The Frankenstein Patent

And G.E. Created Life, and It Was Hungry

BY MICHAEL ROGERS

Schenectady, New York, is a quiet town of two-story frame houses, just north of Albany, that calls itself "The Electric City," a reference not to psychedelia, but to the massive General Electric manufacturing and research complex that dominates the town's economy. The merchandise vending machine in the local Holiday Inn dispenses, along with Certs, pepperoni and pocket razors, a $1.50 plastic slide rule. Inside the city limits, GE manufactures steam and gas turbines; outside, at the Research and Development Center, they manufacture progress.

While the center—a scatter of brick buildings on the bank of the Mohawk River—is not the largest industrial laboratory in the world, it may well be the most diversified. In less than five minutes, in a single building, one can walk from a sophisticated microbiological laboratory complete with ultracentrifuge and costly vials of exotic enzymes, to the two-and-a-half-story-high mechanical press that, two decades ago, produced the first synthetic diamond on the planet.

By now, even the diamond mining De Beers has a license to use GE's patented diamond-making process. Patents, in fact, might well be construed to be the R&D Center's most important product: A display of metal-etched photographs in the reception lobby honors the center employees who have contributed more than 50 patents each year. Last year, GE was granted two-thirds more patents in this country than the nearest runner-up and, on average, the R&D Center produced one of those patents each and every working day.

One of those patent applications, though, was rejected last year and is presently on appeal. An appealed patent application is not unique: The Patent Office appeal board is presently running about two years behind. What is unique, however, about [Cont. on 30]

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The industrial use of microorganisms — yeasts, mold and bacteria — is hardly new. The fermentation of alcoholic beverages with yeast is positively ancient; the use of mold to produce antibiotics like penicillin is, on another time scale, just about as venerable. In recent years the applications have grown numerous and a touch more esoteric; for example, the Japanese produce amino acids as cattle food supplement, and several European corporations are exploring large-scale yeast farming as a protein source.

In the same 24-hour period, while a 1000-pound steer produces one pound of protein, 1000 pounds of high-protein yeast turn into 4000 pounds. The potentials are, clearly, great, and it seemed altogether inevitable that sooner or later, some of the new and sophisticated techniques of molecular genetics—the reengineering of basic organisms in the laboratory—would find commercial application.

That inevitability has come to pass and one of the first such applications is the subject of GE's disputed patent request. It seems that there is a genus of bacteria called *Pseudomonas*, found, generally, in soil and water and displaying an unusually broad appetite that happens, in certain strains, to include crude oil. In the past, in fact, the presence of these strains was even considered a possible indicator of underground petroleum.

The GE researcher, a young and personable Ph.D. named Ananda Chakrabarty, decided to look into the possibility of recruiting *Pseudomonas* as a cleanup squad for oil spills. The idea itself was neither new nor, at the outset, particularly workable. For all their odd appetite, *Pseudomonas* is, at heart, a touch finicky and no single strain exists in nature that will digest all of the components that make up crude oil. And should one dump in a mix of strains—each specializing in one portion of the petroleum—the bacteria end up spending so much time competing with each other that the job of oil digestion proceeds, in all, rather sloppily.

Chakrabarty, however, had already spent a great deal of time studying the genetic basis of *Pseudomonas*'s gastronomic preference and had learned that the genetic information which allows the bugs to digest oil resides not in the large central chromosome but in tiny, extrachromosomal bits of DNA called "plasmids." And plasmids, as molecular biologists have lately learned, are very handy little devices for shuttling genetic information between bacteria—both in nature and in the laboratory.

Chakrabarty isolated the specific plasmids that control petroleum digestion from a set of different *Pseudomonas* strains and then, using some tricky laboratory work, managed to sneak four of them into a single bacterial cell—which then developed the capacity to digest, all by itself, most of the various hydrocarbons that constitute crude oil. That same bacterium, moreover, proceeded to pass the ability on to its descendants.

A new strain of bacteria, in essence, and while Chakrabarty is still at work perfecting his new "bug"—as researchers often refer to their microbes—the commercial wheels have already begun to turn. One possibility GE is considering is to package the bacteria in dry powder form, for application to oil slicks, or perhaps even to premix that powder with the straw that is customarily set down to soak up fresh spills. A GE promo display already includes a color transparency of two glass vials; one contains water, topped by a thick layer of grimy crude oil, the other—which started out the same way—contains only water slightly clouded by the millions of modified *Pseudomonas* that have made dinner of the unsightly petroleum.

Modified *Pseudomonas* culture is not going to show up in hardware stores next week. As Chakrabarty continues to make genetic modifications on his bug, General Electric is in the midst of dealing with the touchier legal questions posed by the creation of what is, essentially, a novel organism.

One question, obviously, is environmental impact: What unforeseen disturbance might be wrought by dumping a genetically engineered supermicrobe into, say, an ocean-borne oil slick? Researcher Chakrabarty is fairly persuasive in minimizing those worries—although GE acknowledges that environmental testing of the new bug prom- [Cont. on 71]

New Life Form

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How complex, even GE may not yet understand. The Environmental Protection Agency, upon whose shoulders the question will fall, is already no stranger to the field of microbiological oil-spill cleanup. For several years now, federal law has provided for the testing of these oil-eating microbes and EPA has, in preparing these guidelines, examined about five such products. The central requirement is that the oil-eating culture may not contain certain specific organisms that cause disease in human beings; fundamental, one might think, but also fairly critical, in view of the fact that just about half of the microbes that EPA originally reviewed would have failed the pathogenicity test outright.

