Synthetic Biology

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A Scientist discovers *that which exists*; an Engineer creates *that which never was*.

-- Theodore Von Kármán
“Synthetic biology is an emerging area of research that can broadly be described as the design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems.”
Technology of synthetic biology
It’s all about DNA…

DNA is the machine language program for biochemical processes
The ability to manipulate this one molecule allows virtually anything biological to be engineered!

DNA is to biology as the electron is to computing
Reading code
1980
500 bp/day (manual)

1987
36,000 bp/day (semi-auto)

1995
144,000 bp/day (semi-auto)

1998
500,000 bp/day (automatic)

2007 – Sequencing by Synthesis
1GB bp/day (automatic)
The breakthrough of our lifetime... the X PRIZE about each of us.

Revolution Through Competition.
280.6 TFLOPS with 131072 nodes
Writing code: synthesis
If we can’t build it, we don’t understand it.
if you can write DNA,
you're no longer limited
to "what is"
but to what you could make
Digital DNA “design”

Physical DNA and outputs
EGFP gene 714 bp
Applications dependent on synthetic capabilities

- Single genes
- Minimal life

Base pairs:
- $10^2$
- $10^3$
- $10^4$
- $10^5$
- $10^6$
- $10^7$

Genetic circuits, viruses, GEMs
Engineered organisms
Sponsored Links

**Blue Heron Bio GeneMaker**
Call now for promotional pricing!
The **DNA Synthesis** Specialists.
www.blueheronbio.com

**Gene Synthesis in a Flash**
1 kb within 8 business days,
3 kb within 13 business days!
www.geneart.com

**Gene Synthesis $1.10/bp**
For small, large & difficult genes.
Free subcloning services
www.celtek-genes.com

**Gene Synthesis $0.69/bp**
Fast Delivery, 100% Sequenced, from
The Constructive Biology Company TM
codondevices.com/constructedclones

**Custom PNA Synthesis**
Peptide nucleic acid conjugates
PNA Chimera, PNA modifications
pnaoligos.com

**Rapid Gene Synthesis**
Superfast Turnaround Guaranteed!
Low Cost, Individualized Support
www.DNA20.com
- -5 years: 0.5 - 5kb, $10-$15/bp
- 0 years: 50 - 500kb $0.50-$1/bp
- +5 years: 5mb - 5gb <$0.0001/bp

18 July 05. Method: Rough Google search. Thus not a thorough survey. No academic facilities.

Data Source: Rob Carlson, U of W, Seattle; www.synthesis.cc, rob@synthesis.cc

Engineering philosophy
Engineering process...

- Some success
- More success
- Even more success

refinement

complexity

- Electronics
- Software
- Aeronautics
- Structures
- Materials
- Automotives
Name: B0015  
Type: Double terminator  
Length 129 bp  
Designed by: Reshma Shetty  
Forward efficiency: 0.984  
Reverse efficiency: .295
STANDARDIZED DATA

System

Device

Part

DNA

Synthetic system or cell

F1760 Sender Device

B0015 terminator

ccaggcatcaaataaaacgaaaggctcagtcgaaagactgggcctttctggtttatatctgttgtttgtcggtgaacgctctctactagagtcacactggctcaccttcgggtgggcctttctgcgtttata
# Transcriptional Regulators

## Available repressible regulators (normally ON)

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Direction</th>
<th>Control</th>
<th>Output Low</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBa 14032</td>
<td>promoter P(Lac)Iq</td>
<td>Forward</td>
<td>aTC, tetracycline</td>
<td>Hi</td>
<td>37</td>
</tr>
<tr>
<td>BBa R0040</td>
<td>promoter (terR, negative)</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>54</td>
</tr>
<tr>
<td>BBa R0051</td>
<td>promoter (lambda cl regulated)</td>
<td>Forward</td>
<td>lambda cl</td>
<td>Hi</td>
<td>49</td>
</tr>
</tbody>
</table>

## Available inducible regulators (normally OFF)

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Direction</th>
<th>Control</th>
<th>Output Low</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBa J12007</td>
<td>Modified lambda Prm promoter (OR-3 obliterated)</td>
<td>Forward</td>
<td>cl</td>
<td>Hi</td>
<td>62</td>
</tr>
<tr>
<td>BBa R0062</td>
<td>Promoter (luxR &amp; HSL regulated -- luxP)</td>
<td>Forward</td>
<td>luxR, HSL</td>
<td>Hi</td>
<td>56</td>
</tr>
<tr>
<td>BBa R0079</td>
<td>Promoter (LasI &amp; PAI regulated)</td>
<td>Forward</td>
<td>PAI</td>
<td>Hi</td>
<td>157</td>
</tr>
<tr>
<td>BBa R0080</td>
<td>Promoter (AraC regulated)</td>
<td>Forward</td>
<td>araC</td>
<td>Hi</td>
<td>149</td>
</tr>
</tbody>
</table>

