still can factor. It speeds up factorization by almost an order of magnitude," says Simmons. Now the Sandia group has refactored a 58-digit number that took them 8.8 hours with their old algorithm in 1.8 hours—a fivefold improvement in speed. They factored a 60-digit number in 2½ hours and a 63-digit "wanted" number in 5.18 hours. They hope to do even better next year when they get a Cray XMP—essentially two Crays hooked back to back. The new machine, they predict, should speed up their factoring by a factor of 4.

A key competitor for the Sandia factoring record is Wunderlich, who is exploiting a new computer at NASA's Goddard Space Flight Center to do the job. Wunderlich's plan is to do the countless trial divisions needed to factor a large number all at once. To do this, he needs to use a parallel processor computer—one that has a number of independent units to do this arithmetic. Wunderlich began planning this work in 1979, intending to use the Illiac IV, the first parallel processor ever built, and one with 64 separate units. But, Wunderlich says, "It was very hard to do anything sustained on that machine. It was an old generation machine and it was torn down shortly after I began. But my experience on the Illiac said to me that this is really the way to do factoring."

Wunderlich next got a grant to try factoring on a British machine called DAP, which has 4096 processors. There are only a few DAP's in the entire world because the machine was expensive and commercially unsuccessful. Wunderlich spent the summer of 1981 working on one of these machines at Queen Mary College in London, where he wrote parts of a factoring program but never got the program entirely running. "It takes a gigantic effort to put a new algorithm on a large machine," he remarks.

Soon afterward, Wunderlich heard from NSA, which asked him to submit a grant proposal. Wunderlich did and received, he says, "generous funding." He is using this grant money to try and factor large numbers on a very new machine called MPP, for Massively Parallel Processor. The computer, which belongs to NASA and is to be primarily used to analyze satellite data, has 16,384 parallel processors. For factoring, however, it seems ideal. "It's the right architecture, the right kinds of languages, and it has lots of support," says Wunderlich. But, he remarks, the machine is still so new that it is barely running. When the MPP is fully operational, however, Wunderlich thinks he will have "one of the fastest factoring programs in existence. I think I will be able to do a 60-digit number in 1 hour."

The third group of researchers in this factoring competition is building its own computer—one that will do only factoring. It is being built by Samuel Wagstaff at Purdue University together with Jeffrey Smith and Carl Pomerance at the University of Georgia, from parts that they order through the mail. They also plan to produce a special-purpose chip to do trial divisions. The investigators call their machine EPOC, for Extended Precision Operand Computer, or, more colloquially, The Georgia Cracker.

The EPOC computer has two features that will speed up factoring, Wagstaff says. First, it has a large word size. Normally, large computers can only handle word sizes of 32 bits. This machine handles 128 bits. "If you add two numbers of 128 bits, it takes ten operations on an IBM or CDC computer," says Wagstaff. "The EPOC does it in one operation." The second special feature of the EPOC is that it does some of the trial divisions in parallel and it does them in a separate part of the computer. Eventually, the EPOC builders plan to have their machine do several hundred of these divisions at the same time. They expect to be able to factor a 78-digit number in 1 day.

What is the future of factoring? Obviously, there must be a limit to the size of number that can be factored, but mathematicians no longer think that the limit depends on the speed of their computers alone. "I'm convinced now that large-scale computational problems such as factoring depend as much on the architecture of the machine as on its brute-force speed. If you can modify the architecture you can make enormous progress," Simmons says. "The exploitation of machine architecture is a whole new way of doing mathematics."

—GINA KOLATA

Specific Expression of Transferred Genes

Foreign genes, which were transferred into mice, appear to be expressed according to more normal patterns of tissue distribution

Two recent reports indicate that investigators may be on the verge of seeing virtually normal activity of foreign genes that have been transferred into mice. Introduction of new genes into mice has been accomplished many times during the past few years by injecting cloned genes into fertilized eggs. Although 20 to 30 percent of the recipient animals carry the transferred genetic material in their cells and can transmit it to their progeny, the genes have not been expressed normally.

The new results, suggesting that expression of an antibody gene and one coding for the protein transferrin may follow more normal patterns of expression, are therefore an important step forward. They follow closely on the heels of similar successes with gene transfer in fruit flies.

Ursula Storb of the University of Washington and Ralph Brinster of the School of Veterinary Medicine of the University of Pennsylvania and their colleagues injected 300 fertilized mouse eggs with the cloned gene coding for an antibody light chain of the kappa class. They eventually obtained six animals, all males, with the new gene. When these mice were mated with normal females, about half of the progeny carried the antibody gene, which is the expected result.

The investigators analyzed the expression of the gene, as indicated by its transcription into messenger RNA (mRNA), the first step of protein synthesis, in the progeny of three of the original animals. Transcription of the transferred gene "was high in the spleen and low in liver, and the mRNA is the size you would expect," Storb says. The spleen is rich in antibody-producing B cells; liver cells do not make antibodies.

"The result looks promising, but it still needs more work to show that [expression] is completely tissue-specific," Brinster cautions. Nevertheless, this is the first indication that a transferred gene might be expressed in mice, under

the control of its own regulatory sequences, in the appropriate tissue but not in an inappropriate one. Moreover, expression is high; about 3000 copies of the mRNA of the transferred gene are made per cell. And the antibody protein itself is found in the blood of the animals.

