ISMB News
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The UCL-Birkbeck Synthetic Biology Network: Synbion

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Seven centres across the UK have just been awarded Network grants in Synthetic Biology. The ISMB is now host to one of these Networks that will be run by John Ward (ISMB, Division of Biosciences, UCL) and Irilenia Nobeli (Dept of Crystallography, Birkbeck). We have named our Network Synbion and it comprises researchers across 6 departments at UCL and Birkbeck and also includes 5 other universities in the UK.

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What is Synthetic Biology?

Synthetic Biology is an emerging research area that aims to use the knowledge we now have of the components of biological systems and use these in a defined way to design and build novel artificial biological systems.

Traditional biology has sought to understand existing biological systems. We are now beginning to understand enough of the 'rules' of the construction of these natural systems to be able to design and build simple 'components' that can be used in a standardised manner and combine these to construct novel genetic devices, metabolic pathways, optical or electronic devices. It is built on the ease with which it is now possible to synthesise genes and large DNA fragments and the standardisation of the ways these can be put together in bacteria. In the USA, who are well ahead of the UK and EU in this area, one centre has coined the term 'Biobrick' to describe a registry of standard biological parts that can be ordered and put together to form a device (http://partsregistry.org/Main_Page). This open source approach is the beginning of using an engineering mind set to having components with defined properties that can be used to build complex devices. Just as in the electronics or car industry the final product is just the combination of much simpler individual components.

The involvement of engineers, physical scientists, chemists and biologists can create designed cells, enzymes and biological modules that can be combined in a defined manner. These could be used to make complex metabolic pathways for pharmaceuticals, novel hybrid biosensors or novel routes to biofuels. A future integration of biological devices and hybrid devices as components in the electronic industry might lead to a whole new high value industry for structured biological entities. Synthetic Biology is a fast growing area of research especially in the US and will have a major economic and social impact on the global economy in the coming decades.

Examples of Synthetic Biology

Some of the research in Synthetic Biology looks like what in the past has been termed

pathway engineering and key pioneers in this field such as Jay Keasling, who has constructed engineered microbial pathways for the antimalarial drug artemisinin (Ro et al, 2006), are now described under the banner of Synthetic Biology. The engineering way of looking at such a system would be to take it one stage further and have the genes in such a pathway constructed in blocks bounded by, for example, by restriction sites such that one can easily add to or replace individual genes or larger segments and build pathways de novo from parts with known or predictable properties. Examples from our recent work are a shown in Figures 1 and 2 where we have used 3 different cytochrome P450's and combined these with different ferredoxin reductases to assess their activity in whole cell biocatalysis. Different restriction sites were used at the boundaries of the segments so we could 'mix and match' the genes. We were able to test 3 CytP450s each with 3 different ferredoxin reductases and then assemble the best performing combinations into short operons.

