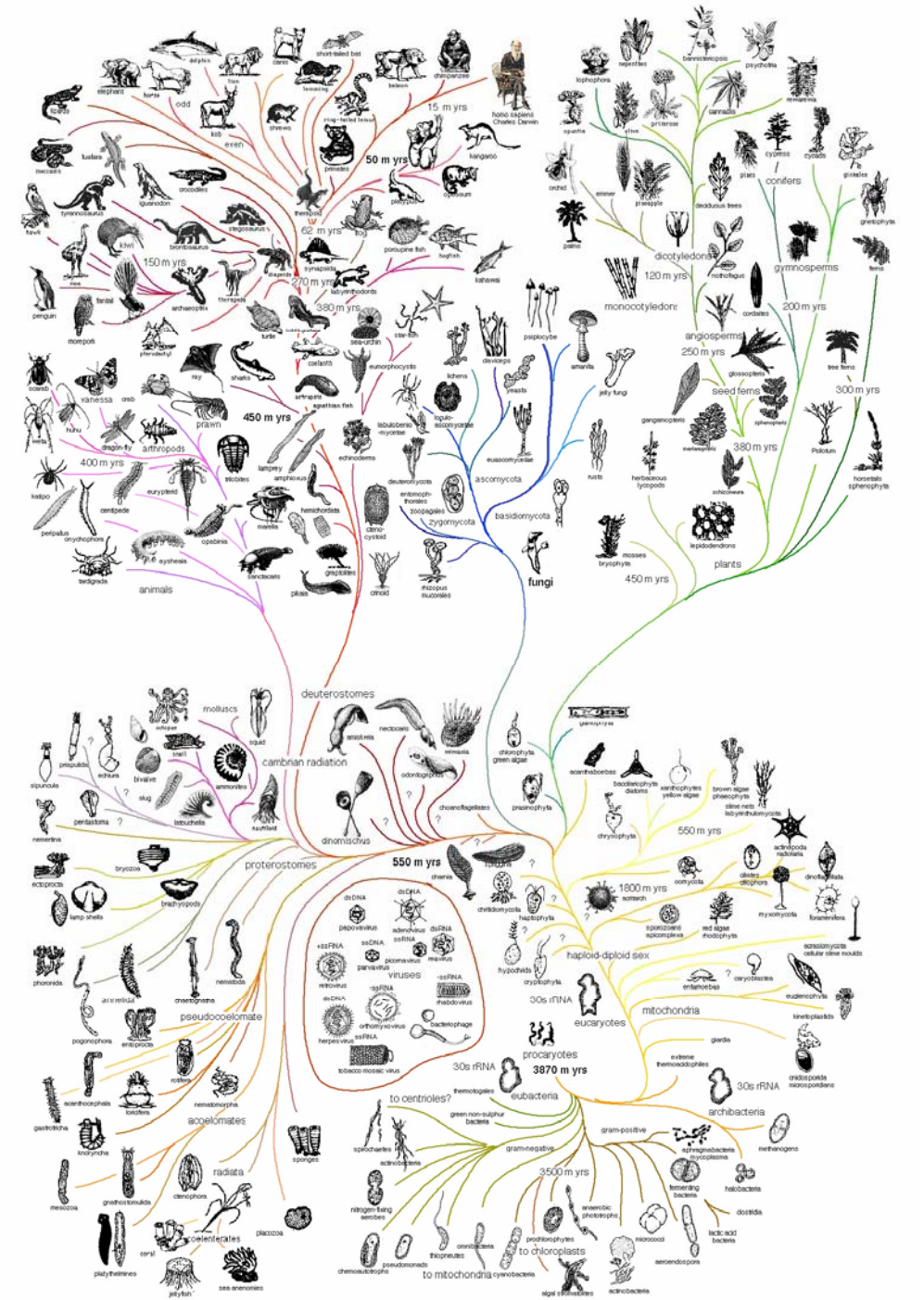
Pimp My Genome!

The mainstreaming of digital genetic engineering

Andrew Hessel
Google Inc. May 3 2007

Biology is the study of life

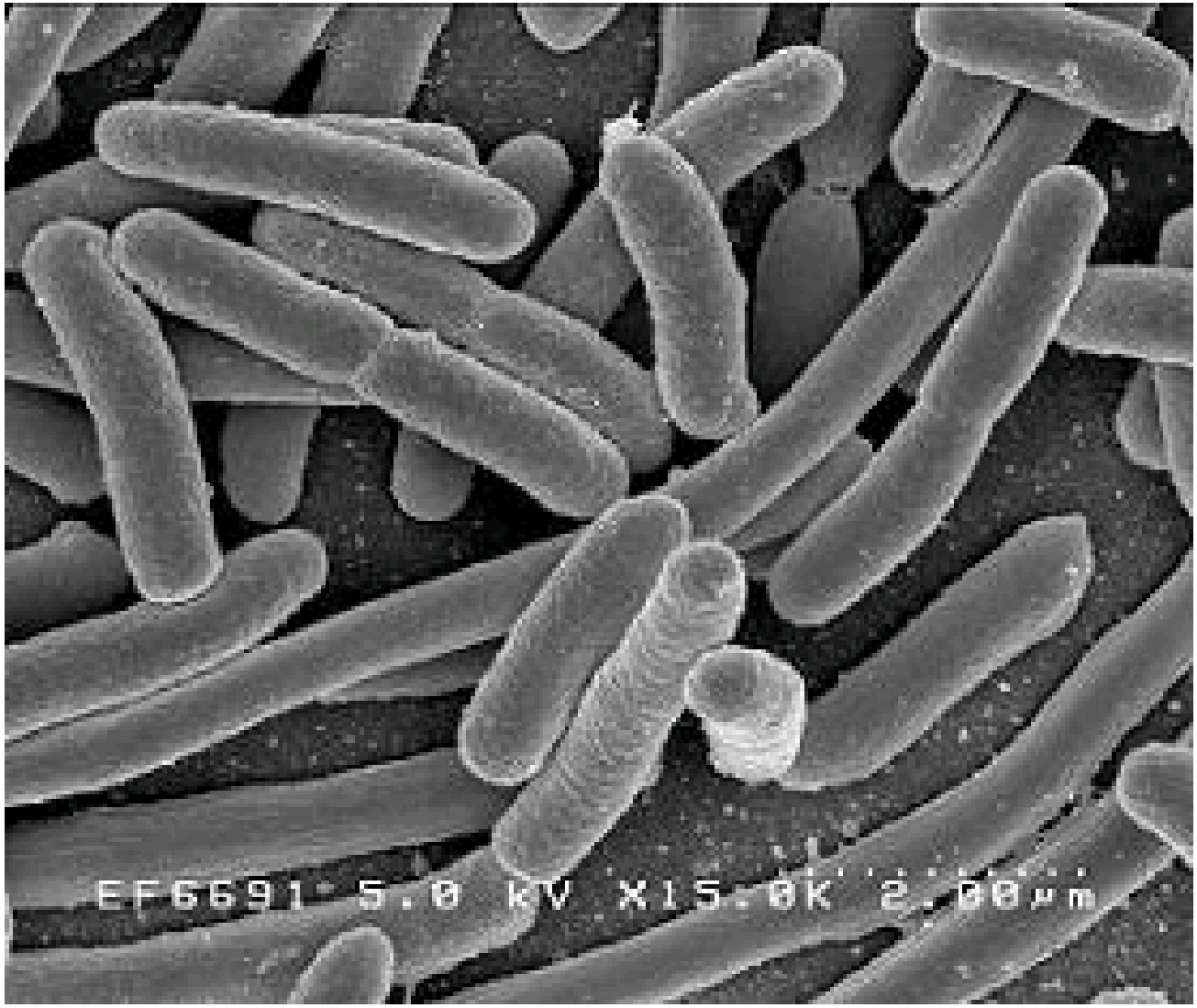


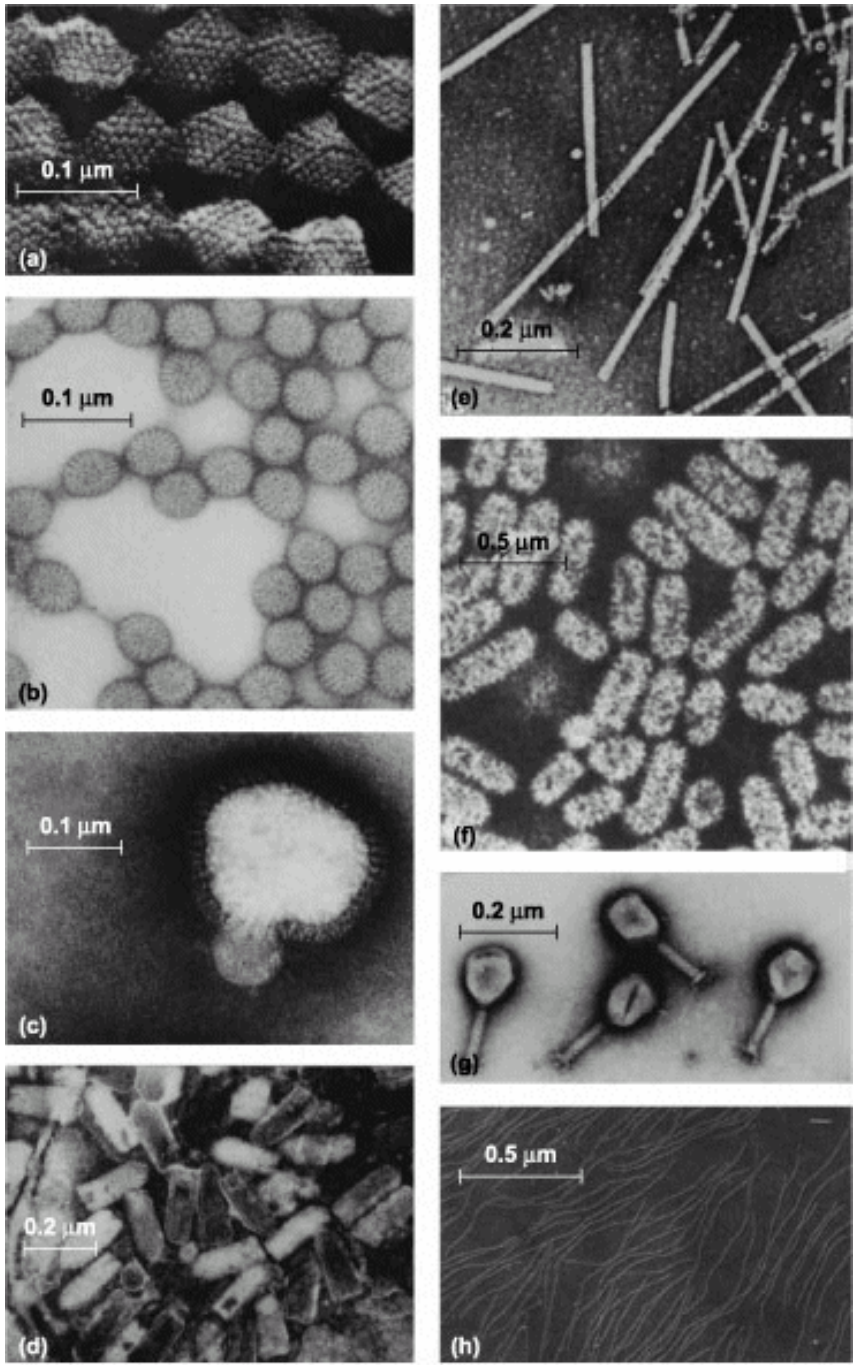
http://www.dhushara.com/book/evol/trevol.jpg

http://www.mccullagh.org/image/10d-17/elephant-side.html

http://www.hoinews.com/uploadedImages/whoi/News/Stories/greenhouse.gif

http://entomology.si.edu/images/EntCollTedJonDave1000.jpg


EF6691 5.0 kV X15.0K 2.00µm



http://content.answers.com/main/content/img/McGrawHill/Encyclopedia/images/CE733500FG0010.gif

Between 2 and 100 million species

We know virtually nothing about microorganisms

http://www.sciencedaily.com/releases/2003/05/030526103731.htm

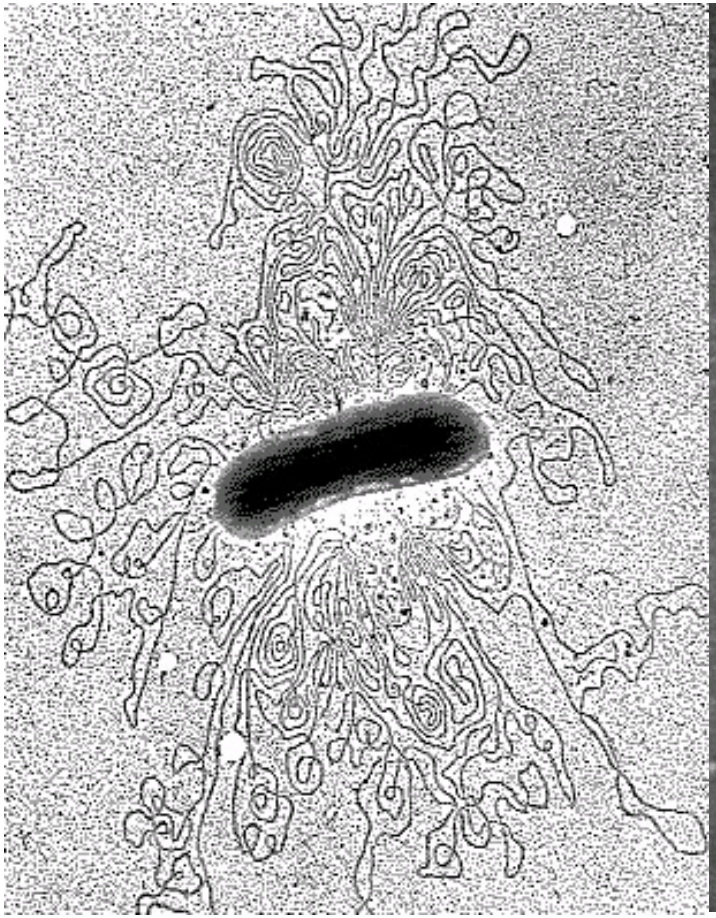
OPEN ACCESS Freely available online

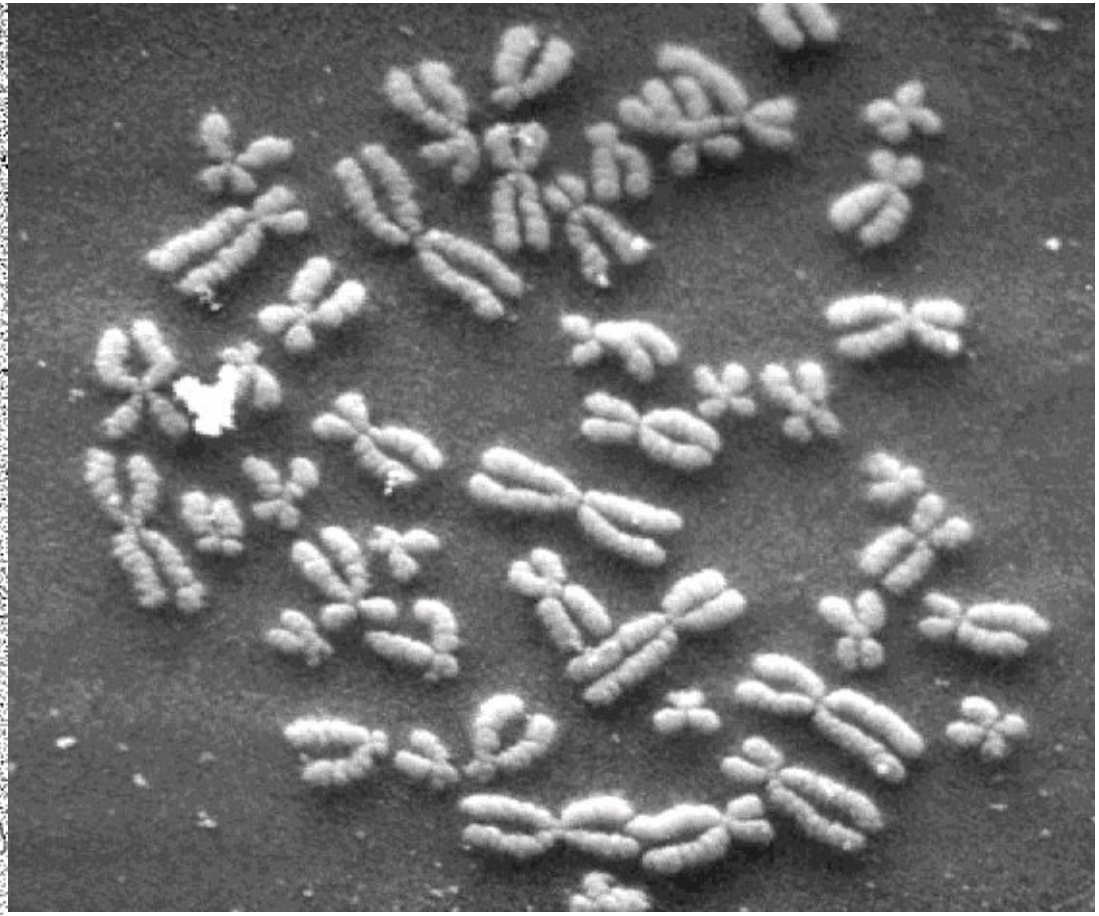
PLoS BIOLOGY

The *Sorcerer II* Global Ocean Sampling Expedition: Northwest Atlantic through Eastern Tropical Pacific

Douglas B. Rusch[1*], Aaron L. Halpern[1], Granger Sutton[1], Karla B. Heidelberg[1,2], Shannon Williamson[1], Shibu Yooseph[1], Dongying Wu[1,3], Jonathan A. Eisen[1,3], Jeff M. Hoffman[1], Karin Remington[1,4], Karen Beeson[1], Bao Tran[1], Hamilton Smith[1], Holly Baden-Tillson[1], Clare Stewart[1], Joyce Thorpe[1], Jason Freeman[1], Cynthia Andrews-Pfannkoch[1], Joseph E. Venter[1], Kelvin Li[1], Saul Kravitz[1], John F. Heidelberg[1,2], Terry Utterback[1], Yu-Hui Rogers[1], Luisa I. Falcón[5], Valeria Souza[5], Germán Bonilla-Rosso[5], Luis E. Eguiarte[5], David M. Karl[6], Shubha Sathyendranath[7], Trevor Platt[7], Eldredge Bermingham[8], Victor Gallardo[9], Giselle Tamayo-Castillo[10], Michael R. Ferrari[11], Robert L. Strausberg[1], Kenneth Nealson[1,12], Robert Friedman[1], Marvin Frazier[1], J. Craig Venter[1]

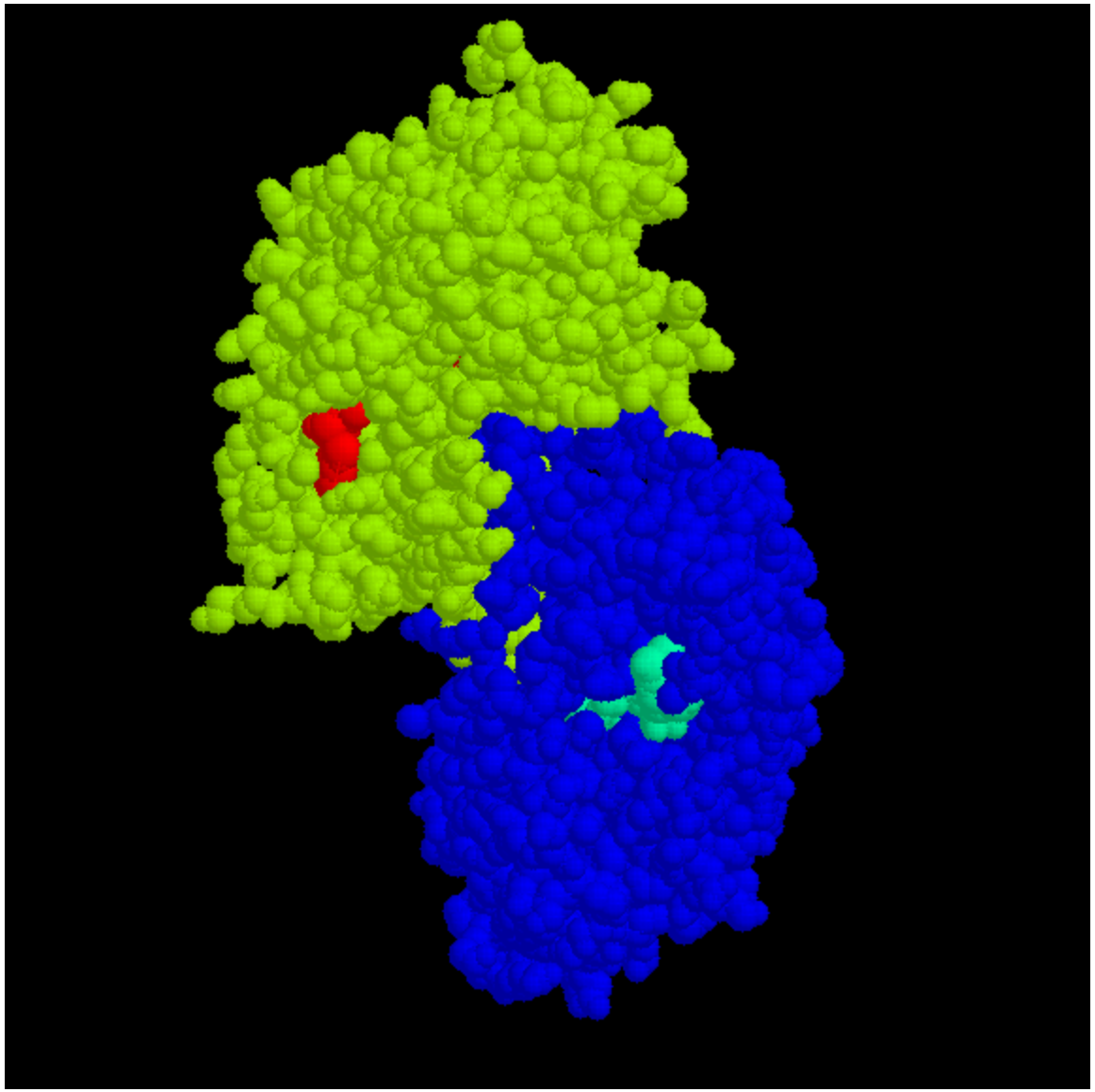
1 J. Craig Venter Institute, Rockville, Maryland, United States of America, 2 Department of Biological Sciences, University of Southern California, Avalon, California, United States of America, 3 Genome Center, University of California Davis, Davis, California, United States of America, 4 Your Genome, Your World, Rockville, Maryland, United States of America, 5 Departmento de Ecologia Evolutiva, Instituto de Ecologia, Universidad Nacional Autónoma de México, Mexico City, Mexico, 6 Department of Oceanography, University of Hawaii, Honolulu, Hawaii, United States of America, 7 Bedford Institute of Oceanography, Dartmouth, Nova Scotia, Canada, 8 Smithsonian Tropical Research Institute, Balboa, Anton, Republic of Panama, 9 Departamento de Oceanografía, Universidad de Concepción, Concepción, Chile, 10 Escuela de Química, Universidad de Costa Rica, San Pedro, Costa Rica, 11 Department of Environmental Sciences, Rutgers University, New Brunswick, New Jersey, United States of America, 12 Department of Earth Sciences, University of Southern California, Los Angles, California, United States of America



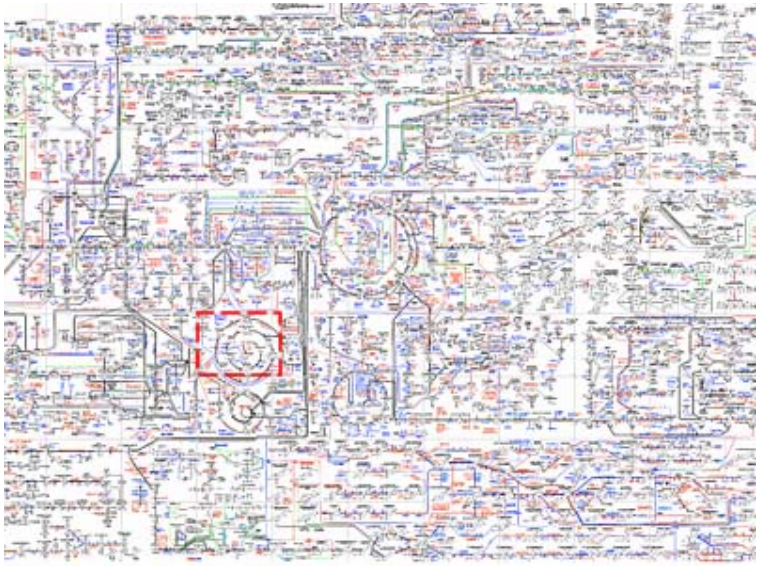


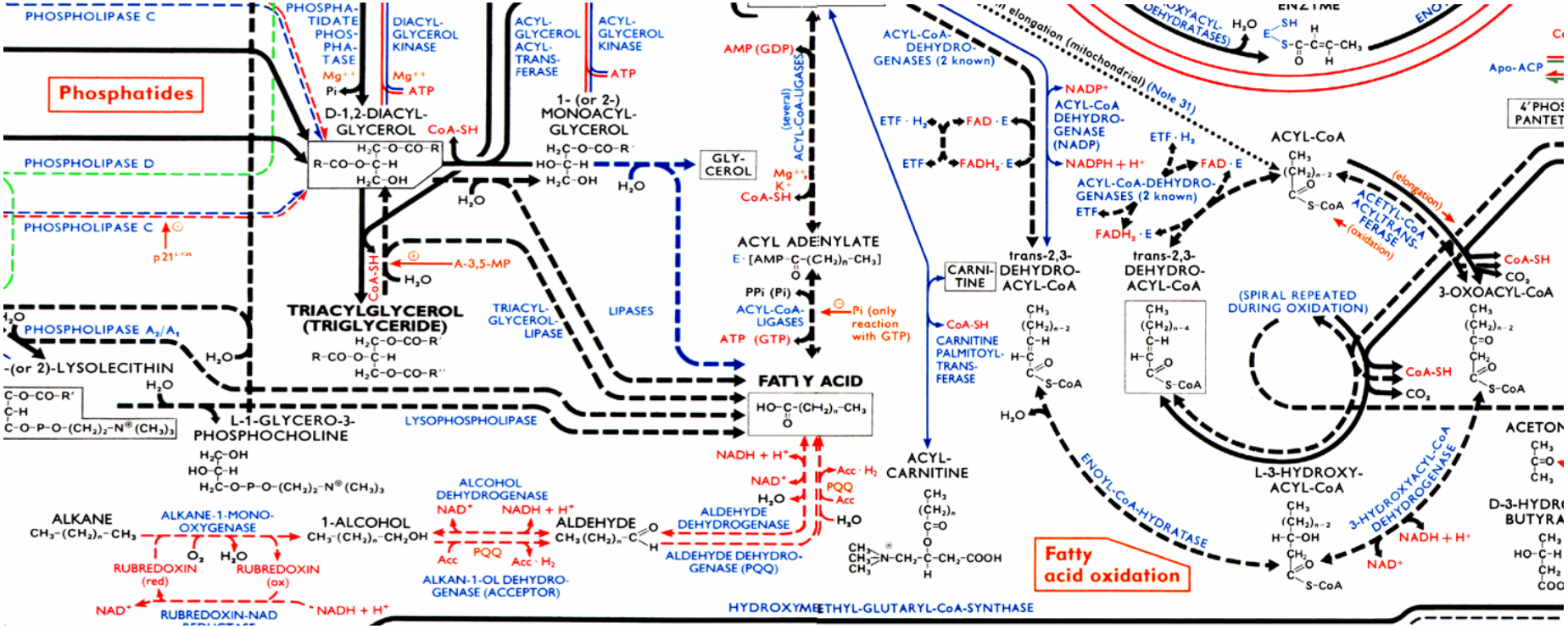
http://www.colorado.edu/MCDB/MCDB1111/intrographics/bacterial%20chromosome.jpg

http://academy.asd20.org/kadets/lundberg/ethics/images/chromosomes.jpg



http://www.cryst.bbk.ac.uk/PPS95/course/9_quaternary/6adh2.gif





http://www.expasy.ch/cgi-bin/show_image?D8&right

July 14, 2006

Made 1L LB Agar in order to make 500 mL (20 plates) of Ampicillin and ~~500~~ 250 mL (~~20~~ 10 plates) Kanamycin plates. ~~see next~~ page

Found H15 on plate #2 which is part BBa_I13522 which is GFP with a constitutive promoter on PSB1A2 vector. (pUC19 derived).

