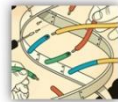


Brewing-up the technologies of tomorrow with synthetic biology

Imperial College
London



Ellis Lab

CSYNBI
Centre for **S**ynthetic **B**iology and Innovation

 **BBSRC**
bioscience for the future

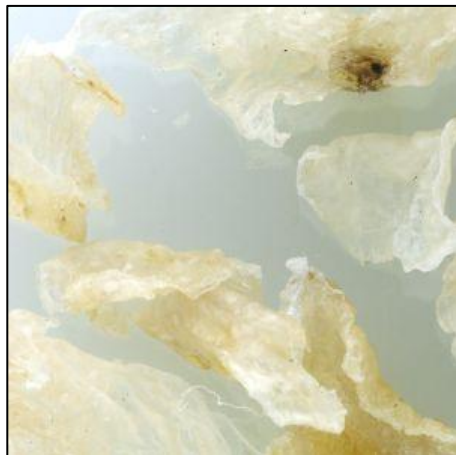
Dr Tom Ellis

EPSRC

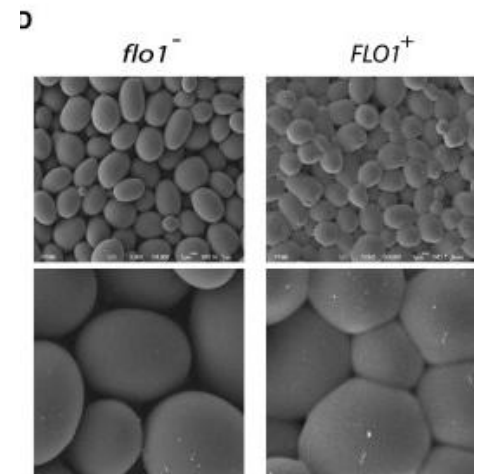
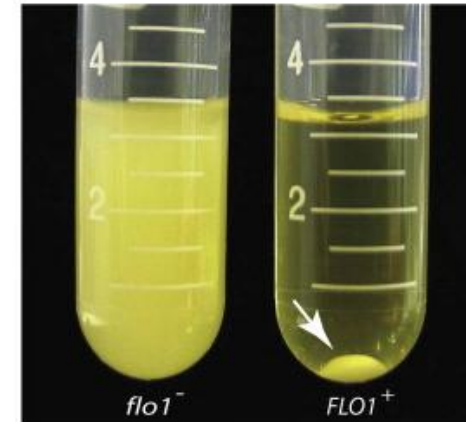
Centre for Synthetic Biology and Innovation
Department of Bioengineering
Imperial College London



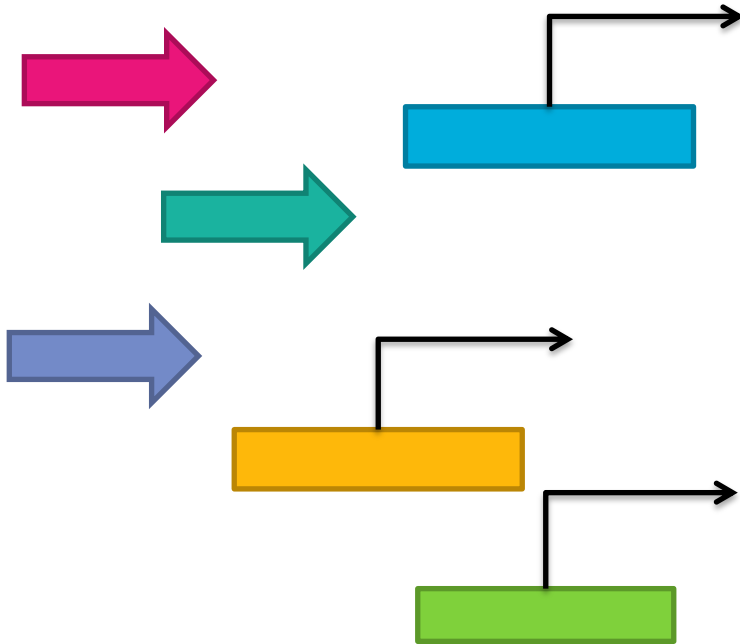
Sedimentation of yeast by flocculation genes



Because flocculation is unpredictable, brewers use *isinglass* or mechanical purification using huge centrifuges and big filters

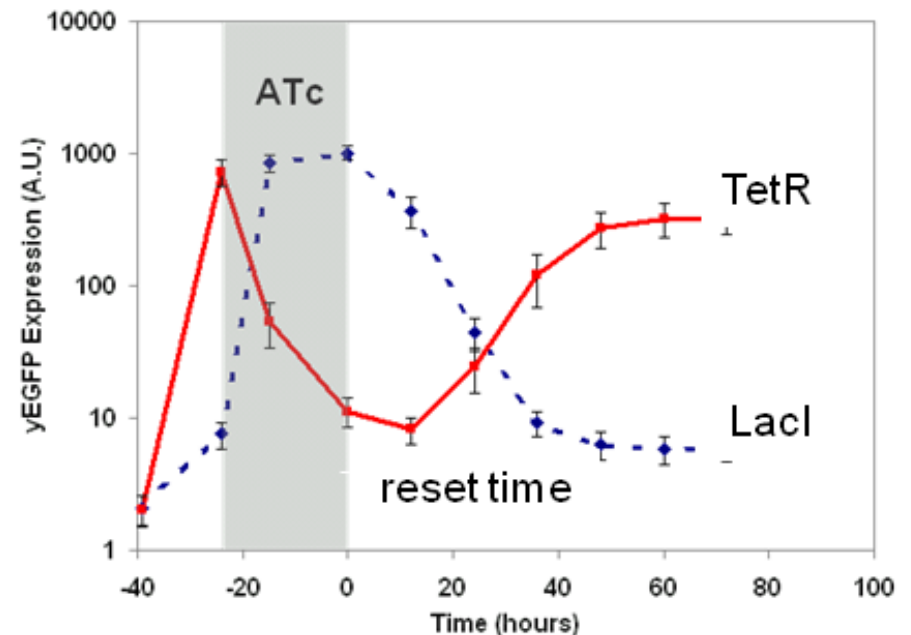
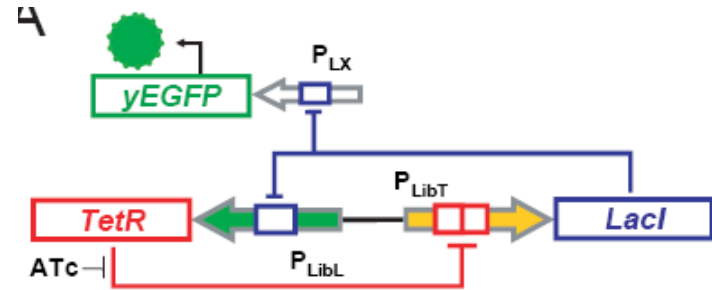


Design & build a DNA-coded timer from parts

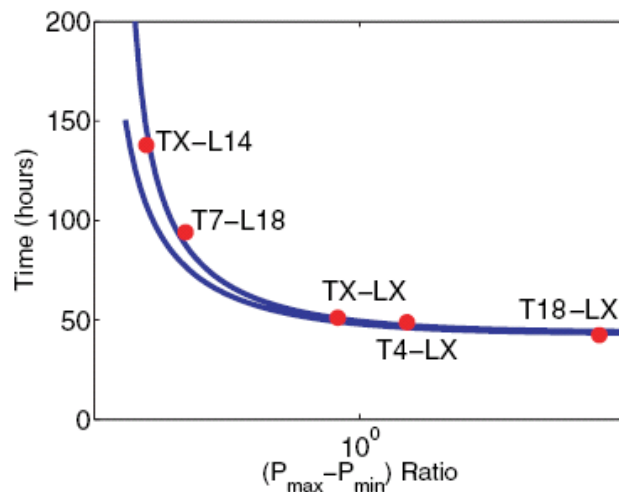
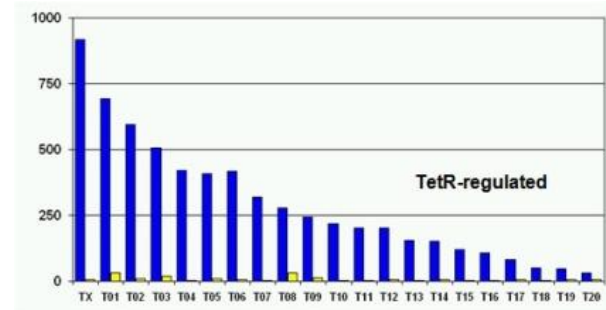
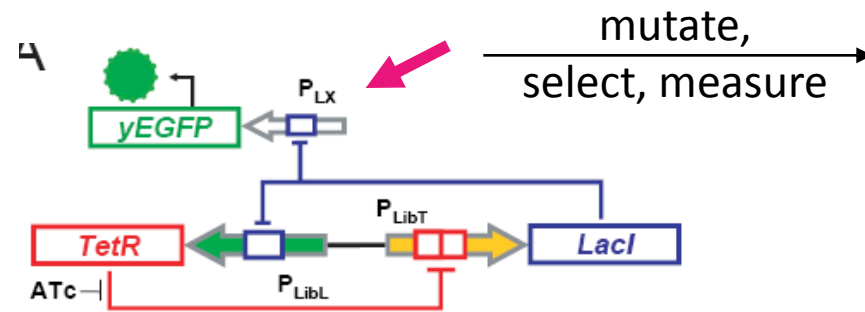


