Brewing-up the technologies of tomorrow with synthetic biology

Dr Tom Ellis

Centre for Synthetic Biology and Innovation
Department of Bioengineering
Imperial College London
Sedimentation of yeast by flocculation genes

Because flocculation is unpredictable, brewers use isinglass or mechanical purification using huge centrifuges and big filters.
Design & build a DNA-coded timer from parts

**PARTS:**
GENES and GENETIC SWITCHES

**SOURCE DNA:**
BACTERIA, PLANTS, JELLYFISH
Timer ‘networks’ that can be tuned predictably

3 promoter ‘nodes’, 20 promoters per library = 8000 possible networks

Predictable custom gene networks with diverse reset times
Timer networks control yeast sedimentation

Modular timer networks ‘wired in’ to control flocculation rather than GFP
Synthetic Biology

Synthetic biology is the **engineering** of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature.

*Source: High-level Expert Group European Commission*
Engineering Biology
Synthetic biology is ‘hacking’ the code books for life: DNA genomes
There's almost a limitless amount of DNA to play with

- Biology is now an *information science* based on DNA code
- Custom DNA sequence can be ordered to be written chemically

Feb 2012: 137,384,889,783 bp
Re-wiring microbiology for new applications

Synthetic Biology

The Cell

Microbes respond and make decisions using networks of interacting genes
Example synthetic biology **Apps**

Adaptive Learning Networks:  *e.g.*  associated memory

Intelligent Biosensors:  *e.g.*  navigating bacteria

Next-generation synthetic gene networks
Timothy K Lu, Ahmad S Khalil & James J Collins
Nature Biotechnology 27, 1139 - 1150 (2009)
Rewriting whole Operating Systems

2010: J. Craig Venter Institute

Complete synthesis of a 1 million base pair bacterial genome from electronic code
Sc2.0 – A Human-made Yeast Genome

Project = Synthetic Yeast 2.0       http://biostudio.bme.jhu.edu/sc2/

A major international project now in 4 countries: USA, China, UK and India

Complete synthesis and assembly of a modified synthetic yeast genome of 11 million base pairs
Swapping natural DNA sequence for synthetic in yeast

Reiterative Recombination Method

Requires two selectable markers

Makes use of yeast’s ability to recombine matching sequences

SERIAL process
Sc2.0 – A global project

Dec 2012 status
MADE  INT
20%    0%
48%    8%
100%   100%
0%     0%
90%    8%
100%   70%
0%     0%
20%    0%
100%   95%
0%     0%
13%    0%
75%    22%
0%     0%
0%     0%
0%     0%
Synthetic Yeast to Brew beyond beer

Penicillin Biosynthesis encoded into synthetic yeast chromosomes
Amazing Apps have been built by students

Following an abstraction similar to electronic engineering
2005 – Students at a summer school
iGEM is a synthetic biology competition
iGEM uses BioBricks – modular DNA parts

Registry of Standard Parts

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Promoter Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>B0034</td>
<td>lac cassette right promoter</td>
<td>tggattgtgggaattctgaggtgata</td>
</tr>
<tr>
<td>B0035</td>
<td>lac promoter</td>
<td>gggttgtgggaattctgaggtgata</td>
</tr>
<tr>
<td>B0036</td>
<td>Modified lambda P11M promoter (expressed by 434 cpo)</td>
<td>aacaacctttaattttgagtttctg</td>
</tr>
<tr>
<td>B0037</td>
<td>Modified lambda P11M promoter (cooperative repression by 434 cpo)</td>
<td>ttttcttcttattttgagtttctg</td>
</tr>
<tr>
<td>B0038</td>
<td>Modified lambda P11M promoter</td>
<td>ttttcttcttattttgagtttctg</td>
</tr>
</tbody>
</table>

Standard Modular Assembly

Open source distributed parts kit
Project AuxIn aims to help fight desertification by promoting plant root growth using engineered bacteria. Re-vegetation is one of the most effective ways to prevent soil erosion. The project consists of three modules – Phyto-Route, Auxin Xpress, and Gene Guard. (Click to learn more)
Parasight

Welcome to the Imperial College London iGEM 2010 project! It’s been a busy four months, and there have been highs and lows, but we’re happy with how things have turned out. Here’s a brief introduction...