Amp Stock: 100 mg/mL
Kan Stock: 50 mg/mL

Final [Amp]: 100 μM (250μL stock in 250 mL media)
Final [Kan]: ~~50~~ μM (250 μL stock in 250 mL)

AmpR Plasmid is High copy number (100+)
KanR Plasmid is Low copy number (10+)

Plasmids Transformed Today:

AMP	70₁	Bba_R0040	Constitutive Promoter (strong)
AMP	30₁	Bba_B0034	High Copy RBS
AMP/KAN	11₁	Bba_B0015	2x Terminator
AMP	H15₍₂₎	Bba_I13522	GFP Device

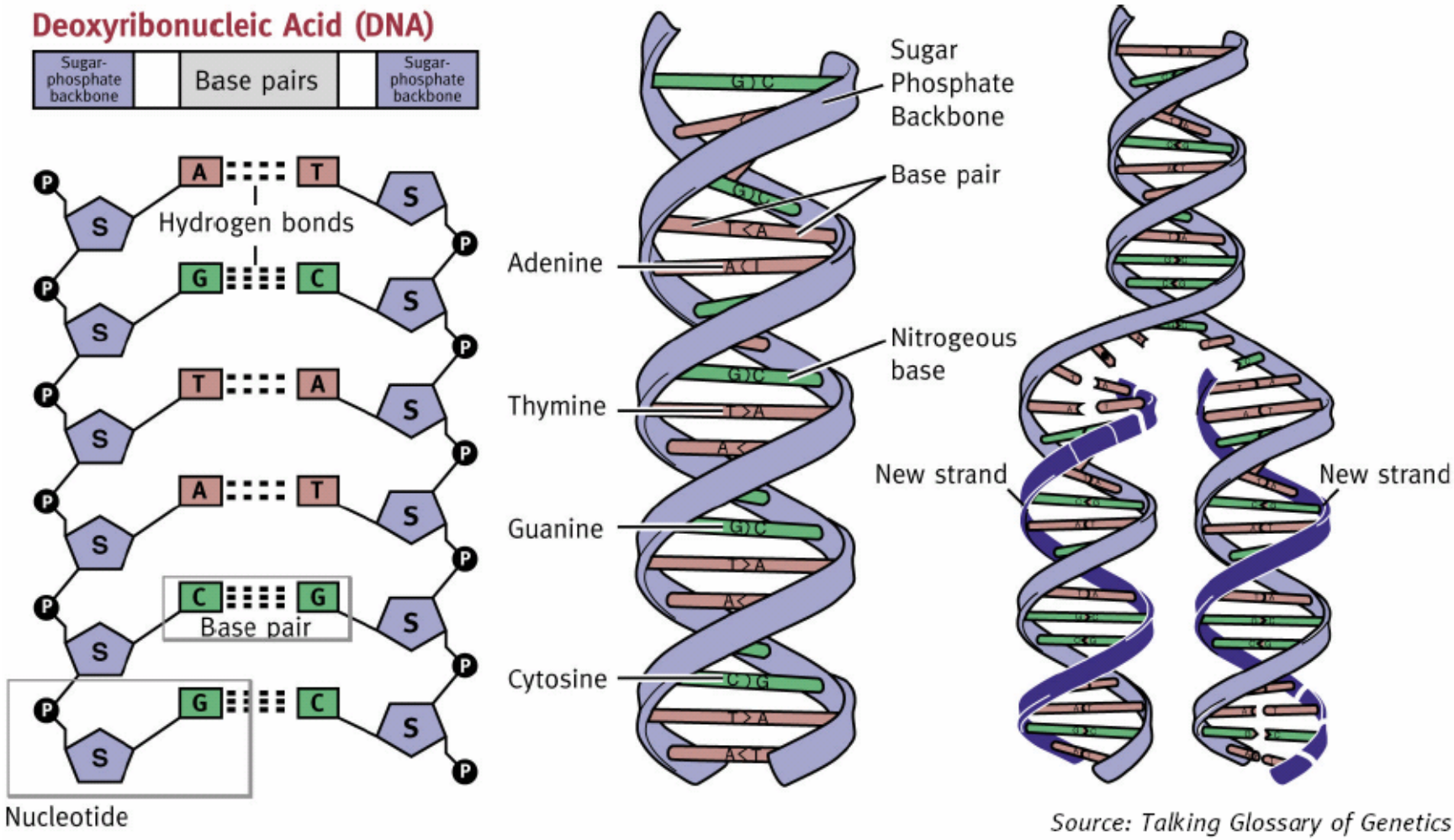
Subscript is which plate the DNA for that part (plasmid) is.

Device ≡ Working System ≡ D.

Not using DH5A, using TOP10

Digital Biology

Genomics



Source: Talking Glossary of Genetics

DNA is the machine language program for biochemical processes

Genomes are programs encoding:

- Biochemical processors
- Machinery to duplicate and install the program onto processors

Homo sapiens (human)	2900 million bases	~30,000	1 gene per 100,000 bases	46
Rattus norvegicus (rat)	2,750 million bases	~30,000	1 gene per 100,000 bases	42
Mus musculus (mouse)	2500 million bases	~30,000	1 gene per 100,000 bases	40
Drosophila melanogaster (fruit fly)	180 million bases	13,600	1 gene per 9,000 bases	8
Arabidopsis thaliana (plant)	125 million bases	25,500	1 gene per 4000 bases	10
Caenorhabditis elegans (roundworm)	97 million bases	19,100	1 gene per 5000 bases	12
Saccharomyces cerevisiae (yeast)	12 million bases	6300	1 gene per 2000 bases	32
Escherichia coli (bacteria)	4.7 million bases	3200	1 gene per 1400 bases	1
H. influenzae (bacteria)	1.8 million bases	1700	1 gene per 1000 bases	1

**Information extracted from genome publication papers below.*

Genome size does not correlate with evolutionary status, nor is the number of genes proportionate with genome size.

http://www.ornl.gov/sci/techresources/Human_Genome/faq/compgen.shtml#genomesize


danielg 072006 - S3is

Reading code

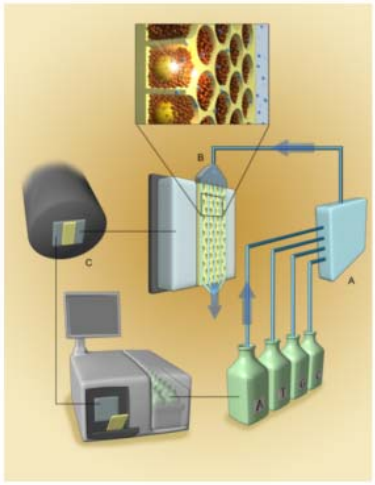
Nobel foundation

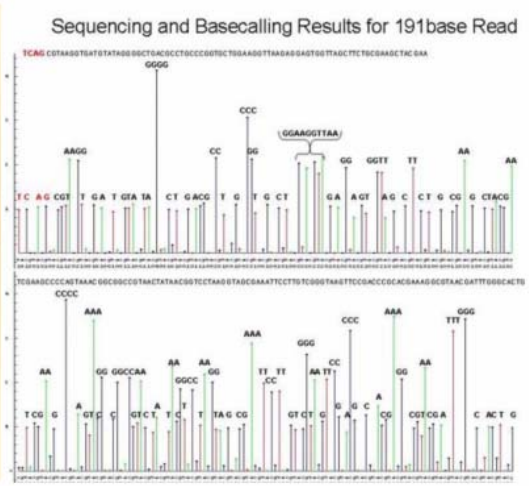
1980
500 bp/day (manual)

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

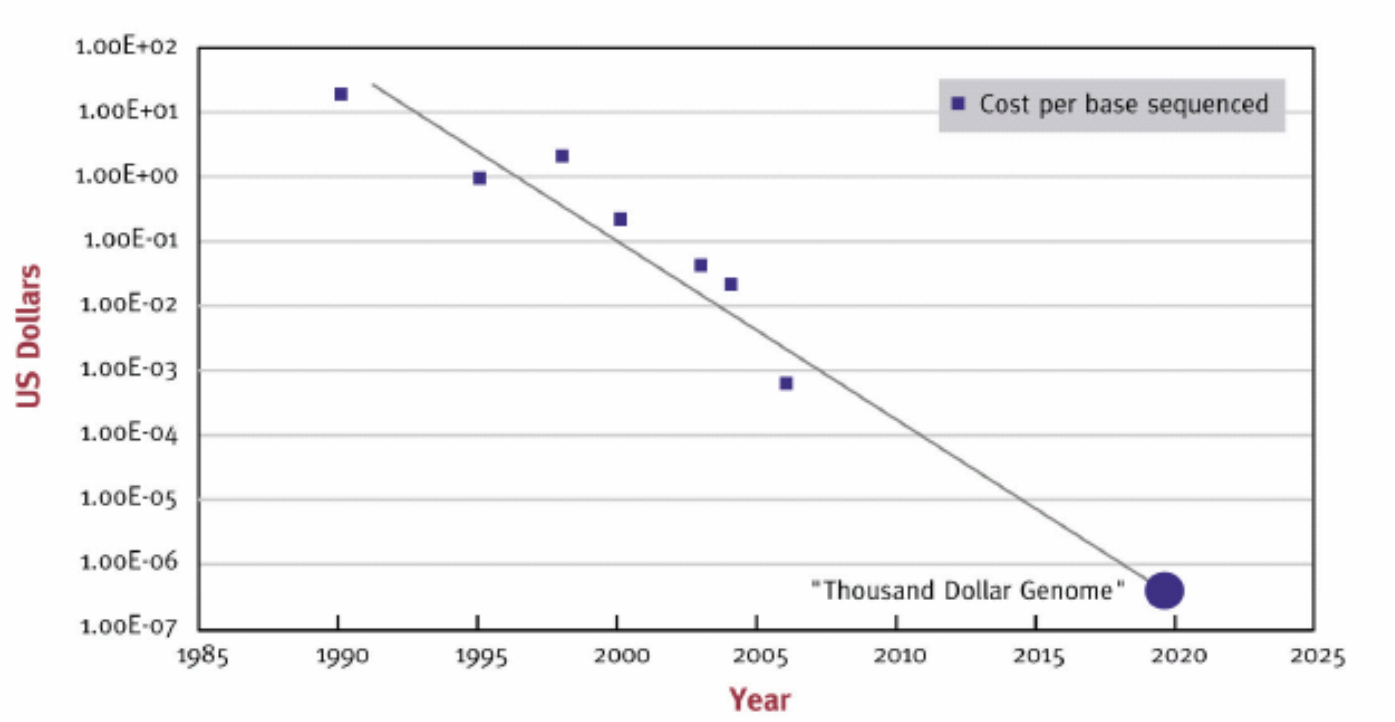
1995
144,000 bp/day (semi-auto)

1998
500,000 bp/day (automatic)





2007 – Sequencing by Synthesis
1GB bp/day (automatic)



Source: R. Carlson, Bio-era

Comprehension

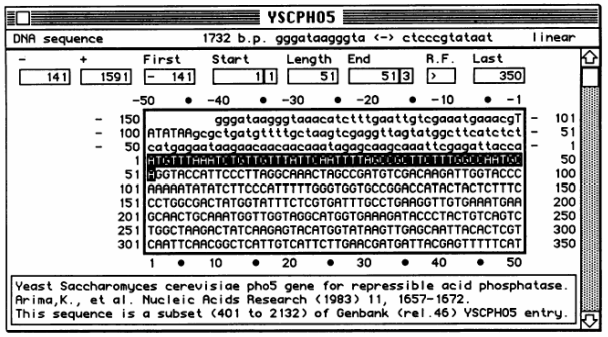
Volume 16 Number 5 1988 Nucleic Acids Research

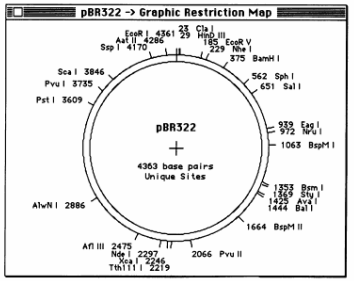
'DNA Strider': a 'C' program for the fast analysis of DNA and protein sequences on the Apple Macintosh family of computers

Christian Marck

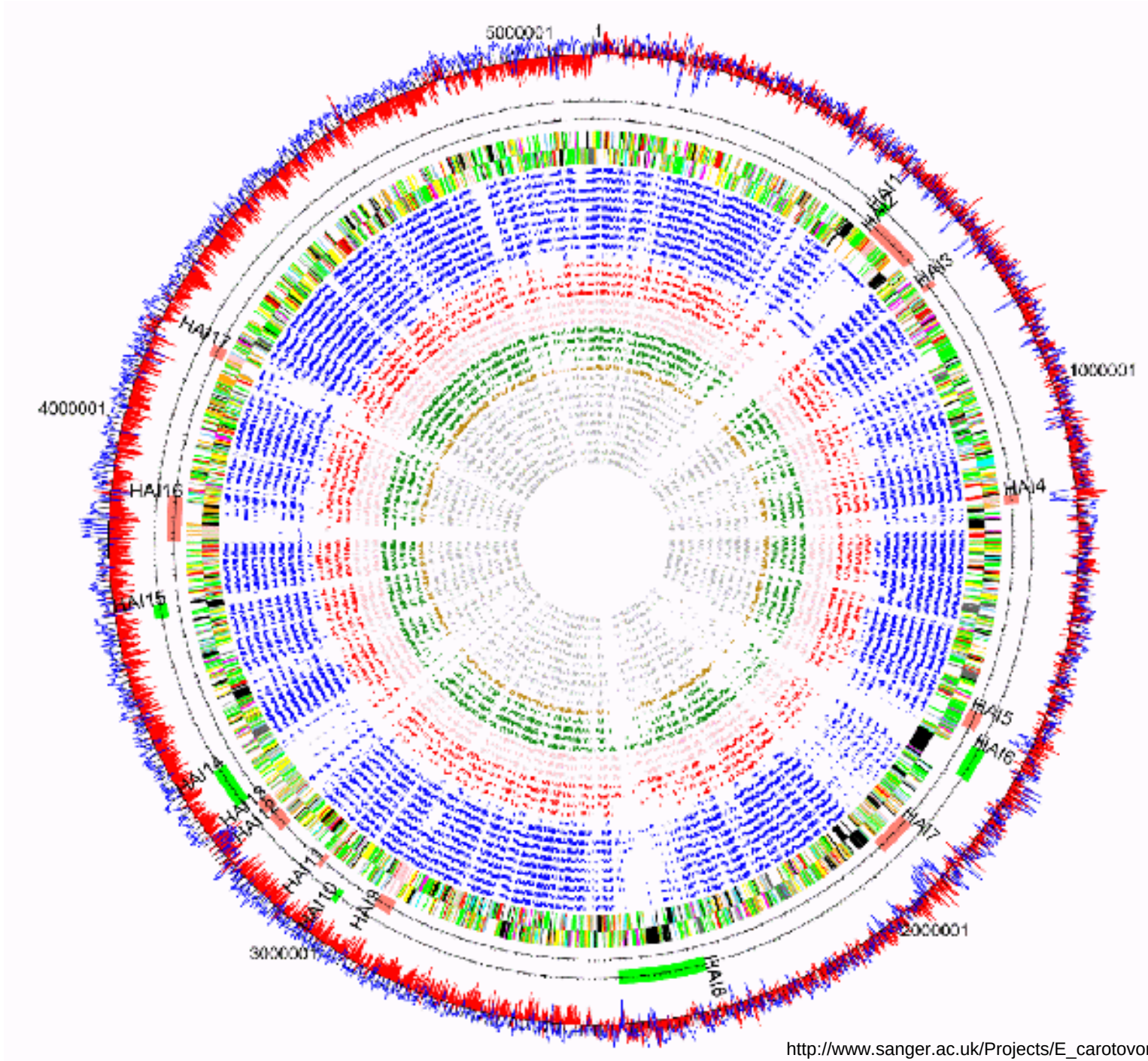
Service de Biochimie, Bâtiment 142, Département de Biologie, Centre d'Etudes Nucléaires de Saclay, 91191 Gif-sur-Yvette Cedex, France

Received August 17, 1987; Revised and Accepted November 15, 1987

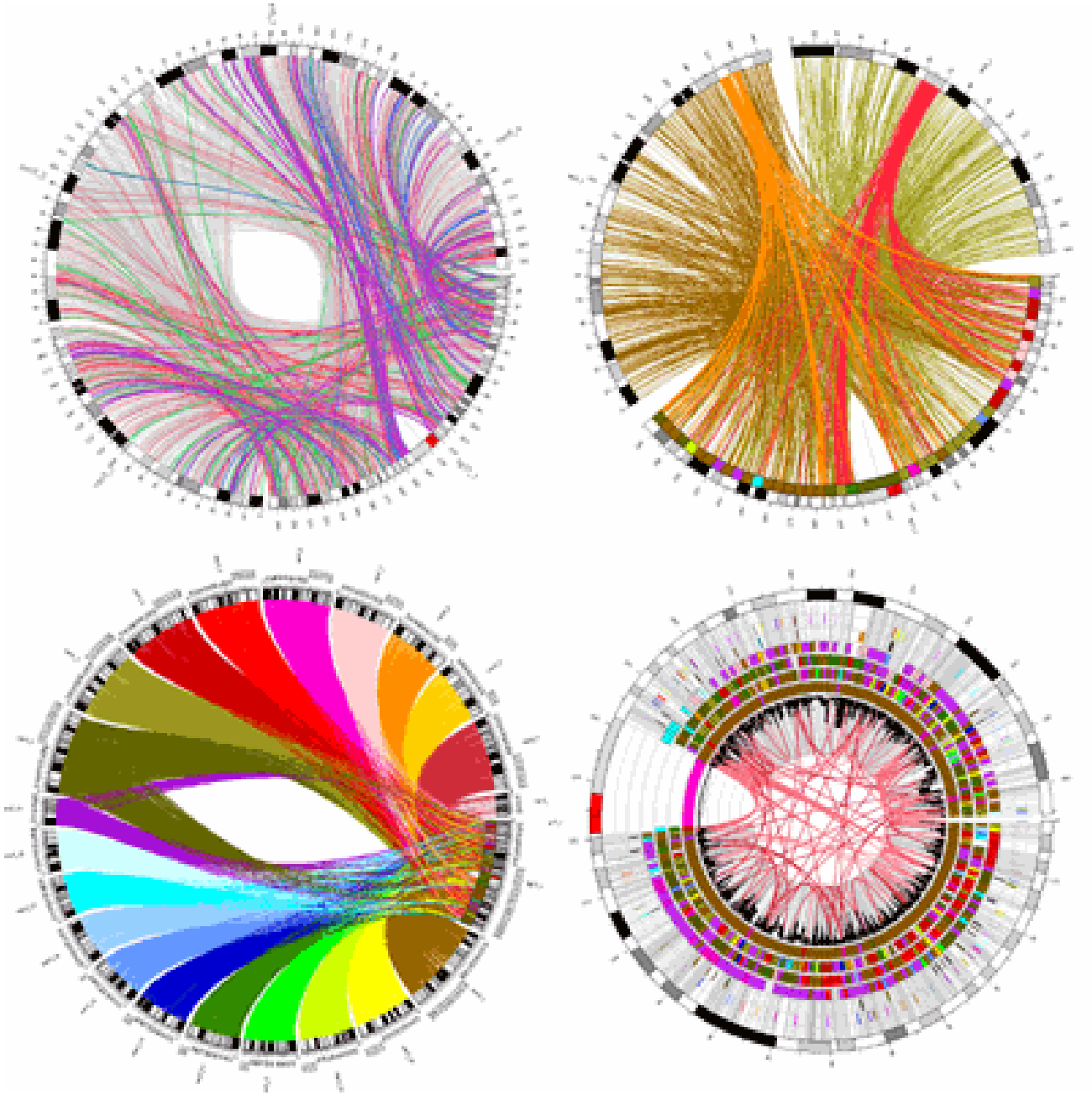




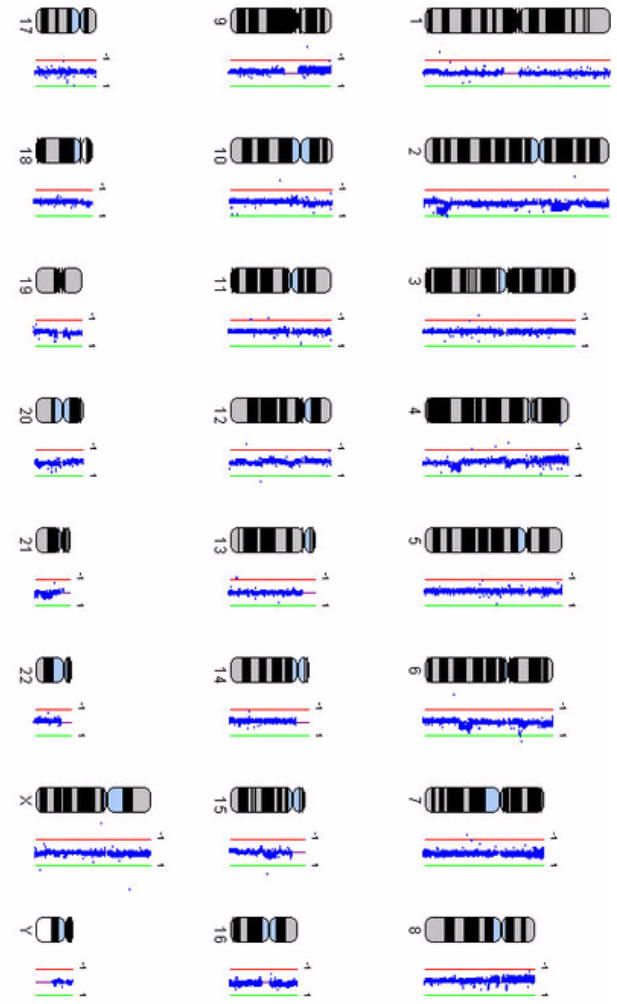
280.6 TFLOPS with 131072 nodes

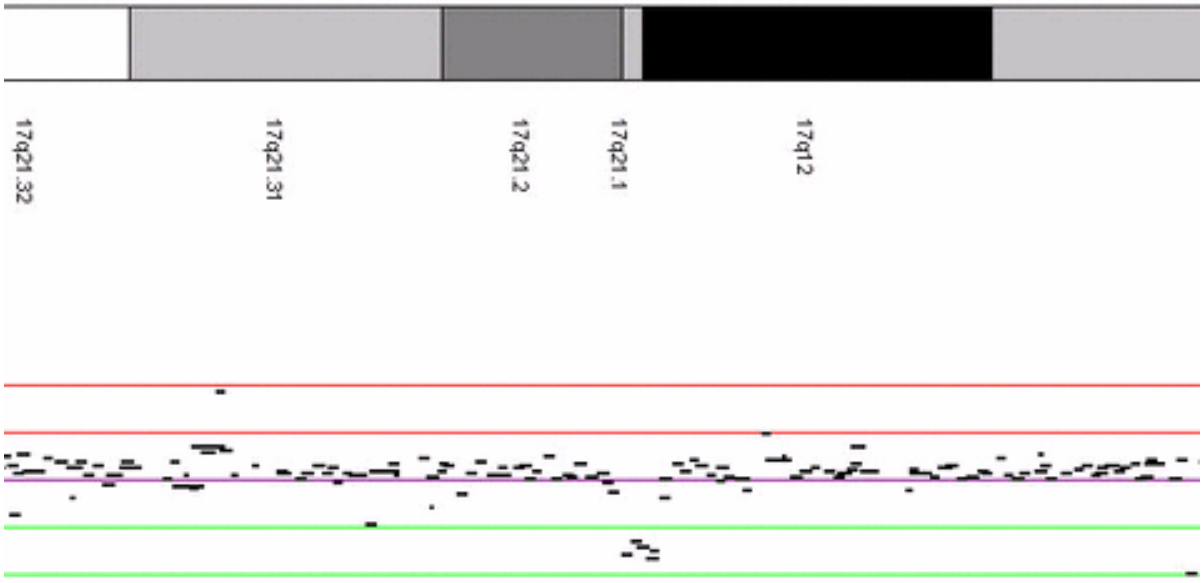


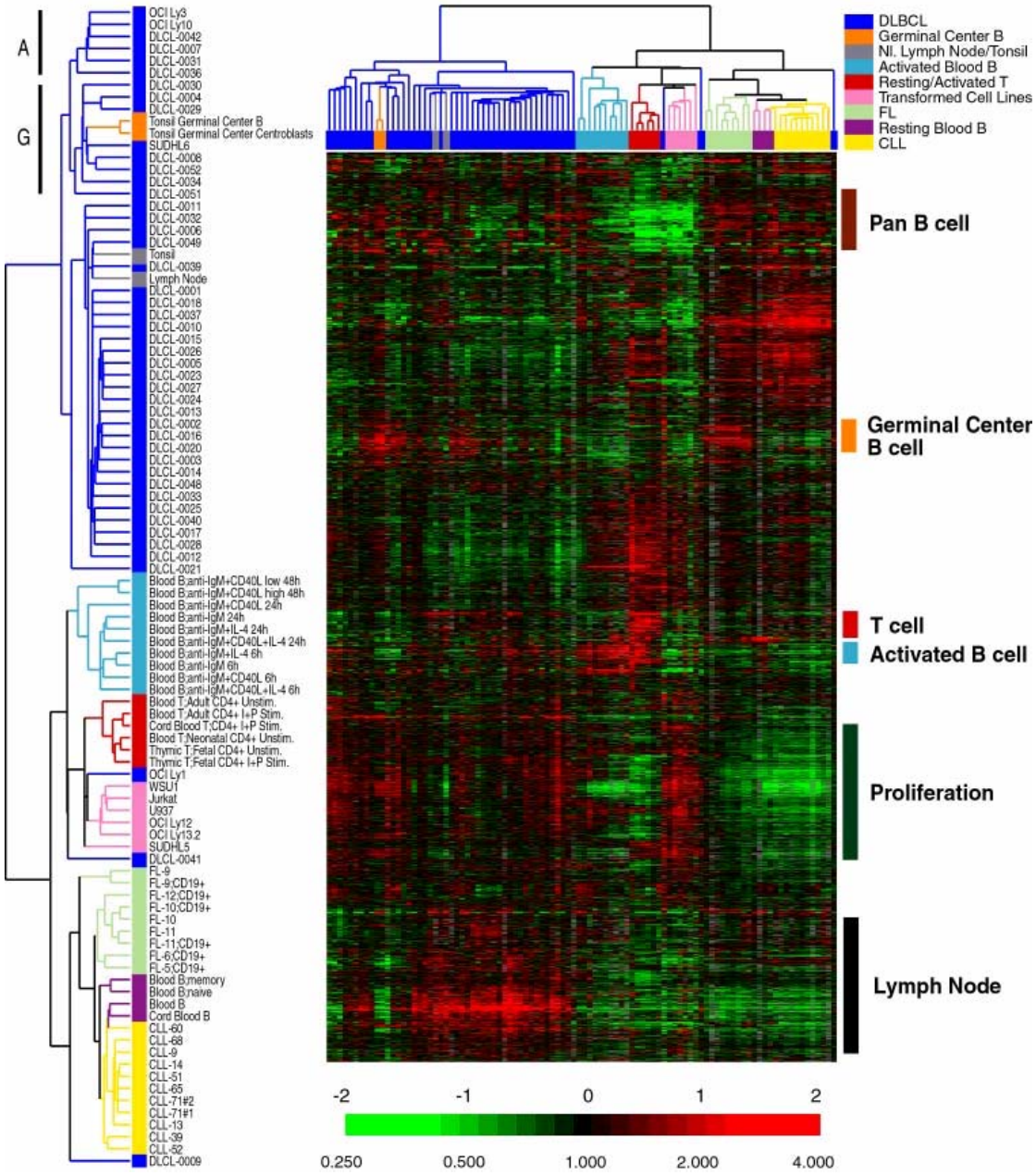
http://www.sanger.ac.uk/Projects/E_carotovora/gfx/erwinia.gif



