ones discovering cliffs. Last year, 4 million people went rock climbing in the United States alone, and they left their mark on these fragile ecosystems, as Knight and Camp report in studies in the December 1998 issue of *Conservation Biology* and the April issue of the *Wildlife Society Bulletin*. Some Joshua Tree prominences are now hung with so many ropes that they look like Gulliver tied down by Lilliputians. To keep regular routes safe, climbers routinely "garden" them, pulling plants and soil out of cracks and wire-brushing lichens off protruding handholds.

Not surprisingly, Knight and Camp's studies show that climbers reduce plant cover and drive off birds. Independent botany consultant Victoria Nuzzo of Rockford, Illinois, showed that climbers reduced lichen cover and species by half and took out three-quarters of threatened cliff goldenrod plants at one site in northern Illinois's Mississippi Palisades State Park. Perhaps worst of all, climbers on the Niagara Escarpment are clearing the way by cutting down the old trees. Survivors may be used to fasten ropes, which strips their bark. Dendrochronologist Kelly has meticulously documented the damage; he dated one tree that germinated in 1215—and had its main axis sawed off in 1992.

Because the recognition of cliff life is so new, few parks have gotten around to making rules. As studies build, that may change. "I like to think that the more we learn about these places, the more we can demonstrate how special they are," says Kelly. –KEVIN KRAJICK

Kevin Krajick is a writer in New York City.

BIOTECHNOLOGY

Engineering Metabolism For Commercial Gains

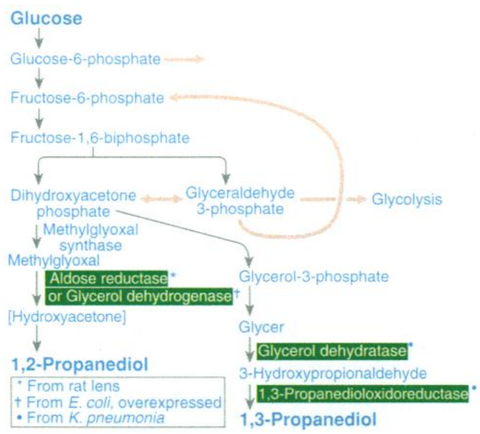
Researchers are using genetic engineering to turn bacteria into chemical reactors that perform multistep synthesis of bulk chemicals

The chemical industry is going back to the future. Until the 1930s, most bulk chemicals came from microbes, which made them by fermenting biomass such as corn and potatoes. But after learning how to "crack" petroleum into simpler hydrocarbons, chemists took over. They devised complex, multistep schemes to convert these building blocks into bulk chemicals as well as smaller scale specialty products. Now, microbes are poised to reenter the bulk chemical business.

Two decades of advances in microbial genetics and a new understanding of cells' metabolic pathways are helping researchers turn microbes into one-pot chemical reactors, able to perform multiple enzymatic steps to convert sugars and other raw materials into industrial chemicals or pharmaceuticals. By combining several chemical steps into one reaction vessel, so to speak, the strategy can save large amounts of money. As a result, the chemical industry is now getting set to reintroduce fermentation as an economical means of producing many bulk chemicals.

For example, DuPont, in Wilmington, Delaware, is planning to put a modified bacterium to work turning glucose into 1,3-propanediol, a monomer that can be linked to form a polyester called polytrimethylene terephthalate, now found in some carpeting and textiles. "We have a tremendous opportunity here to make an impact with a highly efficient and cost-effective biological process," says Richard LaDuca, the project coordinator at Genencorp International in Rochester, New York, which is working with DuPont. Two different multistep processes are now used commercially to make 1,3-propanediol.

Genencorp is also working with Eastman Chemical, of Kingsport, Tennessee, to commercialize a microbial process that transforms glucose into 2-keto-L-gulonic acid, the key intermediate in the industrial synthesis of ascorbic acid (vitamin C). The collaboration—which included several other companies and Argonne National Laboratory, in Argonne, Illinois—engineered an undisclosed bacterium to carry out the four-step metabolic pathway. According to chemical engineer Michael Cushman, Eastman's project director, this biological process is now, "without a doubt, the cheapest way to make ascorbic acid." If adopted, this one-step process would replace the current seven-step method.