“More than two billion people around the world live with unrelenting illness due to parasites” - WHO Director General Lee Jong-won.

Synthetic biology offers great opportunity for biosensors, however current designs require hours of waiting before a detectable output is produced. To tackle this issue in the field, it is crucial that a new generation of biosensors be designed that can respond in minutes. With this in mind, we have engineered a fast, modular sensor framework which allows for quick detection of a range of different parasites, and may also be used as an environmental tool for mapping their spread. In particular we have designed and modified B. subtilis to give a clearly visible color readout upon detecting the waterborne Schistosoma parasite which affects 200 million people worldwide.

You can take a look at our cellular overview below. Follow the link below to take a quick tour of the wiki. The links on the right lead to elements we feel are interesting additions to the core project. Or just head for the main menu above if you know what you’re looking for.

Click here to take the tour...

Welcome to a very basic model of our cell. The main features are the **cell wall**, the **cytoplasm**, a **two component signaling** system, and our **sinecistatins**.
E. Chromi

The Cambridge 2009 iGEM team has created two kits of parts that will facilitate the design and construction of biosensors in the future.

Previous iGEM teams have focused on genetically engineering bacterial biosensors by enabling bacteria to respond to novel inputs, especially biologically significant compounds. There is an unmistakable need to also develop devices that can 1) manipulate input by changing the behaviour of the response of the input-sensitive promoter, and that can 2) report a response using clear, user-friendly outputs. The most popular output is the expression of a fluorescent protein, detectable using fluorescence microscopy. But, what if we could simply see the output with our own eyes?

We successfully characterised a set of transcriptional systems for calibrated output - Sensitivity Tuners. We also successfully expressed a spectrum of pigments in E. coli, designing a set of Colour Generators.
What could synthetic biology give us?

With James King and Daisy Ginsberg
What could synthetic biology give us?

With Nicola Morgan (RCA Fashion)
What could synthetic biology give us?

• 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
What could synthetic biology give us?

• Cell-based computers and hard-drives
• Buildings that grow and change
• Yoghurt that makes your farts smell like mint
• Microbes to colonise Mars

• Targeted bio-weapons such as personalised viruses or crop-spoiling pests
Is this safe?
Bringing together disciplines

Synthetic Biology

High School iGEM

iGEM HS runs from August to May, with finals in June. Allows leaders to work with students schedules and allow school students to experience synthetic biology.
Mini-iGEM and Work-Experience iGEM

Two weeks to:
• brainstorm and develop a project idea
• write-up a description of the project
• consider the implications of it
• code a simulation of how it works
• present the project to the class
Further Information

Synthetic Biology at Imperial College London
http://www3.imperial.ac.uk/syntheticbiology

The Ellis Lab
http://openwetware.org/wiki/Ellis_Lab

Synthetic Biology: A Primer Textbook
http://www.amazon.co.uk/Synthetic-Biology-Paul-S-Freemont/dp/1848168632
Further Information

The iGEM competition and Schools iGEM
http://igem.org/Main_Page

The BioBricks Parts Registry
http://partsregistry.org/Main_Page

The BioBricks Foundation
http://biobricks.org/

The Woodrow Wilson Project: synthetic biology 101
http://www.synbioproject.org/topics/synbio101/
Further Information

Short excellent video describing synthetic biology
http://www.youtube.com/watch?v=rD5uNAMbDaQ

David Shukman visits Imperial’s Synthetic Biology Centre

BBC News article by David Shukman

Horizon 1 hour special on Synthetic Biology with Adam Rutherford
http://www.bbc.co.uk/programmes/b01b45zh