

Topic 1 Topic 2 Topic 3 Topic 4 Topic 5

Foundations for Synthetic Biology



Topic 1 Topic 2 Topic 3 Topic 4 Topic 5

Standard for Physical DNA Composition



Topic 1 Topic 2 Topic 3 Topic 4 Topic 5

# Standards for Functional Composition



Topic 1 Topic 2 Topic 3 Topic 4 Topic 5

**Characterising Biological Parts** 



Topic 1 Topic 2 Topic 3 Topic 4 Topic 5

**Building Systems from BioBricks** 



#### Be Aware





Topic 1 Topic 2 Topic 3 Topic 4 Topic 5

Foundations for Synthetic Biology

Vincent Rouilly
Bioengineering Departement
Imperial College London

**Press Review** 

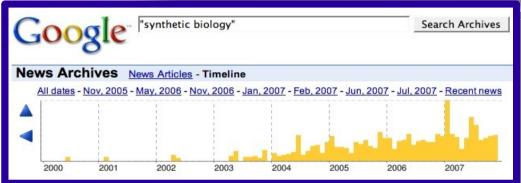
**Current Research** 

Finding our SB Definition

SB Principles Ethics & Society



#### **Press Review**



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Past month

#### Archives

#### All dates

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2003-04 1990s

Before 1990 Other dates

Mews Alerts

#### Scientists Call For Global Push To Advance Research In Synthetic...

Science Daily - Science Daily (press release) - Jun 26, 2007

That research area is synthetic biology -- the construction or redesign of ... Synthetic biology offers solutions to these issues: microorganisms that ...

Scientists Call For Global Push To Advance... - innovations report

All 3 related - Related web pages

#### Synthetic Biology? Memory In Yeast Cells Synthesized

Science Daily - Science Daily (press release) - Sep 17, 2007

ScienceDaily (Sep. 17, 2007) - Harvard Medical School researchers have successfully synthesized a DNA-based memory loop in yeast cells, findings that mark a ...

Scientific American: Nothing Says "Early... - Scientific American

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#### Biology's New Forbidden Fruit

New York Times - Feb 11, 2005

But synthetic biology could also make us safer. Last month, shortly after the journal Nature published an article by Dr. George M. Church of the Harvard ...

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#### ... Synthetic Biology - Genes and Heredity - Cloning - Biology ...

New York Times - Jul 8, 2007

By NICHOLAS WADE. FORGET genetic engineering. The new idea is synthetic biology, an effort by engineers to rewire the genetic circuitry of living organisms. ...

#### The Technology Chronicles: From God to Darwin to Synthetic Biology

San Francisco Chronicle - Aug 8, 2006

In the beginning an all-powerful diety created the universe in six days and then rested. Or perhaps everything started with a Big Bang followed by billions ...

Related web pages

Gates foundation to promote synthetic biology

Vincent Koully @ Imperial College London, ∠006



#### Press Review: Main Stream



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OPINION

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Some think bank with tradition.

We think 150 years of innovation.

Special Report Get article

Synthetic biology

Life 2.0

Aug 31st 2006 | BERKELEY, CAMBRI From The Economist print edition

The new science of synthetic its time will soon come



#### Architect of Life

Matthew Herper 10.02.06

Drew Endy aims to reinvent the biotechnology industry.

To Drew Endy, all the great breakthroughs in biotechnology of th killing crops and glowing fish--they're simply the result of moving precisely, to rewrite DNA one unit at a time, using this genetic de succeeds it will change the way mankind interacts with the living

The 36-year-old professor at Massachusetts Institute of Technol genetic material, much as bits of mortar or silicon are used to er these wonderful living objects that make copies of themselves,

In coming years, Endy says, we'll begin to see the first customtumor cells. These "devices" will guard against disease, create r very early days; scientists do not know how to build such device micromachines.

Endy, along with three synthetic-biology comrades, started a cor \$13 million in backing from Flagship Ventures and three other fin intends to produce its own creations, but that accomplishment is

Initially Codon's goal is to dominate the gene-synthesis market. recently shipped the biggest piece of DNA ever made, a hunk of

Codon claims it will have more production capacity by year-end t 1999, and DNA 2.0, founded in 2003, both of which also deliver



#### Synthetic biology

#### Playing demigods

From The Economist print edition



Economist. Aug 2006

Synthetic biology needs to be monitored, but not stifled

THERE will be no thunderstorm, no bolts of lightning channelled through giant switchgear, and definitely no hunchbacks called Igor. But sometime soon a line will be crossed in a laboratory somewhere and the first unarguably living thing created from scratch by the hand of man will divide itself in two and begin to reproduce When it does so, it will abolish, once and for all, a distinction as old as human thought: that between animate and inanimate matter



It is not considered polite, in the circles of synthetic biology as the subject is known, to mention the "F" word. Yet behind almost every discussion of the ethics of modern biology lurks the grinning spectre of Mary Shelley's novel, "Frankenstein", a parable on the unintended consequences of creating life. In truth, there is not much that is ethically dubious about making a bacterium from scratch. Making life is less worrying than modifying life—and modifying it in ways that are accidentally or deliberately harmful to mankind.

Synthetic biology is more than the mere tinkering of biotechnology. That just moves single genes around. Synthetic biologists plan to move lots of genes and to industrialise the process in a way that will let people order biological parts as routinely as they order electrical components. If this vision is realised (and there is still a long way to go) biotechnology will become a true branch of engineering, with benefits for industry, medicine and agriculture (see article and article). But biotechnology will also become a game that almost anyone can play-for fun or profit, recklessly or responsibly, for good or ill.