Microbial industry. Equipped with genetically engineered enzymes (green), bacterial metabolism can transform glucose into propanediol.

Other chemical companies are also trying to harness microorganisms to produce bulk chemicals. But they are generally tight-lipped about their efforts, because of both the financial stakes and the strategy's history of difficulties. "Replacing chemistry with biochemistry was one of the very first things to cross people's minds when genetic engineering first came about in the early 1980s," says Douglas Cameron, recently hired away from the University of Wisconsin, Madison, by food-processing giant Cargill to build a metabolic engineering group at its Minneapolis research and development center. "But to do this on a commercial scale was a far more difficult task than anyone thought."

"Putting the new enzymes into an organism is really the easy part," adds Bernhard Palsson, professor of bioengineering at the University of California, San Diego. Indeed, it can be almost trivial, says Cameron, who is more forthcoming than many others working in industry. Developing bacteria capable of producing 1,2-propanediol—used today as a food additive, particularly for making semimoist pet food—took him and his group just a month, he notes.

They took advantage of *Escherichia coli*'s ability to convert glucose into small amounts of the compound methylglyoxal as a normal part of sugar metabolism. They knew that either of two enzymes—aldose reductase or glycerol dehydrogenase—would turn methylglyoxal into 1,2-propanediol. By consulting online databases, the group identified the appropriate genes for the enzymes and engineered them into *E. coli*. Current production of 1,2-propanediol by this engineered *E. coli* is a mere 0.2 grams per liter, "but these are our initial results and far from optimized," explains Cameron. He sees no reason to doubt that further engineering will increase production to the 100-grams-per-liter level needed to make the process commercially viable.

But coaxing a bacterium to shift much of its metabolic resources into making a particular compound is a challenge nonetheless. The production of an individual metabolite via a particular pathway is affected by the ebb and flow of dozens of other pathways in a cell's metabolism. "Eventually, you have to start looking at metabolic fluxes in the organism, in an attempt to choose pathways to get rid of or down-regulate in order to shunt more metabolic energy into the pathway you've engineered," says Palsson.

He and others, including James Bailey of the Swiss Federal Institute of Technology in Zurich, Gregory Stephanopoulos of the Massachusetts Institute of Technology, and Jans Nielsen of the Technical University of Denmark, have developed computer models of these metabolic fluxes in *E. coli*. One model correctly predicted the metabolic effects of 73 different mutations, Palsson says. He is now trying to predict which of *E. coli*'s metabolic pathways are absolutely essential for life, and is working with Harvard geneticist George Church to knock out the pathways one by one to see if the model's predictions match reality. Ultimately, these models should help researchers who have introduced new enzymes into an organism to plan a second round of metabolic engineering, bolstering or shutting off specific pathways to maximize the amount of product.

Microbiologist Mary E. Lidstrom of the University of Washington, Seattle, is hoping to do the same kind of metabolic engineering on *Methylobacterium extorquens*, a bacterium capable of growing on one-carbon sources such as methanol. Because methanol is easy to make from methane, found in natural gas, genetically engineered *Methylobacterium* could replace some of the existing chemical processes for turning this readily available feedstock into the dozens of commodity chemicals that go into the manufacture of almost every polymer now in use. Lidstrom has already created an efficient vector system for introducing new genes into the organism, and she has worked out most of the metabolic pathways this organism uses to grow on methanol. Her research group is also sequencing the remainder of the organism's genome. That, she says, "will give us the tools to greatly reduce the time it takes us to engineer new pathways in this organism."

The promise of genomics is what makes metabolic engineers so hopeful these days. "With all of the genome sequences we now have and with a better understanding of cellular metabolism, we now have the tools to engineer new metabolic pathways and increase yield of a desired product on a time frame that competes with chemistry," says Genencorp's LaDuca. **–JOSEPH ALPER**

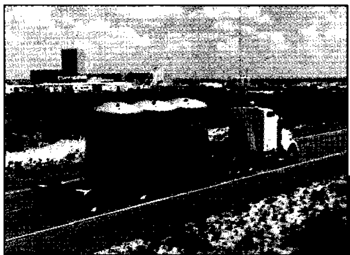
Joseph Alper is a writer in Louisville, CO.

