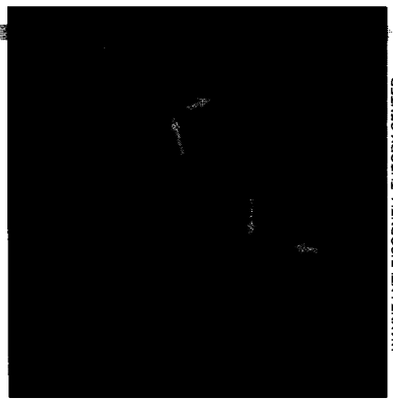
lier than expected, other times later. A statistical analysis showed periodicities in the timing data. Wolszczan then concluded that the pattern was produced by the gravitational pull of two orbiting planets on the pulsar. The star consequently "wobbles back and forth, so the pulses get periodically delayed and advanced," he says.



WAYNE LYTLE/CORNELL THEORY CENTER

**Pulsar planets.** Gravitational tugs *(red)* affected the planets' orbits, altering the pattern of radio signals from the pulsar.

Though Wolszczan had few doubts, some in the astronomical community have been cautious in accepting their claim—they pointed to an earlier pulsar planet that turned out to be a mistake (*Science*, 24 January 1992, p. 403). But the presence of more than one planet in this case—the timing data reveals two bodies about three times the mass of Earth with orbits of 67 and 98 days respectively—offered the potential for an elegant proof. Rasio and others immediately calculated that the pull of the planets on each other should significantly alter their orbits. The affect of these changing orbits on the star's wobble would also be detectable within the arrival times of the star's pulses.

These perturbations, however, are orders of magnitude more subtle than the ones that originally revealed the planets. For statistical validity, concluded astronomers, the pulsar would have to be monitored for quite some time. "I thought it would take 5 years to dig out—if at all," says Wolszczan. But by this January, with only 3 years of data in hand, he was ready to claim success. A primary reason for the quick triumph was the fortuitous 3:2 ratio of orbital periods of the planets. The planets thus pass each other fairly frequently at the same place in relation to the pulsar. "The inner planet is getting a kick from the outer planet—and vice versa—in the same place," says Thorsett. This alignment sped up the orbital changes enough that they became quietly evident; otherwise, "it might have been centuries," he says.

Even though two planets are already safely in pocket, astronomers are far from finished with this pulsar system. Wolszczan now says the timing data point to a third orbiting body—a moon-sized object that circles the star every 25 days— as well as hints of a fourth with a much larger orbit. Attempts to image the planets have failed, though that failure was not unexpected. "It's probably just too far away for optical and infrared measurements," says Wolszczan.

Confirmation of the existence of the pulsar planets has given a welcome lift to those wondering whether our solar system is a rare event and planning searches for other planets (see box, p. 506). "I'm personally very impressed with the pulsar planet work," says University of Arizona's Donald McCarthy, a veteran planet searcher. Indeed, "if pulsars have planets, then almost anything can," says Thorsett, referring to the fact that most astronomers had considered pulsars unsuitable planetary homes, since they're the remnants of stars that have exploded in supernovae. The blasts would presumably have destroyed existing planets along with any material from which future planets might condense.

Or would they? Thorsett and Rachel Dewey at NASA's Jet Propulsion Lab calculated last year that preexisting planets might occasionally ride out the blast, depending on where their orbits placed them at the time of the supernova.

That kind of luck may not even be necessary to explain Wolszczan's and Frail's planets; their pulsar is a relatively old one, thought to have spun up by accreting material from a now-invisible companion. Such systems would have plenty of time to recover from a supernova, say astronomers. Moreover, the companion could have provided the seeds of future planets, says Rasio. Astronomers have observed a number of "eclipsing pulsars" where the pulsar boils material off its stellar companion. This freed material could then form a circumstellar disc, from which planets are thought to form.

Wolszczan himself is keen on another explanation: a cataclysmic merger of two inward-spiraling white dwarf stars, which would produce a pulsar—and possibly a circumstellar disk. At the moment, almost any explanation can have its partisans, since there's little data with which to weed out theories. "I haven't seen a real consensus forming," says Princeton's Joseph Taylor, who shared last year's Nobel prize in physics for his studies of pulsar timing. Most researchers do agree on one thing: These planets aren't likely to vanish into thin air as have so many others.