Life, Reinvented

A group of MIT engineers wanted to model th

### Press Review: Science/Tech



Biologists are crafting libraries of interchangeable DNA parts and assembling them inside microbes to create programmable, living machines

#### **Designs on life**

Earlier this month, students from around the world locked horns in competition. Their challenge vas to build functioning devices out of biplogical parts. Erika Check finds out how they got or

Nature, Nov 2005

By W. Wayt Gibbs

volution is a wellspring of cre- one species to another for 30 years, vet tation and competition have en-

genetic engineering is still more of a craft

Scientific American, May 2004

Reprints | Issue Contents

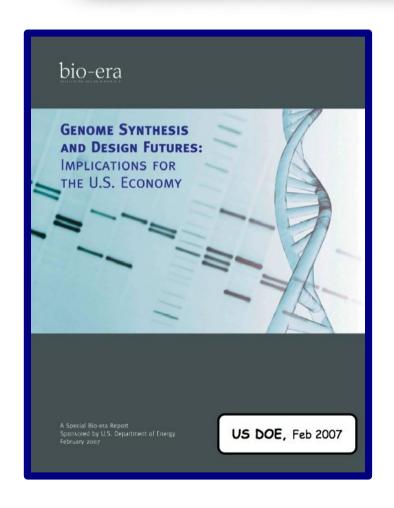
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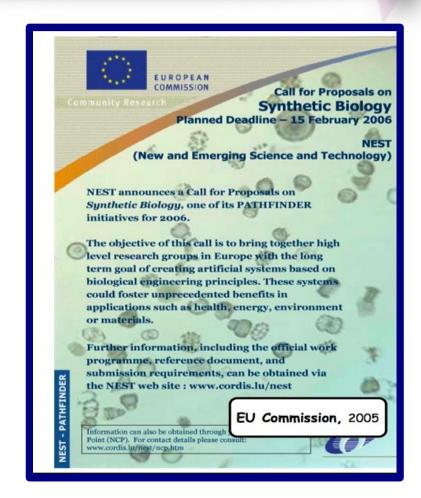
Just What Is Synthetic Biology?

Vincent Rouilly @ Imperial College London, 2008



## Press Review: Govt Institutions





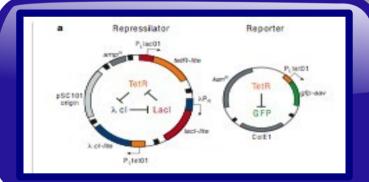


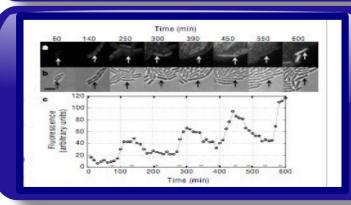
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#### A synthetic oscillatory network of transcriptional regulators

Michael B. Elpwitz & Stanislas Leibler

Departments of Malecular Biology and Physics, Princeton University, Princeton, New Jersey 08544, USA





year 2000

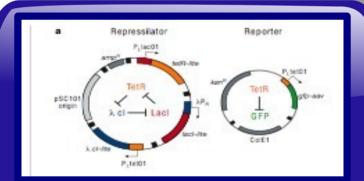
## Seminal Research Papers

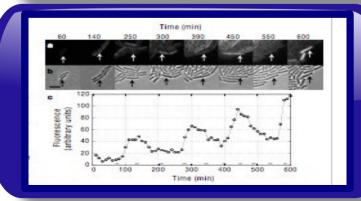
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## synthetic oscillatory network of transcriptional regulators

Michael B. Elowitz & Stanislas Leibler

Departments of Molecular Biology and Physics, Princeton University, Princeton, New Jersey 08544, USA



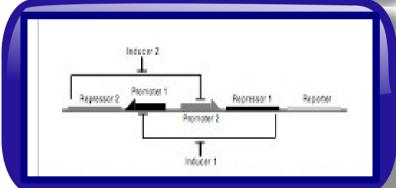


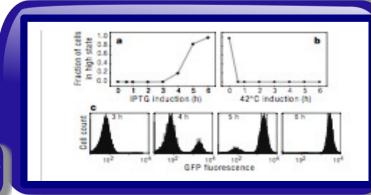
Cited +500X

#### construction of a genetic toggle switch in *Escherichia coli*

Timothy S. Gardner\*†, Charles R. Cantor\* & James J. Collins\*†

\* Department of Biomedical Engineering, † Center for BioDynamics and ‡ Center for Advanced Biotechnology, Boston University, 44 Cummington Street, Boston, Massachusetts 02215, USA

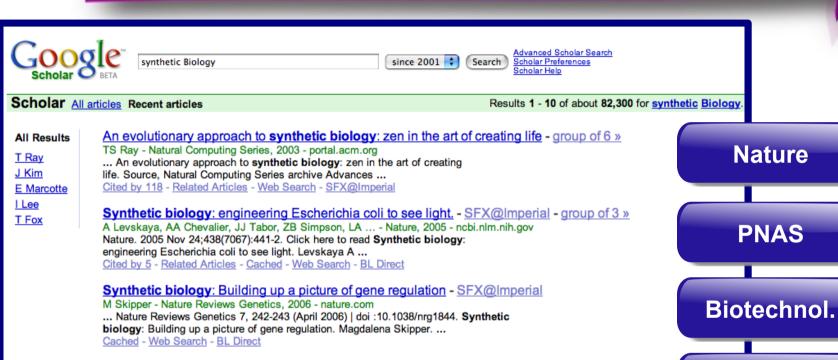




year 2000



## Science in the Making



Synthetic biology: Designs on life - SFX@Imperial - group of 3 »

E CHECK - Nature, 2005 - nature.com

... 438417a. Synthetic biology: Designs on life. Erika ... Synthetic biology aims to merge engineering approaches with biology. Researchers working ...