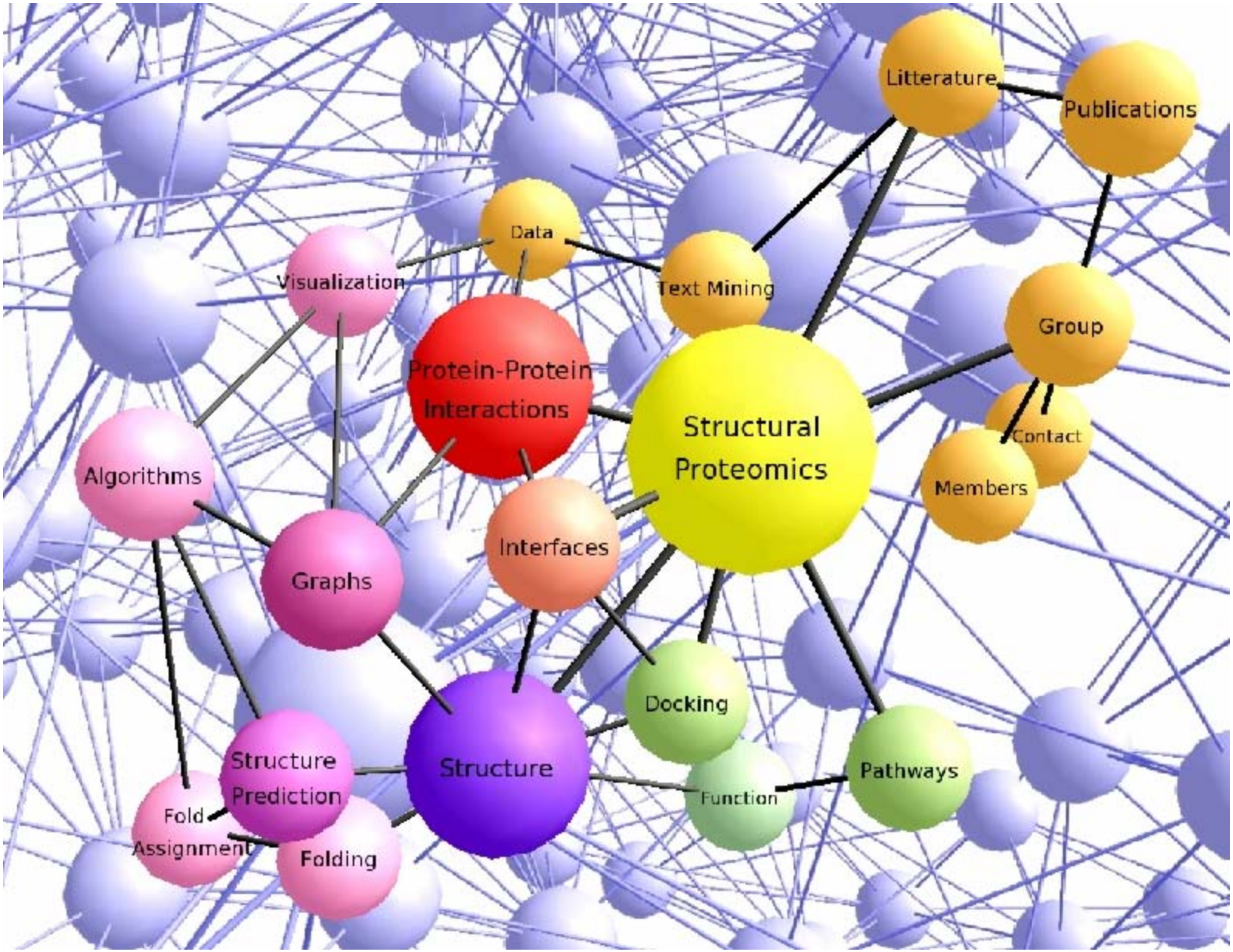
http://mkweb.bcgsc.ca/circos/tutorial/004/summary.png


17
9
1
18
10
2
19
11
3
20
12
4
21
13
5
22
14
6
X
15
7
Y
16
8

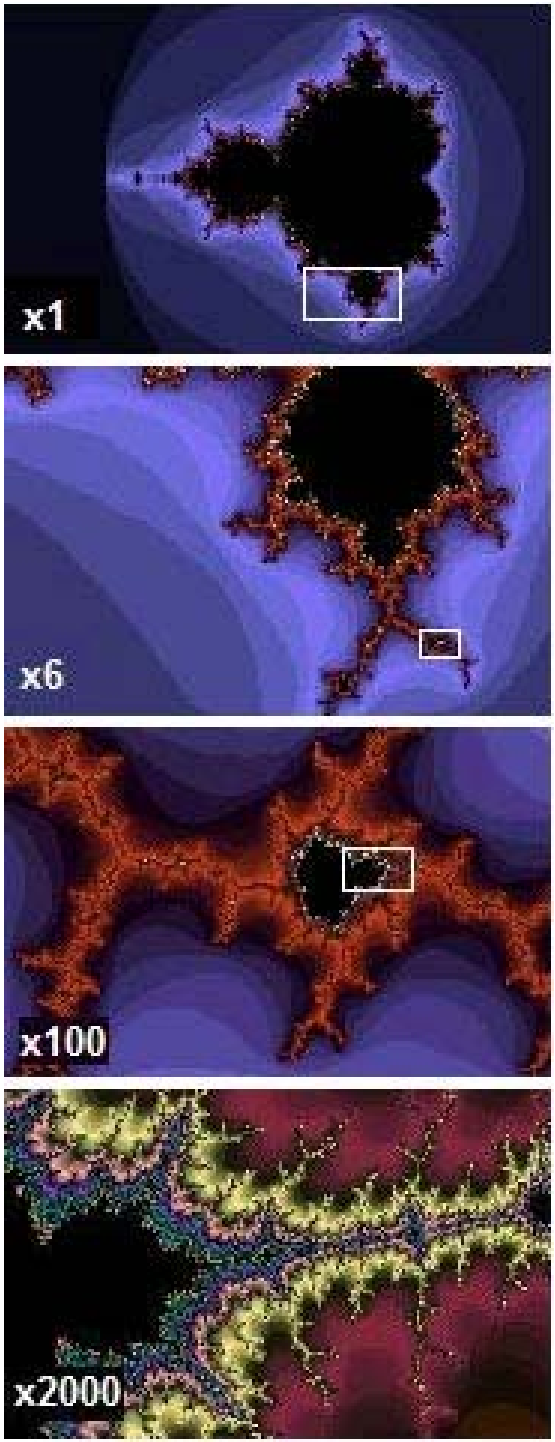

17q21.32
17q21.31
17q21.2
17q21.1
17q12



http://llmpp.nih.gov/lymphoma/images/large_figure1.jpg



http://www.molgen.mpg.de/~lappe/photos/final_webPict.jpg

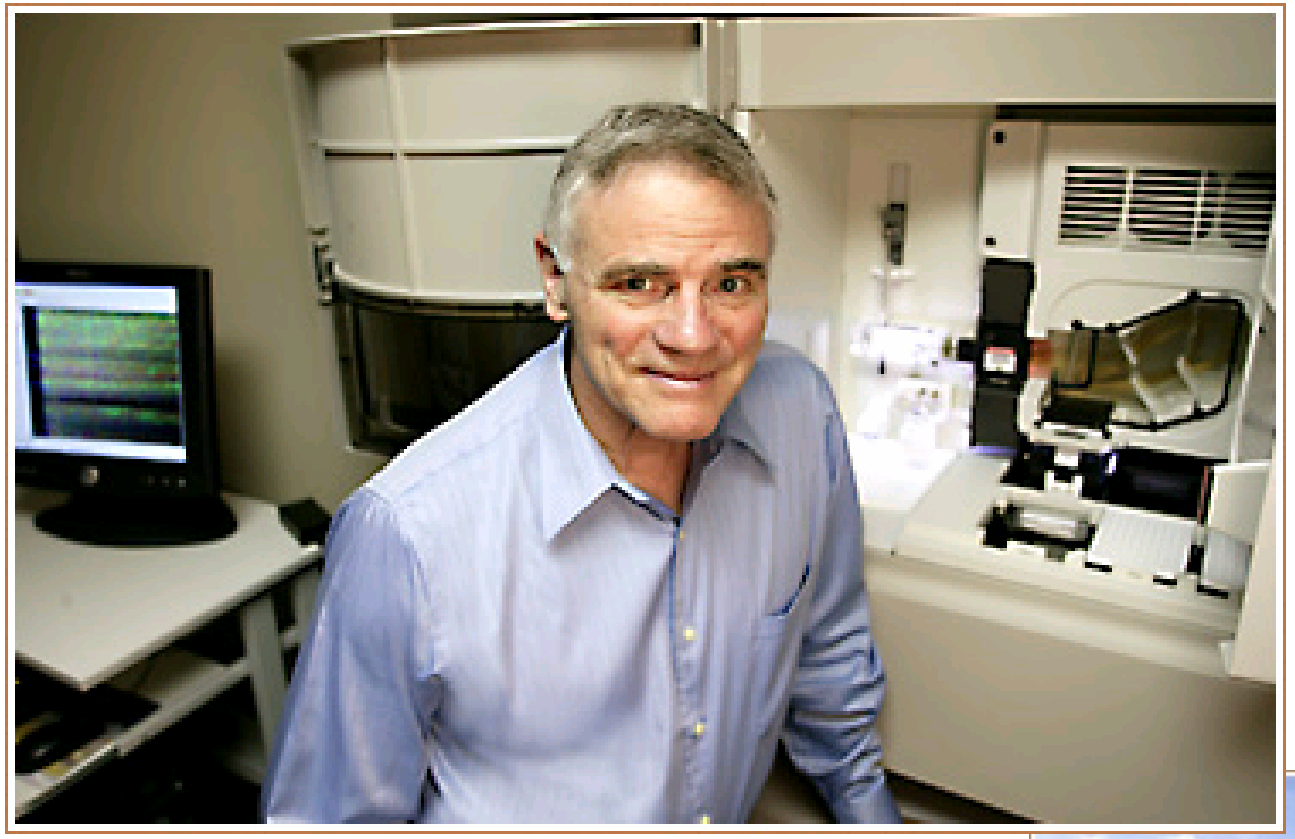


Reduction ⟺ Complexity

http://www.linesandcolors.com/category/digital-art/

Biological understanding

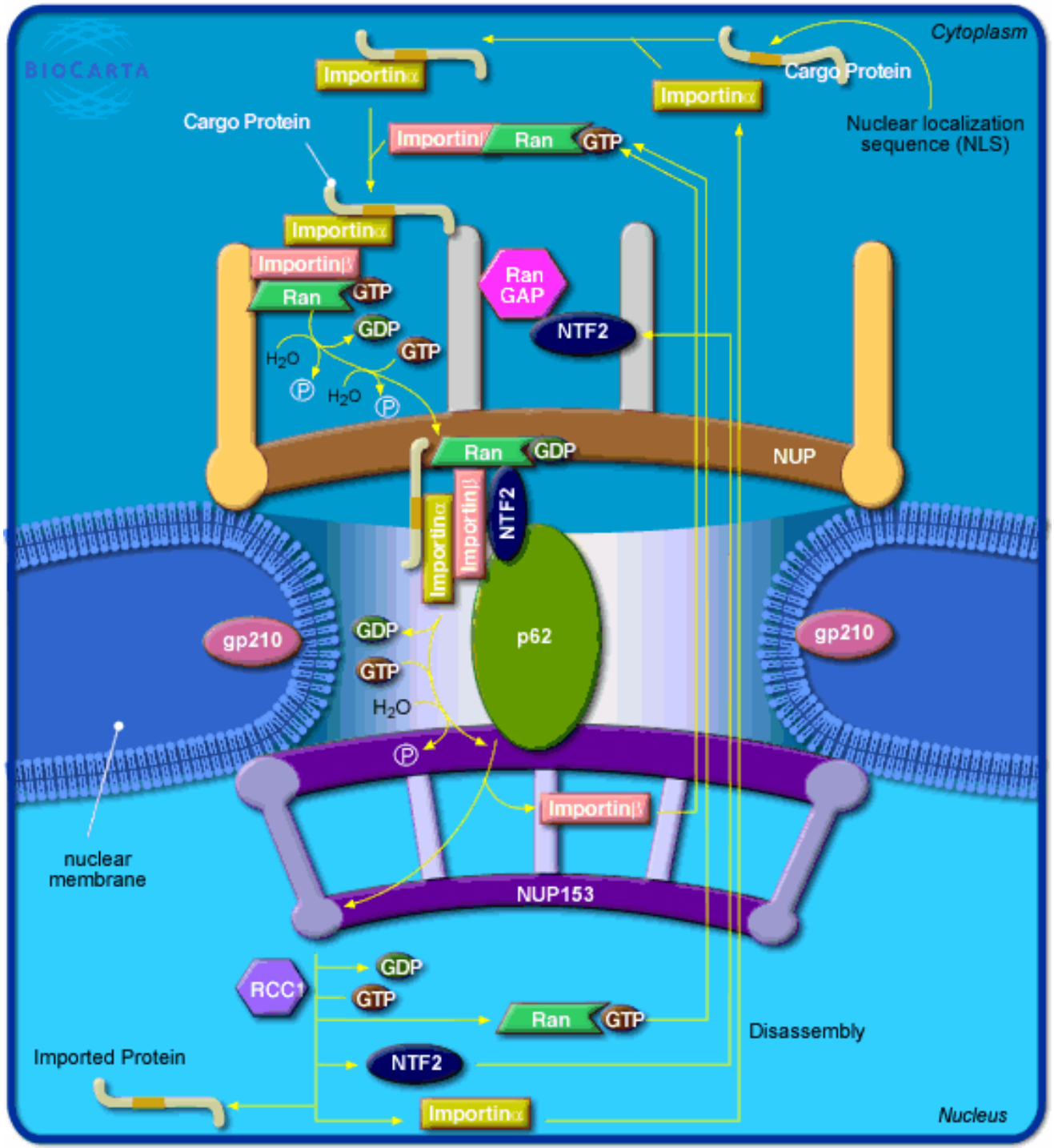
- Just storing data is a challenge
- Finite human comprehension > finer specializations > greater barriers
- Machine-learning, self-organizing, and other naïve techniques increasing necessary – ***Systems Biology***

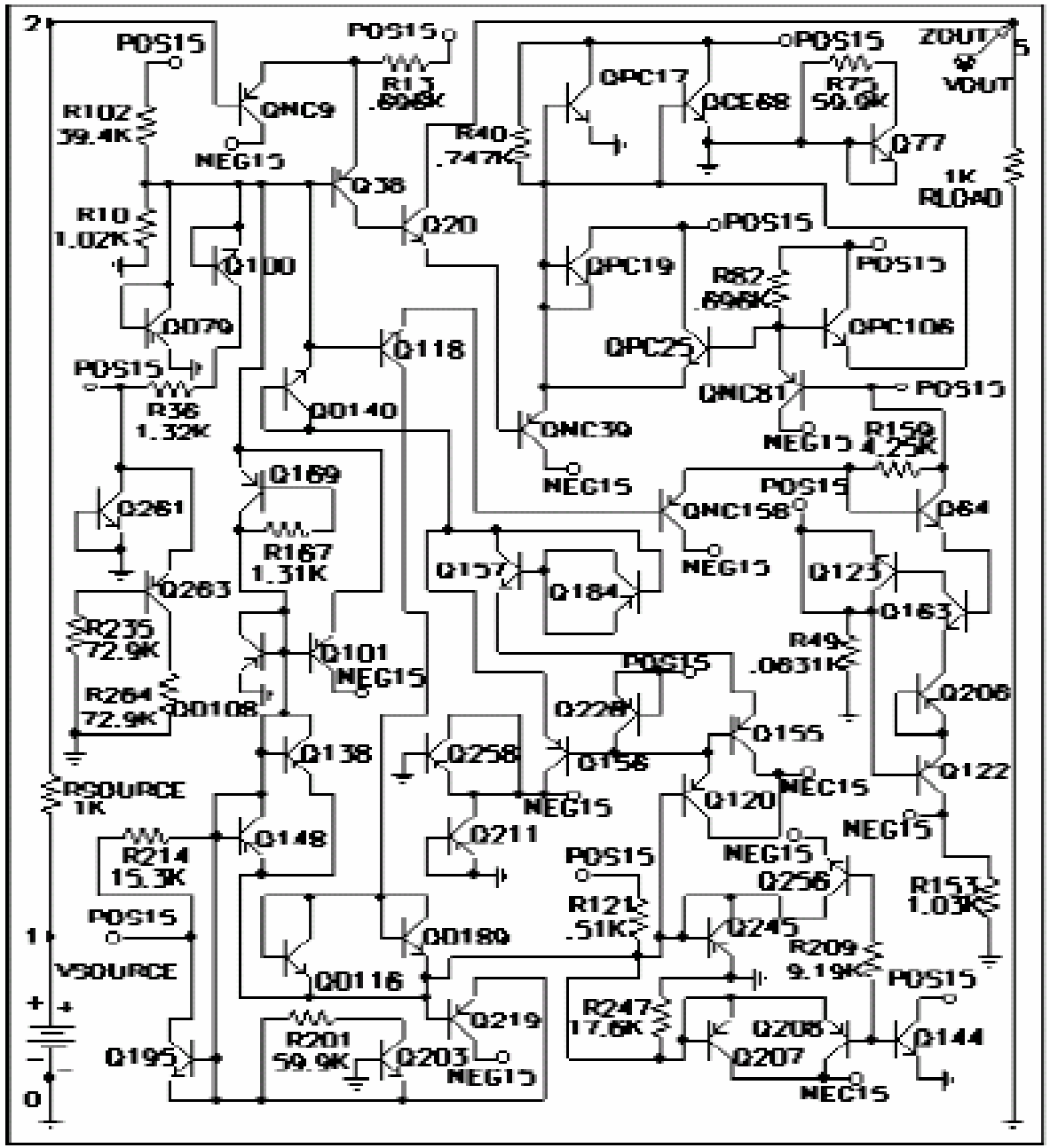


Perspectives of Systems Biology

"Perhaps surprisingly, a concise definition of systems biology that most of us can agree upon has yet to emerge."

Ruedi Aebersold, Ph.D.
Faculty Member
Institute for Systems Biology


BIOCARTA
Cytoplasm
Importinα
Cargo Protein
Importinα
Cargo Protein
Nuclear localization sequence (NLS)
Cargo Protein
Importinβ
Ran
GTP
Importinα
Importinβ
Ran
GTP
Ran GAP
NTF2
GDP
GTP
H2O
P
H2O
P
Ran
GDP
NUP
Importinα
Importinβ
NTF2
gp210
GDP
GTP
H2O
p62
gp210
P
Importinβ
nuclear membrane
NUP153
RCC1
GDP
GTP
Ran
GTP
Disassembly
Imported Protein
NTF2
Importinα
Nucleus



J.R. Koza et al.
Automatic creation of computer programs for designing electrical circuits using genetic programming.

http://www.genetic-programming.com/jkpdf/acdm1998.pdf

Genetic “Engineering”

Writing code

If we can’t build it, we don’t understand it.

Proc. Nat. Acad. Sci. USA
Vol. 69, No. 10, pp. 2904–2909, October 1972

Biochemical Method for Inserting New Genetic Information into DNA of Simian Virus 40: Circular SV40 DNA Molecules Containing Lambda Phage Genes and the Galactose Operon of *Escherichia coli*

(molecular hybrids/DNA joining/viral transformation/genetic transfer)

DAVID A. JACKSON*, ROBERT H. SYMONS†, AND PAUL BERG

Department of Biochemistry, Stanford University Medical Center, Stanford, California 94305

Contributed by Paul Berg, July 31, 1972

First rDNA molecule reported, October 1972

Proc. Nat. Acad. Sci. USA
Vol. 70, No. 11, pp. 3240–3244, November 1973

Construction of Biologically Functional Bacterial Plasmids *In Vitro*

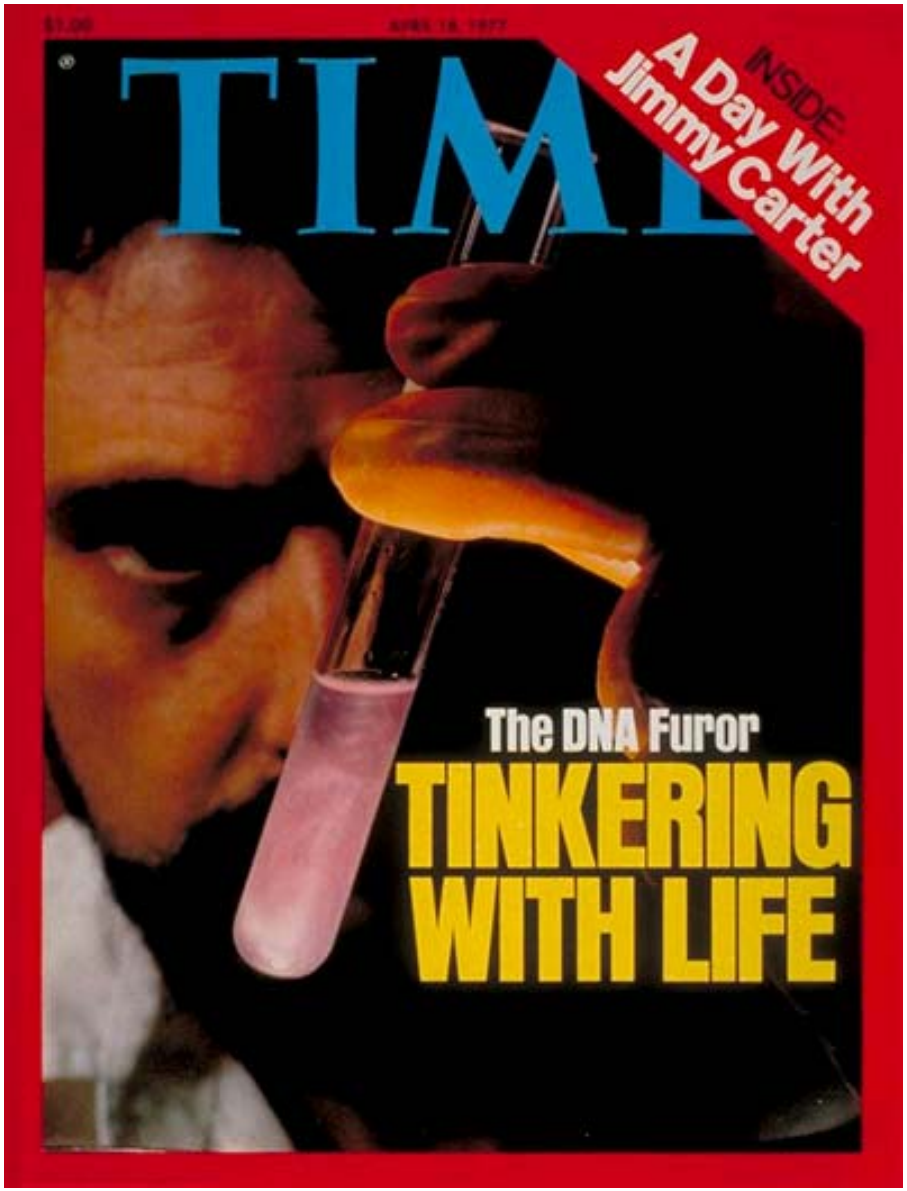
(R factor/restriction enzyme/transformation/endonuclease/antibiotic resistance)

