

Synthetic Biology

*an overview
bits and bases*

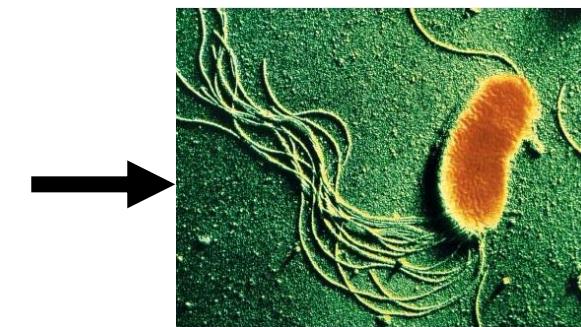
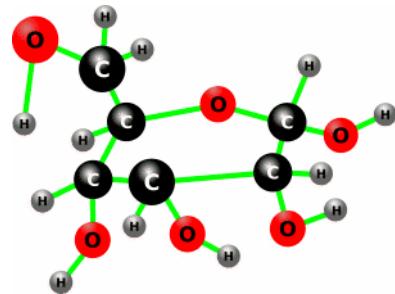
*April 14, 2008
Washington DC*

Andrew Hessel
ahessel@gmail.com

Image: flickr.com see <http://www.marshallartstudios.com>

DNA is a programming language

Input(s) → “Computer” → Output(s)