Related Articles - Cached - Web Search - BL Direct

How synthetic biology can avoid GMO-style conflicts. - SFX@Imperial

M Tepfer - Nature, 2005 - ncbi.nlm.nih.gov

Comment on: Nature. 2005 Aug 18;436(7053):894-5. Click here to read How synthetic biology can avoid GMO-style conflicts. Tepfer ...

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RNA synthetic biology.

F. League D. Duwor H. Colline Nat Biotechnol 2005, pobliple più gov

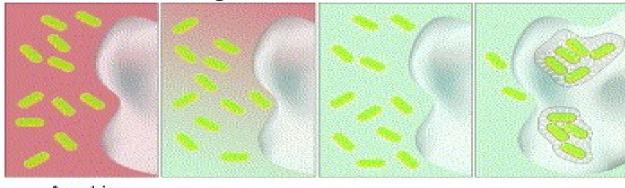
Chem. Eng

Nat. Computing



### **Current Research: Biomedical**

#### Tumor-Killing Bacteria, JC Anderson et al, 2004.



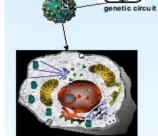
Aerobic Conditions Low Cell Density OFF

Hypoxia High Cell Density ON

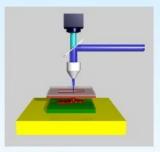
inv Induction

Invasion

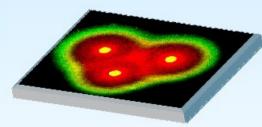
#### Programmed Tissue (Re)generation



Step #1: genetically engineer new communication & differentiation pathways Ron Weiss' Lab, Princeton.



Step #2: Laser Direct Write\* of cells onto a substrate

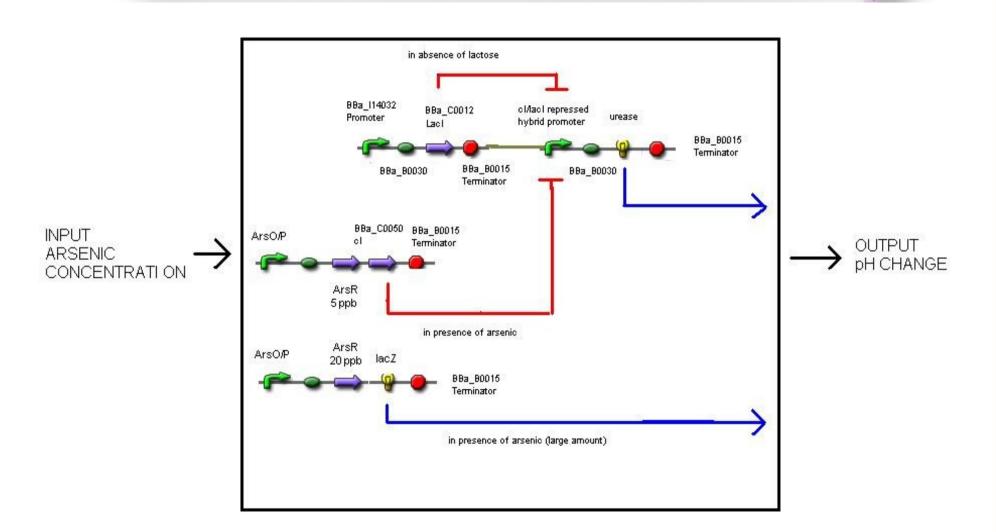


Step #3: pattern formation and tissue generation based on engineered cellcell communication

