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Baby Steps to New Life-Forms

By OLIVIA JUDSON

Olivia Judson on the influence of science and biology on modern life.

Intelligent design. That's one goal of synthetic biology, a field that was catapulted into the news last week with the announcement that a group of biologists had manufactured a genome that exists nowhere in nature and inserted it into a bacterial cell. The dream is that, one day, we'll be able to sit and think about what sort of life-form we'd like to make — and then design and build it in much the same way we make a bridge or a car.

Realizing this dream is still some way off. But before I get to that, let me briefly describe the state of play.

Synthetic biology is predicated on the fact that, to a large extent, organisms can be broken down into a set of parts. For example, the information contained in DNA comes in discrete chunks — namely, genes. Genes contain the instructions for making proteins — molecules that come in different shapes and sizes — as well as information about where and when those proteins should be used. Proteins interact with each other, driving many of the functions of the cell.

Some genes are essential: without the proteins they encode, the organism cannot exist. But many genes are "optional" — in the laboratory at least, the organism gets on fine without them.

Likewise, having an "extra" gene or two isn't usually a problem. Already, we have exploited this fact to insert new genes into organisms as diverse as petunias and goats. Since the 1980s, human insulin has been mass-produced by bacterial cells genetically engineered to make it.

Already, we have improved on nature to create versions of genes and proteins that do not exist in the wild. Green fluorescent protein, for example, is naturally made by jellyfish; we humans have altered the gene so that the protein has a stronger fluorescence and occurs in other colors. It is now an essential tool in cell biology, as the fluorescence allows cells, genes and proteins, to be tagged and their activities monitored.

And, recently, we have begun to build genomes in the laboratory. The first to be made, eight years ago, was poliovirus. Then it became possible to make synthetic copies of existing bacterial genomes. Now, with the results published last week, we can begin to manufacture genomes for bacteria that do not exist in nature.

The difficulties, however, remain great. Last week's announcement, while an enormous and complex technical achievement, was a baby step toward designer life, not a giant leap. The resulting bacterium is little different from a bacterium that already exists. The principal difference is that its DNA carries some "watermarks" — special sequences — that identify it as having been made, not evolved.

One problem with creating life from the drawing board is that evolved biological systems are complex, and often behave in ways we cannot (thus far) predict. Although we can specify the DNA sequence to make a particular protein, we cannot always predict what the protein will look like or how it will interact with other proteins in the cell. Also, to a large extent, biological systems are not standardized: Yes, we have become good at making DNA, but we do not yet have a "basic" cell, into which everything else can be slotted. In short, while we can copy genomes, and edit them lightly, we are a long way from writing one from scratch.

Although we cannot yet express ourselves fluently in nature's genetic language, however, there is the tantalizing possibility that we might one day write our own. We have begun to engineer proteins that include components that do not normally occur in living beings, and we are starting to build molecules that resemble DNA in terms of their capacity to store information, but that can be read differently by the machinery of the cell. This would allow us to create a "second nature" — a set of organisms that use a different genetic language, and cannot readily interact with the life-forms that evolved in the wild.

What I love about this is that the process of inventing a new genetic language will help us to understand more about the one that actually evolved. Indeed, this has already begun. Early attempts to manufacture DNA alternatives quickly revealed that the "bannisters" of the double helix — the chains that run down the outside of the molecule — are more essential to how the molecule works than anyone had thought.

There are many ways we could use designer organisms, some good and some bad. But the most fundamental aspect of the enterprise is that by trying to build life, we gain a more profound understanding of its evolved nature.

Notes:

The field of synthetic biology is enormous and contains many applications I have not described here. For interesting overviews of the possibilities see, for example, Benner, S. A. and Sismour, A. M. 2005. "Synthetic biology." Nature Reviews Genetics 6: 533-543; Endy, D. 2005. "Foundations for engineering biology." Nature 438: 449-453; Carr, P. A. and Church, G. M. 2009. "Genome engineering." Nature Biotechnology 27: 1151-1162; and Khalil, A. S. and Collins, J. J. 2010. "Synthetic biology: applications come of age." Nature Reviews Genetics 11: 367-379. Please also refer to these papers for discussions of the hurdles to be overcome, including the ones that I mention (the lack of a basic cell, the problems of prediction) towards the end of the article.