PARTS:
GENES and GENETIC SWITCHES

SOURCE DNA:
BACTERIA, PLANTS, JELLYFISH



Timer 'networks' that can be tuned predictably



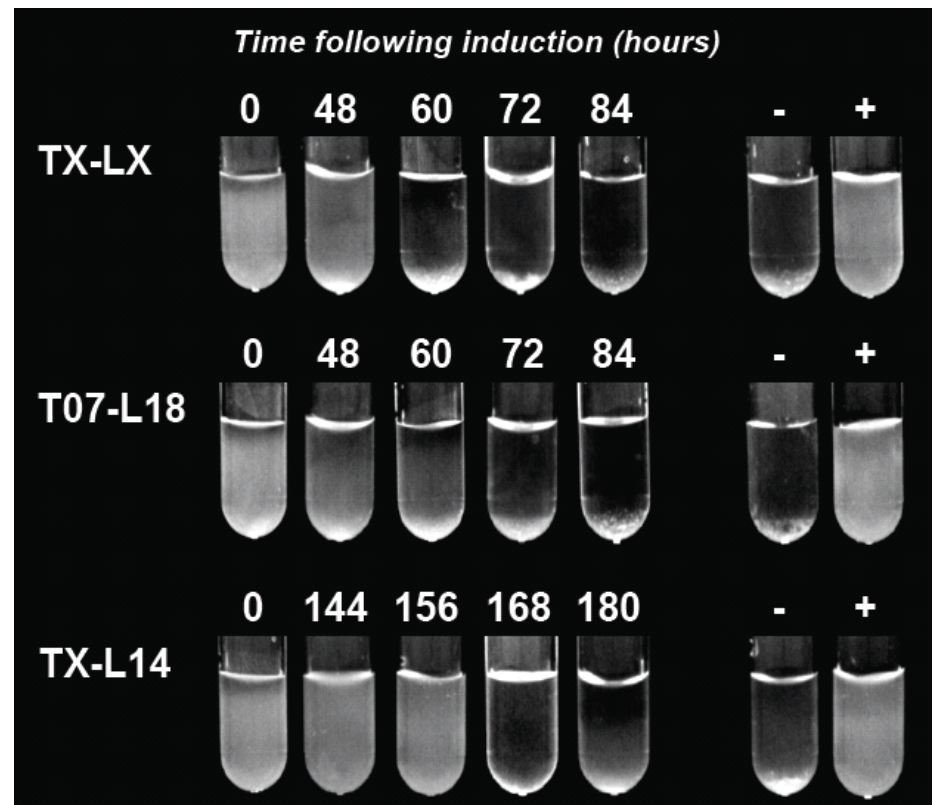
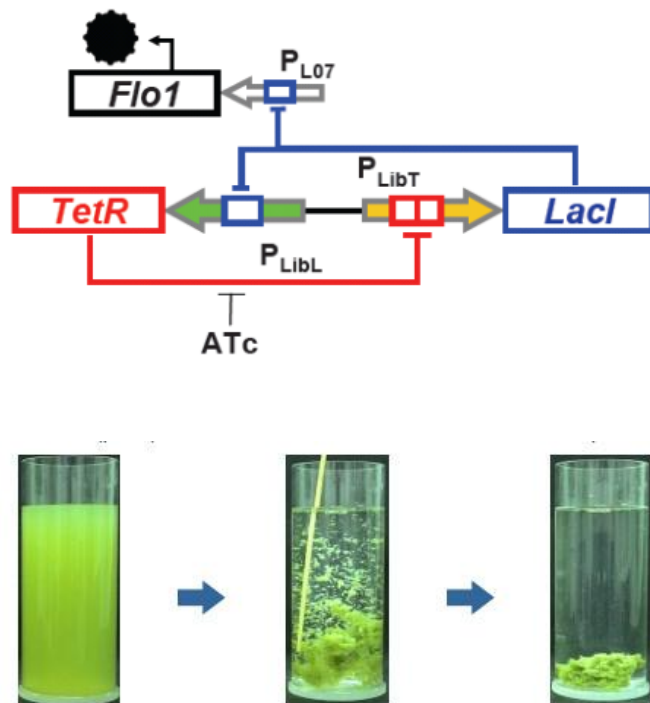
input data
predictive model

Promoter	Max Output	error	Min Output	error
LX	717.38	21.06	13.06	0.77
L01	399.90	25.02	11.11	0.60
L02	372.59	16.87	9.71	0.11
L03	292.11	11.60	83.05	1.09
L04	282.01	13.61	50.55	1.92
L05	246.73	6.42	151.75	2.77
L06	228.45	15.37	23.79	0.31
L07	139.99	8.43	5.40	0.35
L08	141.86	6.23	7.67	0.35
L09	134.04	9.73	23.54	1.55
L10	129.13	8.04	4.96	0.30
L11	108.27	4.18	5.74	0.45
L12	107.35	4.73	5.07	0.36
L13	103.58	9.54	4.37	0.29
L14	82.32	1.50	4.15	0.23
L15	70.91	4.42	20.83	0.96
L16	72.03	3.05	4.28	0.23
L17	56.97	1.77	5.15	0.36
L18	47.16	1.33	3.91	0.28
L19	44.10	2.25	4.25	0.20
L20	37.08	2.12	9.41	0.69

