whether this mechanism is acting in humans has not yet been determined.

Despite that uncertainty, scientists familiar with the RA study are encouraged because it has expanded the applications of oral tolerization, fueling hopes that it may be useful in the treatment of other autoimmune diseases, whose targets range from the thyroid gland to the neuromuscular junction. "Any of these T cell mediated diseases might be targets for this kind of therapy," says Ohio State University immunologist Caroline Whitacre, who is also studying oral tolerization. And the treatment seems to have virtually no side effects, a welcome improvement over present RA treatments.

Nevertheless, most researchers contacted by *Science* say they will remain skeptical until they see whether larger studies also produce encouraging results. "It's certainly very promising," says clinical immunologist Noel Rose of Johns Hopkins University. But, he adds, "these diseases are notoriously remitting and exacerbating. You need fairly long-term studies on large numbers of people to get truly reliable results."

A more specific concern relates to Trentham's study design. Joel Kremer, head of rheumatology at Albany Medical College, was one of several immunologists who reviewed the study for AutoImmune, and he says the reviewing team noted that the study lacked an initial drug-free period. Such "washout periods" allow the effects of previous medications to wear off. During the washout time, the symptoms of patients with active disease should flare up, establishing a baseline for testing collagen's effects.

Without the washout, "there are two possible interpretations," says Kremer. "One is that this drug really does something because it can stop [post medication] flares, which are the most serious forms of the disease that we see." Or the disease could have been in remission, in which case the collagen had little to suppress.

Trentham acknowledges that the study had a bit of a "quick and dirty" character to it, because he was "still seeking a yes or no answer as to whether there was anything there or not." With a qualified "yes" from this study, he and AutoImmune are designing a larger, multicenter trial that would include a washout period and 6 months of treatment with a range of collagen doses. Recruitment for the trial will begin early next year, with results anticipated sometime in 1995.

Before those next results are in, the researchers caution RA sufferers against popping over-the-counter collagen pills. If the findings hold up, dosage is likely to be crucial, and there's little chance that such supplements could provide the right amount of type II collagen. Pill-poppers would only add frustration to their stiffness and pain.

–Marcia Barinaga

MICROELECTRONICS

Is the Third Time a Charm for A Superconducting Computer?

Ten years ago yesterday (on 23 September 1983), dreams of creating ultrafast computers from superconducting materials seemed to die when IBM announced the end of its highly publicized $100 million program of research and development on Josephson junctions. These devices—nothing more than two layers of superconductor separated by a thin insulating barrier—had seemed highly promising as the basis for a new generation of computers. But 20 years of research led IBM to conclude that, fast as they might be, they would never manage to stay far enough ahead of silicon technology to make a large investment pay. Eight years later, in 1991, an equally grandiose Japanese effort sponsored by the Ministry of International Trade and Industry came to a barren end.

Yet in spite of these two failures, the dream of challenging silicon with superconducting circuits remains alive in an effort Konstantin Likharev of the State University of New York at Stony Brook calls "the third major attempt—and probably the last"—to harness Josephson technology in computer circuits. Likharev and his collaborators have already built a variety of devices based on the technology, which they plan to test next summer. Parallel projects are under way at other institutions including the University of Rochester and the National Institute of Standards and Technology.

All these efforts combine Josephson junctions with a new kind of logic, invented by Likharev and his colleagues, that promises to overcome the drawbacks of earlier strategies. Instead of using voltage differences to represent the 0s and 1s of data—the downfall of the earlier effort because it limited the switching speed—Likharev's scheme relies on single quantum units of magnetism. IBM physicist Mark Ketchen calls the strategy, known as rapid single flux quantum logic (RSFQ), the best bet yet to "see what really is the potential of superconducting technology for high-speed digital computation."

If this third try succeeds, it could open the way to computers or communications circuits that live up to the original hopes for Josephson junctions. Already, simple RSFQ circuits made of the low-temperature superconductor niobium are running at speeds of 50 billion cycles a second, 1000 times faster than the fastest personal computers and 100 times faster than the fastest silicon devices. "If we improve the technology," says Likharev, an avowed optimist, "which is relatively easy to do, we hope to achieve speeds of around 300 billion operations a second." And because the devices are superconducting, the energy consumed is infinitesimal. "We're spending 10^{-19} joules per operation," says Likharev, "which is something like a million times less than the usual silicon memory cell in your computer would require."