\* Collaboration with Craig Arnold's Lab



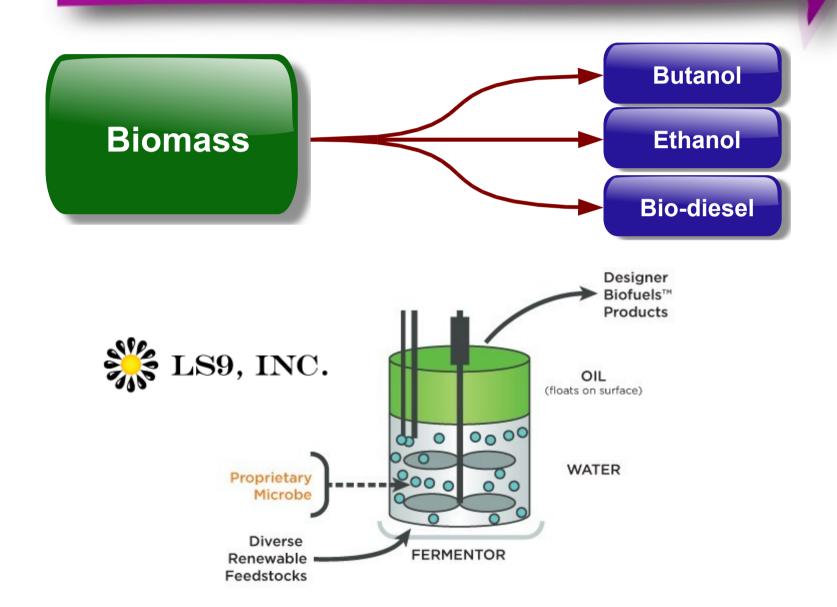
## Current Research: Environment



Arsenic Biosensor, iGEM 2006, Edinburgh Team



# Current Research: Bio-Energy



Vincent Rouilly @ Imperial College London, 2008



# Current Research: Drug Development

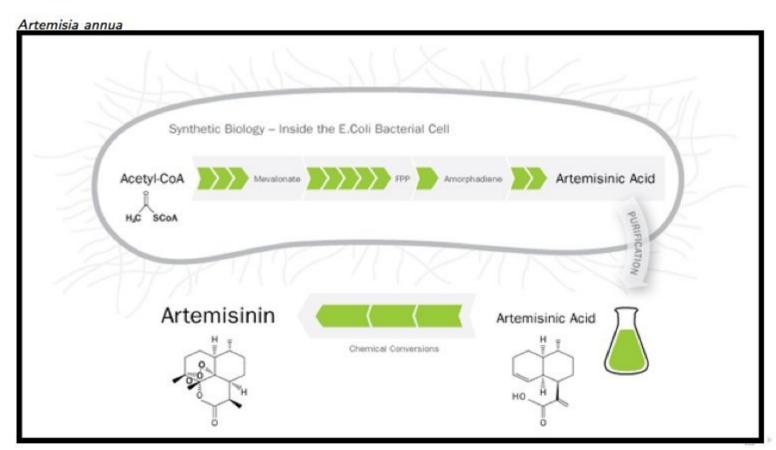
#### Bacterial drug factories







Institute for OneWorld Health
A Nonprofit Pharmaceutical Company

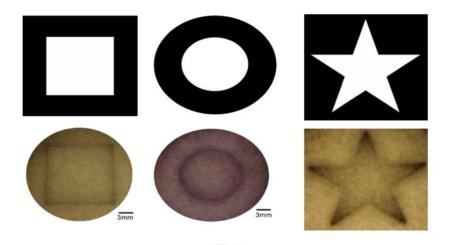


\* from Austin Che's presentation

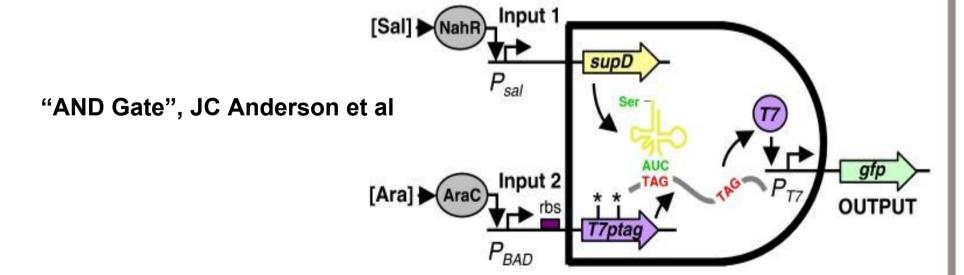


## Current Research: Information Processing

Bacterial signal processing for edge detection



"Bacterial Edge Detector", Jeffrey Tabor



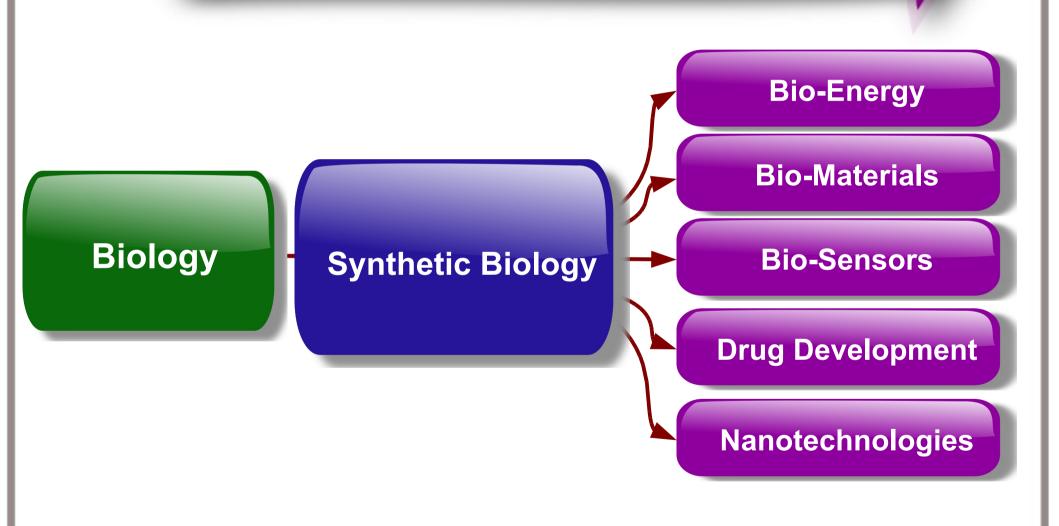


# **Synthetic Biology Definition**

- - -

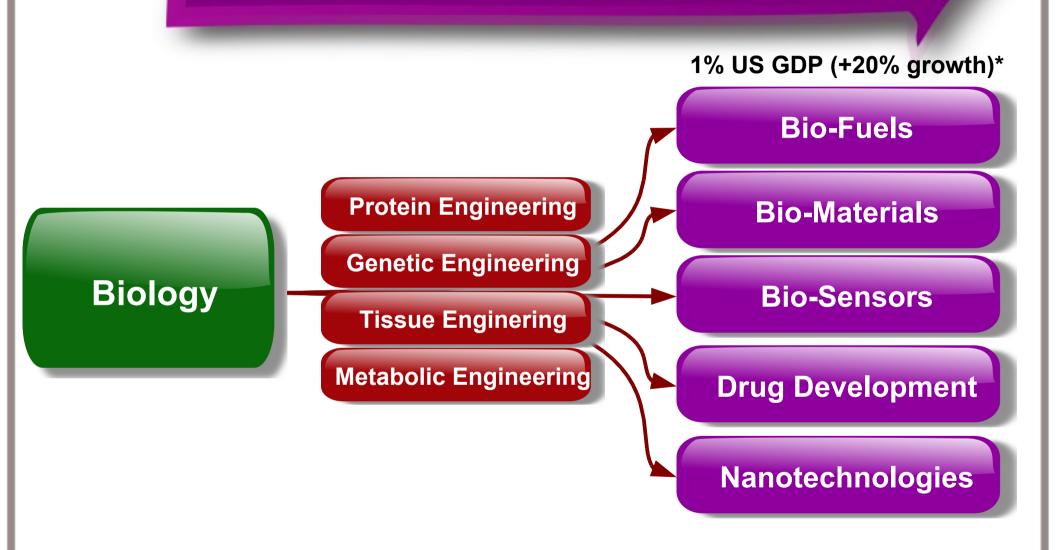


# Defined by its areas of application?





# Defined by its areas of application?



\* Carlson, 2008.



# Defined by its technological platform

# Synthetic Biology Toolbox

**Recombinant DNA** 

**Cloning – Directed Evolution** 

DNA Sequencing DNA Synthesis

High-throughput technologies (NMR, micro-arrays, automation)

Computational Modelling



# Defined by its technological platform '

Synthetic Biology Toolbox

**Protein Engineering** 

**Genetic Engineering** 

**Tissue Enginering** 

**Metabolic Engineering** 

**Recombinant DNA** 

**Cloning – Directed Evolution** 

DNA Sequencing DNA Synthesis

High-throughput technologies (NMR, micro-arrays, automation)

Computational Modelling



# SyntheticBiology.org

#### **Synthetic Biology**

#### Synthetic Biology is

- A) the design and construction of new biological parts, devices, and systems, and
