qbio quantitative biology

UNIVERSITÉ DE MONTPELLIER

An introduction to synthetic biology

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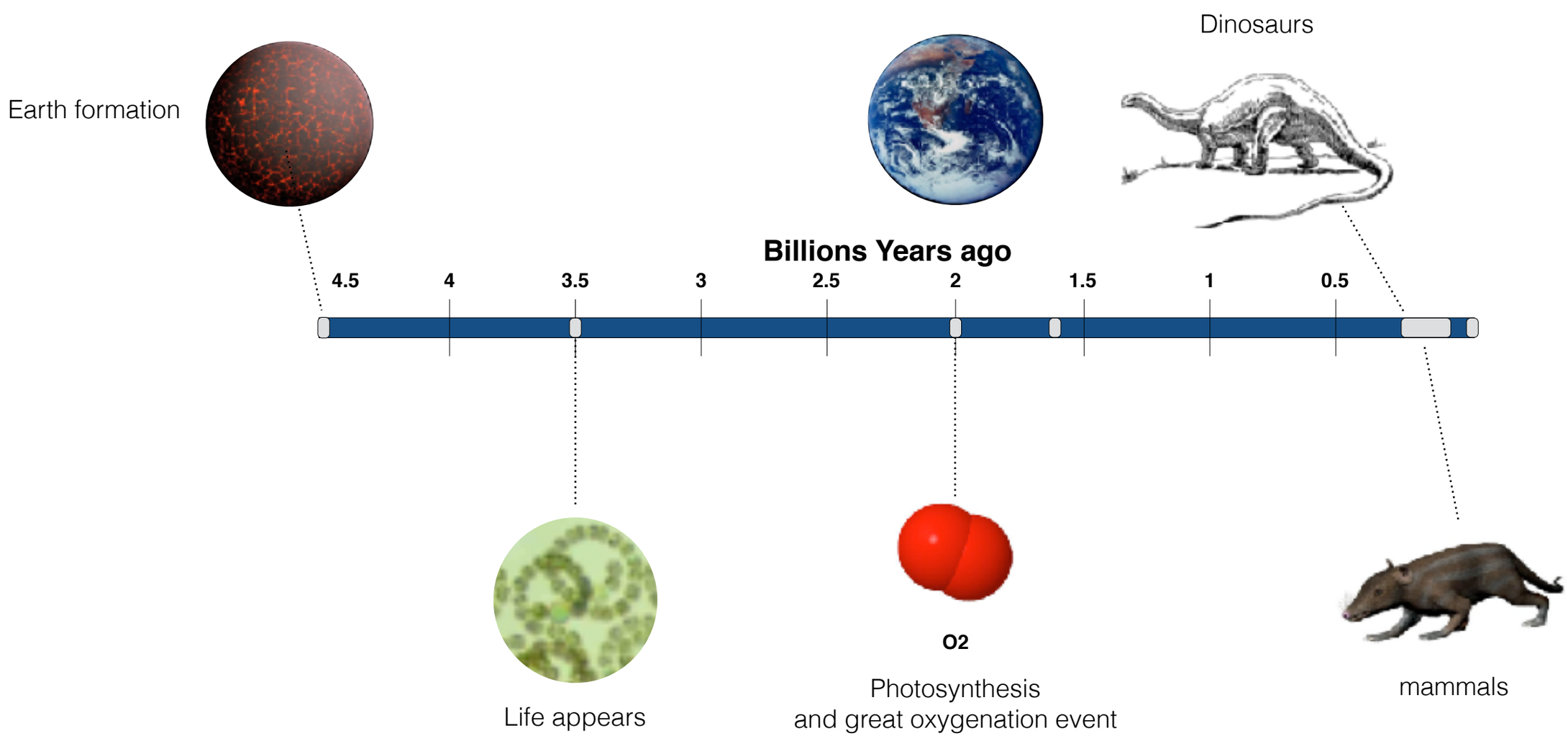
QBio Master 1- synthetic biology, 2021

https://qbio.umontpellier.fr/

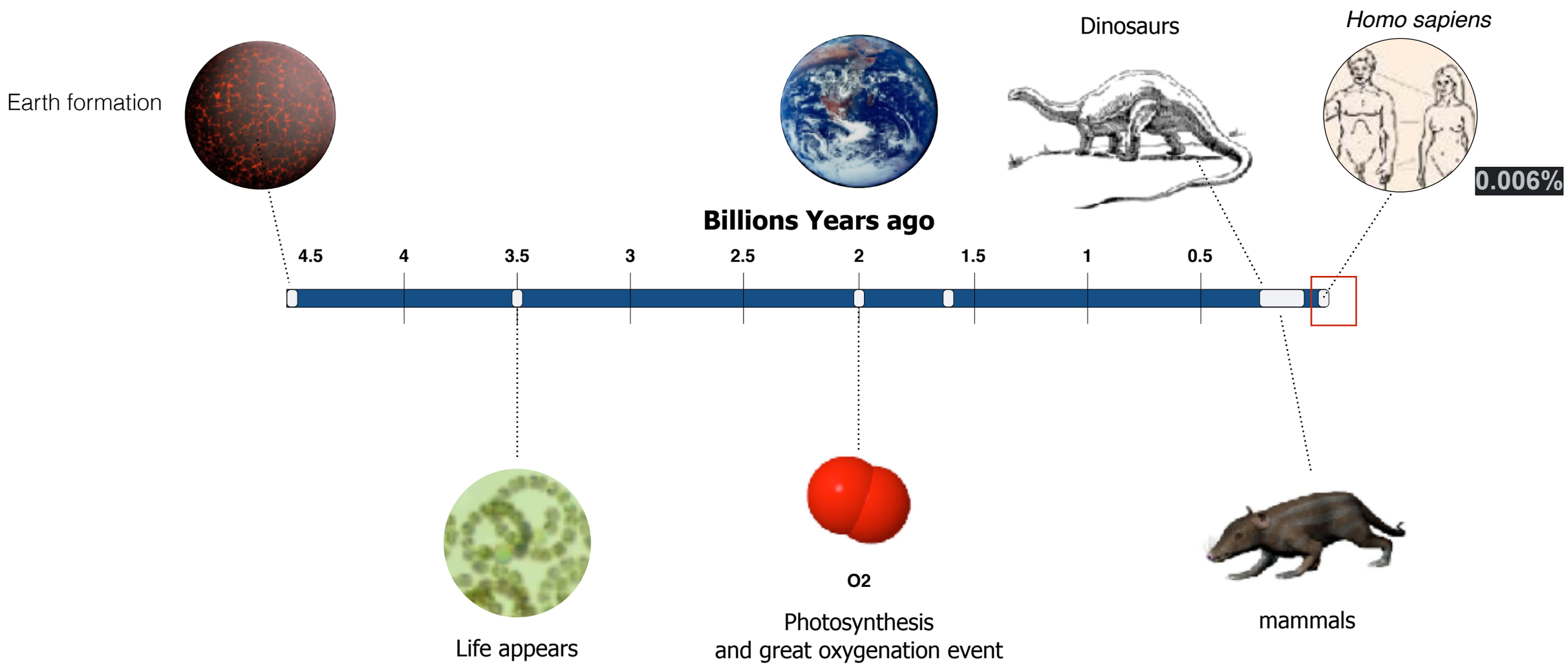
https://github.com/qbiomaster/SynBio


Earth formation
Dinosaurs
Billions Years ago
4.5
4
3.5
3
2.5
2
1.5
1
0.5
O2
Life appears
Photosynthesis
and great oxygenation event
mammals

James Temple

N. Hobgood

Arturo de Frias Marques

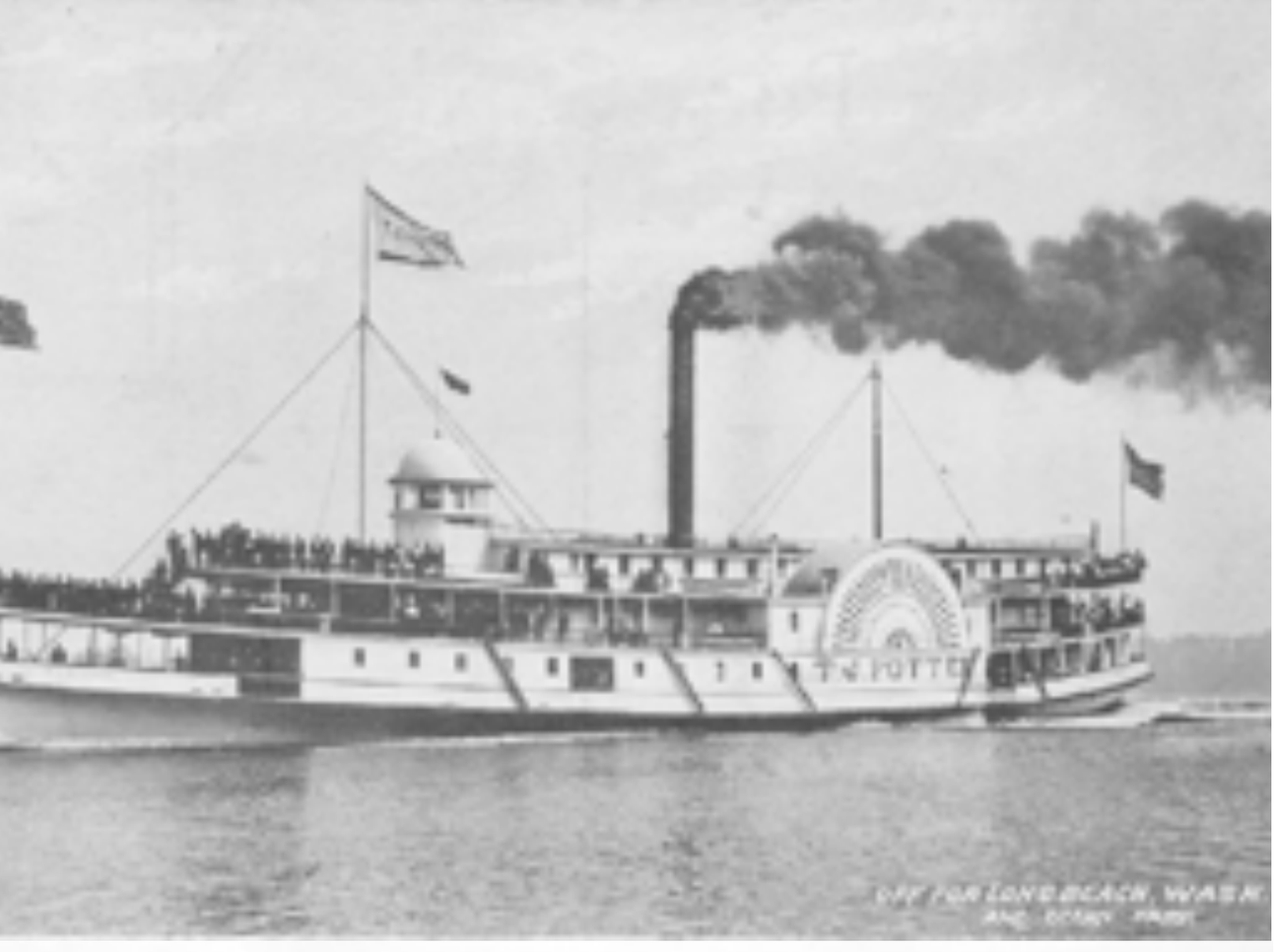

Earth formation
Dinosaurs
Homo sapiens
0.006%
Billions Years ago
4.5
4
3.5
3
2.5
2
1.5
1
0.5
O2
Life appears
Photosynthesis
and great oxygenation event
mammals

Bifaces-2.6-Million-year

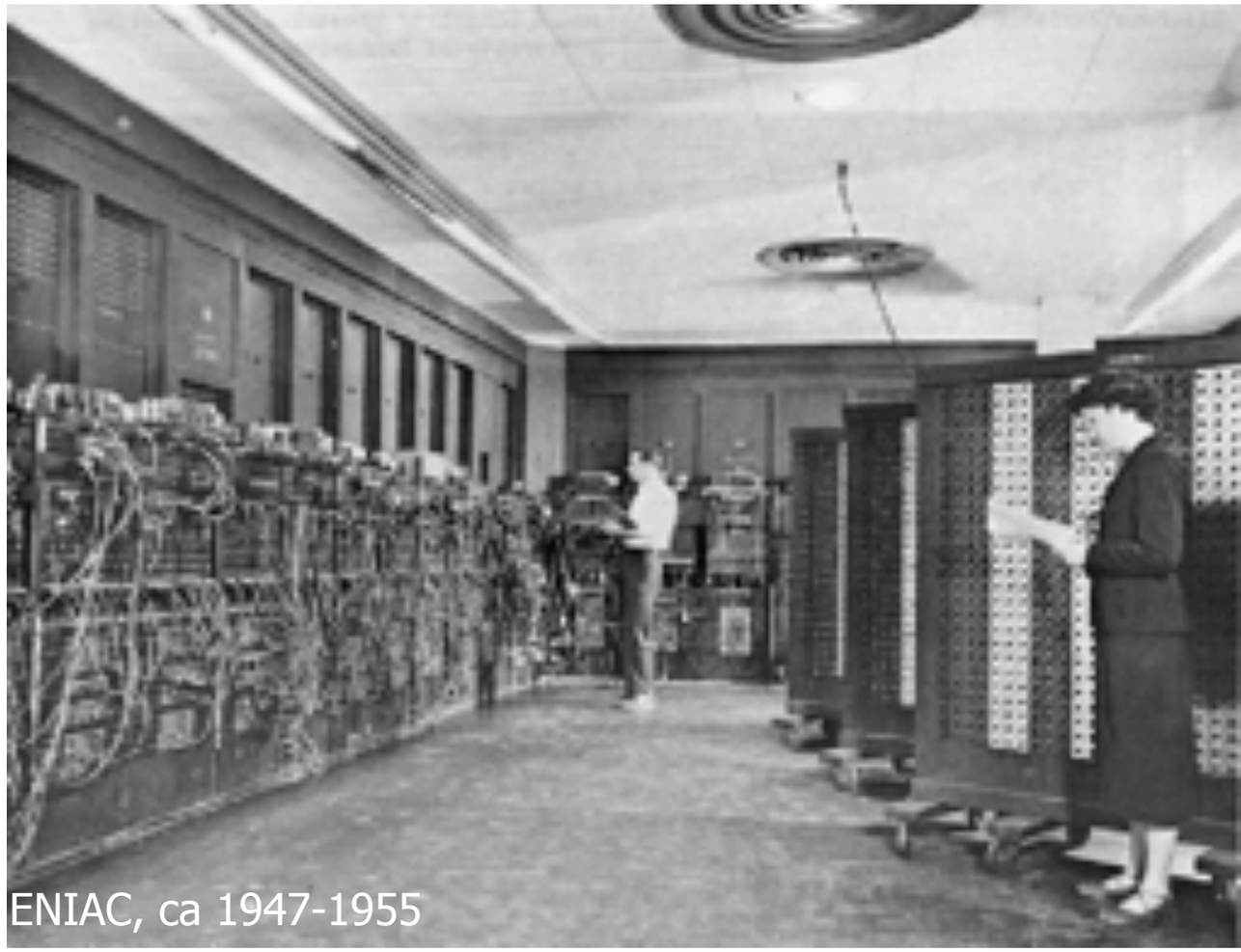
Picture by José-Manuel Benito Álvarez

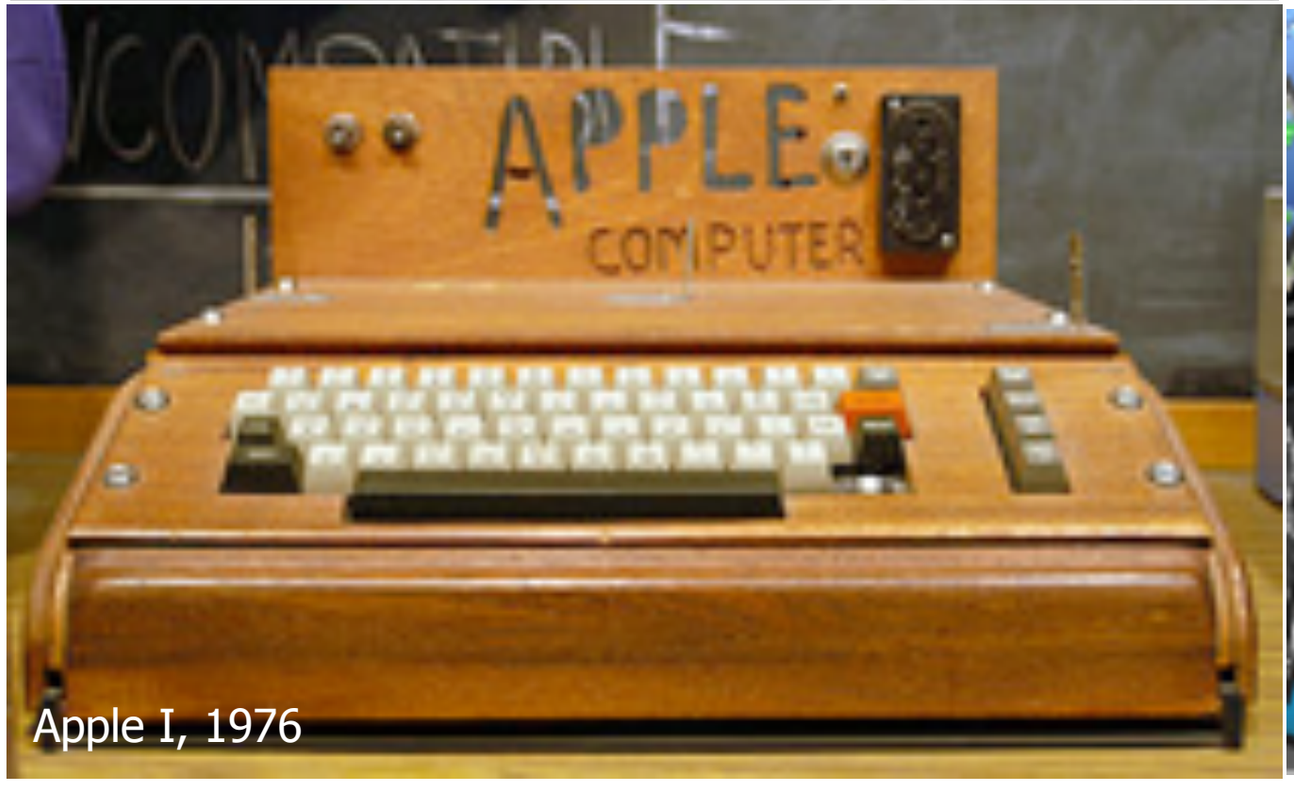
Bronze artifacts- 800BC

Daegok-ri, Hwasun, Korea- National Museum of Korea


OFF FOR LONG BEACH, WASH.

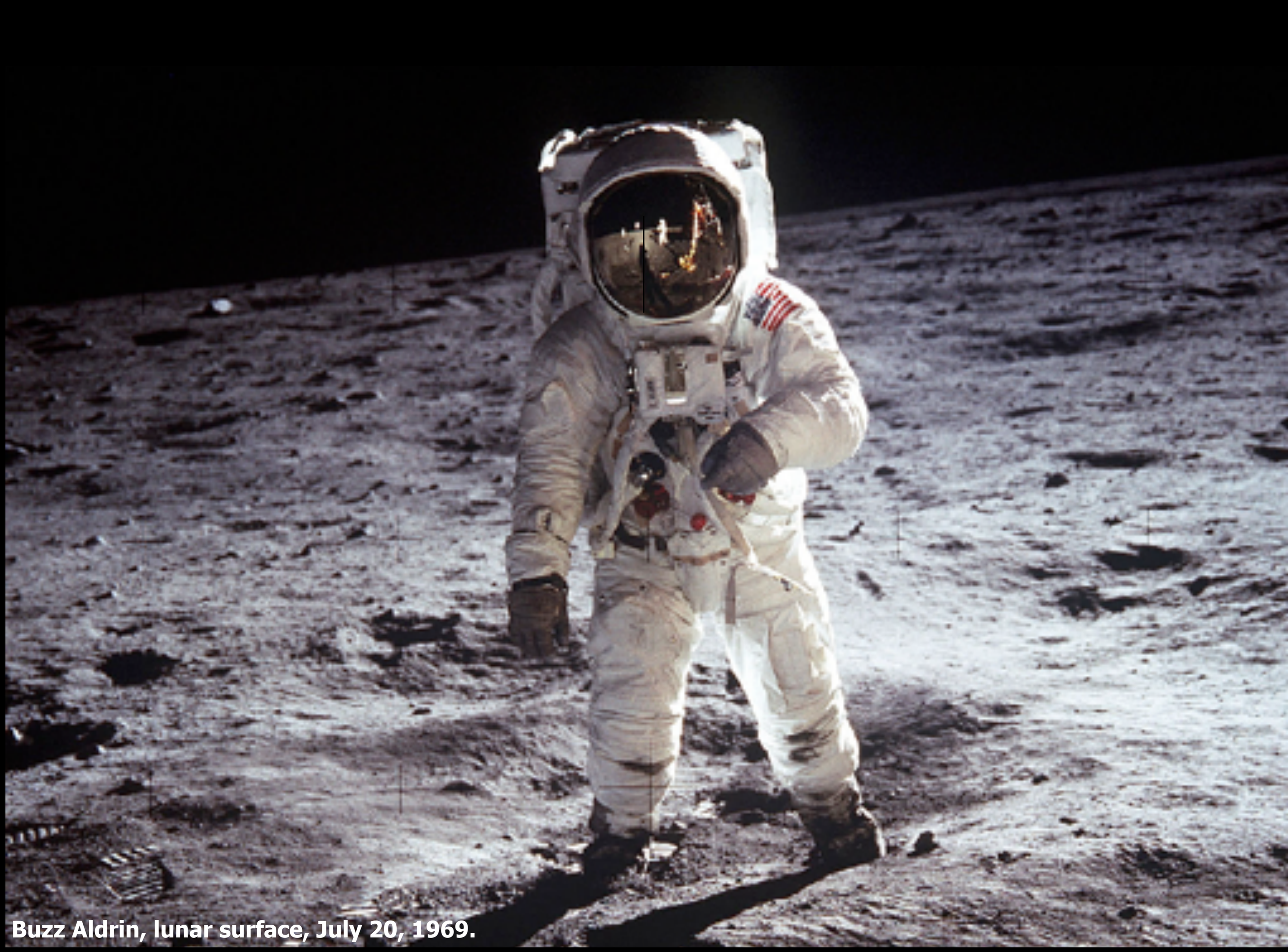
Human computers, ca 1920


ENIAC, ca 1947-1955



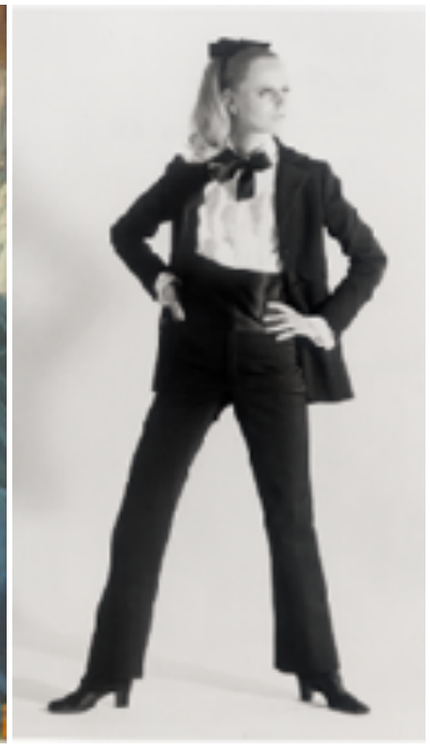
Apple I, 1976

Grotte Chauvet, Ardeche, France, 30000 years ago



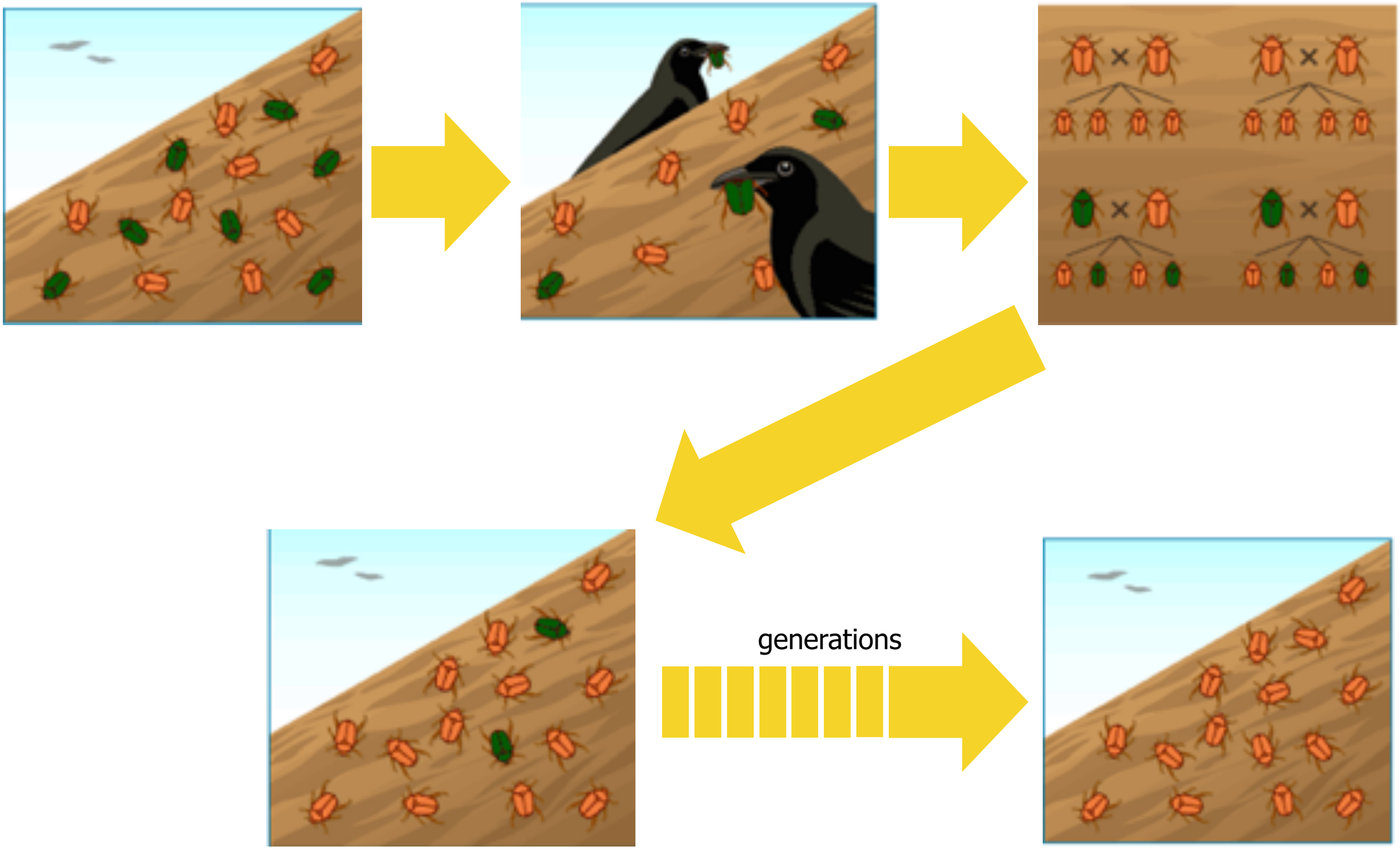
Buzz Aldrin, lunar surface, July 20, 1969.

Maks Karochkin



Penicillin (antibiotic)

Darwinian evolution: Variation et natural selection

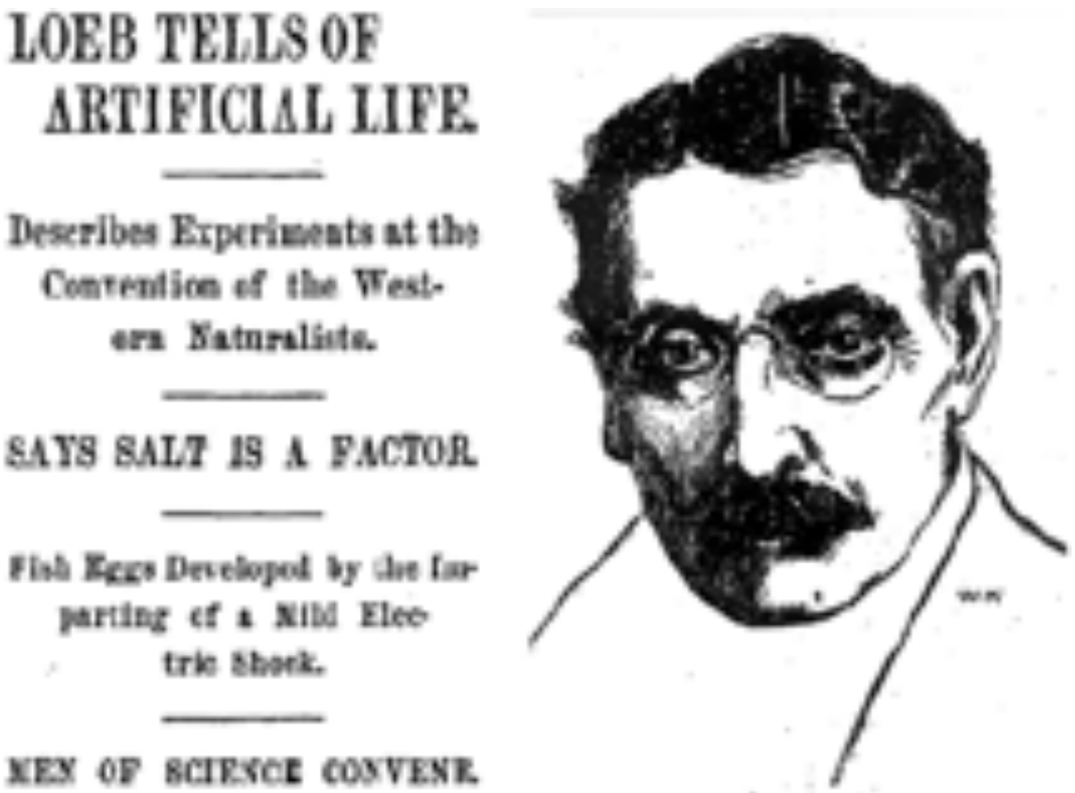


http://evolution.berkeley.edu

We shaped the living world via selective breeding

1900's

Jacques Loeb



LOEB TELLS OF ARTIFICIAL LIFE.

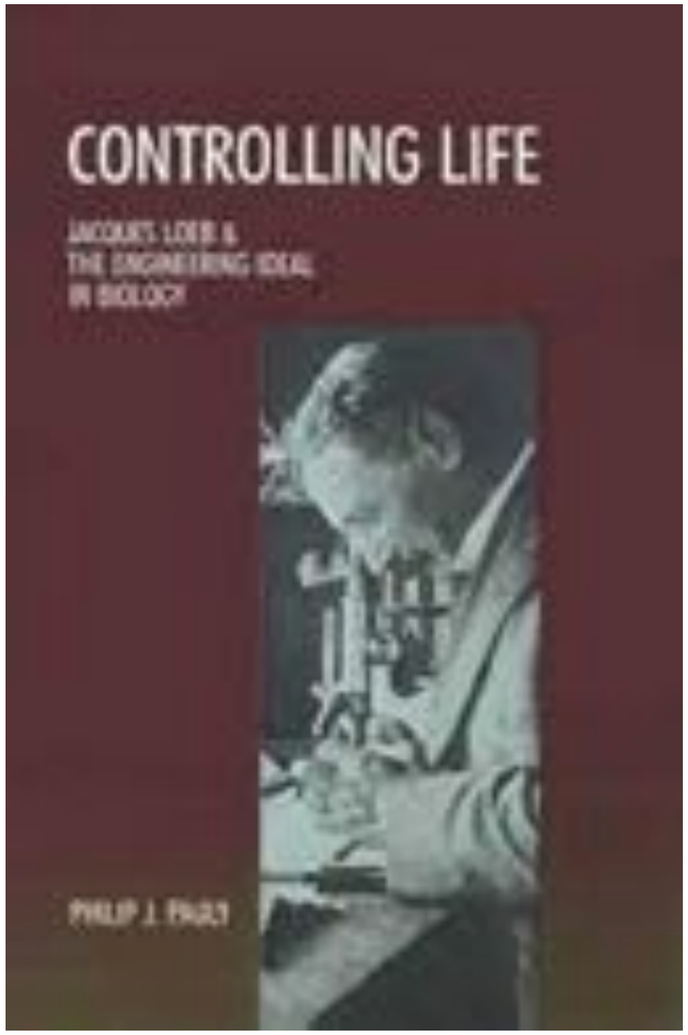
Describes Experiments at the Convention of the Western Naturalists.

SAYS SALT IS A FACTOR.

Fish Eggs Developed by the Imparting of a Mild Electric Shock.

MEN OF SCIENCE CONVENE.