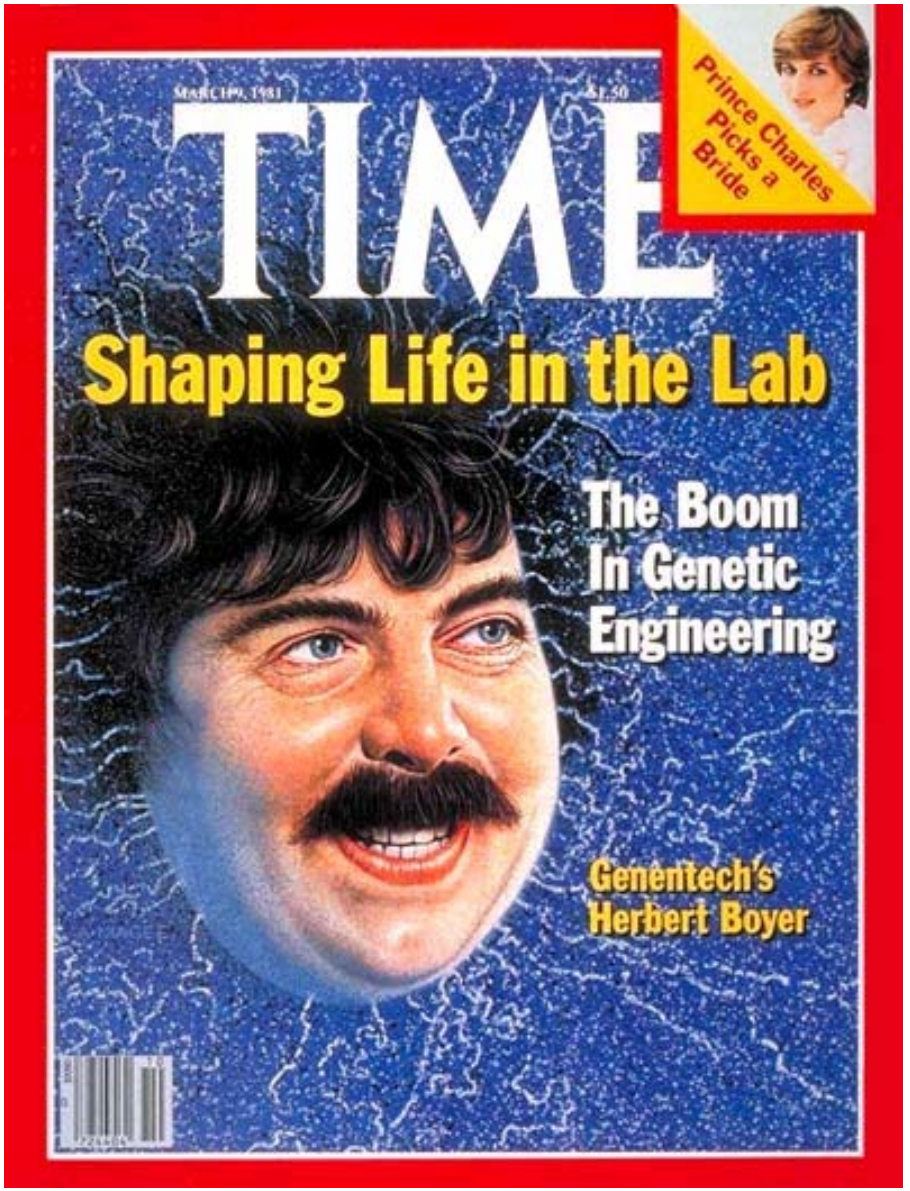
STANLEY N. COHEN*, ANNIE C. Y. CHANG*, HERBERT W. BOYER†, AND ROBERT B. HELLING†

* Department of Medicine, Stanford University School of Medicine, Stanford, California 94305; and † Department of Microbiology, University of California at San Francisco, San Francisco, Calif. 94122

Communicated by Norman Davidson, July 18, 1973

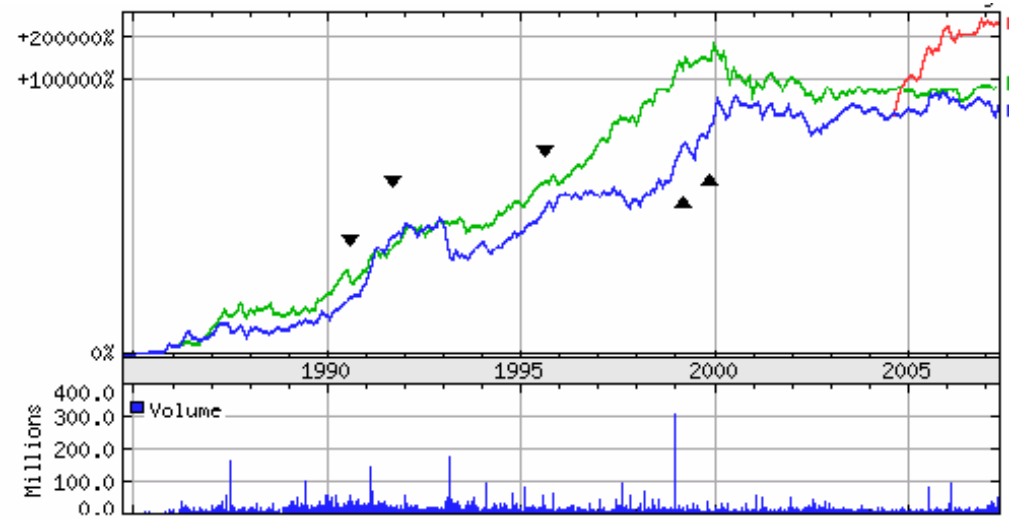
First synthetic DNA molecule reported, November 1973


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


TIME
Prince Charles Picks a Bride
Shaping Life in the Lab
The Boom In Genetic Engineering
Genentech's Herbert Boyer

DNA vs Electronics

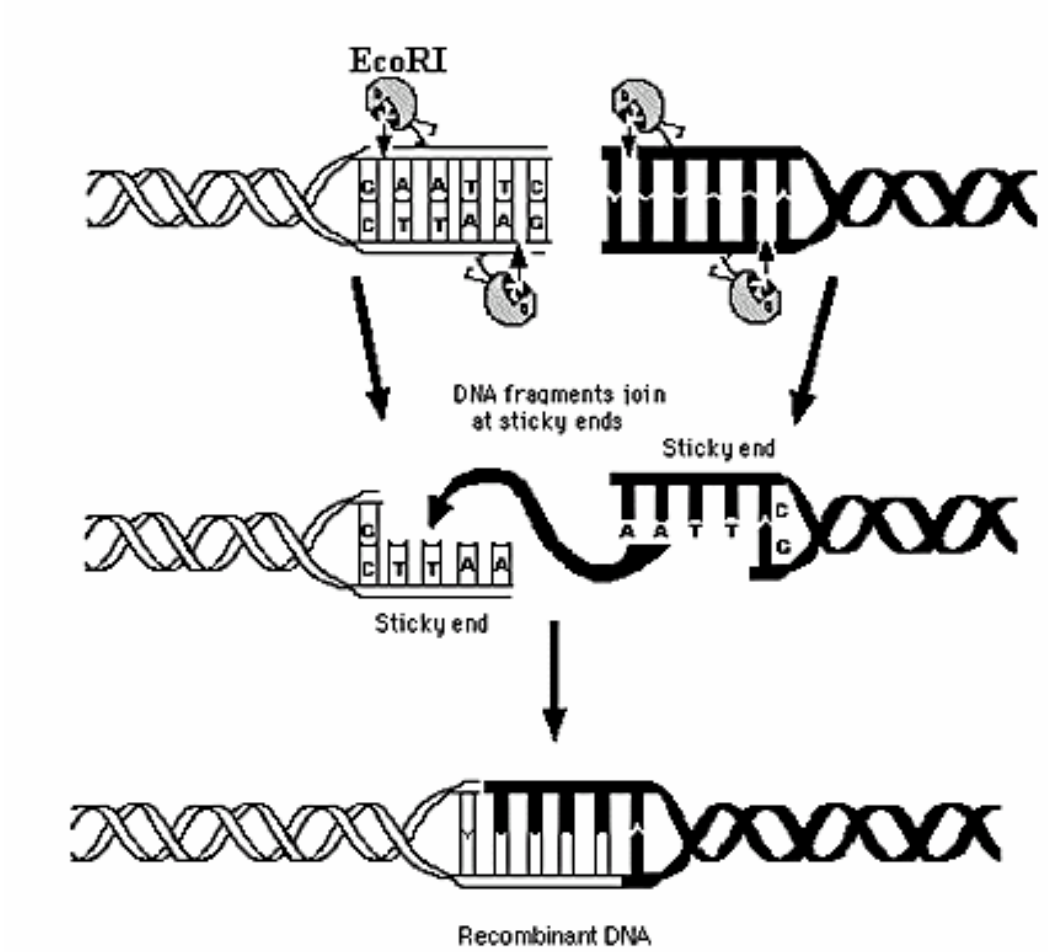
- Basic elements: DNA (1953/nobel ‘62) and transistor (1947/nobel ‘56)
- Similar potential for great influence on society
- Similar industry growth curves



REBASE®

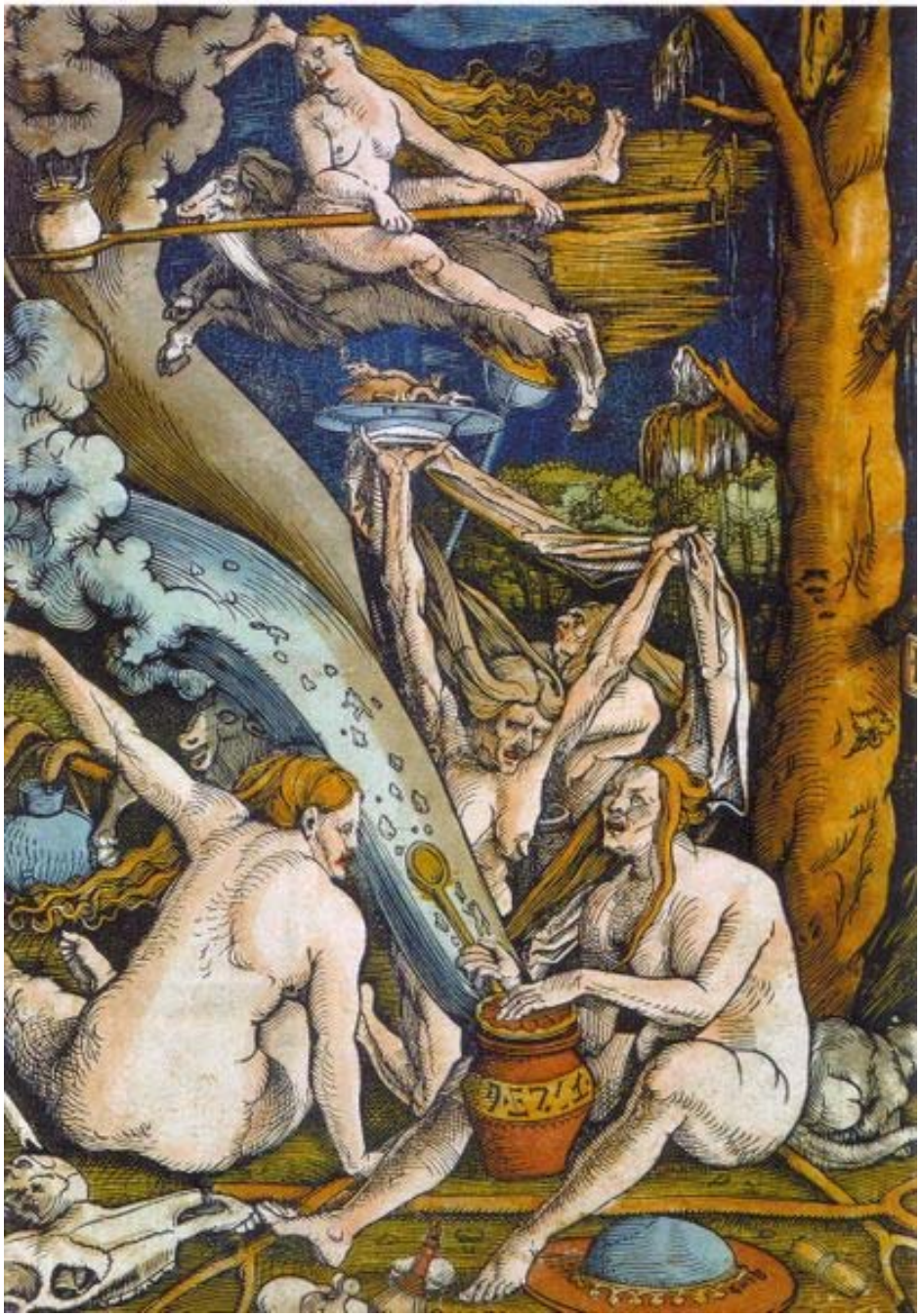
home page...

rebase.neb.com

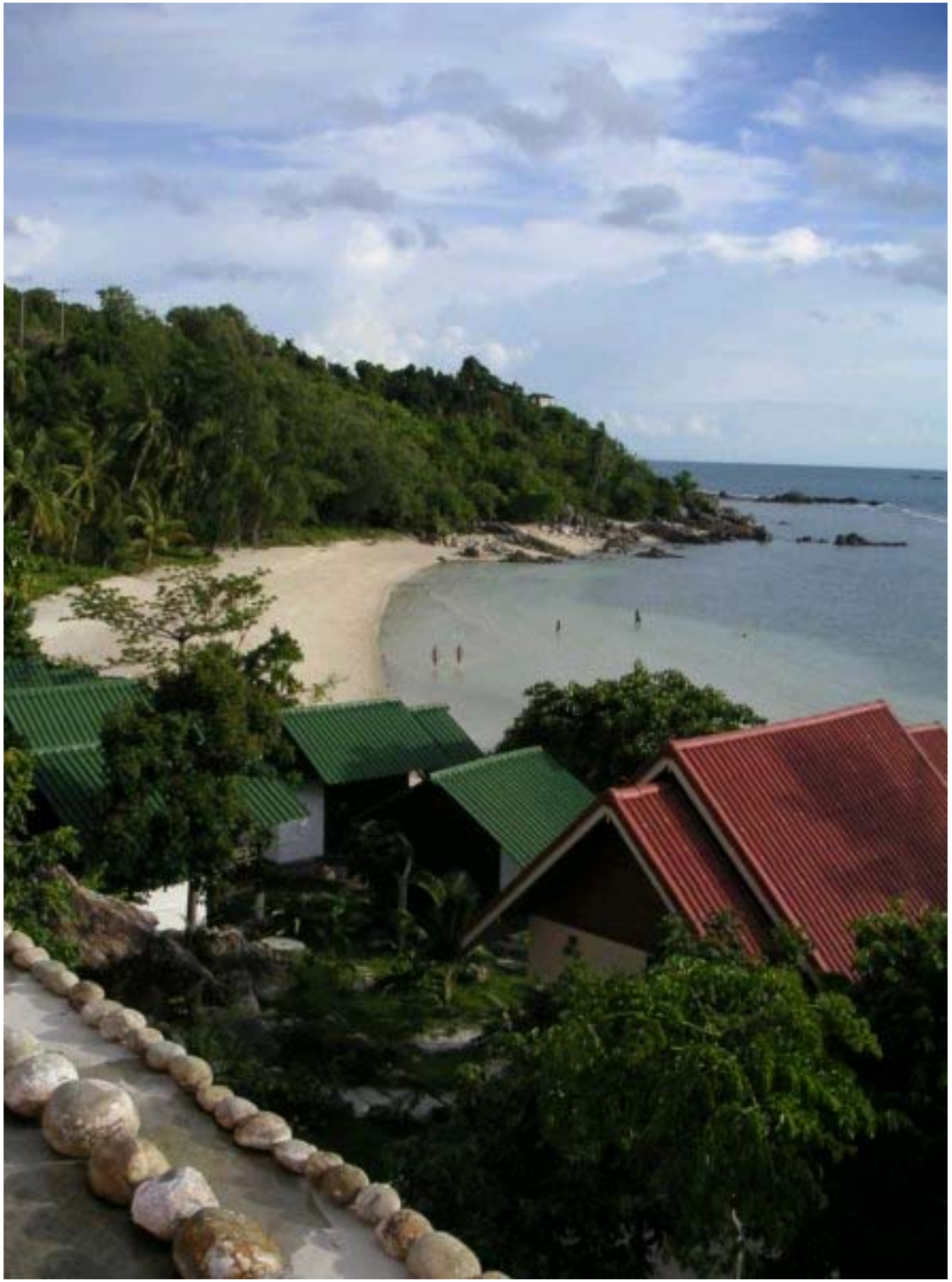


Restriction Enzyme Action of EcoRI

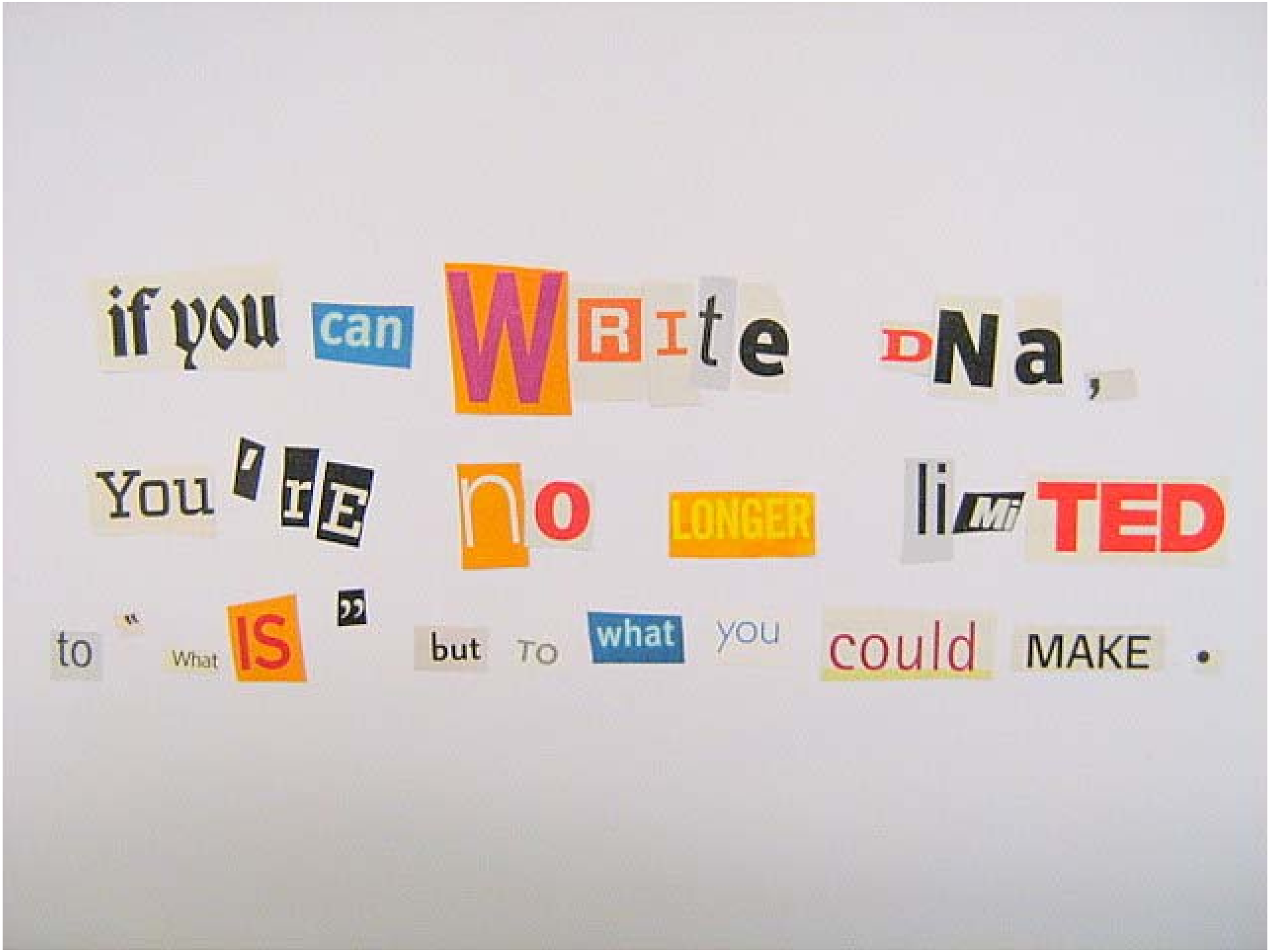

WARNING



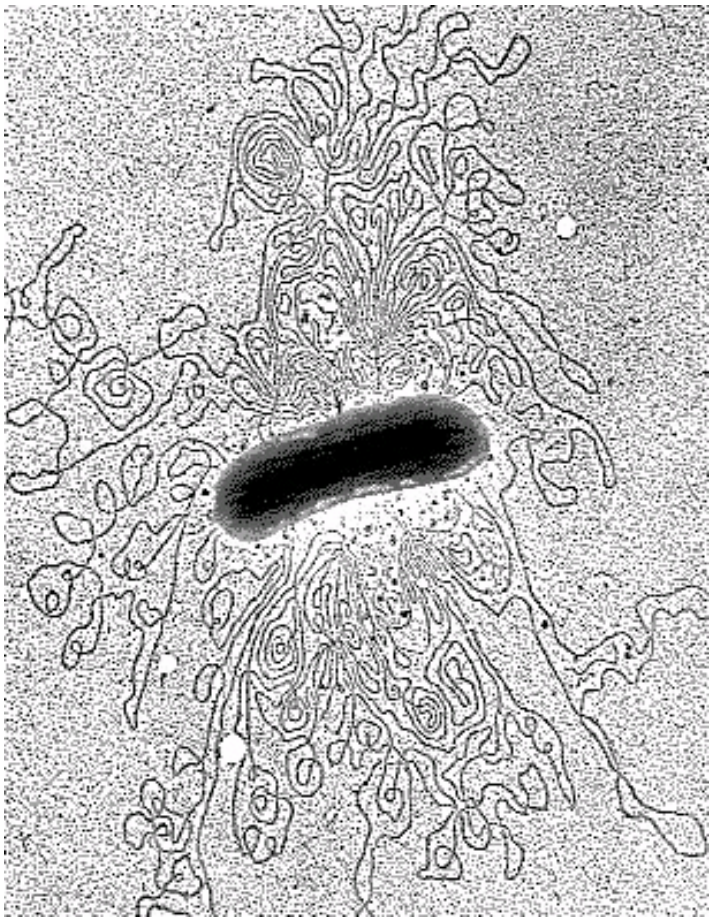
Hand Baldung Grien: Witches. Woodcut 1508



Genomic programming


if you can WRIte DNa,
You 're no LONGER limiTED
to " What IS " but TO what you could MAKE .

