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Pursuing Synthetic Life, Dazzled by Reality

By NATALIE ANGIER

When scientists announced on Jan. 24 that they had reconstituted the complete set of genes for a microbe using just a few bottles of chemicals, the feat was hailed as a kind of shining Nike moment in the field of synthetic biology, the attempt to piece together living organisms from inert scratch.

Reporting in the journal Science, Dr. J. Craig Venter and his colleagues at the J. Craig Venter Institute said they had fabricated the entire DNA chain of a microbial parasite called Mycoplasma genitalium, exceeding previous records of sustained DNA synthesis by some 18-fold. Any day now, the researchers say, they will pop that manufactured mortal coil into a cellular shell, where the genomic code will "boot up," as Dr. Venter puts it, and the entire construct will begin acting like a natural-born M. genitalium — minus the capacity, the researchers promise, to infect the delicate tissues that explain the parasite's surname.

Yet even as researchers rhapsodize about gaining the power to custom-design organisms that will supply us with rivers of cheap gasoline, better chemotherapeutic agents or — here's my latest fantasy — a year-round supply of fresh eggnog, the most profound insights to emerge from the pursuit of synthetic life just may be about real life.

Scientists who seek to imitate living cells say they can't help but be perpetually dazzled by the genuine articles, their flexibility, their versatility, their childlike grandiosity. No matter what outrageous or fattening things we may ask our synthetic cells to do, scientists say, it's nothing compared with what cells already have done of their own accord, usually in the format of bacteria. Microbes have been found to survive and even thrive in places where if they had any sense they would freeze, melt, explode, disintegrate, starve, suffocate, or at the very least file a very poor customer review.

"We have micro-organisms that live in such strong acid or base solutions that if you put your finger in, the skin would dissolve almost instantly," Dr. Venter said in an interview. "There's another organism that can take three million rads of radiation and not be killed." How can a microbe withstand a blast of radioactivity that is a good 1,500 times greater than what would kill any of us virtually on the spot? "Its chromosome gets blown apart," Dr. Venter said, "but it stitches everything back together and just starts replicating again."

Given the wealth of biological and metabolic templates that nature has invented over nearly four billion years of evolutionary tinkering, scientists say, any sane program to synthesize new life forms must go hand in hand with a sustained sampling of the old. "My view is that we know less than 1 percent of what's out there in the biological universe," Dr. Venter said.

Last year, he and his colleagues went prospecting for new organisms in the deep midocean, long thought to be one of earth's least animate regions. Sure, life evolved in the seas, but shallow seas, where sunlight can penetrate, were considered the preferred site for biodiversity. Even with the startling discovery in the 1980s of life on the ocean floor, around the hydrothermal vents, the midocean waters couldn't shake their reputation as an impoverished piece of real estate: too far down for solar energy, too high up for its geothermal equivalent.

Yet when the Venter team began sampling the waters for the most basic evidence of life, the presence of genetic material, they found themselves practically awash in novel DNA. “From our random sequencing in the ocean, we uncovered six million new genes,” he said, genes, that is, unlike any yet seen in any of the mammals, reptiles, worms, fish, insects, fungi, microbes or narcissists that have been genetically analyzed so far. With just that first-pass act of nautical sequencing, Dr. Venter said, “we doubled the number of all genes characterized to date.”

Researchers assume that most of the novel DNA is microbial in origin, but they have yet to identify the organisms or see what they can do, because most microbes are notoriously difficult to cultivate in the lab. Bacteria may happily swim through toxic waste, but when it comes to confinement on an agar plate, thank you, they’d rather be dead.

Technical challenges notwithstanding, scientists have made some progress in investigating preposterous life forms and tallying the biochemical tools that such extremophiles use. Thermophilic microbes, for example, which can withstand temperatures of 238 degrees Fahrenheit, well above the boiling point of water, have stiffening agents in their membranes, to keep them from melting away, and they build their cell proteins with a different assortment of amino acids than our cells do, allowing the construction of strongly bonded protein chains that won’t collapse in the heat.

By contrast, said Steven K. Schmidt, a microbiologist at the University of Colorado in Boulder, when you look at organisms that thrive in subzero conditions, “their membranes are really loosey-goosey, very fluid,” and so resist stiffening and freezing. It turns out there are a lot of these loosey-gooses around. Dr. Schmidt and his colleagues study the fridgophile life forms that make their home in glacial debris high in the Andes Mountains, 20,000 feet above sea level, where the scene may look bleak, beyond posthumous, but where, he said, “we’ve been pretty amazed at the extreme diversity of things we’ve found.” The complexity of the Andean microbial ecosystem, he said, “is greater than what you’d find in your garden.”

Yes, microbes were here first, and they’ve done everything first, and synthetic lifers are happy to scavenge for parts and ideas. Drew Endy, an assistant professor in the biological engineering department at the Massachusetts Institute of Technology, and his colleagues are putting together a registry of standardized biological parts, which they call BioBrick parts. The registry consists of the DNA code for different biological modules, interchangeable protein parts that they hope may someday be pieced together into a wide variety of biological devices to perform any task a bioengineer may have in mind, rather like the way nuts, bolts, gears, pulleys, circuits and the like are assembled into the machines of our civilization. Numbering some 2,000 parts and growing, the registry contains many recipes for clever protein modules invented by bacteria. One sequence engineered by researchers in Melbourne, Australia, encodes the instructions for a little protein balloon, for example. “It’s based on a natural part found in a marine micro-organism that controls the buoyancy of the cell,” Dr. Endy said.

Invisible though it may be, the microbial community ever keeps us afloat.