Chicago Daily Tribune, December 28, 1900



- **ISBN13** 9780195042443

1912

ÉTUDES DE BIOPHYSIQUE

LA BIOLOGIE SYNTHÉTIQUE

PAR

STÉPHANE LEDUC

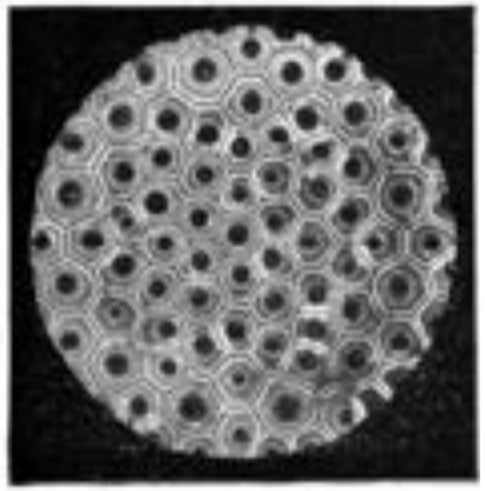
AVEC 110 FIGURES DANS LE TEXTE

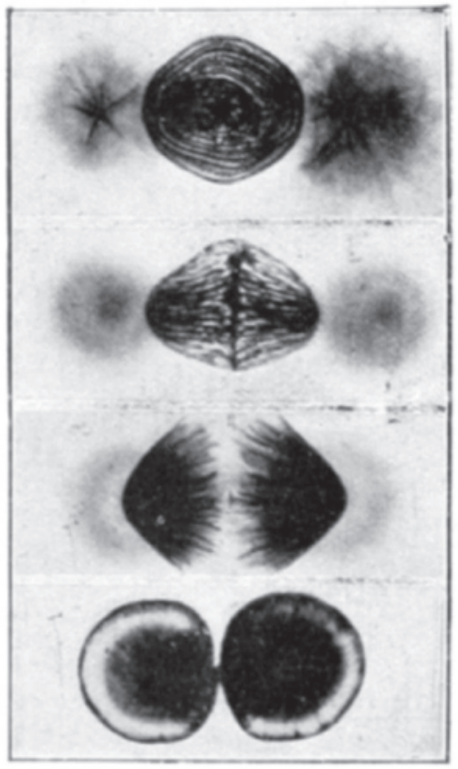
A. POINAT, ÉDITEUR

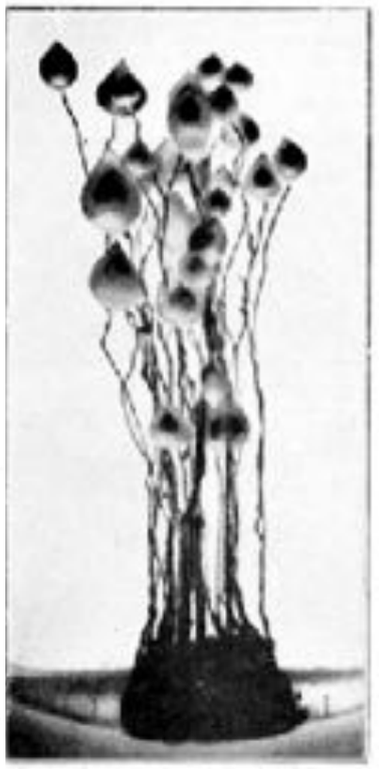
Stephane Leduc

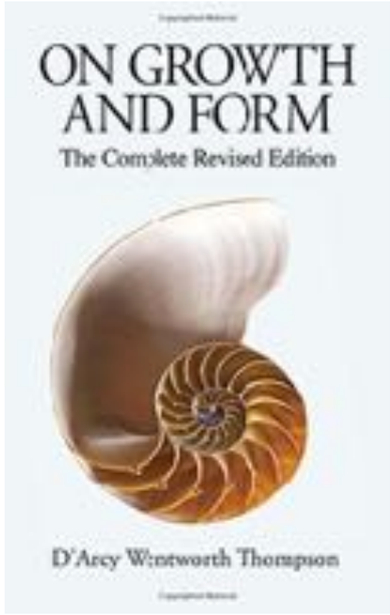
"When we have come to know the physical mechanism of the production of an object or a phenomenon, it becomes possible to reproduce the object or the phenomenon, science has become synthetic.

Biology is a science like any other, it must be successively descriptive, analytical and synthetic. "

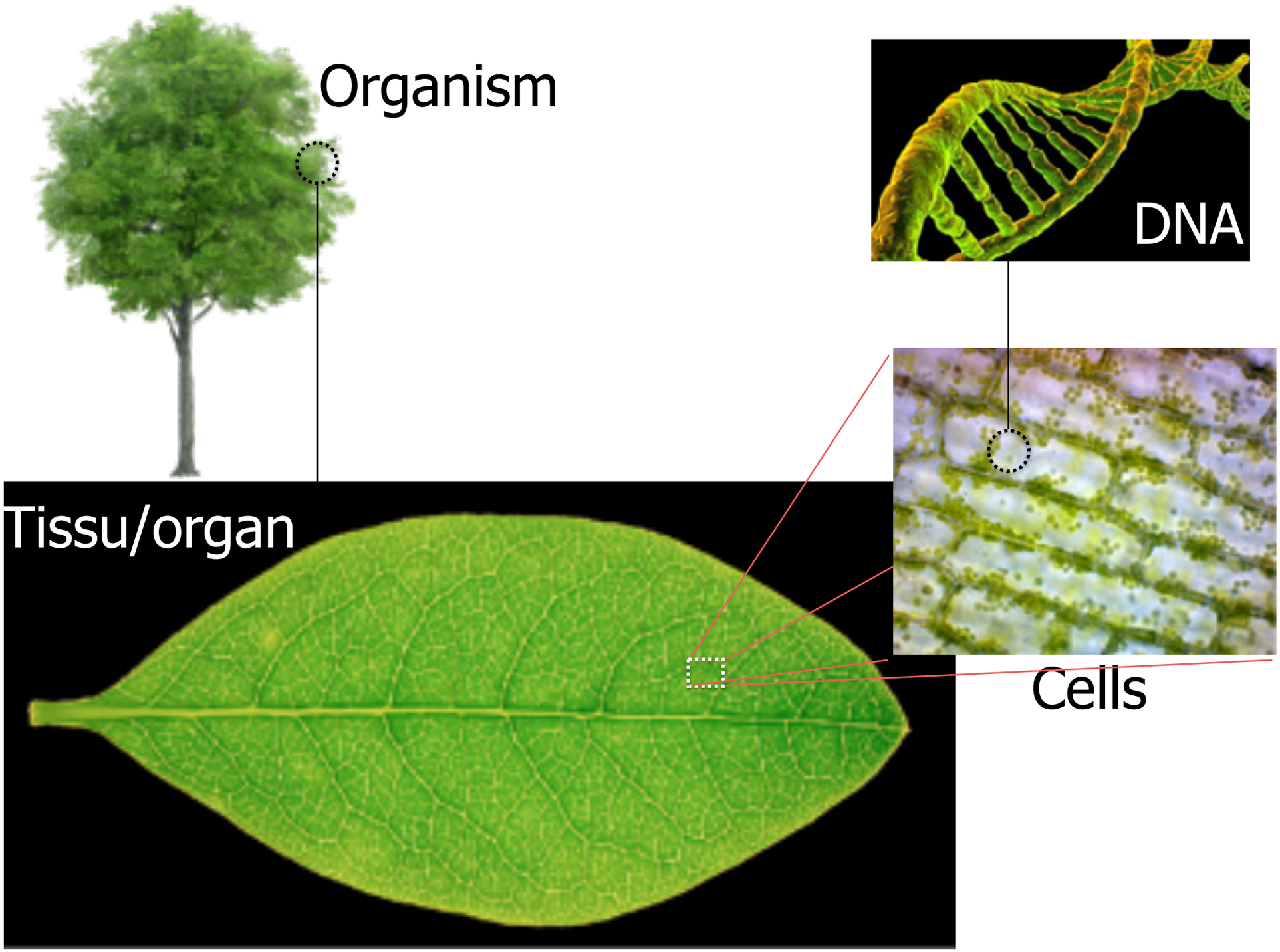




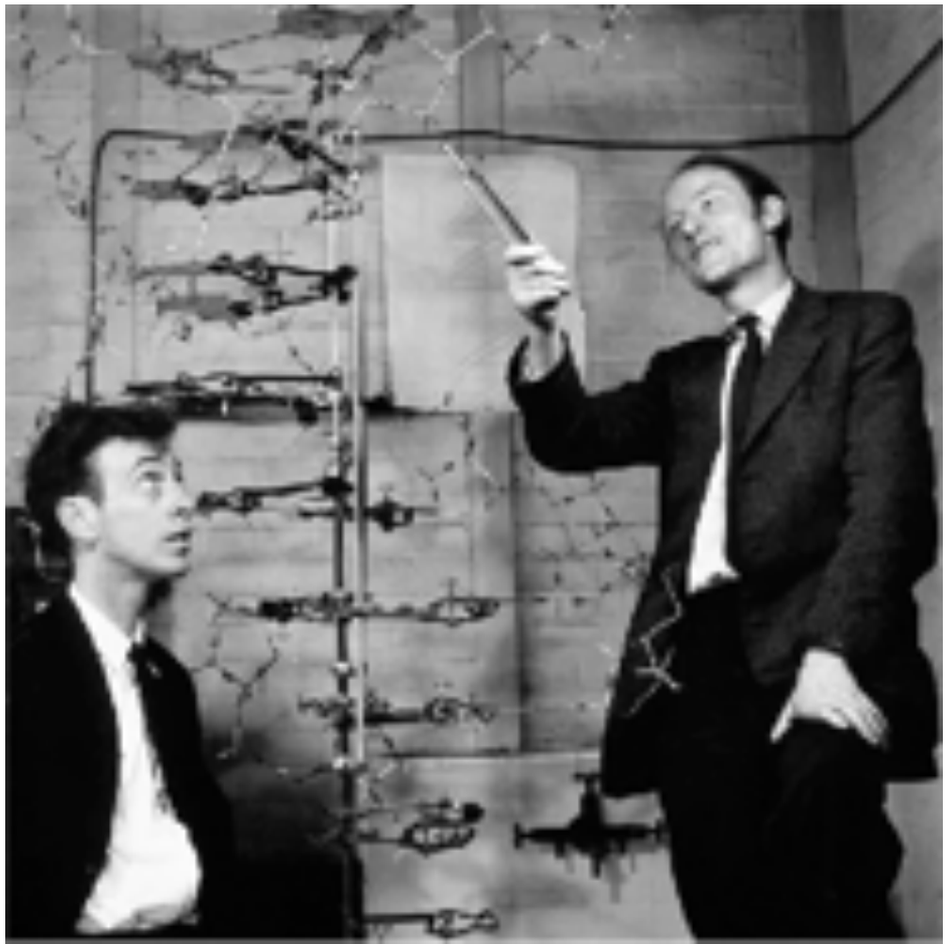




https://www.gutenberg.org/ebooks/33862

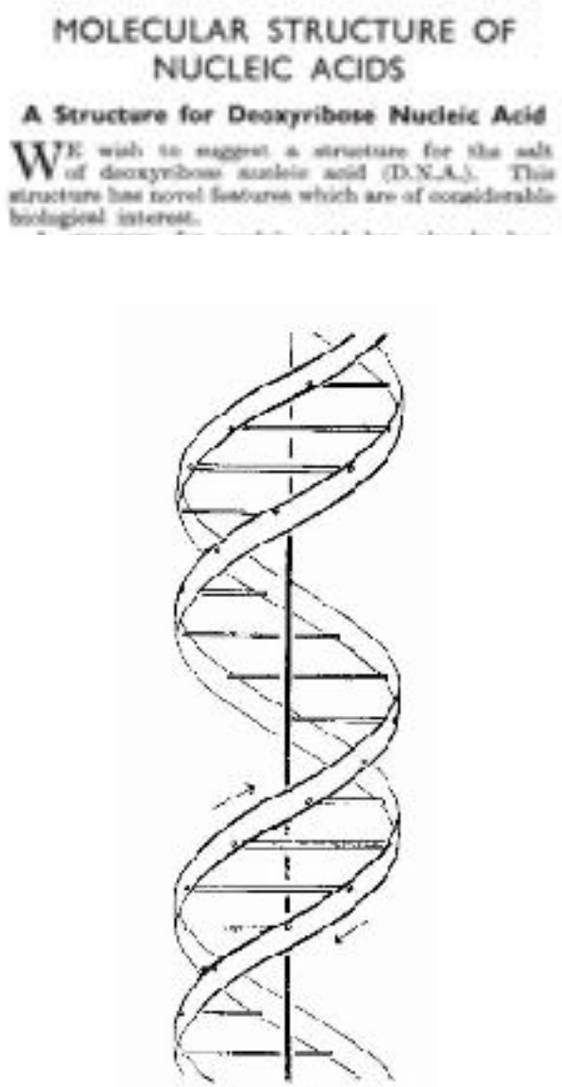

Organism
DNA
Tissu/organ
Cells

1953



James Watson Francis Crick

Rosalind Franklin



MOLECULAR STRUCTURE OF NUCLEIC ACIDS

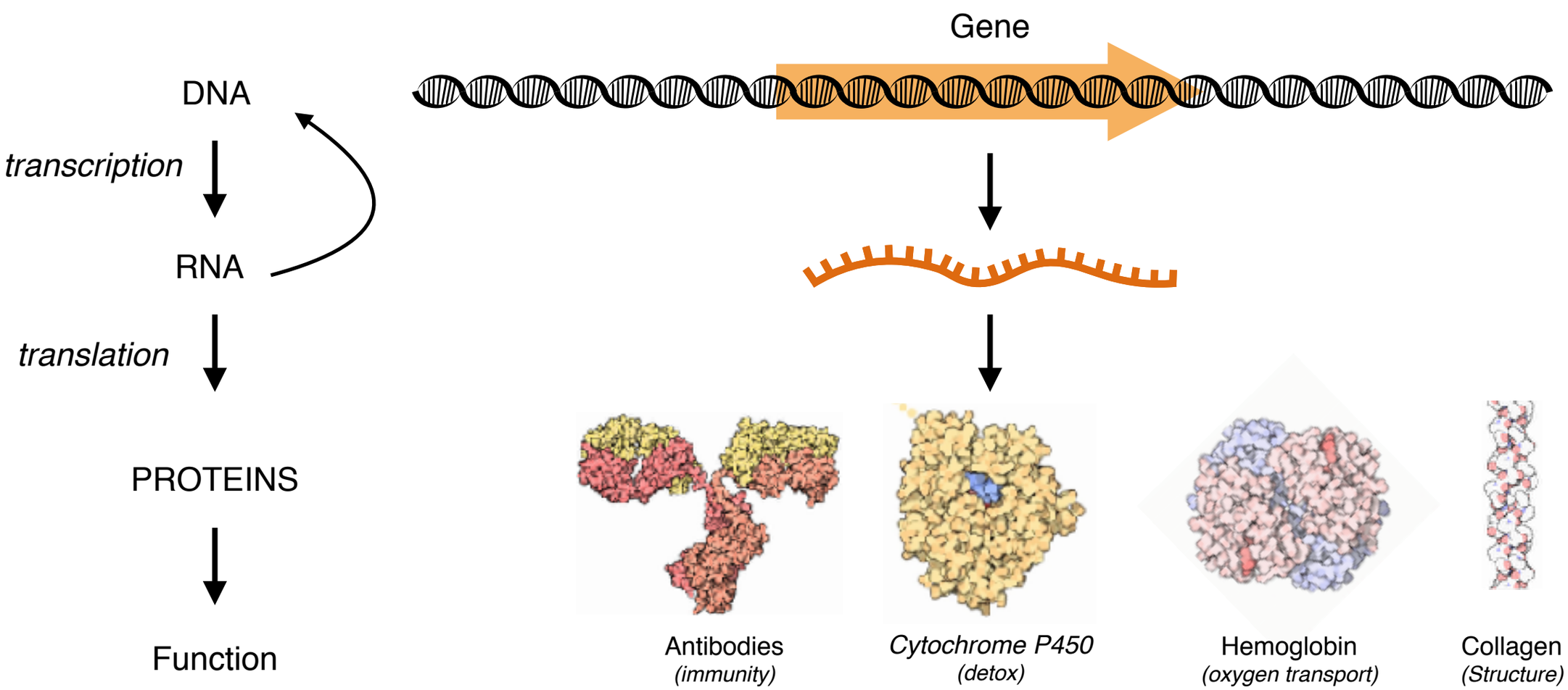
A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

Nature, 1953

Francois Jacob Jacques Monod André Lwoff

The central dogma of molecular biology



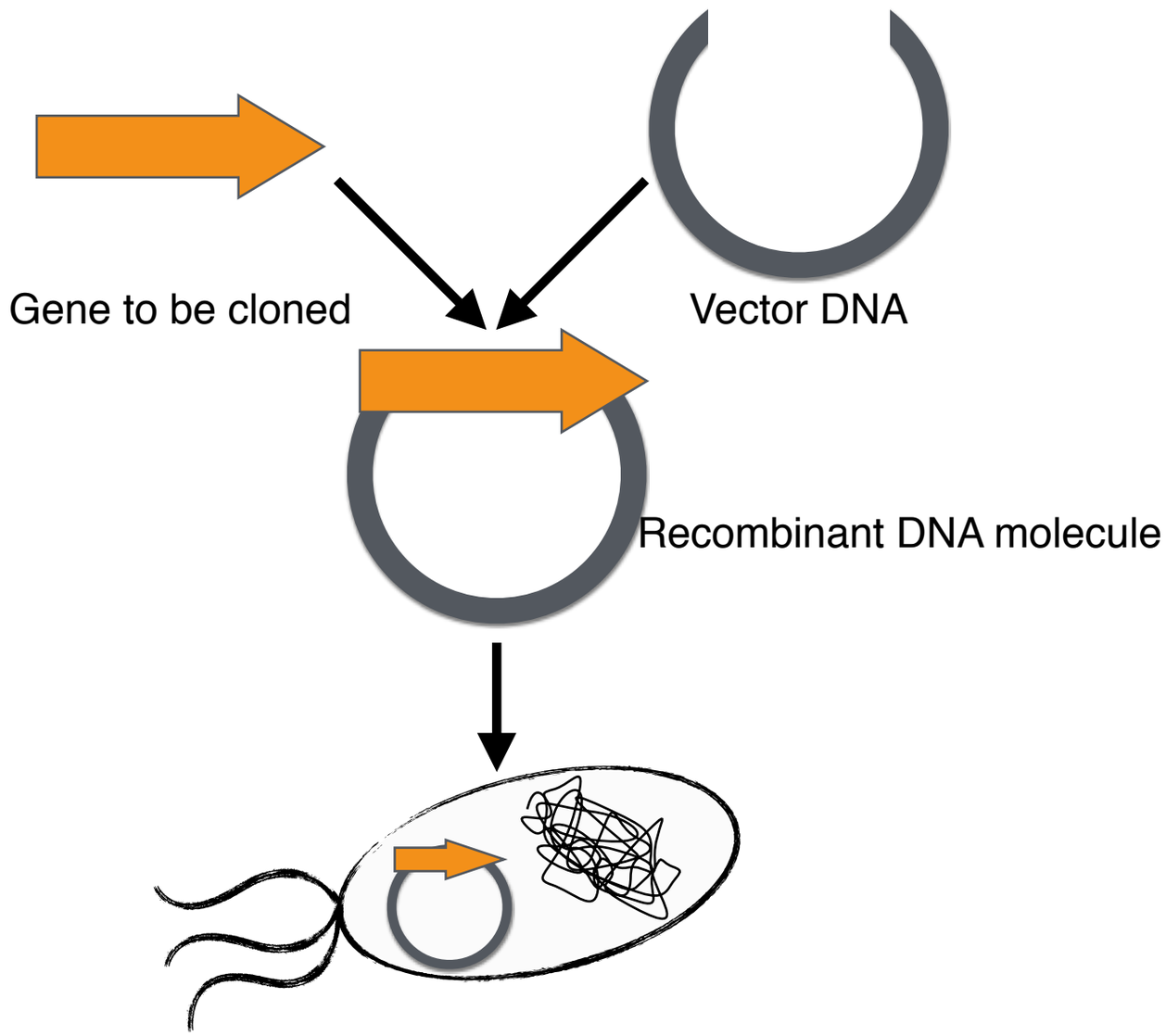
1966

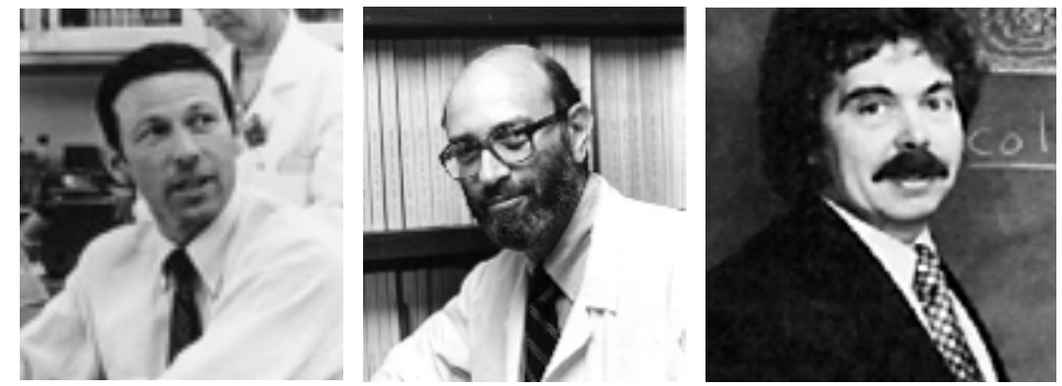
http://vega.org.uk/video/programme/156

I”t is conceivable that one day we can build a synthetic cell”

1970's

Genetic "engineering"





Paul Berg Stanley Cohen Herbert Boyer

Le détergent glouton!

Ses multi-enzymes dévorent les taches.

Chaque paquet d'Ala contient une forte concentration de multi-enzymes. Ils dévorent les taches de fruits, œuf, herbe, sauce, chocolat, etc. Mais ils respectent les couleurs et les tissus. Ala contient également un nouveau détergent à grande efficacité contre la saleté.

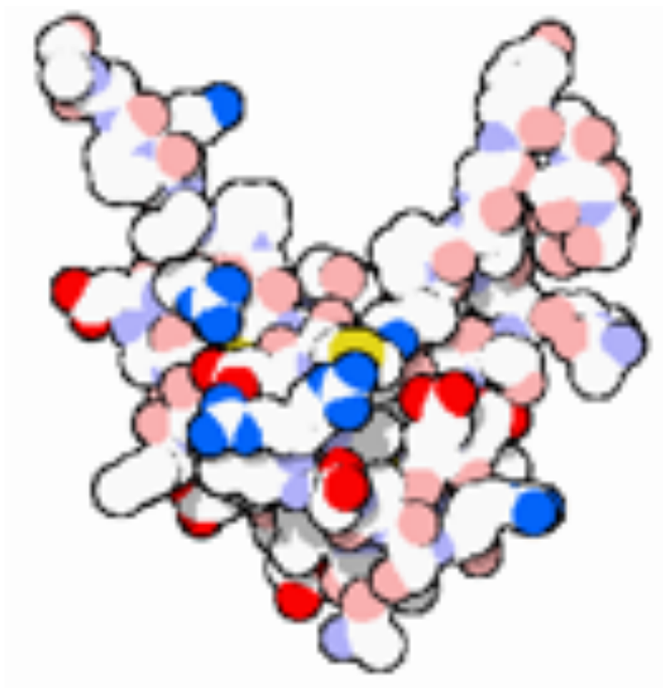
Conçu spécialement pour le lavage en machine, Ala est également supérieur dans tous autres modes de lavage. Sa mousse, normale en lavabo, est discrète en machine. C'est pourquoi Ala convient tout particulièrement à votre machine à tambour.

ala donne à votre linge la propreté totale.

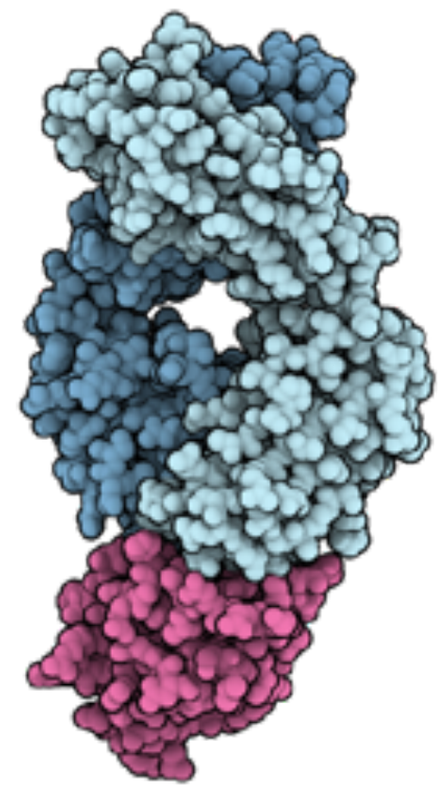
http://blogpub.canablog.com

recombinant insulin

Human Growth Hormone



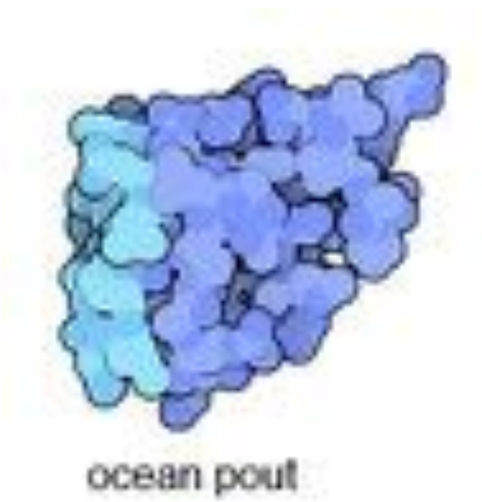
Therapeutic antibodies



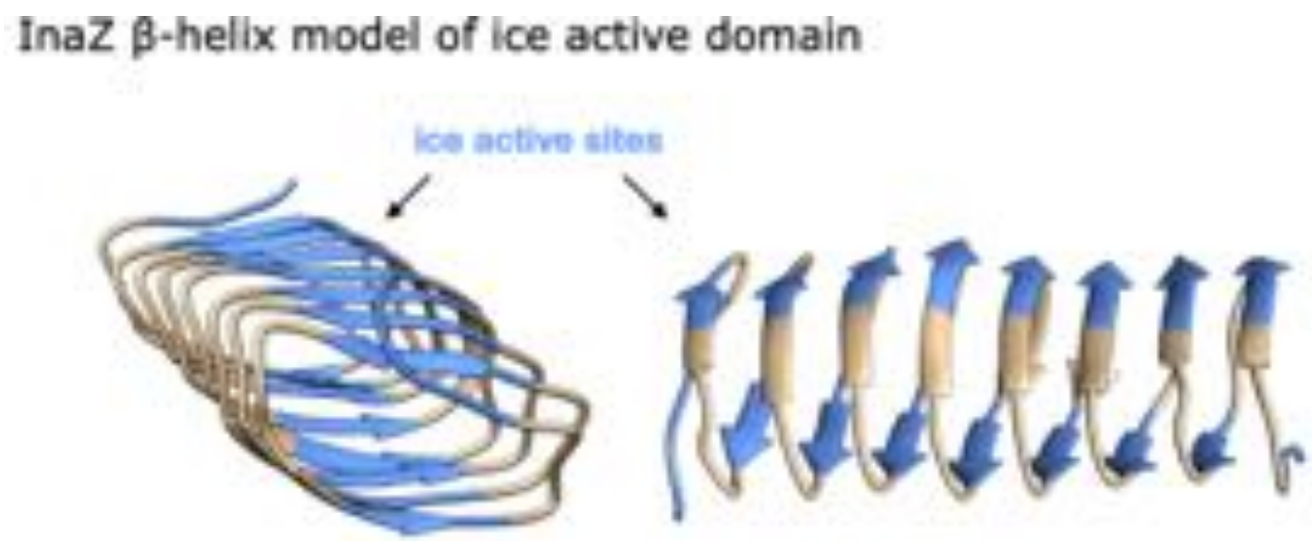
Anti-PDL1

Atezolizumab

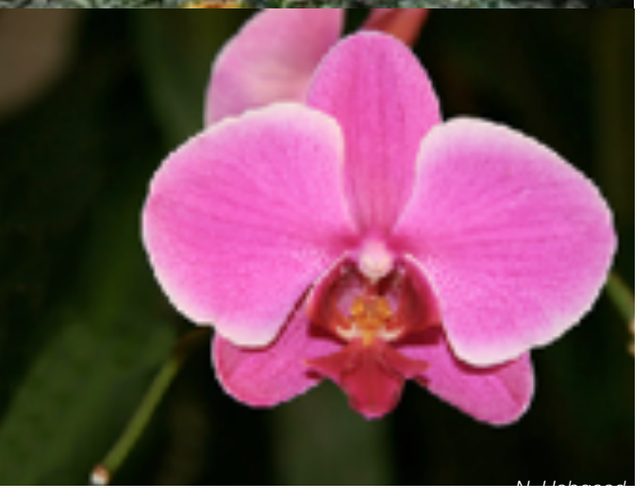
Antifreeze proteins



Ice nucleating proteins

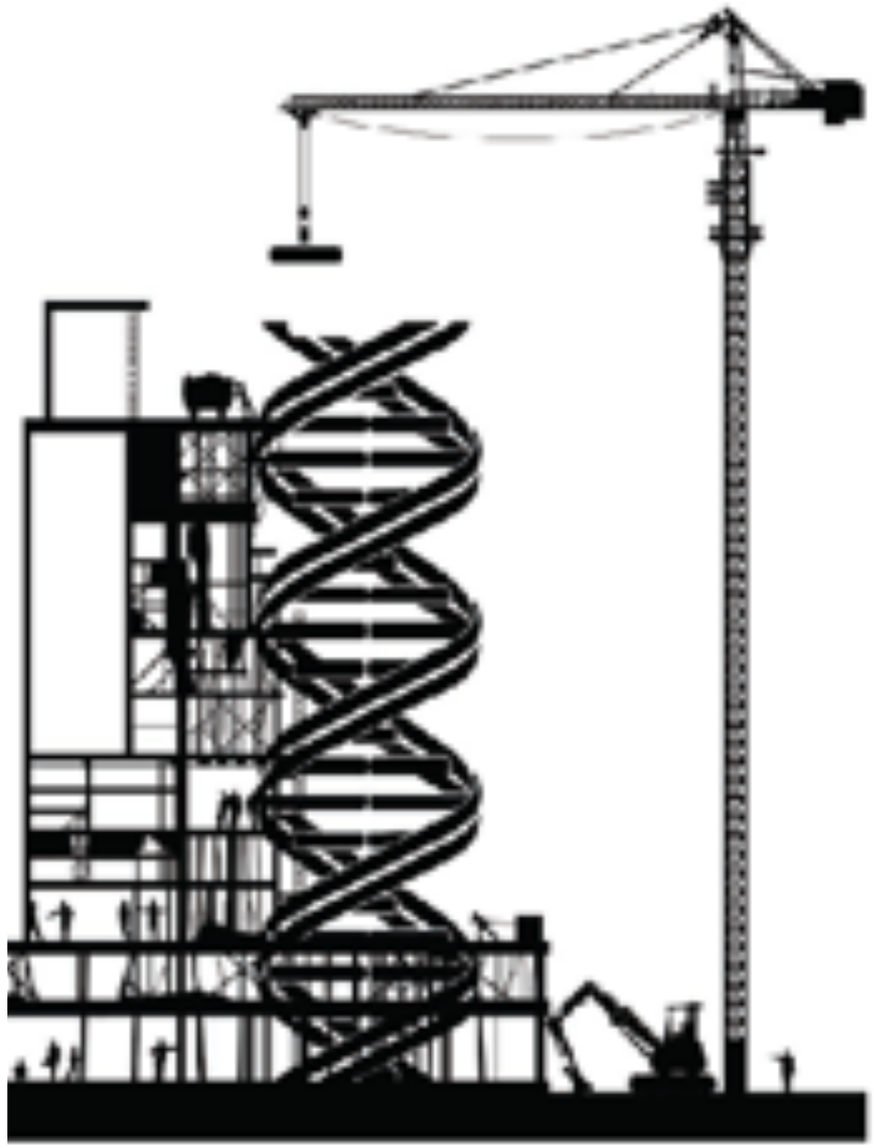


James Temple



Arturo de Frias Marques

Synthetic Biology:
Rational engineering of new biological systems and functions



Fact: Biotech methods almost unchanged in 40 years

1973

Construction of biologically functional bacterial plasmids in vitro

Cohen et al., PNAS, 1973

MATERIALS AND METHODS

E. coli strain W1485 containing the R6F1010 plasmid, which carries resistance to streptomycin and sulfonamide, was obtained from S. Falkow. Other bacterial strains and R factors and procedures for DNA isolation, electron microscopy, and transformation of *E. coli* by plasmid DNA have been described (1, 7, 8). Purification and use of the *EcoRI* restriction endonuclease have been described (8). Plasmid heteroduplex studies were performed as previously described (9, 10). *E. coli* DNA ligase was a gift from P. Modrich and R. L. Lehman and was used as described (11). The detailed procedures for gel electrophoresis of DNA will be described elsewhere (Helling, Goodman, and Boyer, in preparation); in brief, duplex DNA was subjected to electrophoresis in a tube-type apparatus (Heatter Scientific Instruments) (0.6 × 15-cm gel) at about 20° in 0.7% agarose at 20.5 V with 40 mM Tris-acetate buffer (pH 8.00) containing 20 mM sodium acetate, 2 mM EDTA, and 18 mM sodium chloride. The gels were then soaked in ethidium bromide (5 μg/ml) and the DNA was visualized by fluorescence under long wavelength ultraviolet light ("black light"). The molecular weight of each fragment in the range of 1 to 200 × 10⁶ was determined from its

1985

Cloning and expression of the human erthropoietin gene

Lin et al., PNAS, 1985

Assembly of Expression Vector for the Epo Gene. For direct expression of the genomic Epo gene, the 4.8-kilobase (kb) *Bst*EII–*Bam*HI fragment of λHE1 (see *Results*), which contains the entire Epo gene, was used. After converting the *Bst*EII site into a *Bam*HI site with a synthetic linker, the fragment was inserted into the unique *Bam*HI site of the expression vector pDSVL (unpublished data), which contains a dihydrofolate reductase (DHFR) minigene from pMg1 (24). The resulting plasmid pDSVL-gHuEPO (Fig. 1*A*) was then used to transfect Chinese hamster ovary (CHO) DHFR⁻ cells (25) by the calcium phosphate microprecipitate method (26). The transformants were selected by growth in medium lacking hypoxanthine and thymidine. The culture medium used was Dulbecco's modified Eagle's medium supplemented with 10% fetal bovine serum, penicillin, streptomycin, and glutamine (25).