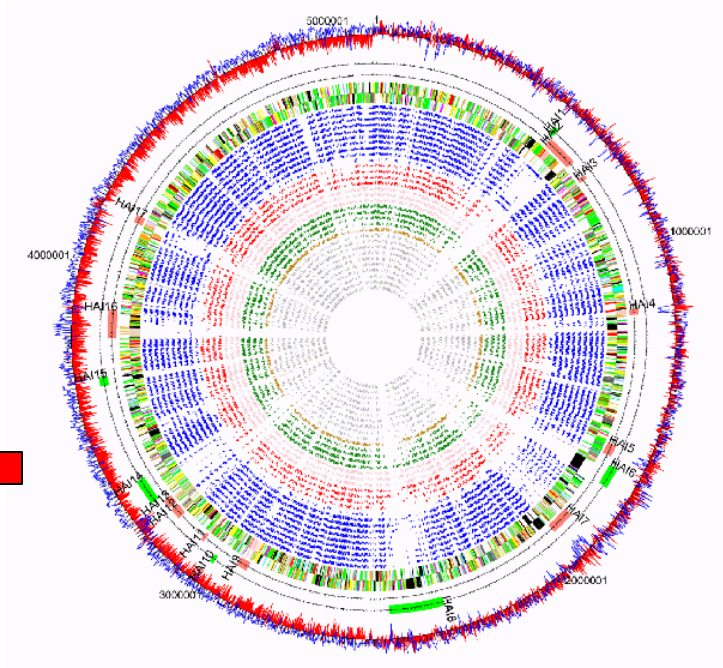
http://en.wikipedia.org/wiki/Image:Metal_movable_type.jpg



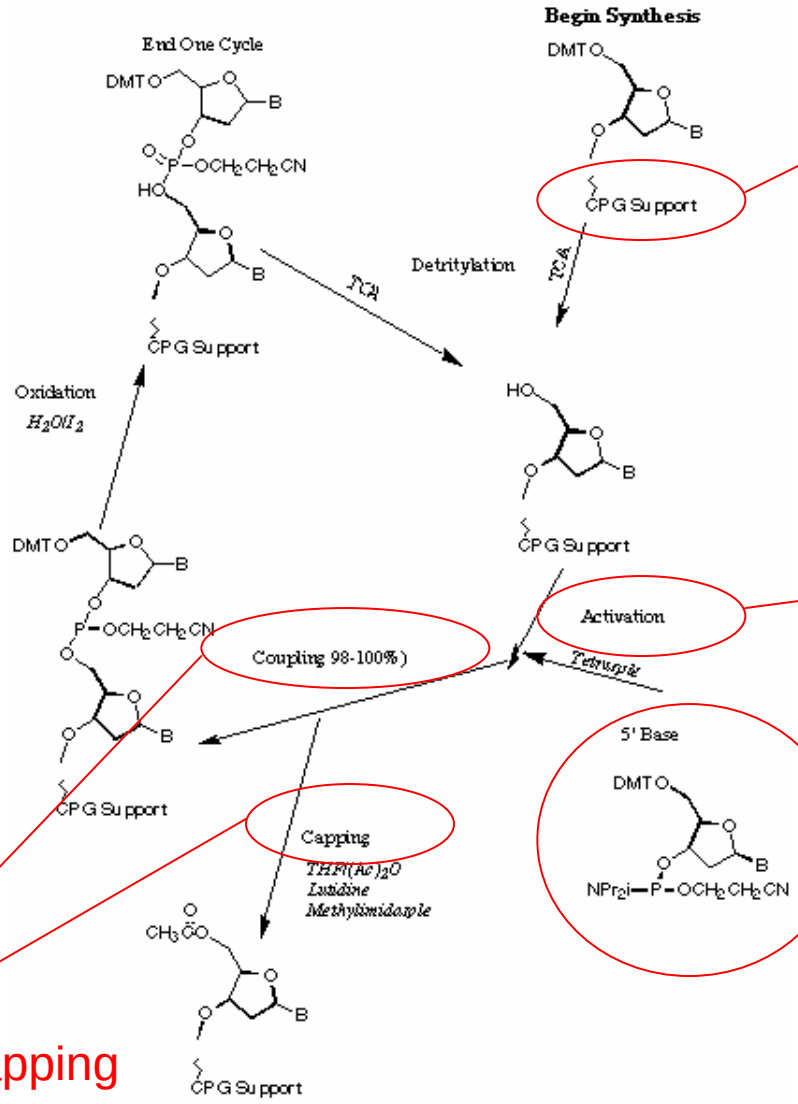
Physical DNA

sequencing

synthesis



Digital DNA

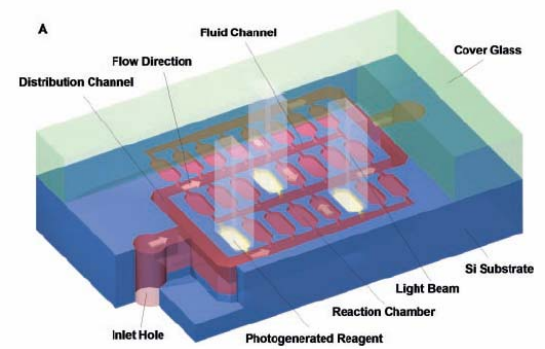


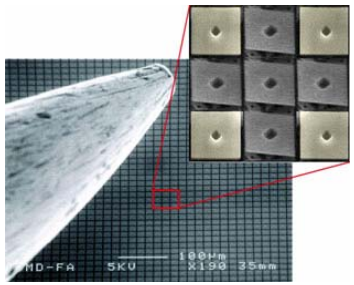
Controlled Pore Glass Solid Support

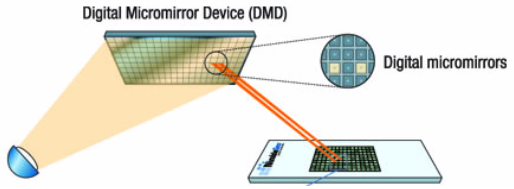
Activation (acid) and new base addition

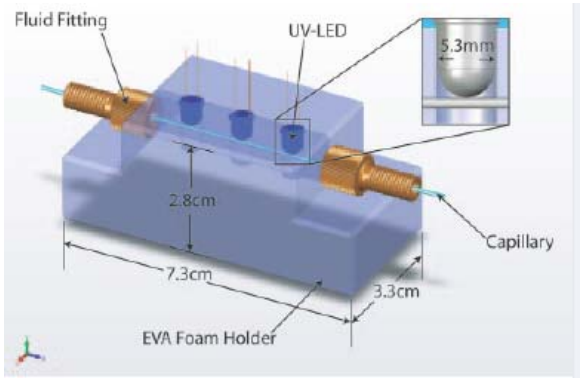
Coupling and Capping


BECKMAN


A
Fluid Channel
Flow Direction
Distribution Channel
Cover Glass
Si Substrate
Light Beam
Reaction Chamber
Inlet Hole
Photogenerated Reagent




Digital Micromirror Device (DMD)
Digital micromirrors


Fluid Fitting
UV-LED
5.3mm
2.8cm
Capillary
7.3cm
3.3cm
EVA Foam Holder

Milli GEN/Biosearch 8700 DNA Synthesizer

Seller of this item? Sign in for your status

1 of 6

Supersize

Starting bid:	**US $89.99** Place Bid >
End time:	**May-04-07 08:30:40 PDT** (1 day 7 hours)
Shipping costs:	Check item description and payment instructions or contact seller for details
Ships to:	United States
Item location:	Saint Louis, Missouri, United States
History:	0 bids
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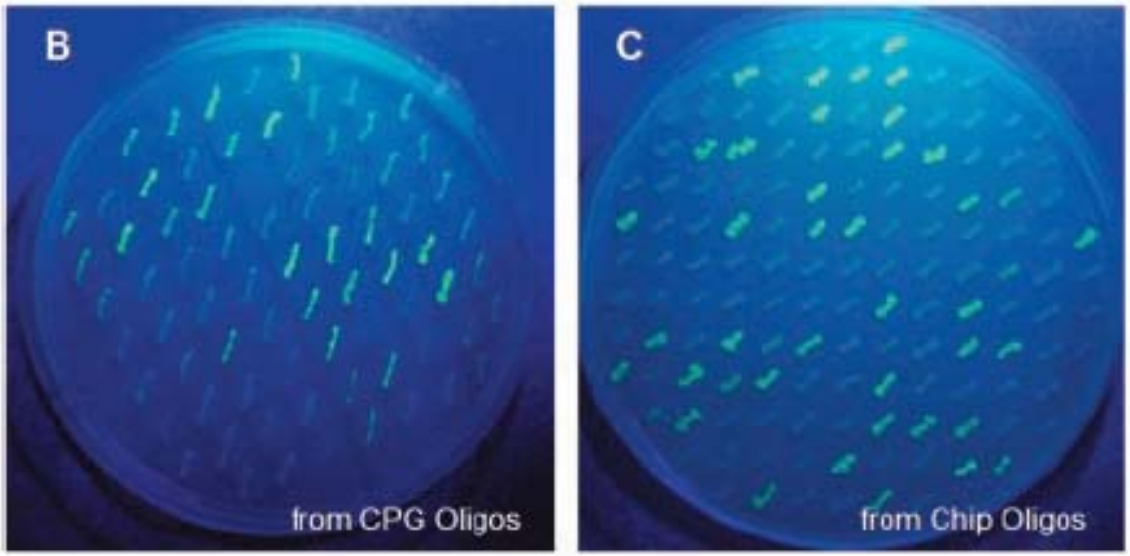
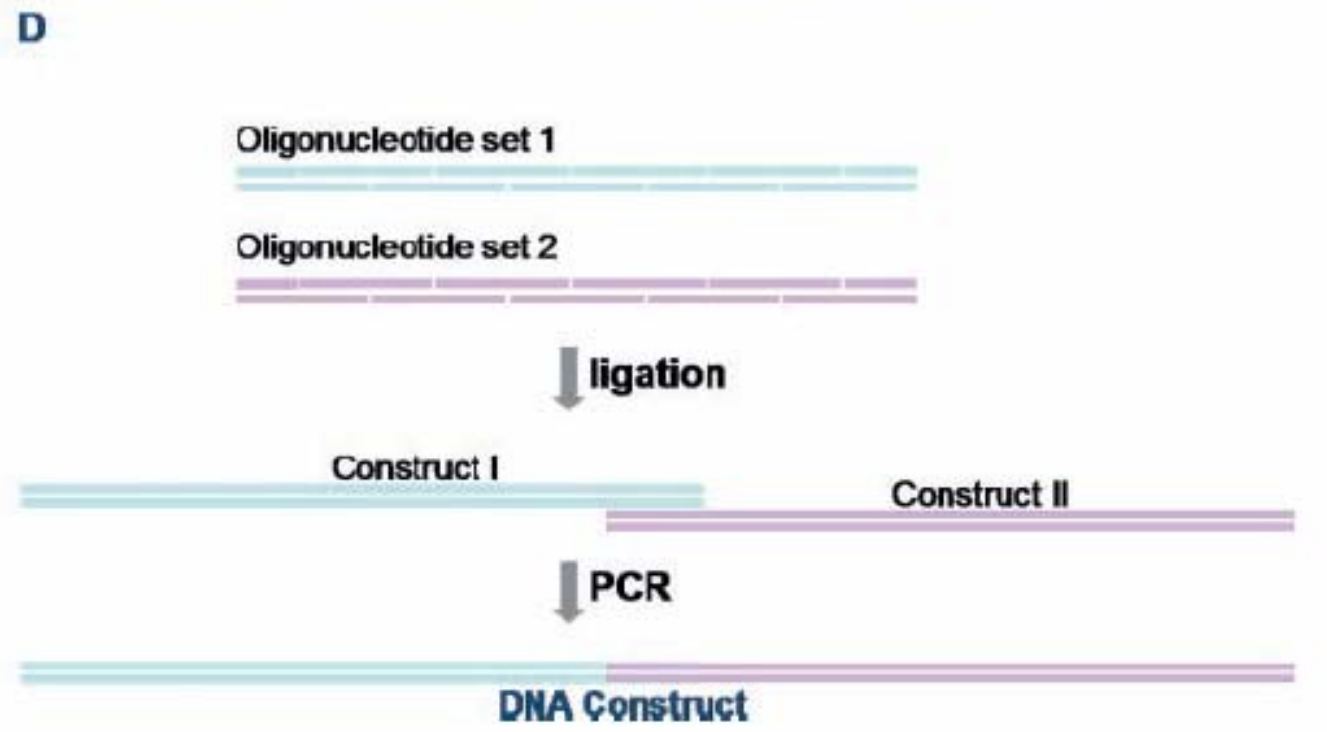


EGFP gene 714 bp



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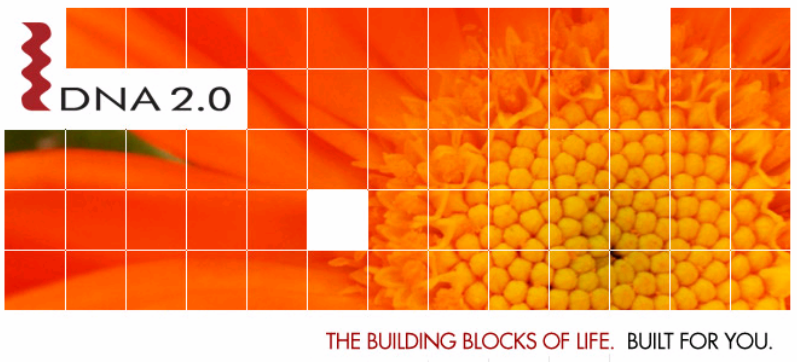

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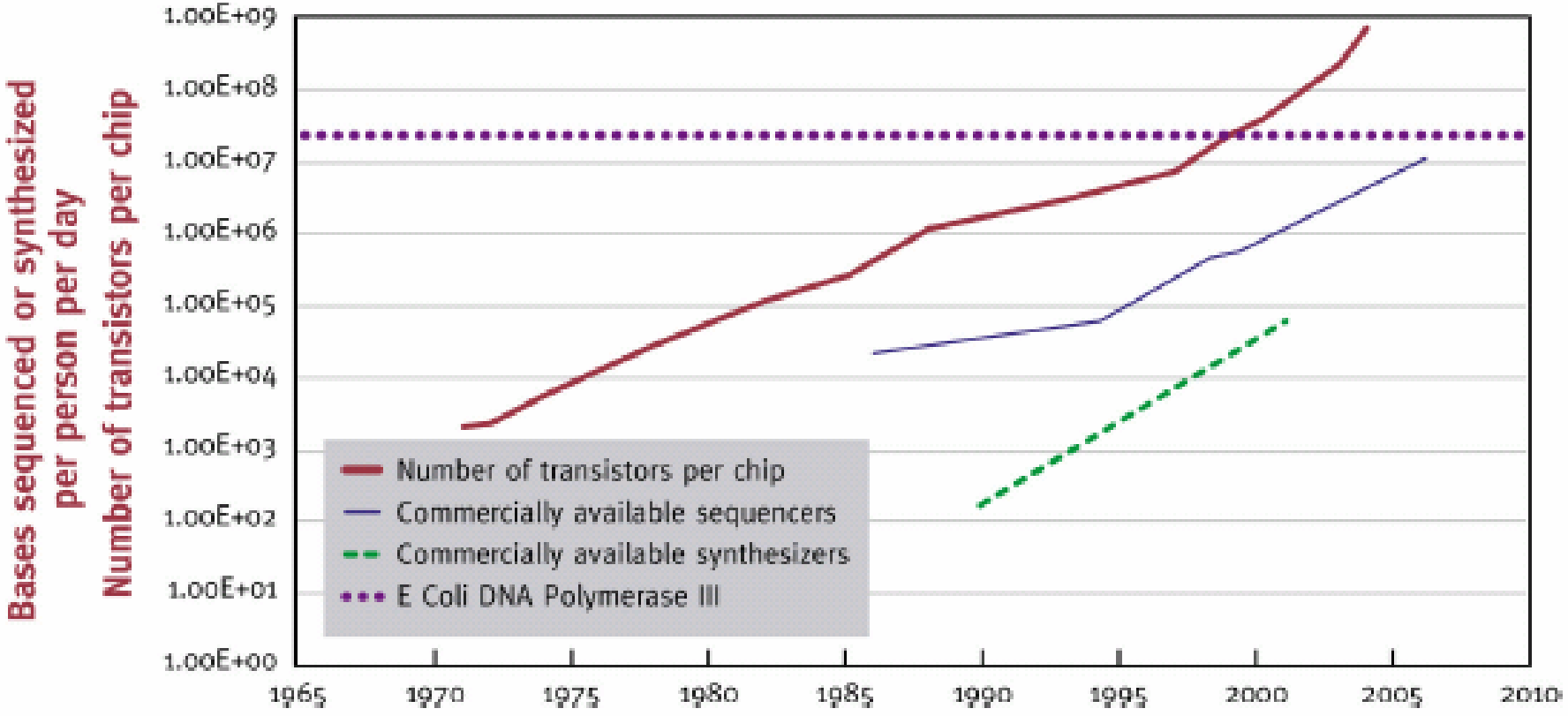
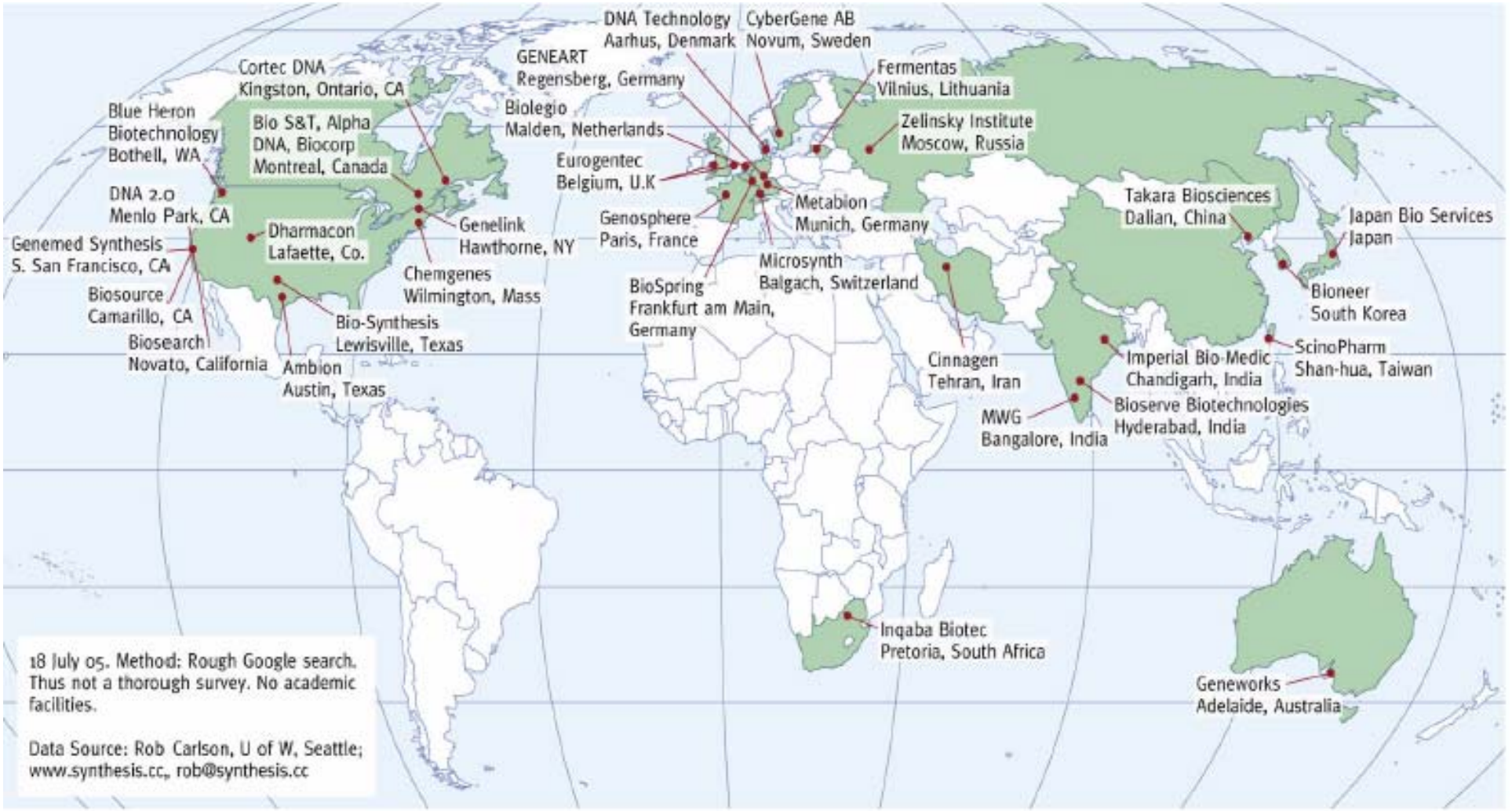
BIOTECHNOLOGY

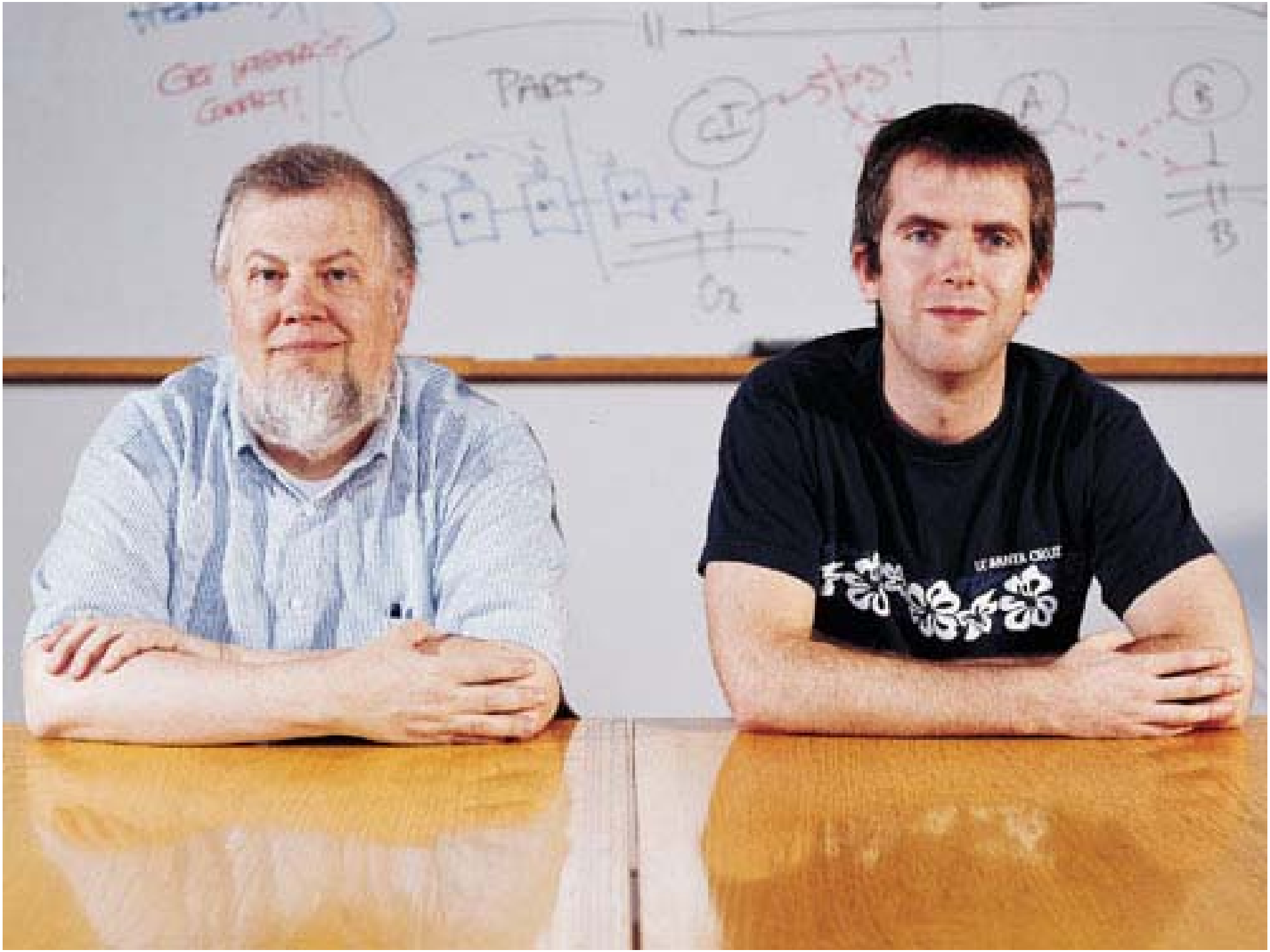


Source: R. Carlson, Bio-era.

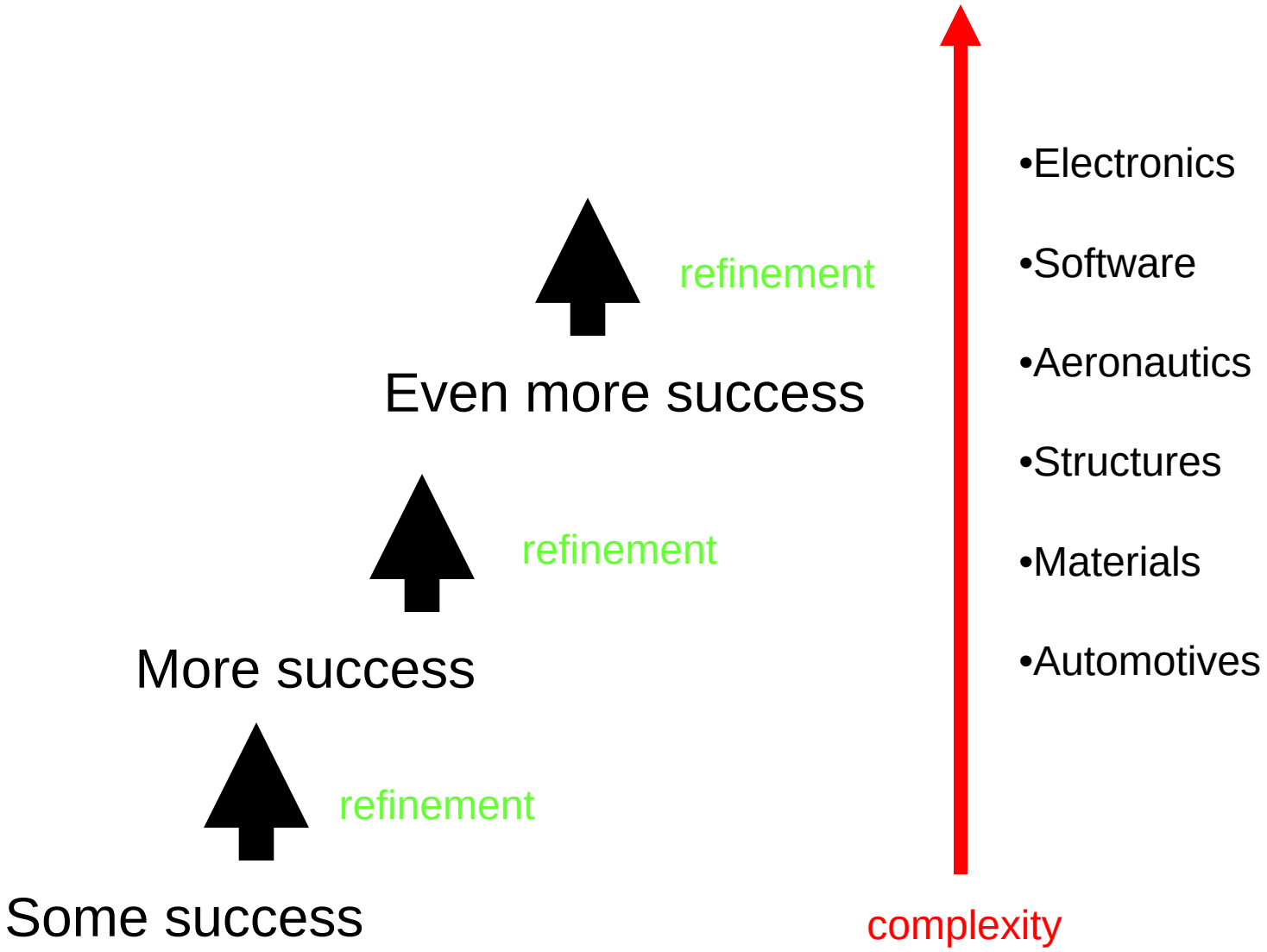


Sources: Source: R. Carlson, G. Epstein, A. Yu (2005)


open sources 2.0
THE CONTINUING
EVOLUTION
O'REILLY


PARTS

Engineering process…



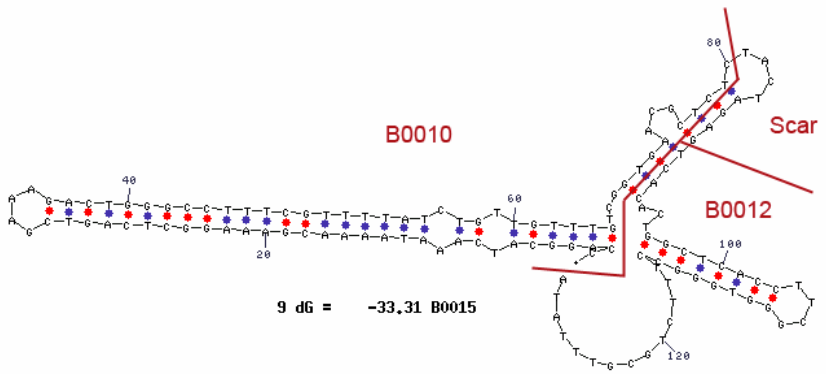
F1760

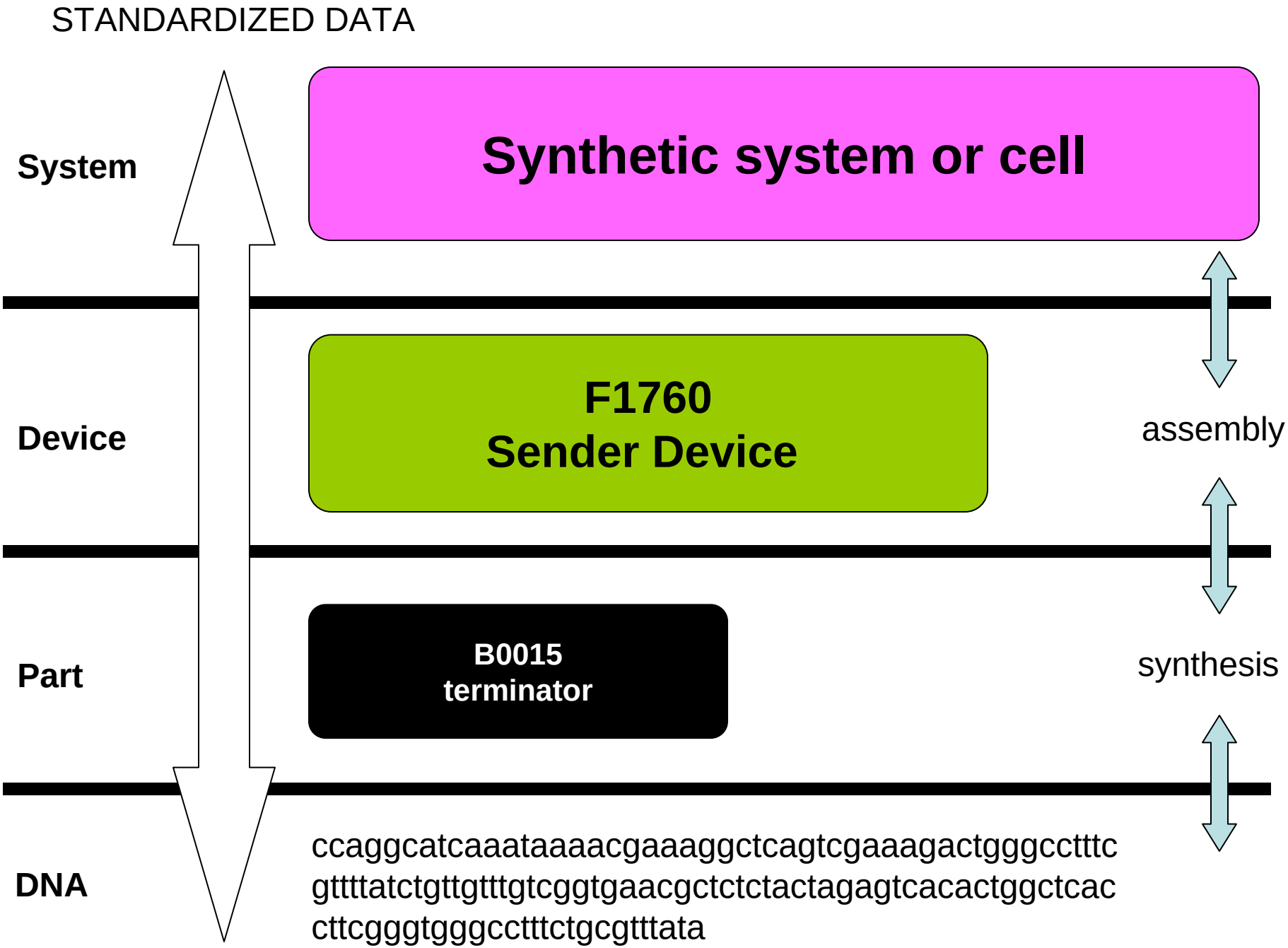
Sender Device

B0015

terminator

Name: B0015
Type: Double terminator
Length 129 bp
Designed by: Reshma Shetty
Forward efficiency: 0.984
Reverse efficiency: .295