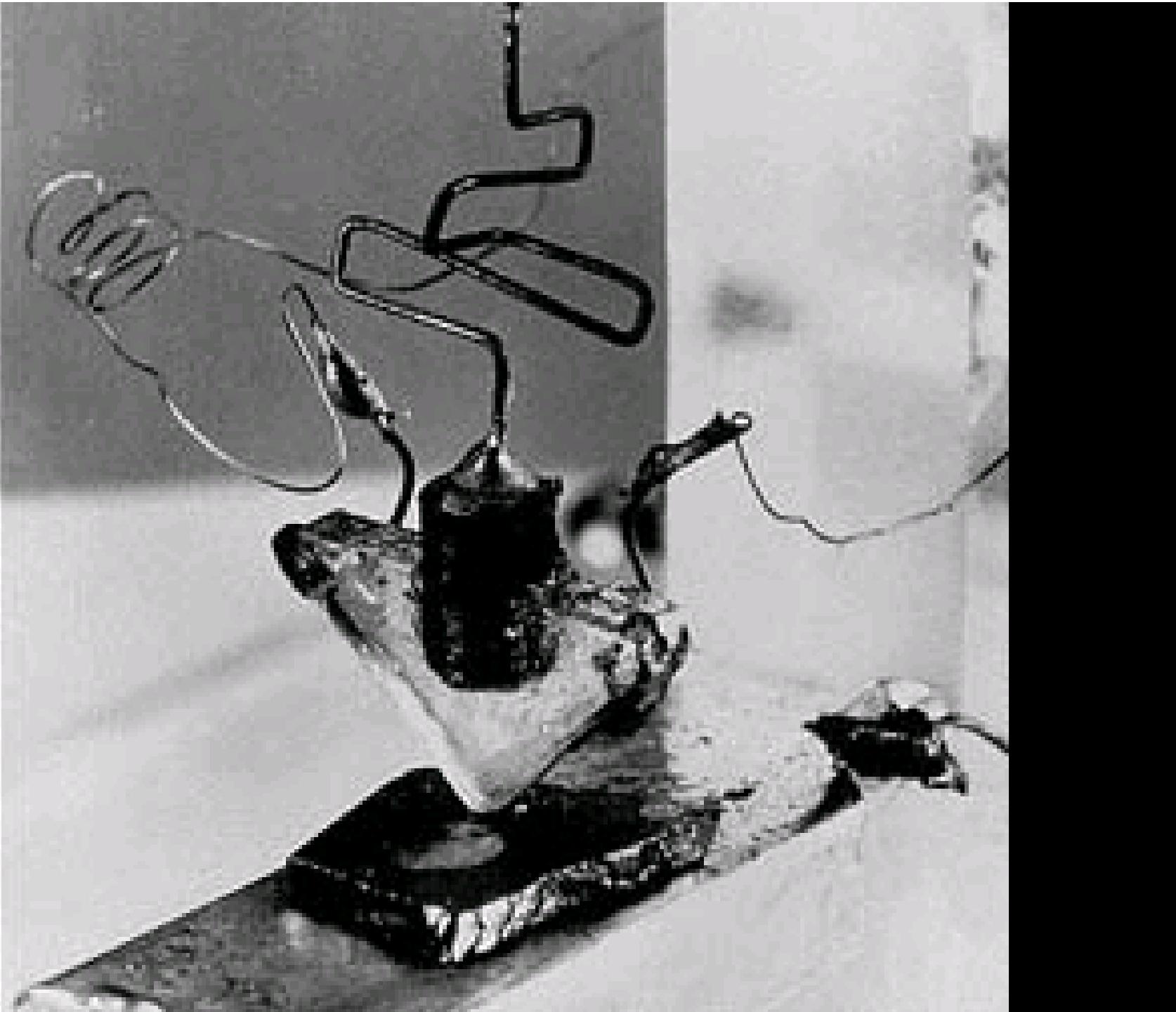
→ Swim toward sugar

Bits (0, 1's) encode software for electronic processors