2006

Production of the antimalarial drug precursor artemisinic acid in engineered yeast

Ro et al., Nature, 2006

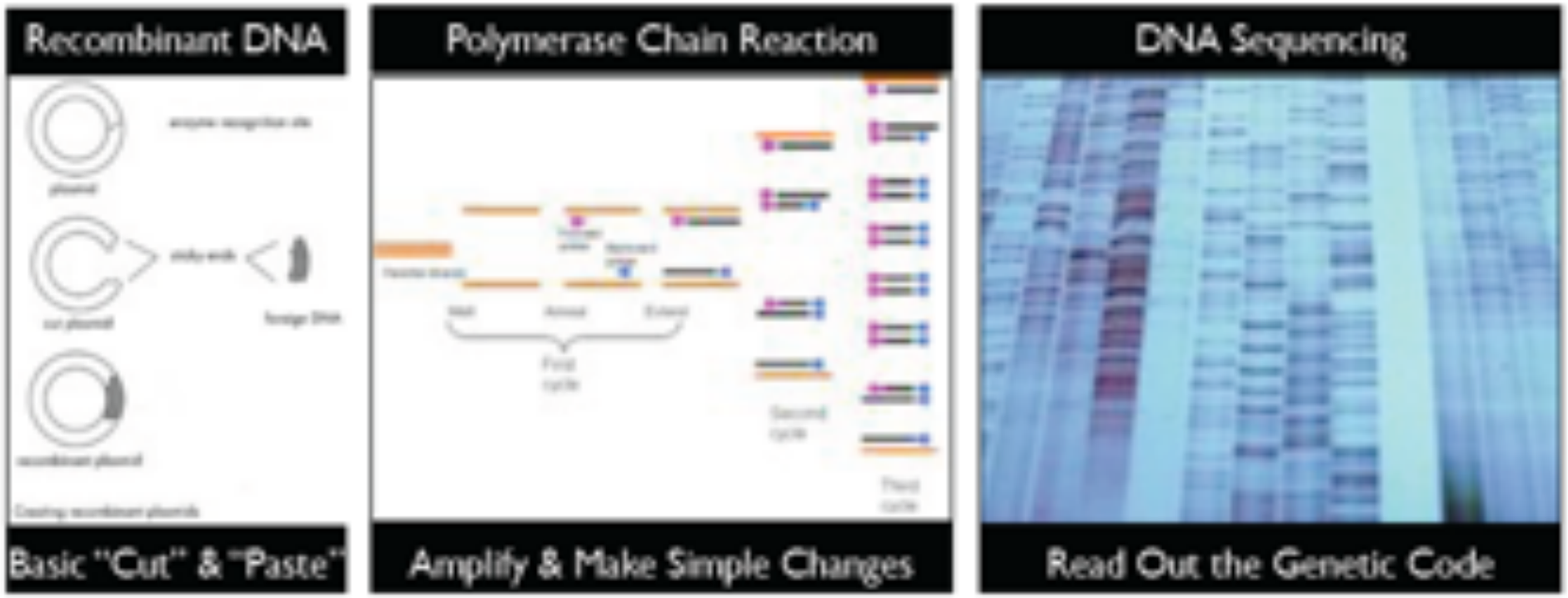
Plasmid construction. To create plasmid pRS425-ADS for expression of ADS with the GAL1 promoter, ADS was PCR amplified from pADS[1] using primer pair 9 and 10 (Supplementary Table 3). Using these primers the nucleotide sequence 5′-AAAAGA-3′ was cloned immediately upstream of the start codon of ADS. This consensus sequence was used for efficient translation[7] of ADS and the other galactose-inducible genes used in this study. The amplified product was cleaved with SpeI and XhoII and cloned into SpeI and XhoII digested pRS425GAL1[7].

For integration of an expression cassette for ADS6GA, plasmid pJ-ADS6GA was constructed. First SacII restriction sites were introduced into pRS426GAL1[7] at the 5′ end of the GAL1 promoter and 3′ end of the CYC1 terminator. To achieve this, the promoter-multiple cloning site-terminator cassette of pRS426GAL1 was PCR amplified using primer pair 11 and 12. The amplified product was cloned directly into PmeII-digested pRS426GAL1 to create a vector pRS426-SacII. The vector digested with

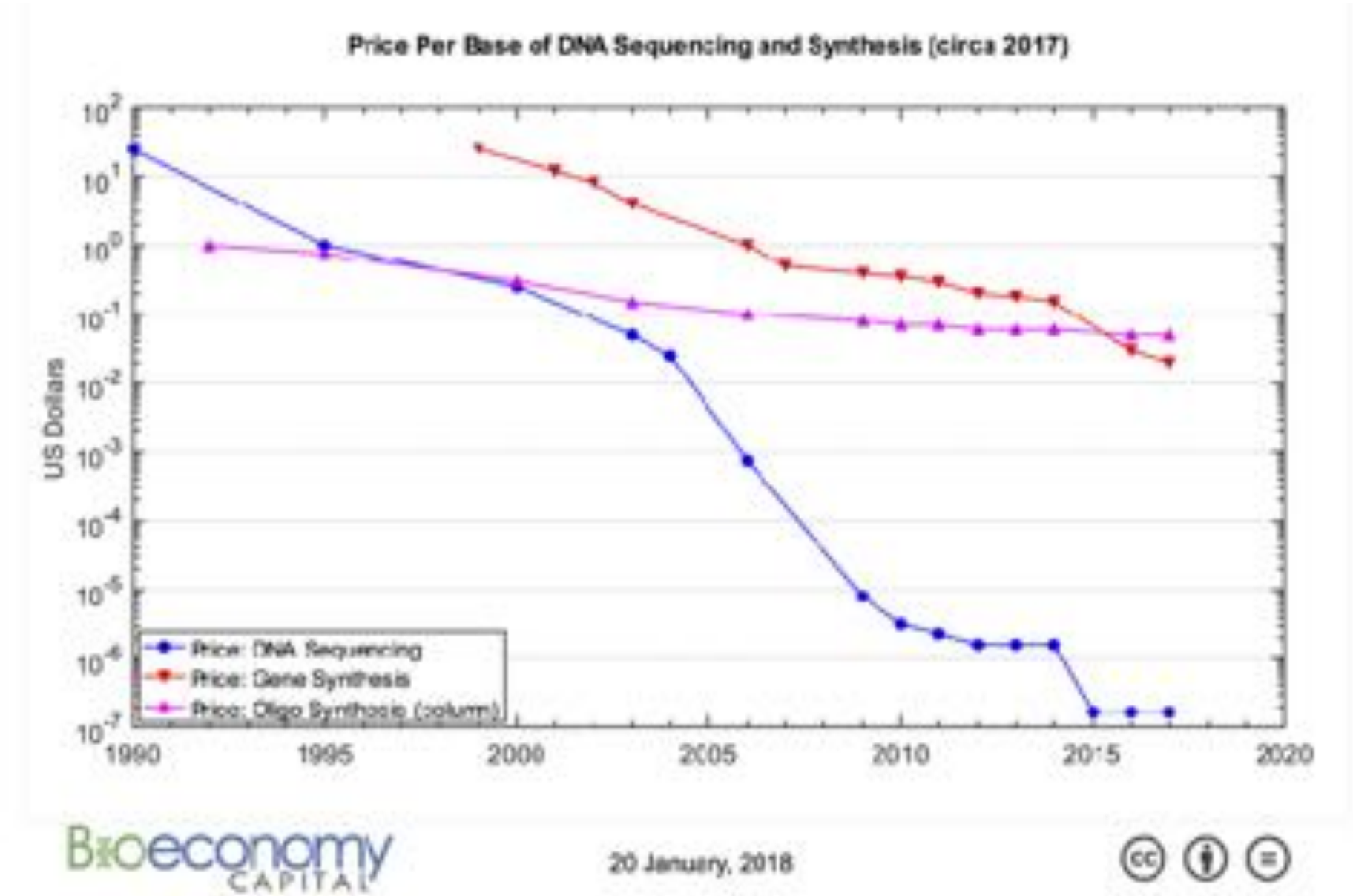
Synthetic biology is enabled by a tool revolutions

Synthetic biology= tools revolution

First Gen. Biotech =



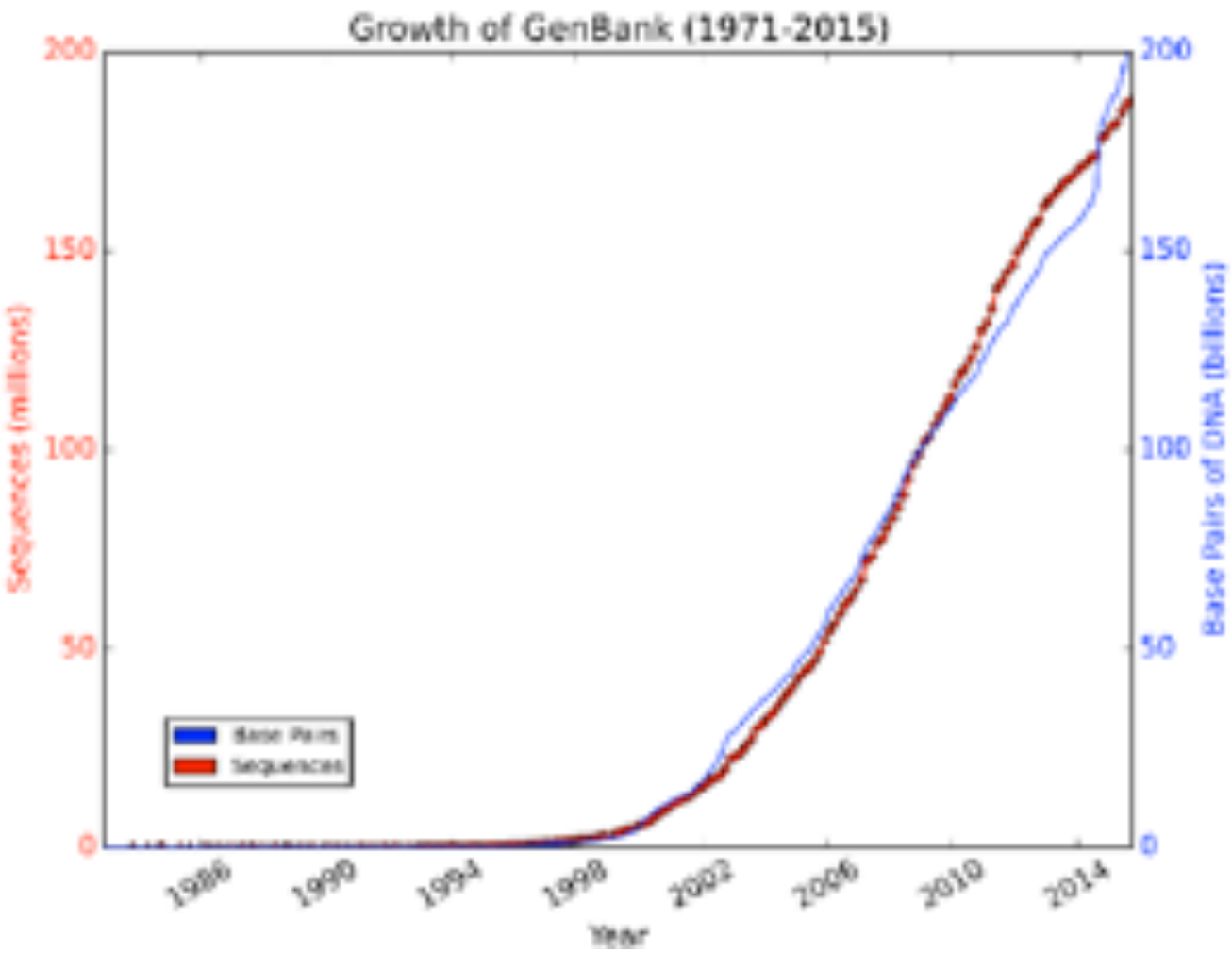
Massive improvements in sequencing and synthesis technologies



Massive price drops

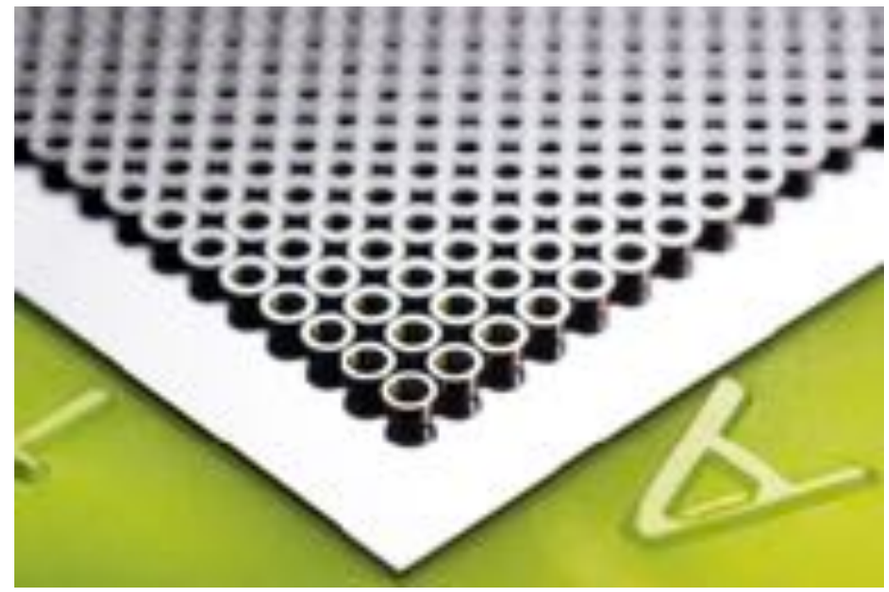
Technological revolution #1: DNA sequencing

Exponential increase of the number of sequences databases



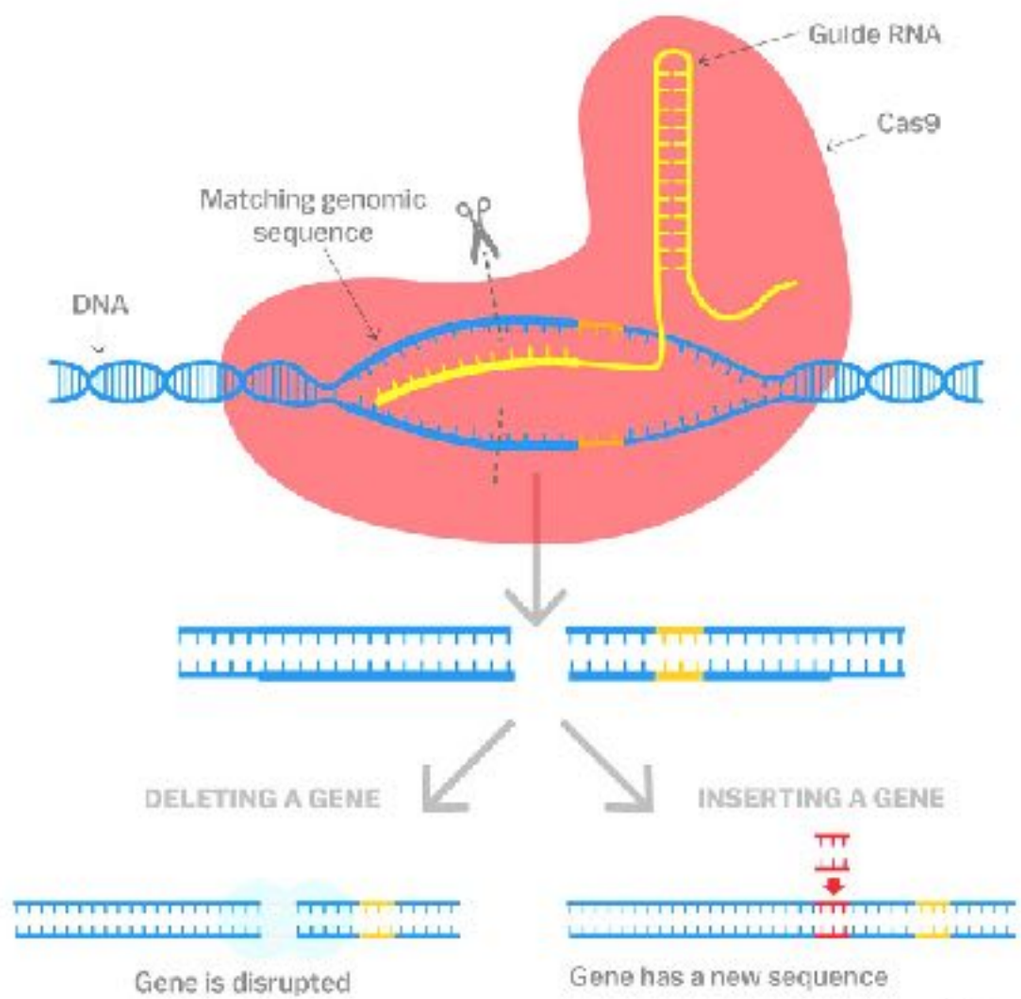
Human genome: 1000$

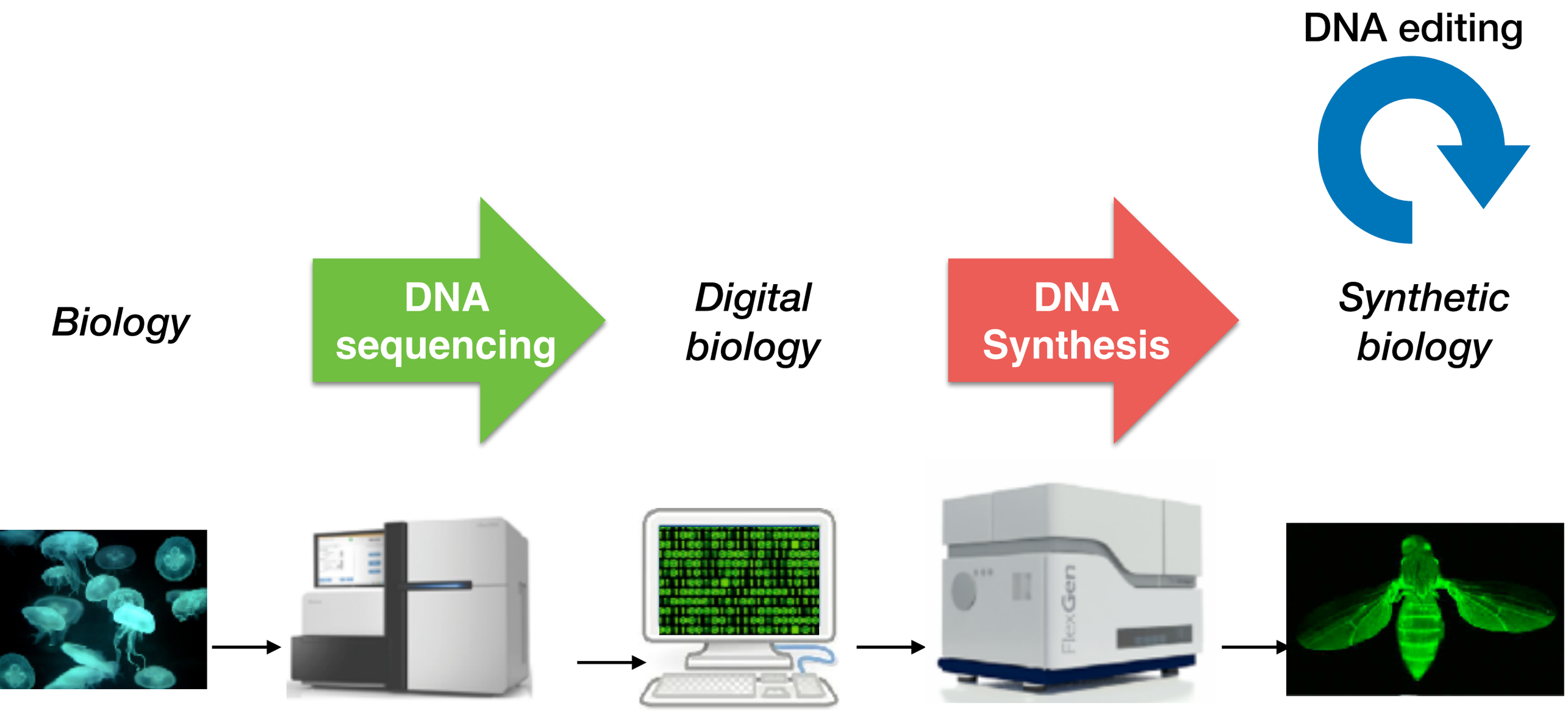
Technological revolution #2: DNA synthesis



Last updated: 0,07 $/bp
Average gene: 70$

Technological revolution #3: DNA editing via CRISPR




DNA editing
Biology
DNA sequencing
Digital biology
DNA Synthesis
Synthetic biology
FlexGen

Sequence design

email

gene synthesis

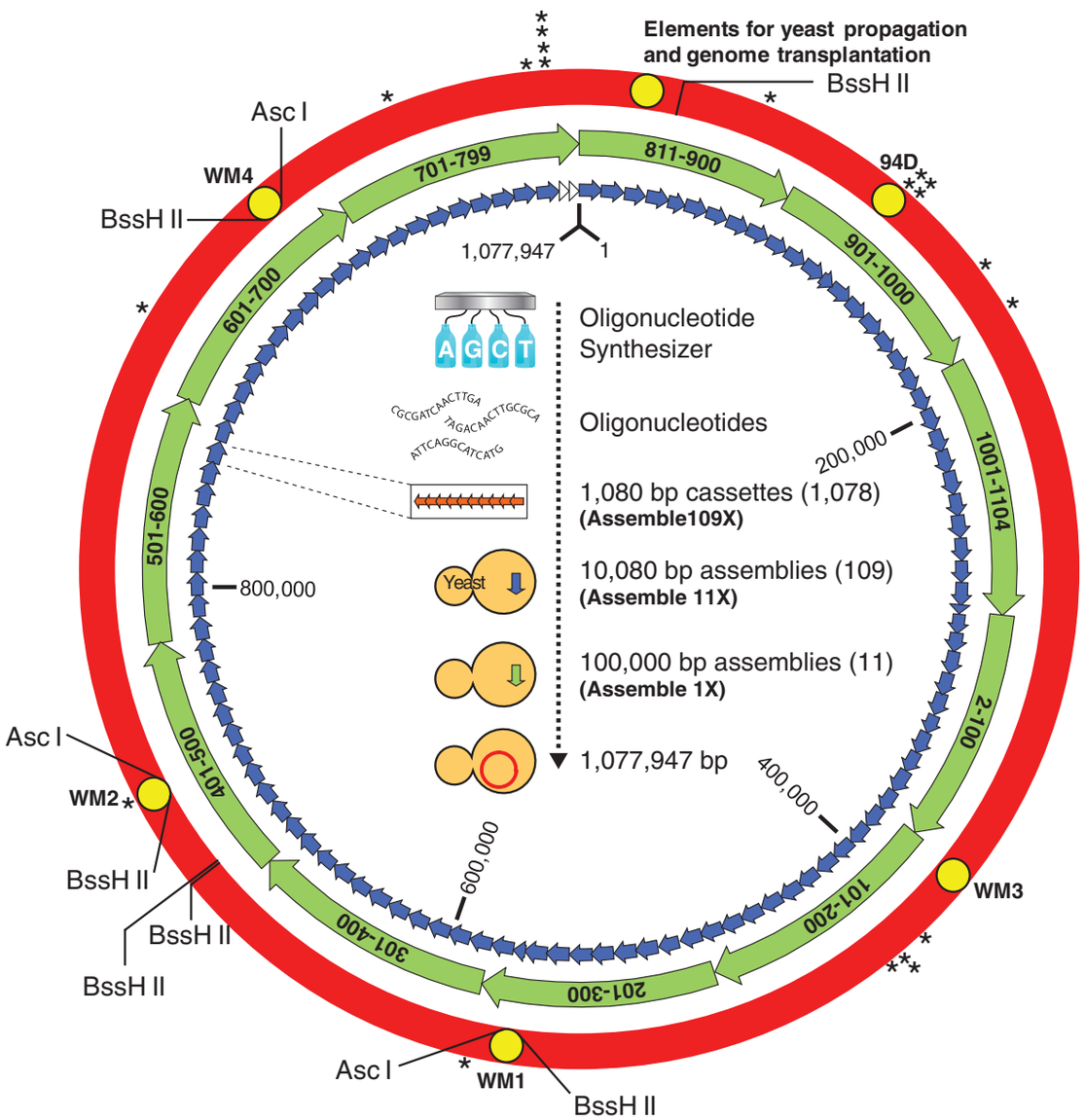
4 jours à 2 semaines

Test

mail

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,[1] John I. Glass,[1] Carole Lartigue,[1] Vladimir N. Noskov,[1] Ray-Yuan Chuang,[1] Mikkel A. Algire,[1] Gwynedd A. Benders,[2] Michael G. Montague,[1] Li Ma,[1] Monzia M. Moodie,[1] Chuck Merryman,[1] Sanjay Vashee,[1] Radha Krishnakumar,[1] Nacyra Assad-Garcia,[1] Cynthia Andrews-Pfannkoch,[1] Evgeniya A. Denisova,[1] Lei Young,[1] Zhi-Qing Qi,[1] Thomas H. Segall-Shapiro,[1] Christopher H. Calvey,[1] Prashanth P. Parmar,[1] Clyde A. Hutchison III,[2] Hamilton O. Smith,[2] J. Craig Venter[1,2]*



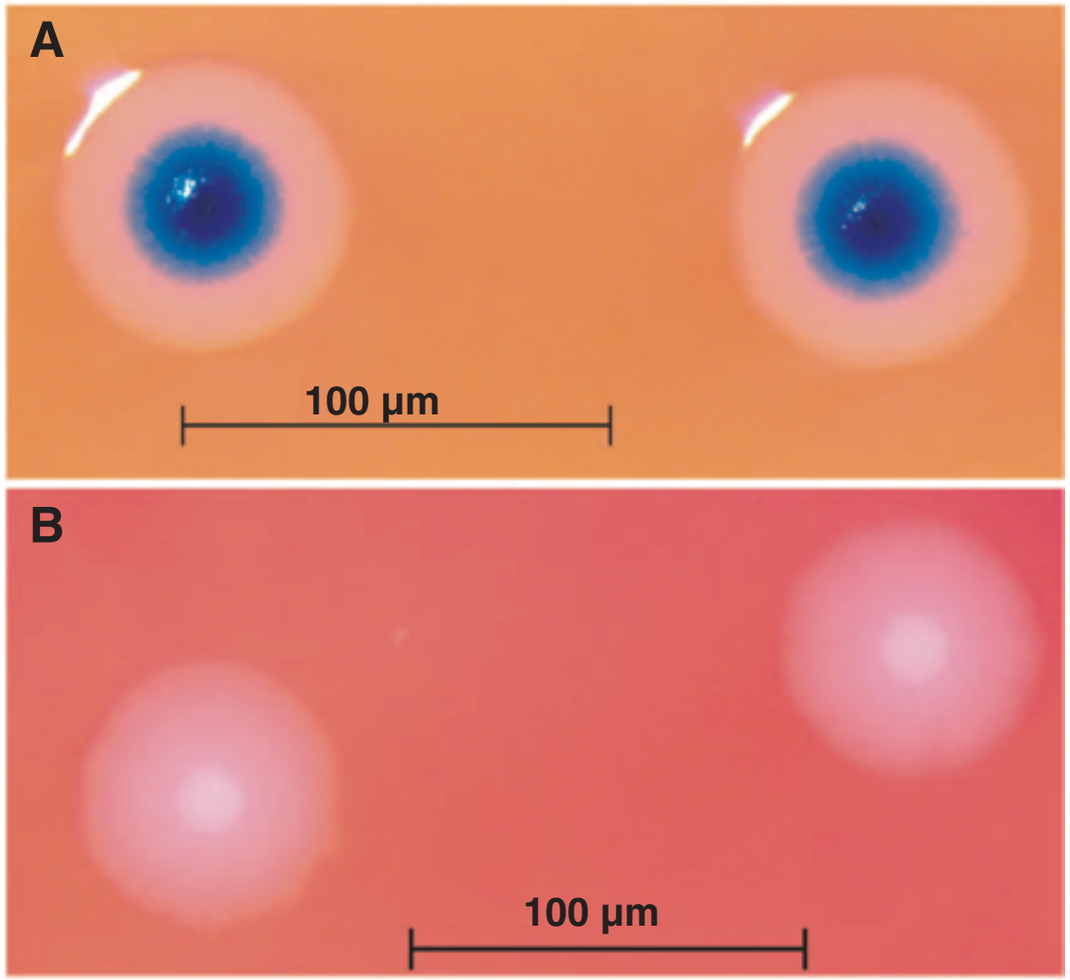
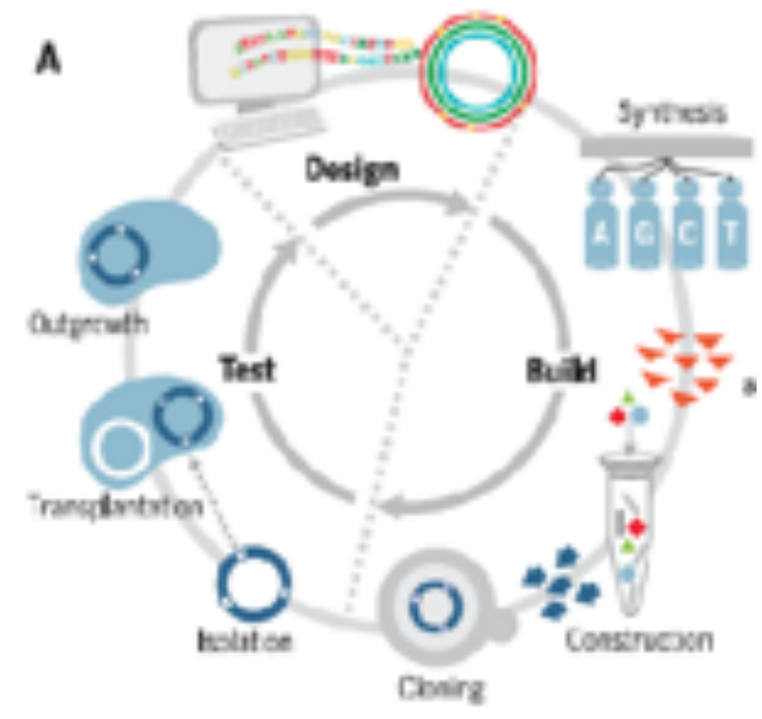


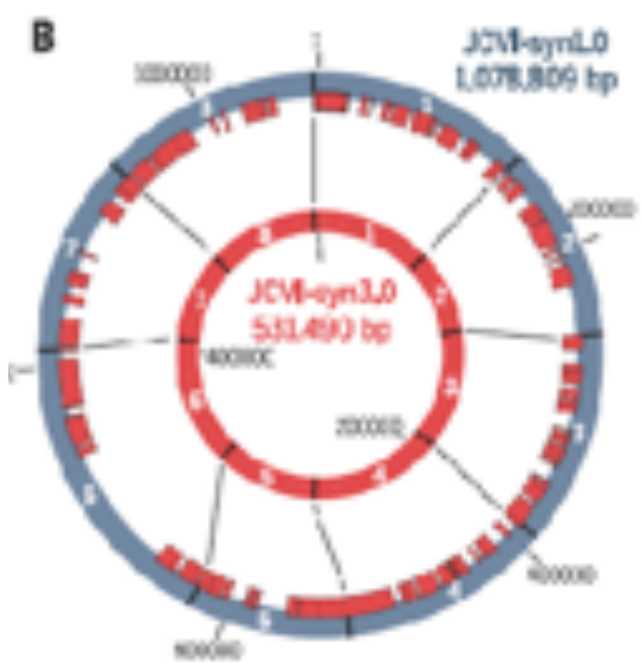
Fig. 1. The assembly of a synthetic *M. mycoides* genome in yeast. A synthetic *M. mycoides* genome

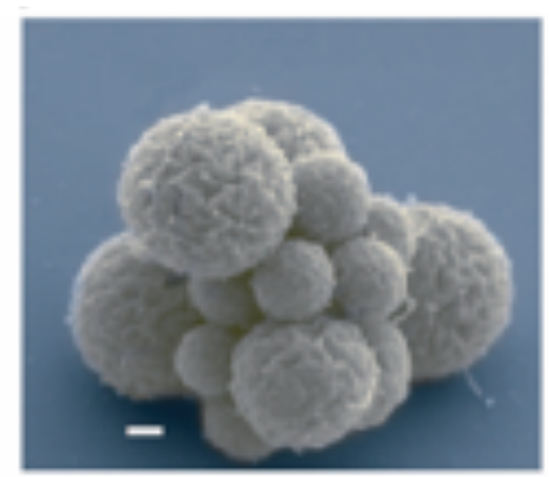
Design and synthesis of a minimal bacterial genome

Clyde A. Hutchison III,[1*] | Ray-Yuan Chuang,[1]†‡ Vladimir N. Noskov,[1]
Nacyra Assad-Garcia,[1] Thomas J. Deerinck,[2] Mark H. Ellisman,[2] John Gill,[1]
Krishna Kannan,[1] Bogumil J. Karas,[1] Li Ma,[1] James F. Pelletier,[1]§ Zhi-Qing Qi,[1]
R. Alexander Richter,[1] Elizabeth A. Strychalski,[1] Lijie Sun,[1]‖ Yo Suzuki,[1]
Billyana Tsvanov,[1] Kim S. Wise,[1] Hamilton O. Smith,[1,3] John I. Glass,[1]
Chuck Merryman,[1] Daniel G. Gibson,[1,3] J. Craig Venter[1,4*]

We used whole-genome design and complete chemical synthesis to minimize the 1079-kilobase pair synthetic genome of *Mycoplasma mycoides* JCVI-syn1.0. An initial design, based on collective knowledge of molecular biology combined with limited transposon mutagenesis data, failed to produce a viable cell. Improved transposon mutagenesis methods revealed a class of quasi-essential genes that are needed for robust growth, explaining the failure of our initial design. Three cycles of design, synthesis, and testing, with retention of quasi-essential genes, produced JCVI-syn3.0 (531 kilobase pairs, 473 genes), which has a genome smaller than that of any autonomously replicating cell found in nature. JCVI-syn3.0 retains almost all genes involved in the synthesis and processing of macromolecules. Unexpectedly, it also contains 149 genes with unknown biological functions. JCVI-syn3.0 is a versatile platform for investigating the core functions of life and for exploring whole-genome design.