STANDARDIZED DATA
System
Synthetic system or cell
Device
F1760
Sender Device
assembly
Part
B0015
terminator
synthesis
DNA
ccaggcatcaaataaaacgaaaggctcagtcgaaagactgggcctttc
gttttatctgttgtttgtcggtgaacgctctctactagagtcacactggctcac
cttcgggtgggcctttctgcgtttata

Transcriptional Regulators

jump to part

BBa_

navigation

- Main Page
- Browse Part Types
- iGEM Wiki
- Community portal
- Recent changes
- Recent part changes

resources

- User Accounts
- Add a Part
- Part Searches
- DNA Repositories
- Sequence Analysis
- Assembly Tool
- Help

search

Go Search

toolbox

- What links here

Available repressible regulators (normally ON) -?-

Show 0 more parts

Edit

-?-	Name	Description	Direction	Control -?-	Output Low	Output High	Length
A W	BBa_I14032	promoter P(Lac) IQ	Forward				37
A W	BBa_R0040	promoter (tetR, negative)	Forward	aTc, tetracyline			54
A W	BBa_R0051	promoter (lambda cI regulated)	Forward	lambda cI			49

Available inducible regulators (normally OFF) -?-

Show 0 more parts

Edit

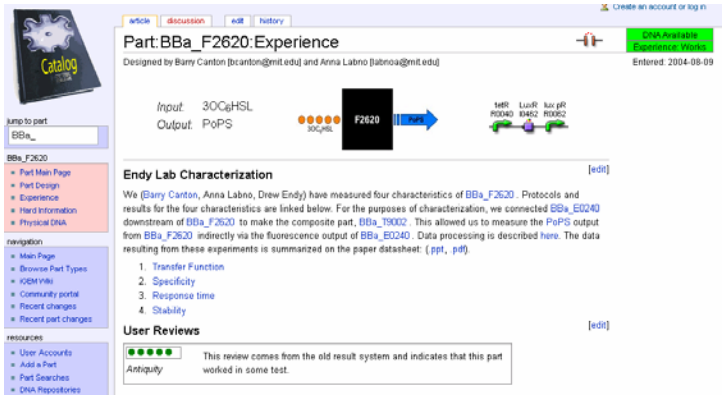
-?-	Name	Description	Direction	Control -?-	Output Low	Output High	Length
A	BBa_I12007	Modified lambda Prm promoter (OR-3 obliterated)	Forward	cI			82
A	BBa_R0062	Promoter (luxR & HSL regulated -- lux pR)	Forward	luxR, HSL			55
A	BBa_R0079	Promoter (LasR & PAI regulated)	Forward	PAI			157
A	BBa_R0080	Promoter (AraC regulated)	Forward	araC			149

Available other regulators

Show 172 more parts

Edit

-?-	Name	Description	Direction	Control -?-	Output Low	Output High	Length
A W	BBa_I0500	Inducible pBad/araC	Forward	araC, arabinose			1210
A W	BBa_I13453	Pbad promoter					130
A W	BBa_J13002	TetR repressed POPS/RIPS generator	Forward	ATc			74
A W	BBa_J13023	3OC6HSL+LuxR dependent POPS/RIPS generator					117
A W	BBa_J23100	constitutive promoter family member					35
A W	BBa_J23101	constitutive promoter family member					35
A W	BBa_J23102	constitutive promoter family member					35
A W	BBa_J23103	constitutive promoter family member					35
A W	BBa_J23104	constitutive promoter family member					35
A W	BBa_J23105	constitutive promoter family member					35
A W	BBa_J23106	constitutive promoter family member					35
A W	BBa_J23107	constitutive promoter family member					35
A W	BBa_J23108	constitutive promoter family member					35
A W	BBa_J23109	constitutive promoter family member					35
A W	BBa_J23110	constitutive promoter family member					35
A W	BBa_J23111	constitutive promoter family member					35



BBa_F2620

3OC$_6$HSL → PoPS Receiver

http://parts.mit.edu/registry/index.php/Part:BBa_F2620

Authors:
Barry Canton [bcanton@mit.edu]
Anna Labno [labnoa@mit.edu]

Last Update: 15 January 2007

Description

A transcription factor (LuxR, BBa_C0062) that is active in the presence of cell-cell signaling molecule 3OC$_6$HSL is controlled by a TetR-regulated operator (BBa_R0040). Device input is 3OC$_6$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.

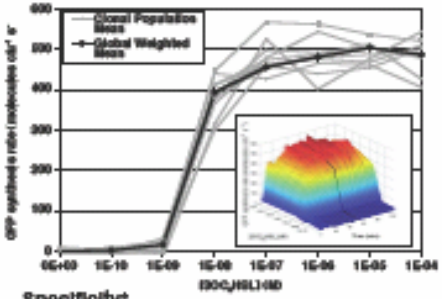
Characteristics

Input Swing: 1E-9 to 1E-6 M 3OC$_6$HSL, exogenous
Output Swing: 0±1 to 503±1 GFP molecules cfu^{-1} s^{-1}
Switch Point: 7±1 nM 3OC$_6$HSL, exogenous
LH Response: 9 min ($t_{50\%}$), 27 min ($t_{90\%}$)

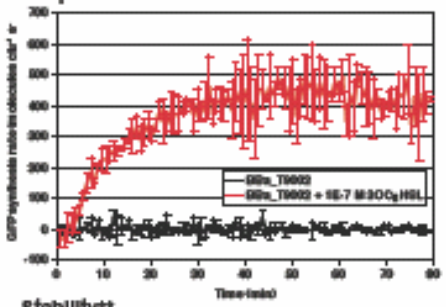
Key Parts

BBa_R0040: TetR-regulated operator
BBa_C0062: luxR ORF
BBa_R0062: LuxR-regulated operator

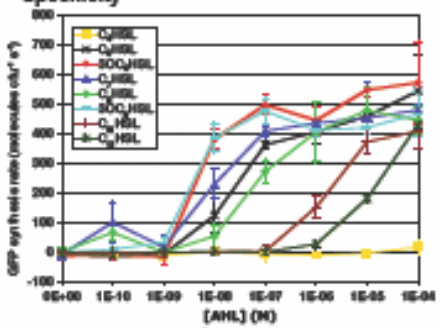
Transfer Function*



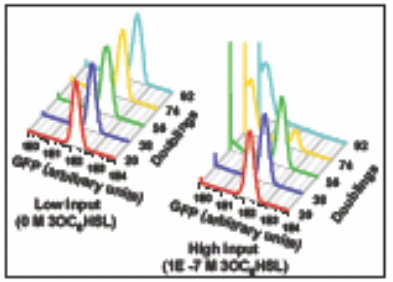
Response Time*



Specificity*



Stability**



Demand (low/high input)

Translational: 256/8048 ribosomes cfu^{-1}
3.8E3/1.2E5 charged tRNA cfu^{-1} s^{-1}

Stability (low/high input)

Genetic: >92/74 replication events**
Performance: >92/74 replication events**

Compatibility

Chassis: Compatible with *MC4100*, *MG1655*, and *DH5α*
Plasmids: Compatible with *pSB3K3* and *pSB1A2*
Devices: Compatible with *E0240*, *E0430* and *E0434*
Crosstalk with systems containing *TetR (C0040)*
Signaling: Crosstalk with input molecules similar to 3OC$_6$HSL

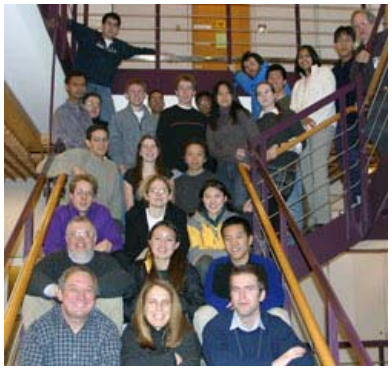
Conditions (abridged)

Output: Indirect via *BBa_E0240*
Vector: pSB3K3
Chassis: MG1655
Culture: Supplemented M9, 37°C
**Equipment:* PE Victor3 plate reader
***Equipment:* BD FACScan cytometer

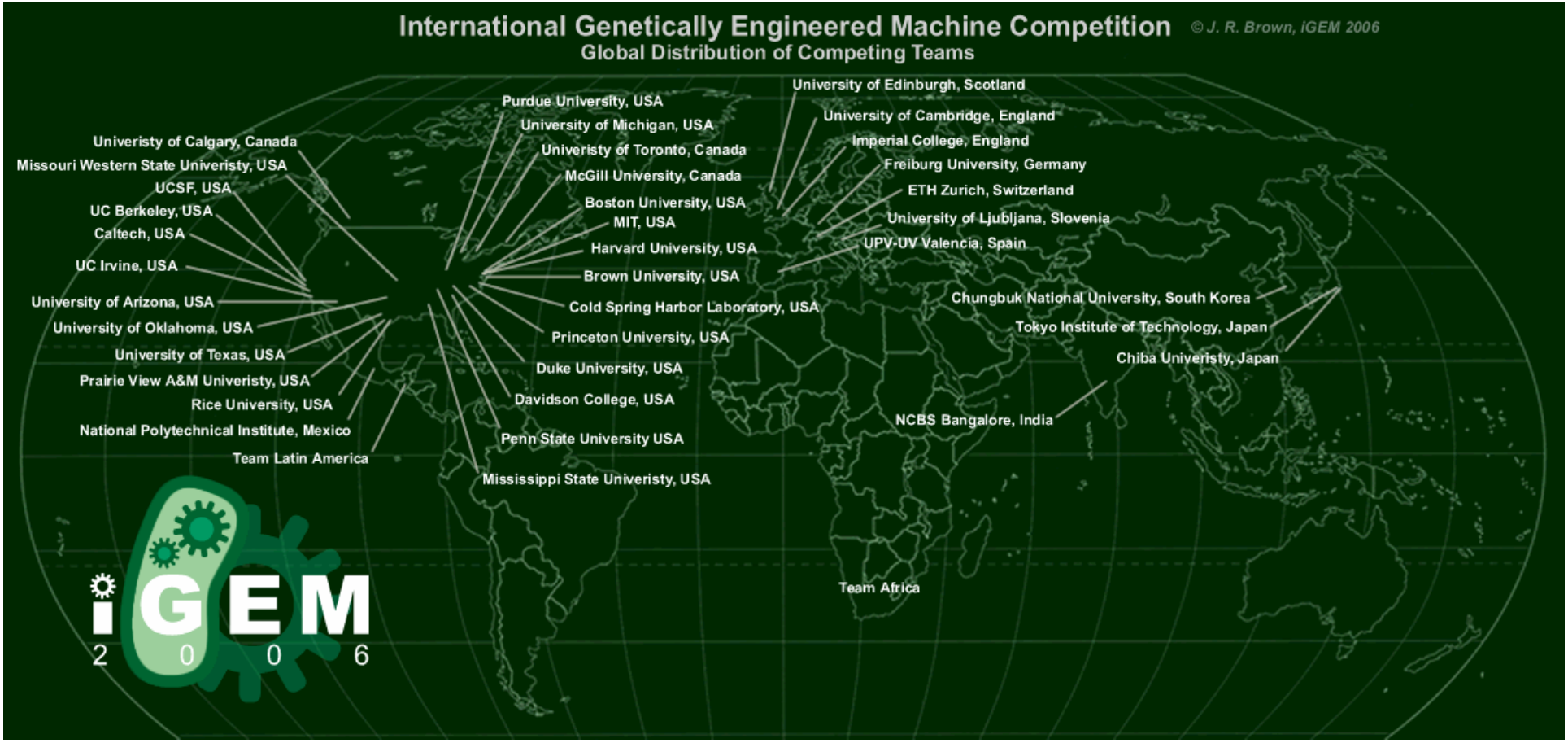
Signaling Devices

Shares:

- DNA parts
- DNA code
- Protocols
- Experience
- Publications
- Only one rule: share back!



2006 Jamboree – 400 gengineers


International Genetically Engineered Machine Competition
© J. R. Brown, iGEM 2006
Global Distribution of Competing Teams
University of Edinburgh, Scotland
Purdue University, USA
University of Cambridge, England
University of Michigan, USA
Imperial College, England
Univeristy of Calgary, Canada
Univeristy of Toronto, Canada
Freiburg University, Germany
Missouri Western State Univeristy, USA
McGill University, Canada
ETH Zurich, Switzerland
UCSF, USA
Boston University, USA
University of Ljubljana, Slovenia
UC Berkeley, USA
MIT, USA
UPV-UV Valencia, Spain
Caltech, USA
Harvard University, USA
UC Irvine, USA
Brown University, USA
Chungbuk National University, South Korea
University of Arizona, USA
Cold Spring Harbor Laboratory, USA
Tokyo Institute of Technology, Japan
University of Oklahoma, USA
Princeton University, USA
Chiba Univeristy, Japan
University of Texas, USA
Duke University, USA
Prairie View A&M Univeristy, USA
Davidson College, USA
Rice University, USA
NCBS Bangalore, India
National Polytechnical Institute, Mexico
Penn State University USA
Team Latin America
Mississippi State Univeristy, USA
iGEM
2006
Team Africa

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**

Designs on life

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

Even if you're thinking big, you usually have to start small. Especially, as a group of Swiss students found, when big means counting to infinity. The team was drawing up a blueprint for the world's first counting machine made entirely of biological parts. Although they had their sights on loftier numbers, they opted to go no higher than two. If the plan worked, it would be a proof-of-principle for a much larger tallying device.

The group, from the Federal Institute of Technology (ETH) in Zurich, was one of 17 teams unveiling their projects at the first international Intercollegiate Genetically Engineered Machine (iGEM) competition, held at the Massachusetts Institute of Technology (MIT) in Cambridge on 5 and 6 November. The event attracted students from all over the world to design and build machines made entirely from biological components such as genes and proteins. They drew up grand designs for bacterial Etch-a-Sketches, photosensitive t-shirts, thermometers and sensors. And if none of the designs succeeded completely, that was more because of the limitations of the nascent science of synthetic biology than any lack of enthusiasm, creativity or hard work.

Synthetic biology aims to merge engineering approaches with biology. Researchers working at the most basic level are copying simple biological processes, such as the production of a protein from a gene. They break the process down into its component elements, such as a gene and the pieces of DNA and other molecules that control its activity. They then string these elements together to build a module they know will behave in a particular way — say, oscillate between producing and not producing a protein, or produce a protein that can switch another module on or off.

It is these kinds of components — oscillators and switches — that engineers order from suppliers and link together to build more complex electronic circuits and machines. Synthetic biologists are trying to develop a similar armoury of biological components, dubbed BioBricks, that can be inserted into any genetic circuit to carry out a particular function. Scientists at MIT have established a Registry of Standard Biological Parts, a catalogue of BioBricks that theoretically

Bidding for glory: teams from the ETH in Zurich (top), Cambridge, UK, (bottom right) and Massachusetts at the first International Intercollegiate Genetically Engineered Machine competition.

from the ground up. To do so, they have commandeered a time-honoured engineering tradition: the student competition. The iGEM event began life as a project class for MIT students in 2003. Last year, it was thrown open to other US universities, and this year it went international. The organizers hope to attract 30 to 50 [illegible]

selection of designs. Students from the University of Cambridge, UK, tried to make a circuit that could control the movement of *Escherichia coli* bacteria. They aimed to engineer the bacteria to contain a switch governing their sensitivity to the sugar maltose. With the switch off, the microbes would ignore the sugar. Tripping

BRIEF COMMUNICATIONS

Engineering *Escherichia coli* to see light

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

We have designed a bacterial system that is switched between different states by red light. The system consists of a synthetic sensor kinase that allows a lawn of bacteria to function as a biological film, such that the projection of a pattern of light on to the bacteria produces a high-definition (about 100 mega-pixels per square inch), two-dimensional chemical image. This spatial control of bacterial gene expression could be used to 'print' complex biological materials, for example, and to investigate signalling pathways through precise spatial and temporal control of their phosphorylation steps.

Plants and some bacteria use a class of protein photoreceptors known as phytochromes to control phototaxis, photosynthesis and the production of protective pigments[1–3]. Photoreceptors are not found in enterobacteria, such as *Escherichia coli*, so we created a light sensor that functions in *E. coli* by engineering a chimaera that uses a phytochrome from a cyanobacterium.

A phytochrome is a two-component system that consists of a membrane-bound, extracellular sensor that responds to light and an intracellular 'response-regulator'. The response-regulators of most phytochromes do not have DNA-binding domains and do not directly regulate gene expression, so we fused a cyanobacterial photoreceptor to an *E. coli* intracellular histidine kinase domain (Fig. 1a, and see supplementary information). This design was based on the well studied *E. coli* EnvZ–OmpR two-component system, which normally regulates porin expression in response to osmotic shock[4]. The EnvZ histidine kinase domain has been used for the construction of functional chimaeras[5,6], and a plant phytochrome has

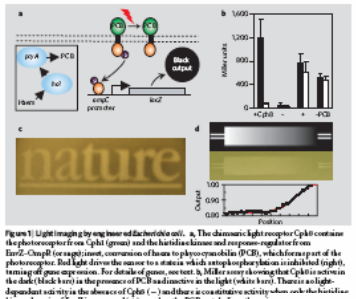


Figure 1 | Light imaging by engineered *Escherichia coli*. a, The chimaeric light receptor Cph8 contains the photoreceptor from Cph1 (green) and the histidine kinase and response-regulator from EnvZ–OmpR (or vice versa; insert, conversion of beam to phycocyanobilin (PCB), which forms part of the photoreceptor. Red light drives the sensor to a state in which autophosphorylation is inhibited (right), turning off gene expression. For details of genes, see text. b, Miller assay showing that Cph8 is active in the dark (black bars) as the precursor of PCB and inactive in the light (white bars). There is a light-dependent activity in the absence of Cph8 (−) and there is constitutive activity when only the histidine kinase domain of EnvZ is expressed (+), or when the PCB metabolic pathway is [illegible]. c, When an image is projected on to a bacterial lawn, the LacZ reporter is expressed in the illuminated regions. d, Transfer function of the circuit. As the intensity of the light is increased in a linear gradient projected from a 35-mm slide, the circuit output gives a graded response.

enzymatically produces a black compound.

The part of the photoreceptor that responds to light, phycocyanobilin, is not naturally produced in *E. coli*. We therefore introduced two phycocyanobilin-biosynthesis genes (*ho1* and *pcyA*) from *Synechocystis* that convert haem into phycocyanobilin[8] (parts [illegible]_I15008, BBa_I15009; MIT Registry of Standard Biological Parts) (Fig. 1a, Inset). Individual Cph1–EnvZ chimaeras were then incubated at 37 °C for 4 h with broad-spectrum light and assayed for expression of the LacZ reporter. The chimaera Cph8 (BBa_I15010) produced a particularly strong response to light (Fig. 1b).

For bacterial photography, we grew a lawn of bacteria on agar. The lacZ reporter was visualized by addition of 5-gal (3,4-cyclohexenoesculetin-β-D-galactopyranoside); LacZ catalyses the formation of a stable, insoluble, dark precipitate from 5-gal. Light repressed the expression in the bacteria, giving a high-contrast replica of the applied image on the biological film, [illegible] appeared light and dark (Fig. 1c, and see supplementary information). The lacZ activity showed a increasing light intensity, the brightest light (Fig.

Our creation of a novel an image-processing f the power and accessibil methods available in th thetic biology. The pri light regulation should to be spatially and tar individual cells and in potential application in raphy, manufacture o composites and the s signalling networks.

Anselm Levskaya*, Aaron J. Tabor†, Zachary Booth Lauer†, Matthew Levy†, Alexander Scouras†, Andrew D. Ellington†, Edward M. Marcotte†‡, C

Genetic 'Jamboree' draws innovators

The Boston Globe

Science students the world over share research

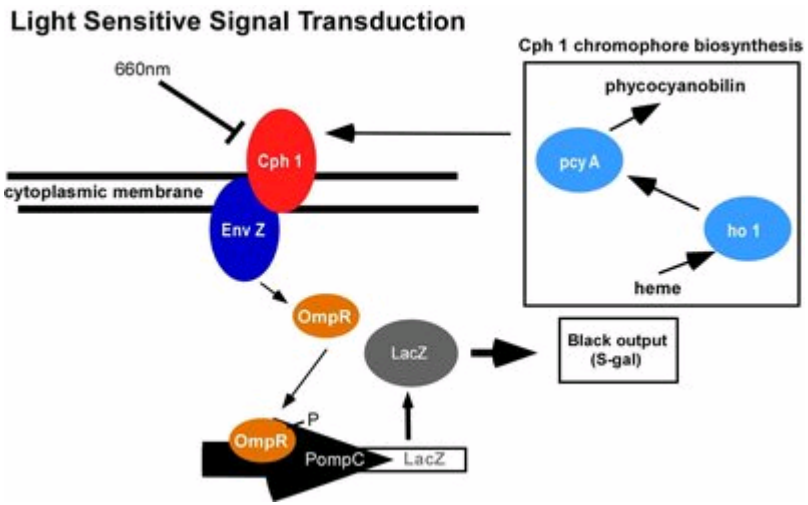
At MIT's International Genetically Engineered Machine Competition yesterday, the audience listened to a presentation on synthetic biology. (John Tlumacki/ Globe Staff)

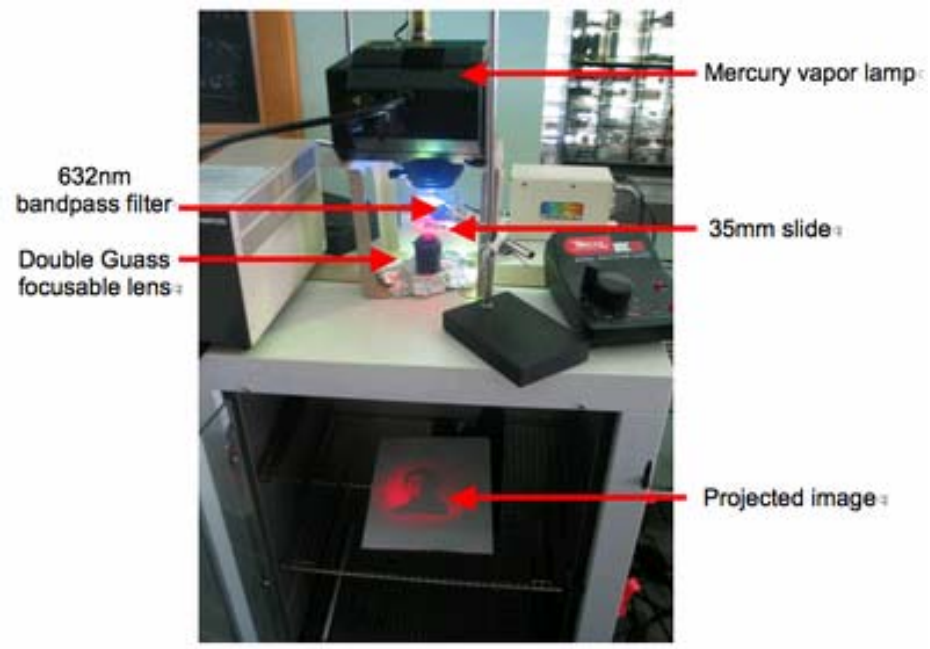
COVER STORY

By Carl Zimmer

Scientist of the Year

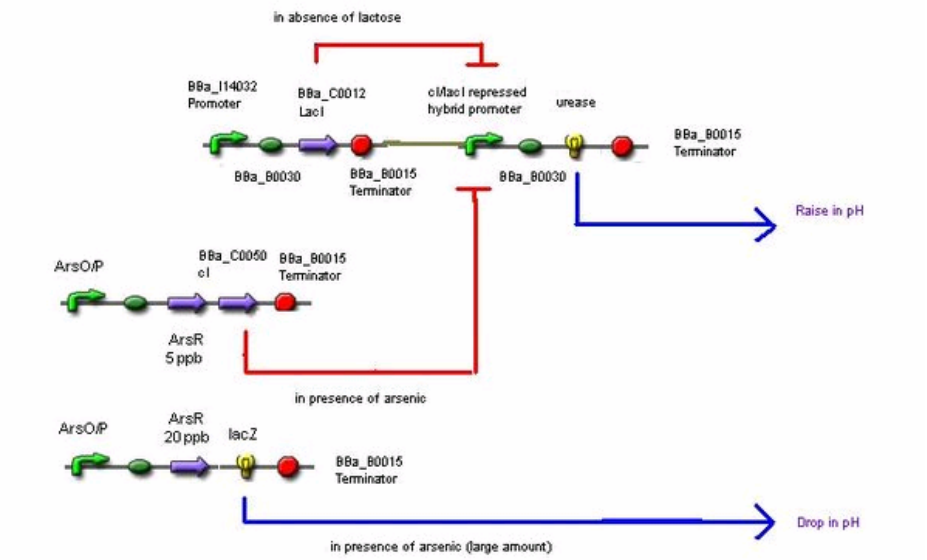
Jay Keasling is developing ways to program DNA as easily as people program computers.

