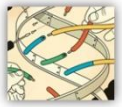
Brewing-up the technologies of tomorrow with synthetic biology

Imperial College London



Ellis Lab

CSynBI
Centre for Synthetic Biology and Innovation

BBSRC
bioscience for the future

EPSRC

Dr Tom Ellis

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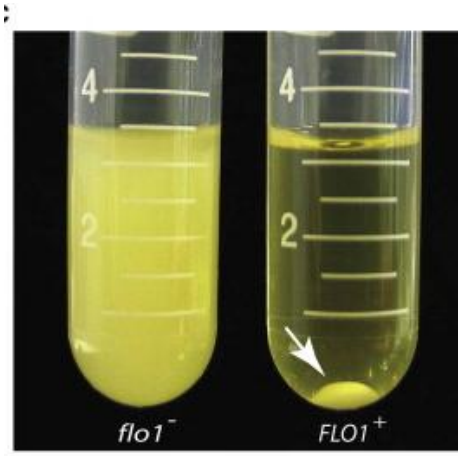
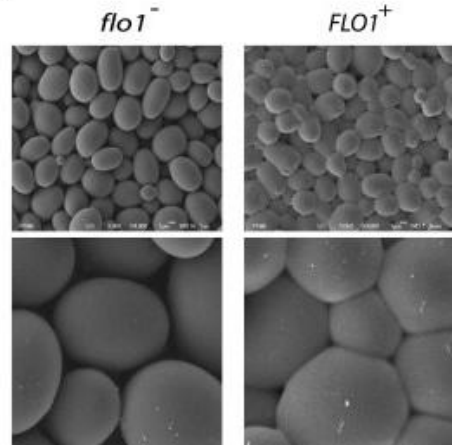
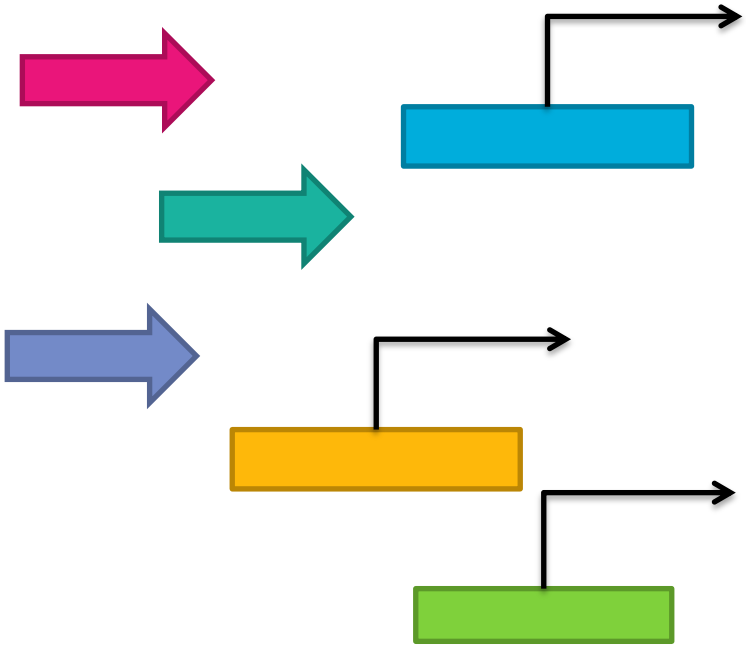
Sedimentation of yeast by flocculation genes

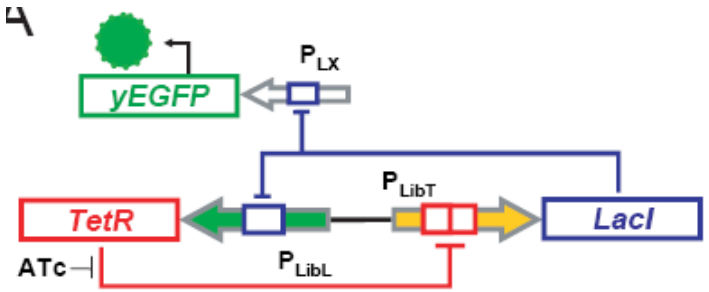


Because flocculation is unpredictable, brewers use *isinglass* or mechanical purification using huge centrifuges and big filters



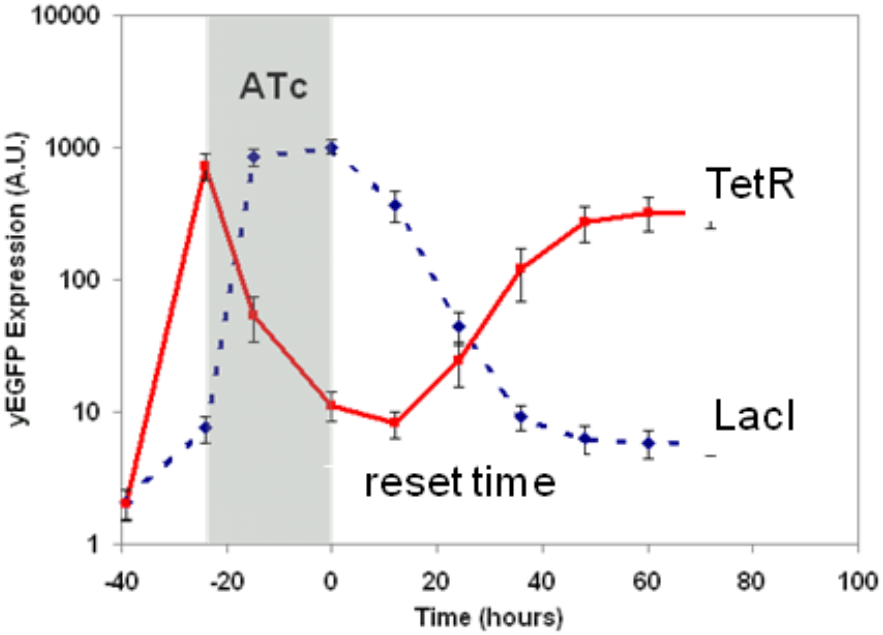
Design & build a DNA-coded timer from parts



