How can we Engineer Biology and why should we do it ? on 19 May 2017

Dr Tom Ellis said bio-engineering had become a popular subject, particularly in America in recent decades. The discovery of the structure of DNA by Watson & Crick in 1950s was the start of a subject which has led on to the study of the base pairs, pioneered by Sanger in America who decoded a million in 1985. By 1995 advances made a hundred million practicable, and the number keeps rising. A sequence of base pairs can now be manufactured for 1 cent per pair compared with $100 in 1988. One can look up a sequence (many are free on the web) and buy it – it comes in a small plastic tube. Synthetic yeast is available.

DNA can be analysed by applying a voltage to drive it through a nanopore device – the pore taken from a cell. As each base passes it generates a characteristic voltage; this can be done at a million bases per second.

Genes are coded in DNA with four bases: Guanine which pairs with Cytosine; and Adenine pairing with Thymine. A gene is introduced by a promoter section, then the coding sequence and a termination. When a cell divides the coding sequence is transcribed into mRNA which is translated into a protein by a ribosome, ready to be formed into daughter DNA.

Dr Ellis showed how biological engineering can be compared with conventional electronic engineering principles, with circuits, modules, computers and networks replaced by a hierarchy of Proteins, Genes, Cells and Tissues – involving bio-reactions which follow a pathway.

Genes can be added to make a cell do a new function, much as 'apps' can be entered into 'phones. The new function will propagate down subsequent generations. It is possible to change the sequence of genes in a cell - in 2010 J Craig Venter created the "first synthetic cell" though the cell apparatus was still there. He rebuilt an existing genome (with about a thousand bases) but with some differences. Just shuffling the existing chromosomes – hyper speed evolution - can make a difference. About 95% of deliberate differences will stop the cell from working – but 5% don't, and may even enhance its performance.

Dr Ellis is working on **yeast**. There is a worldwide study on "Synthetic Yeast 2.0", with work in Australia, China, Singapore, the USA and the UK. At Imperial College they are working on chromosome 11, of the 16 chromosomes in yeast. This has 670,000 base pairs, out of the 12 million base pairs in a yeast cell.

A switch can be made by inserting a gene that responds to, for instance, lactose to set one state or an antibiotic to set the other. Introducing more such genes (with different chemo-reactants) can give a yeast cell with an adaptive learning function. This can take minutes, and a whole system might need an hour to 'learn' a new trick. Producing a new strain of yeast cells can be done in a day, followed by growth and screening stages within a week. Various genes have been inserted into yeasts: zylose, from wood, not found in natural yeasts; raspberry genes to give flavour; even penicillin can be made by suitably modified yeast. Yeasts can be made to show the presence of a chemical by producing a coloured dye.

Dr Ellis also spoke about similar work being done with bacteria, to make ultra-pure cellulose. In one application of this project the cellulose is used to make water purification filters, for use in parts of the world where water is otherwise undrinkable.

He briefly went on to talk about the **human genome**. It contains a high proportion of 'junk' DNA, which does indeed seem to be junk, although it is conserved in cell division – mysterious; he noted that birds, with weight limitations, have a lower proportion of 'junk' DNA. Modelling biological processes, both natural and experimental, is improving – and sequencing the human genome has been achieved.

Dr Ellis gave us an insight into the engineering discipline of synthetic biology that, since 2000, treats DNA as engineerable code, and has gone from building simple small genetic systems that add memory to bacteria to projects making entirely synthetic organisms and developing new forms of therapies. What could synthetic biology give us? Some developments being worked on are:

- Biofuels and hydrogen to replace petrol and oil, made from sunlight and CO_2
- Cheaper, faster production of anti-malarials and rare or new antibiotics
- Bacteria that enrich soil with natural fertilisers
- Plants that detect explosives from landmines
- Rapid 'printing' of new vaccines
- Microbes or viruses to detect and kill cancers

Ethics obviously come into what is becoming a pervasive tool in science, accessible to school students and citizen scientists as well as those in biotech and universities. There are dangers whether through malice or unintended consequences. Responsible innovation in Synthetic Biology requires its practitioners to ask:

- What is the purpose?
- Why do you want to do it?
- What are you going to gain from it?
- What else is it going to do?
- How do you know you are right?