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

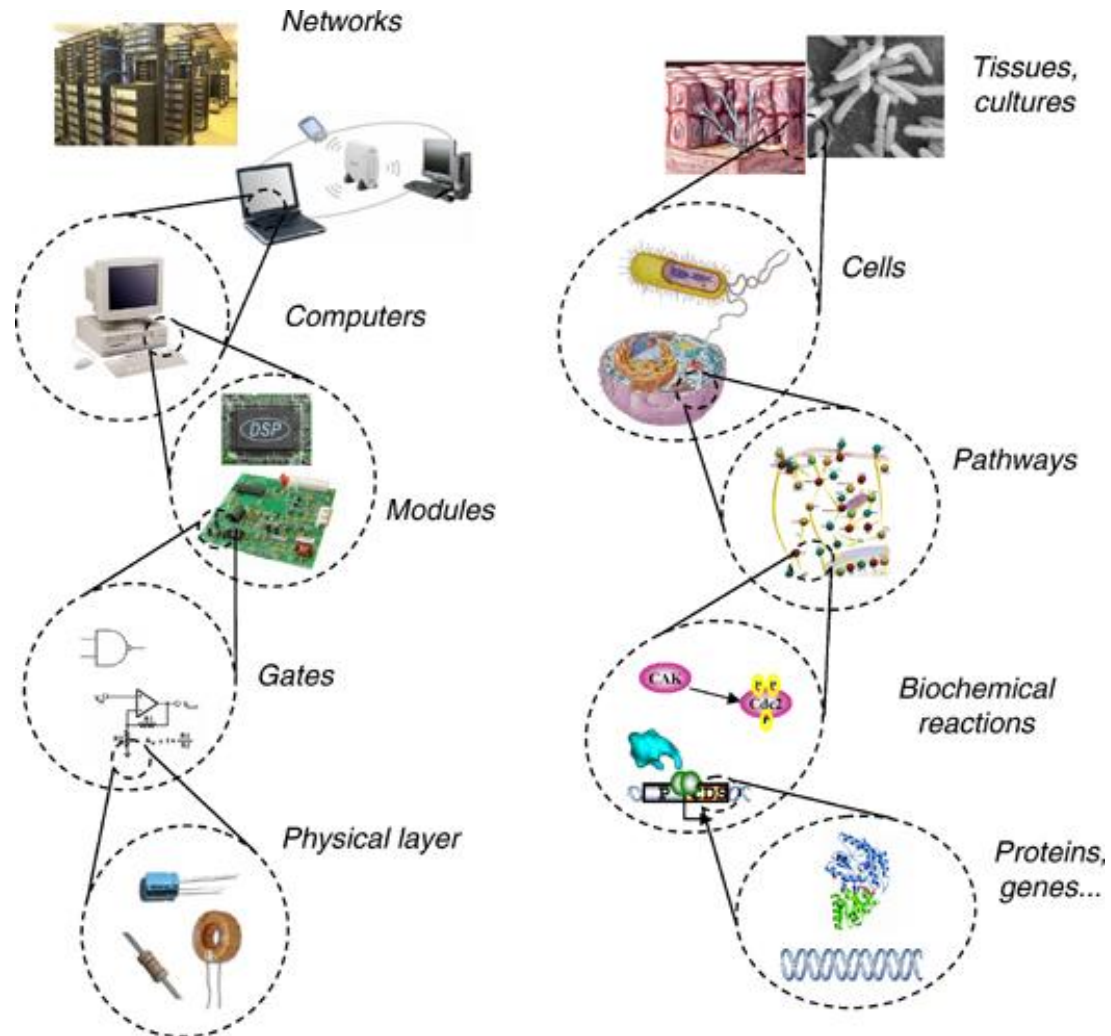


Synthetic Biology

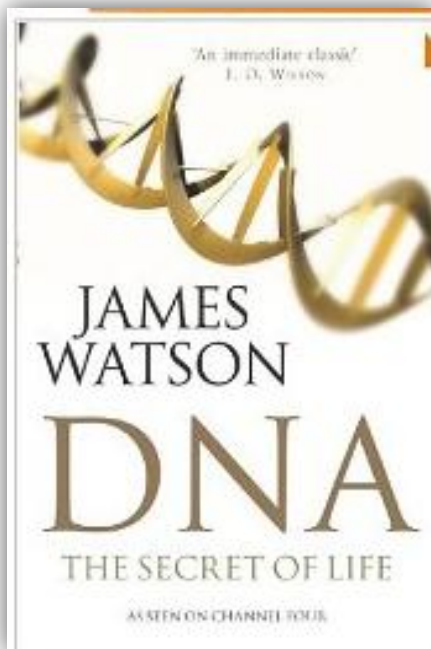
Synthetic biology is the **engineering** of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature.

Source: High-level Expert Group European Commission

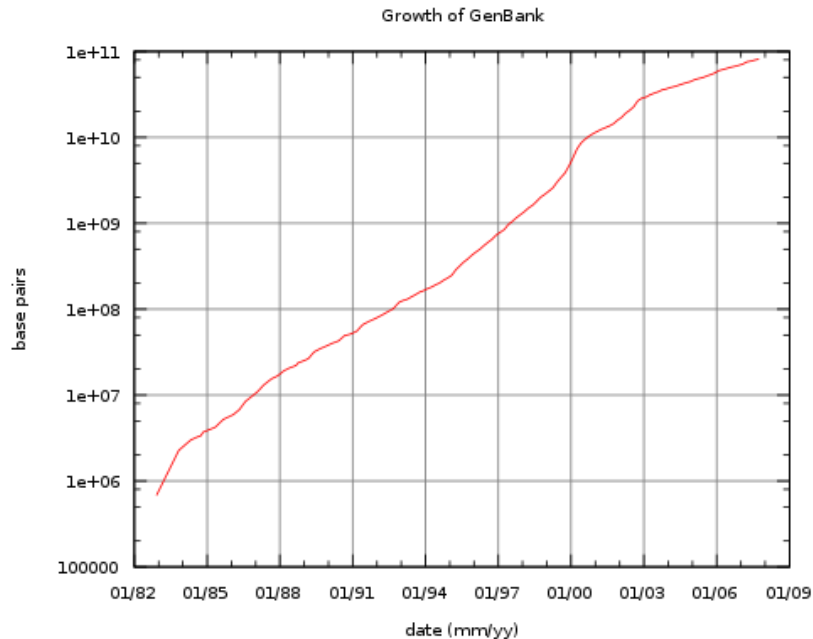
Engineering Biology



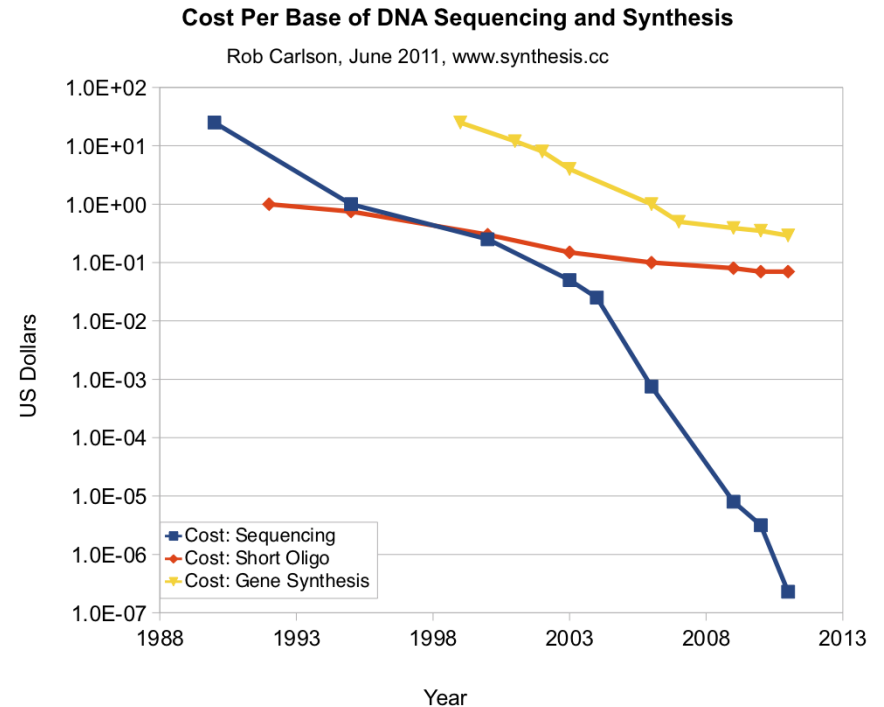
Synthetic biology is 'hacking' the code books for life: DNA genomes



