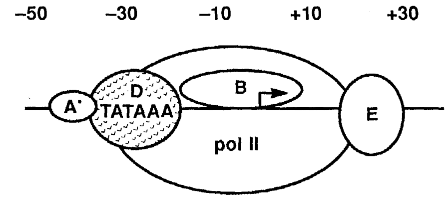

Turning genes on. *The TATA regulatory sequence first binds transcription factor II D (D), followed in order by the proteins A, B, polymerase II, and E. [Adapted from S. Buratowski, S. Hahn, L. Guarente, and P. A. Sharp,* Cell ***56****, 549 (1989)]*

(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, coleader 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.

But since the Hodel outburst, even industry estimates have dipped, bringing them into rough agreement with the Interior estimates. The bottom line? Counting an additional 306 trillion cubic feet of reserves, the United States would thus have a 35-year gas supply. Alternatives to conventional gas include gas trapped in the seams of coal deposits and in impermeable rock.

A number of factors contributed to these less optimistic estimates, according to Mast and his colleagues. Much of the change came from the oil and gas industry itself. Spurred by high prices, it launched a frenzied drilling effort in the early 1980s that would test the optimism of the 1981 estimates. In almost all areas, that confidence was misplaced. In the frontiers of oil and gas exploration of Alaska, the offshore Atlantic, and the thrust belts of the West, disappointing drilling results forced downward reassessments of the resources left to be discovered. In better known areas, the continued decline in the size of newly discovered fields confirmed that regions that have been producing new discoveries for decades are drying up as fast as feared.

The modest amount of oil and gas that was discovered between the two reports not only reduced the general optimism, it inevitably shrank the new estimates. The transfers of the new oil and gas from the undiscovered category to reserves accounted for 15% to 20% of the decreases.

There were also less precisely determined contributions to the drops in undiscovered resources. One was the shifting economics of oil and gas extraction. The lower the price for the product, as set by worldwide market forces, the less likely that small, hard to drill, out of the way deposits in the United States will be drawn on. When the 1981 estimates were being prepared, the world price of oil was rapidly approaching $30 per barrel. It is now about $18 per barrel and not expected to soar as high as thought earlier. That would mean that the United States would "run out of oil" with oil left in the ground that, under other economic conditions, would be in the undiscovered category. In addition to economics, more detailed and objective techniques for sizing up as yet unseen deposits, always a tricky business, left less room for the ingrained optimism of oil explorationists.

"There isn't an unlimited amount of oil," notes Mast, "particularly at today's prices." Those prices might not rise that fast before 1993, when the next Department of Interior estimates are due. The burst of exploratory drilling that reined in earlier optimism has faded away under low prices. That can only hinder the next evaluation of undiscovered oil and gas. ■ RICHARD A. KERR

Japan: Superconductor Hopes Drop

Japanese researchers and industry leaders are less optimistic now than they were a year ago about how quickly high-temperature superconductors can be moved into the marketplace, according to an article in the Japanese journal *Nikkei High Tech Report*.

Published by the Nikkei Research Institute of Industry and Markets, the article estimates that it will be at least 10 years before the first simple devices made with high-temperature superconductors are available commercially, and more like 20 years for the ambitious applications, such as superconducting supercomputers, magnetically levitated trains, electric generators, motors, magnetic resonance imaging units, and power transmission cables.

"I think in the beginning [the Japanese attitude] was unreasonably optimistic," says Mildred Dresselhaus, a Massachusetts Institute of Technology physicist who concurs with the conclusions of the report. Dresselhaus recently chaired a panel organized by the Japanese Technology Evaluation Center to compare the Japanese superconductivity effort with the one in the United States (see *Science*, 11 August, p. 594). Especially among Japanese businessmen, she says, "people got very excited," but "there is less euphoria now because the easy things have been done."

Part of the reason for the early enthusiasm in Japan, Dresselhaus suggests, was that Japanese researchers were at the forefront of the basic research into high-temperature superconductivity. "Japan was more of a focus than usual in a scientific discovery, which led to a great deal of national pride and excitement," she explains.

The MIT physicist says that, judging from her own trips to Japan, the experience of the past year has made the Japanese more aware of the problems involved with commercializing high-temperature superconductivity and brought them down to earth. Still, she adds, they remain more optimistic than people in the United States, partly because the long-term outlook of the Japanese makes their business and government leaders more cheerful about the possibility of a lengthy development period. "Ten years is nothing to them," she says.

The article in *Nikkei High Tech Report* recounts a number of the well-known difficulties facing the development of high-temperature superconductors. "The most pressing and expensive problem will be how to form superconducting wires," it says. "Wires hundreds of meters long will have to be manufactured, without losing the superconducting properties" in order to make magnets and motors. And superconducting magnets and motors will need other parallel developments, including new refrigeration systems and analytical methods for early detection of deterioration or failures.

"Thin films pose even more complications," the report says. Thin films will be needed for such applications as magnetic shielding, superconducting electronics and interconnections, and superconducting quantum interference devices, or SQUIDs. "Any bumps or indentations in the surface must be no larger than 0.1 nanometer. The smoothest surfaces possible at present still have irregularities 100 times the target uniformity, so some kind of breakthrough will be required."

Refrigeration of superconducting devices down to liquid nitrogen temperatures or colder will also pose various technical problems, depending on the particular application under consideration. "Magnetic shielding calls for techniques capable of cooling large surface areas, while power transmission cables have to be cooled over long distances—up to tens of kilometers," the report says. "No clear solution is on the horizon as yet."

The article goes on to list several other practices that must be mastered before high-temperature superconductors can be used in applications, including processing tiny superconductor electronic circuits, putting silicon and superconductors on the same chip, and improving the reliability and durability of superconductors. "Still, even with so many difficulties remaining to be addressed," the article says, "many researchers remain optimistic—particularly in Japan. Overall, they see the matter mainly as a question of setting priorities on R&D to find practical solutions to the problems, one by one."

One question that remains to be answered is whether the optimistic attitude of the Japanese or the more cautious attitude of the Americans will prove to be the better one in the long-term competition for the coming high-temperature superconductor market. ■ ROBERT POOL