**–John Travis**

CARDIOVASCULAR DISEASE

# Gene Transfer to Spark a Failing Heart

Just as the walled cities of ancient times had sentries at the gates, the cell has it own molecular sentries—proteins called receptors embedded in the cell membrane. These sentries consent to deal with only a few of the thousands of molecules that bathe the cell. As a result, those chosen few—hormones and other key messengers—have their messages passed along to the cell interior, where they receive a response. The past decade's leaps in understanding how these cellular sentries do their job may soon allow researchers to apply that knowledge to a surprising practical realm: gene therapy for congestive heart failure.

On page 582, receptor biologist Robert Lefkowitz of Duke University School of Medicine and his colleagues report that giving mice extra copies of the human gene for a specific cellular receptor (the $\beta_2$-adrenergic receptor, which responds to adrenaline) greatly strengthens the beating of the animals' hearts, even in the absence of adrenaline. "The result is really exciting, and it may ultimately give us a better understanding of how congestive heart disease progresses," says cardiologist Michael Bristow of the University of Colorado Health Sciences Center in Denver.

That understanding might one day also become a practical form of therapy for the condition, which results when the heart muscle cannot contract with enough power to circulate blood efficiently. Although congestive heart failure may be treated with adrenaline-like drugs, the patients' hearts respond weakly both to the drugs and to adrenaline itself. And as the heart continues to weaken, the drugs may become even less effective. But the Duke group's work suggests that it may be possible to reduce—even eliminate—use of drugs in therapy by introducing extra copies of the gene for the $\beta_2$-adrenergic receptor ($\beta_2$-AR) into a failing heart.

Lefkowitz decided to undertake the transgenic mouse experiments, he says, because Colorado's Bristow had shown that the β-adrenergic receptors are less abundant and less active in the hearts of congestive heart failure patients. He therefore reasoned that increasing the number of $\beta_2$-AR might well improve the heart's performance.

For their first experiments, the Duke group introduced into mice the gene for a $\beta_2$-AR mutant that constantly sends its signals to the cell interior, assuming this would be the most efficient way to aid the heart. However, these animals' hearts didn't have very many of the mutant receptors. Speculating that the heart cells couldn't tolerate the mutant receptor, the group introduced the normal $\beta_2$-AR gene into another batch of mice—with much better results. These animals showed anywhere from a 100- to 200-fold increase in $\beta_2$-AR expression. "I was blown away by how high the expression was," Lefkowitz says. The high expression

of the $\beta_2$-AR gene correlated with the increased contractility of the heart muscle both in the living animals and in lab tests. Since the animals hadn't been given any adrenaline, the group asked how the receptor alone could increase contractility.

One possibility is that the plethora of receptors was allowing the heart to respond to the animals' existing low levels of adrenaline. But when Lefkowitz and his colleagues gave the mice a drug that blocked the receptors' ability to respond to adrenaline, the heart continued to pump just as hard. So Lefkowitz and his colleagues concluded that a small percentage of the receptors are always sending messages to the cell's interior. Increasing the total number of receptors would therefore mean that the animals would have a greater number of active receptors. "Suppose 2% of the receptors are naturally in the active form and you have a 200-fold increase in total receptors, you have a maximumly stimulated cell," explains Lefkowitz.

Surprisingly, even though the animals' hearts are on permanent overdrive, the mice appear normal. "Intuitively, you would think this couldn't be good for the animals," Lefkowitz says. But "they're happy out to 8 or 9 months—which is as far as we have looked at them."

Lefkowitz's results encourage cardiologist Judith Swain at the University of Pennsylvania Hospital, who is excited about the possibility for cardiac gene therapy. "Because you can dramatically change the contractility of the mouse heart, you can easily see how one could make changes in human heart function using a gene therapy approach," says Swain. Both Swain and Lefkowitz agree, however, that gene therapy is still far in the future.

First, the Lefkowitz group will have to find out if their approach works on animals with diseased hearts. Also, before there is any practical gene therapy for congestive heart disease, researchers will have to overcome such major obstacles as finding a safe and effective way of putting the gene directly into heart muscle cells rather than into early embryos as in the current experiments—a requirement if the method is ever to be applicable to human patients.

Lefkowitz has begun a collaboration with gene therapy pioneer Ronald Crystal at Cornell University Medical College in New York City to achieve just that goal. They plan to explore using a virus to carry the gene to the heart. Alternatively, the gene might be introduced into cardiac muscle cells, which can then be transplanted into hearts (*Science*, 1 April, pp. 31 and 98). If all goes well, Lefkowitz says, it might some day be possible to use therapy with receptor genes to treat heart failure and other illnesses.