There's almost a limitless amount of DNA to play with

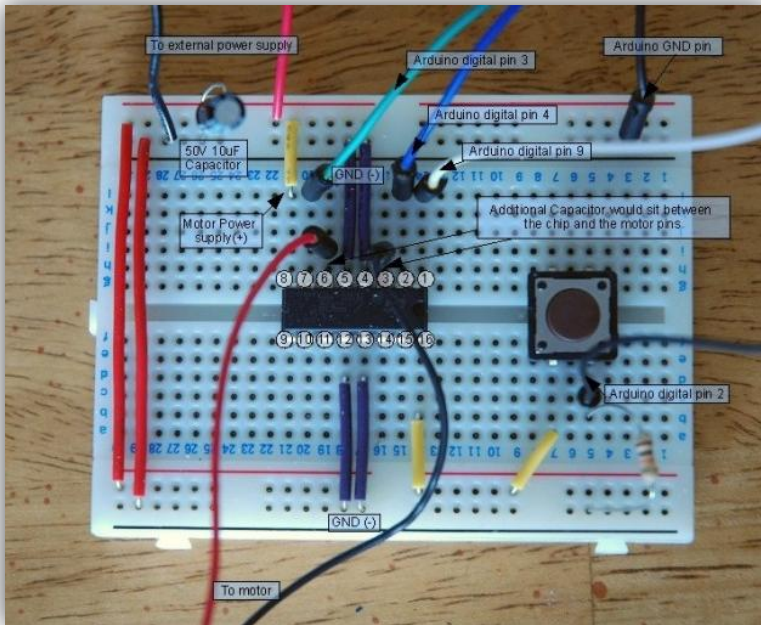


Feb 2012: 137,384,889,783 bp



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

Re-wiring microbiology for new applications



Synthetic Biology

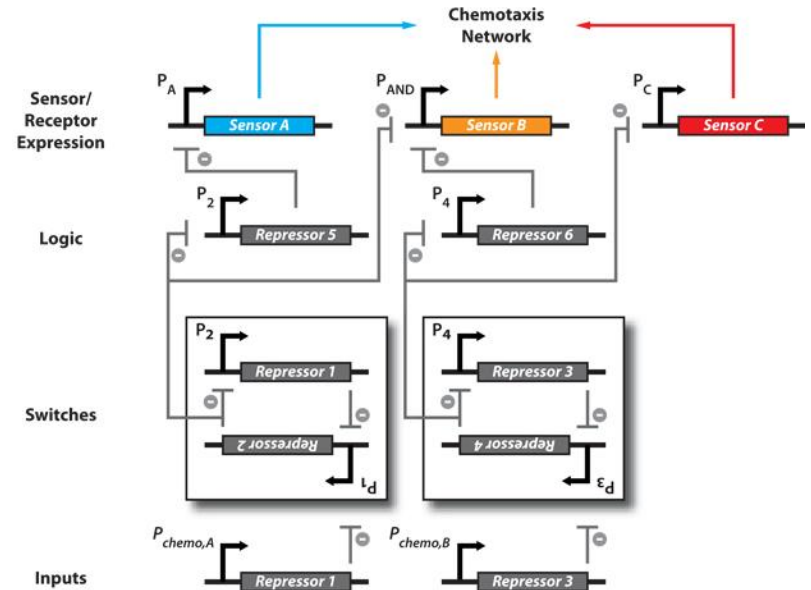
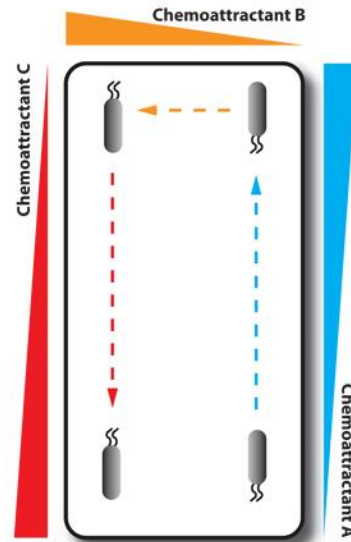
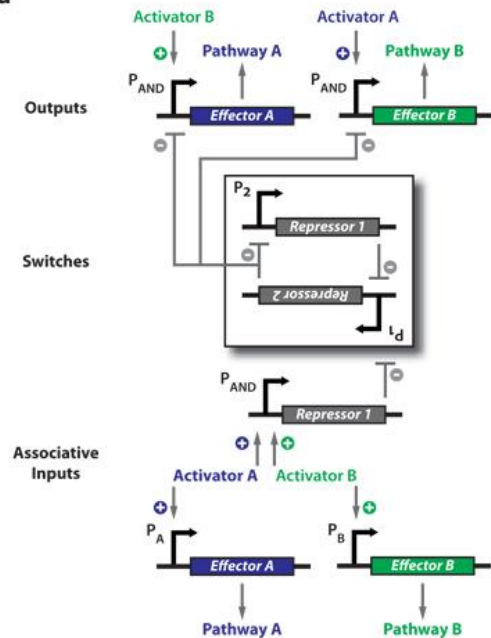


The Cell

Microbes respond and make decisions using networks of interacting genes

Example synthetic biology Apps

a



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

Intelligent Biosensors: *e.g.* navigating bacteria

Genes	Repressor 1	0	0	1	1
	Repressor 2	1	1	0	0
	Effector A	0	1	1	1
	Effector B	0	0	1	1
Proteins	Activator A	0	1	1	1
	Activator B	0	0	1	0
	Effector A	0	1	1	1
	Effector B	0	0	1	1

Activator

Diagram illustrating the activation of the network. Activator A and Activator B are shown as inputs to the network. Activator A is represented by a blue arrow pointing to the network, and Activator B is represented by a green arrow pointing to the network. The network is shown as a box with multiple layers of regulation.

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

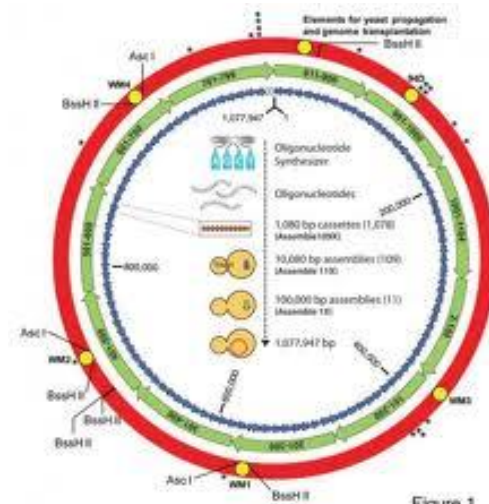


Figure 1

Sc2.0 – A Human-made Yeast Genome

Project = Synthetic Yeast 2.0

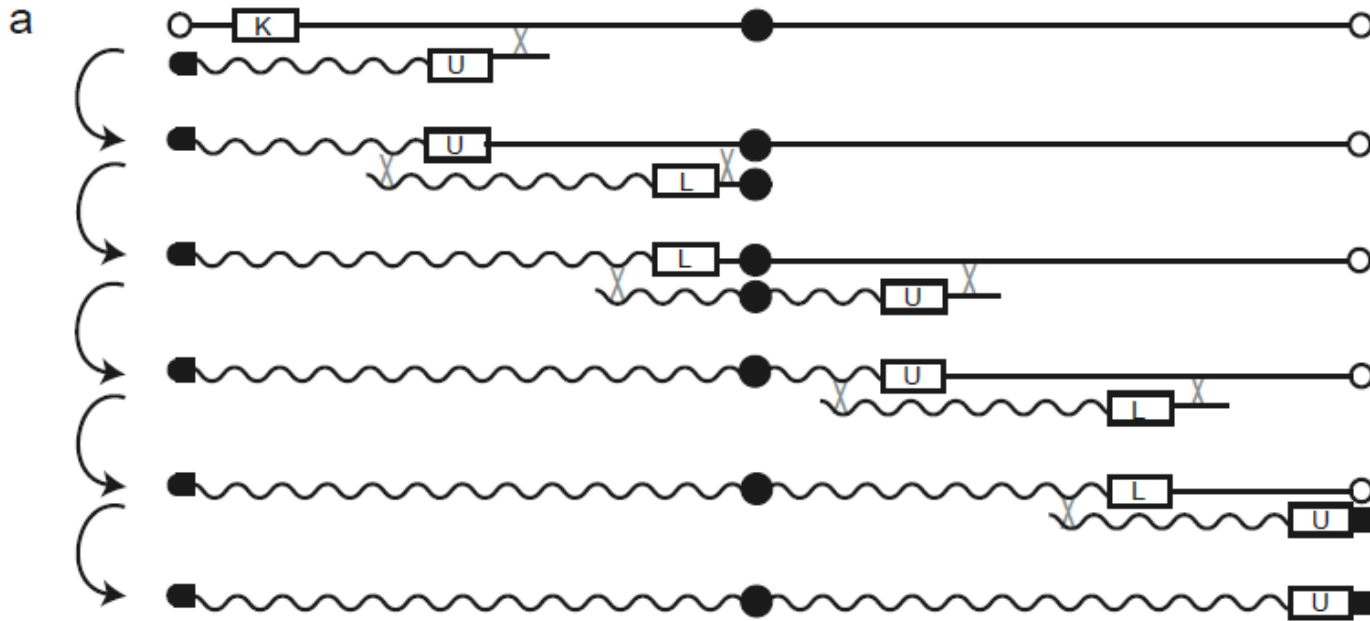
<http://biostudio.bme.jhu.edu/sc2/>

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

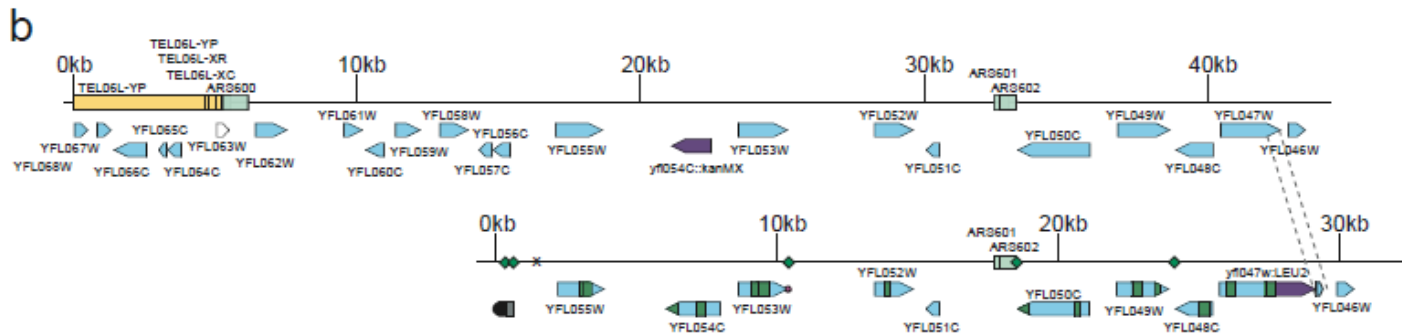
Swapping natural DNA sequence for synthetic in yeast