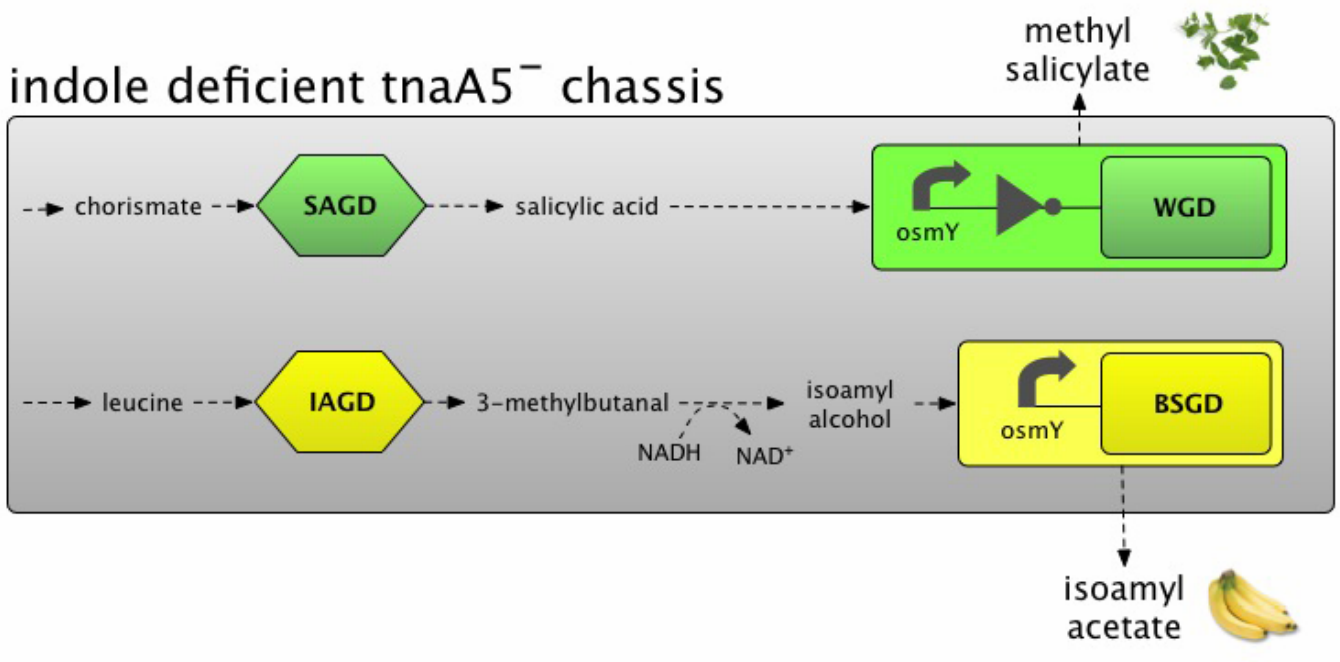

Light Sensitive Signal Transduction
Cph 1 chromophore biosynthesis
660nm
phycocyanobilin
Cph 1
pcy A
cytoplasmic membrane
Env Z
ho 1
heme
OmpR
LacZ
Black output
(S-gal)
P
OmpR
PompC
LacZ


Mercury vapor lamp
632nm
bandpass filter
35mm slide
Double Guass
focusable lens
Projected image


Hello
World


HOOK 'EM HORNS


in absence of lactose
BBa_I14032
Promoter
BBa_C0012
LacI
cI/lacI repressed
hybrid promoter
urease
BBa_B0015
Terminator
BBa_B0030
BBa_B0015
Terminator
BBa_B0030
Raise in pH
ArsO/P
BBa_C0050
cI
BBa_B0015
Terminator
ArsR
5 ppb
in presence of arsenic
ArsO/P
ArsR
20 ppb
lacZ
BBa_B0015
Terminator
Drop in pH
in presence of arsenic (large amount)


indole deficient tnaA5⁻ chassis
methyl salicylate
chorismate
SAGD
salicylic acid
osmY
WGD
leucine
IAGD
3-methylbutanal
NADH
NAD+
isoamyl alcohol
osmY
BSGD
isoamyl acetate


2006
Ljubljana, Slovenija
iGEM

BERKELEY CENTER FOR SYNTHETIC BIOLOGY

A JOINT PROGRAM OF THE CALIFORNIA INSTITUTE FOR QUANTITATIVE BIOMEDICAL RESEARCH (QB3) AND LAWRENCE BERKELEY NATIONAL LABORATORY (LBNL)

The California Institute for Quantitative Biomedical Research (QB3) and Lawrence Berkeley National Laboratory (LBNL) have joined forces to accelerate the growth of synthetic biology, a new field that promises major new advances in preventing and treating disease, generating new energy sources, and preventing and mitigating environmental threats.

Opening in spring 2005 in a spacious, modern building in west Berkeley, the Berkeley Center for Synthetic Biology gives renowned scientists and engineers the chance to pool their talents and collaborate in new ways, with enormous potential benefits for California's citizens in the form of advances in biomedicine and energy renewables and economic growth.

Synthetic biologists study the control and design of biological components and new organisms to solve a host of important health, energy, and environmental problems that cannot be solved using naturally occurring biological entities. The inherently

QB3 and LBNL scientists occupy lab space in a building renovated in 1997 for biotech research, previously leased by Bayer, featuring large labs, viral suites, and tissue culture rooms. UCSF Mission Bay and numerous biotech firms are nearby.

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.

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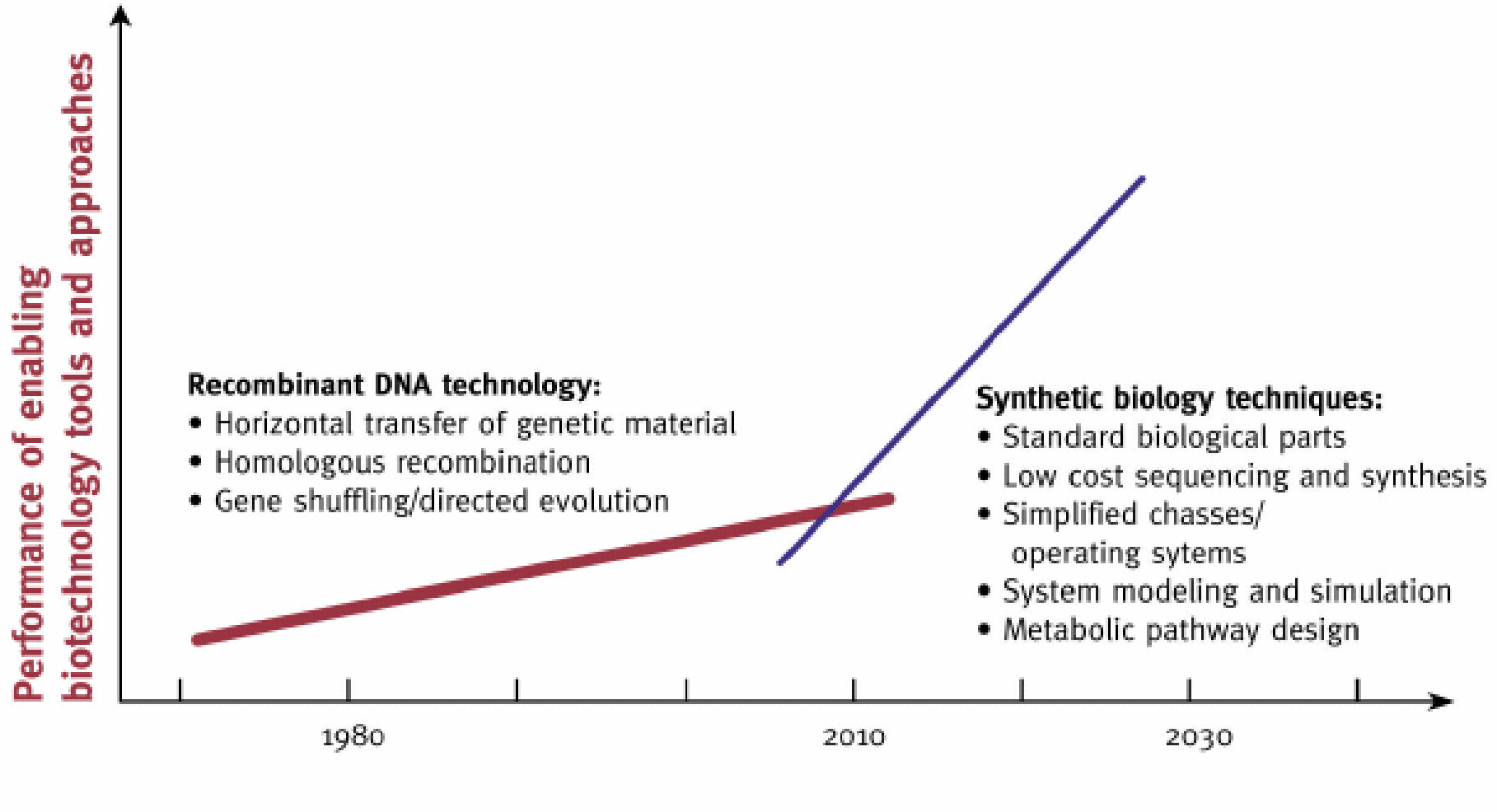
Looking forward



Source: Bio era

Driving Forces

- Rapid advance of DNA sequencing, synthesis, and other enabling technologies
- Global growth of biotech R&D, knowledge, and applications
- Geopolitics; new security concerns
- Energy prices and climate change
- Urbanization and industrialization in developing economies

Major Uncertainties

- How quickly will biological engineering advance?
- Will governments attempt to restrict access to advanced biotech tools?
- How will public attitudes toward biological engineering evolve?
- Will the assertion of intellectual property rights slow innovation in synthetic biology?
- Will terrorists or governments use genome engineering techniques to create biological weapons?

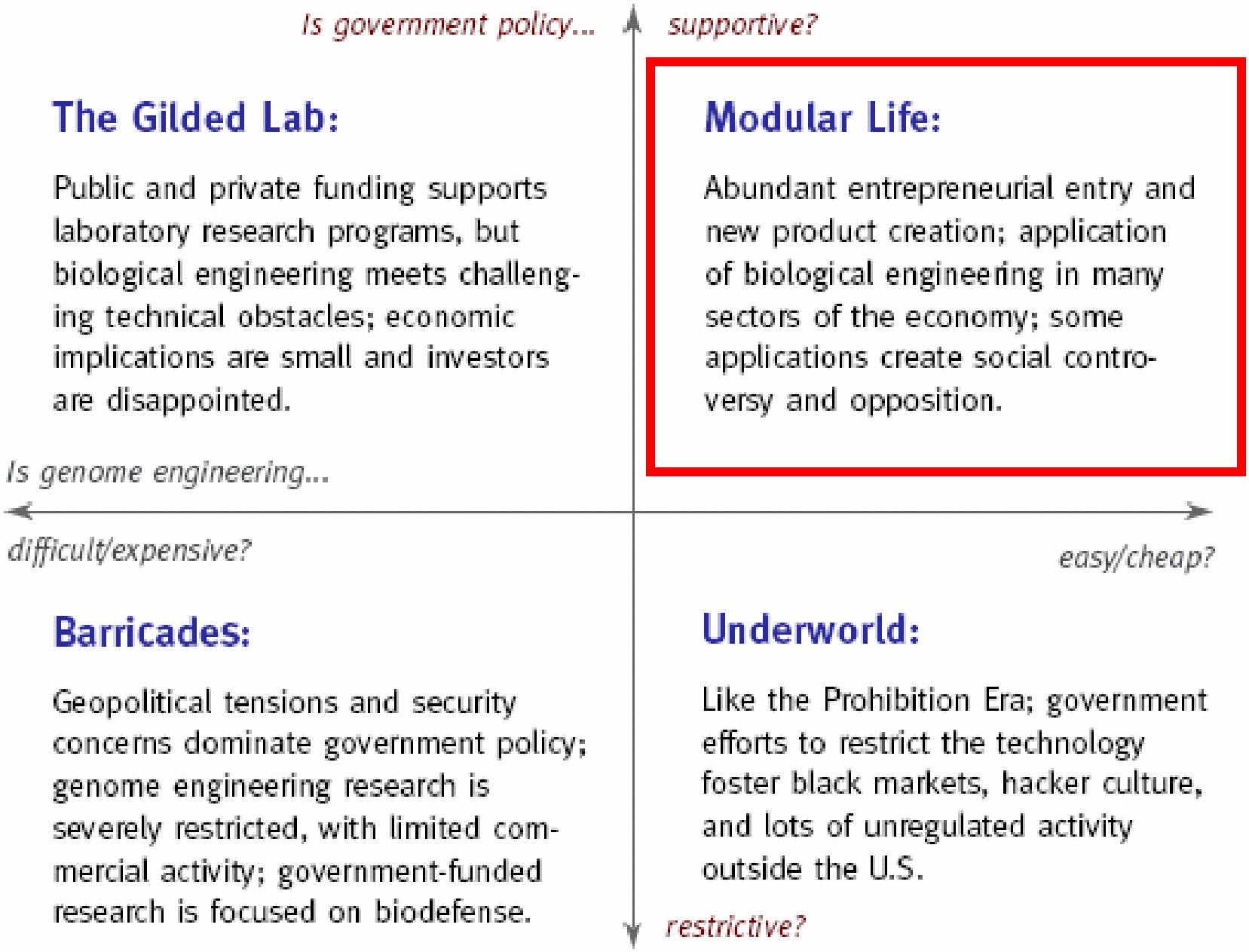
Predetermined Elements

- Increasing environmental stress on global ecosystems
- Growing infectious disease threats to human and animal populations
- Human curiosity & technical innovation
- Growing healthcare needs of aging populations

Prime Movers

- U.S. government: DOE, NIH, NSABB, USPTO
- Biological engineering researchers
- "Open source" biology community
- Bioterrorists
- Energy, chemical, and pharmaceutical industries

Source: Bio era



Source: Bio era

Photo Credit: By Joby Warrick -- The Washington Post Photo

Essential genes of a minimal bacterium

John I. Glass, Nacyra Assad-Garcia, Nina Alperovich, Shibu Yooseph, Matthew R. Lewis, Mahir Maruf, Clyde A. Hutchison III, Hamilton O. Smith*, and J. Craig Venter

Synthetic Biology Group, J. Craig Venter Institute, 9704 Medical Center Drive, Rockville, MD 20850

Contributed by Hamilton O. Smith, November 18, 2005

Mycoplasma genitalium has the smallest genome of any organism that can be grown in pure culture. It has a minimal metabolism and little genomic redundancy. Consequently, its genome is expected to be a close approximation to the minimal set of genes needed to sustain bacterial life. Using global transposon mutagenesis, we isolated and characterized gene disruption mutants for 100 different nonessential protein-coding genes. None of the 43 RNA-coding genes were disrupted. Herein, we identify 382 of the 482 *M. genitalium* protein-coding genes as essential, plus five sets of disrupted genes that encode proteins with potentially redundant essential functions, such as phosphate transport. Genes encoding proteins of unknown function constitute 28% of the essential protein-coding genes set. Disruption of some genes accelerated *M. genitalium* growth.

urogenital pathogen, is the extreme manifestation of this genomic parsimony, having only 482 protein-coding genes and the smallest genome, at ~580 kb, of any known free-living organism capable of being grown in axenic culture (13). Although more conventional bacteria with larger genomes used in gene essentiality studies have on average 26% of their genes in paralogous gene families, *M. genitalium* has only 6% (Table 1, which is published as supporting information on the PNAS web site). Thus, with its lack of genomic redundancy and contingencies for different environmental conditions, *M. genitalium* is already close to being a minimal bacterial cell.

In our 1999 report (4) on the essential microbial gene for *M. genitalium* and its closest relative *Mycoplasma pneumoniae*, we mapped ~2,200 transposon insertion sites in these two species, and

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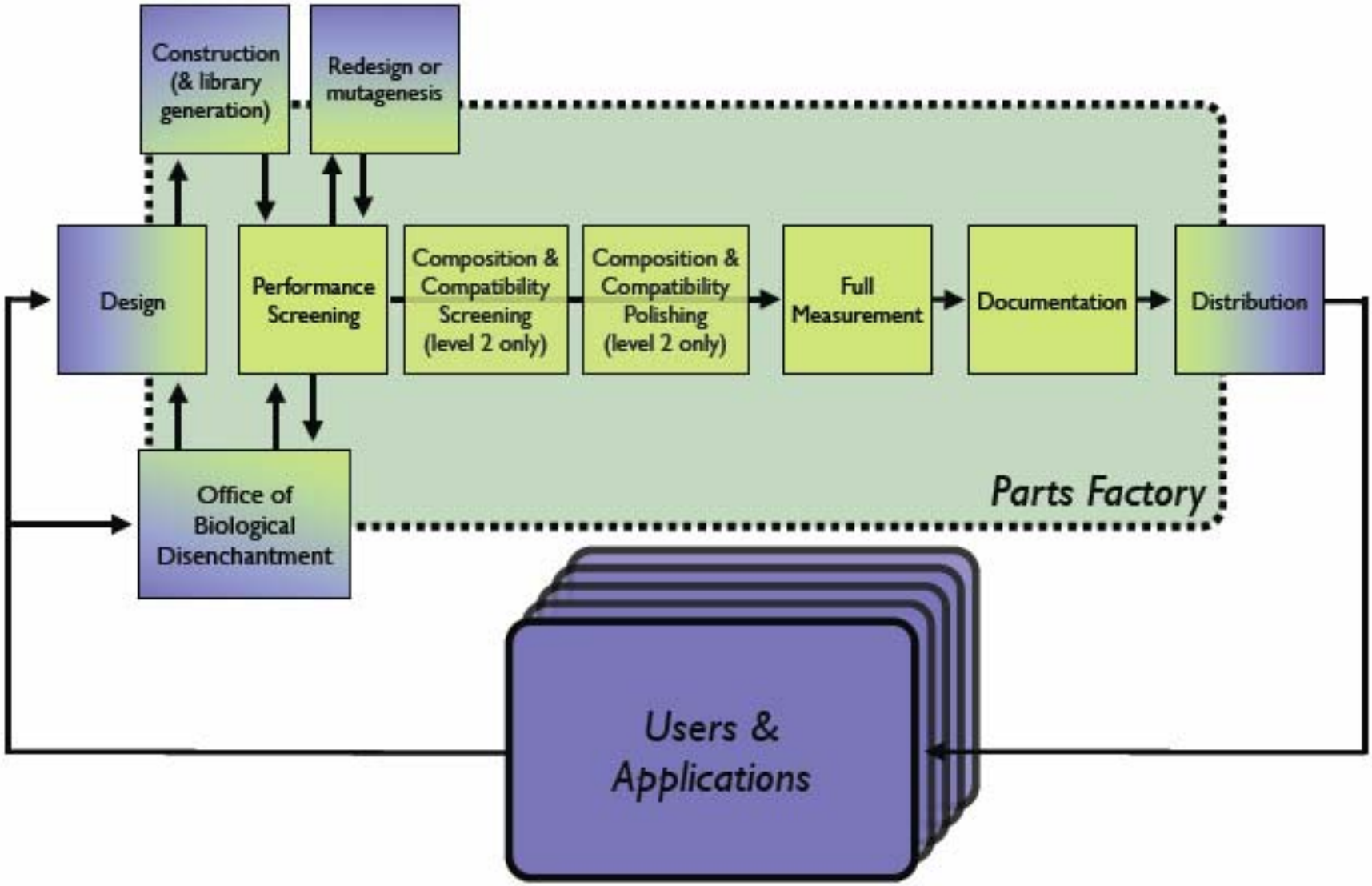
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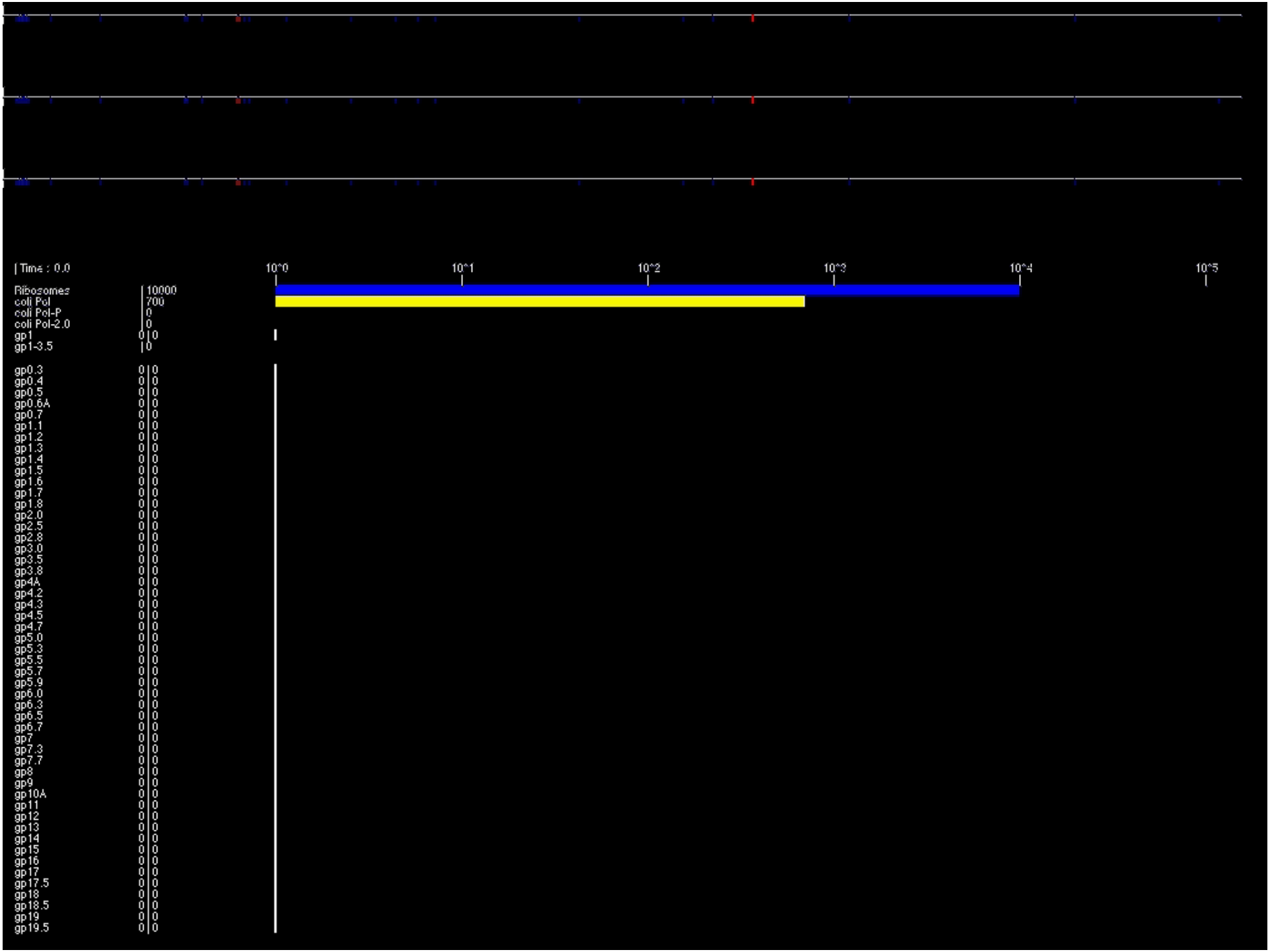
The Methuselah Foundation is a non-profit 501(c)(3) volunteer organization dedicated to raising public awareness of the near-term potential for evidence-based interventions in the aging process. To this end, we perform research focused on repairing the damage that accumulates at the cellular and molecular level with time causing age-related dysfunction, and offer the multi-million dollar Methuselah Mouse Prize (Mprize) for significant, scientifically reproducible life extension in already aged lab mice.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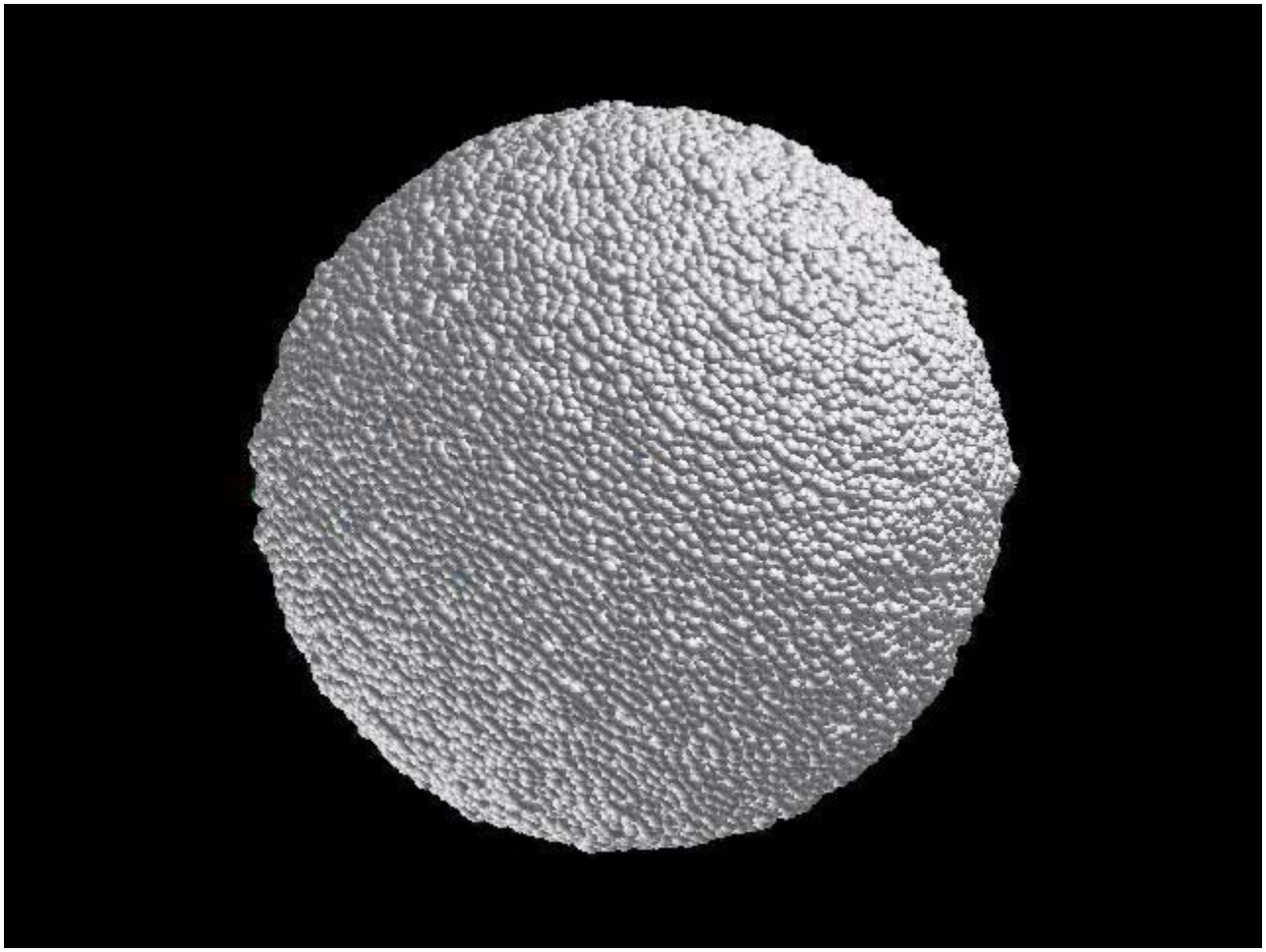