–Lisa Seachrist

SOLID-STATE PHYSICS

# A New Laser Promises to Put An End to Band Gap Slavery

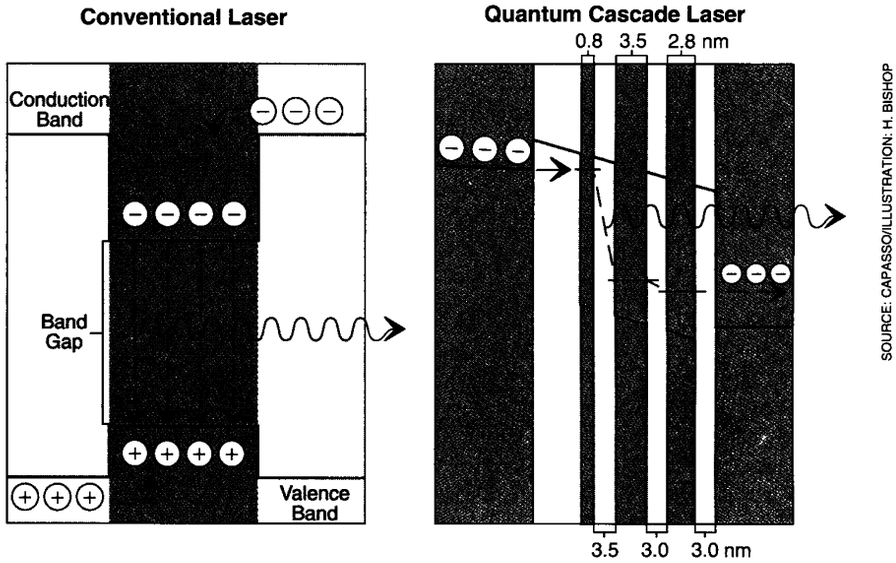
If you are a naturally enthusiastic researcher, one of the few drawbacks to creating a unique new scientific device is the need to restrain your own enthusiasm. For Federico Capasso of AT&T Bell Laboratories—an upbeat man to begin with—and postdoc Jerome Faist, that's a double challenge, because their quantum cascade laser can be viewed both as an advance in laser physics and also as a potential technological coup.

Faced with these prospects, Capasso oscillates between expansiveness and caution. "It's really a nitty-gritty technical advance" with implications that could be "quite mind-boggling," Capasso, head of Bell Labs' quantum phenomena and device research department, says in an unguarded moment. Then, swinging to caution, he adds that it would be a mistake to "toot the technological thing" because it could take years for the laser to become practical. So he settles for calling it "a very significant research achievement." Most other researchers who know of the work, described on page 533 of this issue of *Science*, echo that judgment.

What Faist and Capasso have built, in collaboration with Alfred Cho, Deborah Sivco, Carlo Sirtori, and Albert Hutchinson, is the first semiconductor laser whose wavelength is set entirely by an artificially created physical structure—dozens of atoms-thick sandwiches of semiconductor known as quantum wells—rather than by the laser's chemical composition. Whereas a conventional semiconductor laser generates light when excited electrons drop across a material's intrinsic "band gap" into the ground state, the new AT&T device extracts light from electrons cascading down energy steps created by the quantum wells. Because those stair steps, unlike a band gap, can be tailored at will by changing the thickness of the wells, the laser should open up regions of the infrared spectrum that are critical for monitoring pollutants or detecting objects through the atmosphere, but are now difficult to reach with semiconductor lasers.

Before that can happen, say other physicists, Faist and his colleagues must prove that the laser can emit light continuously (so far it fires only in pulses) and can operate efficiently at temperatures above that of liquid nitrogen. But even if the quantum cascade laser doesn't turn out to be a technologically useful device, says Dan Botez of the University of Wisconsin, it will stand as a tour de force of physics. University of California, Berkeley, physicist Charles Townes, who shared the Nobel Prize in 1964 for the invention of the laser, agrees, calling the quantum cascade laser "a beautiful piece of solid-state and laser physics."

What impresses Townes is the sharp departure from conventional laser design. Conventional semiconductor lasers fire when electrons in the semiconductor are excited from their ground states—known as the valence band—across the band gap into states




**Tripping the light.** In a conventional semiconductor laser, a material's intrinsic band gap sets the wavelength. In a quantum cascade laser, it's the result of energy levels *(red)* created by a series of sandwich-like quantum wells. The diagram shows one of the laser's 25 active regions.