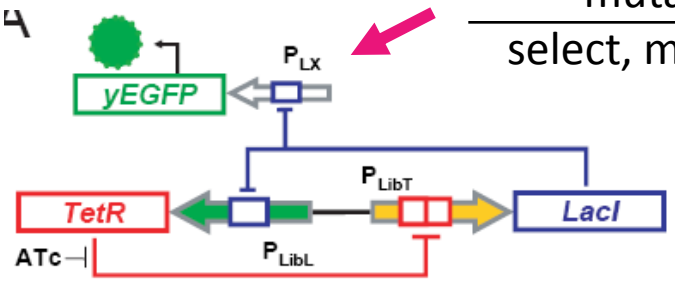


PARTS:
GENES and GENETIC SWICTHES

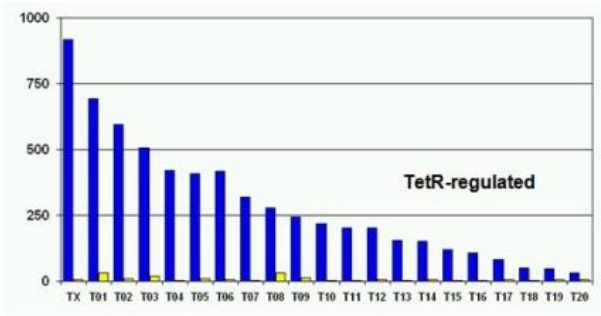
SOURCE DNA:
BACTERIA, PLANTS, JELLYFISH

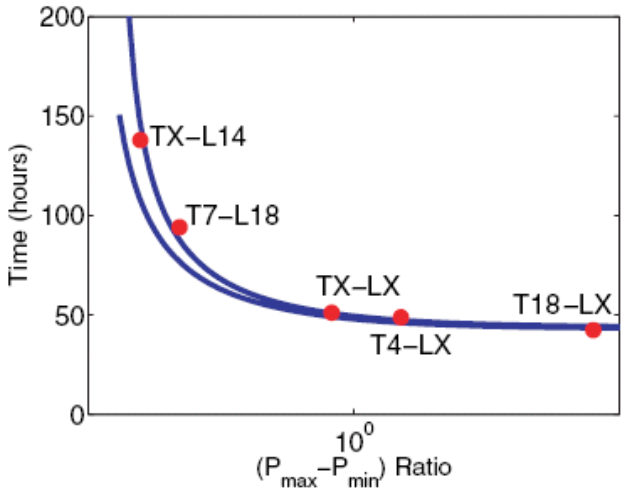


Timer ‘networks’ that can be tuned predictably



mutate,
select, measure





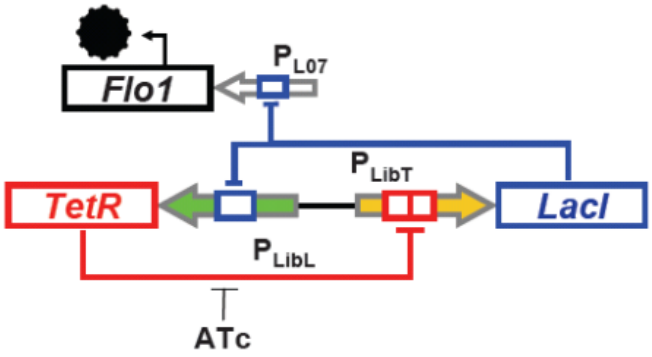
input data
predictive model

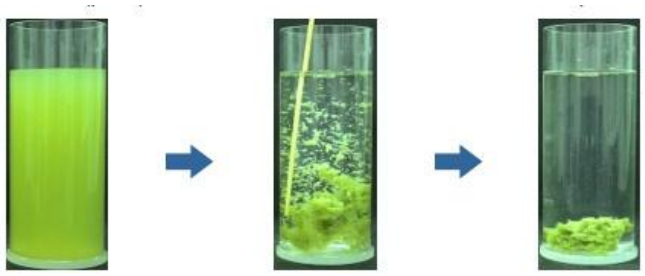
Promoter	Max Output	error	Min Output	error
LX	717.38	21.06	13.06	0.77
L01	399.90	25.02	11.11	0.60
L02	372.59	16.87	9.71	0.11
L03	292.11	11.60	83.05	1.09
L04	282.01	13.61	50.55	1.92
L05	246.73	6.42	151.75	2.77
L06	228.45	15.37	23.79	0.31
L07	139.99	8.43	5.40	0.35
L08	141.86	6.23	7.67	0.35
L09	134.04	9.73	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

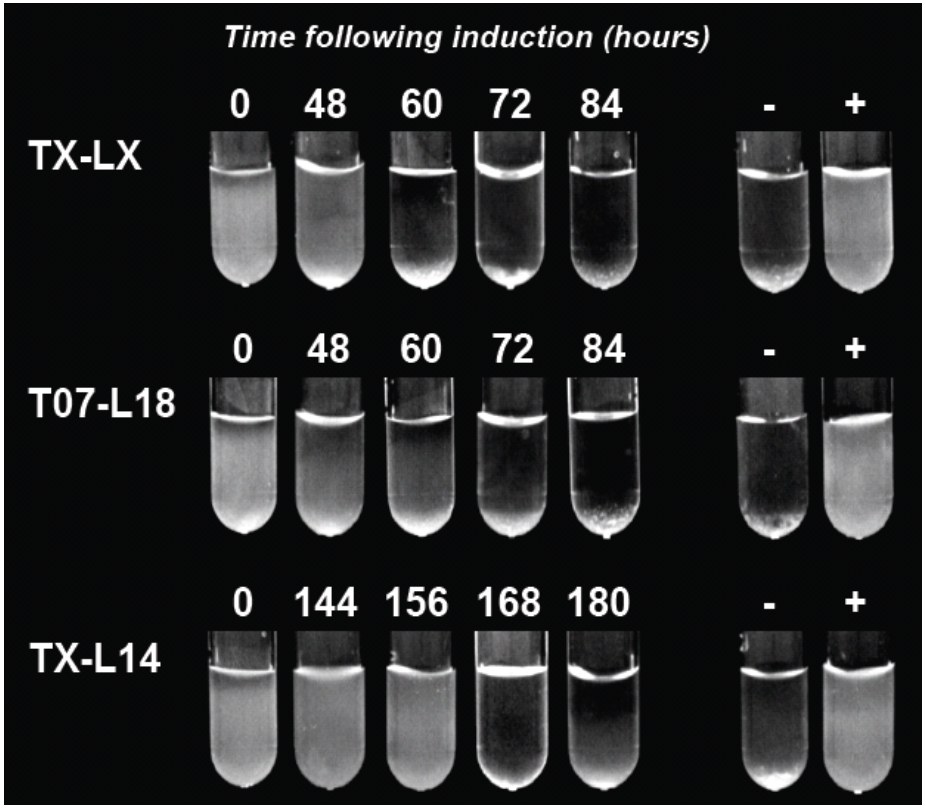
3 promoter ‘nodes’, 20 promoters per library = 8000 possible networks
Predictable custom gene networks with diverse reset times

Timer networks control yeast sedimentation

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





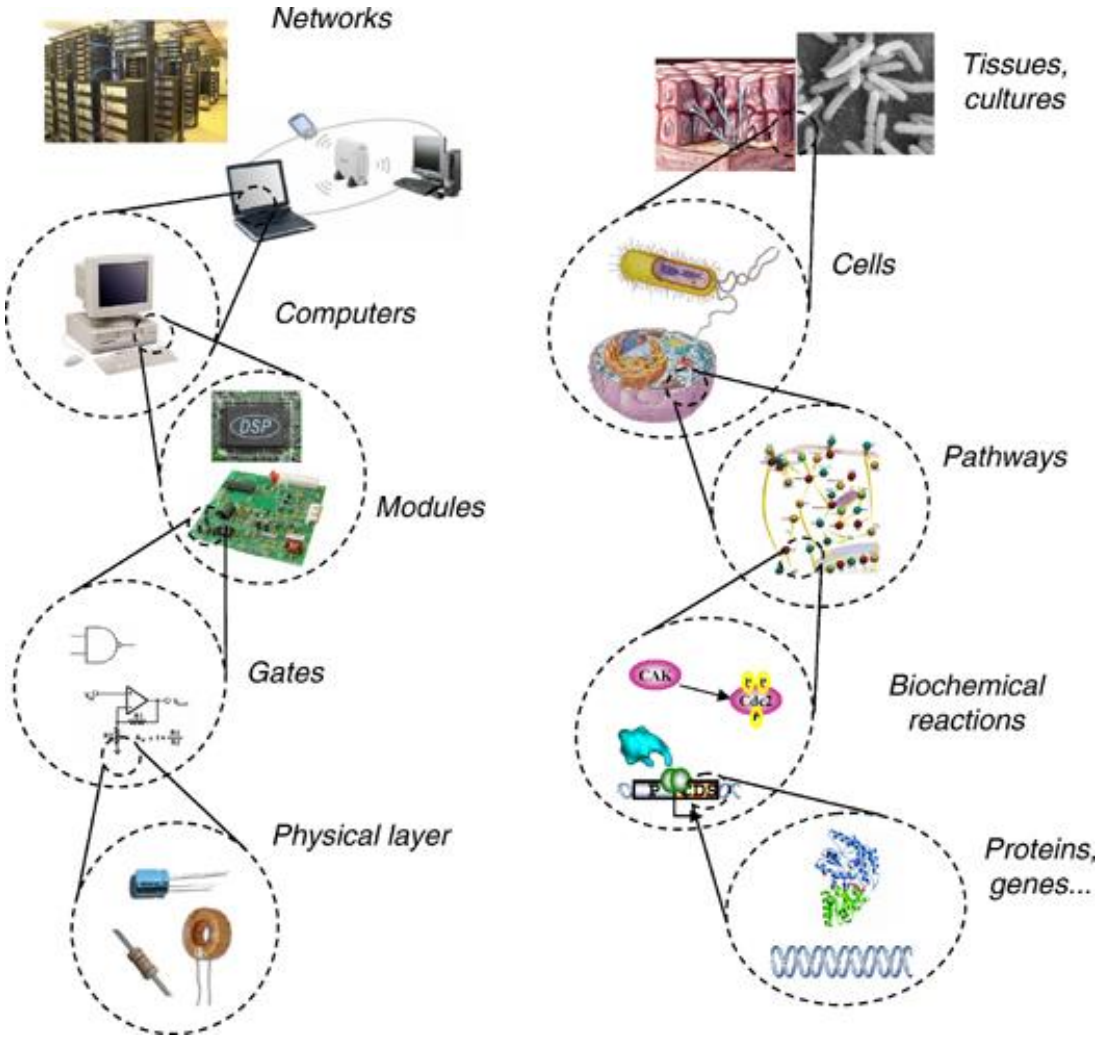


Synthetic Biology

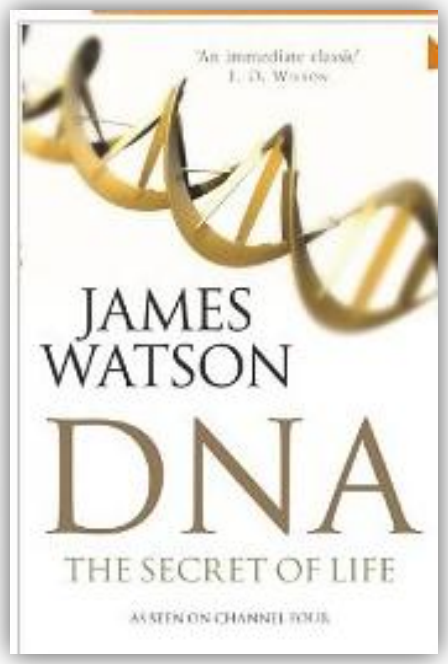
Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature.

