Three pillars of synthetic biology

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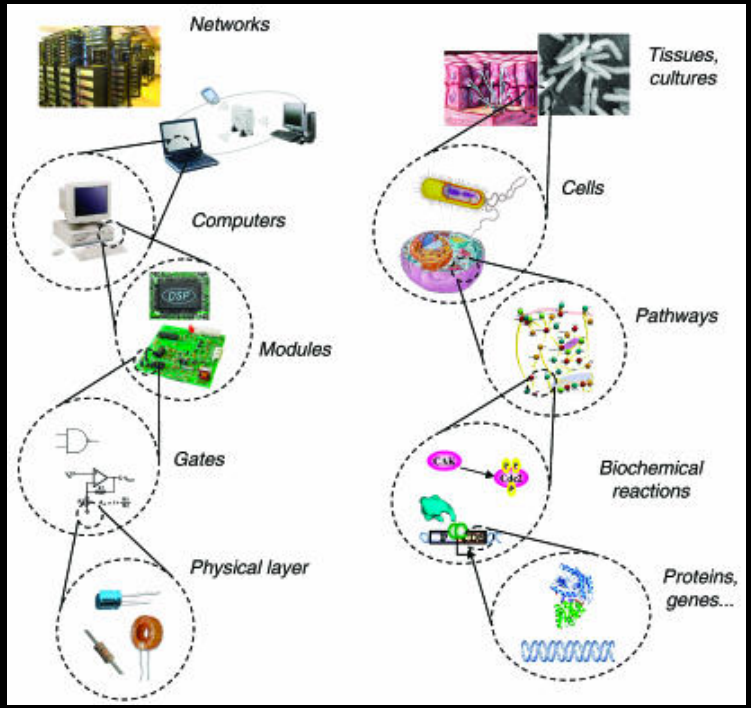
The Economist
The new era of corporate scandal
Algeria kicks out its dictator
Why Europe's banks are so rotten
Great wheels of China
APRIL 6TH–12TH 2019
Redesigning life
The promise of synthetic biology

April 2019

Synthetic biology's vision: cell as computer



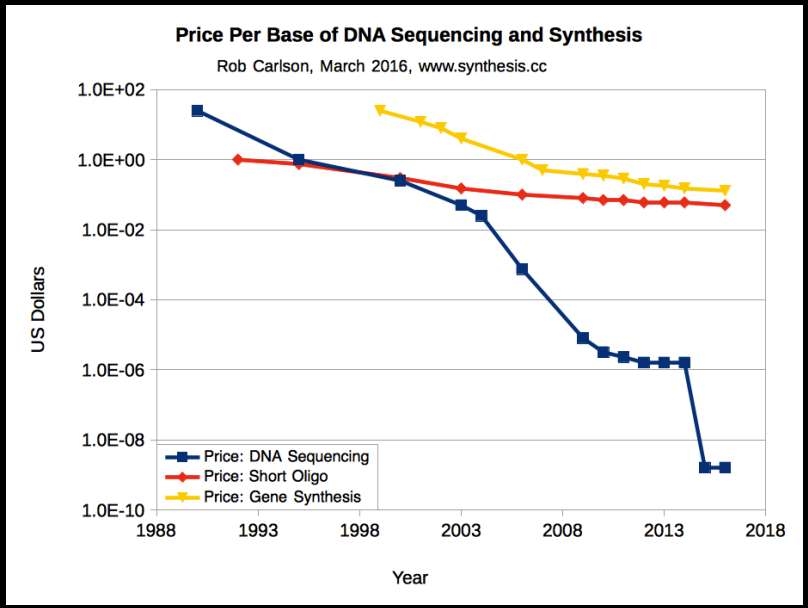
Weiss 2009

1

Synthesizing DNA of any length and sequence

It is harder to write DNA than to read it

Many efforts to reduce the error rate in DNA synthesis



It is harder to write DNA than to read it

SGI desktop DNA printer
500,000 SEK

Build to learn

SCIENCE

Researchers Say They Created a 'Synthetic Cell'

By NICHOLAS WADE MAY 20, 2010

New York Times 2010

"WHAT I CANNOT CREATE, I DO NOT UNDERSTAND"

Encoded into genome of "M. laboratorium."
500 necessary genes have unknown function

What will we (try to) build next?