Reiterative
Recombination
Method

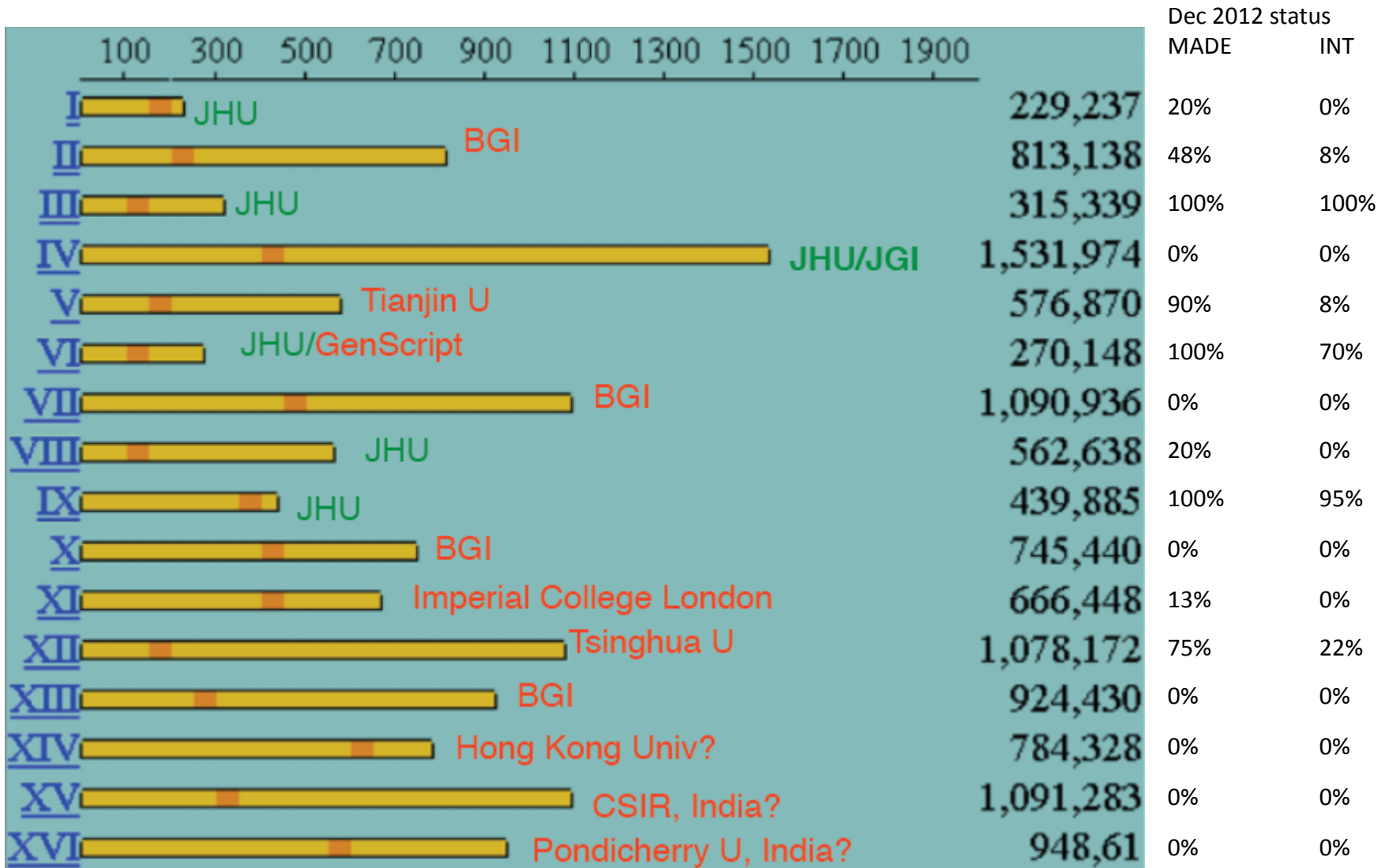
Requires two
selectable
markers

Makes use of
yeast's ability to
recombine
matching
sequences

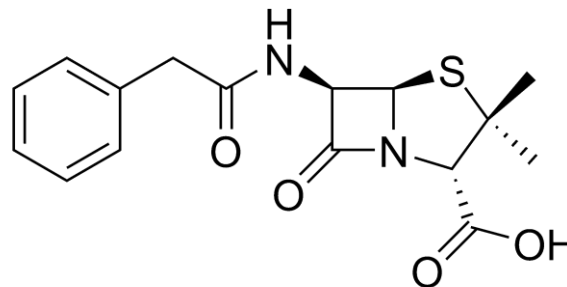
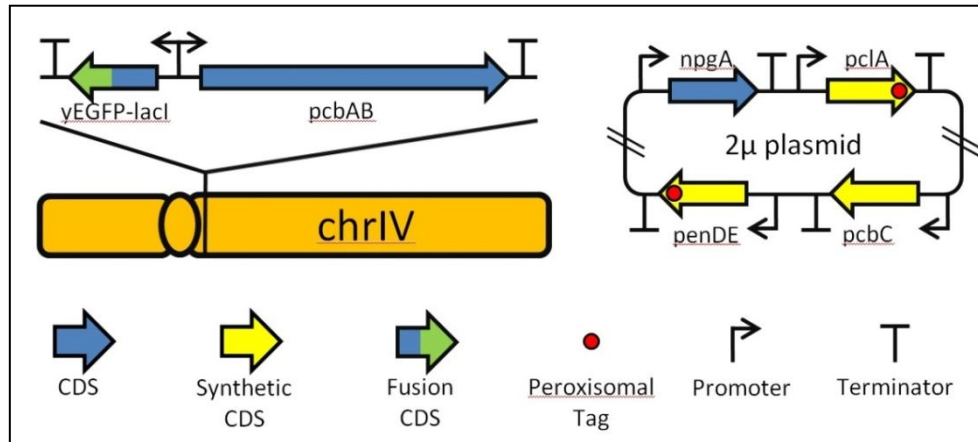


SERIAL process

Sc2.0 – A global project

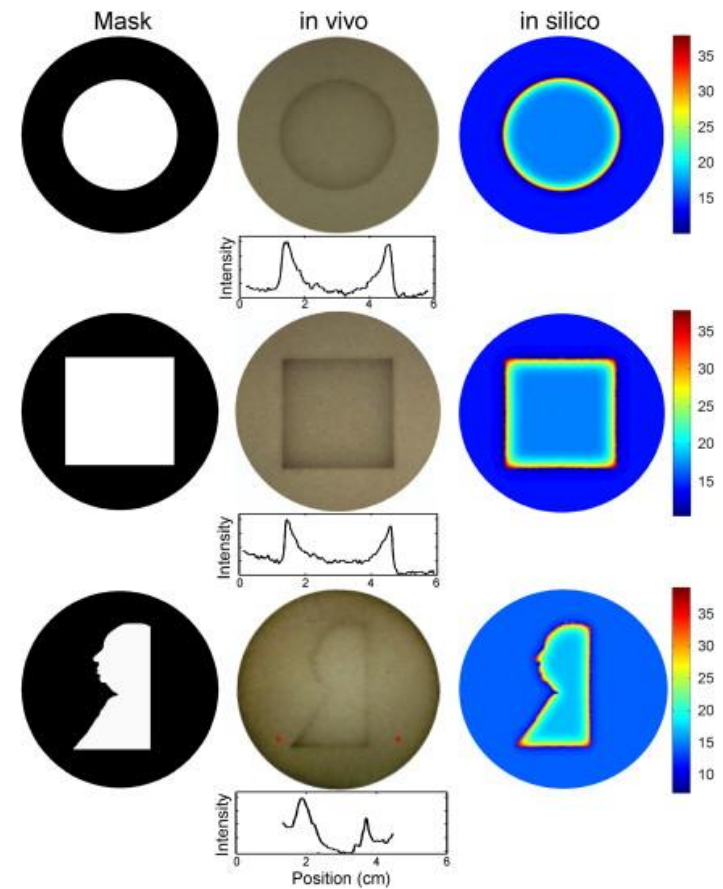
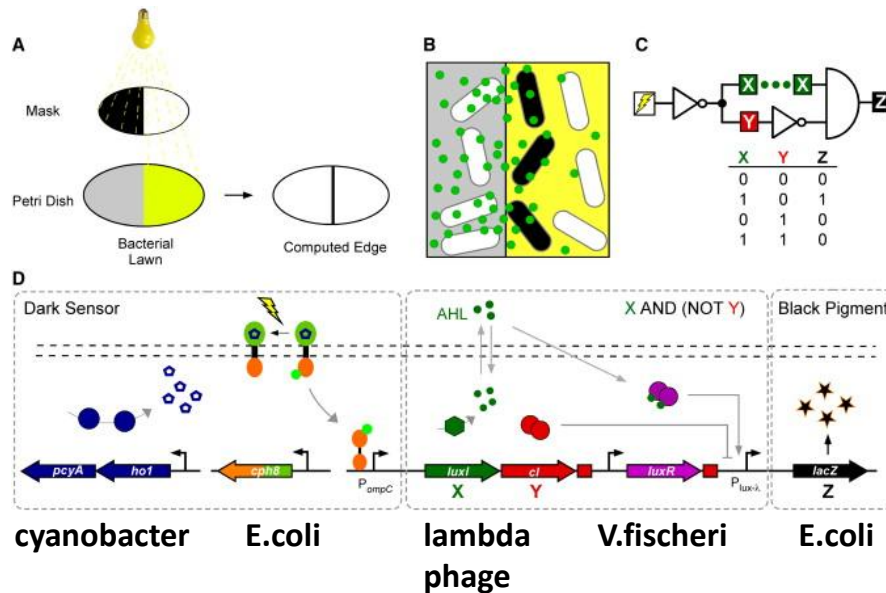