Bases (A,T,G,C's) encode software for cells

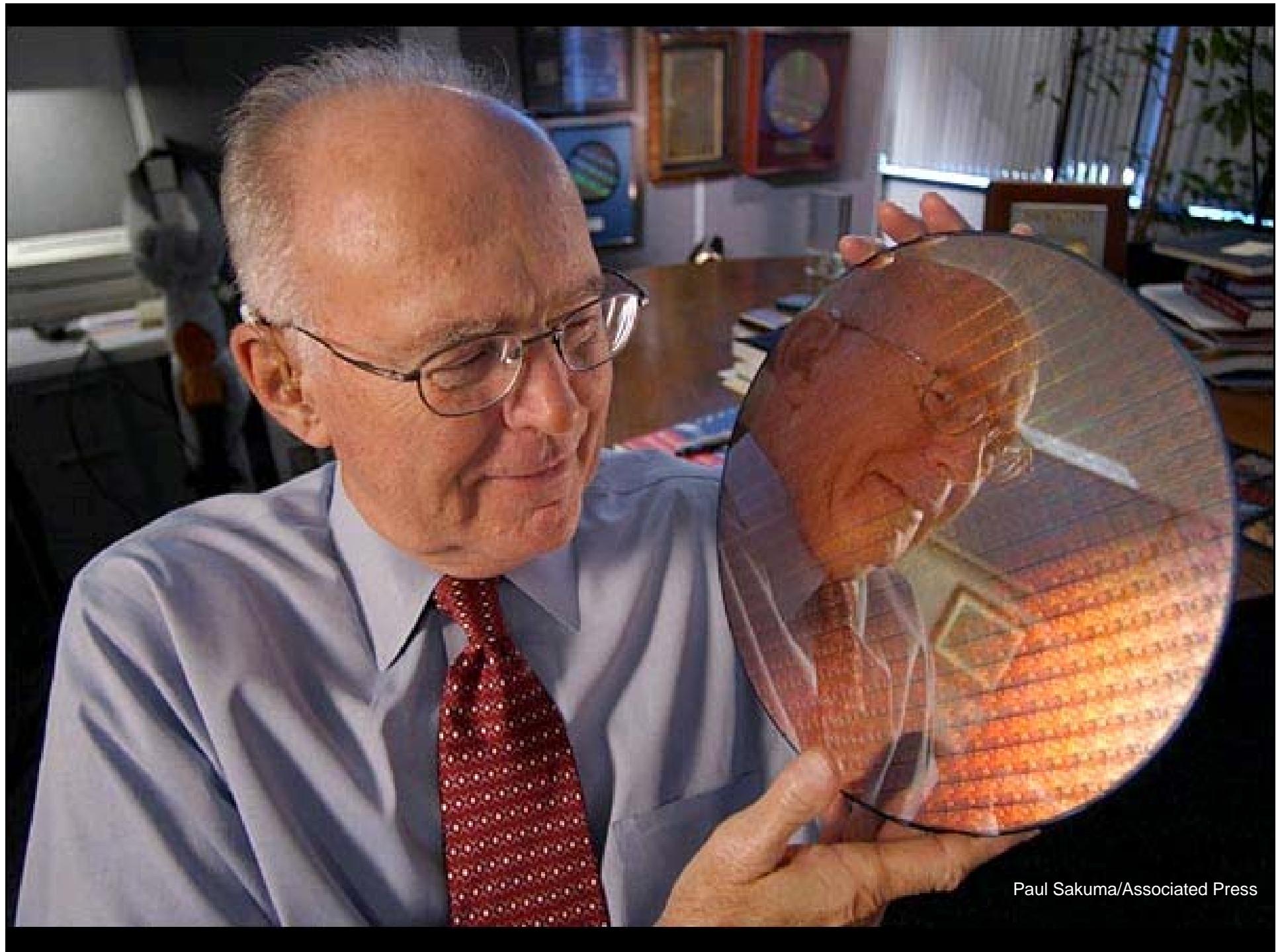
DNA is source code for cells.

