per second from the roughly tenfold larger distance of Jupiter.

Under normal circumstances, the backup antenna's glacial rate of communication would be adequate. But suppose something goes wrong with the spacecraft as it whips by Venus? JPL mission controllers would have to diagnose the problem through this extremely slow communications channel and then try to radio correction commands the same way—a process one engineer close to the project compares to groping your way through a dark room where your 3-year-old may or may not have scattered toys on the floor. You can do it—slowly. But it would certainly be easier and safer if you could increase the data rate and, in effect, turn up the lights.

"The low data rate is something we didn't want to do," says Ausman. But he remains a cautious optimist. "We have assessed the problem, and we believe we have sufficient visibility to always reconstruct what's going on in the spacecraft."

He admits that 40 bits per second is too low for the controllers to exercise and calibrate Galileo's attitude-control system, which is what maintains the pointing. But that will be done shortly after launch, when the available data rates are much higher, he says. "We can't think of any failure modes near Venus that would require us to recalibrate immediately."

So in the last analysis, does sending Galileo past Venus bring it too near the edge? Is the mission about to set a new NASA record for technical risk?

Well—probably not, says Ausman. "The design margins we built into the spacecraft at the outset have been almost miraculously maintained," he says. "We've been able to satisfy the fundamental thermal and power constraints unchanged throughout the mission." He maintains that he and his colleagues are comfortable with the mission as it stands.

In many ways, in fact, Galileo today is in better condition than it was in 1986. During the 3-year delay caused by the Challenger disaster, a number of the science instruments were upgraded. And several hardware glitches were found—at least two of which could have caused serious problems in flight if they had not been fixed. One involved cracked solder in the computer electronics and the other overheating in the attitude-control thrusters.

Still, everyone will be much happier once Galileo has looped back and made its first pass at Earth in December 1990. From then on it will remain outside Earth's orbit, where the sunlight is cooler—and where the high-gain antenna can at last be safely unfurled. ■ M. MITCHELL WALDROP

Gene Control Research Gets a Boost

Researchers clone the gene for a critical cog in the gene control machinery of higher organisms

FIVE RESEARCH TEAMS—four in the United States and one in Europe—are about to announce a significant advance in biologists' struggle to understand how the cells of higher organisms turn their genes on and off. They have discovered the gene that directs the synthesis of the TATA protein, one of the most elusive—and critical—components of the gene regulatory machinery. "The TATA protein is a key factor in gene transcription, the one that the other regulatory factors talk to," says Leonard Guarente, the leader of one of the U.S. teams.

How cells control their genes so that they manufacture the necessary proteins at just the right times is key to much of basic cell biology. This includes the orchestration of embryonic development as well as the adaptations that cells must make in everyday life as they respond to the environment. In addition, derangements in gene activities may contribute to the development of cancer and other diseases.

No wonder then that over the past several years molecular biologists have expended a great deal of time and energy trying to analyze the biochemical machinery that controls gene expression. They have been very successful in doing this in the bacteria, but in more complicated organisms the problem has proved to be a much more difficult nut to crack.

Researchers learned that genes in the higher organisms, like those in bacteria, are activated by proteins that bind to specific DNA sequences connected to the genes. But the molecular control machinery in the higher organisms proved to be very complex, involving several proteins that have to act together to turn on any given gene. On top of that, some of the crucial regulatory proteins could not be isolated.

The TATA protein, which is particularly critical because it is the first of the proteins to bind to a gene regulatory site—the sequence known as the TATA box—was one of those that could not be isolated, and its absence presented a major roadblock to researchers who wanted to understand the biochemical basis of gene control. The new achievement—the cloning of the yeast gene for the TATA protein—ought to break through that roadblock.

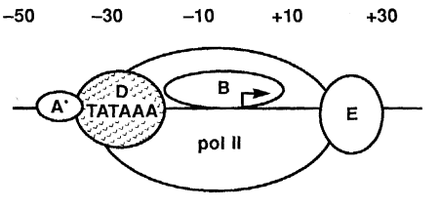
Guarente, who works at the Massachusetts Institute of Technology, and his former postdoc Steven Hahn, who is now at the Fred Hutchinson Cancer Research Center in Seattle, cloned the gene with Stephen Buratowski and Phillip Sharp, who are at MIT. The gene has also been cloned independently by Fred Winston's group at Harvard Medical School, by Robert Roeder's group at Rockefeller University, by Martin Schmidt and Arnold Berk at the University of California in Los Angeles, and by Pierre Chambon at the University of Strasbourg in France. The MIT and Harvard workers describe their results in the 22 September issue of *Cell*. The Roeder group's paper is scheduled to appear in the 28 September issue of *Nature* and that of the Berk group is in press at the *Proceedings of the National Academy of Sciences*. Chambon has also submitted a paper to the *Proceedings*.

The search for the factors that control gene activity in higher organisms began about 10 years ago when molecular biologists found that genes carry identifiable regulatory sequences that are needed for normal gene activation. One of the first regulatory sequences identified was the TATA box, which was so named because it contains the bases thymine and adenine in a roughly alternating sequence.

The researchers already knew that bacterial genes are turned on by the binding of specific proteins to their regulatory sequences. So the discovery of the TATA box ignited an intensive search for the proteins that might control genes in higher organisms by binding to that sequence.

Ironically, the efforts yielded an embarrassment of riches. Researchers found that four different regulatory proteins plus RNA polymerase II bind in and around the TATA box. The polymerase is the enzyme that gets gene expression under way by copying the DNA of genes into messenger RNAs, which make the proteins the cells need.