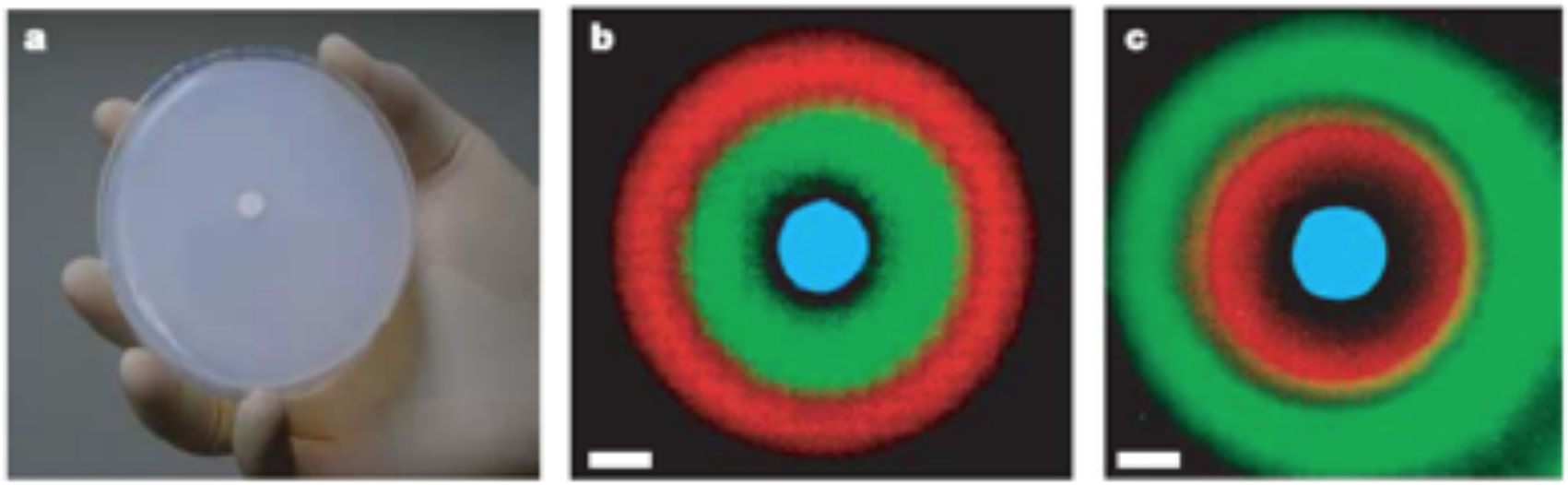


Science 2016

A synthetic multicellular system for programmed pattern formation

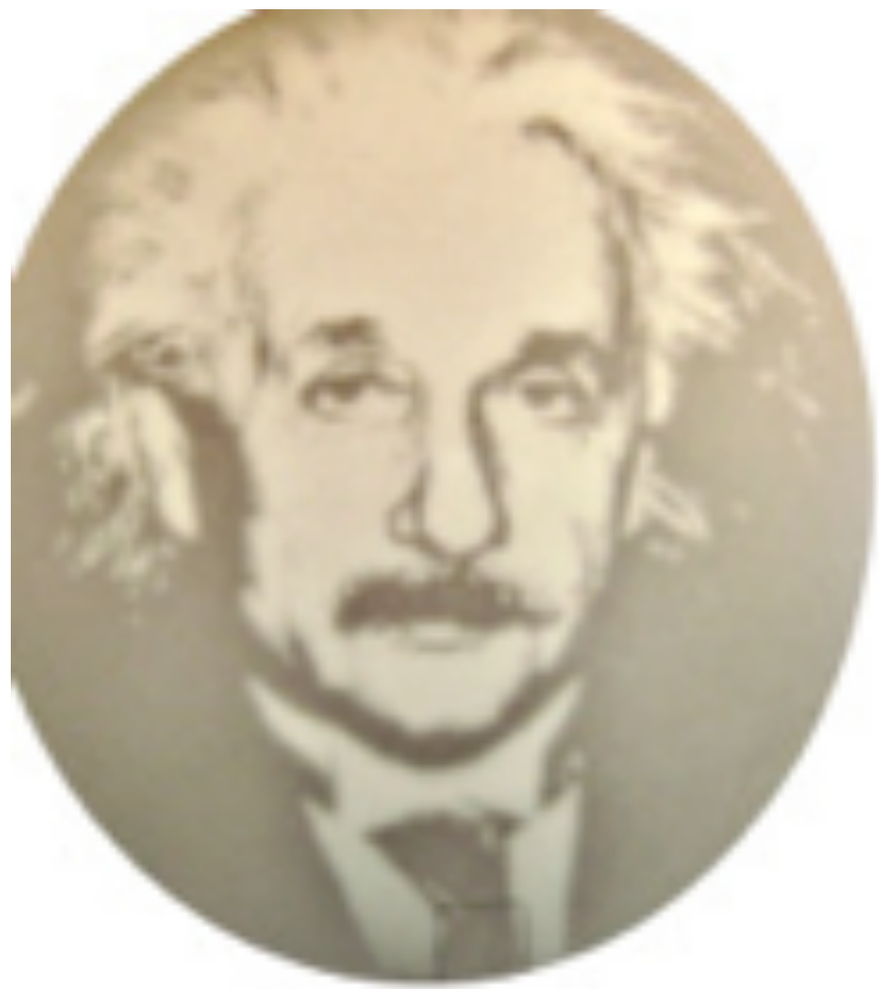
Subhayu Basu[1], Yoram Gerchman[1], Cynthia H. Collins[3], Frances H. Arnold[3] & Ron Weiss[1,2]

[1]*Department of Electrical Engineering and* [2]*Department of Molecular Biology, Princeton University, Princeton, New Jersey 08544, USA*
[3]*Division of Chemistry and Chemical Engineering, California Institute of Technology 210-41, Pasadena, California 91125, USA*



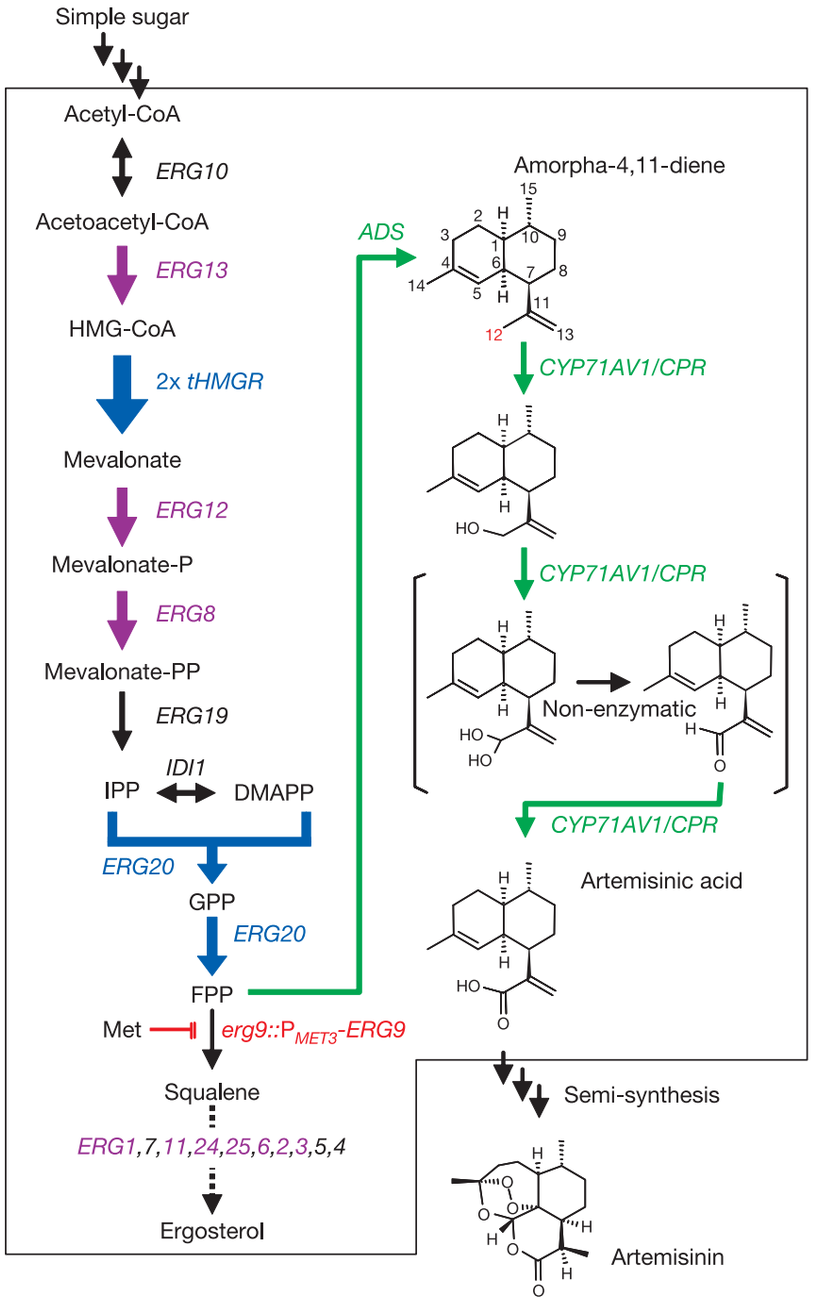
Engineering *Escherichia coli* to see light

These smart bacteria 'photograph' a light pattern as a high-definition chemical image.



Production of the antimalarial drug precursor artemisinic acid in engineered yeast

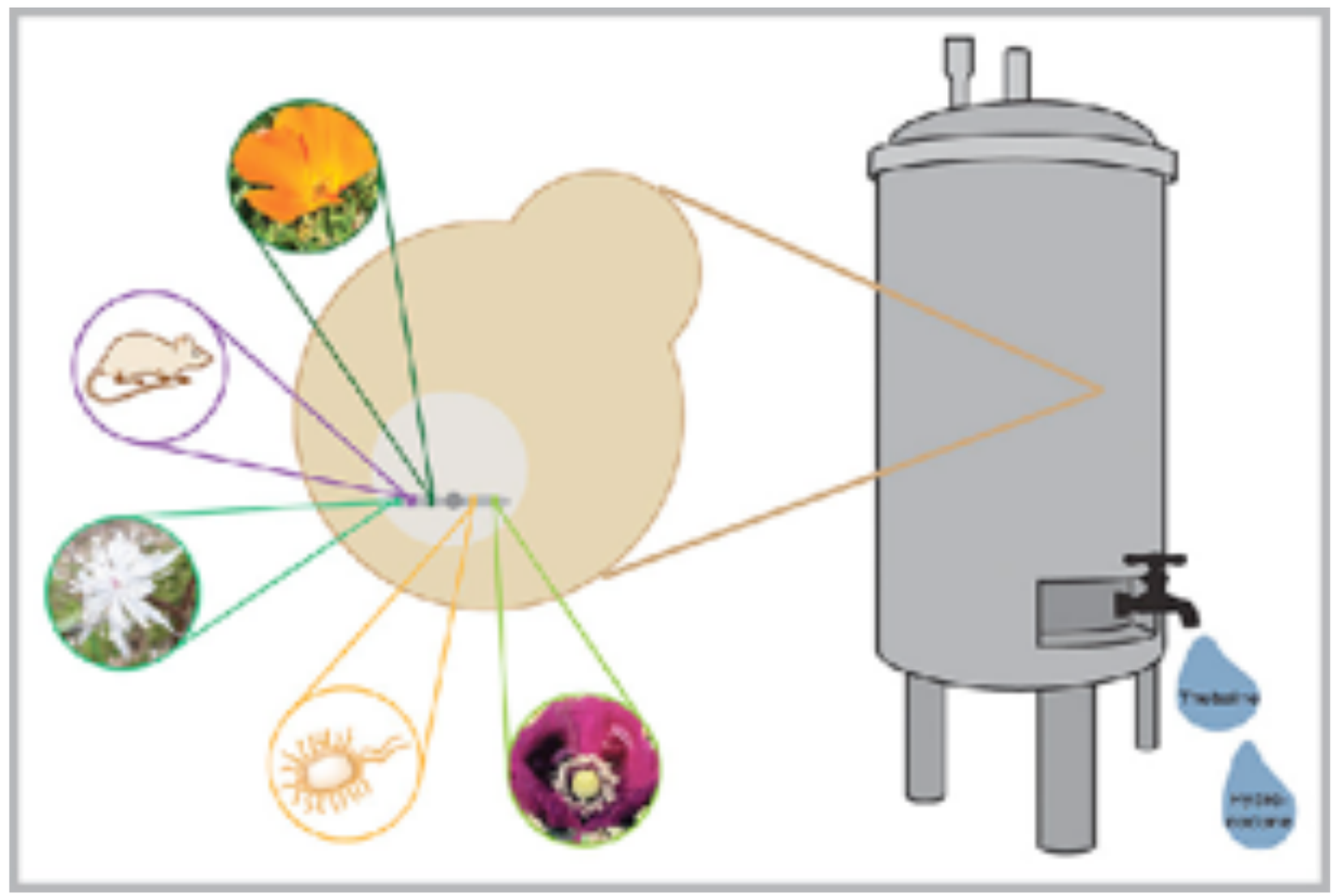
Dae-Kyun Ro[1]*, Eric M. Paradise[2]*, Mario Ouellet[1], Karl J. Fisher[6], Karyn L. Newman[1], John M. Ndungu[3], Kimberly A. Ho[1], Rachel A. Eachus[1], Timothy S. Ham[4], James Kirby[2], Michelle C. Y. Chang[1], Sydnor T. Withers[2], Yoichiro Shiba[2], Richmond Sarpong[3] & Jay D. Keasling[1,2,4,5]



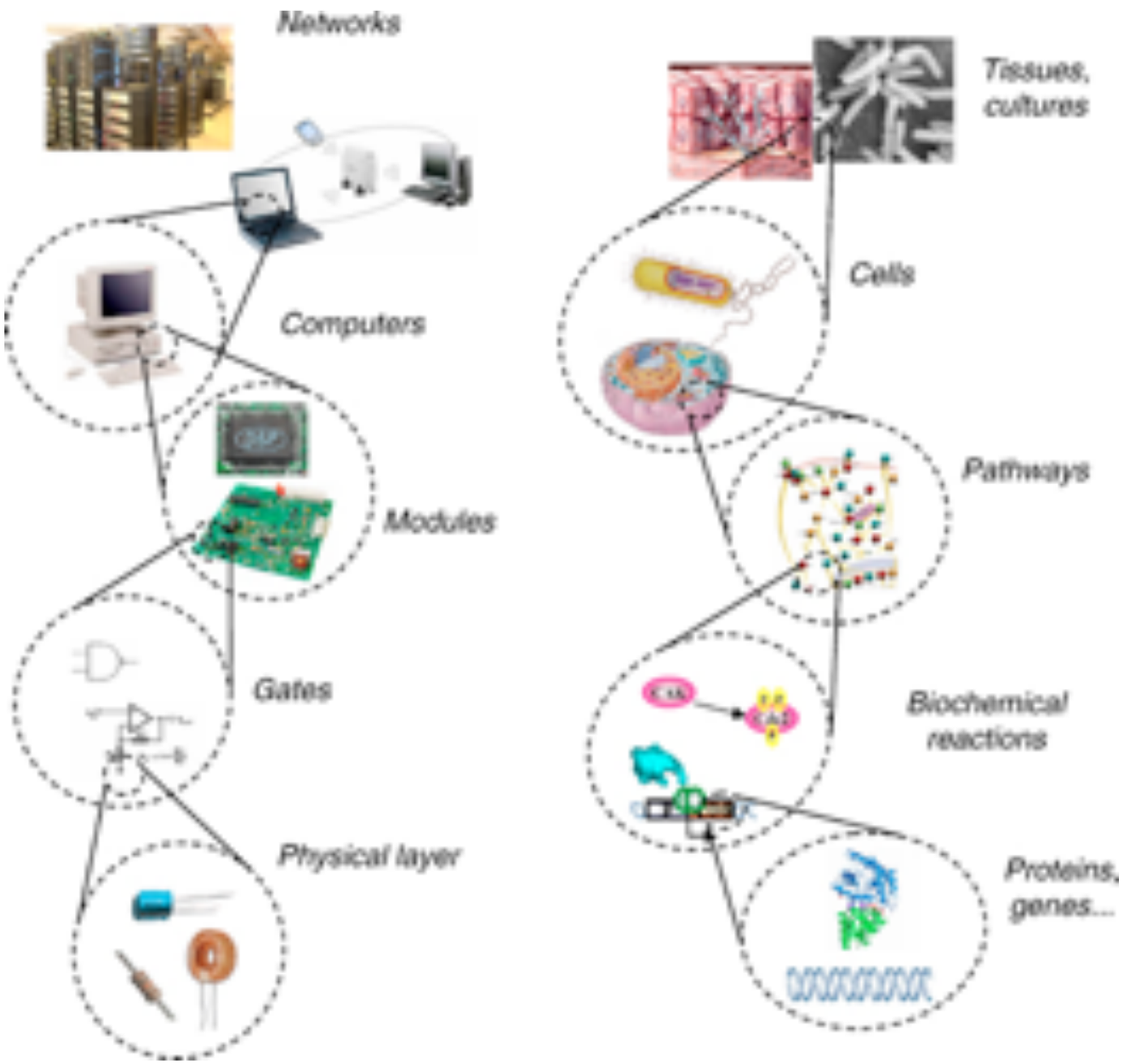
SYNTHETIC BIOLOGY

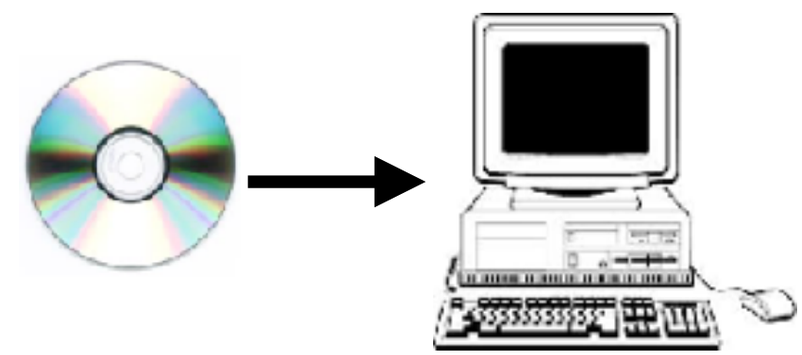
Complete biosynthesis of opioids in yeast

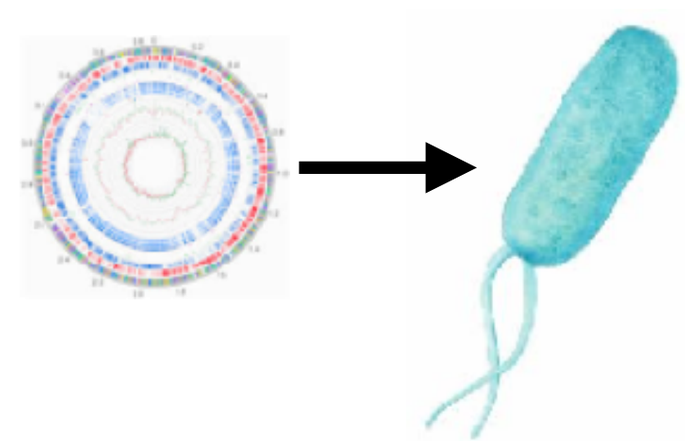
Stephanie Galanie,[1] Kate Thodey,[2] Isis J. Trenchard,[2]
Maria Filsinger Interrante,[2] Christina D. Smolke[2*]



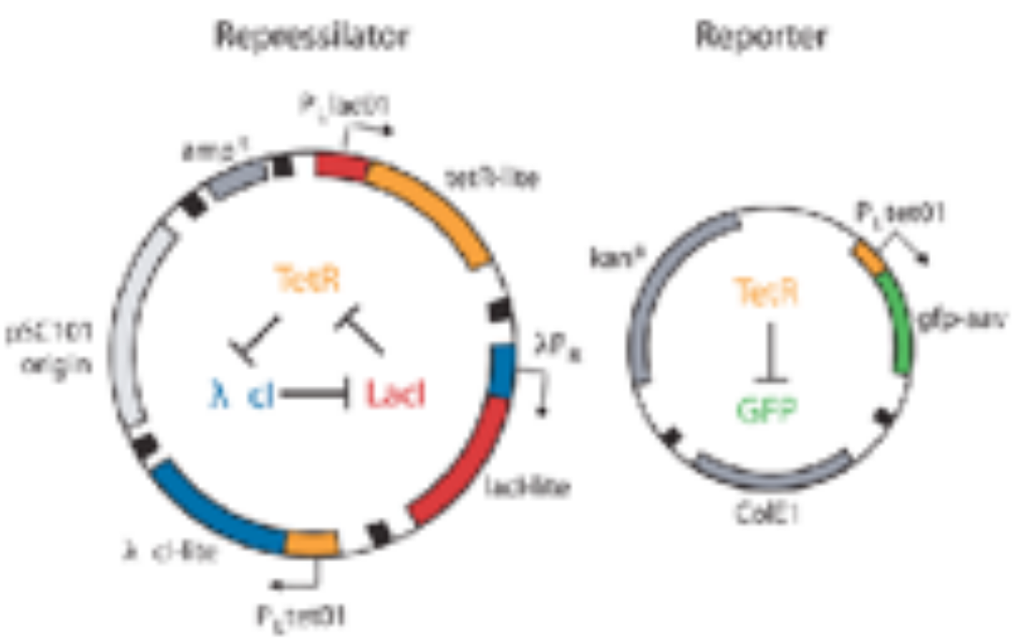
Inspirations: mature engineering sciences example with electronics





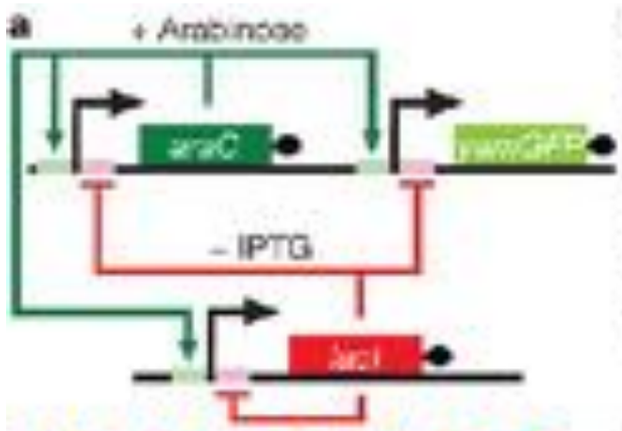


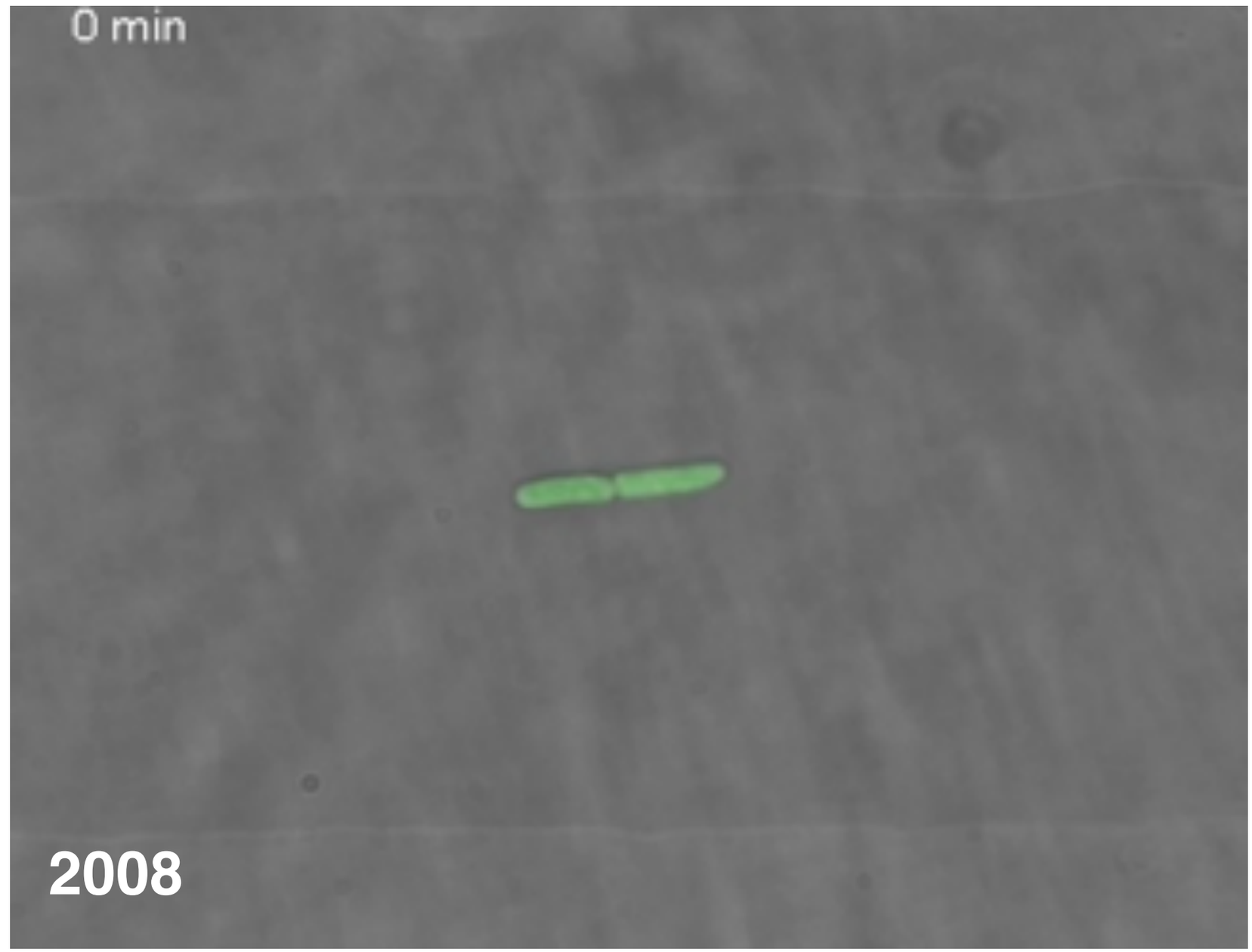
Genetic oscillators



Elowitz, 2000

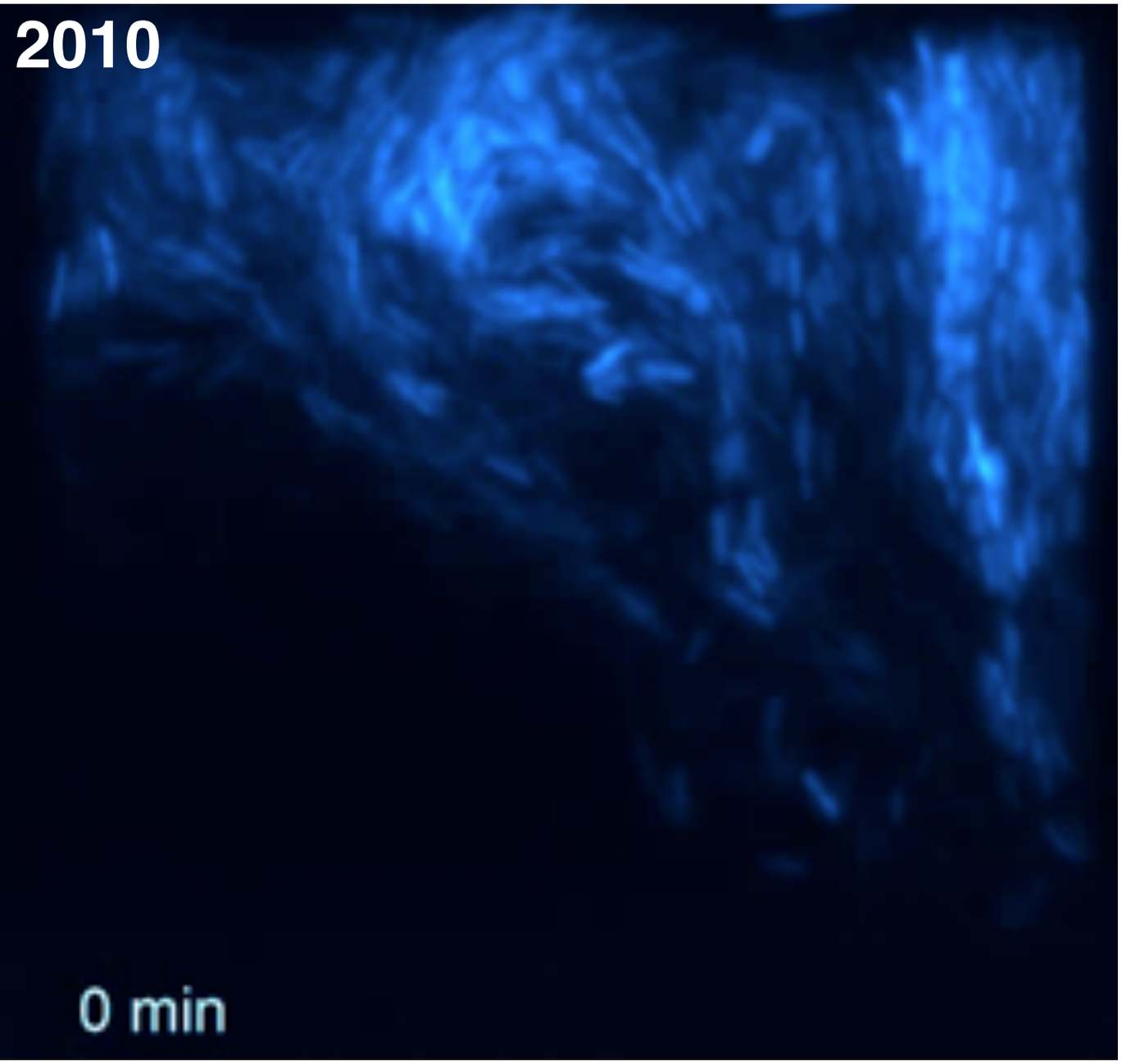
Genetic oscillators





Striker, 2000

Synchronized genetic oscillators



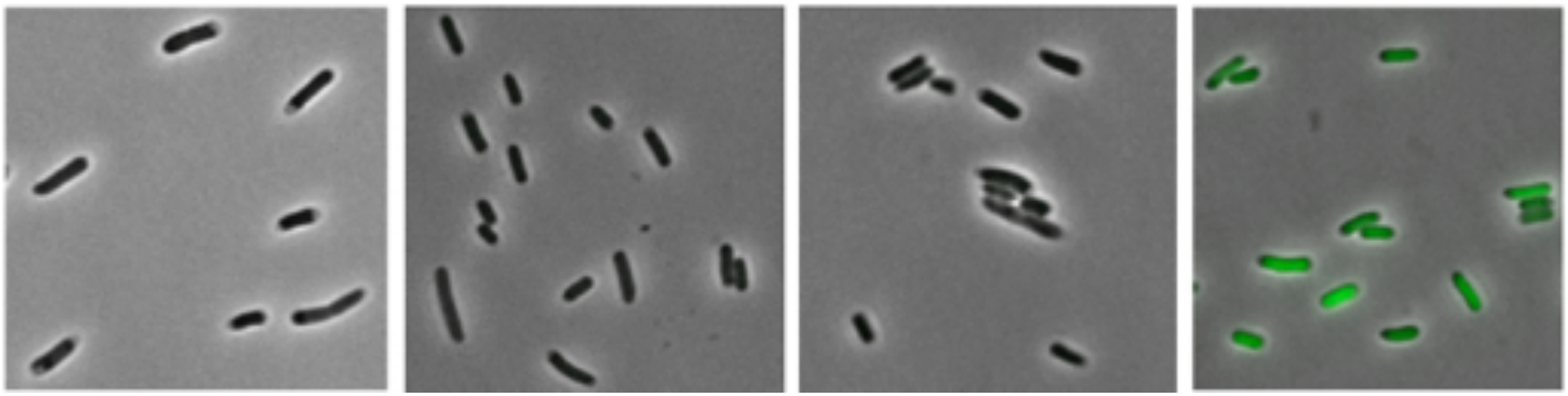
Hasty lab, UC San Diego

Amplifying Genetic Logic Gates

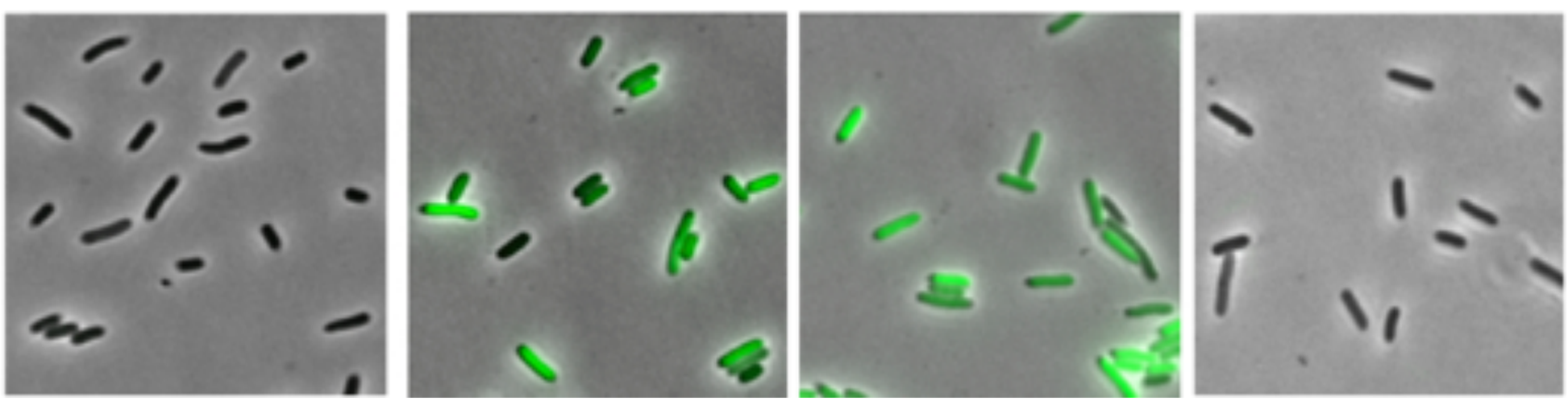
Jerome Bonnet, Peter Yin,* Monica E. Ortiz, Pakpoom Subsoontorn, Drew Endy†

no inducer | Molecule A | Molecule B | A+ B

AND



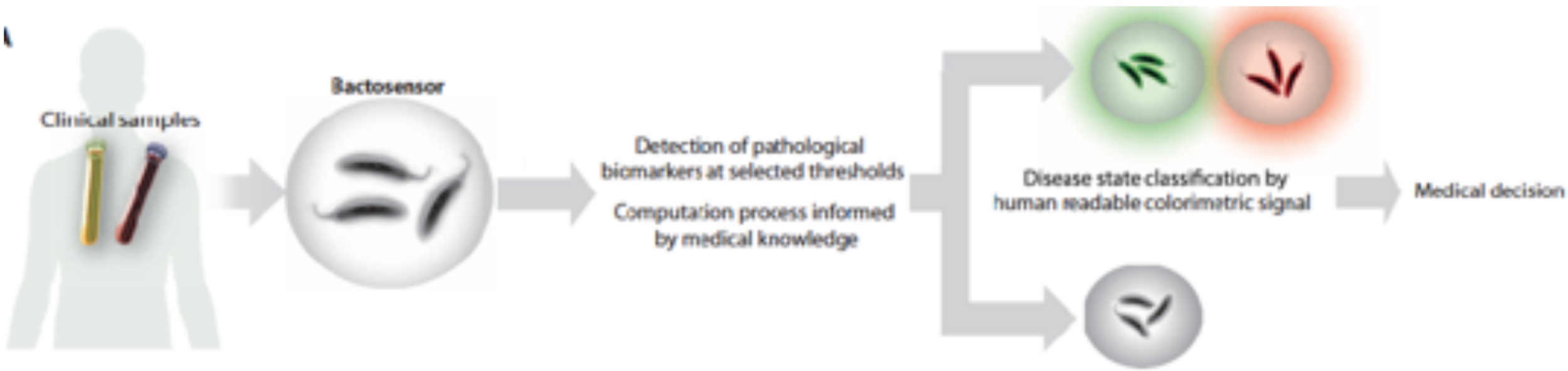
XOR

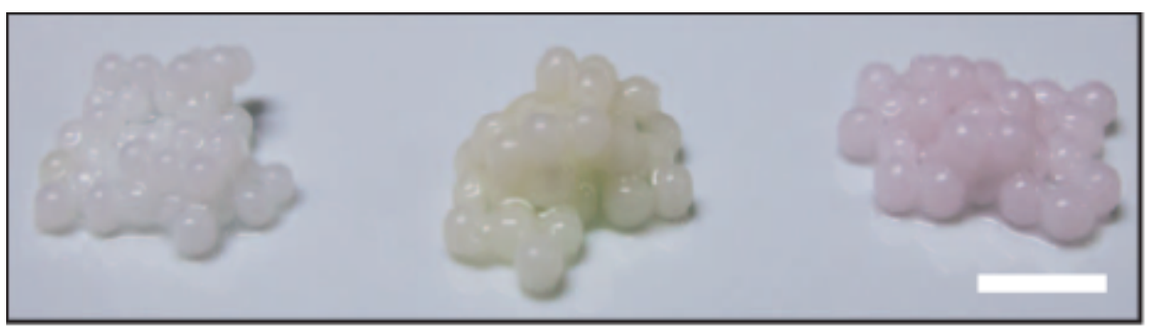


Next class

Detection of pathological biomarkers in human clinical samples via amplifying genetic switches and logic gates