Synthetic Yeast to Brew beyond beer



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

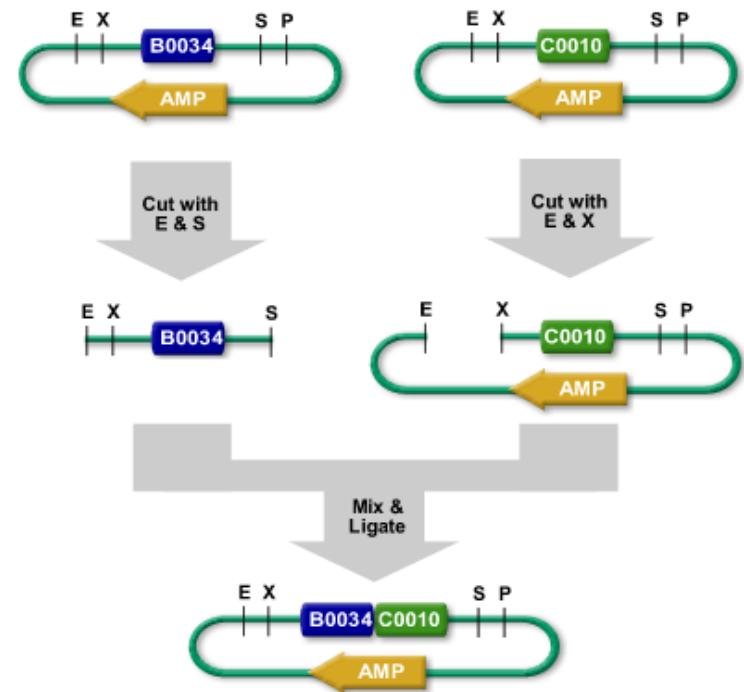


iGEM uses BioBricks – modular DNA parts

Registry of Standard Parts

-?-	Name	Description	Promoter Sequence	
A	BBa_I1051	Lux cassette right promoter	...tggtatagtcgaatacctcggcggtgata	1
A	BBa_I12001	Promoter (PRM+)	...gatttaacgtatcagcacaaaaaagaacc	
A	BBa_I12006	Modified lamdba Prm promoter (repressed by 434 cl)	...attacaaactttctgtatagatttaacgt	1
A	BBa_I12036	Modified lamdba Prm promoter (cooperative repression by 434 cl)	...ttctgtatagattacaatgtatctgt	1
A	BBa_I12040	Modified lambda P(RM) promoter: -10 region from P(L) and cooperatively repressed by 434 cl	...ttctgtatagattacaatgtatctgt	1
A	BBa_I12212	TetR - TetR-4C heterodimer promoter (negative)	...actctgtaagatagagtggtacacaaaa	
A	BBa_I14015	P(Las) TetO	...tttggtacactcctcctcagtgatagaga	1
A	BBa_I14016	P(Las) CIO	...cttttggtacactcctcggcggtgata	1
A	BBa_I14032	promoter P(Lac) IQ	...aaacctttcggtatgcatgacatagcgcc	
A	BBa_I714889	OR21 of PR and PRM	...tatttacctctggtgataatggttgc	
A	BBa_I714924	RecA_DlexO_DLacO1	...actctggcatgacgagctgacaaagtaa	
B ?	BBa_I715003	hybrid pLac with UV5 mutation	...ttgtagcggtataacaatattgtgacaca	
A	BBa_I718018	dapAp promoter	...cattgagacactgtttgcacagaggatgg	
A	BBa_I731004	FecA promoter	...ttctgttcgactatagctgaacacaaca	2
A	BBa_I732200	NOT Gate Promoter Family Member (D001O1w1)	...gaattgtgagcggtataacaattggatccgg	
A	BBa_I732201	NOT Gate Promoter Family Member (D001O11)	...ggaattgtgagcgctcaaatggatccgg	
A	BBa_I732202	NOT Gate Promoter Family Member (D001O22)	...ggaattgtgagcgcttacaattggatccgg	
A	BBa_I732203	NOT Gate Promoter Family Member (D001O33)	...ggaattgtgaaacgtttacaattggatccgg	

Standard Modular Assembly



Open source
distributed parts kit



Auxin

Imperial College
London

Project AuxIn

Achievements

Human Practice

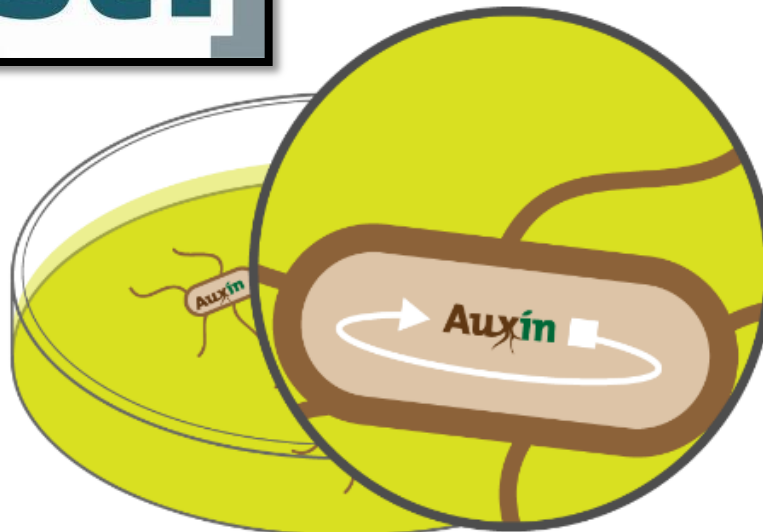
Extras

Team

If you cannot view the photo gallery below, please click [here](#) to view our alternative home page or download the Adobe Flash Player [here](#).

PHOTO GALLERY

dstl



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)

©copyright Flash Slideshow by Flash-Gallery.com

AT A GLANCE

MAIN RESULTS

DATA

Follow us on



The Radio_iGEM Show



The Radio_iGEM Show

[Jamboree Part 3 - The Results](#)



INFO



FANS



TRACKS



CHAT



EPISODES

Project

Plan

Results

Extras

Parasight | Parasite detection with a rapid response

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-wook.

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 colour readout upon detecting the waterborne *Schistosoma* parasite which affects 200 million people worldwide.

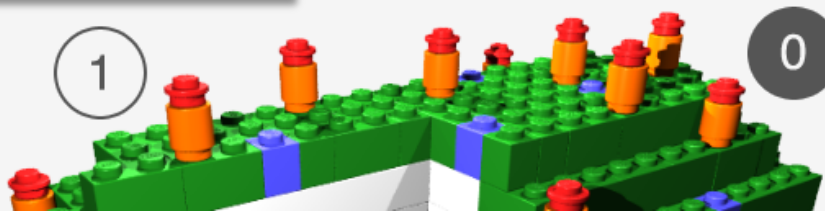
You can take a look at our cellular overview below. Follow the link below to take a quick tour of the wiki. The links on the right lead to elements we feel are interesting additions to the core project. Or just head for the main menu above if you know what you're looking for.