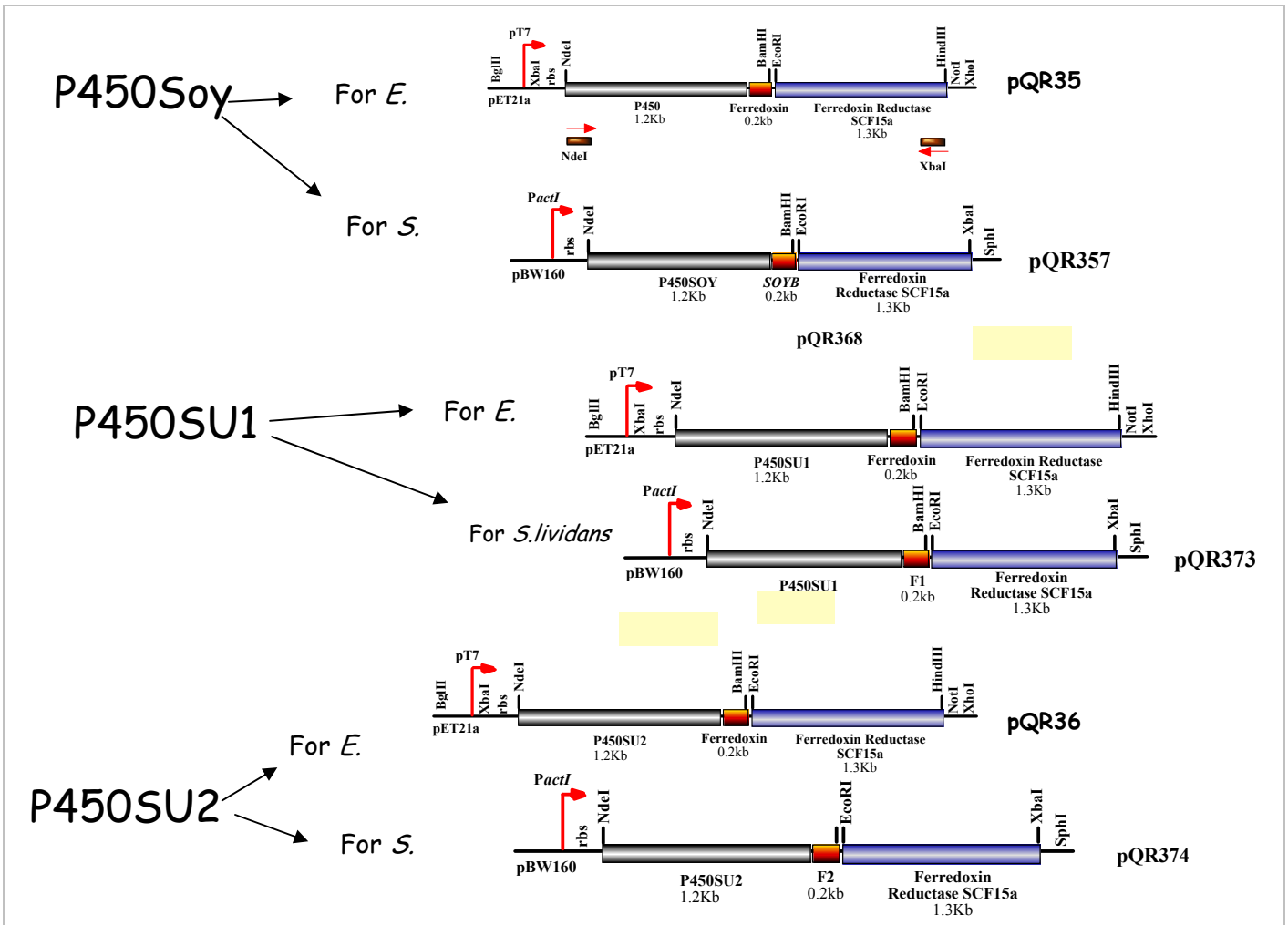

Figure 1

Figure 1 shows the best combinations and this is taken one step further by taking the operons and placing in vectors for expression in the filamentous soil bacterium Streptomyces lividans. We have designed de novo pathways using the enzymes transketolase, TK, and transaminase, TAm, (Ingram et al, 2006) and Figure 2 shows the

compounds made with E. coli wild type TK and a TAm from Chromobacterium violaceum. Figure 2 shows a hypothetical set of compounds that could be made with modified TKs and TAms that can give defined chiral products and by combining each of these in the correct combination with CytP450s, complex chiral products can be formed.