Alexis Courbet,[1] Drew Endy,[2] Eric Renard,[3] Franck Molina,[1]* Jérôme Bonnet[4]*



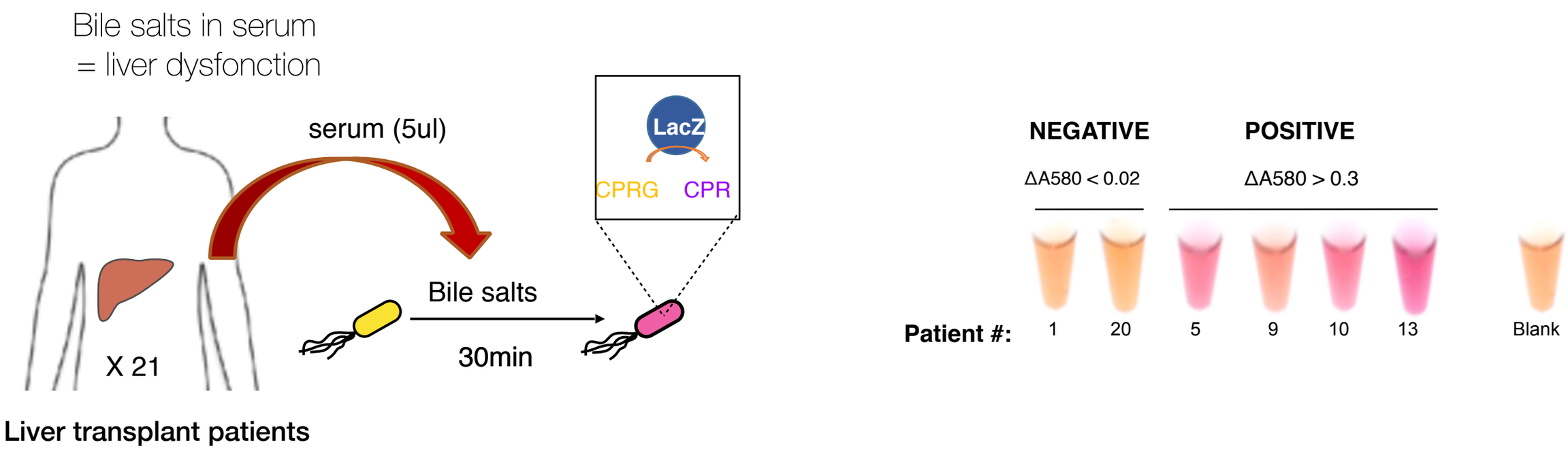


ARTICLE

https://doi.org/10.1038/s41467-021-25538-y OPEN

Programmable receptors enable bacterial biosensors to detect pathological biomarkers in clinical samples

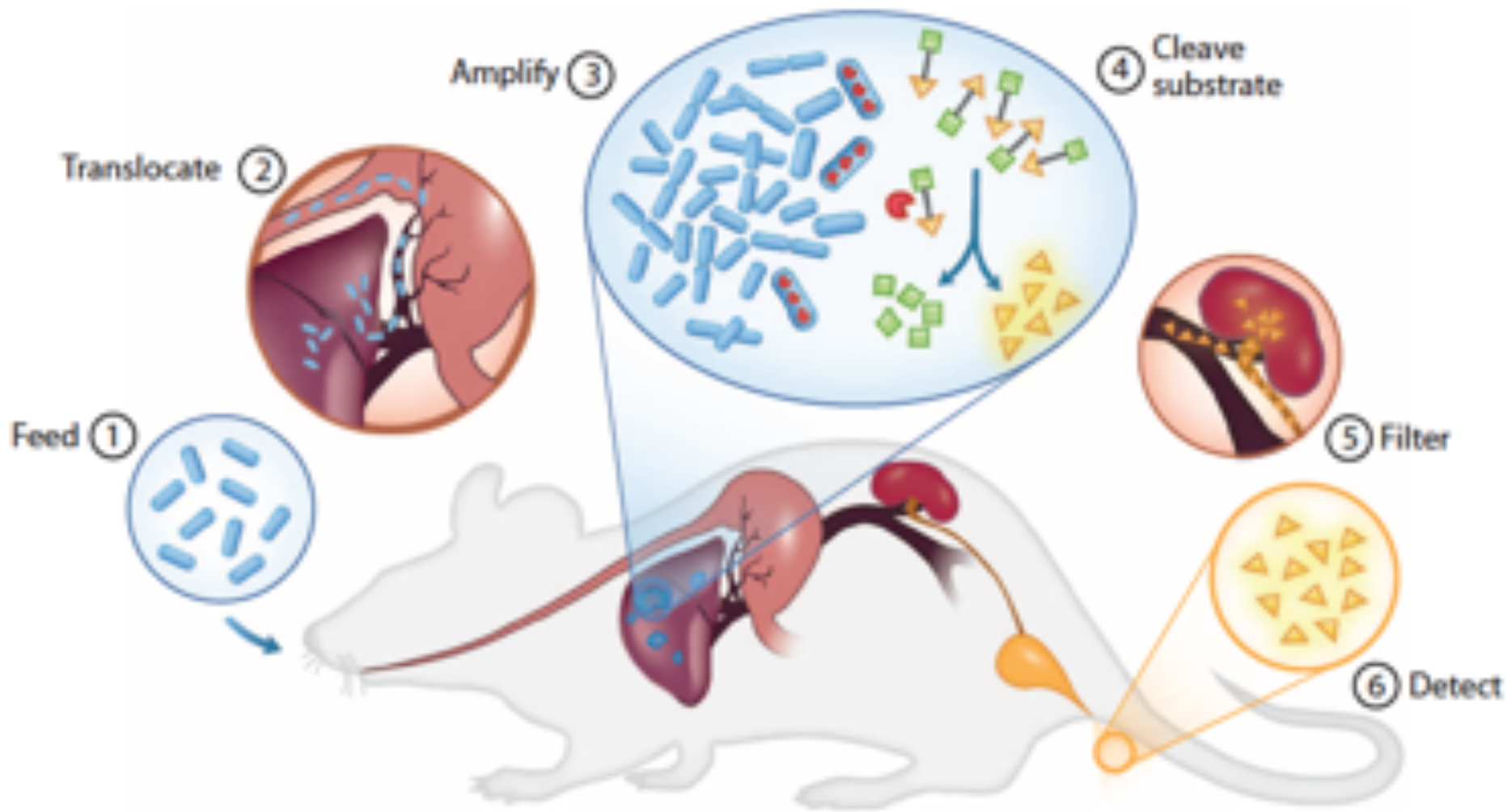
Hung-Ju Chang[1], Ana Zúñiga[1], Ismael Conejero[1,2,3], Peter L. Voyvodic[1], Jerome Gracy[1], Elena Fajardo-Ruiz[1], Martin Cohen-Gonsaud[1], Guillaume Cambray[1], Georges-Philippe Pageaux[4], Magdalena Meszaros[4], Lucy Meunier[4] & Jerome Bonnet[1]✉



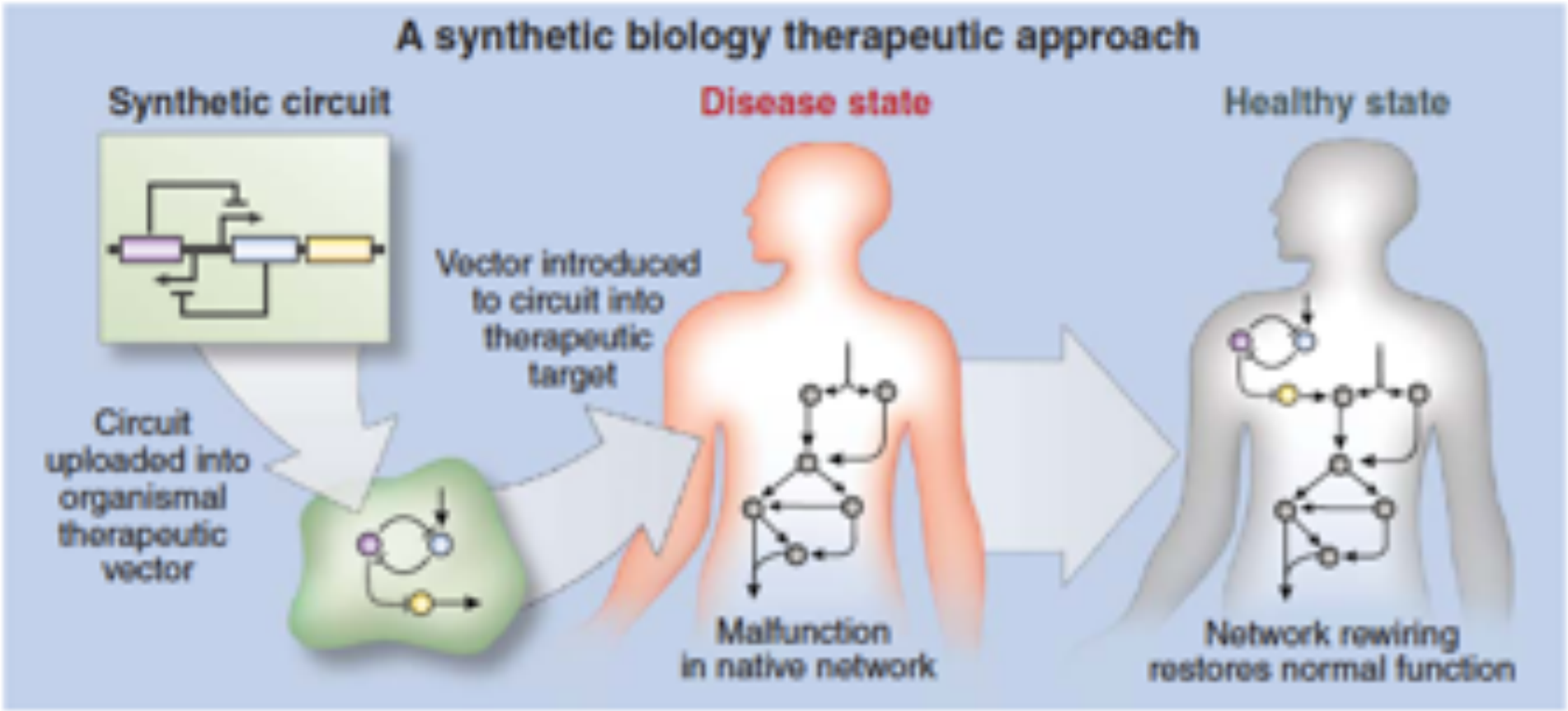
Chang et al. ***Nature Communications****, 2021*
https://doi.org/10.1038/s41467-021-25538-y

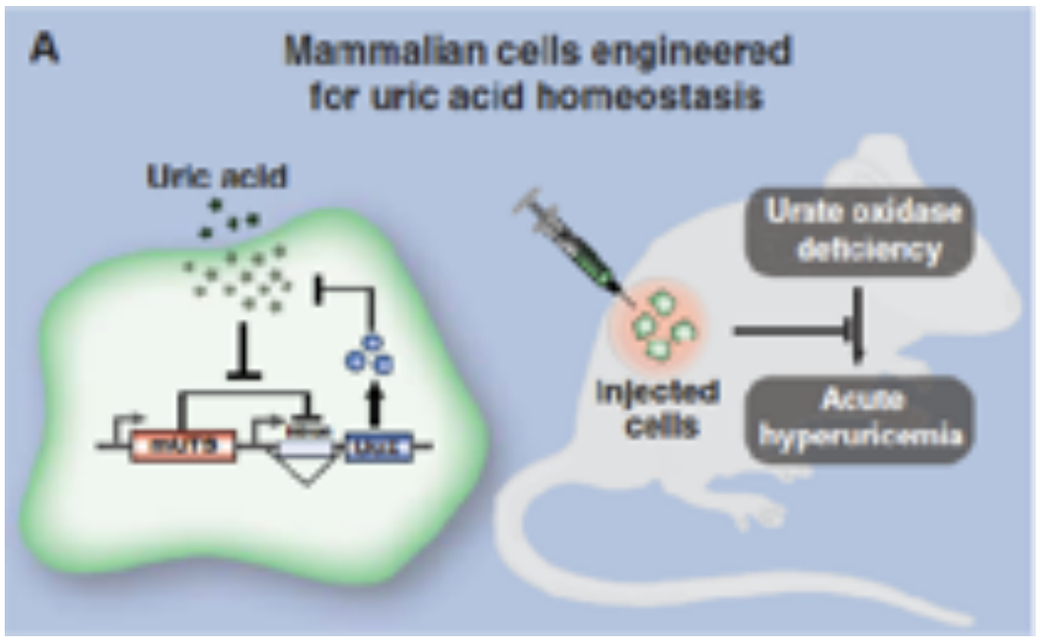
Programmable probiotics for detection of cancer in urine

Tal Danino,[1*] Arthur Prindle,[2*] Gabriel A. Kwong,[1†] Matthew Skalak,[1] Howard Li,[2] Kaitlin Allen,[1] Jeff Hasty,[2,3,4‡] Sangeeta N. Bhatia[1,5,6,7,8‡§]



Prosthetic gene networks

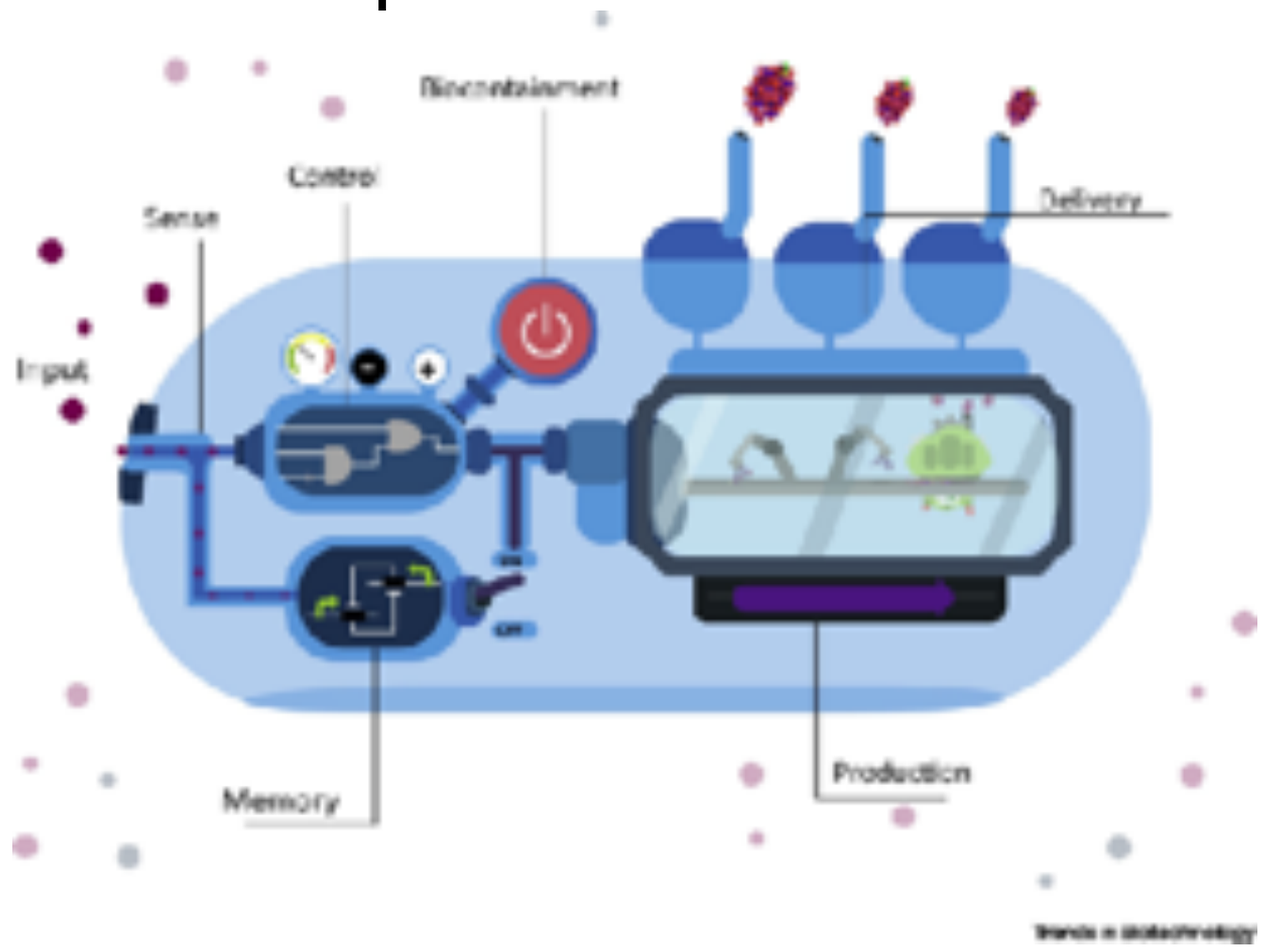


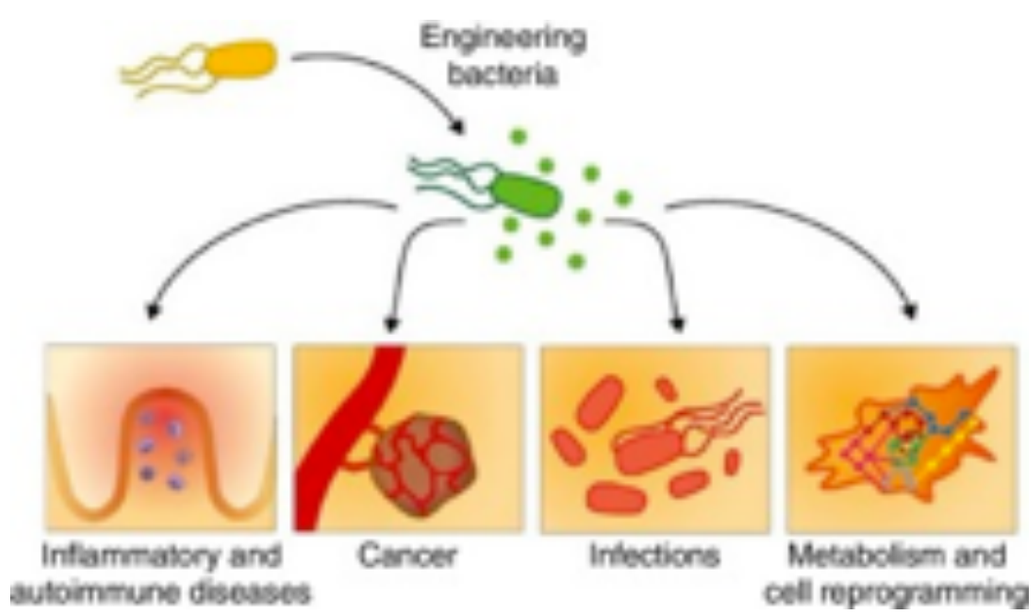


Rudder et al., 2011

gout

Engineered bacterial therapeutics

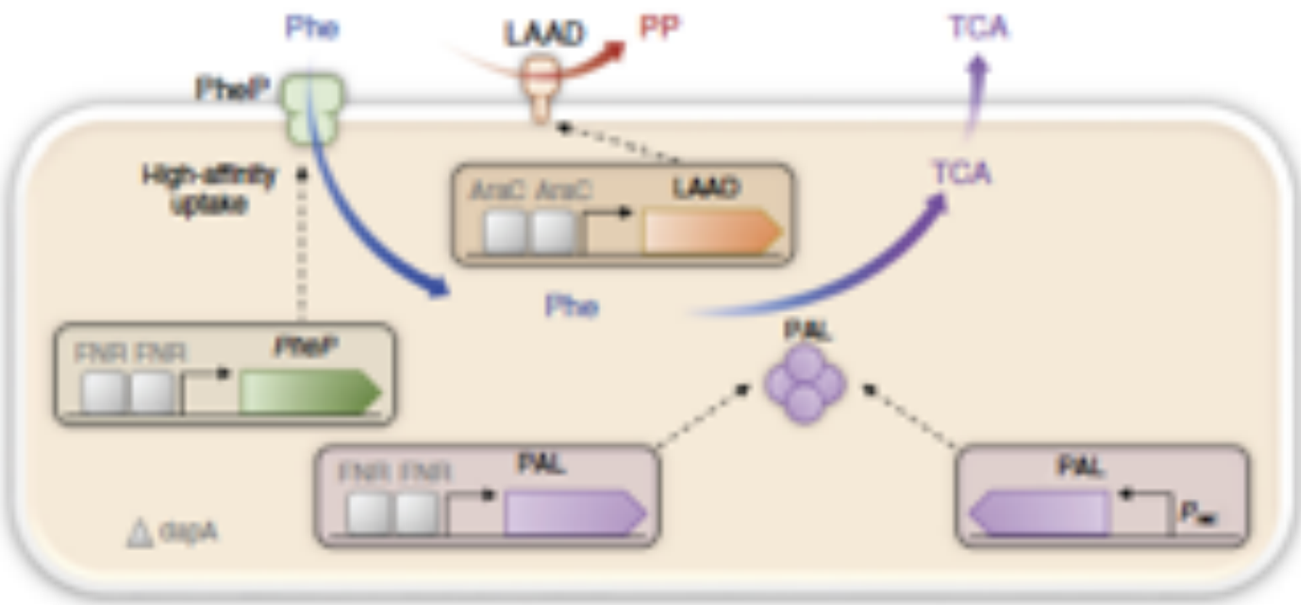


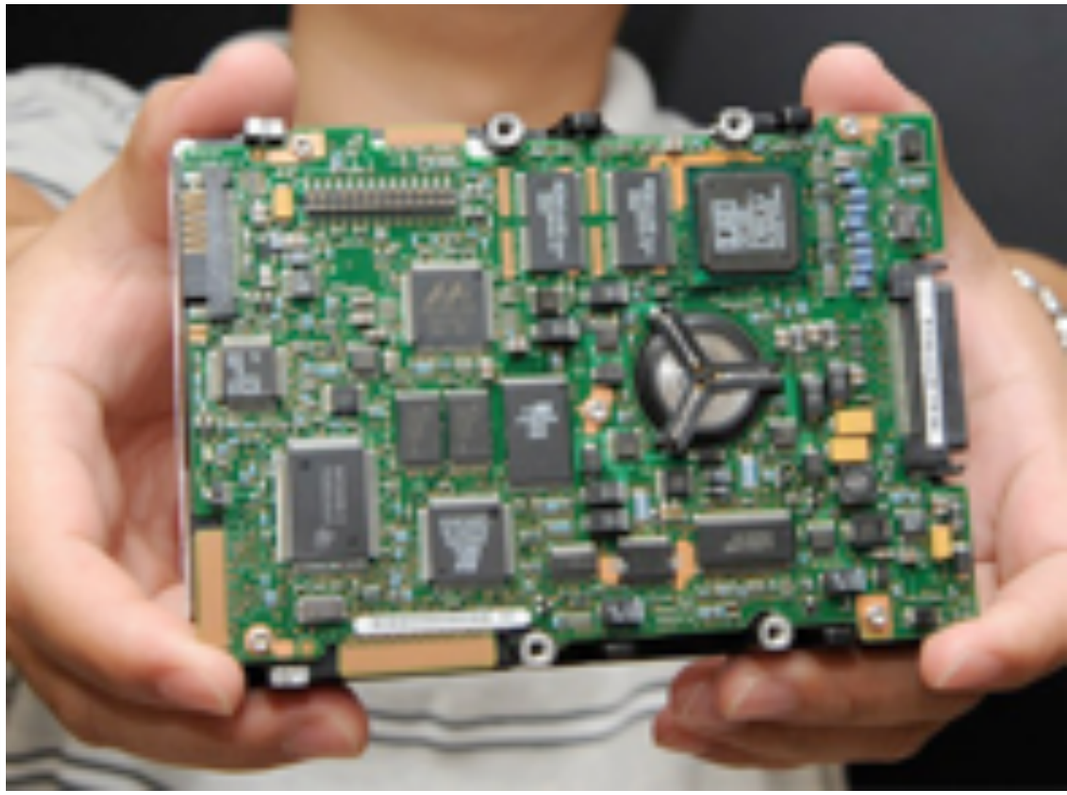


Pinero-Lambea at al., Curr. Op. Biotech. 2015

Development of a synthetic live bacterial therapeutic for the human metabolic disease phenylketonuria

Vincent M Isabella[1], Binh N Ha[1], Mary Joan Castillo[1], David J Lubkowicz[1], Sarah E Rowe[1,2], Yves A Millet[1], Cami L Anderson[1], Ning Li[1], Adam B Fisher[1], Kip A West[1], Philippa J Reeder[1], Munira M Momin[1], Christopher G Bergeron[1], Sarah E Guilmain[1], Paul F Miller[1], Caroline B Kurtz[1] & Dean Falb[1]

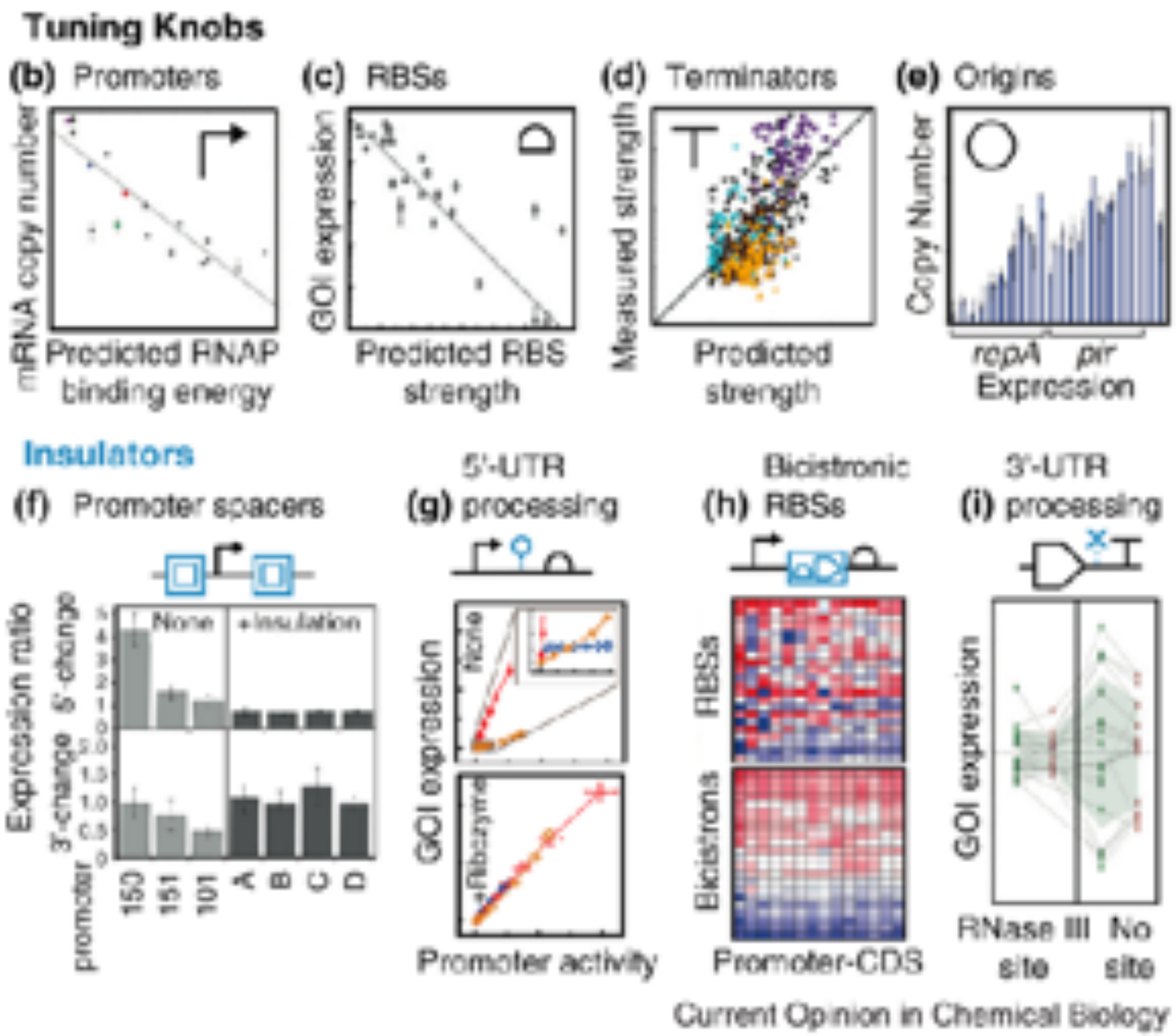




Inspirations from mature engineering disciplines

Dolmen des blancs fossés,
France, ~ 1800 av. JC

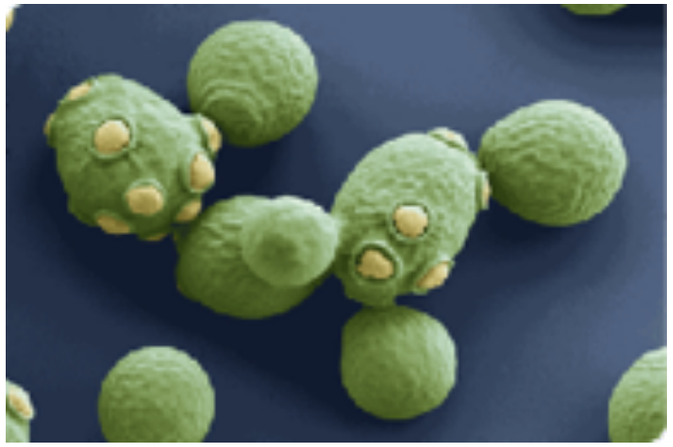
Well-characterized parts libraries are available for E. coli…



biofab

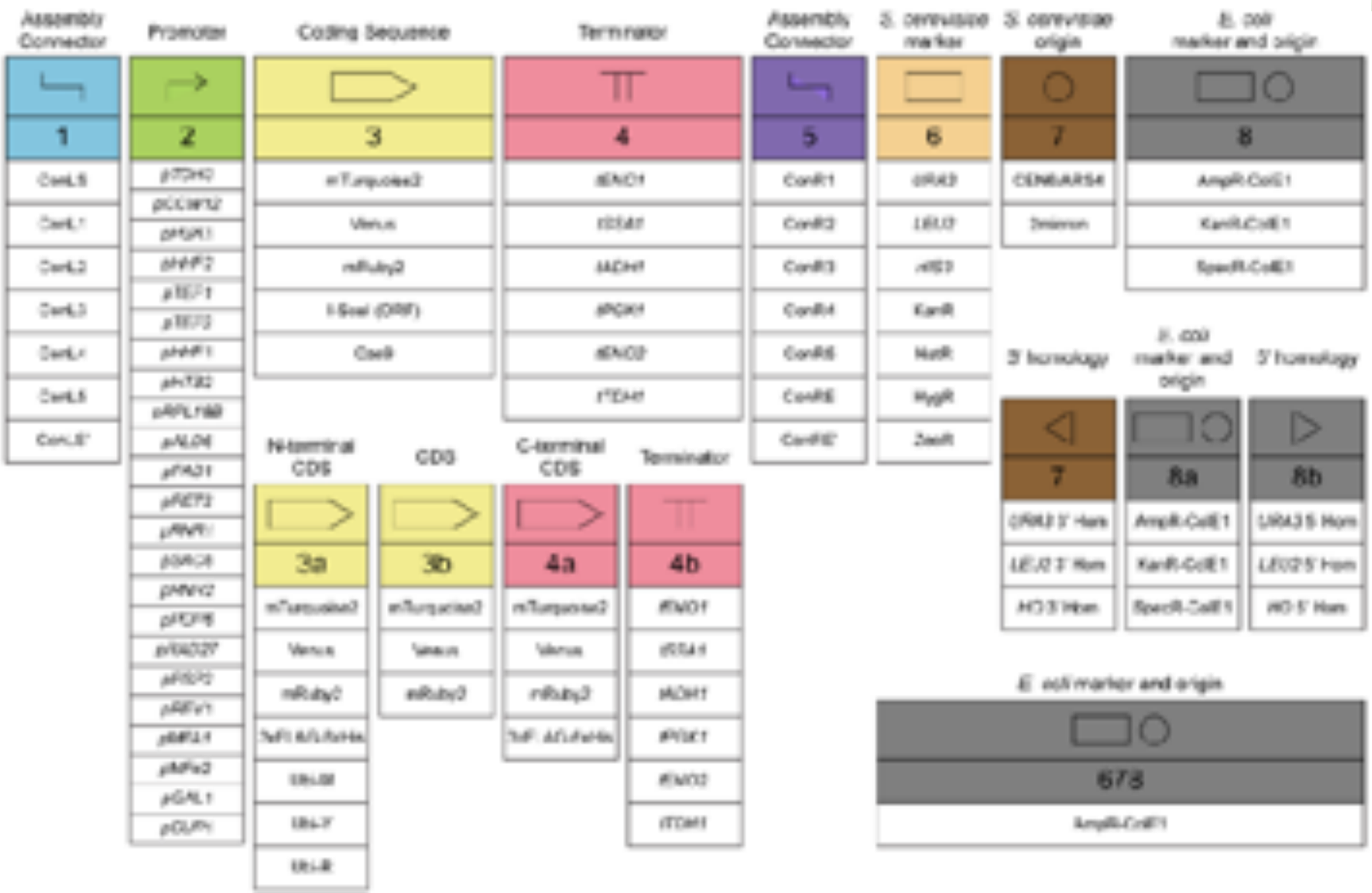
Nielsen et al. 2014

As well as for yeast…

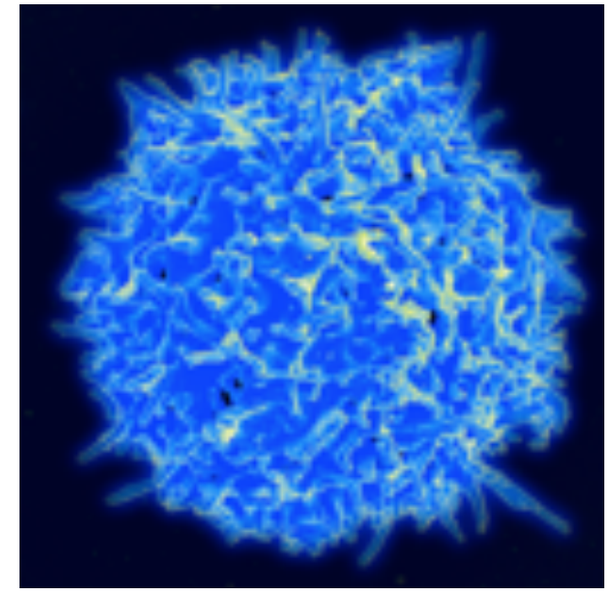


A Highly Characterized Yeast Toolkit for Modular, Multipart Assembly

Michael E. Lee,[†,‡,⊥] William C. DeLoache,[†,‡,⊥] Bernardo Cervantes,[†,⊥] and John E. Dueber*[,†,§,∥]