GE's *Pseudomonas* culture is a nonpathogenic strain and should have no difficulty on that account (although, according to the EPA, they have made no formal application thus far). The real question, however, remains: Precisely what long-term effect might the release of a modified organism have on the environment?

"That's a good question," says a researcher at the EPA laboratory in Edison, New Jersey, "and based on our current procedures, it wouldn't be answered." The question is, though, one that GE will probably have to answer. Even after the bug has been EPA certified, on-site approval must be given—at each oil spill—before application is allowed. And that approval involves state and local environmental regulation. One would suspect that it will require fairly persuasive evidence from the manufacturer to convince local environmental watchdogs that a genetically engineered microbe is also the sort of microbe that one would want in one's own harbor.

On that front, General Electric will likely choose to argue that their modified *Pseudomonas* is not really, all in all, so different from the strains that already exist in nature. On another front, however, GE seems to be gearing up to present precisely the opposite argument. And that front, as suggested earlier, is the United States Patent Office.

In the spring of 1974, Chakrabarty and General Electric were granted a patent on the complex microbiological process, involving ultraviolet irradiation, that allowed the researcher to fit his *Pseudomonas* with a series of plasmids that would not, in nature, normally coexist in the same bacterium. The product of that process—the modified *Pseudomonas*—was at the same time denied patent.

According to GE's Research and Development Center's patent operation, the rejected patent regarding the microbe has been appealed and will be reviewed by the Board of Patent Appeals within two years. If appeal fails on that level, the case may then go outside of the patent office; to District Court or to the Court of Customs and Patent Appeals.

At this point, the details of the case are obscure. The issue at question appears to be whether one can patent a novel living organism, and the precedents seem both aged and foggy. One can, for example, patent hybrid plants, as long as they can be vegetatively reproduced.

Past that, however, no real precedent seems to exist in the GE case. One ruling, often cited, is more than a century old. At one point, according to a lawyer involved, GE even briefly considered calling the novel *Pseudomonas* bacterium a plant, since precedent already exists in that situation. The notion was immediately dismissed and by now the die appears cast: GE wants to patent its super bug, and they are willing to argue about it.

The Patent Office offers no comment. An examiner involved in the GE application for modified *Pseudomonas* says that "I can't even acknowledge that there has been such an application"; such secrecy is standard procedure in the sphere of proprietary processes—those held by a company without the benefit of patent.

So the GE super bug—presently slumbering, Pyrex bound, in a small laboratory overlooking the Mohawk — may yet lend its name to some precedent-setting judicial decisions. Or perhaps not: The overall utility of microbiological techniques for oil-spill removal is still considered rather dubious and, at some point, the legal flak may overwhelm commercial potential of even the hungriest *Pseudomonas*.

But even so, *Pseudomonas* is only the beginning. GE, for example, is already publicly discussing the engineering of microorganisms capable of concentrating gold or platinum from waste substances—the innards of discarded automotive catalytic converters, for example — which bacteria can then be harvested and purified. And past that, numerous researchers, in this country and in Europe, are designing genetically engineered microbes tailored to turn out a variety of pharmaceutical substances from enzymes to antibiotics. Bacteria engineered to turn out insulin is a possibility that arises regularly in speculative discussions.

The questions — both environmental and legal—created by commercial use of engineered microorganisms cannot possibly go long without answers. In a sense, the environmental and public health issues have already been recognized and, at this writing, have already been the subject of more than one year's vociferous discussion within the research community (see "The Pandora's Box Congress," RS 189, 1975). That discussion, which has thus far produced both a voluntary research moratorium and a still disputed set of guidelines, deals with the most sophisticated genetic engineering techniques presently available; the artificial recombination of DNA particles that would never meet in nature. Chakrabarty's GE work, while it reads out in terms of a microbe that has never really previously existed in nature either, does not approach the implications of those more controversial techniques.

If the public health issues remain unresolved, the legal issues are even more so. Even the keenest legal mind will likely soon founder in the complexities of separating a patentable process from the nonpatentable microorganism that was designed to perform it in the first place.

It would seem to demand almost preternatural caution, at this stage of the game, to draft legal precedents regarding the rights to novel life forms. Yet without the right of patent, the whole field of genetically engineered microorganisms might well drift into the alchemical realm of closely guarded secret industrial formulae; a condition in the case of colas or perfumes but which may well be far different when it comes to the artificial manipulation of life.

The solutions may turn out to be much simpler than expected. Only within the last 18 months or so have questions of this nature occurred on levels as practical as patent offices or agencies of environmental impact. The questions have been sudden, and for all their foreshadowing in speculative literature, fairly unforeseen in their specifics. That suddenness, perversely, is almost guaranteed to be belied only by the length of time those same questions will remain with us.

PLASMID *pSC*101 is shadowed with platinum-palladium and enlarged 230,000 diameters in an electron micrograph made by the author. A plasmid is a molecule of DNA that exists apart from the chromosome in a bacterium and replicates on its own, often carrying the genes for some supplementary activity such as resistance to antibiotics. This plasmid, a small one made by shearing a larger plasmid native to the bacterium *Escherichia coli*, is a circular, or closed-loop, molecule of DNA about three micrometers in circumference that carries the genetic information for replicating itself in *E. coli* and for conferring resistance to the antibiotic tetracycline. It was the "vehicle" for the first gene-manipulation experiments by the author and his colleagues. Foreign DNA was spliced to it and the plasmid was introduced into *E. coli*, where it replicated and expressed both its own and the foreign DNA's genetic information.