- B) the re-design of existing, natural biological systems for useful purposes.

(Español)





# SyntheticBiology.org

#### **Synthetic Biology**

#### Synthetic Biology is

- A) the design and construction of new biological parts, devices, and systems, and
- B) the re-design of existing, natural biological systems for useful purposes.

(Español)



**Protein Engineering** 

**Tissue Enginering** 

**Genetic Engineering** 

**Metabolic Engineering** 



# iGEM Perspective

#### iGEM - The international Genetically Engineered Machine competition



**iGEM addresses the question:** Can simple biological systems be built from standard, interchangeable parts and operated in living cells? Or is biology simply too complicated to be engineered in this way?

www.parts.mit.edu/wiki



## iGEM Perspective

#### **iGEM** - The international Genetically Engineered Machine competition



**iGEM addresses the question:** Can simple biological systems be built from standard, interchangeable parts and operated in living cells? Or is biology simply too complicated to be engineered in this way?

www.parts.mit.edu/wiki

#### **True Engineering Approach to Biology**

**Standard** 

Interchangeable

**Parts** 

Protein Enginearing

Tisue Enginering

Genetic Englineering

Metabelic Engineering

Vincent Rouilly @ Imperial College London, 2008



# **Engineering Approach**

#### **Industrial Revolutions**

# MechanicalTransportChemicalDigitalMachine Tool<br/>Nuts & BoltsTrains<br/>Car / RoadLarge scale productionHardware<br/>Communication protocolsFile Format