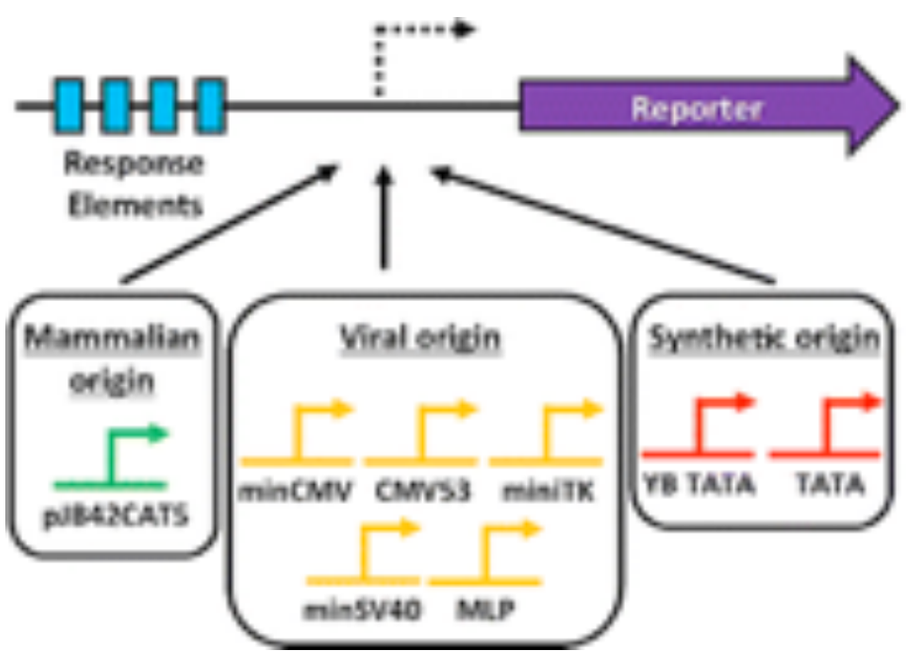
Or mammalian cells….

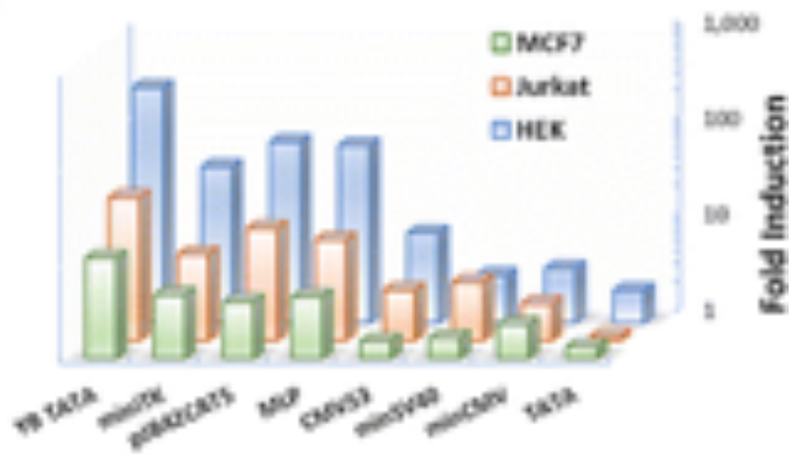


Quantitative Analyses of Core Promoters Enable Precise Engineering of Regulated Gene Expression in Mammalian Cells

Christopher Ede, Ximin Chen, Meng-Yin Lin, and Yvonne Y. Chen*

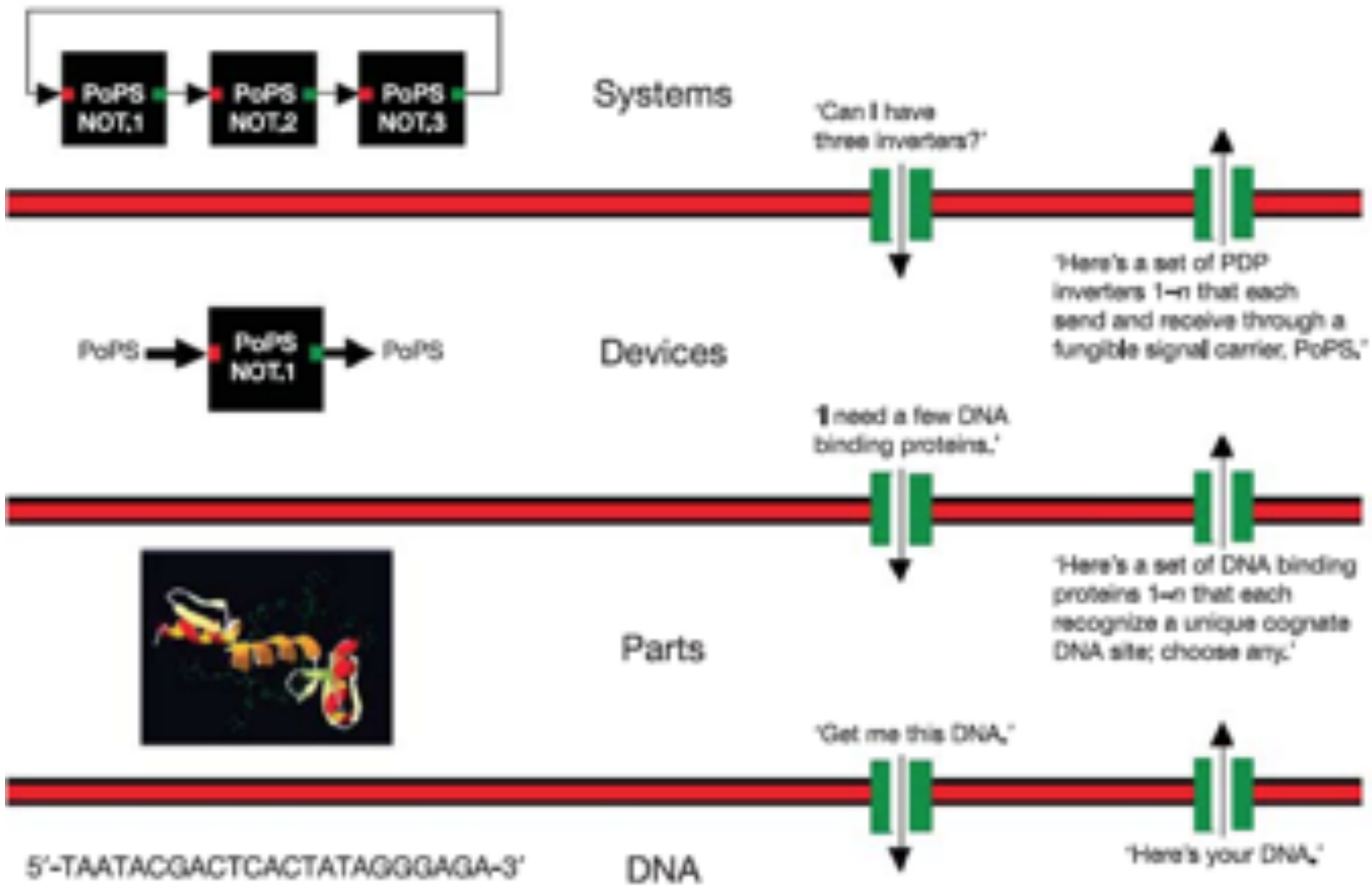
Department of Chemical and Biomolecular Engineering, University of California—Los Angeles, Los Angeles, California 90095, United States





ACS Synthetic Biology, 2016

Abstraction hierarchy



Synthetic biology based on standard parts

International Genetically Engineered Machine Competition

http://igem.org/

Registry of Standard Biological Parts

page discussion view source history

Welcome to the Registry of Standard Biological Parts.

The Registry is a collection of ~3200 genetic parts that can be mixed and matched to build synthetic biology devices and systems. Fo the Registry is part of the Synthetic Biology community's efforts to make biology easier to engineer. It provides a resource of availabl iGEM teams and academic labs.

The Registry is based on the principle of "get some, give some". Registry users benefit from using the parts and information available from the R their engineered biological systems. In exchange, the expectation is that Registry users will, in turn, contribute back information and data on ex parts that they make to grow and improve this community resource.

Catalog of parts & devices

Help

Users & groups

(Apply for an account)

DNA repositories

Registry tools

- Search parts (?)
- Add a part
- Send parts to the Registry
- Sequence analysis

You'll notice some significant changes to the Registry recently. In particular, the Registry catalog of parts has been entirely re easier browsing of the available parts and devices. You can now browse parts and devices by type, by chassis and by stand that the documentation and help pages for each class of parts have been greatly enhanced.

The Registry of Standard Biological Parts is "always" a work in progress. Please browse the new catalog and let us know wh to edit and improve the pages further.

http://partsregistry.org/

parts.igem.org

tools catalog repository assembly protocols learn BBa_ login 0

Registry of Standard Biological Parts

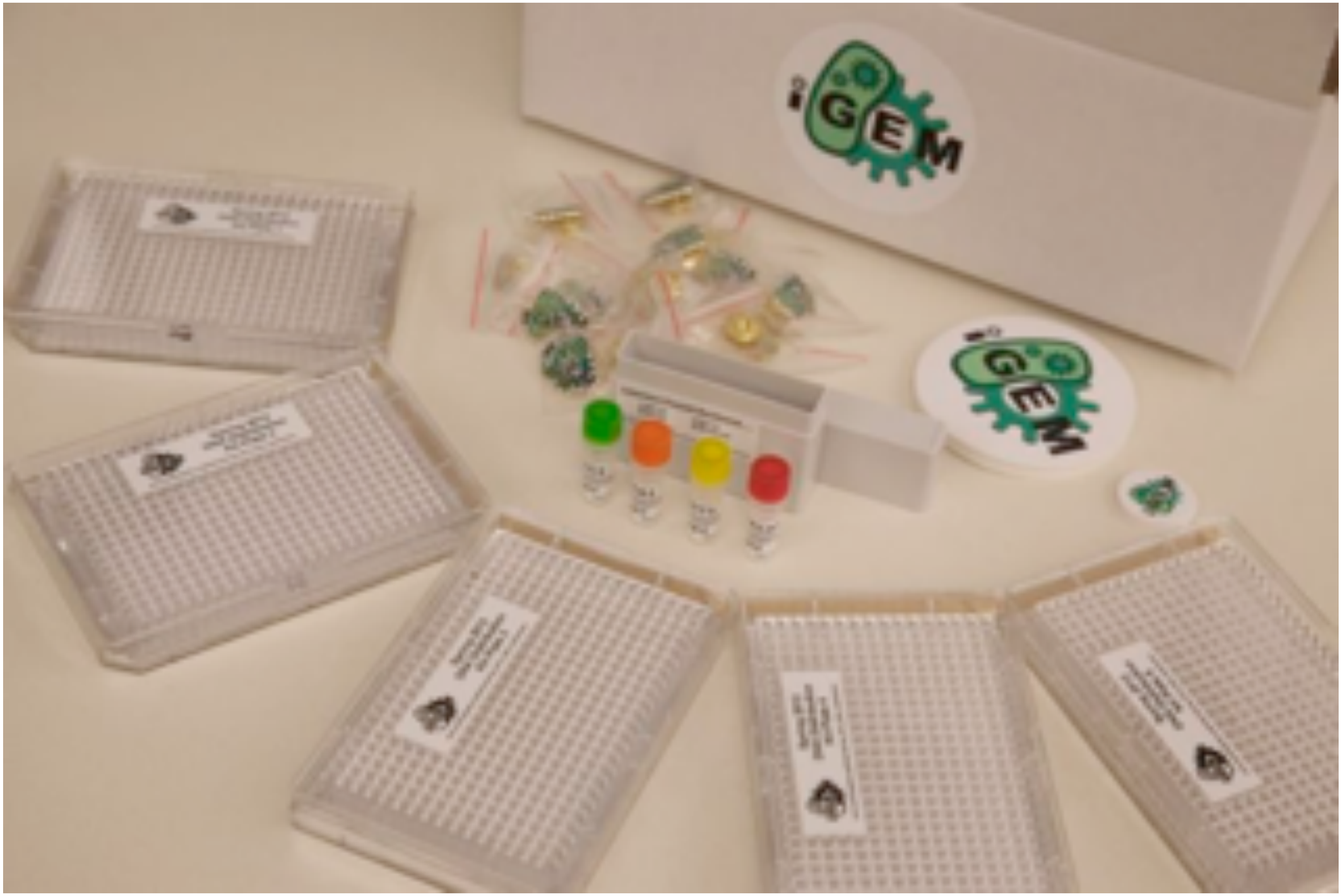
Odor

< Back to Catalog

Odorants are volatile compounds that have an aroma detectable by the olfactory system. Odorant enzymes convert a substrate to an odorant product. Recently, the DNA sequences for several odorant enzymes have been obtained.

More...

Name	Type	Description	Length
BBa_I742107	Coding	COMT	1101
BBa_I742109	Translational_Unit	COMT gene with ribosome binding site	1117
BBa_I742111	Translational_Unit	Limonene synthase gene with ribosome binding site	1687
BBa_J45001	Coding	SAM:salicylic acid carboxyl methyltransferase; converts salicylic acid to methyl salicylate (winter	1155
BBa_J45002	Coding	SAM:benzoic acid carboxyl methyltransferase; converts benzoic acid to methyl benzoate (floral odor)	1098
BBa_J45003	Coding	SAM:jasmonic acid carboxyl methyltransferase; converts jasmonic acid to jasmine odor	1170
BBa_J45004	Coding	SAM:benzoic acid/salicylic acid carboxyl methyltransferase I; converts salicylic acid to methyl sali	1074
BBa_J45005	Coding	SAM:salicylic acid carboxyl methyltransferase; converts salicylic acid to methyl salicylate (winterg	1083
BBa_J45006	Coding	alcohol acetyltransferase I (ATF1)	1581
BBa_J45007	Coding	SAM:benzoic acid/salicylic acid carboxyl methyltransferase II; converts salicylic acid to methyl sal	1074
BBa_J45008	Coding	branched-chain amino acid transaminase (BAT2); converts leucine to alpha-ketoisocaprsate	1134
BBa_J45009	Coding	ketoisocaproate decarboxylase (THI3); converts alpha-ketoisocaproate to 3-methylbutanal	1830
BBa_J45014	Coding	alcohol acetyltransferase I; converts isoamyl alcohol to isoamyl acetate (banana odor)	1581
BBa_J45017	Coding	isochorismate pyruvate-lyase and isochorismate synthase (pchBA); converts chorismate to salicylate	1736
BBa_J45099	Generator	Wintergreen odor enzyme (BSMT1) generator	1232
BBa_J45100	Generator	Wintergreen odor enzyme (BSMT1) generator	1294
BBa_J45119	Generator	Wintergreen odor enzyme (BMST1) generator	1230



+ de 3000 composants génétiques

2005

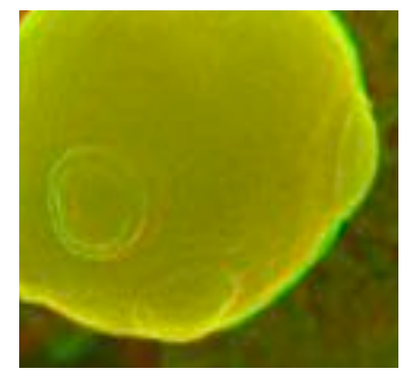
2006

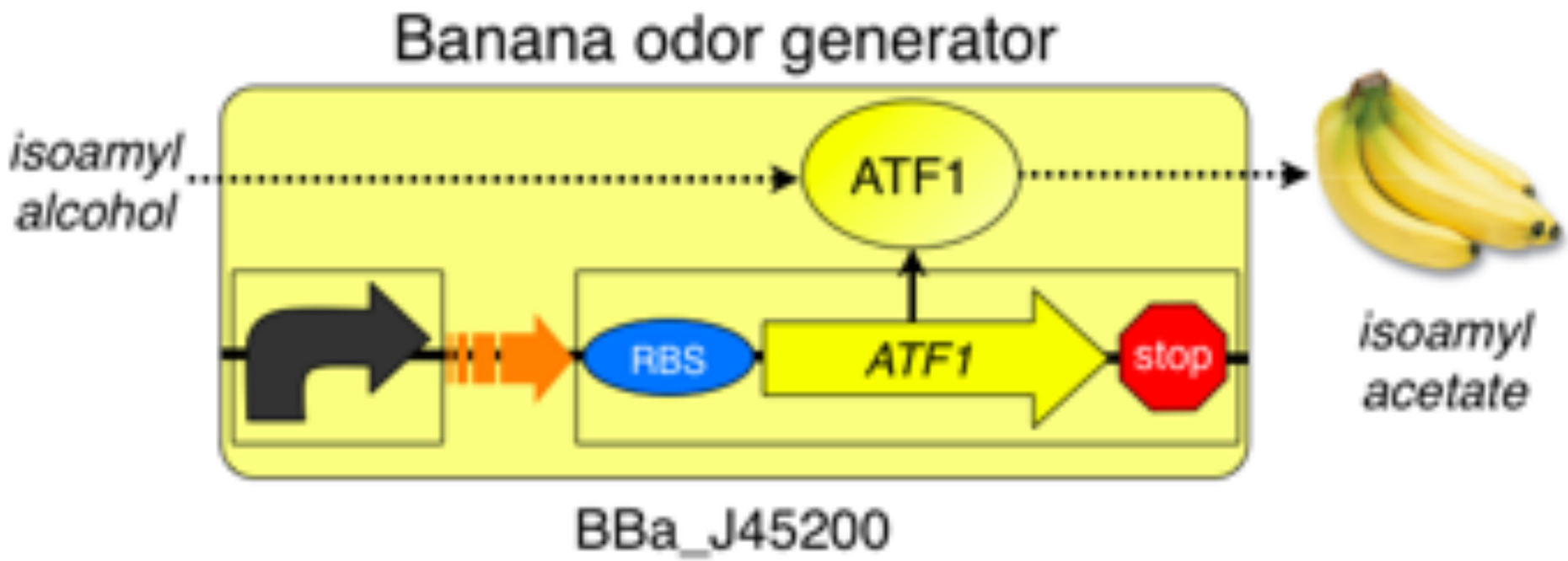
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
2009

2013

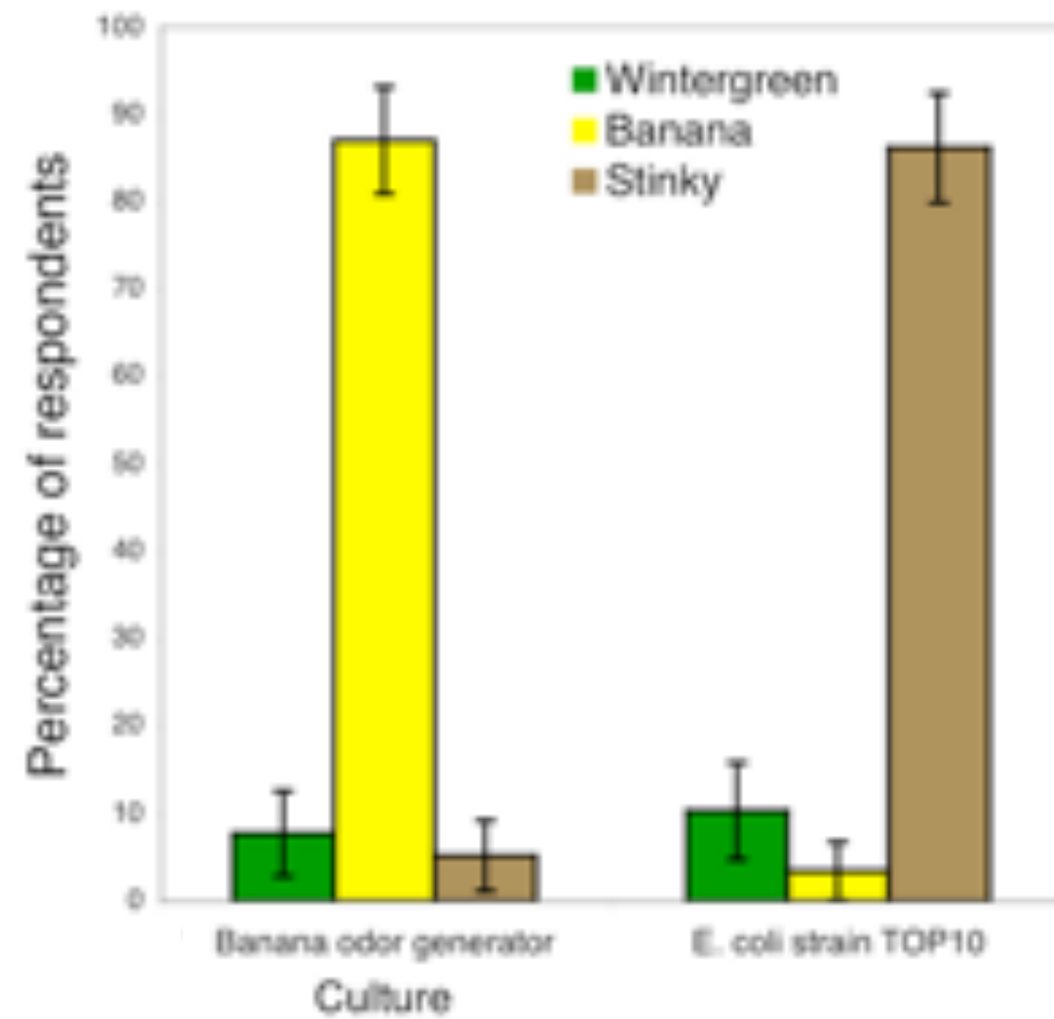
2700 Participants
280 Equipes

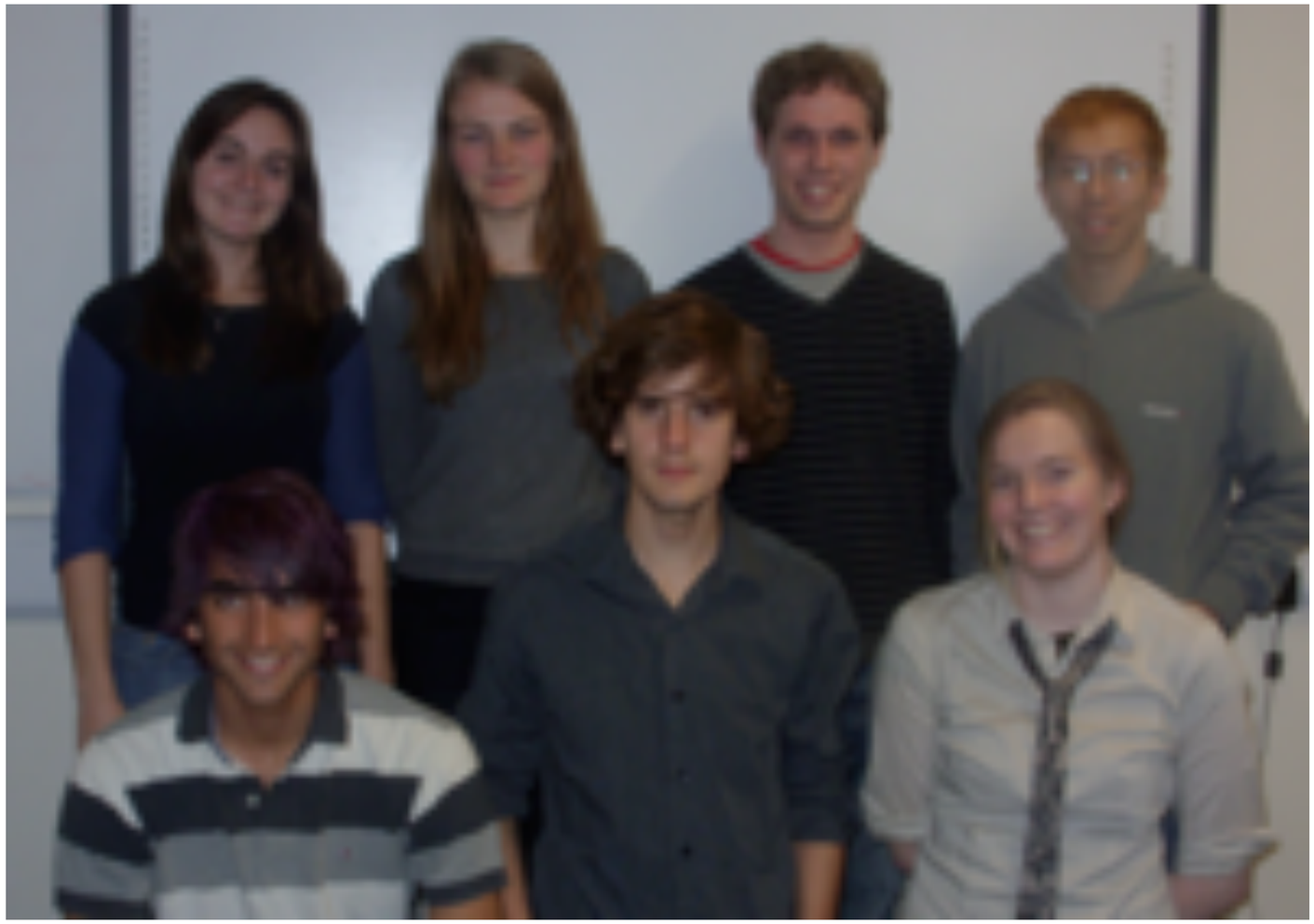
iGEM MIT 2006

A. thaliana	*O. basilicum*	*A. majus*	*C. breweri*	*S. cerevisiae*
				
JMT	CCMT	BAMT	BSMT	ATF1
jasmine	cinnamon	fresh / floral	wintergreen	banana


Banana odor generator
isoamyl alcohol
ATF1
RBS
ATF1
stop
isoamyl acetate
BBa_J45200

Smell test


Wintergreen
Banana
Stinky
Percentage of respondents
0
10
20
30
40
50
60
70
80
90
100
Banana odor generator
E. coli strain TOP10
Culture