## Available other regulators

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Direction</th>
<th>Control</th>
<th>Output Low</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBa J0500</td>
<td>Inducible pBAD/araC</td>
<td>Forward</td>
<td>araC, arabinose</td>
<td>Hi</td>
<td>1210</td>
</tr>
<tr>
<td>BBa J3453</td>
<td>Pbad promoter</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>130</td>
</tr>
<tr>
<td>BBa J3002</td>
<td>TetR repressed POPS/RIPS generator</td>
<td>Forward</td>
<td>ATc</td>
<td>Hi</td>
<td>74</td>
</tr>
<tr>
<td>BBa J3023</td>
<td>AOCBHL/LuxR dependent POP/RIPS generator</td>
<td>Forward</td>
<td></td>
<td>Hi</td>
<td>117</td>
</tr>
<tr>
<td>BBa J23101</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23102</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23103</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23104</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23105</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23106</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23107</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23108</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
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<tr>
<td>BBa J23109</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23110</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
<tr>
<td>BBa J23111</td>
<td>constitutive promoter family member</td>
<td>Forward</td>
<td></td>
<td>Low</td>
<td>35</td>
</tr>
</tbody>
</table>
**Part BBa_F2620: Design**

**BBa_F2620**: 3OC_HSL → PoPS Receiver

**Description**
A transcription factor (LuxR, BBA_C0062) that is active in the presence of cell-cell signaling molecule 3OC_HSL is controlled by a TetR-regulated operator (BBa_R0040). Device input is 3OC_HSL. Device output is PoPS from a LuxR-regulated operator. If used in a cell containing TetR then a second input signal such as aTc can be used to produce a Boolean AND function.

**Characteristics**
- **Input Swing**: 1E-9 to 1E-6 M 3OC_HSL, exogenous
- **Output Swing**: 0±1 to 50±1 GFP molecules cm⁻2 s⁻¹
- **Switch Point**: 7±1 nM 3OC_HSL, exogenous
- **LH Response**: 5 min (t₀), 27 min (t₅₀)

**Response Time**
- **Specificity**
- **Stability**

**Key Parts**
- **BBa_R0040**: TetR-regulated operator
- **BBa_C0062**: luxR ORF
- **BBa_R0002**: LuxR-regulated operator

**Transfer Function**

**Registration**

Registry of Standard Biological Parts
making life better, one part at a time

License: Public
Shares:

• DNA parts
• DNA code
• Protocols
• Experience
• Publications
Designs on life

Earlier this month, students from around the world locked horns in competition. Their challenge was to build functional biological circuits out of biological parts. BioBrick found out how they got on.

Genetic 'Jamboree' draws innovators

Science students the world over share research.
Light Sensitive Signal Transduction:

- **Cph1** chromophore biosynthesis:
  - Cph1
  - Phycocyanobilin
  - pcyA
  - to 1
  - heme

Black output (G-gal):

- Black output

**Env Z**

**OmpR**

**LacZ**

**PompC**

**LacZ**

632nm bandpass filter

Double Guass focusable lens

Mercury vapor lamp

35mm slide

Projected image
indole deficient tnaA5^- chassis

chorismate \rightarrow SAGD \rightarrow salicylic acid

leucine \rightarrow IAGD \rightarrow 3-methylbutanal

NADH \rightarrow \text{isoamyl alcohol}\rightarrow NAD^+

methyl salicylate \rightarrow osmY \rightarrow WGD

\text{isoamyl acetate}
iGEM 2007

- 57 teams – 20 countries
  - USA (26)
  - Scotland (3)
  - Colombia
  - Italy (2)
  - Mexico
  - Taiwan
  - Russia
  - Germany
  - South Africa
  - Middle East
  - Canada (6)
  - Japan (2)
  - Australia
  - England
  - Switzerland
  - China (4)
  - Spain
  - India
  - France
  - Slovenia
U of A iGEM Team

• Biobutanol project – “Plan B”
• Moving metabolic pathway from Clostridium into E. coli
Opportunities for Alberta
Synthetic biology is going to grow fast!

Source: Bio era
PIMP MY GENOME!
SYNTHETIC BIOLOGY:
A PLAN FOR ENGINEERING BIOLOGY

Wednesday April 4, 2007
University of Alberta, Telus Centre, Room 150
111 Street and 87 Avenue
Edmonton, AB
Doors open and refreshments - 3:00 PM
Presentation - 3:30 PM
Complimentary return bus transportation will be provided to guests from the University of Calgary.

Join Drew Endy, a leader in synthetic biology from MIT, for an engaging look at how biological engineering is changing. Find out how the latest advances in this new area of biology are helping make WAR better, cheaper and easier.