*Synthetic biology is about how to program cells
efficiently and reliably*

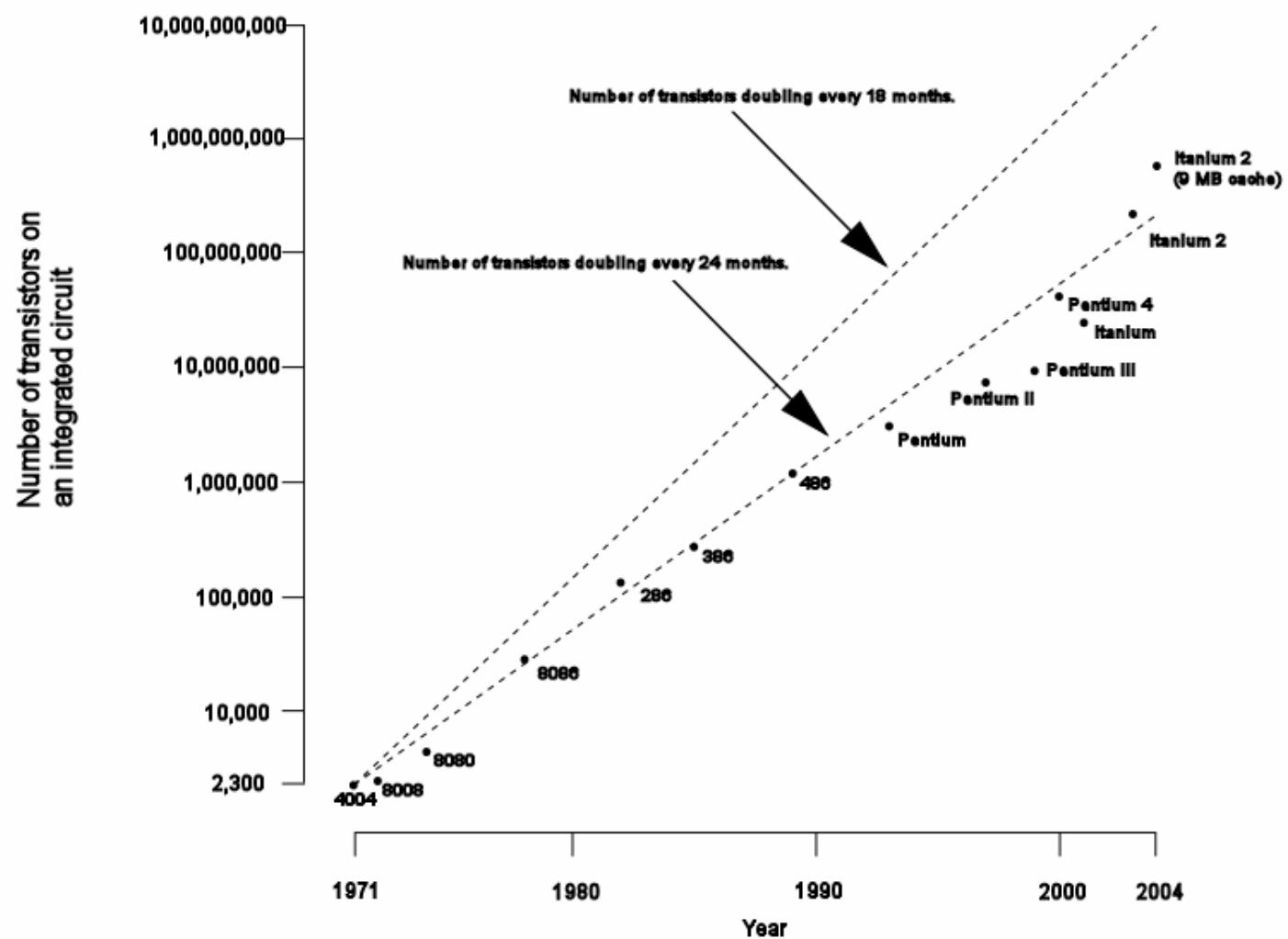
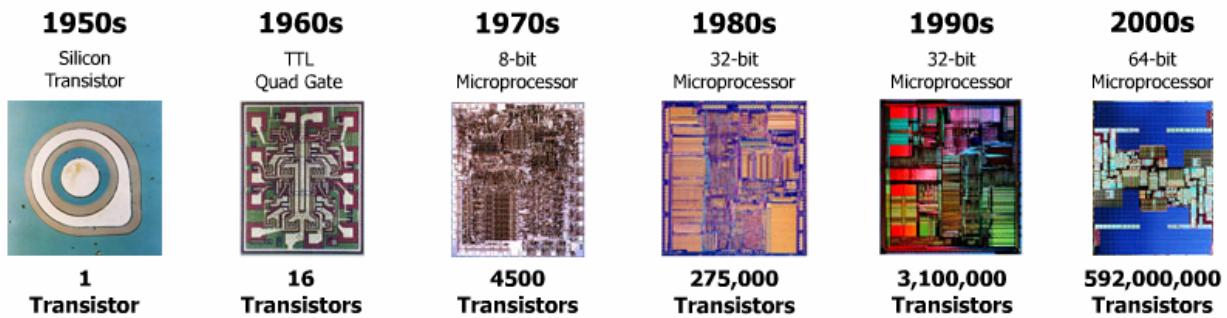