Extra Links



[Click here to take the tour...](#)

BILL & MELINDA
GATES foundation



Welcome to a very basic model of our cell. The main features are the cell wall, the cytoplasm, a two component signaling



Categories :

Home

Team

Sponsors

Parts Submitted to Registry

Image Gallery

Leave a Message!

Project :

Overview

Sensitivity Tuner

--- Characterisation

--- Modelling

Colour Generators

--- Carotenoids (Orange/Red)

--- Melanin (Brown)

--- Violacein (Purple/Green)

The Future

Safety

Notebook :

Week 1

Week 2

Week 3

Week 4

Week 5

Week 6

Week 7

Week 8

Week 9

Week 10

Team Logistics :

Protocols

Stock List

Research

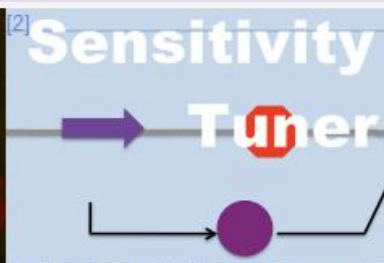
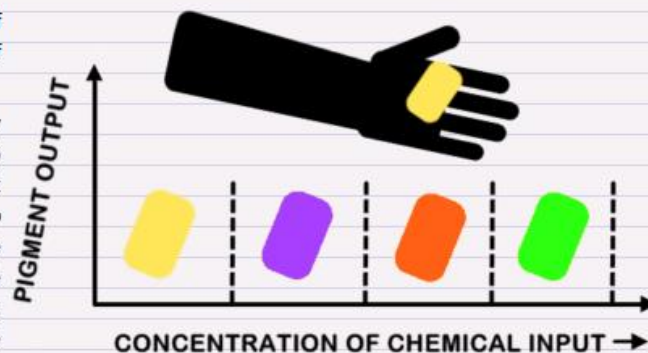
Shared Links and Help

E. Chromi

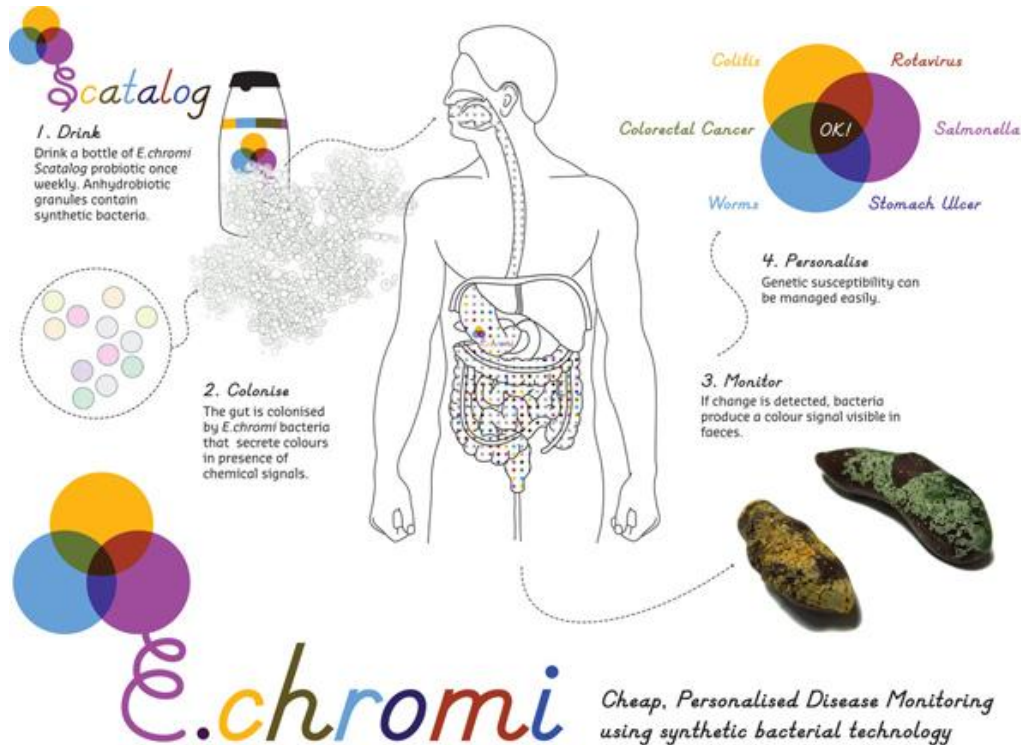
The Cambridge 2009 iGEM team has created two kits of parts that will facilitate the design and construction of biosensors in the the future.

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](#).

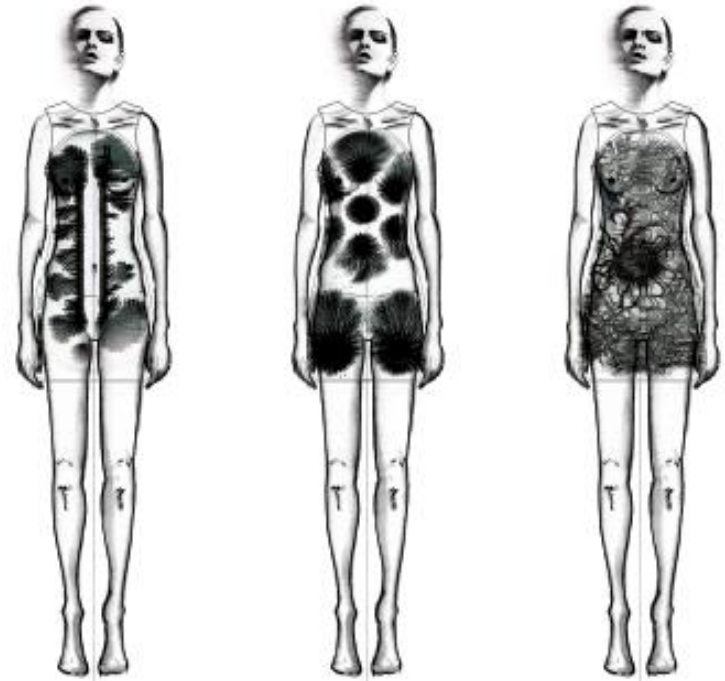


What could synthetic biology give us?



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 CO₂
- 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?



Synthetic Biology Dialogue

SYNDUSTRY

The news of "Synthia," the world's first human-made species, is just the latest from a rapidly growing artificial life industry. Synthetic biology (or "Syn Bio") aims to profit from the design and construction of industrially useful life-forms.

THE EMERGING SYNTHETIC BIOLOGY INDUSTRY

Syn Bio's Big Shots

Global corporations are investing in synthetic biology labs and partnering with start-up companies.

"Over the next 20 years synthetic genomics is going to become the standard for making anything." - Craig Venter

- Cargill**: Agribusiness giant. Supports synthetic biology R&D.
- BP**: Energy giant. \$500 million partnership on synthetic biology with University of California Berkeley; holds equity stake in Craig Venter's Synthetic Genomics, Inc.
- Du Pont**: Chemical giant. Developed first commercial syn bio product with Genencor and sugar giant Tate & Lyle - a fibre called Sorona.
- Pfizer**: Pharma giant. Conducts in-house syn bio research for drug development.
- Virgin Group**: Includes Virgin Fuels, investor in synthetic biology. Controlled by celebrity billionaire Richard Branson.

Synthetic Startups

A bevy of 'pure play' syn bio companies is attempting to design synthetic microbes for fuel, chemicals and drugs. Many are university spin-offs.

- gevo**: (USA) Developing synthetic biofuels with support from Virgin.
- Mascoma**: (USA) Developing synthetic biofuels.
- Synthetic Genomics**: (USA) Constructing synthetic life forms for biofuels and carbon sequestration.
- LS9**: (USA) Developing synthetic biofuels and industrial chemicals.
- AMYRIS**: (USA) Developing cellular factories to produce drugs, fuels and industrial chemicals.
- ProtoLife**: (Italy) Developing synthetic living systems.

DNA Synthesis Foundries

DNA foundries produce the raw material for creating artificial life: synthetic DNA (sDNA). Over 70 DNA foundries worldwide manufacture sDNA for genetic engineers and synthetic biologists. The market for sDNA already exceeds a billion dollars annually. Even long DNA sequences - entire genes, for example - can be ordered over the Internet and delivered within two weeks. The speed of producing accurate DNA sequences is doubling every two years and costs are halving even faster.