For the announcement that a team of biologists has made a synthetic bacterial genome, see Gibson, D. G. et al. 2010. "Creation of a bacterial cell controlled by a chemically synthesized genome." Science Express 20 May 2010.

For a look at which genes are essential and which are not, see for example, Glass, J. I. et al. 2006. "Essential genes of a minimal bacterium." Proceedings of the National Academy of Sciences USA 103: 425-430. The insertion of novel genes into both plants and animals is now routine, and can be read about in any modern biology textbook. For the original paper showing the synthesis of human insulin in bacteria see, Goeddel, D. V. 1979. "Expression in Escherichia coli of chemically synthesized genes for human insulin." Proceedings of the National Academy of Sciences USA 76: 106-110. Human insulin is just one of a large number of compounds produced in genetically engineered bacteria. For an interesting overview of what bacteria are making for us, see Lee, S. Y. et al. 2009. "Metabolic engineering of microorganisms: general strategies and drug production." Drug Discovery Today 14: 78-88.

For improved, brighter green fluorescent protein, see Crameri, A. et al. 1996. "Improved green fluorescent protein by molecular evolution using DNA shuffling." Nature Biotechnology 14: 315-319. For a look at the smorgasbord of color possibilities, see Shaner, N. C., Steinbach, P. A., and Tsien, R. Y. 2005. "A guide to choosing fluorescent proteins." Nature Methods 2: 905-909. For an amazing demonstration of how fluorescent proteins can be used, see the brainbow paper: Livet, J. et al. 2007. "Transgenic strategies for combinatorial expression of fluorescent proteins in the nervous system." Nature 450: 56-63.

For synthetic poliovirus, see Cello, J., Paul, A. V. and Wimmer, E. 2002. “Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template.” Science 297: 1016-1018. For synthetic copies of existing bacterial genomes, see Gibson, D. G. et al. 2008. “One-step assembly in yeast of 25 overlapping DNA fragments to form a complete synthetic Mycoplasma genitalium genome.” Proceedings of the National Academy of Sciences USA 105: 20404-20409.

For a fascinating overview of how we may be able to write our own, novel, genetic languages see for example Schmidt, M. 2010. “Xenobiology: a new form of life as the ultimate biosafety tool.” BioEssays 32: 322-331. This paper also includes the term “second nature”, which I am borrowing. The potential for engineering to reveal aspects of why the world is the way it is has been much discussed by the authors I mention in the first paragraph of these notes. Benner and Sismour 2005 give a good account of how early efforts to make DNA alternatives revealed unsuspected properties of DNA, especially the importance of the bannisters. For an overview of recent progress in incorporate “unnatural” amino acids into proteins, see Wang, Q. et al. 2009. “Expanding the genetic code for biological studies.” Chemistry and Biology 16: 323-336.

91 Readers' Comments

1.
May 28th, 2010
1:38 pm
This comment has been removed. Comments are moderated and generally will be posted if they are on-topic and not abusive. For more information, please see our Comments FAQ.
2.
J.
New York
May 28th, 2010
1:38 pm
It strikes me that "synthetic biology" remains an ambiguous term that tries to capture a whole range of scientific, engineering, and business projects. While some ventures aim to, as you write, "gain a more profound understanding of its evolved nature" others seek squarely to strip out the complexity of evolved life to make organisms that behave more like machines. As we consider the ethics of these projects, there may be an important distinction between projects that seek to unravel mysteries of biology life and those that seek to industrialize it into a "second nature." A commitment to the science of the former may not necessarily demand enthusiasm for the latter.
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3.
Clara
NY
May 28th, 2010
1:38 pm
What seems most interesting, and at the same time most frightening about this is the possibilities which appear for mutations of humans. Creating a new life form sounds nice, but what happens when we mix it with humans? Will the results be human anymore, and what if we all share in these new creations (as they might help fight diseases and so on)? It's both exciting and very scary. An interesting discussion on evolution and eugenics:
http://www.pandalous.com...
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4.
Louis
Austin
May 28th, 2010
1:38 pm
Just one bit of advice - Read Mary Shelley's "Frankenstein" or at least know the basic premise.
Recommend Recommended by 6 Readers
5.
Gemli
Boston
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