IBM 701 1953



Paul Sakuma/Associated Press





1956



danielig 072006 - S3is





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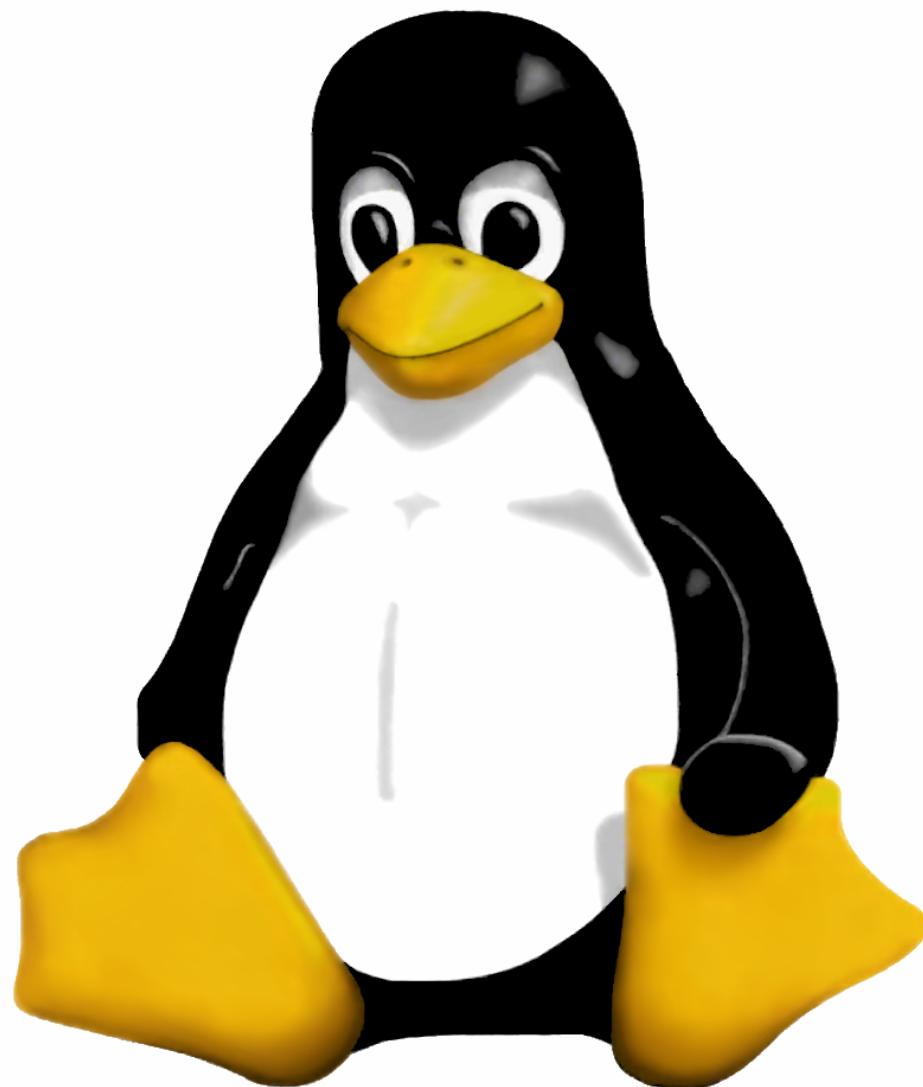
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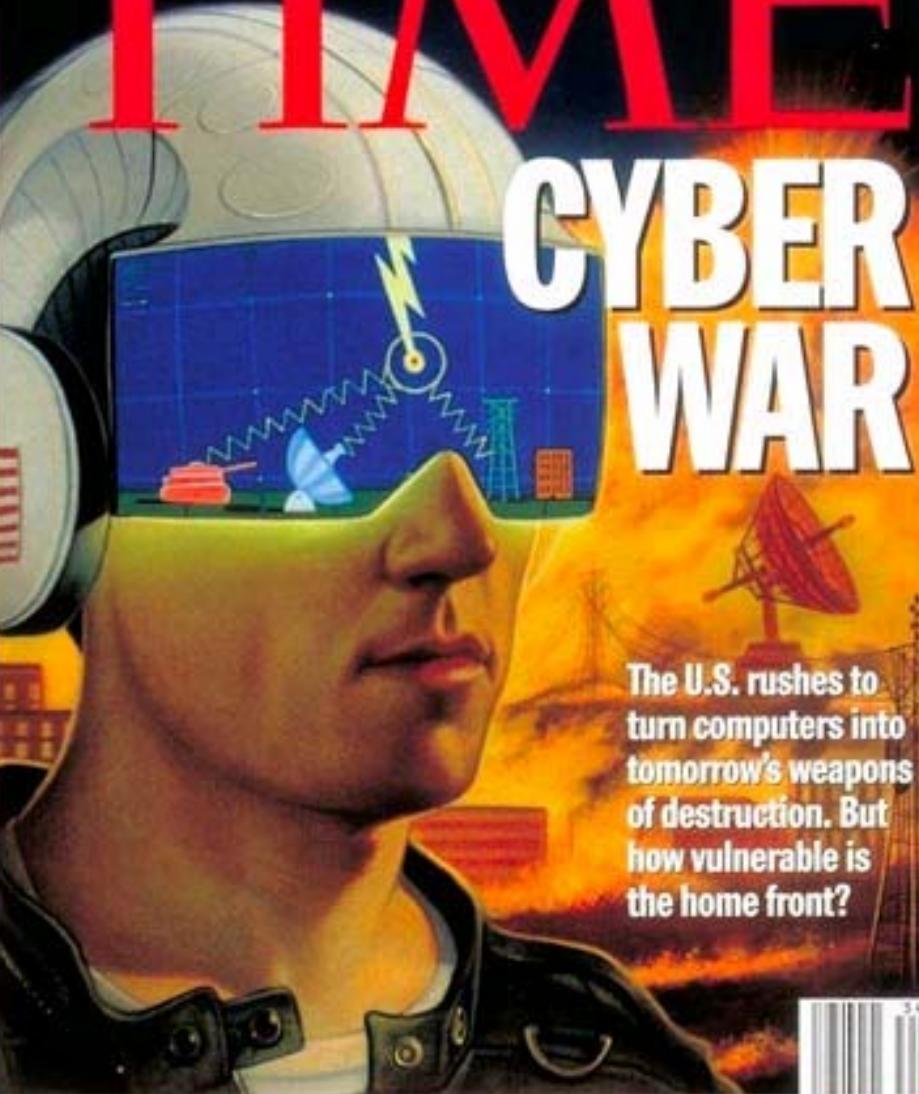
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HE'S GONE: Jerry Garcia Dead at 53

TIME

CYBER WAR



The U.S. rushes to turn computers into tomorrow's weapons of destruction. But how vulnerable is the home front?