Then a few years ago, Roeder, Sharp, and Chambon brought some order out of the confusion by pinpointing the particular protein that actually recognizes the TATA sequence. Only after this protein, which is designated transcription factor IID



Turning genes on. *The TATA regulatory sequence first binds transcription factor II D (D), followed in order by the proteins A, B, polymerase II, and E. [Adapted from S. Buratowski, S. Hahn, L. Guarente, and P. A. Sharp,* Cell ***56****, 549 (1989)]*

(TFIID), binds to the DNA can the other regulatory proteins and the polymerase join in to initiate gene expression. It is the yeast gene for transcription factor IID that the five research groups have now cloned.

They chose the yeast gene because no one could isolate the equivalent protein from mammalian cells. Having the protein encoded by the gene targeted for cloning is necessary because the amino acid sequence data can be used to design probes to fish the gene out of the genome.

"The initial breakthrough came 2 years ago when Sharp and Guarente and Chambon showed that the yeast factor could substitute for the human factor," Roeder says. This gave the researchers a good assay for purifying the yeast factor. It also helped that yeast cells make more of the factor than mammalian cells do and that the yeast protein is smaller and possibly more stable than the mammalian protein.

In any event, the Guarente-Sharp, Roeder, Berk, and Chambon groups all used the yeast transcription factor as their stepping stone to the gene. Winston and his colleagues got there by another route.

Winston, a yeast geneticist, had identified a number of mutations that affect gene transcription in that organism. One mutation in particular behaved as if the gene affected might encode a transcription factor, and the Harvard researcher set out to clone it. He and Guarente and Sharp were aware of each other's work, and they kept in touch while pursuing their respective genes. Eventually Winston and Steven Hahn compared notes on the gene structures. "We were both stunned to find out that the genes matched up," Winston says.

Not only that but the Harvard group has also shown that the TFIID gene is necessary for normal yeast growth and gene transcription. This is the first direct evidence that the transcription factor has an essential role in a living organism. All the previous biochemical studies of the factor and its activities had been done in cell-free extracts. The Winston group's findings indicate, Sharp says, that the biochemical results "are likely to be a valid reflection of what is going on in the cell. It's what you'd expect, but it's nice to have the data."

The TFIID gene sequence reveals that it encodes a protein with a molecular weight of 25,000, with no strong resemblance to any other protein, including other known DNA-binding proteins. The sequence shows a slight similarity to that of a bacterial transcription factor, but there is some disagreement about what this might mean. Sharp, for one, thinks that the resemblance is simply fortuitous, whereas Roeder suggests it might have functional significance.

He, as well as the other researchers, will be able to test their hypotheses on how the TATA factor works. With the gene now in hand, they can modify it in specific ways and see how the changes affect the function of the proteins produced by the altered genes.

They can also explore how the TATA-binding proteins interact with the other proteins that regulate gene activity. Some of these bind to sites located hundreds of base pairs before the TATA site, but work from Roeder's group, among others, shows that the transcription factors that work at the distant sites can nonetheless interact with the TATA factor to influence gene expression. "The $64,000 question," says Sharp, "is how do these upstream elements do it?"

Now this and other questions can be addressed in yeast, a species much more amenable to genetic and biochemical analysis than are mammalian cells. In addition, the yeast gene should provide an entrée to identifying the TATA factor gene in mammalian cells and eventually cracking that system.

The easiest way to do this would be to use the yeast gene DNA itself as a probe for the corresponding mammalian gene. Unfortunately, the various groups have already shown that this is probably not going to work. A variety of other approaches, although more cumbersome, are still possible, however. "I'm confident that one approach will work and we will eventually get the human factor," Berk says. ■ JEAN L. MARX

Oil and Gas Estimates Plummet

In the spring of 1988, then Secretary of the Interior Donald Hodel was fuming. His own U.S. Geological Survey had reduced by almost 40% its estimate of the oil and natural gas remaining to be discovered in the United States, making dependence on foreign sources and high-priced alternatives appear that much closer. Hodel did not like that. "I will say one thing with absolute confidence," he told oil and gas industry representatives, "after we review the [study's] methodology, the numbers will change. It's guaranteed."

So much for guarantees. Hodel left with the switch of administrations, and after considerable external review of the study, "there has been no change in the numbers," says Richard Mast of the USGS in Denver, co-leader of the study.

If the new estimates of the country's undiscovered oil and gas resources hold up, it would solidify a new realism in the USGS view of energy resources. In 1972 the agency claimed that there were 450 billion barrels of oil and 2100 trillion cubic feet of gas left to be found—figures that the USGS itself soon characterized as four times too high. But even the 1981 USGS estimates of 83 billion barrels and 594 trillion cubic feet were soon viewed by some experts as overly optimistic.

The recently released 1989 estimates, made in cooperation with Interior's Minerals Management Service, are the lowest ever from Interior and fall within the range of recent private and industry estimates, which have been none too encouraging. The estimate of oil remaining to be found has plunged to only 35 billion barrels.

If this estimate is correct, where does that put the United States? The nation has already consumed 143 billion barrels of domestic oil in its 100-year history of oil production and has 51 billion barrels of recoverable oil thought to remain in known fields. That is not as much oil as it might seem. At the recent rate of consumption of 5.4 billion barrels per year, these reserves and the estimated undiscovered oil represent only a 16-year supply. With imports from the Mid-East and elsewhere providing 50% of U.S. needs, as they do now, the domestic supply stretches to 32 years. To get beyond the year 2020, then, the United States would have to increase its reliance on other energy sources. Importing more oil would risk once again becoming hostage to the cartel. Turning to less conventional oil sources at home—such as the mining of oil-impregnated rock—would be costly.

Drawing more on natural gas might help, but the estimate of undiscovered gas did not fare any better. From the 594 trillion cubic feet estimated in 1981, undiscovered gas deposits are now believed to add up to only 263 trillion cubic feet. It was this drop in particular that upset Hodel, who saw gas looming large in America's energy future.