Source: High-level Expert Group European Commission

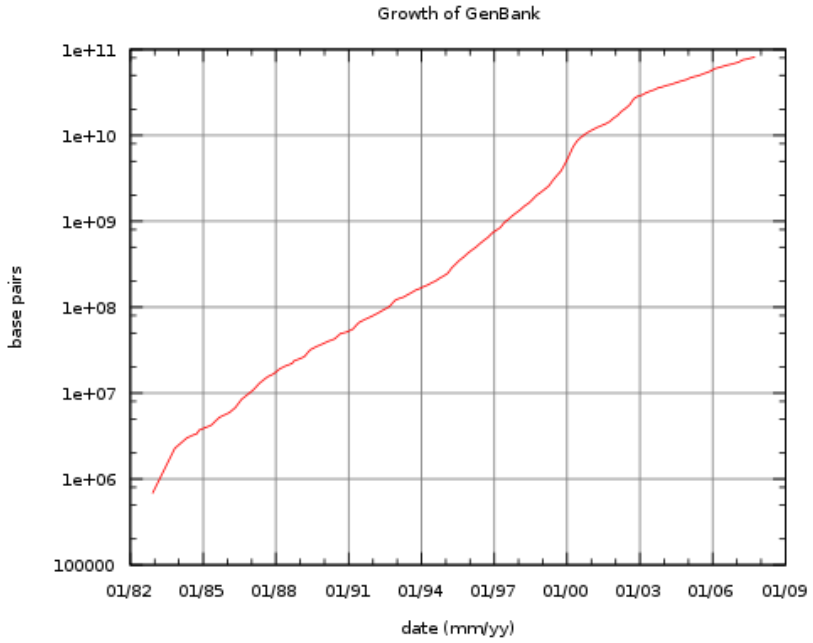
Engineering Biology

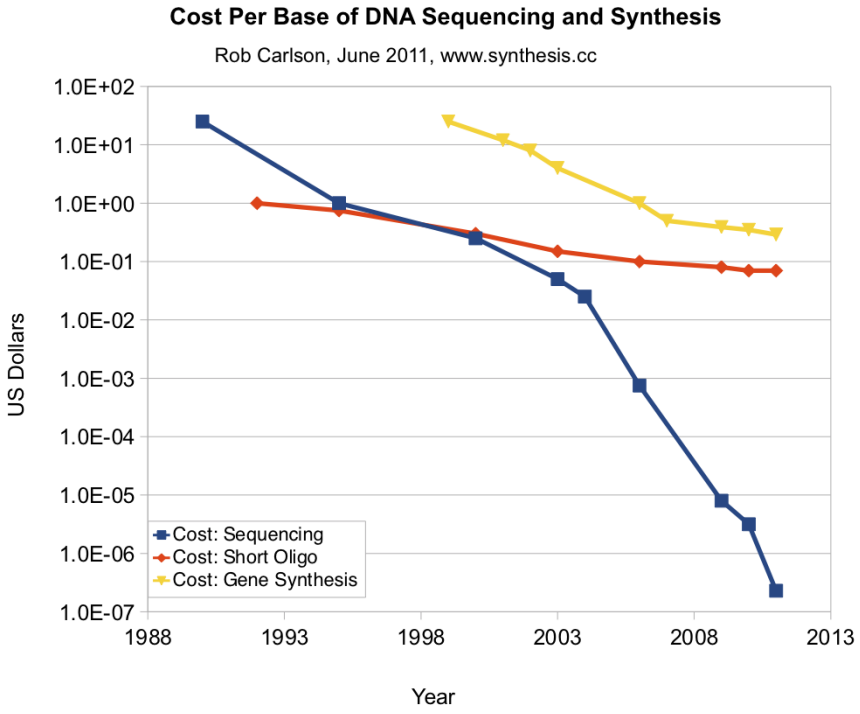


Synthetic biology is ‘hacking’ the code books for life: DNA genomes



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

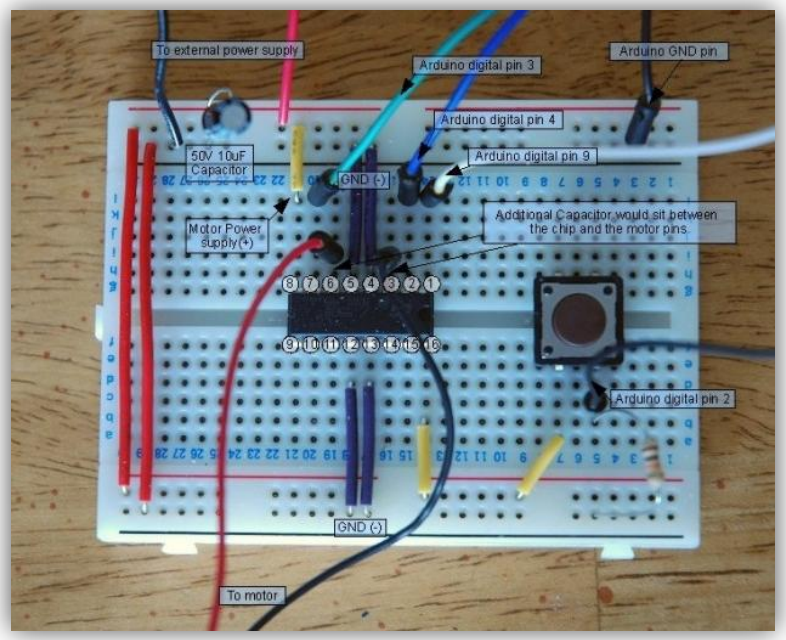




Feb 2012: 137,384,889,783 bp

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

Re-wiring microbiology for new applications

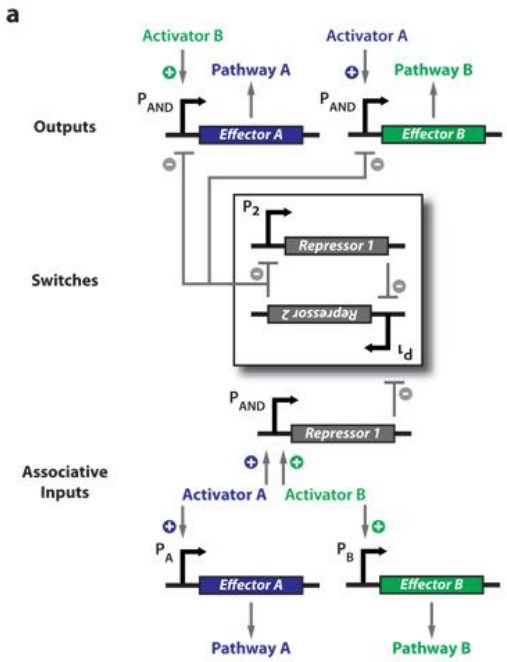


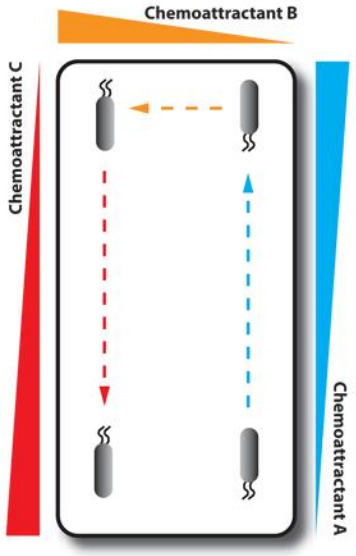
Synthetic Biology

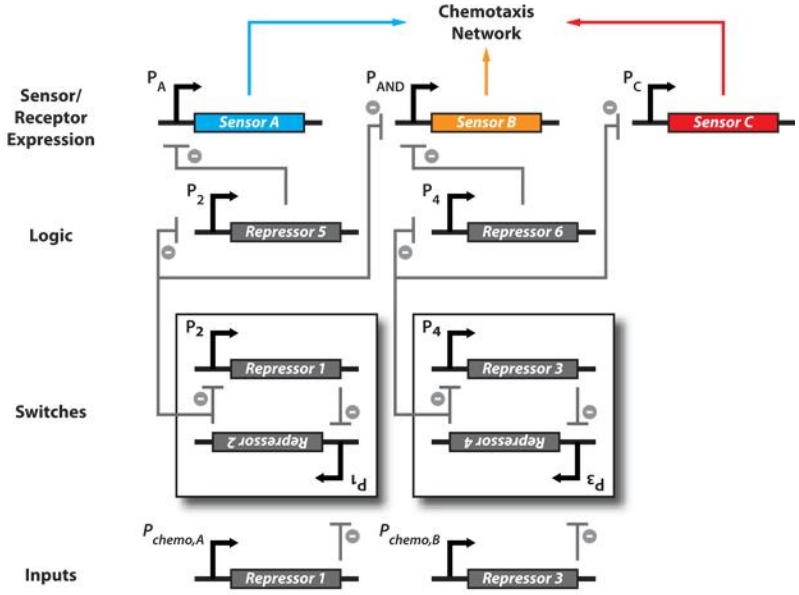
The Cell

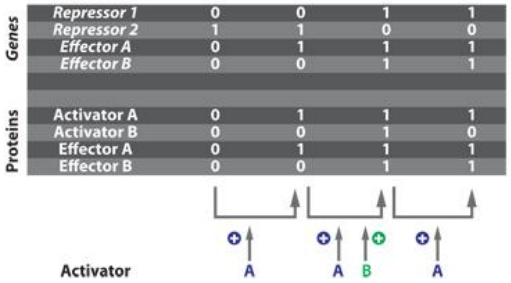
Microbes respond and make decisions using networks of interacting genes