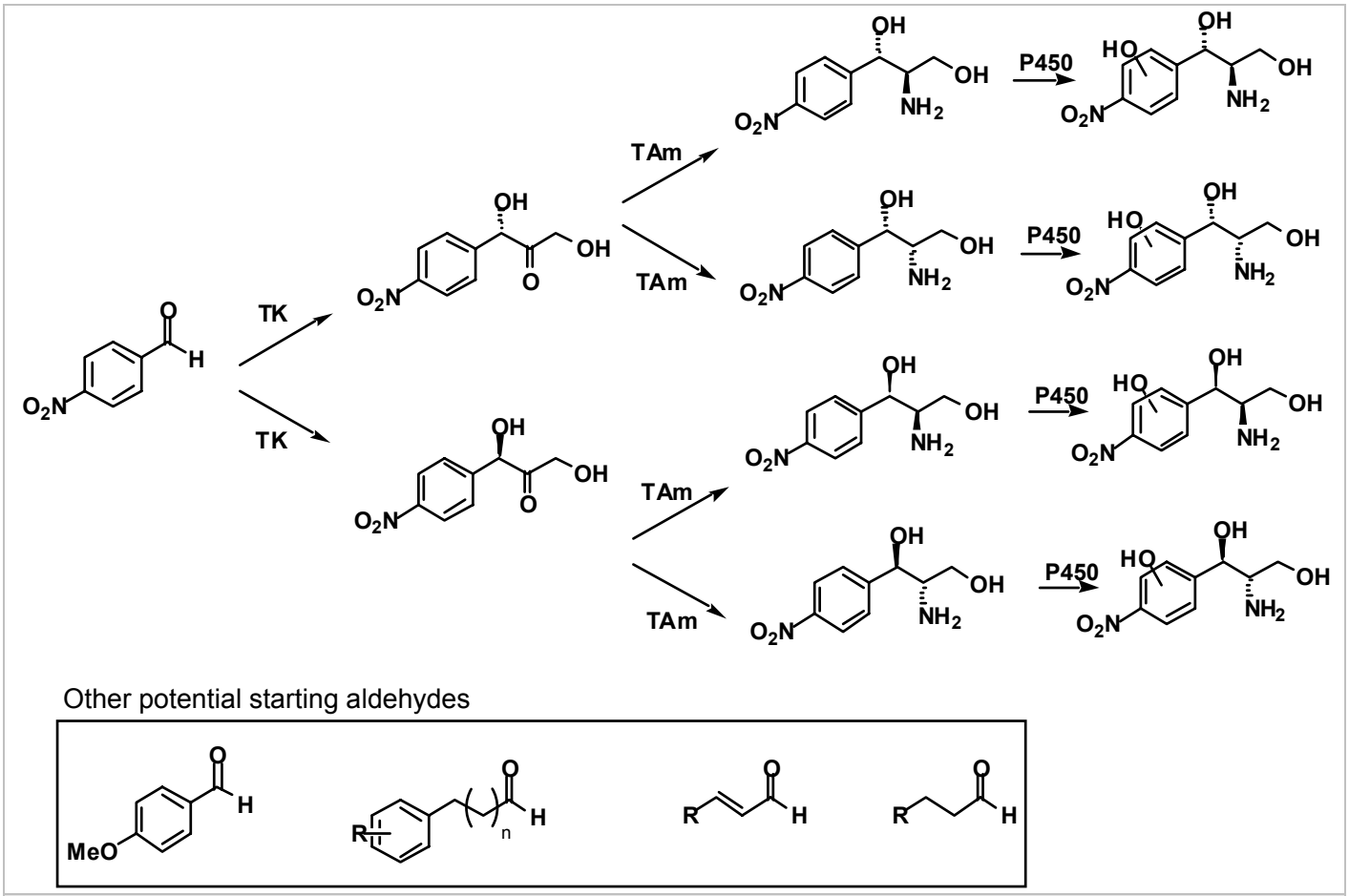

Figure 2

Synbion

The aim of the Synbion Network will be to explore the full range of what biologically designed elements (e.g. proteins) could achieve in the fields of electronics, optics, opto-electronics and magnetics and combinations of these fields. These could be designed as active modules that can then be combined on a framework to assemble the modules. One of the frameworks we see as being important in building novel devices are phages, particularly filamentous phages.