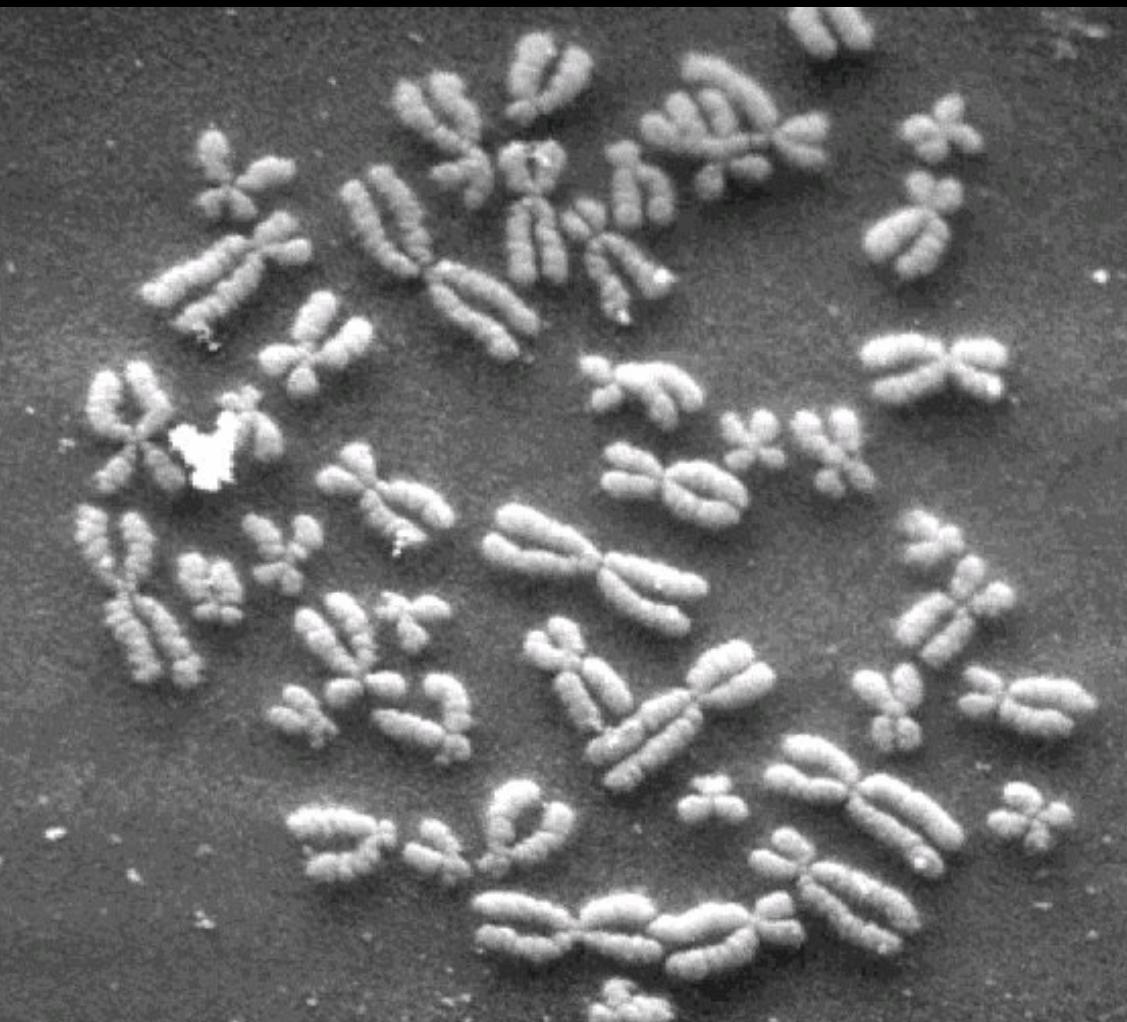




So what about biological processors?