Example synthetic biology **Apps**









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

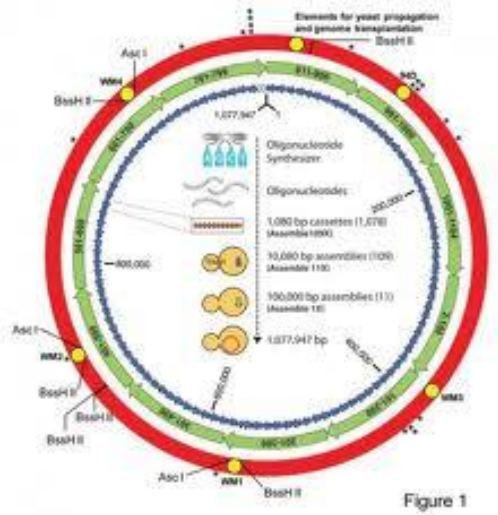
Intelligent Biosensors: *e.g.* navigating bacteria

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



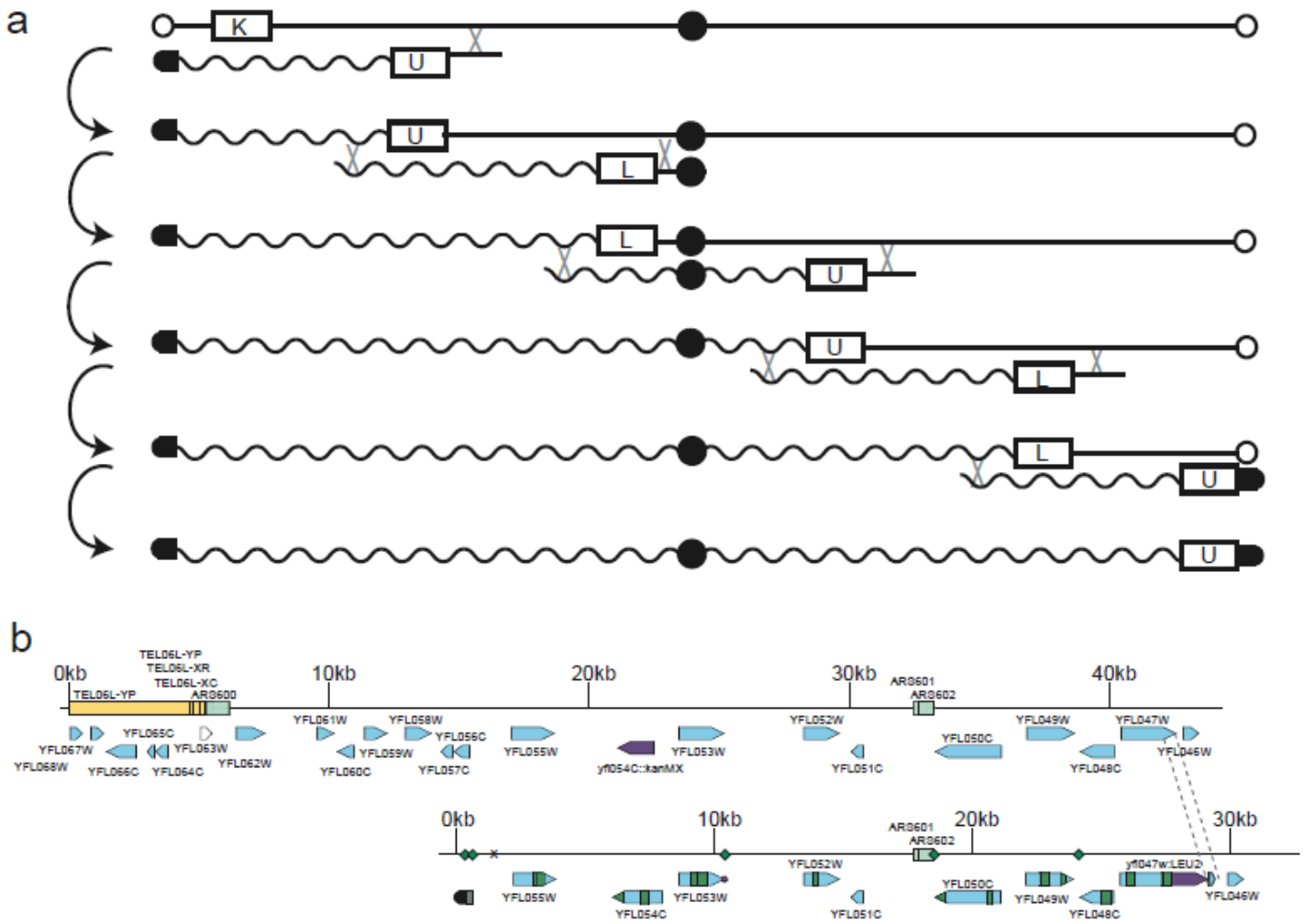
Sc2.0 – A Human-made Yeast Genome

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



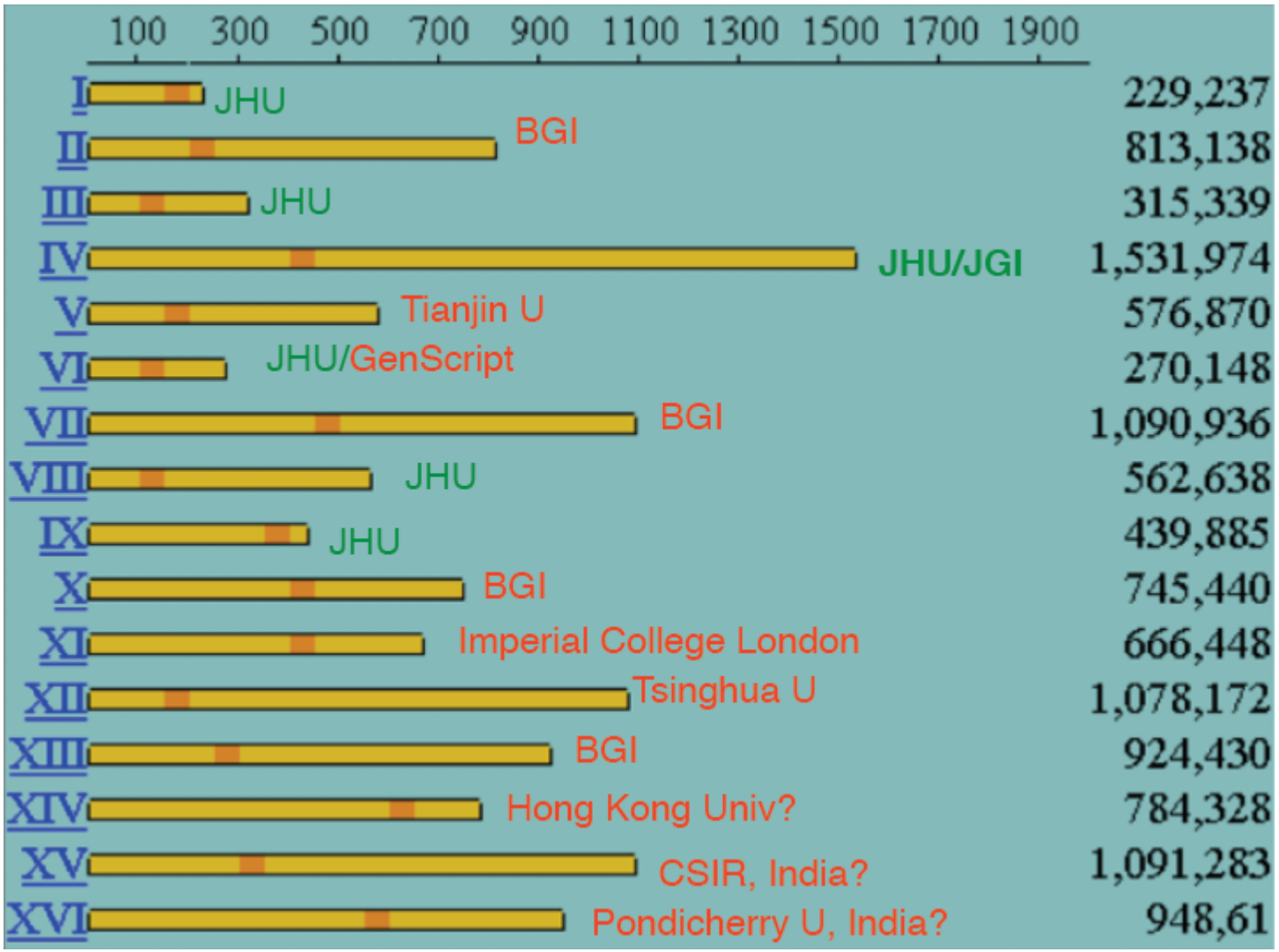
Reiterative Recombination Method

Requires two selectable markers

Makes use of yeast's ability to recombine matching sequences

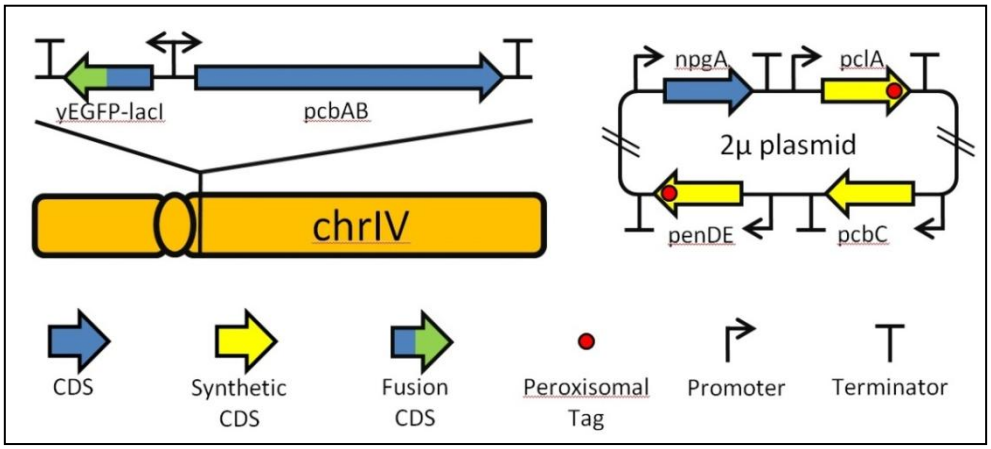
SERIAL process

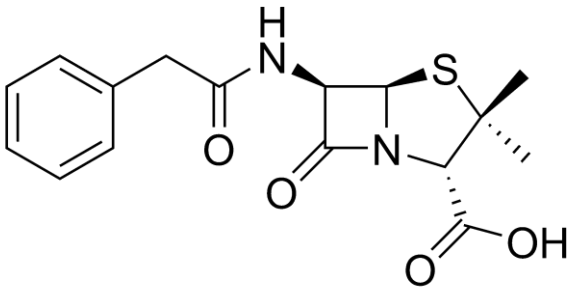
Sc2.0 – A global project



	Dec 2012 status	
	MADE	INT
229,237	20%	0%
813,138	48%	8%
315,339	100%	100%
1,531,974	0%	0%
576,870	90%	8%
270,148	100%	70%
1,090,936	0%	0%
562,638	20%	0%
439,885	100%	95%
745,440	0%	0%
666,448	13%	0%
1,078,172	75%	22%
924,430	0%	0%
784,328	0%	0%
1,091,283	0%	0%
948,61	0%	0%