Drew is a fellow in the Department of Biology and the Biomedical Engineering Division at MIT. He co-founded the MIST Synthetic Biology working group and the Registry of Standard Biological Parts. He is also co-founder of IGEM, the international Genetically Engineered Machine competition. Codon Devices Inc., a venture-funded startup that is working to develop next-generation DNA synthesis technology, and the Biodesign Foundation, a non-profit organization that is working to develop legal and economic strategies needed to support open biotechnology. Drew’s work has been featured in The Economist, Forbes, Wired, Scientific American and the New York Times.

For registration and more information, please visit www.albertaingenuity.ca.

The Alberta Ingenuity Fund supports science and engineering research at the highest levels to create a prosperous future for the province. It does this through funding from a $1.5 billion endowment established and managed by the Government of Alberta to build the capacity for innovation, especially in areas with long lasting social and economic impact.
Engineering synthetic biological constructs will become the foundational technology of the 21st century Tom Knight, MIT, SB3

- Biology > Physics ($, staff, discoveries)
- Biology is more important than physics, as measured by its economic outputs, ethical implications, and effects on human welfare
- Alberta already has a vibrant bio-economy
- Well-positioned to become a global leader in synthetic biotechnologies is we act quickly and decisively
MIT establishes groundbreaking biological engineering major

February 17, 2005

The Massachusetts Institute of Technology faculty yesterday approved a new course of study for undergraduates, in biological engineering, the first entirely new curriculum established at the Institute in 29 years.
2/1/2007 - BP awards $500 million bioenergy grant
Global energy firm BP has selected UC Berkeley, in partnership with Lawrence Berkeley National Laboratory and the University of Illinois, to lead an unprecedented $500 million research effort to develop new sources of energy and reduce the impact of energy consumption on the environment. The funding will create the Energy Biosciences Institute, which initially will focus its research on biotechnology to produce biofuels. QB3 helped coordinate the research proposal and will help administer the project. More >

6/26/2007 - Bay Area partnership to host DOE bioscience center
The U.S. Department of Energy has announced the creation of a new bioenergy research center, with UC Berkeley and Lawrence Berkeley National Laboratory as two of its six collaborating institutions. The Joint BioEnergy Institute — to be headquartered in the East Bay and led by Jay Keasling — will receive approximately $125 million in DOE funding over five years. More >

8/3/2006 - New center poised to transform biotech
Aided by a $16 million NSF grant, QB3 has launched the Synthetic Biology Engineering Research Center at UC Berkeley, with collaborators at UC San Francisco, MIT, Harvard, and Prairie View A&M University. Researchers hope to make it as quick and easy to engineer biology as it now is to assemble microprocessors, hard drives, and memory chips into a computer. More >
Build a bio-fab to support research community and next-gen companies
Monday, April 09, 2007

DNA Factories

Cheaply churning out made-to-order DNA could revolutionize molecular biology.

By Emily Singer
Welcome

Amyris Biotechnologies is translating the promise of synthetic biology into solutions for real-world problems. Building on advances in molecular, cell and systems biology, we are engineering microbes capable of producing high-value compounds to address major global health and energy challenges. We are employing these living chemical factories to produce novel pharmaceuticals, renewable fuels, and specialty chemicals.
• Applications (health, biofuels, bioproducts)

• Software: Metabolic and genomic design tools

• Hardware: Advanced synthesis hardware, biological test and measurement devices

• Ethics and social policy of synthetic biology

• Educational program development

• Next-generation biotechnology company development
ADVENTURES IN SYNTHETIC BIOLOGY

STORY: DREW ENDY  ISADORA DEESE
THE MIT SYNTHETIC BIOLOGY WORKING GROUP
ART: CHUCK WADEY  www.chuckwadey.com

ENGINEERED GENETIC DEVICES

I KNOW BACTERIA BALLOONS WOULDN'T WORK...

IF ONLY THERE WAS SOME WAY TO STOP THEM FROM BURNING 

UNTIL THEY EXPLODE!

PARTS OF AN INVERTER

1. RBS - Basic elements that start the process of protein 

synthesis.

2. Repressor - A gene that encodes a particular 

proteins that inhibit the expression of certain 

genes.

3. Terminator - Special elements that 

down-regulate the expression of DNA. 

and so on.

4. Operator - Special elements that 

inhibit the expression of DNA. 

INVERTER!

OK, PAY ATTENTION!

AN INVERTER IS A COMBINATION OF BASIC 

DNA PARTS THAT...

WORKING TOGETHER, TURN OFF 

SOMETHING INSIDE 

BECAUSE OFF 

LOW REGULATES HIGH, 

AND SO ON.

YOU COULD HAVE USED AN 

INVERTER DEVICE TO HELP 

PREVENT BUDDY'S 

UNFORTUNATE ACCIDENT.

WHAT THE HECK IS AN 

INVERTER?

IT COULD BE THE ANSWER YOU'RE LOOKING FOR.
For ages 8 and up
Adult Supervision Required
Materials included except for the items listed.
Through play, hands-on projects, patterns and puzzles
this book and kit explores the amazing DNA story.