The E. coli filamentous phage (M13, Ff and fd) have a length to width ratio of 138:1 (6.5nm:900nm) - see figure 3a and b, and are like filamentous hair-like macromolecules (Fig 3c). By removing parts of the genome, smaller lengths can be made and some naturally occurring mutants (that cant replicate on their own) are known which are called 'microphage' and are 500 Å by 65 Å = 7.7:1. These phages have coat proteins, Fig 3d, into which fusions can be made such that proteins are displayed on the surface. It is with these type of coat protein fusions that the 'active modules' could be displayed and assembled. Like having an 'enzyme on a stick'.

Other self assembling structures could be used and devices could be designed and

constructed that could carry current, absorb or transmit light or convert one type of energy to another.

Networks don't carry out bench research, but bring together researchers in disparate fields to discuss and design the devices. Over the three years the Network members will be challenged to discuss not only the design of novel bio-electronic and bio-optical devices and also to consider how to best manufacture and scale-up such devices. The initial network has biologists (molecular biologists, microbiologists, biophysicists and bioinformaticians), social scientists, physicists, chemists, chemical and biochemical engineers. The ability to design and construct novel genetic entities leads to issues of ethical, social and legal challenges which we are addressing at UCL with members of the Science and Technology Studies department.

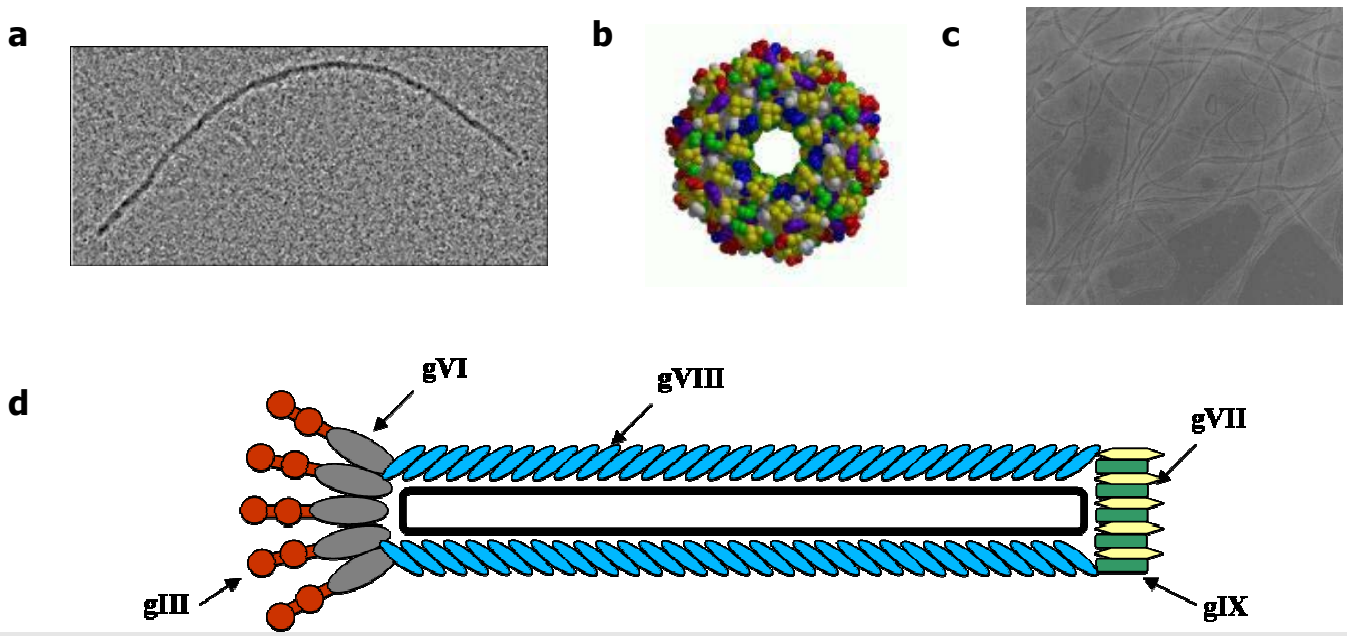

Figure 3

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