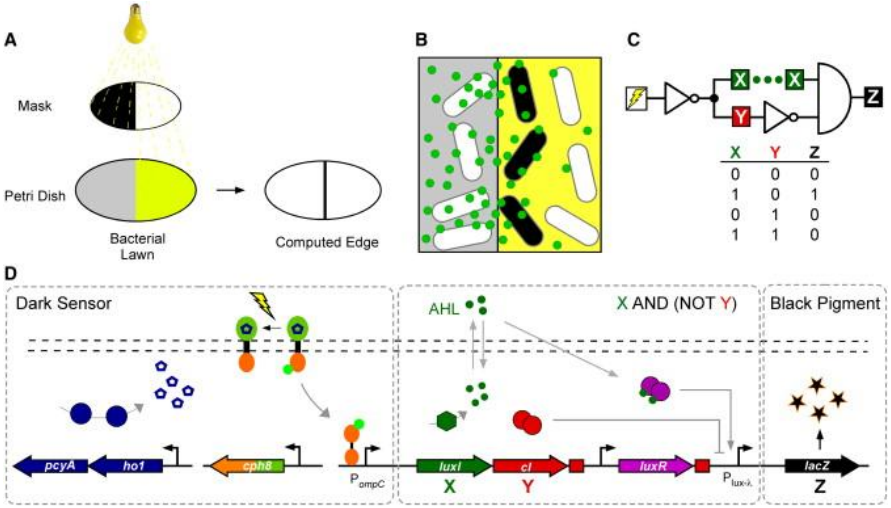
Synthetic Yeast to Brew beyond beer

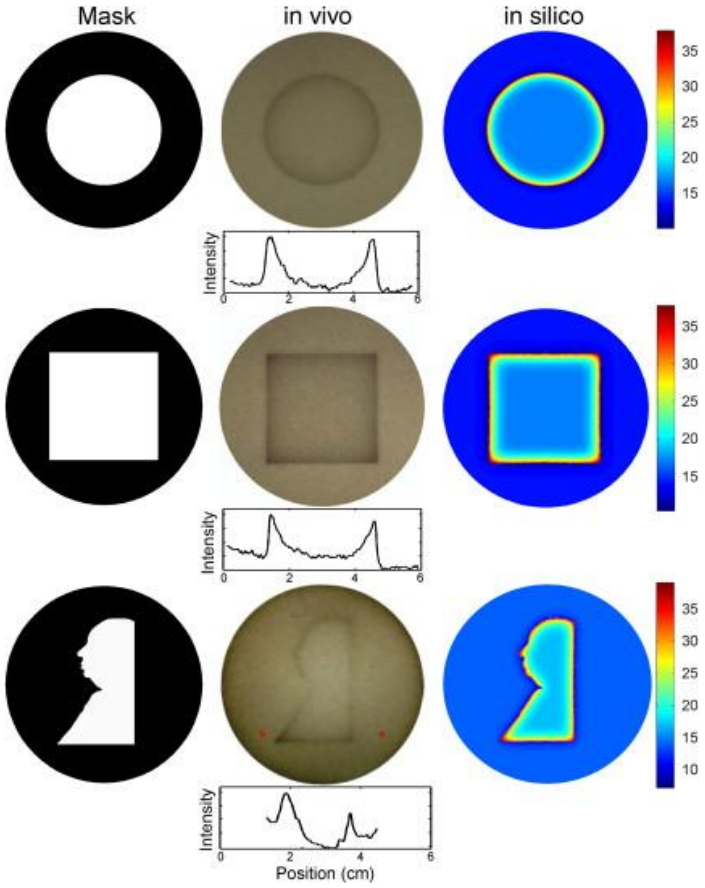




Penicillin Biosynthesis encoded into synthetic yeast chromosomes

Amazing Apps have been built by students





Following an abstraction similar to electronic engineering

2005 – Students at a summer school

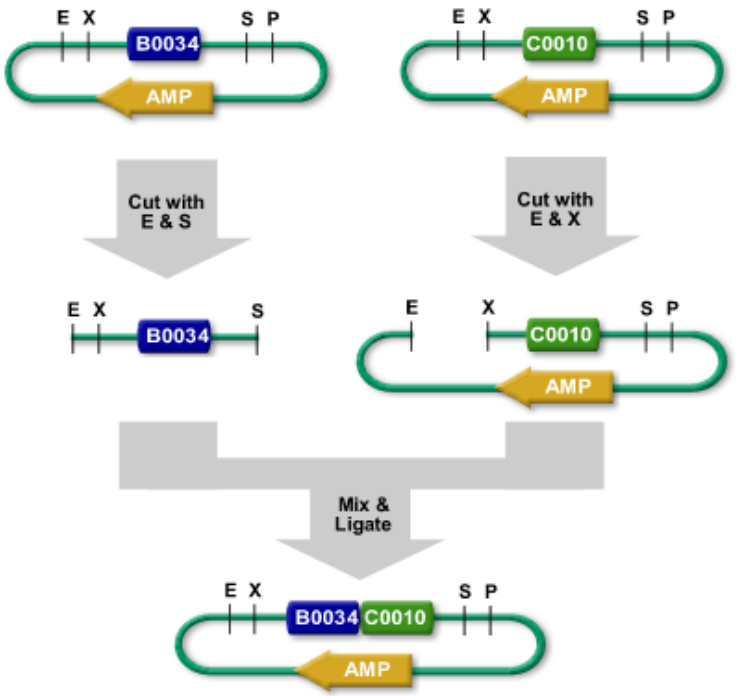
iGEM is a synthetic biology competition

iGEM uses BioBricks – modular DNA parts

Registry of Standard Parts

-?-		Name	Description	Promoter Sequence	
A		BBa_I1051	Lux cassette right promoter	... tgttatagtcgaatacctctggcggtgata	1
		BBa_I12001	Promoter (PRM+)	... gatttaacgtatcagcacaaaaaagaaacc	
A		BBa_I12006	Modified lamdba Prm promoter (repressed by 434 cI)	... attacaaactttcttgtatagatttaacgt	1
A		BBa_I12036	Modified lamdba Prm promoter (cooperative repression by 434 cI)	... tttcttgtatagatttacaatgtatcttgt	1
A		BBa_I12040	Modified lambda P(RM) promoter: -10 region from P(L) and cooperatively repressed by 434 cI	... tttcttgtagatacttacaatgtatcttgt	1
		BBa_I12212	TetR - TetR-4C heterodimer promoter (negative)	... actctgtcaatgatagagtggattcaaaaa	
A		BBa_I14015	P(Las) TetO	... ttttggtacactccctatcagtgatagaga	1
A		BBa_I14016	P(Las) CIO	... ctttttggtacactacctctggcggtgata	1
A	W	BBa_I14032	promoter P(Lac) IQ	... aaacctttcgcggtatggcatgatagcgcc	
A	W	BBa_I714889	OR21 of PR and PRM	... tattttacctctggcggtgataatggttgc	
A	W	BBa_I714924	RecA_DlexO_DLacO1	... actctcggcatggacgagctgtacaagtaa	
B	?	BBa_I715003	hybrid pLac with UV5 mutation	... ttgtgagcggataacaatatgttgagcaca	
