

Synthetic life – too much, too soon?

Michael Reinsborough asks whether synthetic biologists are rushing ahead with development of associated technologies before the science is properly understood.

In the early history of Europe, written knowledge, available only to a select few, was hand copied by monks. By copying ancient manuscripts, the monk would learn to write. Only after a lifetime of copying the great books, or perhaps never, would a monk be able to consider writing something himself. This relationship of learning to write by copying is also the origin of synthetic biology. Recombinant DNA splicing (now over thirty years old) is the process of cutting and pasting a gene from one organism into another, much like copying a letter or a word found in one manuscript into another. As part of gene mapping projects seeking to 'read' DNA code, researchers had to copy short strands of DNA in order to compare them. This artificial synthesis of short strands of DNA, initially very expensive and time consuming, has led from mapping DNA to the possibility of writing or even rewriting genetic code. With the hubris of a junior monk aspiring to be Plato or to improve upon the Latin bible, a new generation of synthetic biologists aspire to rearrange all the paragraphs, all the words, and all the letters at the same time.

The synthetic biology paradigm sees the DNA sequence of a cell as a sort of software that an engineer can decode, rewrite, and improve. The engineer uses a computer to represent and arrange genetic code, and then sends their new design to one of the many make-to-order gene synthesis companies who synthetically construct the genetic material for them. In the lab this new material can then be introduced into a microorganism. This past year Synthetic Genomics Inc. lead by Craig Venter, made world headlines¹ when they announced that they had copied the entire genome of the *Mycoplasma* bacterium synthetically, added a marker gene to enable recognition, and reinserted it into an existing bacterium that had had its own DNA removed. This organism was then able to divide and reproduce using the synthetic DNA. While this was not the creation of man-made life that sound-bite science journalism suggested (the existing cell in which the synthetically made DNA was inserted was not itself artificially created), it was a significant proof-of-concept experiment for a potential synthetic biology industry estimated to be worth billions of dollars in the future.

The uses of synthetic biology (if it can be made to work) are enormous. Anything made in nature could,

in theory, be manufactured cheaply in biochemical factories. Synthetic biology advocates emphasise the possibility of a cure for malaria, cheap biofuels, and potential solutions for climate change, all very media-friendly goals. But early investors in synthetic biology are attempting to patent the basic processes at the beginning of any synthetic biology revolution and therefore achieve sweeping monopoly control over any potential benefits. Besides venture capital firms from the dotcom sector, the infamous oil company BP, agribusiness giant Cargill, chemical company Du Pont, Virgin Fuels, and pharmaceuticals giant Pfizer are some of the global corporations bankrolling R&D and funding start-up companies in synthetic biology.

But success is not the only thing to be concerned about in risky synthetic biology. Both bio-terror and 'bio-error' are concerns. With mail-order gene foundries available on the internet, a laptop and a garage laboratory are the new resource threshold for weaponising viruses.² The possibility that experimental bugs will escape into the environment with unforeseen consequences is also a major concern. But for a scientist, it is perhaps the breathtaking reductionism of the synthetic biology paradigm that is most concerning. In fact, many synthetic biologists are not biologists at all but come from disciplines such as computer science and electrical engineering. The application of explicitly computer science models and electrical circuit diagrams is new to genetic biology.

A gene is a small unit of DNA originally thought to express a specific trait, for example, the production of a protein.³ In reality, genes and parts of genes interact in complex ways producing proteins that suppress or promote the behaviour of other genes, creating a system of cellular regulation (including timing and amount) for the production of a protein. Building a cell that will make a particular protein would involve changes to not just one gene but to many genes at various locations within a strand of DNA. Synthetic biologists are attempting to represent these genetic pathways for controlling the metabolism of a cell in something similar to electric circuit diagrams. Any DNA for which a purpose cannot be found (so called 'junk DNA') is stripped out of the synthetic biologists' model for the cell. Synthetic biologists also want to work below the level of the gene at what is called the codon. A codon codes for one of 20 distinct amino acids that make up proteins. The codon is a set of three rungs on the DNA spiral ladder, each of which can be one of four different letters in the DNA code (C,G,T,A). Because there are 64 different codons that represent only 20

distinct amino acids the synthetic biologist can choose between several codons that express the same amino acid (codon optimisation).

While synthetic biologists are definitely involved in copying all of their information from existing patterns in nature, they are making assumptions about the modular independence of this information and moving it out of its original biological context. This reductionism may miss complex checks and balances that create stability in natural systems. Perhaps it would be better to spend more time reading and faithfully copying the great manuscripts of life before we decide we can scramble all the paragraphs, all the words, and all the letters of all the books at the same time.

Dr Michael Reinsborough holds a PhD in the history of science from Queens University Belfast.

Notes and references

(web links correct as of 1 December 2010)

1. For example, see: Gill V (2010). 'Artificial life' breakthrough announced by scientists. BBC news online, 20 May. <http://www.bbc.co.uk/news/10132762>
2. p.51 of: Langley C (2005). Soldiers in the Laboratory. Scientists for Global Responsibility. <http://www.sgr.org.uk/publications/soldiers-laboratory>
3. DNA produces RNA, which builds proteins. Proteins – made up of amino acids – are the stuff of which life is made.