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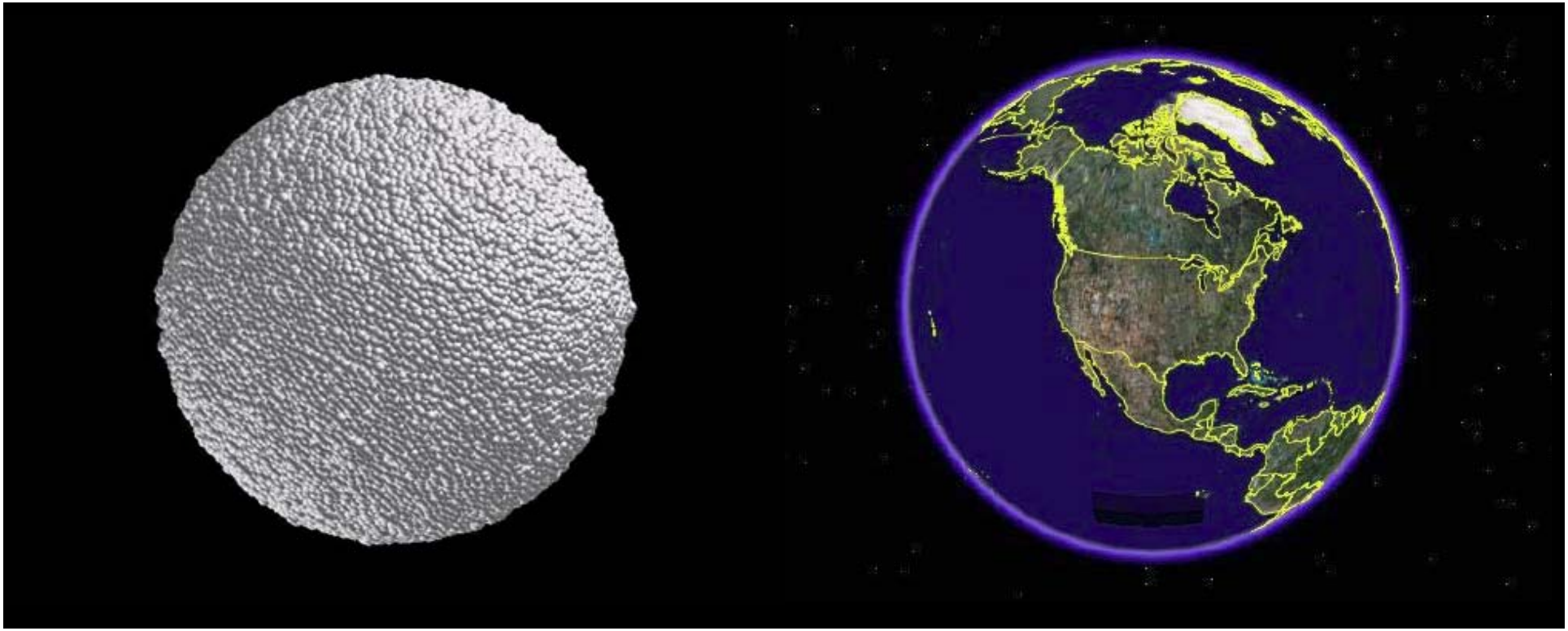
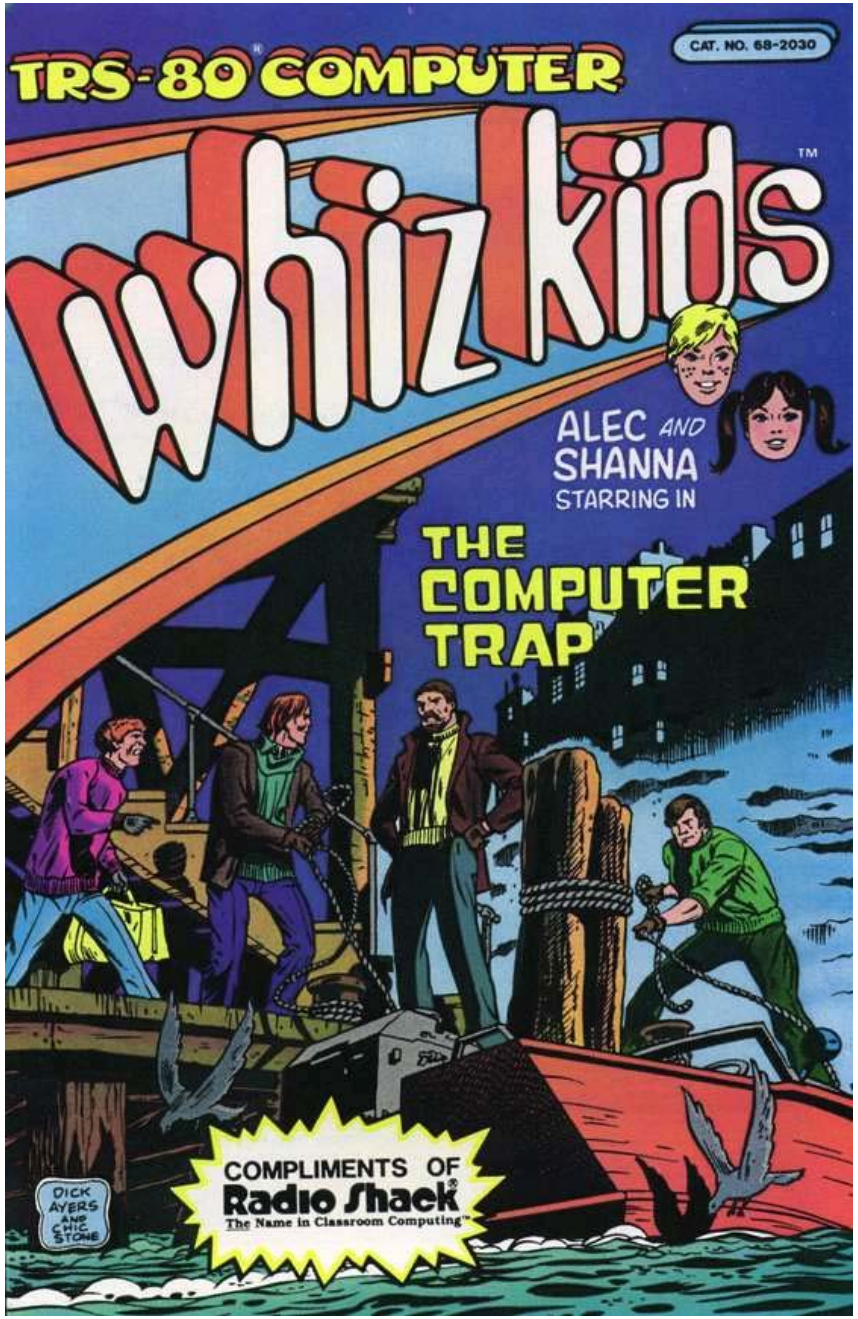



MAY 3, 1982
$1.50
TIME
-.3%
INFLATION VANISHES!
At Least for A Month
COMPUTER GENERATION
A New Breed of Whiz Kids


TRS-80® COMPUTER
CAT. NO. 68-2030
whizkids™
ALEC AND SHANNA STARRING IN
THE COMPUTER TRAP
COMPLIMENTS OF
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The Name in Classroom Computing™
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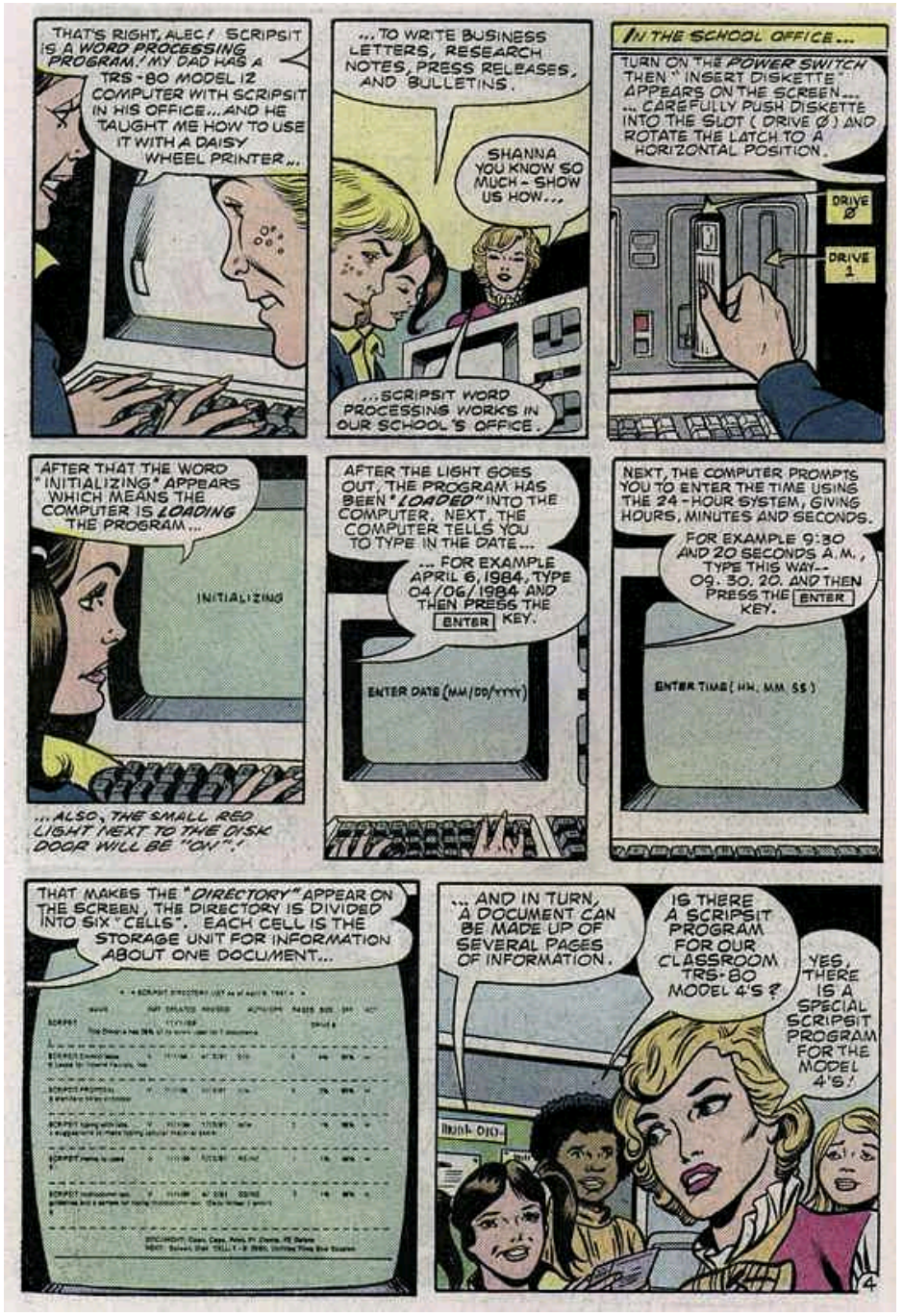
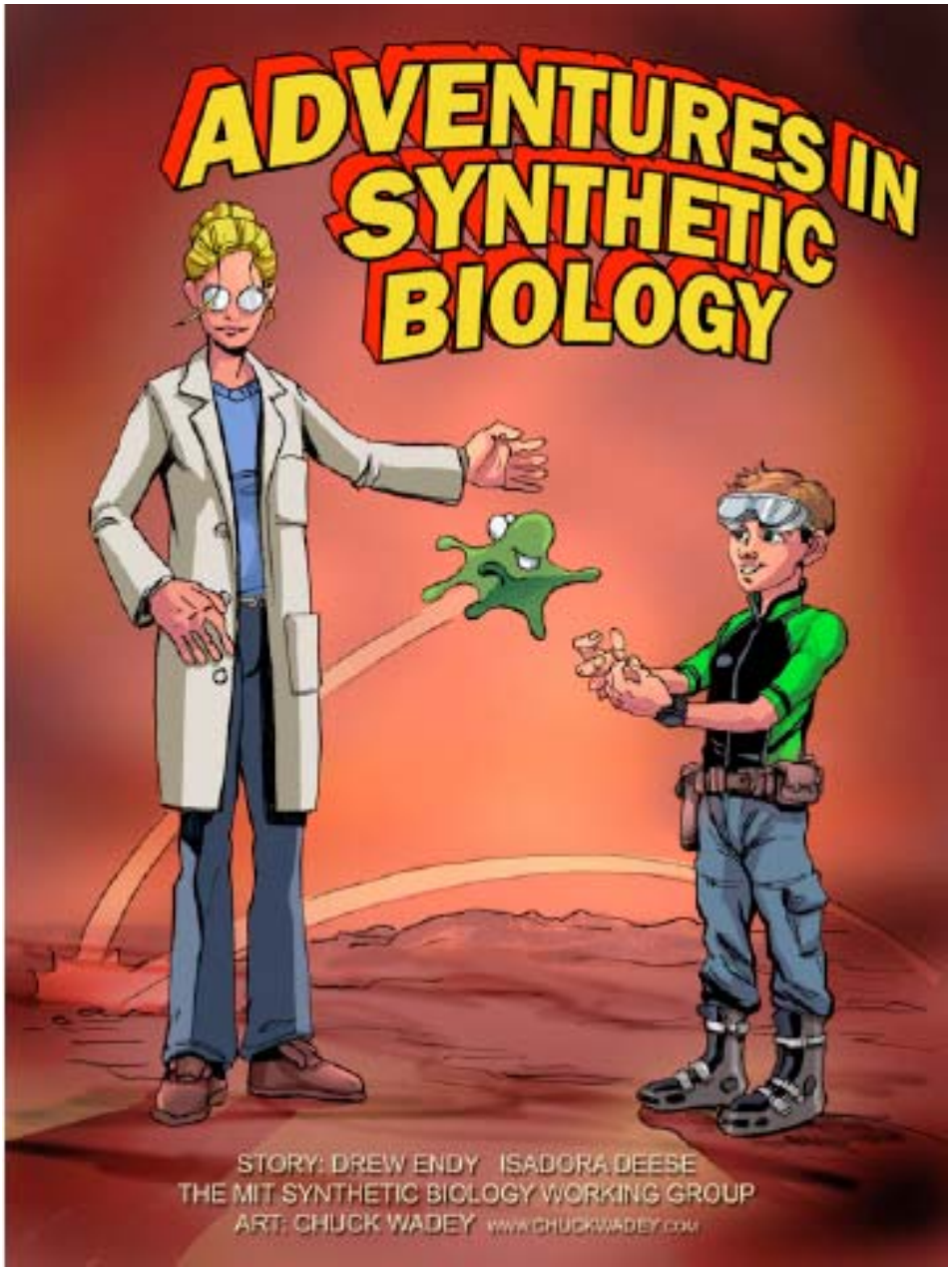
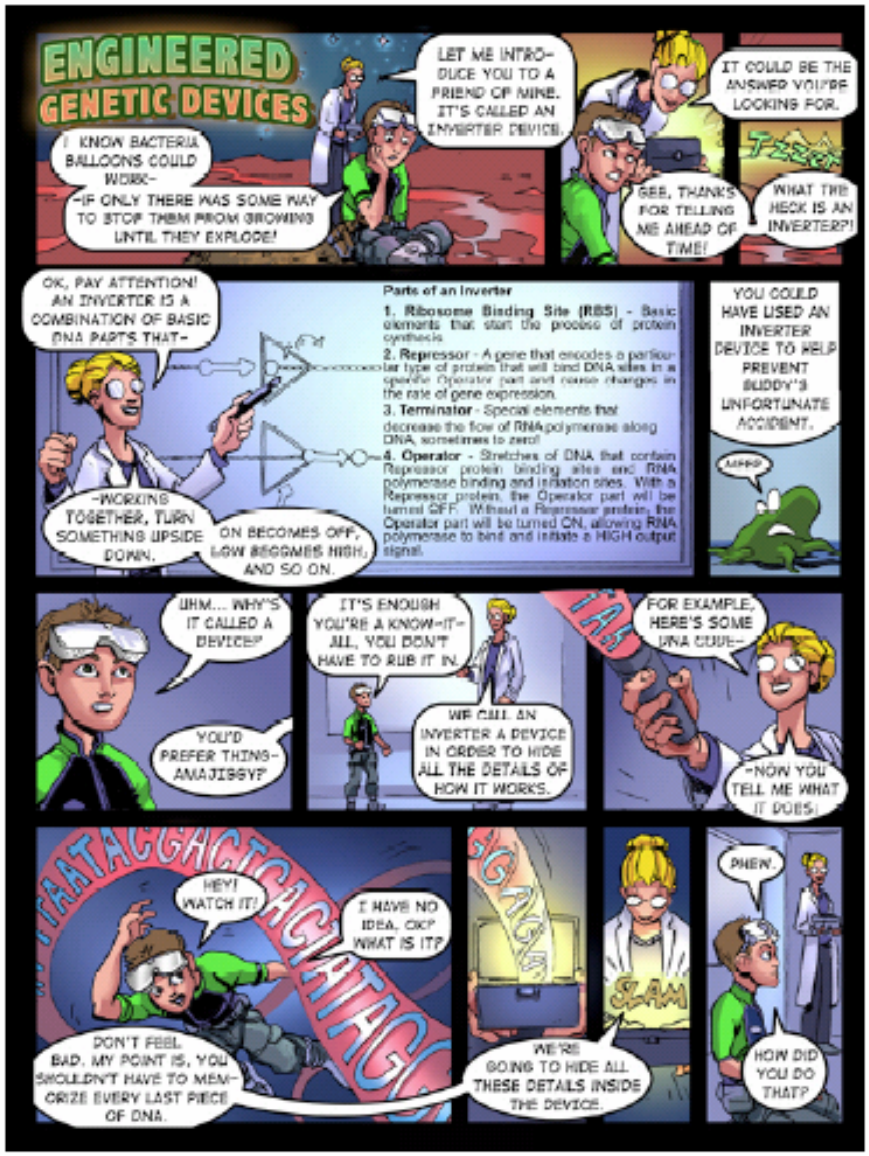
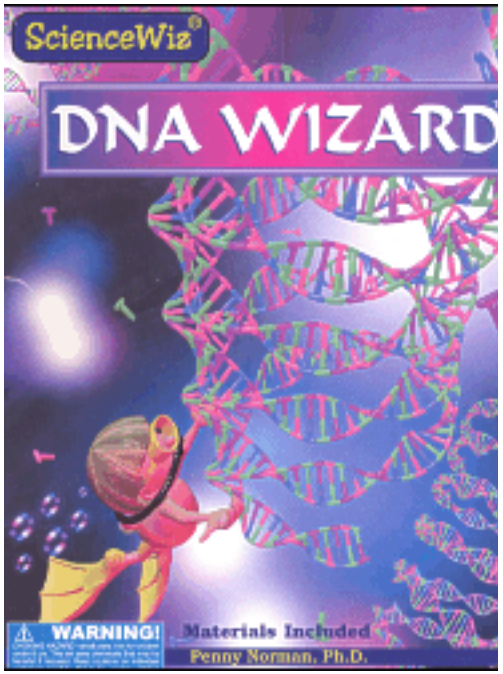

THAT'S RIGHT, ALEC! SCRIPSIT IS A WORD PROCESSING PROGRAM! MY DAD HAS A TRS-80 MODEL 12 COMPUTER WITH SCRIPSIT IN HIS OFFICE... AND HE TAUGHT ME HOW TO USE IT WITH A DAISY WHEEL PRINTER...
...TO WRITE BUSINESS LETTERS, RESEARCH NOTES, PRESS RELEASES, AND BULLETINS.
SHANNA YOU KNOW SO MUCH - SHOW US HOW...
...SCRIPSIT WORD PROCESSING WORKS IN OUR SCHOOL'S OFFICE.
IN THE SCHOOL OFFICE...
TURN ON THE POWER SWITCH THEN "INSERT DISKETTE" APPEARS ON THE SCREEN... ...CAREFULLY PUSH DISKETTE INTO THE SLOT (DRIVE Ø) AND ROTATE THE LATCH TO A HORIZONTAL POSITION.
DRIVE Ø
DRIVE 1
AFTER THAT THE WORD "INITIALIZING" APPEARS WHICH MEANS THE COMPUTER IS LOADING THE PROGRAM...
INITIALIZING
...ALSO, THE SMALL RED LIGHT NEXT TO THE DISK DOOR WILL BE "ON"!
AFTER THE LIGHT GOES OUT, THE PROGRAM HAS BEEN "LOADED" INTO THE COMPUTER. NEXT, THE COMPUTER TELLS YOU TO TYPE IN THE DATE...
... FOR EXAMPLE APRIL 6, 1984, TYPE 04/06/1984 AND THEN PRESS THE ENTER KEY.
ENTER DATE (MM/DD/YYYY)
NEXT, THE COMPUTER PROMPTS YOU TO ENTER THE TIME USING THE 24-HOUR SYSTEM, GIVING HOURS, MINUTES AND SECONDS.
FOR EXAMPLE 9:30 AND 20 SECONDS A.M., TYPE THIS WAY-- 09.30.20. AND THEN PRESS THE ENTER KEY.
ENTER TIME (HH.MM.SS)
THAT MAKES THE "DIRECTORY" APPEAR ON THE SCREEN. THE DIRECTORY IS DIVIDED INTO SIX "CELLS". EACH CELL IS THE STORAGE UNIT FOR INFORMATION ABOUT ONE DOCUMENT...
... AND IN TURN, A DOCUMENT CAN BE MADE UP OF SEVERAL PAGES OF INFORMATION.
IS THERE A SCRIPSIT PROGRAM FOR OUR CLASSROOM TRS-80 MODEL 4'S?
YES, THERE IS A SPECIAL SCRIPSIT PROGRAM FOR THE MODEL 4'S!
4


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 COULD WORK-
-IF ONLY THERE WAS SOME WAY TO STOP THEM FROM GROWING UNTIL THEY EXPLODE!
LET ME INTRODUCE YOU TO A FRIEND OF MINE. IT'S CALLED AN INVERTER DEVICE.
IT COULD BE THE ANSWER YOU'RE LOOKING FOR.
GEE, THANKS FOR TELLING ME AHEAD OF TIME!
WHAT THE HECK IS AN INVERTER?!
OK, PAY ATTENTION! AN INVERTER IS A COMBINATION OF BASIC DNA PARTS THAT-
-WORKING TOGETHER, TURN SOMETHING UPSIDE DOWN.
ON BECOMES OFF, LOW BECOMES HIGH, AND SO ON.
Parts of an Inverter
1. Ribosome Binding Site (RBS) - Basic elements that start the process of protein synthesis.
2. Repressor - A gene that encodes a particular type of protein that will bind DNA sites in a specific Operator part and cause changes in the rate of gene expression.
3. Terminator - Special elements that decrease the flow of RNA polymerase along DNA, sometimes to zero!
4. Operator - Stretches of DNA that contain Repressor protein binding sites and RNA polymerase binding and initiation sites. With a Repressor protein, the Operator part will be turned OFF. Without a Repressor protein, the Operator part will be turned ON, allowing RNA polymerase to bind and initiate a HIGH output signal.
YOU COULD HAVE USED AN INVERTER DEVICE TO HELP PREVENT BUDDY'S UNFORTUNATE ACCIDENT.
MMMF
UHM... WHY'S IT CALLED A DEVICE?
YOU'D PREFER THING-AMAJIBBY?
IT'S ENOUGH YOU'RE A KNOW-IT-ALL. YOU DON'T HAVE TO RUB IT IN.
WE CALL AN INVERTER A DEVICE IN ORDER TO HIDE ALL THE DETAILS OF HOW IT WORKS.
FOR EXAMPLE, HERE'S SOME DNA CODE-
-NOW YOU TELL ME WHAT IT DOES!
HEY! WATCH IT!
I HAVE NO IDEA. OK? WHAT IS IT?
DON'T FEEL BAD. MY POINT IS, YOU SHOULDN'T HAVE TO MEMORIZE EVERY LAST PIECE OF DNA.
WE'RE GOING TO HIDE ALL THESE DETAILS INSIDE THE DEVICE.
SLAM
PHEW.
HOW DID YOU DO THAT?



http://www.electrowiz.com/

Acknowledgements

- Drew Endy
- MIT iGEM program
- Bio Era
- Cybercell
- Jonas Karlsson
- Alberta Ingenuity Fund