Plenty of people think such optimism is cockeyed. They point out that no one has yet standardized the production technology enough to make large-scale computer memories. Furthermore, high-temperature superconductors, which would be much preferable to the low-temperature materials Likharev and his colleagues exploit, are so balky that researchers struggle to fashion even simple circuits and logic devices.

To Likharev and his co-workers, those drawbacks pale in the face of the technology's promise. Any logic element—an ordinary transistor, for example—has to switch between two states, corresponding to the binary digits 0 and 1, in response to an external signal. Because Josephson junctions are superconducting, that signal can be minuscule—less than a millivolt, compared to a volt for a silicon transistor—and a smaller signal means faster switching.

Quick change artists. Both the IBM and Japanese efforts to exploit this responsiveness were based on the Josephson junction's ability to switch between superconducting and non-superconducting states. Ordinarily, pairs of electrons "tunnel" across the gap without resistance, in a superconducting current. But if too large a current surges into the junction, its superconductivity breaks down, and the gap becomes a barrier. That creates resistance to the flow of current, resulting in a voltage difference across the gap. In the IBM and Japanese schemes, these two states—the low voltage tunneling state and the high voltage resistive state—represented 0 and 1, and a junction could be switched between them with a pulse of current.

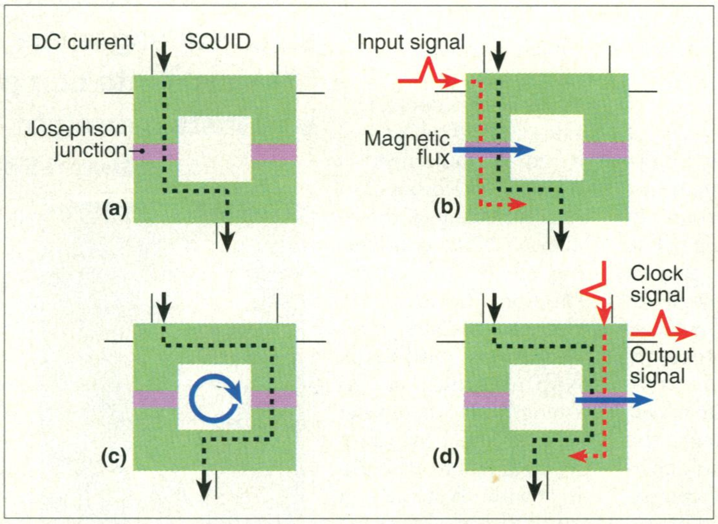
A critical limitation in this scheme, says IBM's Ketchen, is that the junctions don't always reset themselves to 0 when the incoming current abates. Once the Josephson junction is in the voltage state, it lingers there even after the incoming current drops all the way to zero. The faster the circuits are run, the larger the problem becomes; at a billion cycles per second, which is the minimum speed needed to compete with silicon, the junctions don't reset themselves fast enough to keep up. "That phenomenon," says Ketchen, a veteran of the IBM program, "was not originally recognized as being an issue until maybe 1980, when we finally understood what was going on."

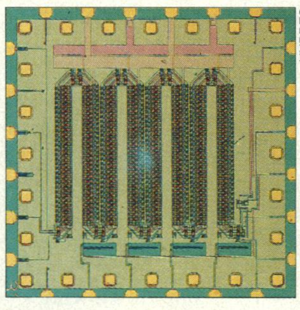
In 1985, while at Moscow State University, Likharev, Vasili Semenov, and Oleg Mukhanov saw a new way to exploit Josephson junctions, one that wouldn't be prey to the resetting problem. Their scheme—RSFQ—doesn't require switching between superconducting and non-superconducting states. Instead, the junction remains superconducting and serves as a gate that admits units of magnetism, generated by external currents, into a tiny superconducting ring known as a SQUID (for Superconducting Quantum Interference Device).

The scheme takes advantage of the fact that, for quantum mechanical reasons similar to those that govern the electronic energy levels of an atom, a ring of superconducting material breaks any magnetic field it encloses into discrete "flux quanta." Ordinarily these magnetic flux quanta are trapped within the superconducting ring. If, however, the ring is interrupted by a gap of insulating material, creating a Josephson junction, individual quanta can sneak in or out through the junction whenever a pulse of current briefly reaches a critical level.