A		BBa_I718018	dapAp promoter	... cattgagacacttgtttgcacagaggatgg	
		BBa_I731004	FecA promoter	... ttctcgttcgactcatagctgaacacaaca	2
	W	BBa_I732200	NOT Gate Promoter Family Member (D001O1wt1)	... gaattgtgagcggataacaattggatccgg	
	W	BBa_I732201	NOT Gate Promoter Family Member (D001O11)	... ggaattgtgagcgctcacaattggatccgg	
	W	BBa_I732202	NOT Gate Promoter Family Member (D001O22)	... ggaattgtaagcgcttacaattggatccgg	
		BBa_I732203	NOT Gate Promoter Family Member (D001O33)	... ggaattgtaaacgtttacaattggatccgg	

Standard Modular Assembly

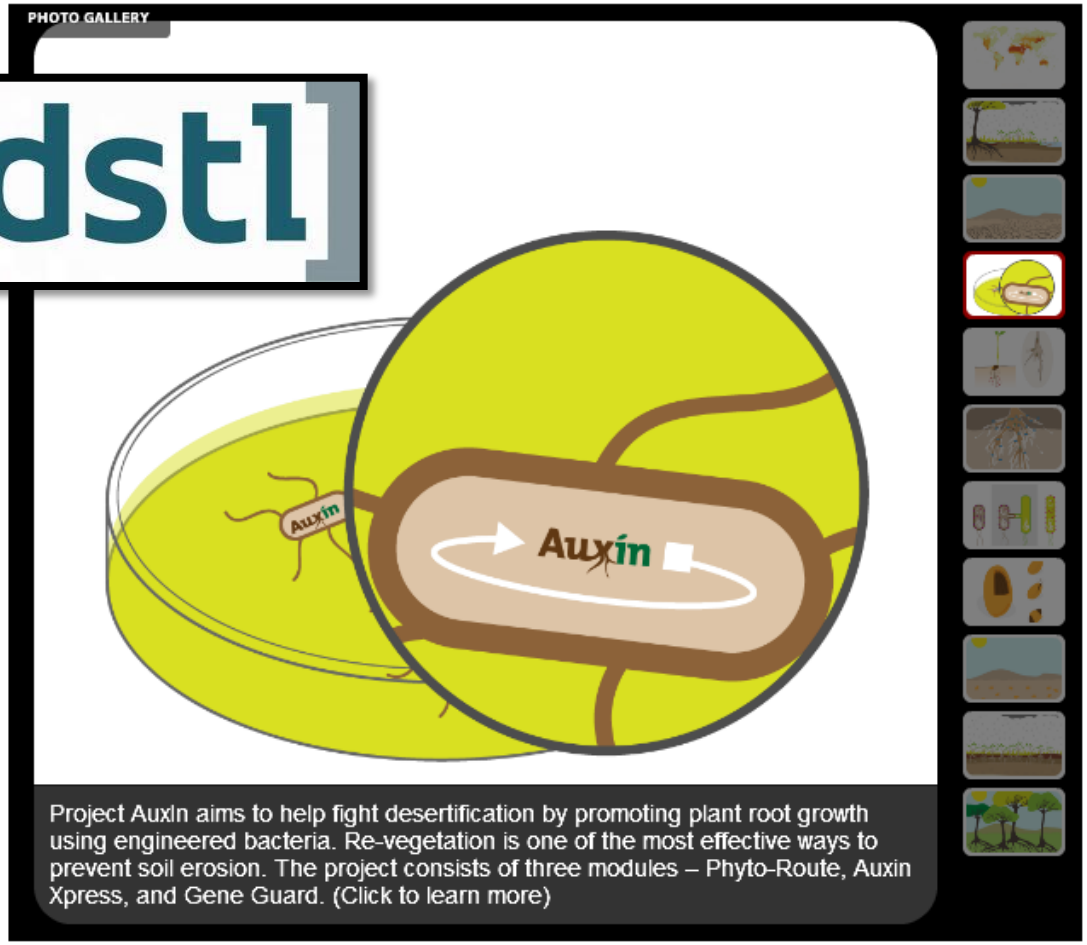


Open source distributed parts kit

Auxin

Imperial College London

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



AT A GLANCE
MAIN RESULTS
DATA

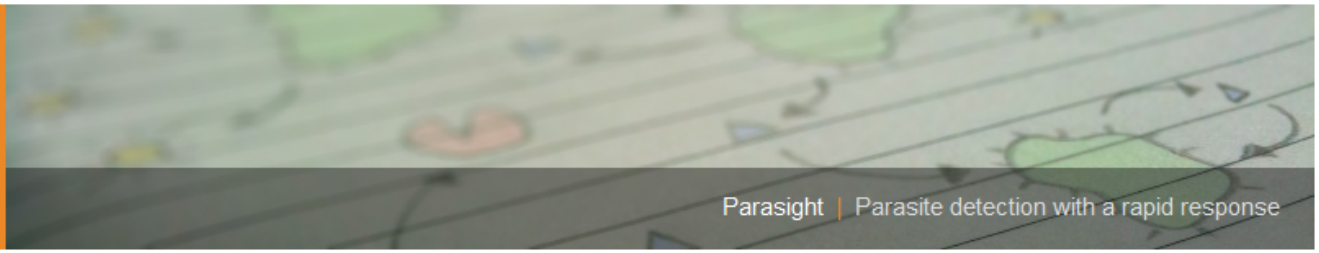
Follow us on

PARASIGHT

Imperial College London

iGEM

CSynBI
Centre for Synthetic Biology and Innovation
Department of Bioengineering
Division of Molecular Biosciences



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.

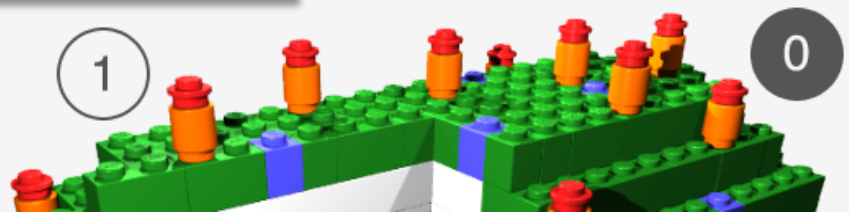
Synthetic biology offers great opportunity for biosensors, however current designs require hours of waiting before a detectable output is produced. To tackle this issue in the field, it is crucial that a new generation of biosensors be designed that can respond in minutes. With this in mind, we have 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*



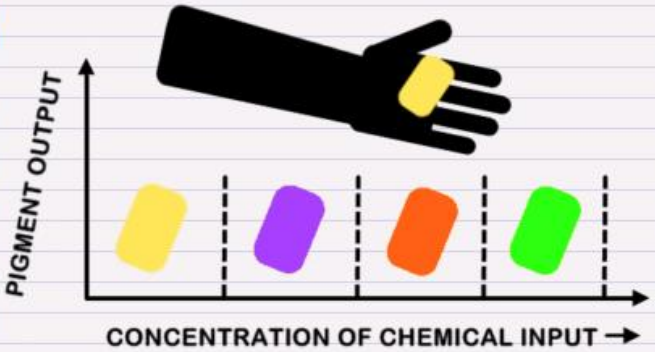
Welcome to a very basic model of our cell. The main features are the cell wall, the cytoplasm, a two component signaling