## **Engineering Approach**

**Abstraction** 

**Standardisation** 

**Quality Control** 

#### **Industrial Revolutions**

Mechanical

Transport

**Chemical** 

**Digital** 

Machine Tool

**Trains** 

Car / Road

Large scale production

Hardware

Communication protocols

File Format

**Nuts & Bolts** 

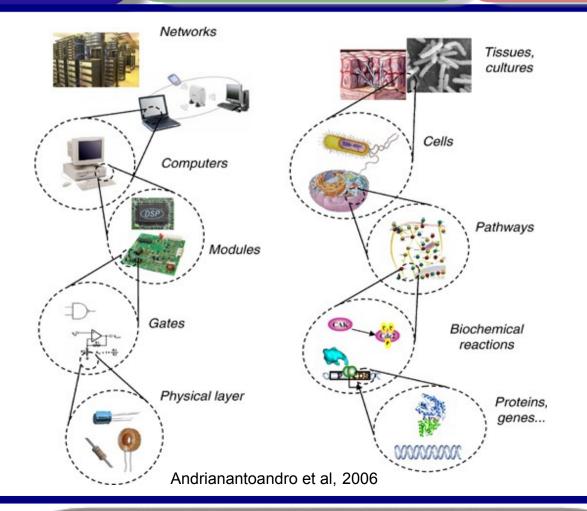


## **Abstraction Principle**

**Abstraction** 

**Standardisation** 

**Quality Control** 



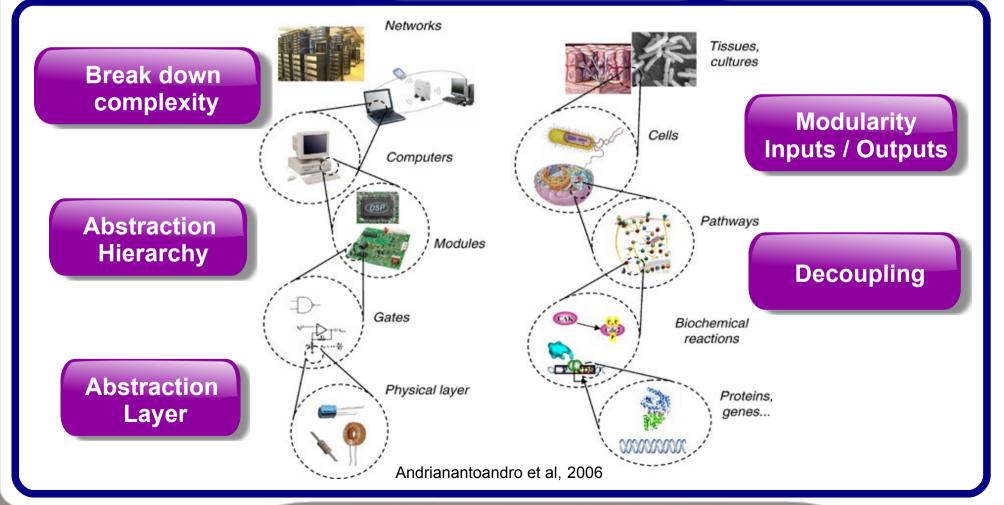


## **Abstraction Principle**

**Abstraction** 

**Standardisation** 

**Quality Control** 



Vincent Rouilly @ Imperial College London, 2008



**Abstraction** 

Standardisation

**Quality Control** 

DNA



**Abstraction** 

**Standardisation** 

**Quality Control** 

**Parts** 



DNA



**Abstraction** 

**Standardisation** 

**Quality Control** 

Devices



**Parts** 



DNA

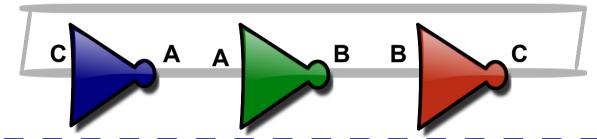




**Standardisation** 

**Quality Control** 





Devices



**Parts** 



DNA



# Standardisation Principle

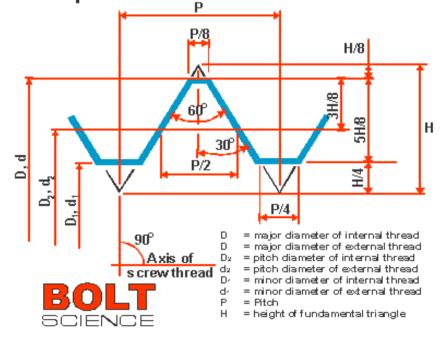
**Abstraction** 

**Standardisation** 

**Quality Control** 



### Basic profile of the Unified and ISO thread form





## Standardisation Principle

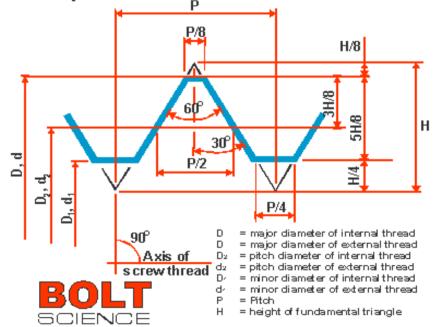
**Abstraction** 

**Standardisation** 

**Quality Control** 



Basic profile of the Unified and ISO thread form



Uniform and agreed

Inter-operability

**Re-usability** 

**Economical Benefits** 



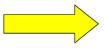
## Standardisation Principles for SB

**Abstraction** 

**Standardisation** 

**Quality Control** 

**Standard Physical DNA composition** 



Topic 2

**Standards Functional Composition** 



Topic 3

**Standard Culture Conditions** 

**Standard Measurements** 

**Standard Cell Host (Chassis)** 



Topic 4

+ Practical



# **Quality Control Principle**

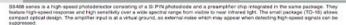
### **Abstraction**

### **Standardisation**

## **Quality Control**

### Si PIN photodiode with preamp S6468 series

High-speed sensor with preamp



- Cut-off frequency (Vcc=5 V)
   S6468 : 15 MHz
   S6468-02: 35 MHz
- Low noise (f=1 MHz)
   S6468 : 25 nVrms/Hz<sup>1/2</sup>
   S6468-02: 28 nVrms/Hz<sup>1/2</sup>
- 3 nin TO-18 nackane

- Optical fiber communication

### ■ Electrical and optical characteristics [Ta=25 °C, Vcc=5 V, Rt=500 Ω, Ct=13 pF] \*

Parameter	Symbol		56468		56465-02				
		Condition	Min.	Тур.	Max.	Min.	Typ.	Max.	Unit
Spectral response range	λ		2000	320 to 1060	1		320 to 1000		nm
Peak sensitivity wavelength	λp			900			800	-	nm
		λ=660 nm	-	13.5	-	-	8.5	-	m/v/µ/W
Photo sensitivity	S	λ=780 nm		15.5	-	- 2	11	-	
		λ=830 nm		16.5	-	-	- 11	-	
Trans-impedance	Rr			30	-		20	-	kΩ
Power supply current	lee	RL==	-	-	3	-	-	3	mA
Output biss voltage "2	Vo	RL=∞ Pin=0 µW	0.55	0.65	0.8	0.65	0.8	0.9	V
Temperature coefficient of output bias voltage		25 - 100-57-00-53	-	-2			-2	-	mV/ °C
Cut-off frequency	fc	Pin=10 µW "3	12	15	-	28	35	-	MHz
Maximum output voltage amplitude		Nonlinear distortion: 10 % Max.	0.5			0.5			Vp-p
Output impedance	Zo	f=5 Hz		30			30		Ω
Output noise voltage	Vn	Pin=0 μW f=1 MHz	20	25	100	8.5	28	-	nW/Hz <sup>10</sup>
Overshoot	S- 0	Pin=10 µW "3			10		-	10	%

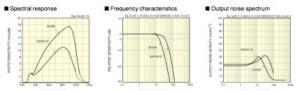
### ■ Absolute maximum ratings

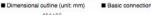
Parameter	Symbol	Min.	Max.	Unit	
Power supply voltage "4"	Voc	-0.5	7	V	
Power dissipation	P		300	mW	
Operating temperature	Topr	-20	70	°C	
Change to see and the	Total	40	****	400	

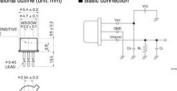
- \*2: Output voltage Vout =Vo-(Pin x S) Pin: incident radiant flux (uW)
- "4: A bypass capacitor (0.01 µF to 0.1 µF ceramic) is connected between the Voc lead and the GND lead.

