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Little progress

Extreme hunter scores big with tiny finds.
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You could call him the real Agent Mulder. Like that indefatigable character from *The X-Files* television series, Jonathan Trent, an astrobiologist with NASA, is driven by a curiosity to find life-forms that can exist on other planets. For the last 15 years, he has dived into oceans, climbed volcanoes, and scoured the world's hot springs to study extremophiles, rare microorganisms that can survive in extreme heat, cold, and even acidic conditions. "These are the types of extraterrestrials that we should be looking for, not funny creatures with bumps on their heads," says Mr. Trent. "The question I have been trying to answer is, How do these organisms survive in these conditions?"

In 1991, his search for "extreme" organisms turned up a breakthrough that may revolutionize a branch of nanotechnology known as molecular manufacturing. In this nascent field of study, scientists assemble structures and materials using atoms and basic molecular forces as primary building blocks.

If molecular manufacturing delivers on its promise, tiny microchips could be created atom by atom – preserving Moore's law well into the next century. New medical devices, like nanobots that roam our blood stream and deliver drugs, could become a kind of backup immune system.

But nanotechnology has made far more progress in press releases and the pages of science fiction novels than it has as a viable science. Thus far, molecules have proven too small to manipulate with precision, even with atomic-force microscopes. For the most part, scientists have been able to do little more than prod, magnetize, or push them around a surface. This means that they cannot really build anything; it is the difference between stacking up cement blocks and actually building a house. If molecular manufacturing were house construction work, we would still be learning to build the wooden frame.

And that is where Mr. Trent and his team at NASA's Ames Research Center in Mountain View, California, come in. The scientists have discovered a substance that can act as that much-needed frame to hold atoms in place and organize them into different structures. The discovery will, they say, make the manufacture of nano-scale devices like microprocessors, memory chips, or drug-delivery modules as easy as mixing a solution in a test tube. Best of all, this substance could enable such items to be produced in large quantities economically.

Mr. Trent's discovery has not gone unnoticed. The research center's Nanotechnology Lab, one of five regional nanotech research centers in the United States, is the largest recipient of the government's $700 million nanotech investment fund. Moreover, NASA is already in licensing discussions with at least one major biotech firm to use it.

The miracle substance is the byproduct of a microbe that has survived the last 3.4 billion years in some of the world's harshest environments. It has survived the ice ages, the extinction of the dinosaurs, and now quite happily thrives in sulfuric hot springs, where temperatures reach 185 degrees Fahrenheit. This little microbe's resilience has helped scientists begin to overcome the obstacles to manufacturing nano-scale devices.

Until now, molecular manufacturing has been constrained by what scientists like to call the "fat fingers" problem. As anybody who has chased a grain of rice around with a pair of chopsticks can testify, it can be very difficult to pick up or place really tiny objects with relatively big tools.

There are, roughly speaking, three basic approaches to molecular manufacturing: binding molecules by mixing them with sticky molecules like fats (chemistry), binding them through genetic engineering (biology), or binding them using physical methods like bombarding them with electrons (physics). But because the scale involved in doing these manipulations is so small, many scientists have concluded that it would be best if nanotech devices organized themselves like chemicals, replicated themselves like living organisms, and functioned as predictably as machines. Overcoming these hurdles surely would require Mr. Trent's express focus on these problems, along with the integration of several different branches of science and a healthy dose of creativity.

Then, as often happens in scientific discovery, serendipity took over. Mr. Trent and his team unearthed a protein called Heat Shock Protein 60 (HSP 60) while studying *Sulfolobus shibatae*, an extremophile microbe that lives in the sulphuric hot springs in Yellowstone National Park. This protein assembles itself into a ring structure called a chaperonin, which fortifies the cell membrane so the microbe can live in extreme conditions.

Closer inspection revealed other fascinating features. First, a chaperonin molecule has an empty core, like a stack of Lifesavers candy, which makes it an ideal manufacturing frame. But the diameter of the core is too narrow to hold enough nanosize particles for practical manufacturing purposes. Chad Paavola, a molecular biologist at NASA, genetically tweaked the protein to widen the "hole" and remove unwanted strands of protein. He then engineered the protein so that it would grow amino acids on the inside of the opening so that nanoparticles would stick there. Otherwise, nanoparticles could bounce out of the chaperonin opening.

Once they were able to increase the diameter of the hole, the molecule could be used to trap and contain nano-size substances like gold, magnetized particles (for storage devices), or toxins that target cancer cells. And chaperonins use little hooks around their outside edges to attach to one another and organize into rows and columns. This ability to self-organize is key: it solves the “fat fingers” problem. Furthermore, because *Sulfolobus shibatae* lives in warm environments, the chaperonin could be used in manufacturing processes that reach temperatures as high as the boiling point of water.

After getting acquainted with these microbes in the lab, NASA biologists employed a common biotech trick: they inserted foreign genetic code into the rapidly replicating *Escherichia coli* bacteria. In this case, they fooled the single-celled organism into producing industrial quantities of chaperonin. “Normally you have to separate out the bacteria and the protein in a costly process,” says Mr. Trent. “But HSP 60 is heat resistant, so you can warm up the solution until you burn off the *E. coli*.” And all that remains is very useful nano-scale scaffolding.

But the work did not end there. NASA scientist Andrew McMillan discovered that the chaperonin could be morphed from its tubular shape into various other shapes, like a honeycomb, which could provide the lattice structure required to assemble a nano-size memory chip.

According to nanotechnology expert David Goldhaber-Gordon, assistant professor of physics at Stanford University, each individual piece of Mr. Trent’s method has been done before. Panasonic and Sony, for example, are working with a protein that binds to magnetized iron particles, which they hope will provide nano-scale storage mediums.

“However, what is unique is combining work such as protein design with self-assembly techniques to make a hybrid organic/inorganic substance,” says Mr. Goldhaber-Gordon. “And it is the versatility of the chaperonin that is new here. Once you have the scaffolding, you can attach pretty much anything you want.”

NASA’s approach is promising because any particle can be mixed in with the chaperonins, which will provide the framing upon which other nano-scale devices can be built.

Whether it is the scary killer bugs in Michael Crichton’s techno-thriller *Prey* or the tiny medical devices that roam our bodies eating cancers in K. Eric Drexler’s visionary book *Engines of Creation*, nanotechnology is billed as both the miracle and the nightmare science of our age. But so far it has made little progress as either. In fact, it will be a few years before we have even a nano-scale computer chip. What we are seeing now is the creation of the materials or building blocks that will perhaps make these things possible. Society will have to decide whether that is good or bad.