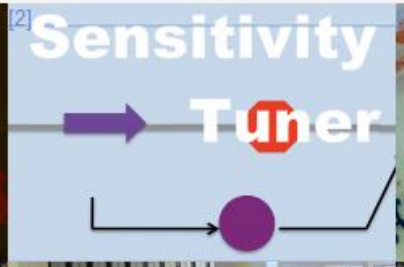
E. Chromi

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

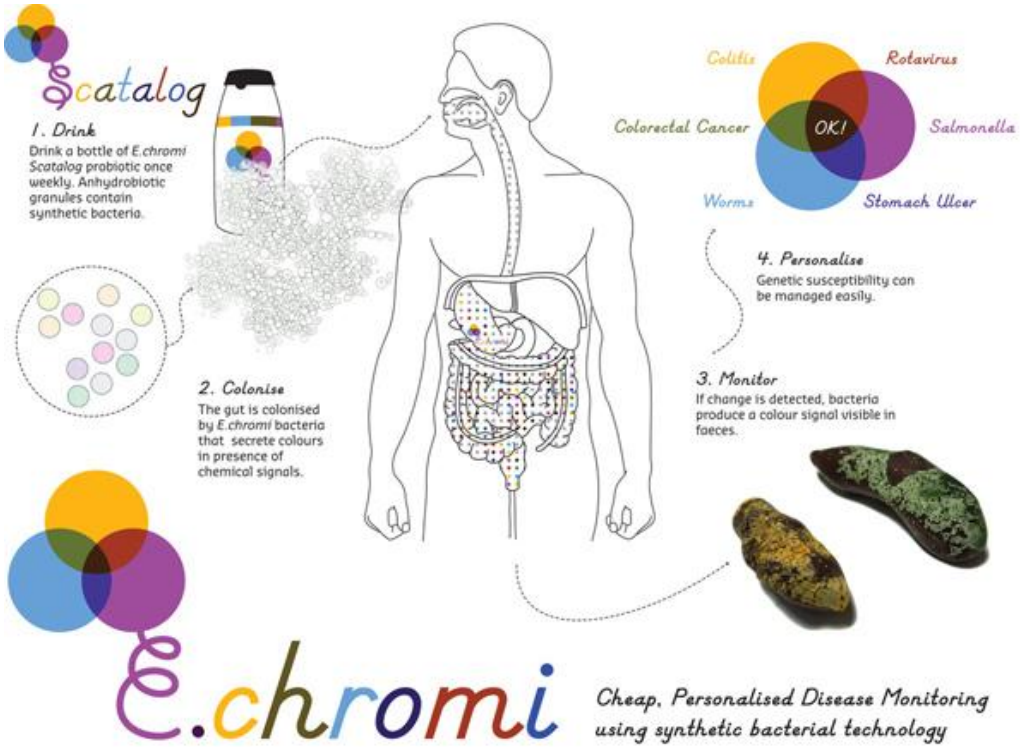
Previous iGEM teams have focused on genetically engineering bacterial biosensors by enabling bacteria to respond to novel inputs, especially biologically significant compounds. There is an unmistakable need to also develop devices that can **1) manipulate input by changing the behaviour of the response 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.



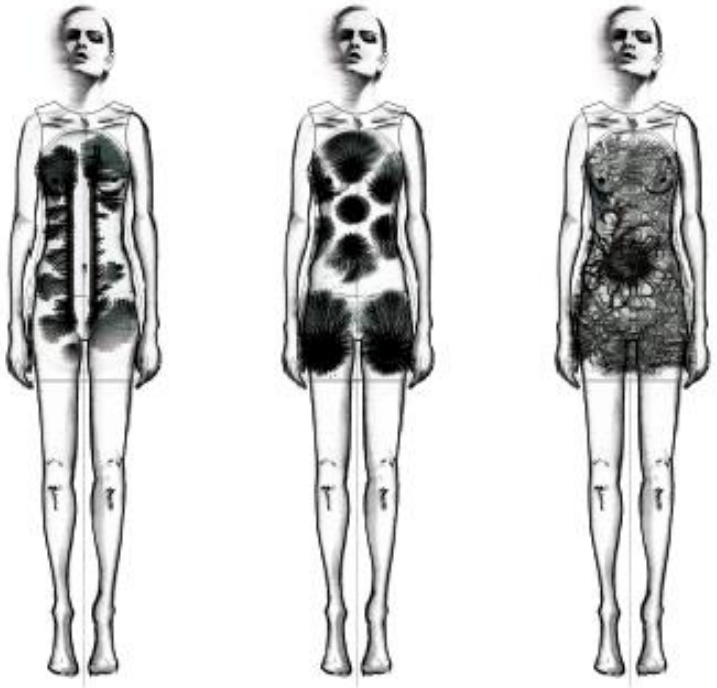


What could synthetic biology give us?



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 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?