STATE

### SI PIN photodiode with preamp S6468 series







◆ ESD S6468 series may be damaged or their performance may deteriorate by such factors as electro static discharge from the human body, surgle voltages from measurement equipment, leakage voltages from soldering irons and pucking materials, etc. As a countermeasure against electro shade discharge, the device, operator, over, buce and measuring jate must all be set at the same potential. The blottering precautions must be observed during user to expend the properties of th

At Bit Cut and profession read after capitation from the profession and the Capitation from the Capitation

### HAMAMATSU



## **Quality Control Principle**

### **Abstraction**

### **Standardisation**

### **Quality Control**

### Si PIN photodiode with preamp S6468 series

High-speed sensor with preamp

S6468 series is a high-speed photodetector consisting of a Si PIN photodiode and a preamptifier chip integrated in the same package. They feature high-speed response and high sentitify over a wide spectra range from visible to near thirdered tight. The small package (TO-18) spectra range from visible to have infriend tight. The small package (TO-18) spectra range from the proper when design the proper special special scan be determined by the proper when the proper special scan be determined by the proper when the proper special scan be designed by the proper special special scan be designed by the proper special scan be designed by the proper special scan be designed by the proper special special scan be designed by the proper special scan be designed by the proper special scan be designed by the proper special special scan be designed by the proper special scan be designed by the proper special scan be designed by the proper special special scan be designed by the proper special scan be designed by the proper special scan be designed by the proper special special scan be designed by the proper special scan be designed by the proper special scan be designed by the proper special special scan be designed by the proper spe

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- Optical fiber communication

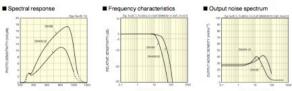
### ■ Electrical and optical characteristics [Ta=25 °C, Vcc=5 V, Rt=500 Ω, Ct=13 pF] \*

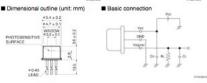
Parameter	Symbol	Condition						Unit	
		Condition	Min.	Тур.	Max.	Min.	Typ.	Max.	Unit
Spectral response range	λ		100000	320 to 1060	1		320 to 1000		nm
Peak sensitivity wavelength	λp	- 1	-	900			800	-	nm
		λ=660 nm	-	13.5	-	-	8.5		mV/µW
Photo sensitivity	S	λ=780 nm	-	15.5	-		11	-	
		λ=830 nm	-	16.5	-	-	- 11	-	
Trans-impedance	Rr	and the same of	-	30	-	-	20	-	ks2
Power supply current	lee	RL==	-	-	3	-	-	3	mA
Output biss voltage "2	Vo	RL=∞ Pin=0 µW	0.55	0.65	0.8	0.65	0.8	0.9	V
Temperature coefficient of output bias voltage		71 000 1700 000	-	-2	-		-2	-	mV/
Cut-off frequency	fc	Pin=10 g/W "	12	15	-	28	35	-	MHz
Maximum output voltage amplitude		Nonlinear distortion: 10 % Max.	0.5			0.5			Vp-p
Output impedance	Zo	f=5 Hz		30			30		Ω
Output noise voltage	Vn	Pin=0 μW f=1 MHz	*6	25	100	6.5	28		nW/Hz <sup>10</sup>
Overshoot		Pin=10 µW "	-		10	-	-	10	%

Parameter	Symbol	Symbol Min.		Unit	
Power supply voltage "4"	Voc	-0.5	7	V	
Power dissipation	P		300	mW.	
Operating temperature	Topr	-20	70	°C	
Storage temperature	Tstg	-40	100	°C	

- \*2: Output voltage Vout =Vo-(Pin x S) Pin: incident radiant flux (uW)

### SI PIN photodiode with preamp S6468 series







♠ ESD S6488 series may be damaged or their performance may deteriorate by such factors as electro static discharge from the human body, surgle voltages from measurement equipment, leakage voltages from soldering mors and packing materials, etc. As a countermeasure against electro static discharge, the device, operating voxyl place and measuring jigs must all be set at the same potential. The florid precautions must be observed during use:

1 by proceedings to be device them electro static discharge which accumulate on the operator or the operator's clothes, use a wrist strap or similar tools to ground the operator's body via a high impediance resister (1 MI).

1 A semiconductive sheet (1 MI3 to 10 MI3) should be flat on both the work table and the floor in the work area.

1 For containing and packing, use of a consolicity material or allumination to its effective. When using an artistatic material, use one with a resistance of V. MiXem\* to 1 GSB.