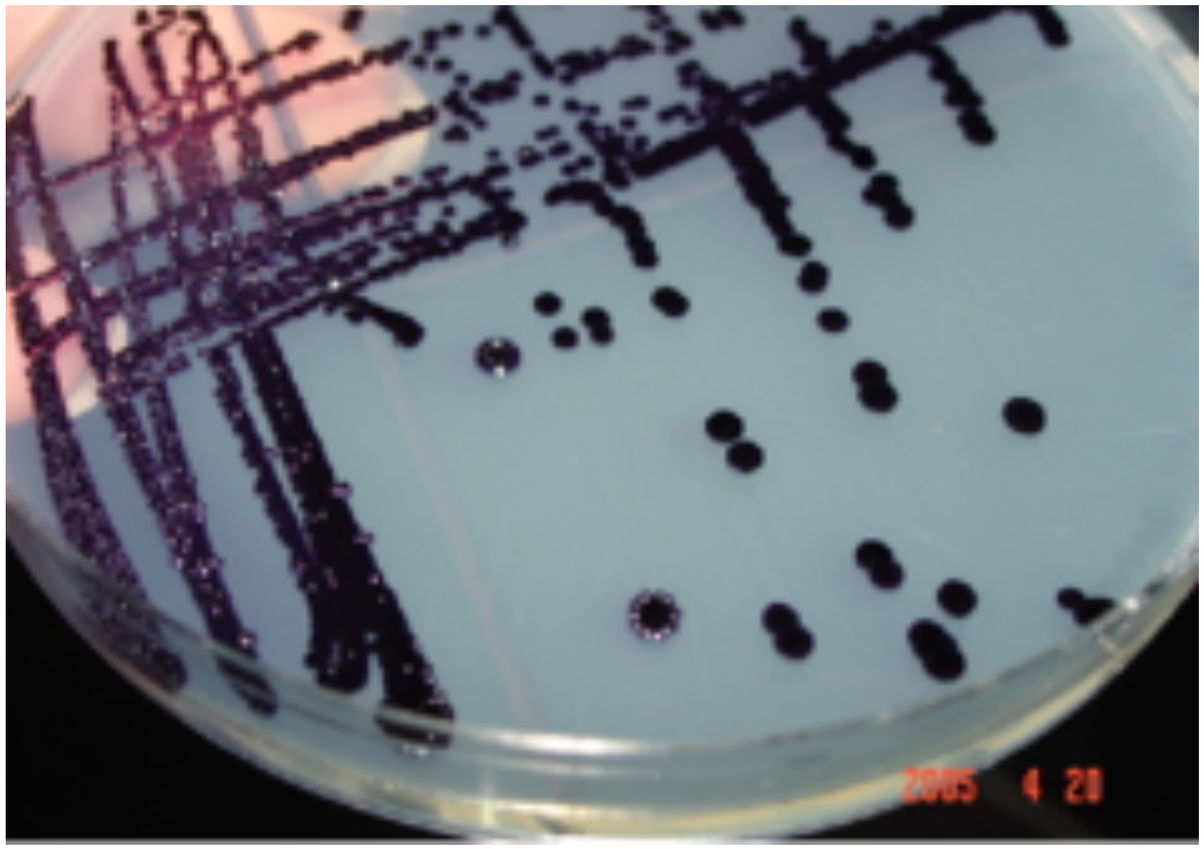


iGEM Cambridge 2009

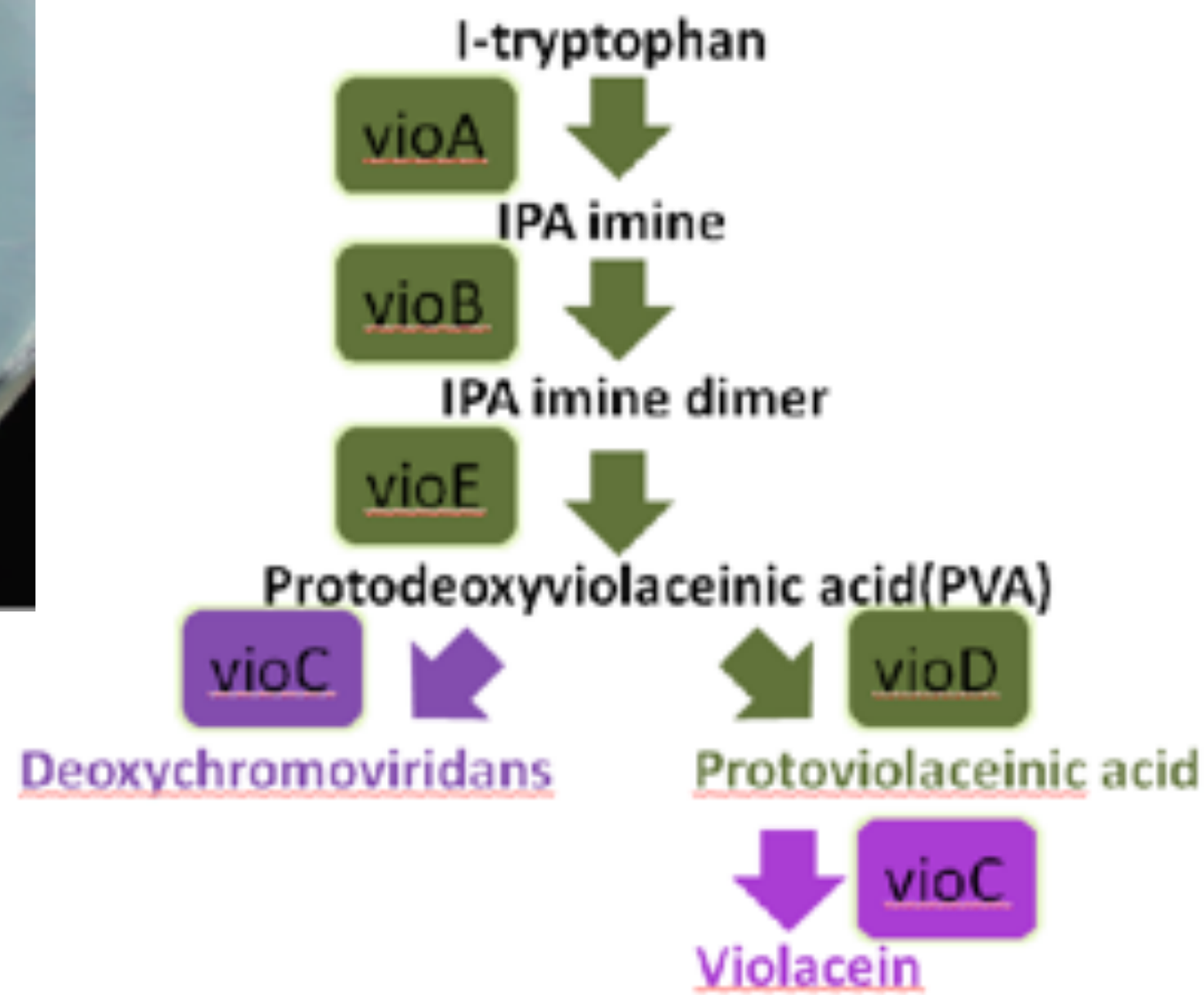
E.chromi ~ living colour from bacteria

iGEM Cambridge 2009

Violaceine



Chromobacterium violaceum



>BBa_K174002 Part-only sequence (7345 bp)

ttaaggaggtaaaaaaaatgaaacattcttccgatatctgcattgttggtgctggtatttctggtttgacgtgcgcaagccatctgctggacagccccggc
atgccgcggtctgagcctgcgtatctttgacatgcagcaagaagcccggtggccgtatccgcagcaaaatgctggatggtaaggcaagcattgaactgggc
gcaggtcgctactcccctcagttgcacccgcatttccaaagccgcaatgcagcactatagccaaaagagcgaagtctatccgttcacccagttgaagttca
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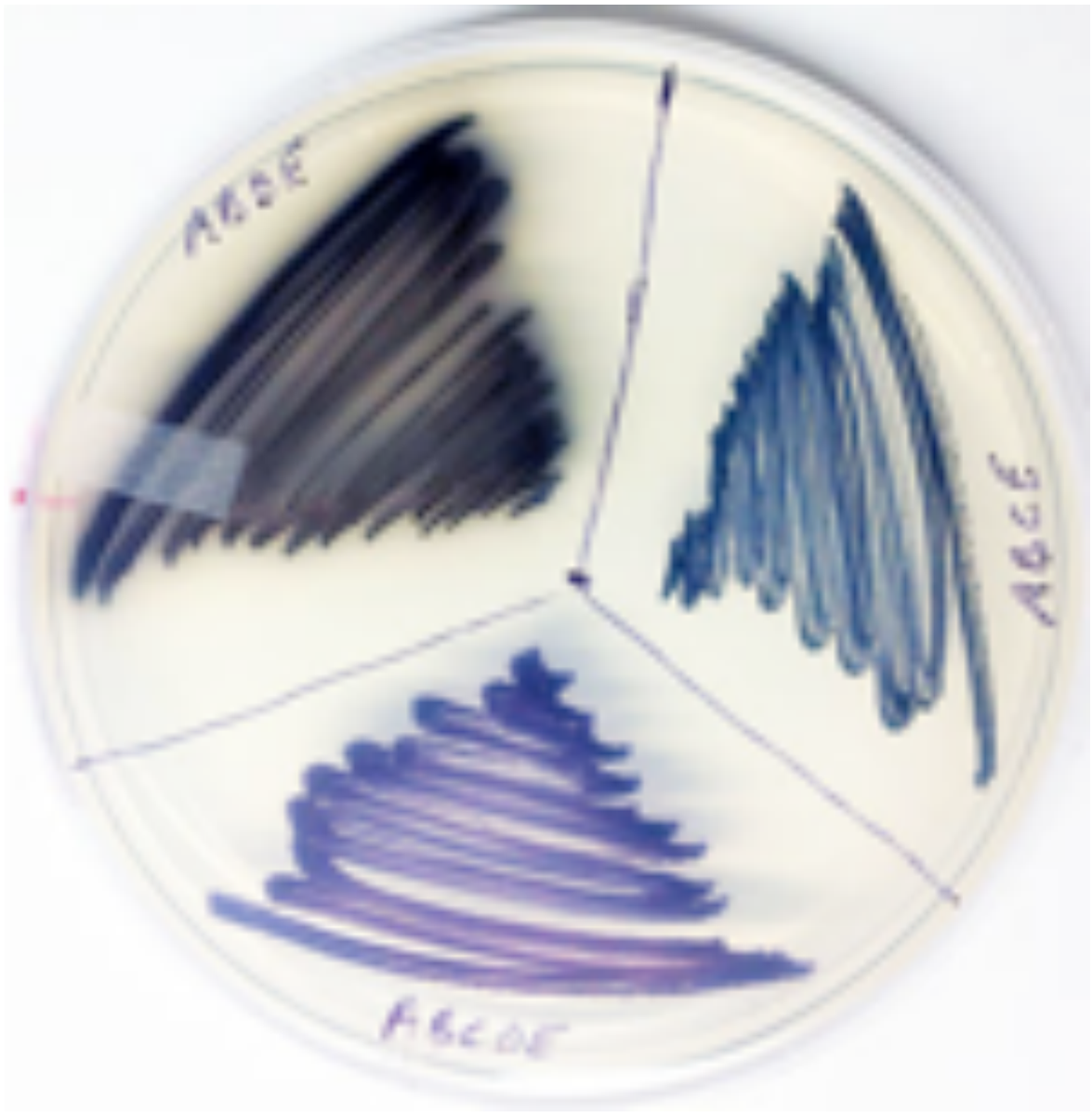
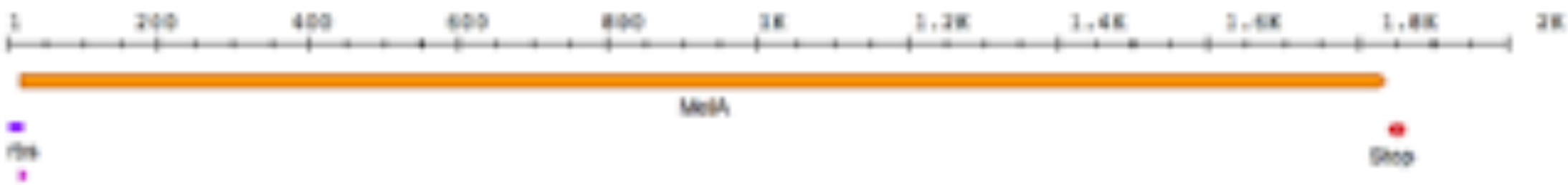

ABCDE
ABCDE
ABCDE

melanin pigment

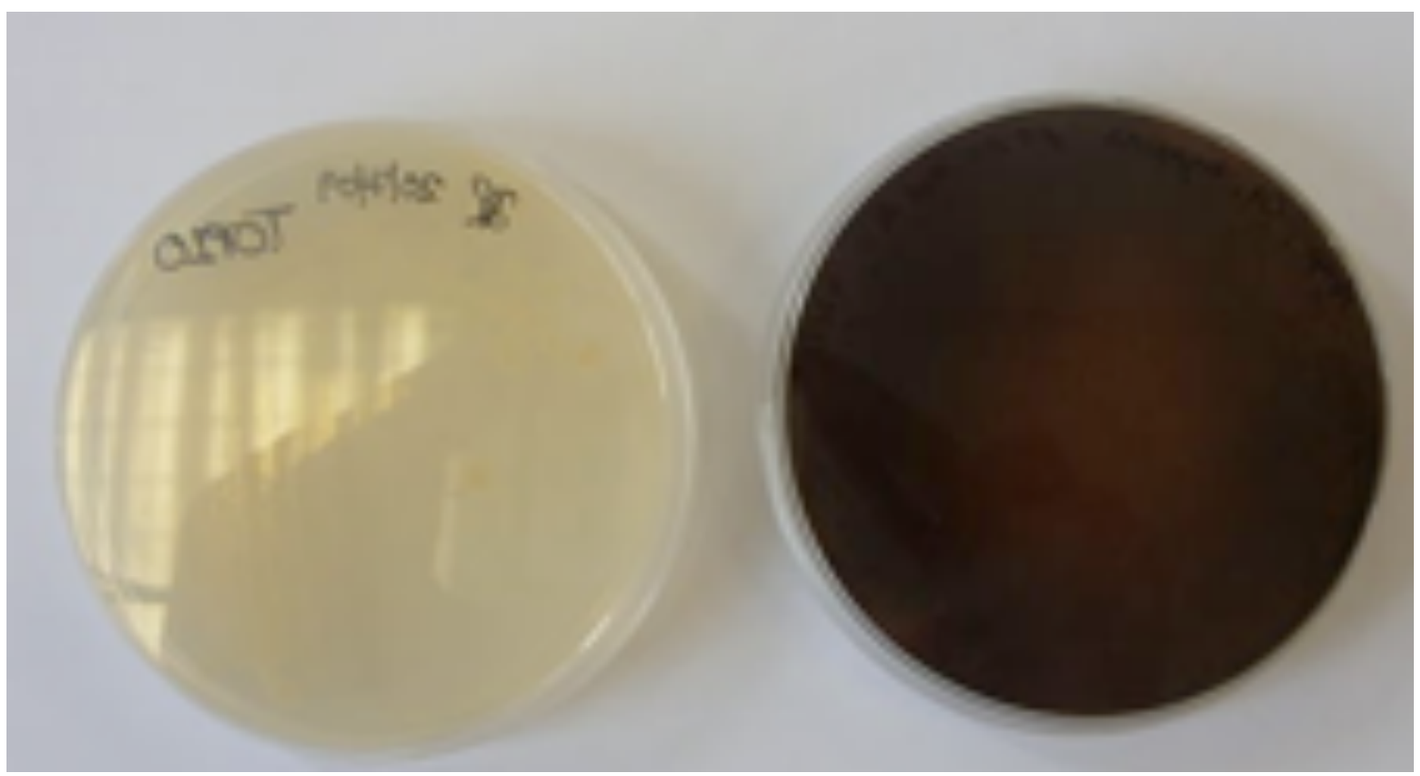
Produces dark brown pigment output. The gene (melA) codes for a tyrosinase which produces the pigment from L-tyrosine. Production of the pigment requires the addition of copper and L-tyrosine supplements (the copper acts as a cofactor for the gene product) but no other precursors. The BioBrick sequence includes the native ribosome binding site.

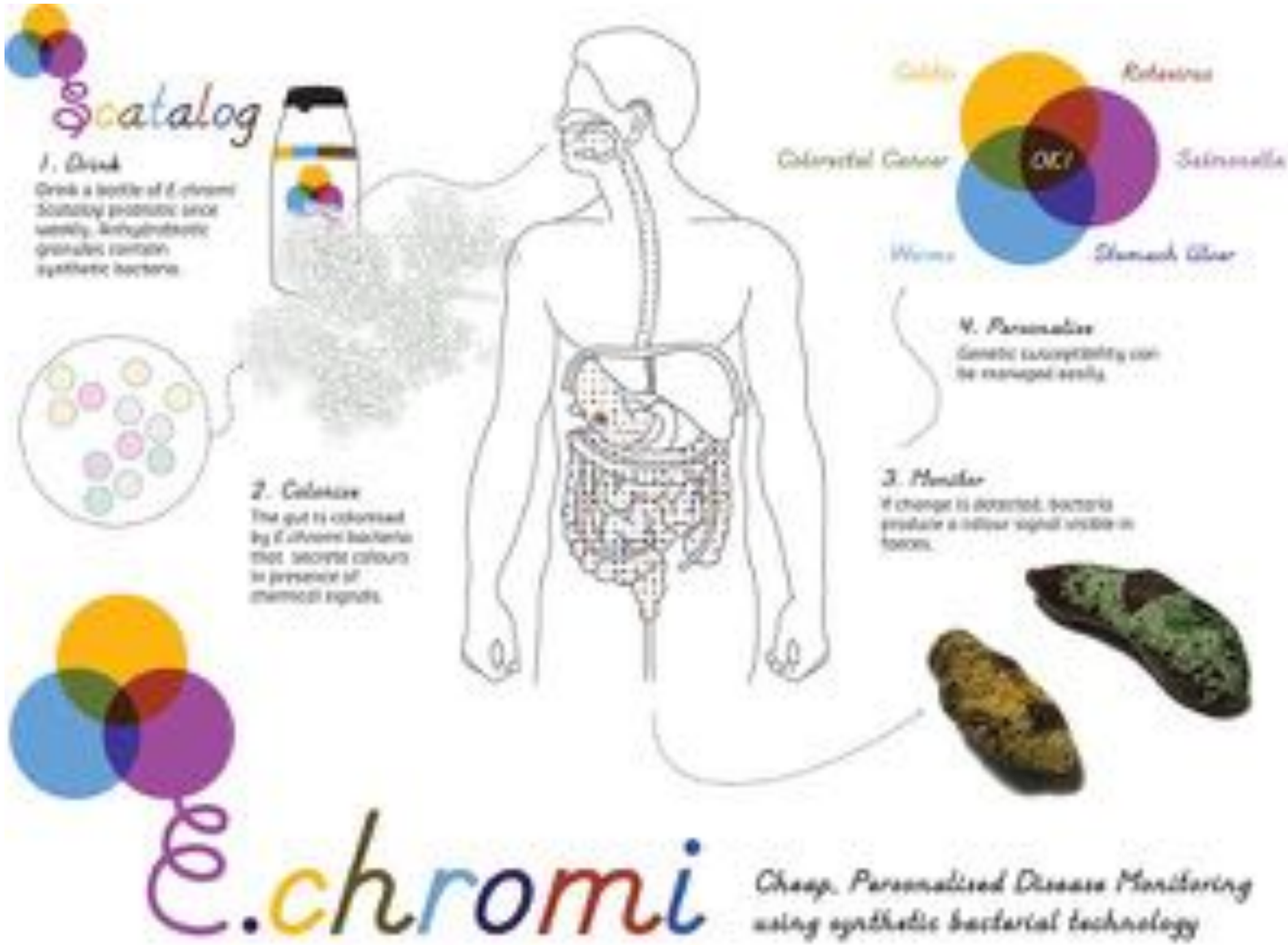
Sequence and Features

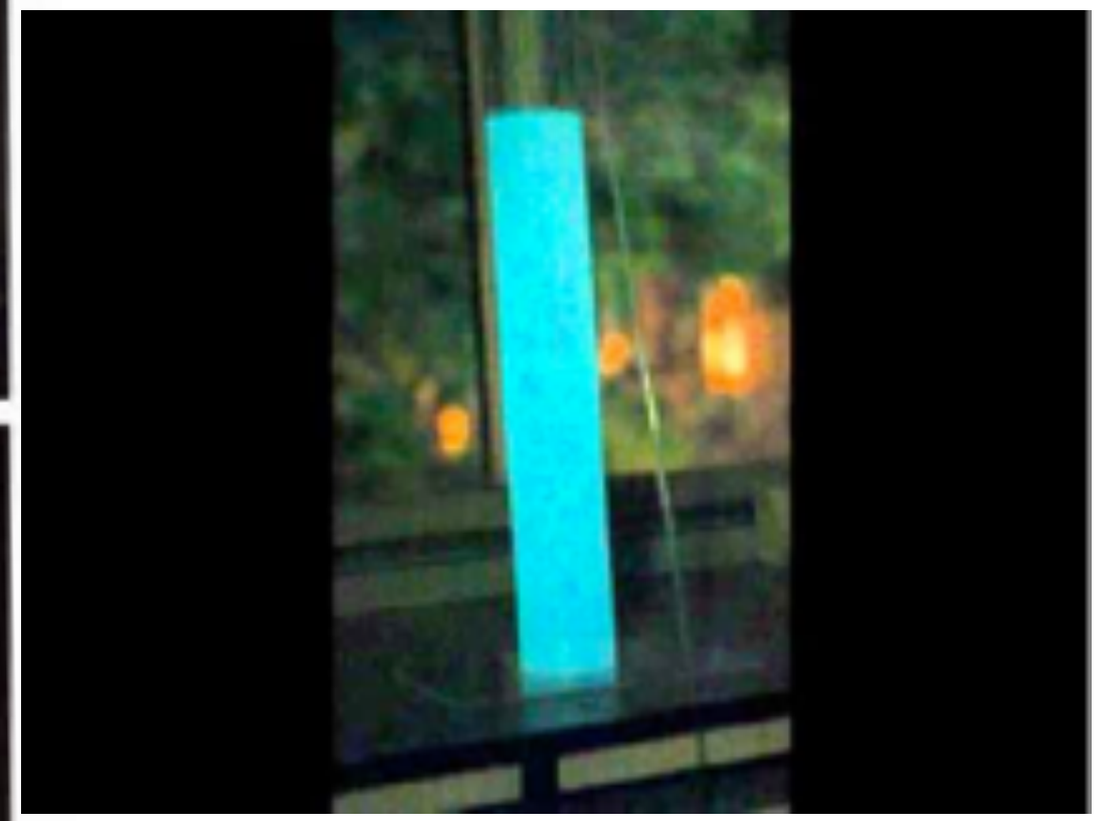
Subparts | **Ruler** | SS | DS **Length: 1844 bp** Get part sequence View plasmid



Assembly Compatibility: 10 12 21 23 25 1000



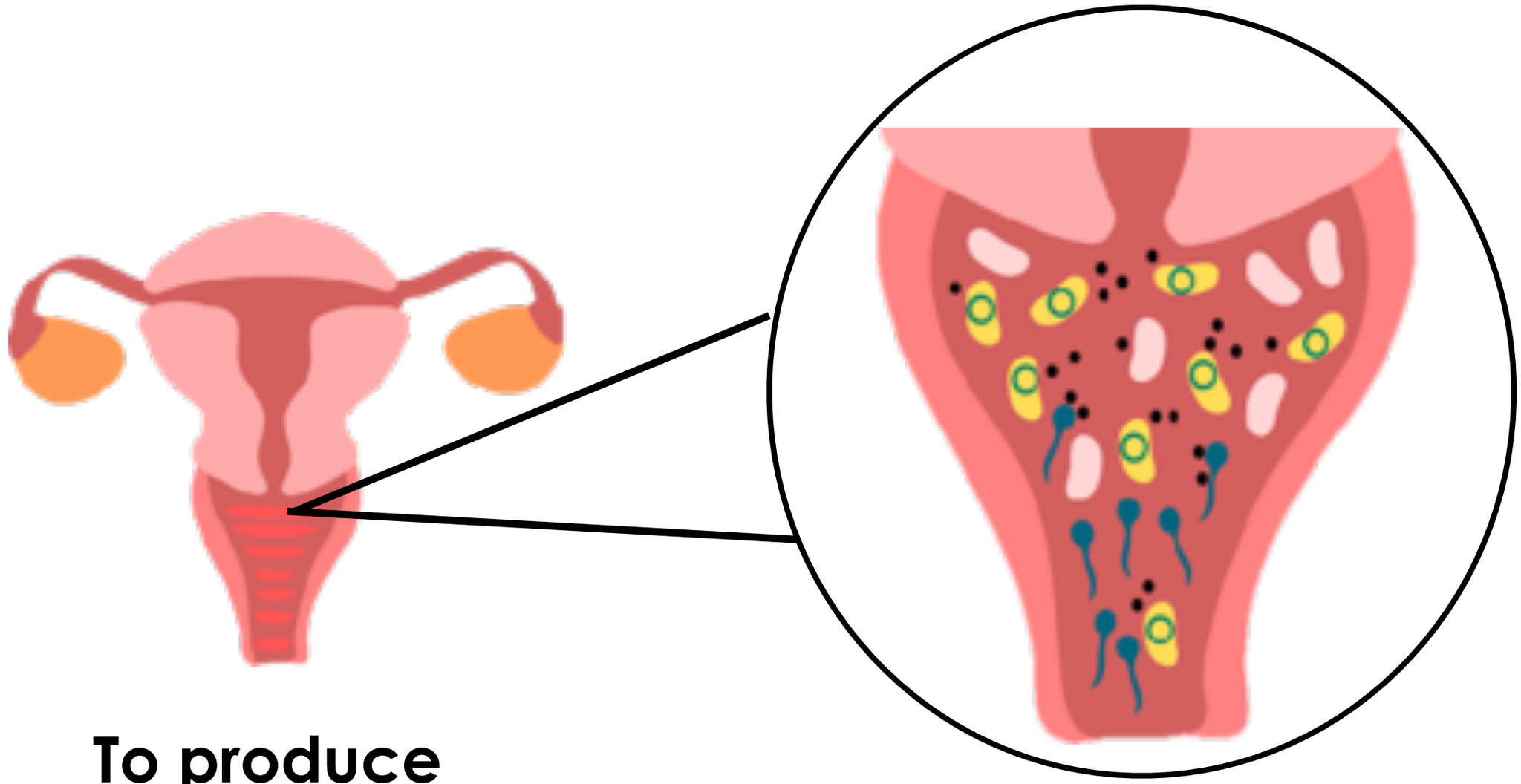

catalog
1. Drink
Drink a bottle of E.chromi Scientific probiotic once weekly. Lyophilisateurs granules contain synthetic bacteria
2. Colonise
The gut is colonised by E.chromi bacteria that secrete colours in presence of chemical signals.
3. Monitor
If change is detected, bacteria produce a colour signal visible in faeces.
Colitis
Rotavirus
Colorectal Cancer
OCT
Salmonella
Worms
Stomach Ulcer
V. Personalise
Genetic susceptibility can be managed easily.
E.chromi
Cheap, Personalised Disease Monitoring using synthetic bacterial technology



iGEM Cambridge 2010

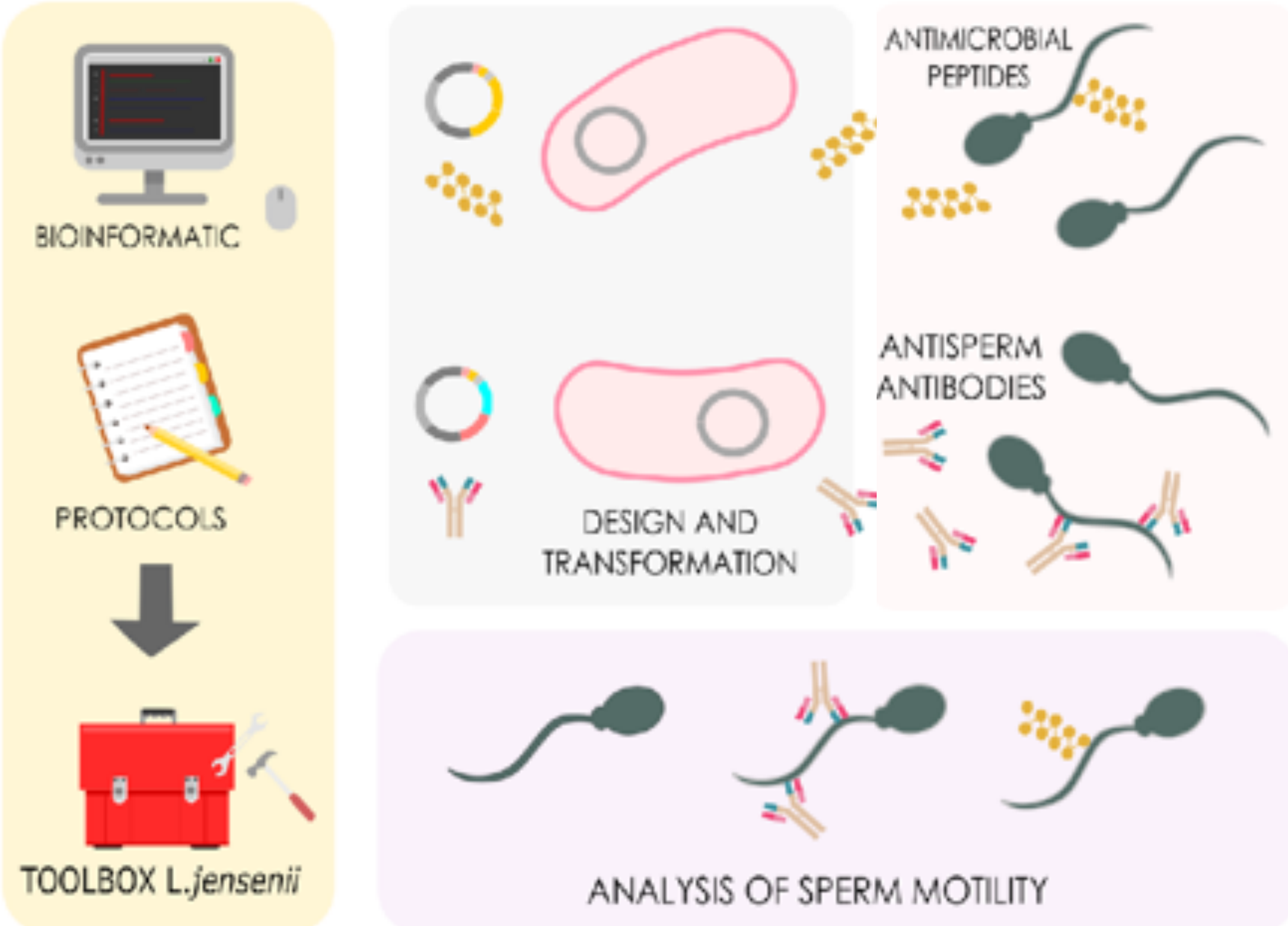
Vagineering
Contraception

Modifying vaginal bacteria



To produce
spermicides!

non hormonal, long-term contraception.


BIOINFORMATIC
PROTOCOLS
TOOLBOX L.jensenii
DESIGN AND TRANSFORMATION
ANTIMICROBIAL PEPTIDES
ANTISPERM ANTIBODIES
ANALYSIS OF SPERM MOTILITY

COMIC

You've probably already heard about our original flora
What we call "flora" goes actually by the name of
MICROBIOTA
but what is it exactly?
No matter if they vary in different...
...there are microbiota inside every organism!
Microbiotas are communities of micro-organisms
Such as VIRUSES, BACTERIAS, FUNGUS and MICROBES
There are 10 times more microbial organisms like them in our body than human cells!
The human body is full of different microbiotas:
nose
stomach
intestine
reproductive system
mouth
skin and skin
So are plants and animals!
And microbiome is different for everyone!
People often think that bacterias are dangerous and gross...
The truth is that only a few of them actually are pathogenics!
Bacterias should not be confounded with illness!
It is a wide subject
that scientists keep studying

WHAT IS SYNTHETIC BIOLOGY?
One DNA part stands for one Lego brick
There are hundreds of different Lego bricks in nature
Take the bioluminescent bacteria jellyfish: it produces BIOLUMINESCENCE which makes it glow
When scientists take the genes responsible for its fluorescence, they create Lego bricks
Then, they place that gene into an organism, a bacteria for instance
The bacteria will soon divide itself...
...making more copies of the gene!
These bacterias will produce light!
It may seem easy, but as nature is very complex, it can be difficult to put any Lego at all inside an organism
That's why scientists created CONSTRUCTS made from different Lego bricks!
With their gene of interest...
...and other bricks, so that they can be correctly read by the host!

Prize for best "Education and Public Engagement" project

AND GOLD MEDAL !

Starting again this year!

Biotech gets out of the lab

http://magazine.ucla.edu/features/outlaw-biology/

Open Source Biology

The GNU Operating System and the Free Software Movement

Richard Stallman

The First Software-Sharing Community

When I started working at the MIT Artificial Intelligence Lab in 1971, I became part of a software-sharing commun
community; it is as old as computers, just as sharing of recipes is as old as cooking. But we did it more than most.

The AI Lab used a time sharing operating system called ITS (the Incompatible Timesharing System) that the Lab's staff
the large computers of the era. As a member of this community, an AI Lab staff system hacker, my job was to improve th

We did not call our software "free software," because that term did not yet exist, but that is what it was. Whenever peo
them. If you saw someone using an unfamiliar and interesting program, you could always ask to see the source code, so

The Collapse of the Community

The situation changed drastically in the early 1980s when Digital discontinued the PDP-10 series. Its architecture, elegan
becoming feasible in the 80s. This meant that nearly all of the programs composing ITS were obsolete.

The AI Lab hacker community had already collapsed, not long before. In 1981, the spin-off company Symbolics had b
unable to maintain itself. (The book *Machines*, by Steve Levy, describes these events, and gives a clear picture of this co
decided to use Digital's non-free timesharing system instead of ITS.

The modern computers of the era, such as the VAX or the 68020, had their own operating systems, but none of them wer

This meant that the first step in using a computer was to promise not to help your neighbor. A cooperating community w

https://www.oreilly.com/openbook/opensources/book/stallman.html

Richard Stalmann

https://www.gnu.org/philosophy/why-free.html

Essay

Synthetic Biology: Caught between Property Rights, the Public Domain, and the Commons

Arti Rai*, James Boyle

Novel artificial genetic systems with twelve bases instead of four [1]. Bacteria that can be programmed to take photographs [2] or form visible patterns [3]. Cells that can count the number of times they divide [4]. A live polio virus "created from scratch using mail-order segments of DNA and a viral genome map that is freely available on the Internet" [5]. These are some of the remarkable, and occasionally disturbing, fruits of "synthetic biology," the attempt to construct life starting at the genetic level. In terms of their scale and ambition, these efforts go beyond traditional recombinant DNA technology. Rather than simply transferring a pre-existing gene from one species to another, synthetic biologists aim to make biology a true engineering discipline.

In the same way that electrical engineers rely on standard capacitors and resistors, or computer programmers rely on modular blocks of code, synthetic biologists wish to create an array of modular biological parts that can be readily synthesized and mixed together in different combinations. The Massachusetts Institute of Technology (MIT) has a Registry of Standard Biological Parts that supports this goal by indexing biological parts that have been built, and offering assembly services to construct new parts, devices, and systems [6]. Systems, devices, parts, and DNA represent descending levels of complexity—systems consist of devices, and devices consist of parts composed of DNA. The idea behind a registry of parts is that these parts can, and should, be recombined in different ways to produce many different types of devices and systems. Although the registry currently contains physical DNA, its developers believe that, as DNA synthesis technology becomes increasingly inexpensive [7], the registry will be composed largely of information and specifications that can be executed in synthesizers just as semiconductor chip designs are executed by fabrication firms.

Synthetic biology has already produced important results, including more accurate AIDS tests and the possibility of unlimited supplies of previously scarce drugs for malaria [8]. Proponents hope to use synthetic organisms to produce not only medically relevant chemicals but also industrial materials, including biofuels such as hydrogen and ethanol [9]. At the same time, synthetic biology has engendered numerous policy concerns. From its inception, commentators have raised issues ranging from bioethical and environmental worries to fears of bioterrorism—indeed, the US Central Intelligence Agency released a report in 2003 called "The Darker Bioweapons Future" that explicitly referred to the dangers posed by the possibility of genetically engineered viruses [10].

There is, however, one area that has been largely unexplored until this point—the relationship of synthetic biology to intellectual property law. Two key issues deserve further attention. First, synthetic biology presents a particularly revealing example of a difficulty that the law has frequently faced over the last 30 years—the assimilation of a new technology into the conceptual limits posed by existing intellectual property rights. There is reason to fear that tendencies in the way that US law has handled software on the one hand and biotechnology on the other could come together in a "perfect storm" that would impede the potential of the technology. Second, synthetic biology raises with remarkable clarity an issue that has seemed of only theoretical interest until now—the tension between different methods of creating "openness." On the one hand, one standard mechanism for creating openness has involved putting material in the public domain, outside the world of property. On the other, synthetic biology researchers may want to use intellectual property rights to create a "commons," just as developers of free and open source software use the leverage of software copyrights to impose requirements of openness on future programmers, requirements greater than those attaching to a public domain work. But synthetic biology, unlike software, is not necessarily protected by copyright. Should we rethink the boundary lines between intellectual property and the public domain as a result?

The Perfect Storm: Flawed Biotech Law Meets Flawed Software Law?

Intellectual property law in the US has already had difficulty incorporating the revolutionary technologies from which synthetic biology draws inspiration—biotechnology and computers. US patent law requires that inventions be

Essays articulate a specific perspective on a topic of broad interest to scientists.