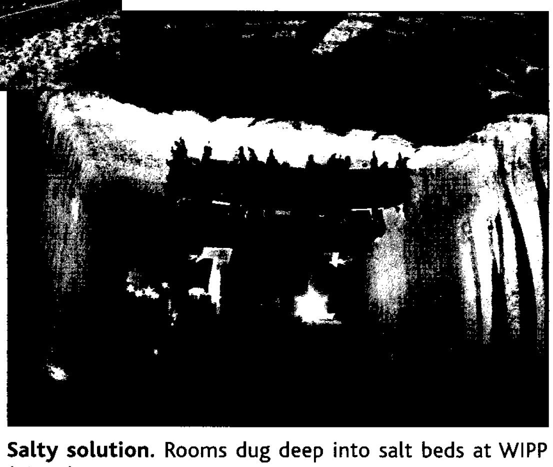
RADIOACTIVE WASTE DISPOSAL

For Radioactive Waste From Weapons, a Home at Last

Independent scientific oversight—and understanding that no site is perfect—helped create the world's only certified deep radwaste repository

For 40 years, scientists and engineers have been crisscrossing the United States searching for likely places to store the mounting tons of radioactive waste created by nuclear weapons production and by nuclear power plants. But everywhere they have looked, they have found geological and political problems. Yucca Mountain, Nevada—the site decreed by Congress as the sole site to be studied as a repository for the nation's most radioactive wastes—is still years from accepting its first curie (see p. 1627). And other nations are even further from actually storing waste: They are still trying to narrow their choices of possible disposal sites.





Salty solution. Rooms dug deep into salt beds at WIPP (*above*) may soon store nuclear waste trucked from bomb production facilities (*top*).

CREDITS: U.S. DEPARTMENT OF ENERGY, CARLSBAD AREA OFFICE

Yet in this frustrating saga, there is one lone success story: the Waste Isolation Pilot Plant (WIPP), a multibillion dollar effort to bury long-lived radioactive wastes in deep salt beds 40 kilometers east of Carlsbad, New Mexico. Unlike any other deep radwaste facility in the world, WIPP has managed to gain approval from scientists and regulators as a safe repository, and even many locals are behind the project. Of course, not everyone is enamored of WIPP. It still faces two lawsuits, filed by environmental groups and the New Mexico attorney general, that challenge its science and due process. But government scientists and lawyers say they're optimistic they'll get favorable judgments. If so, bomb-related wastes could start to be entombed as early as the end of the month.

It's not that WIPP is scientifically a perfect site; indeed, one of the lessons of its history is that there is no such thing. "You never feel quite as comfortable about a site as the day you start to study it," says geophysicist Wendell Weart, who spent more than 20 years as the lead scientist on the project. "If there's anything we've learned" in the course of repository site searches, adds Kevin Crowley, director of the National Research Council's (NRC's) Board on Radioactive Waste Management, "it's that the natural setting is a lot more complicated than we thought it would be. These are first-of-a-kind efforts; they're running into a lot of surprises." Indeed, he says, "it's fair to say things did not go all that smoothly at WIPP, especially in the early days."

The story of how WIPP overcame these obstacles to reach its current status as the world's first certified deep radwaste facility may hold lessons for others struggling along the same path. If there's one overriding lesson, observers say, it is that the technical surprises were handled in an open spirit of scientific inquiry. And a key to this process was an independent scientific advisory board, which provided a thorough—and very public—check on the project scientists.

Deep salt

The road to Carlsbad began in the early 1970s, with a surprise beneath the cornfields of Kansas. Since the 1950s, scientists had pointed to salt as one of the most promising geologic media for a radwaste repository. Laid down in evaporating seas long ago, salt is rock-solid and essentially impermeable. It flows to seal up any excavated cavity and leaves clear traces of any past intrusion of water, the bane of any repository intended to entomb wastes for millennia. In 1970, the Atomic Energy Commission (AEC), a predecessor of the Department of Energy (DOE), tentatively selected an abandoned salt mine near Lyons, Kansas, as a radwaste repository.

Although the nuclear industry was still in its infancy, highly radioactive spent fuel rods from civilian power plants were already piling up. And for decades nuclear weapons production had been generating liquid high-level wastes along with plutonium-contaminated debris—