The key to tissue-specific expression in this case, Storb and Brinster speculate, may be an enhancer sequence located in the large noncoding intron of the antibody gene. Enhancers, which boost gene transcription, have been found in other antibody genes and appear to work only in B cells.

In previous work, the Brinster group, in collaboration with that of Richard Palmiter of the Howard Hughes Medical Institute of the University of Washington found that high expression of a transferred viral gene or of a gene coding for rat growth hormone could be obtained if they were linked to a sequence from the metallothionein gene that very actively promotes gene expression (*Science*, 24 December 1982, p. 1298).

More recently, the Brinster and Palmiter groups have shown that the gene for human growth hormone, which they also linked to the metallothionein promoter, is expressed in mice where it causes growth stimulation, just as the rat hormone did. In both cases, large quantities of the hormones were made in the liver, a pattern of expression that resembles that expected for the metallothionein gene from which the promoter was derived. Growth hormone is normally made in the pituitary gland.

Another gene, that for chicken transferrin, an iron-carrying protein found in blood, also is expressed under the control of its own promoter when transferred into mice, according to Brinster and G. Stanley McKnight, who is at the University of Washington. "Most of the animals expressed the gene," Brinster says, "even though it has a chicken promoter."

Expression of the transferred gene was five to ten times higher in the liver, the normal site of transferrin production, than it was in several other tissues. However, here the case for tissue specificity is not as good as that for the antibody chain gene. The apparent preference for expression in the liver may have simply reflected the high degree of protein synthesis generally occurring in this tissue.

Despite the apparent specificity of expression of the transferred antibody gene, Brinster says, "We don't have anything like what the *Drosophila* people have." He was referring to recent successes in introducing new genes into fruit flies. Three groups of investigators have now found that expression of the transferred genes follows normal developmental patterns in the recipient flies. The genes were active only in appropriate tissues, for example, even though they integrated into the *Drosophila* genome at positions other than the normal ones.

To introduce the genes into fruit flies, the investigators used a method developed by Allan Spradling of the Carnegie Institution of Washington (in Baltimore) and Gerald Rubin, who is now at the University of California at Berkeley; in this method the gene is inserted into a transposable element before injection into the eggs. The transposable element serves as a vehicle for inserting single copies of an intact gene with its flanking sequences into the *Drosophila* genome although there may be several such insertions per cell.

In contrast, when the genes that are injected into mouse eggs become integrated into the genome, several copies are usually linked in a tandem array. Control of genes inserted as single copies may be more normal than when several genes are linked in tandem. Nevertheless, Storb and Brinster note that they see tissue-specific expression of the antibody chain gene in mice even though the numbers and positions of the integrated gene copies vary from animal to animal, a finding that resembles those in *Drosophila*.

Investigators studying *Drosophila* are already in position to begin studying the factors that regulate the normal expression of genes during the development of a living animal. If the observation of tissue-specific expression of the antibody chain gene is verified by further work, similar experiments may soon be possible in a mammal.—**JEAN L. MARX**

Additional Reading

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A Landmark in Fusion

Fusion physicists have hailed it as a milestone, 30 years in coming: on 3 November, scientists at the Massachusetts Institute of Technology's (MIT's) donut-shaped tokamak reactor, the Alcator C, finally achieved the minimum plasma density and confinement time needed for fusion energy breakeven.

While the Alcator C plasma was nowhere near hot enough for sustained fusion, the event had an undeniable symbolic importance. Moreover, the way that the MIT researchers did it has considerable technical importance as well.

Energy breakeven in a deuterium-tritium plasma, which is the easiest fusion fuel to ignite, requires two things. First, the temperature of the plasma must exceed some 200 million degrees Celsius; that milestone was achieved by the Princeton Large Torus in 1978. Second, the product of plasma density and plasma confinement time must exceed the "Lawson" criterion, 6×10^{13} nuclei per cubic centimeter-second; the Alcator C, which is designed for very high densities, came within a factor of 2 of this number in 1981. But then things stalled. When the MIT team tried to increase the density further by raising the fuel supply gas pressure, the confinement time topped out and refused to budge.

This year, however, Alcator team leader Robert Parker and colleagues Martin Greenwald, Dave Gwinn, and Steve Wolfe tried another method, using a kind of high-tech BB gun to inject the plasma with frozen pellets of deuterium. It worked. The evaporating deuterium provided a sudden, massive pulse of fuel that boosted densities to more than 10^{15} nuclei per cubic centimeter with a confinement time of 50 milliseconds—giving a Lawson product of 6×10^{13} to 8×10^{13}.

Pellet injection is not a new idea—the technology used at MIT was developed at Oak Ridge National Laboratory—but it has never before had such a stringent test. "Now I expect that it will be a standard feature on all the advanced machines," says Parker. In particular, it could prove very suitable for the Tokamak Fusion Test Reactor in Princeton, which is expected to achieve *all* the criteria for energy breakeven by 1986 or 1987.

—**M. MITCHELL WALDROP**