Citation: Rai A, Boyle J (2007) Synthetic biology: Caught between property rights, the public domain, and the commons. PLoS Biol 5(3): e58. doi:10.1371/journal.pbio.0050058

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Abbreviations: BIOS, Biological Innovation for an Open Society; HHS, US Department of Health and Human Services; MIT, Massachusetts Institute of Technology

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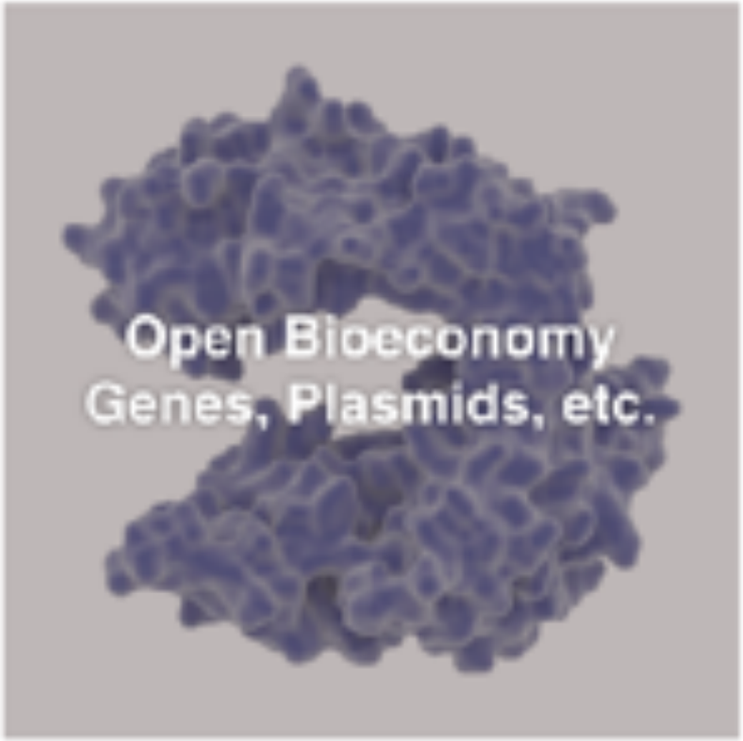
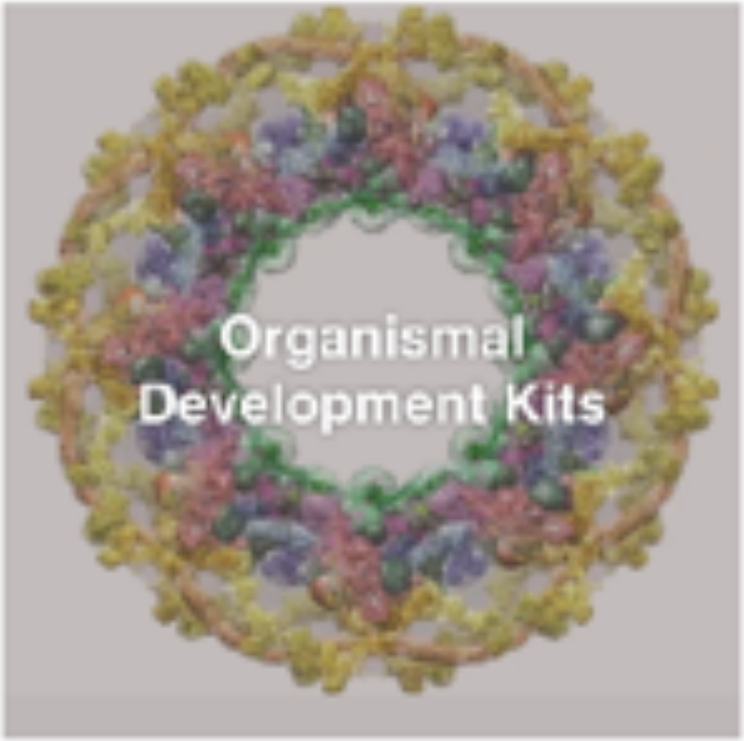
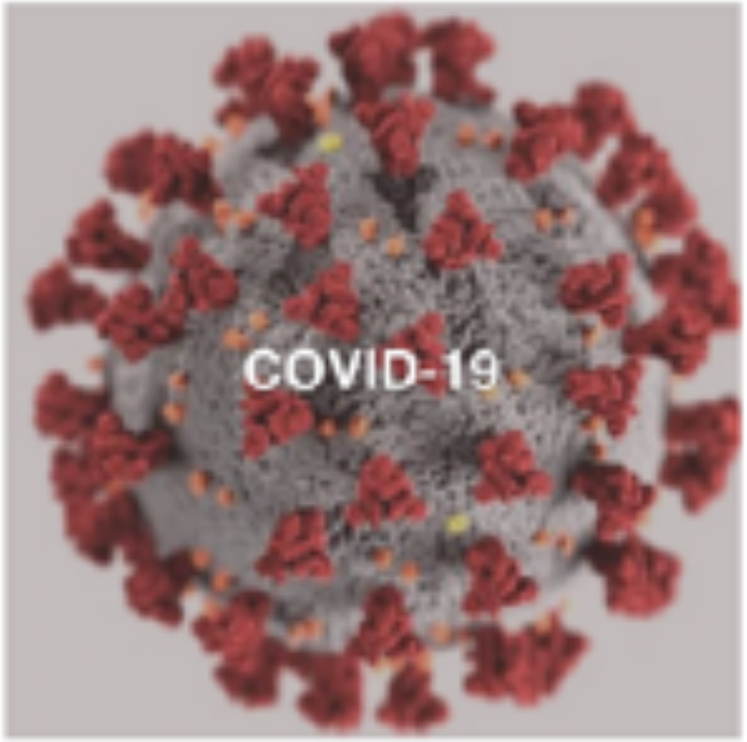
* To whom correspondence should be addressed. E-mail: rai@law.duke.edu

https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.0050058







Open Enzymes 50.00

Open Reporters 50.00

Open Plasmids 50.00

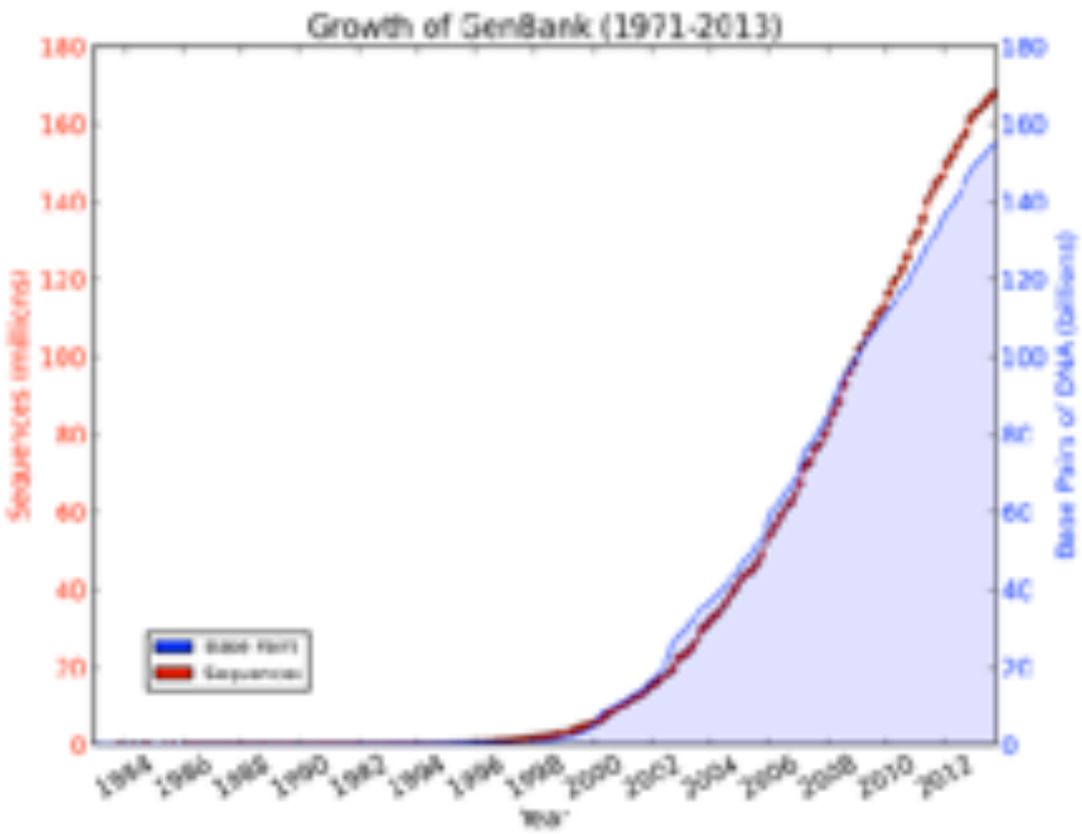
Molecular Diagnostics Toolkit 50.00

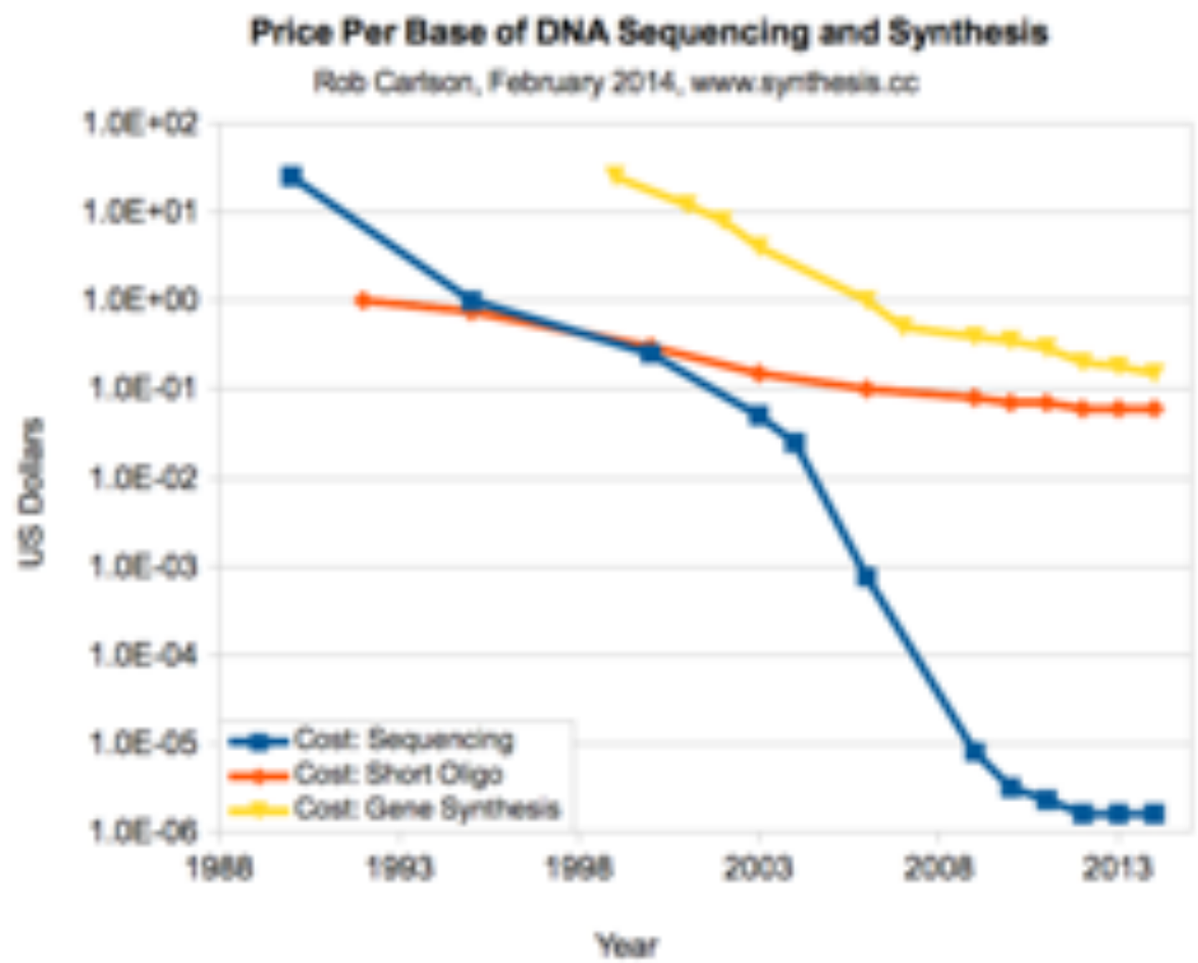
Open PCR

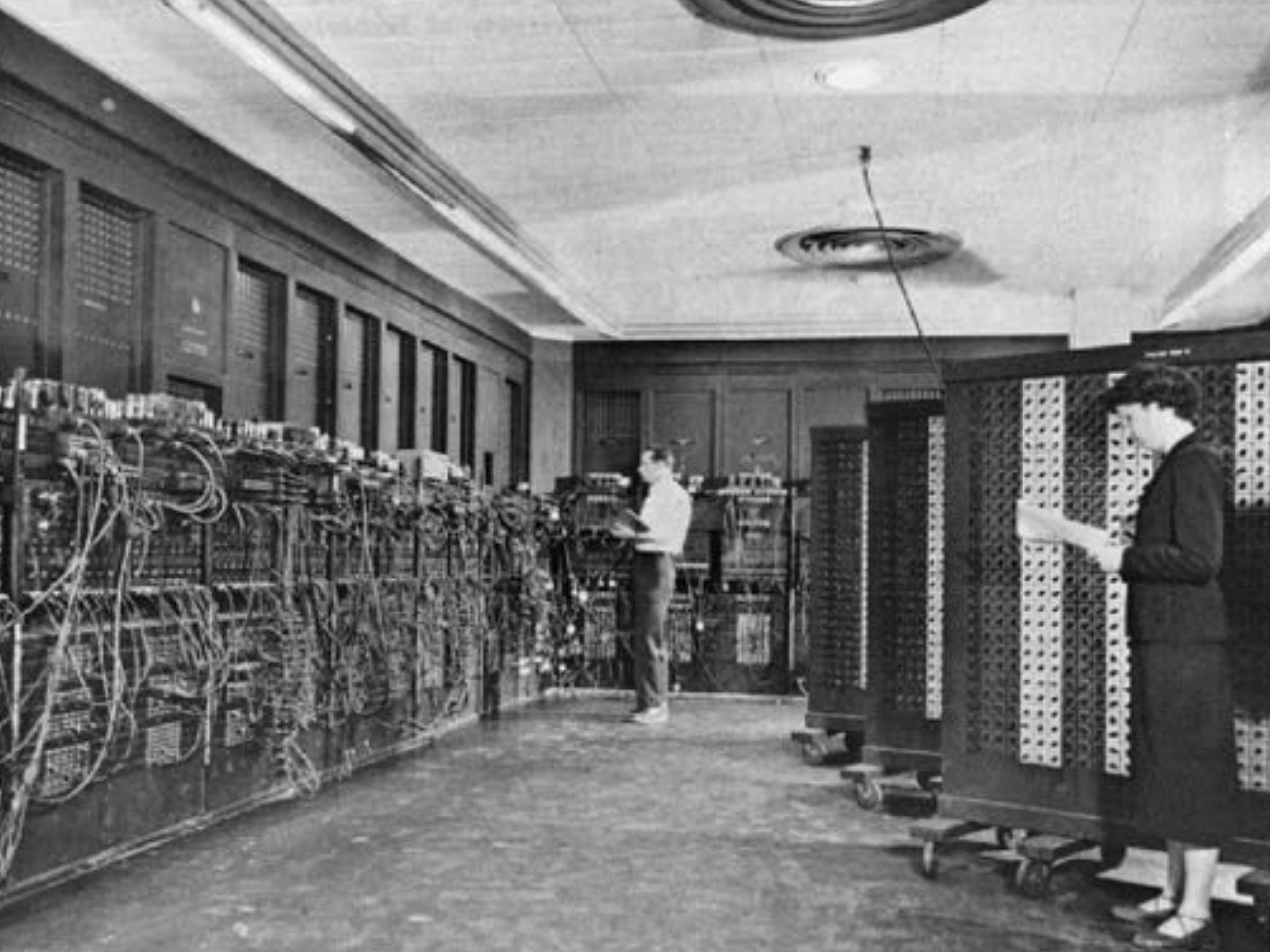
500 Euros

Garage biology

Where is this going?



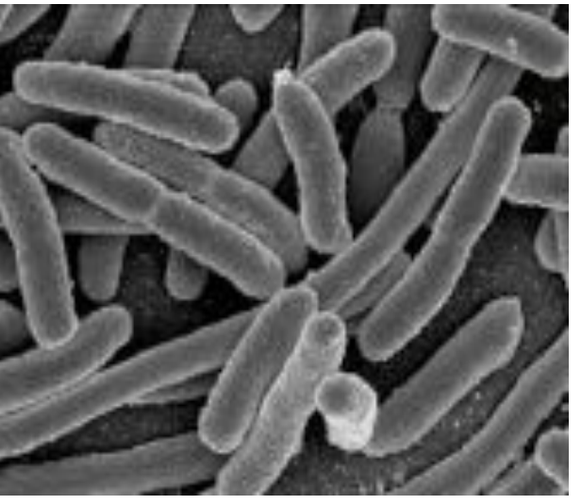




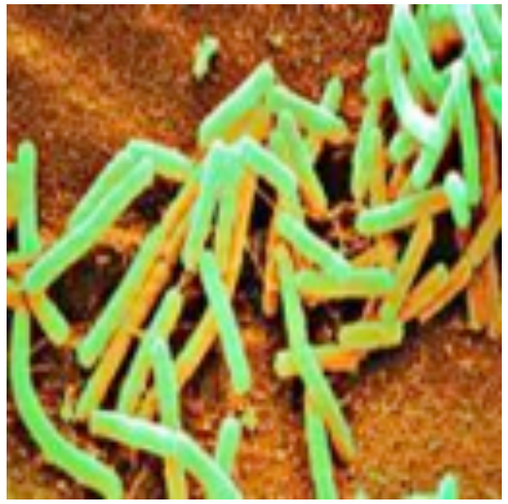
APPLE
COMPUTER

Barrett Lyon / The Opte Project

Visualization of the routing paths of the Internet.

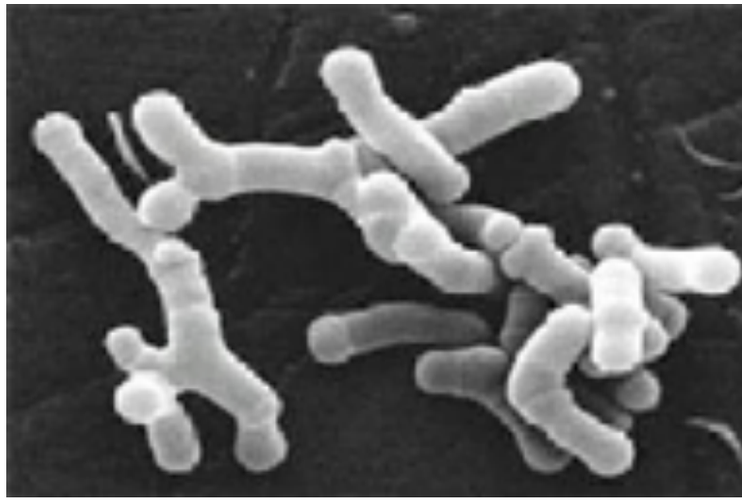


E. coli

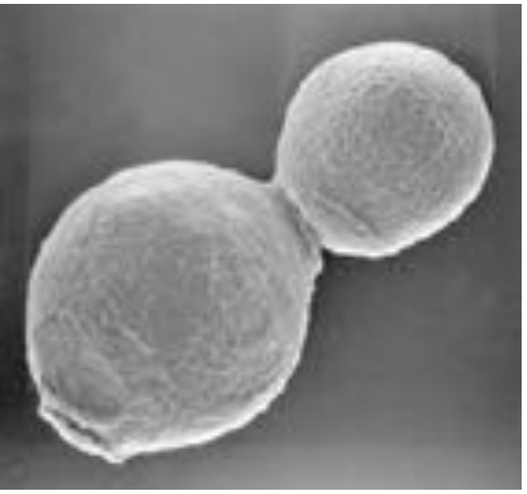


B. subtilis

L. lactis



Bifidobacterium



Yeast

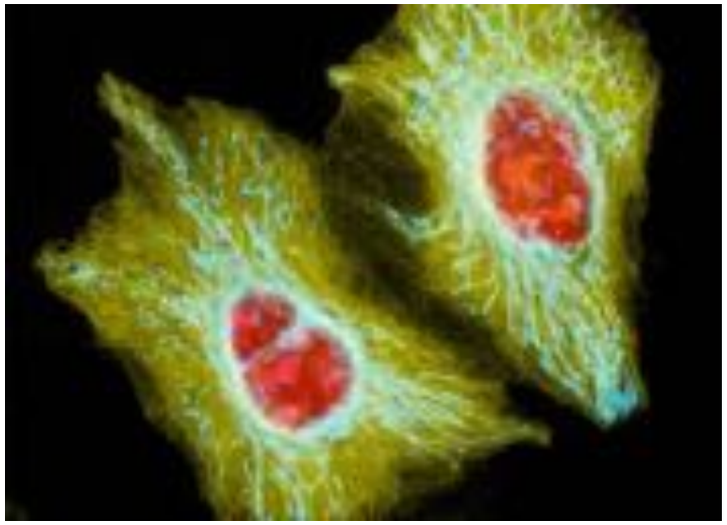
Fly

Frog

Zebrafish

Tunicates

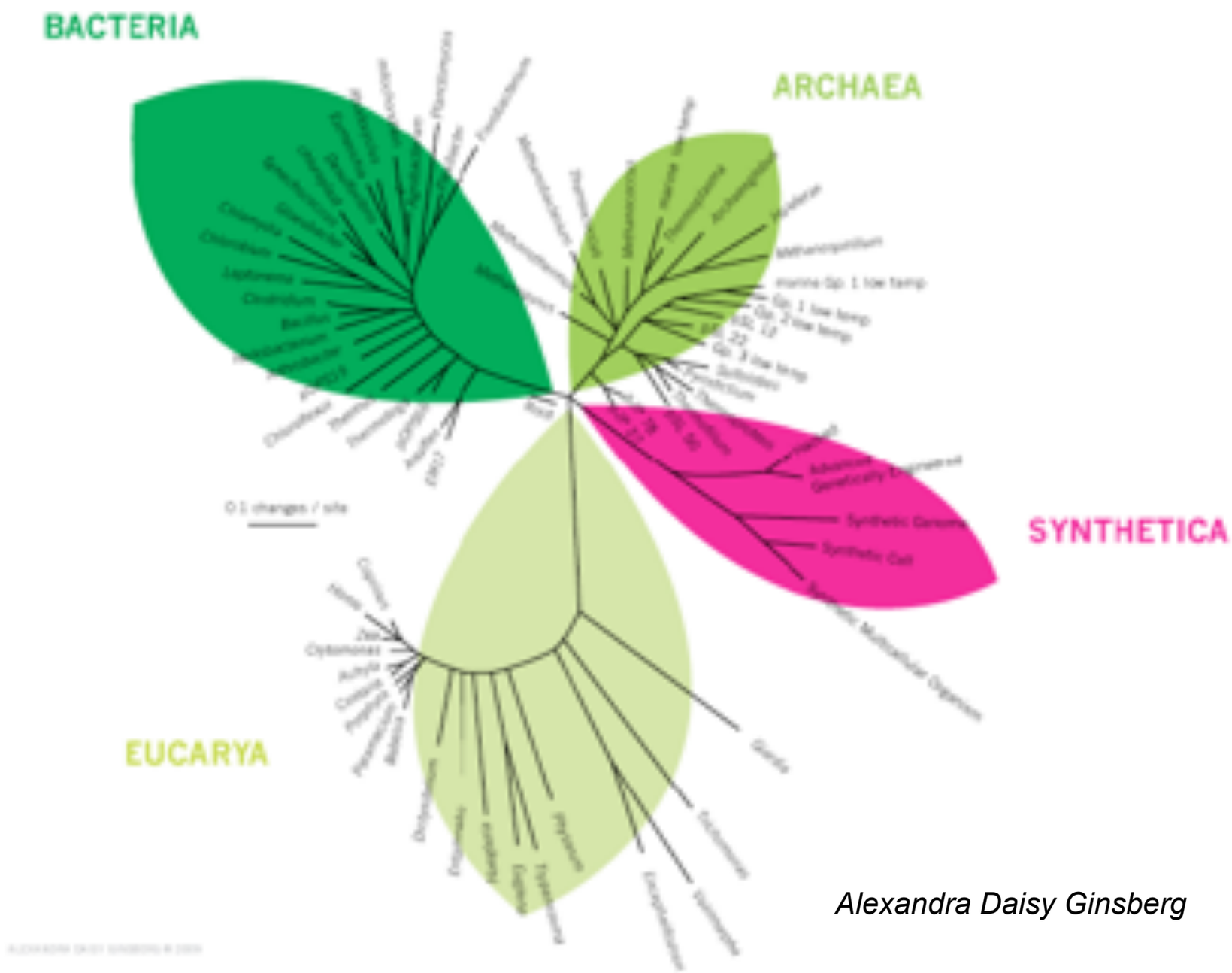
Mice



Human cells

Plants

Choices, future, society



Alexandra Daisy Ginsberg

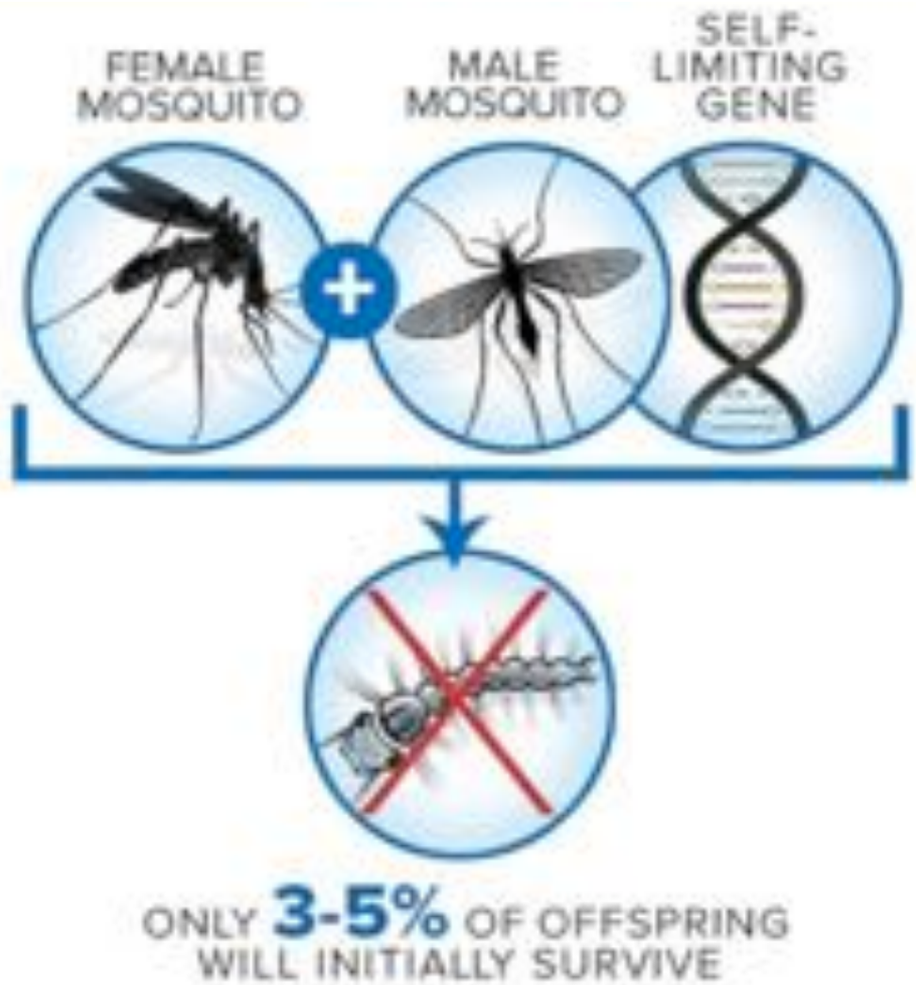
TIME
A Day With Jimmy Carter
The DNA Furor
TINKERING WITH LIFE

1977

TIME
Shaping Life in the Lab
The Boom In Genetic Engineering
Genentech's Herbert Boyer

1981

NO
GMOs


FEMALE MOSQUITO
MALE MOSQUITO
SELF-LIMITING GENE
ONLY 3-5% OF OFFSPRING WILL INITIALLY SURVIVE

SAID NO
TO GMO
MOSQUITOES
SAID NO
TO GMO
MOSQUITOES
GO HOME!

BIOTECHNOLOGY

A prudent path forward for genomic engineering and germline gene modification

A framework for open discourse on the use of CRISPR-Cas9 technology to manipulate the human genome is urgently needed

By David Baltimore,[1] Paul Berg,[2] Michael Bowden,[3] Fiona Cavalli[4] E. Alta Charo,[5] George Church,[6] Jacob E. Corn,[7] George Q. Daley,[8] Jennifer A. Doudna,[9,10] Marsha Fenech,[11] Henry T. Greely,[12] Martin Jinek,[13] G. Steven Martin,[14] Edward Penhoet,[15] Jennifer Puck,[16] Samuel H. Sternberg,[18] Jonathan S. Weissman,[19,20] Keith R. Yamamoto[21]

Genome engineering technology offers unparalleled potential for modifying human and nonhuman genomes. In humans, it holds the promise of curing genetic disease, while in other organisms it provides methods to engineer the biosphere for the benefit of the future developments. The meeting identified immediate steps to take toward ensuring that the application of genome engineering technology is performed safely and ethically.

The promise of so-called "precision medicine" is propelled in part by synergies between two powerful technologies: DNA sequencing and genome engineering. Advances in DNA sequencing capabilities and genome-wide association studies have provided critical information about the genetic changes that influence the development of disease. In the past, without the means to make specific and efficient modifications to a genome, the ability to act on this information was limited. However, this limitation has been upended by the rapid development and widespread adoption of a

CURRENT APPLICATIONS. The simplicity of the CRISPR-Cas9 system allows any researcher with knowledge of molecular biology to modify genomes, making feasible experiments that were previously difficult or impossible to conduct. For example, the CRISPR-Cas9 system enables introduction of DNA sequence changes that correct genetic defects in whole animals, such as replacing a mutated gene underlying liver-based metabolic disease in a mouse model (1). The technique also allows DNA sequence changes in pluripotent embryonic stem cells (4) that can then be cultured to produce specific tissues, such as cardiomyocytes or neurons (2). Such studies are laying the groundwork for refined approaches that could eventually treat human disease.

2015

CRISPR EMBRYOS AND THE LAW

Regulations governing genetic modification in human embryos vary. Some countries ban the practice through legislation that carries criminal penalties; others have unenforceable guidelines.

Genome engineering and species resurrection

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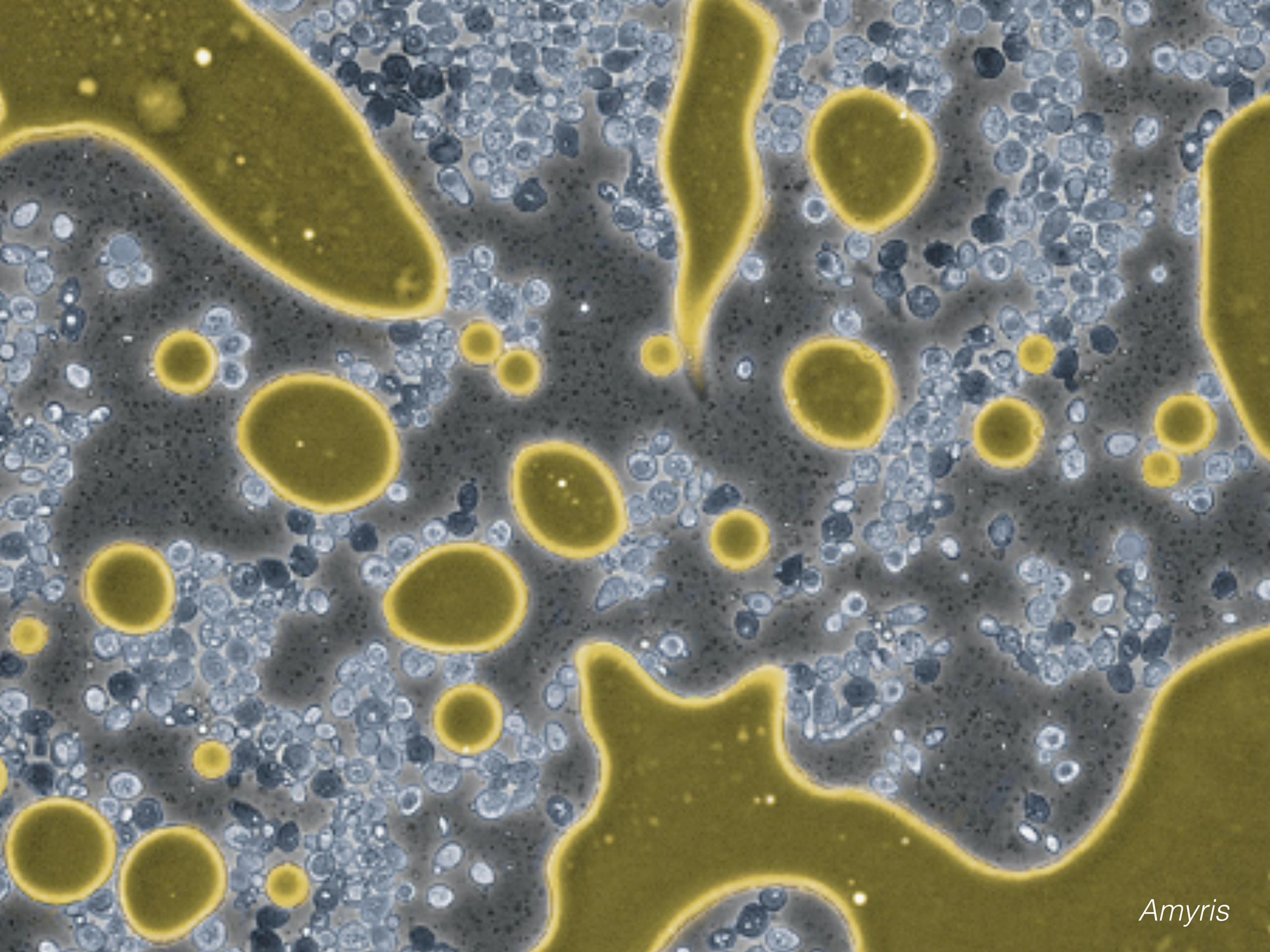
Should scientists seek to clone our ancient hominid cousins?

By **Virginia Hughes**, for National Geographic News

PUBLISHED MARCH 6, 2013

Life finds a way.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Genetic frontiers for conservation

An assessment of synthetic biology and biodiversity conservation

Synthesis and key messages

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Case studies of proposed synthetic biology by scale of application

1. Eradicating invasive rodents from islands.
2. Controlling invasive mosquitoes to prevent bird extinctions in Hawaii.
3. Synthetic biology to address conservation threats to black-footed ferrets.
4. Transgenic American chestnut for potential forest restoration.
5. Corals and adaptation to climate change/acidification.
6. Horseshoe crab replacement for Limulus amebocyte lysate test.
7. Gene drive approach for malaria vector suppression in Africa.
8. Addressing honey bee colony collapse.

iGEM Cambridge 2010

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Carrey, Lim, Reineck, and William. Synthetic Aesthetics

Voltaire
(1694-1778)