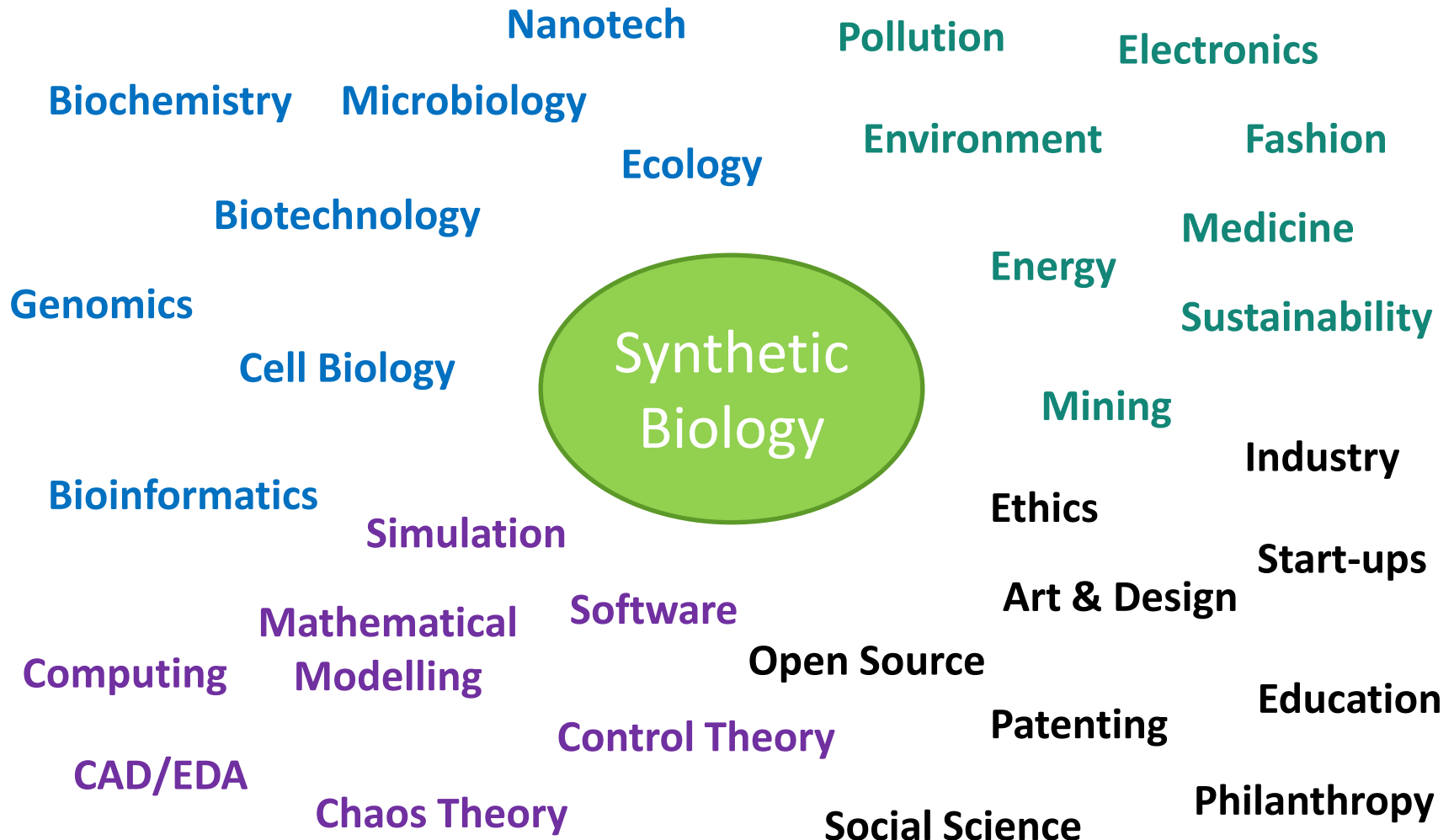
Published by ETC Group Dec 2007 Artwork by Shig

www.etcgroup.org etc

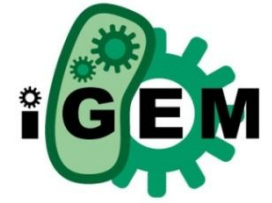
Some Commercial DNA Synthesis Companies:

- Blue Heron Biotech
- Codon Devices
- GeneArt
- Bioneer
- Tech Dragon
- BioServe Biotech
- Inqaba Biotechnical Industries
- GeneWorks
- DNA2.0

Bringing together disciplines



High School iGEM



page discussion view source history teams

Heidelberger Life-Science Lab

Home Team Project Parts Notebook Online Store Sponsors

iGEMS
Unveil the invisible

Idea
Our sunny thought:
How to make bacteria
unveil UV-radiation!

Science
Profound experiments are
followed by shiny results!

Store
Pretty and safe! The new
collection of our iGEMS-jewelry!

Heidelberg LSL 2012

Grand Prize, Winner of the GreenBrick Trophy; Finalist; Best New BioBrick Part, Natural; Best New BioBrick Part or Device, Engineered; Best Experimental Measurement; Best Wiki; Best Presentation

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

The poster for 'Project BioBreeze' is a comprehensive document detailing the team's work. It features a blue header with the 'Mini iGEM' logo and the team names: Tim Boardman, Nicholas Leung, Jonathan Li, and Michael Vanner. The poster is organized into several sections: 'Introduction', 'Chassis', 'Previous iGEM Projects', 'Human Practices', 'Implications', 'Ester Production', 'UV Sensitivity', 'Temperature Sensitivity', 'Future Applications', and 'Special thanks'. Each section contains text, diagrams, and images. The 'Special thanks' section at the bottom left acknowledges Professor Kirby and the team's support. The poster also includes a small photo of the team and a list of references.



Further Information

Synthetic Biology at Imperial College London

<http://www3.imperial.ac.uk/syntheticbiology>

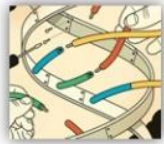
**Imperial College
London**

CSYNBI

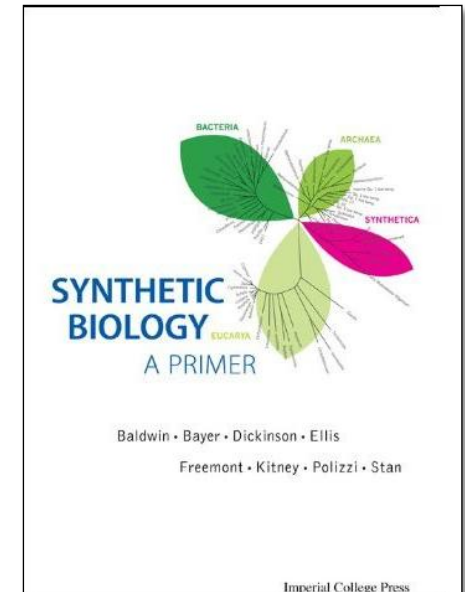
Centre for **S**ynthetic **B**iology and **I**nnovation

The Ellis Lab

http://openwetware.org/wiki/Ellis_Lab



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/>



BioBricks
FOUNDATION

The Woodrow Wilson Project: synthetic biology 101

<http://www.synbioproject.org/topics/synbio101/>

Synthetic
BIOLOGY
PROJECT

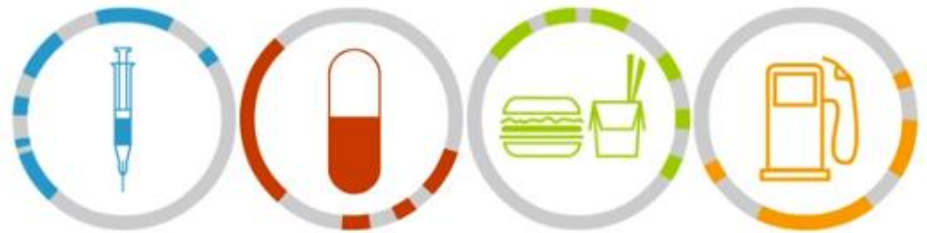


Woodrow Wilson
International
Center
for Scholars

Further Information

Short excellent video describing synthetic biology

<http://www.youtube.com/watch?v=rD5uNAMbDaQ>



David Shukman visits Imperial's Synthetic Biology Centre

<http://www.bbc.co.uk/news/science-environment-17511081>

BBC News article by David Shukman

<http://www.bbc.co.uk/news/science-environment-17436365>

Horizon 1 hour special on Synthetic Biology with Adam Rutherford

<http://www.bbc.co.uk/programmes/b01b45zh>