**Specification Sheet** 

**Characterisation** under Standard Conditions

**Tolerances / Reliability** 

**Trust** 

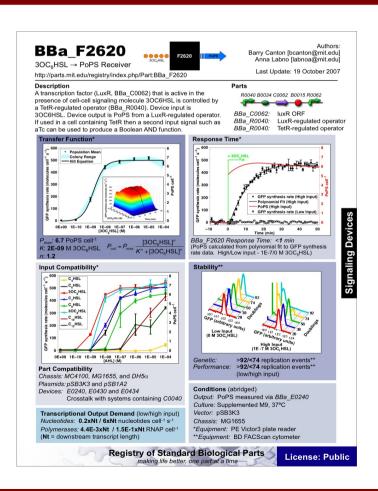


# **Quality Control Principle**

### **Abstraction**

Standardisation

**Quality Control** 

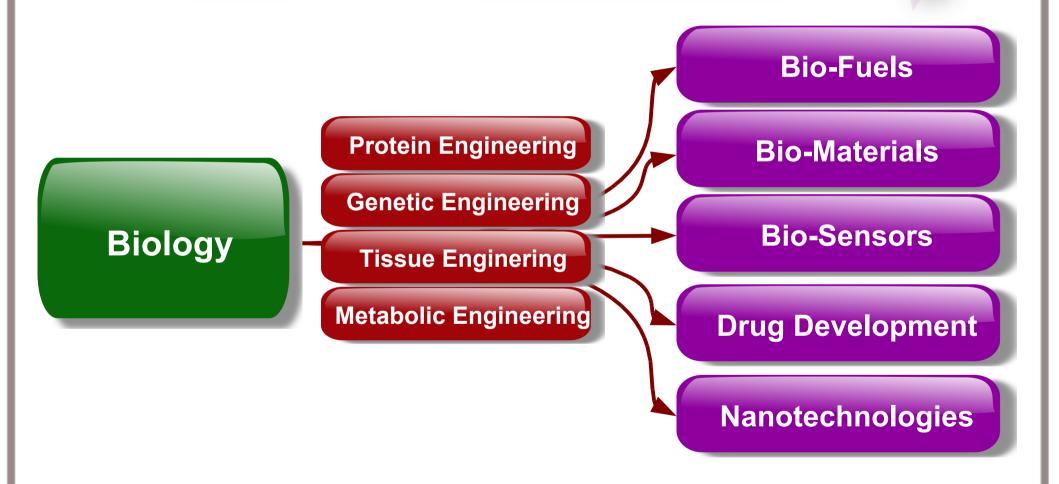




Registry of Standard Biological Parts



# Synthetic Biology Methodology





**Biology** 

# Synthetic Biology Methodology



Registry of Standard Biological Parts

**Protein Engineering** 

**Genetic Engineering** 

Tissue Enginering

**Metabolic Engineering** 

Synthetic Biology Methodology

'build more success on previous success'

**Bio-Fuels** 

**Bio-Materials** 

**Bio-Sensors** 

**Drug Development** 

**Nanotechnologies** 

Vincent Rouilly @ Imperial College London, 2008



# But .... Engineering Challenges Ahead



"What I cannot create, I do not understand."

Richard Feynman (1918-1988)

inspired by Austin Che's presentation



What will be the impact of making biology easier to engineer?



What will be the impact of

making biology easier to engineer?

More People

**More Powerful DNA Programs** 

Faster Development

from Drew Endy's talk, Tianjin 2007

Vincent Rouilly @ Imperial College London, 2008



## Resulting Issues

**Bio Safety** 

**Bio Security** 

Ownership, Sharing, Innovation

**Ethics** 

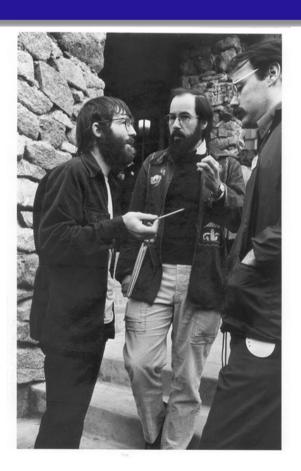
**Community** 

from Drew Endy's talk, Tianjin 2007



### Asilomar (1975)

Recombinant DNA conference



### What has changed?

- 1. Databases populated with sequence information.
- 2. The Internet
- 3. Early improvements in automated DNA construction technology.
- 4. Overnight shipping.
- 5. Expanded concern re: active misapplication of biotech.



Revitalise knowledge of biological safety

Avoid re-militarisation of biological technologies

Regardless, expect that technology will be misapplied. Prepare.

Develop an ownership & sharing framework that maximizes innovation and equity.

Build a community who can lead development of a constructive culture in Biological Engineering.

from Drew Endy's talk, Tianjin 2007



# Synthetic Biology Community

You are now part of it !!!

Engage ... Challenge ... Contribute





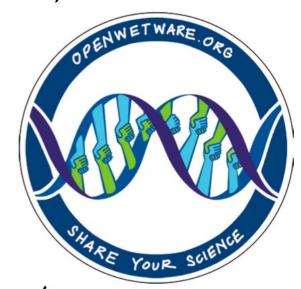




## References



- > Drew Endy's Talks (on OWW)
- > Austin Che Presentations
- > OpenWetWare Folks
- > iGEM Competition
- > BioBricks Foundation

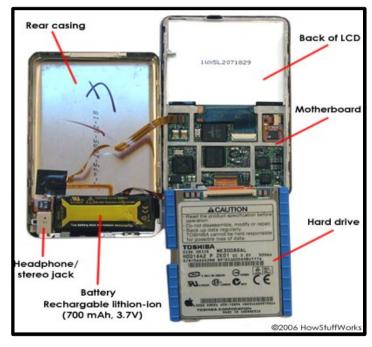






# Example: iPod





### Features:

Audio / Video / Photos External hard drive Calendar / Contacts Games Car Integration