Therein lay the basis for a new kind of binary logic: The presence or absence of a magnetic flux quantum within the ring could represent a 1 or 0. Nudge the SQUID with a critical current, says Likharev, "and it would switch from one state to another, rapidly, in a picosecond or shorter, by changing the number of quanta." Because the Josephson junction in the RSFQ scheme never switches permanently into the non-superconducting, voltage state, it doesn't suffer the resetting problem.

Moreover, as Likharev explains, the passage of a flux quantum into or out of the superconducting ring causes a short pulse of voltage across the Josephson junction. The pulse, in turn, can control the state of a second SQUID. In effect, each SQUID sends out a signal every time it changes its state. And that kind of communication among logical elements can form the basis for complex logic circuitry.





Altered states. In a SQUID—a microscopic ring of superconducting material cut by Josephson junctions—pulses of current admit and release units of magnetic flux. A high-speed signal processing device *(right)* incorporates 4096 SQUIDs.

From 1985 to 1991, while Likharev and his colleagues were still in Moscow, he says, "we did some theoretical development, but in 6 years we tested just four integrated circuits, because fabrication was a big problem in Russia." When the group came to America in 1991, Likharev and Semenov went to Stony Brook, while Mukhanov went to work for Hypres Inc., a manufacturer of niobium superconductors in Elmsford, New York. Their arrival coincided with a Department of Defense program to award university research initiative grants for applied science, and Likharev's group was one of the first to win. At that point, says Likharev, "we started to work fast. Now we're typically fabricating around 10 chips a month." Working with Hypres, Likharev and Semenov have created what Likharev calls a "complete library of elementary gates of this logic." Their goal now is to demonstrate by next summer the prototypes of useful devices —among them an analog-to-digital converter and a digital magnetometer—containing thousands of Josephson junction switches.

Many hurdles. To compete successfully with silicon, however, Ketchen thinks such devices will have to shrink dramatically. The main Stony Brook-Hypres effort has aimed at creating devices of about 2 to 3 microns in size; silicon devices, meanwhile, have shrunk well below a micron, says Ketchen. As a result, a consortium formed by IBM, AT&T, and the Massachusetts Institute of Technology's Lincoln Laboratories, working with Jim Lukens and Manjul Bhushan of Stony Brook, is trying to develop means of shrinking RSFQ circuits further. One thrust of the consortium, says Ketchen, "is to try to fabricate the Josephson junction technologies using the fabrication techniques developed for silicon transistors."

Moreover, even Likharev is concerned that the most sophisticated devices made so far have to be cooled in a bath of liquid helium to maintain their superconductivity, a chore he calls "not difficult, but unpleasant." High-temperature superconductors can be cooled with liquid nitrogen, which is cheaper and easier to handle. For that reason, success at replicating RSFQ circuits in high-temperature materials would mark a big step toward practical applications.

But so far, says John Przybysz of Westinghouse, the state of the art is "crude." Unlike the low-temperature superconductor niobium, the high-temperature materials are not single elements but complicated confections that respond unpredictably when laid down in micron-sized layers. "The processes you need to optimize one layer," says Ketchen, "might screw up what you've done in the layer beneath."

The toughest problem is creating high-temperature junctions that have a consistent critical current. If the critical current is too large, explains Ron Ono of NIST, an incoming pulse won't be strong enough to move a quantum of flux across the junction. If the critical current is too low, the junction will be overly sensitive to noise and external fields and will switch when it's not supposed to. "The problem," says Ono, "is truly a manufacturing one. The niobium [low-temperature] junction is a brilliant device. It's easy to make with extremely tight controls. We don't have anything remotely approaching that particular process in [high-temperature materials]."

Whether even niobium RSFQ could seriously rival silicon in mainstream computer technology, says virtually everyone in the field, still depends on whether or not researchers can successfully tackle the problem of fabricating millions of SQUIDs reliably and linking them into devices that can compete with the massive memory chips now available in silicon. For now, RSFQ researchers are struggling to make 16,000 cell memories out of niobium, and no one has yet made a high-temperature memory of any size.

Likharev insists these are problems of "investment rather than physics." But others worry that even if funding holds out and working devices can be fashioned, the third time won't necessarily be the charm for Josephson junctions. This new technology, says Ketchen, "has to be a lot faster than what you can do with silicon. If it isn't, the silicon guys are going to do it soon. There's so much money and resources they will run you over, if you're not way out ahead."

–**Gary Taubes**