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Making cells like computers

By Erik Parens
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Craig Venter recently announced that his research institute had synthesized the genome of a bacterium. Upon hearing this, observers across the world anxiously suggested that he was on the verge of "synthesizing life."

But Venter has not done what most people mean by "synthesizing life." It is true that he has helped to create a new field that is sometimes called "synthetic biology." Synthetic biologists, however, are far from creating the astonishingly complex systems we call life.

Strictly speaking, what Venter did was to stitch together segments of commercially produced copies of naturally occurring DNA to produce an almost exact replica of the genome of a bacterium. He hopes that by the end of the year, when he transplants that synthesized genome to a naturally occurring bacterial cell, it will take over the naturally occurring genome's role and direct the cell's activities.

His next step, which will be far more difficult, will be to create a stripped-down, "minimal" genome, which will exclude genes that he concludes are irrelevant for creating the gene products he wants.

The final step, which will be still more difficult, is to add a gene or genes to that minimal genome and then place it into a naturally occurring bacterial cell. Ultimately, he aims to get those new genes to "program" such a bacterial cell to produce things like malaria vaccines and cheap biofuels. Venter has no intention of trying to synthesize the marvelously complex bacterial cell membrane or cellular environment.

Essentially, "synthetic biologists" hope to make cells act more like computers and less like biological systems. To understand why they would want cells to act less like biological systems, it helps to understand some recent history of human genetics research.

Once upon a time, many geneticists believed that the human organism would work like a computer - at least in the sense that a given input (a gene) would reliably produce a predictable output (a protein). Based on early discoveries about the role of single-gene mutations in such rare disorders as Huntington's disease, many geneticists hoped that mutations in single genes might also have predictable effects on common traits like cancer.

Venter himself was one of the first geneticists to announce the demise of that hope.

In 2000, Venter's private company published its draft sequence of the human genome. But as he acknowledged shortly before that publication, knowing the sequence could only be a small step on the long road toward understanding how genes actually work in complex biological systems. In his own colorful way, Venter said to a New Yorker writer, "We know (scatological expletive deleted) about biology."

Geneticists today are exquisitely attuned to the staggering complexity of the processes that give rise to common traits and, more generally, to the organisms we are. Hardly a month goes by without a discovery that undermines the old-fashioned, simple story: from discovering that molecules that are not DNA play an important role in the expression of genes, to realizing that single genes can code for myriad proteins, to recognizing the significance of gene-gene and gene-environment interactions.

We are just beginning to understand that what we once called "junk" DNA and "inefficient" repetitions of gene sequences both play important roles in cell functioning. As Francis Collins, the head of the National Human Genome Research Institute, recently said, we are in the midst of a scientific revolution in our understanding of what genes are and how they work.

Perhaps no one was more surprised by this complexity than researchers at the National Human Genome Research Institute. After all, the institute owes its existence to the promise made in 1990, that, if Congress would finance the project to sequence the human genome, cures for terrible diseases would be forthcoming. While progress has surely been made, we do not today use gene-transfer technology to reliably treat even one genetic disease. This is not for lack of intelligence, money or commitment. It is because of the extraordinary complexity of biological systems.

It would be a remarkable technical achievement if Venter were to get a bacterium to work more like a computer and less like a biological system. It is already a remarkable achievement to have synthesized a bacterial genome.

As we appreciate Venter's technical prowess, however, we also need to remember his scatological pronouncement of 2000. Conceivably, we are on the verge of installing synthetic genomes in bacterial cells to create products we want. But we are still a long, long way from doing what most people mean by "synthesizing life."

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Correction:

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