Forbes 2016

Svante Pääbo

ARTICLE

doi:10.1038/nature12886

The complete genome sequence of a Neanderthal from the Altai Mountains

Kay Prüfer[1], Fernando Racimo[2], Nick Patterson[3], Flora Jay[2], Sriram Sankararaman[3,4], Susanna Sawyer[1], Anja Heinze[1], Gabriel Renaud[1], Peter H. Sudmant[5], Cesare de Filippo[1], Heng Li[3], Swapan Mallick[3,4], Michael Dannemann[1], Qiaomei Fu[1,6], Martin Kircher[1,5], Martin Kuhlwilm[1], Michael Lachmann[1], Matthias Meyer[1], Matthias Ongyerth[1], Michael Siebauer[1], Christoph Theunert[1], Arti Tandon[3,4], Priya Moorjani[4], Joseph Pickrell[4], James C. Mullikin[7], Samuel H. Vohr[8], Richard E. Green[8], Ines Hellmann[9]†, Philip L. F. Johnson[10], Hélène Blanche[11], Howard Cann[11], Jacob O. Kitzman[5], Jay Shendure[5], Evan E. Eichler[5,12], Ed S. Lein[13], Trygve E. Bakken[13], Liubov V. Golovanova[14], Vladimir B. Doronichev[14], Michael V. Shunkov[15], Anatoli P. Derevianko[15], Bence Viola[16], Montgomery Slatkin[2], David Reich[3,4,17], Janet Kelso[1] & Svante Pääbo[1]

2

Making DNA “circuits”

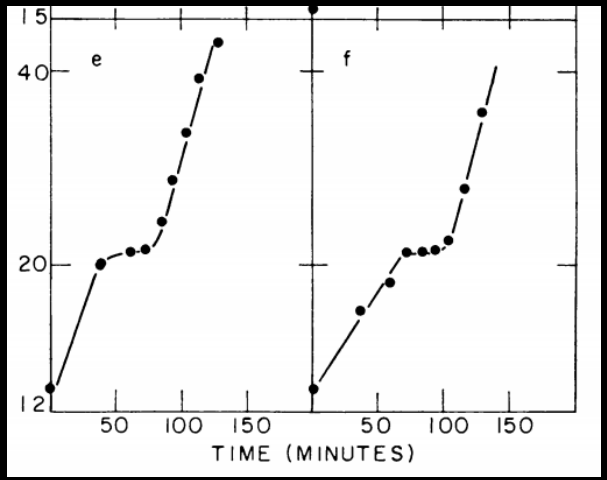
Logic gates for genes have already evolved

JOURNAL OF BACTERIOLOGY, Apr., 1967, p. 1397-1401
Vol. 93, No. 4

Glucose-Lactose Diauxie in *Escherichia coli*

WILLIAM F. LOOMIS, JR.,[1] AND BORIS MAGASANIK
Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts

Received for publication 5 November 1966



"What is true for *E. coli* must also be true for the elephant." *-Monod 1960s*

How it started

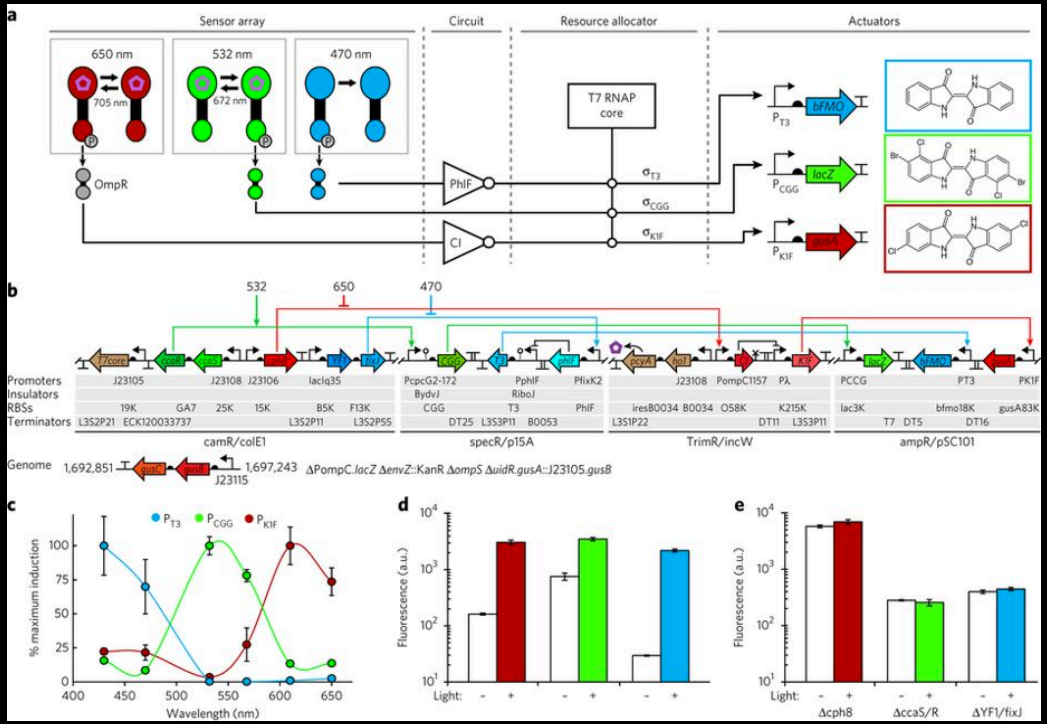
A	B	OUT
0	0	0
1	0	0
0	1	0
1	1	1

A: “Lactose”
B: “No Glucose”

Out: Genes for lactose degrade

How it’s going

Voigt 2017: “Color photography by GMO E. coli”



…circuitry under the hood

“Living therapies” will use logic gates

Seek and destroy (and obey)

3

Editing DNA in the genome

GMOs of the past: not genome edited

Aquabounty

The rapid growth rate of a genetically engineered AquaBounty salmon (left) is obvious when compared to a non-GE salmon (right) of the same age

GloFish (1999)

AquAdvantage salmon (1990)

Gene editing tool was hiding in plain, white sight

Streptococcus thermophilus;
the source of CRISPR/Cas9

The DNA cut is the opportunity for editing

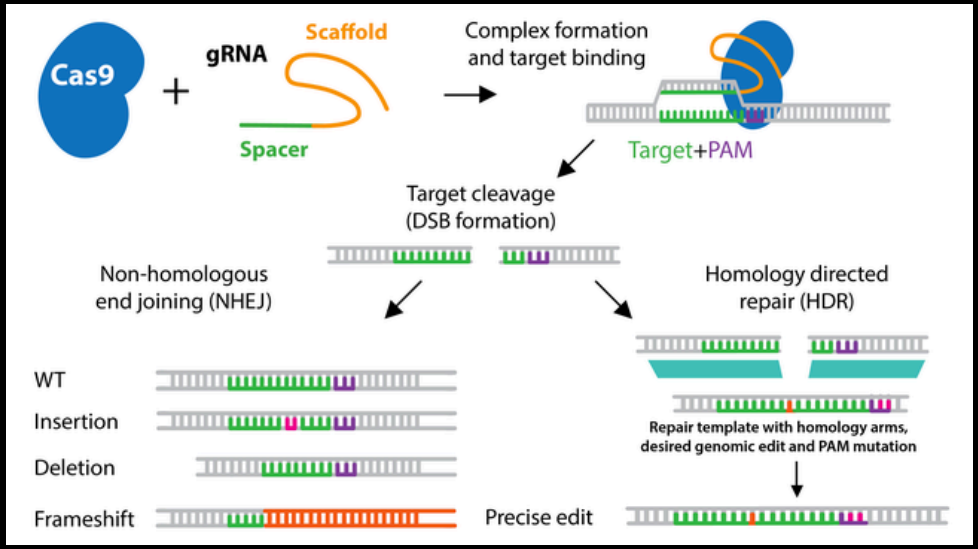


Image: Addgene

Medical biotechnology:
Pigs as clean organ factories

Church lab Harvard, 2015

Industrial biotechnology

SYNTHETIC BIOLOGY

Complete biosynthesis of opioids in yeast

Stephanie Galanie,[1] Kate Thodey,[2] Isis J. Trenchard,[2] Maria Filsinger Interrante,[2] Christina D. Smolke[2]*

Opioids are the primary drugs used in Western medicine for pain management and palliative care. Farming of opium poppies remains the sole source of these essential medicines, despite diverse market demands and uncertainty in crop yields due to weather, climate change, and pests. We engineered yeast to produce the selected opioid compounds thebaine and hydrocodone starting from sugar. All work was conducted in a laboratory that is permitted and secured for work with controlled substances. We combined enzyme discovery, enzyme engineering, and pathway and strain optimization to realize full opiate biosynthesis in yeast. The resulting opioid biosynthesis strains required the expression of 21 (thebaine) and 23 (hydrocodone) enzyme activities from plants, mammals, bacteria, and yeast itself. This is a proof of principle, and major hurdles remain before optimization and scale-up could be achieved. Open discussions of options for governing this technology are also needed in order to responsibly realize alternative supplies for these medically relevant compounds

Smolke lab, Stanford 2015

Three pillars of synthetic biology

1. Synthesizing DNA of any sequence
2. DNA “circuits” that respond to stimulus
3. Genome editing

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