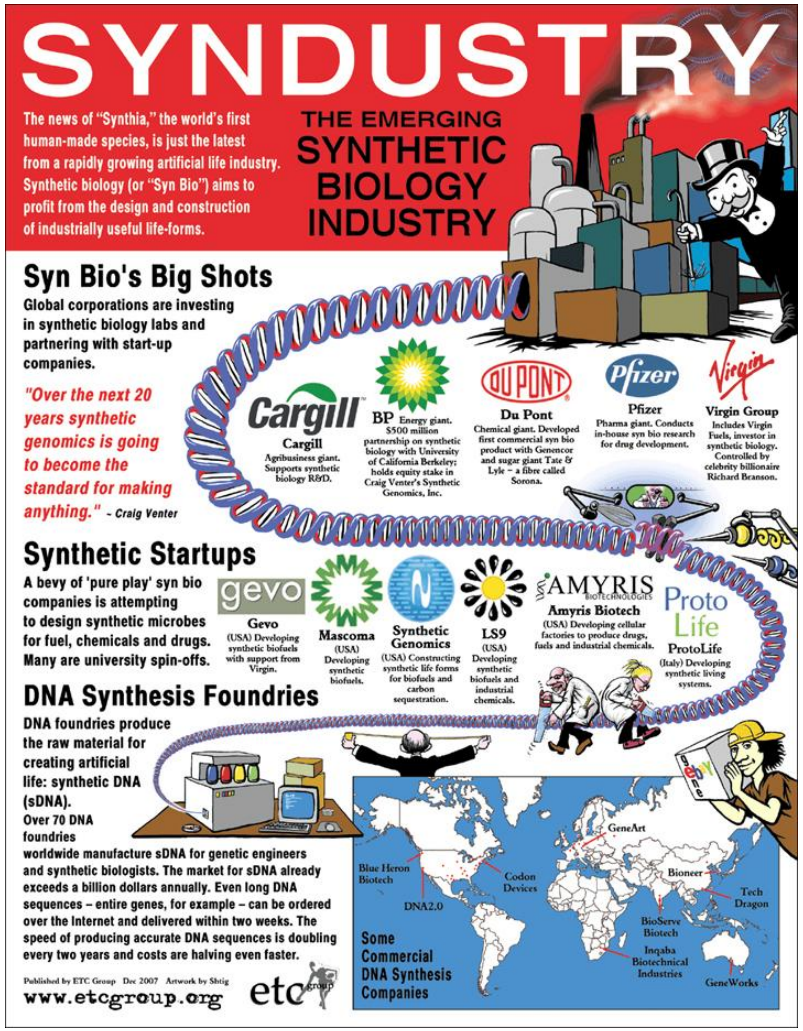
DIY BIO

BBSRC bioscience for the future

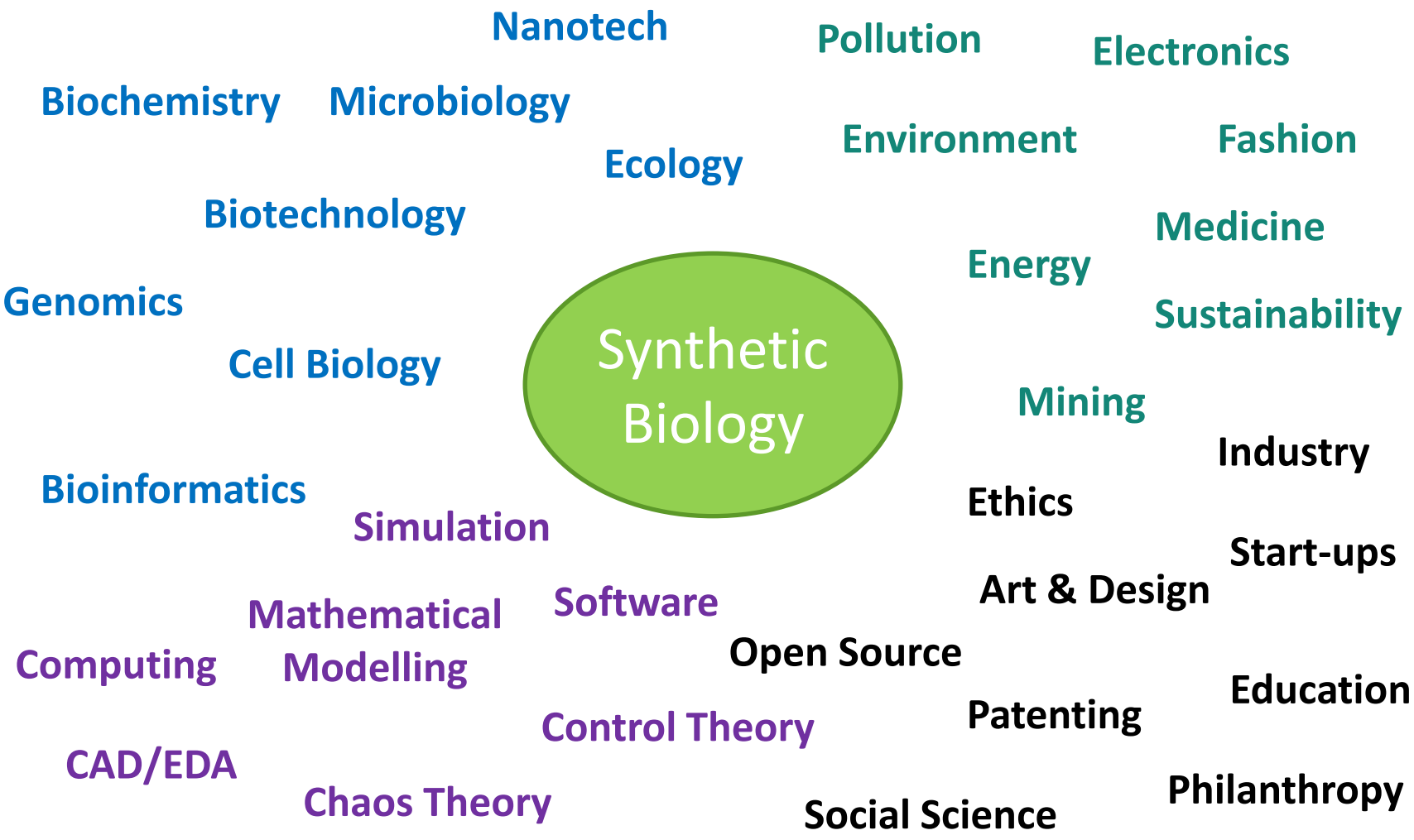
EPSRC Pioneering research and skills

sciencewise

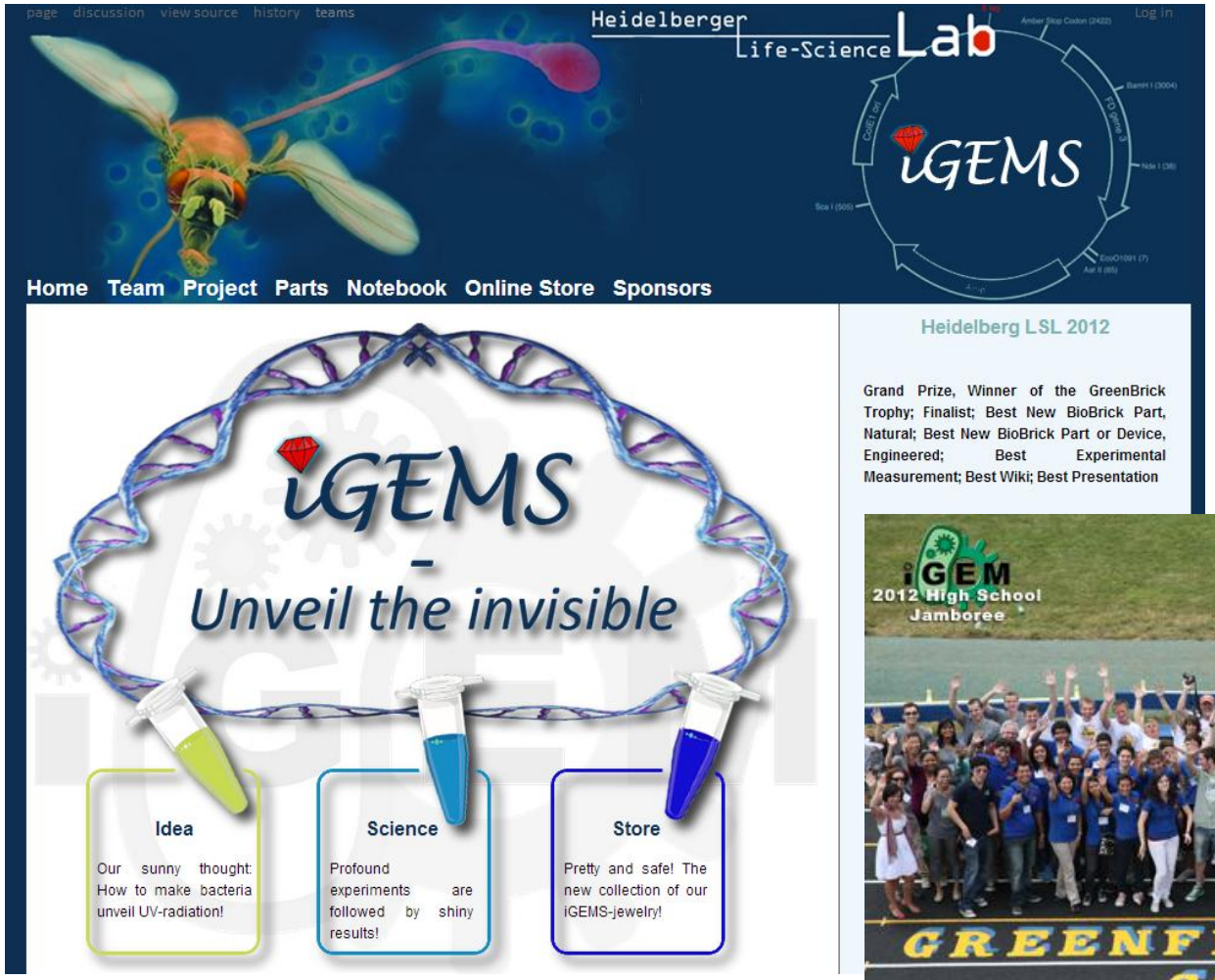
Synthetic Biology Dialogue



Bringing together disciplines



High School iGEM

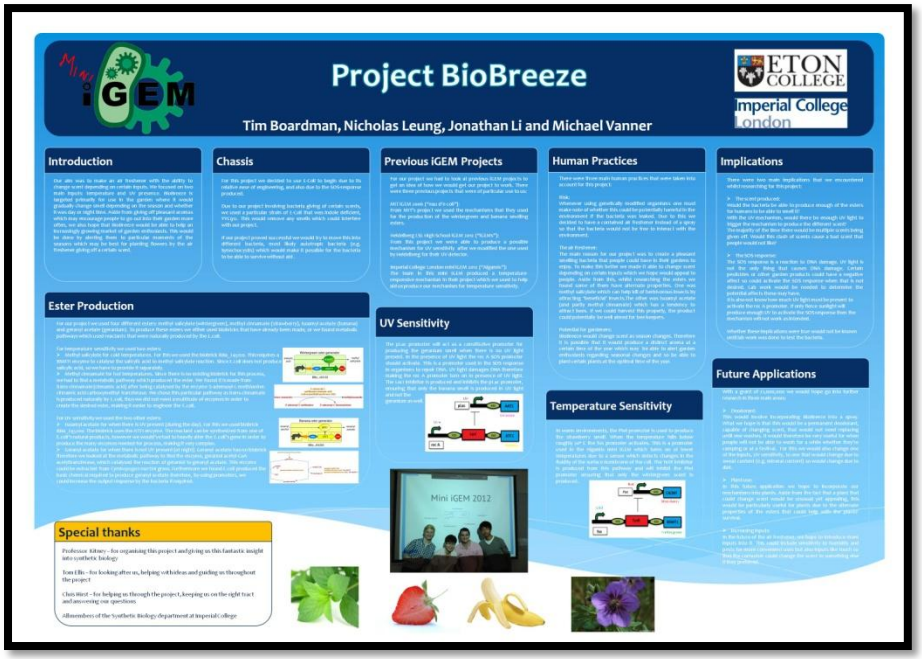


iGEM HS runs from August to May, with finals in June. Allows leaders to work with students schedules and allow school students to experience synthetic biology.

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



Imperial College London

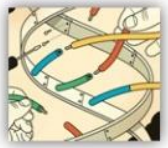
Further Information

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

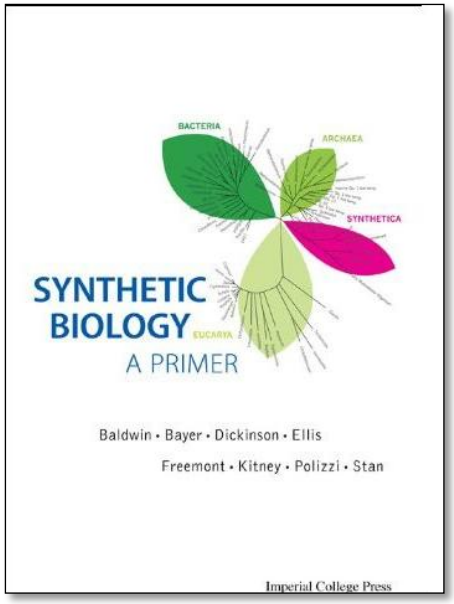
Imperial College London

CSynBI
Centre for Synthetic Biology and Innovation

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/

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
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