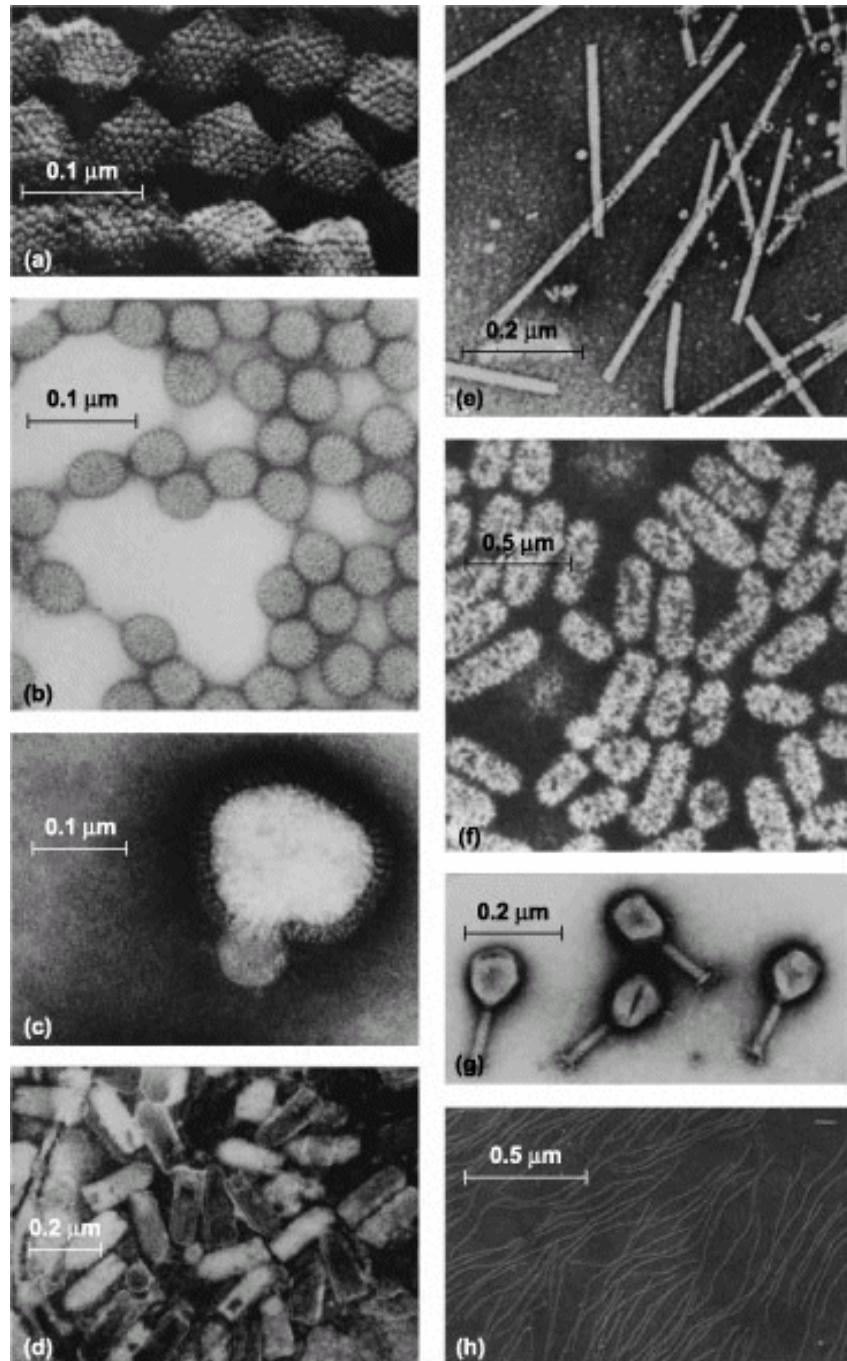






<http://www.colorado.edu/MCDB/MCDB111/intrographics/bacterial%20chromosome.jpg>

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



So why aren't programmed cells an everyday thing today, like computers?

REVERSING

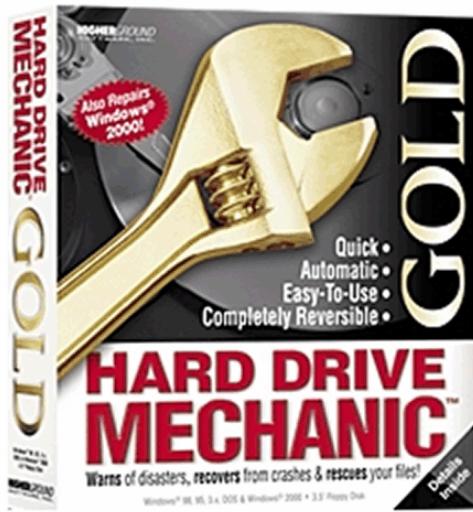
Secrets of Reverse Engineering



What Is Reverse Engineering?

Reverse engineering is the process of extracting the knowledge or design blueprints from anything man-made. The concept has been around since long before computers or modern technology, and probably dates back to the days of the industrial revolution. It is very similar to scientific research, in which a researcher is attempting to work out the "blueprint" of the atom or the human mind. The difference between reverse engineering and conventional scientific research is that with reverse engineering the artifact being investigated is man-made, unlike scientific research where it is a natural phenomenon.

Eldad Eilam

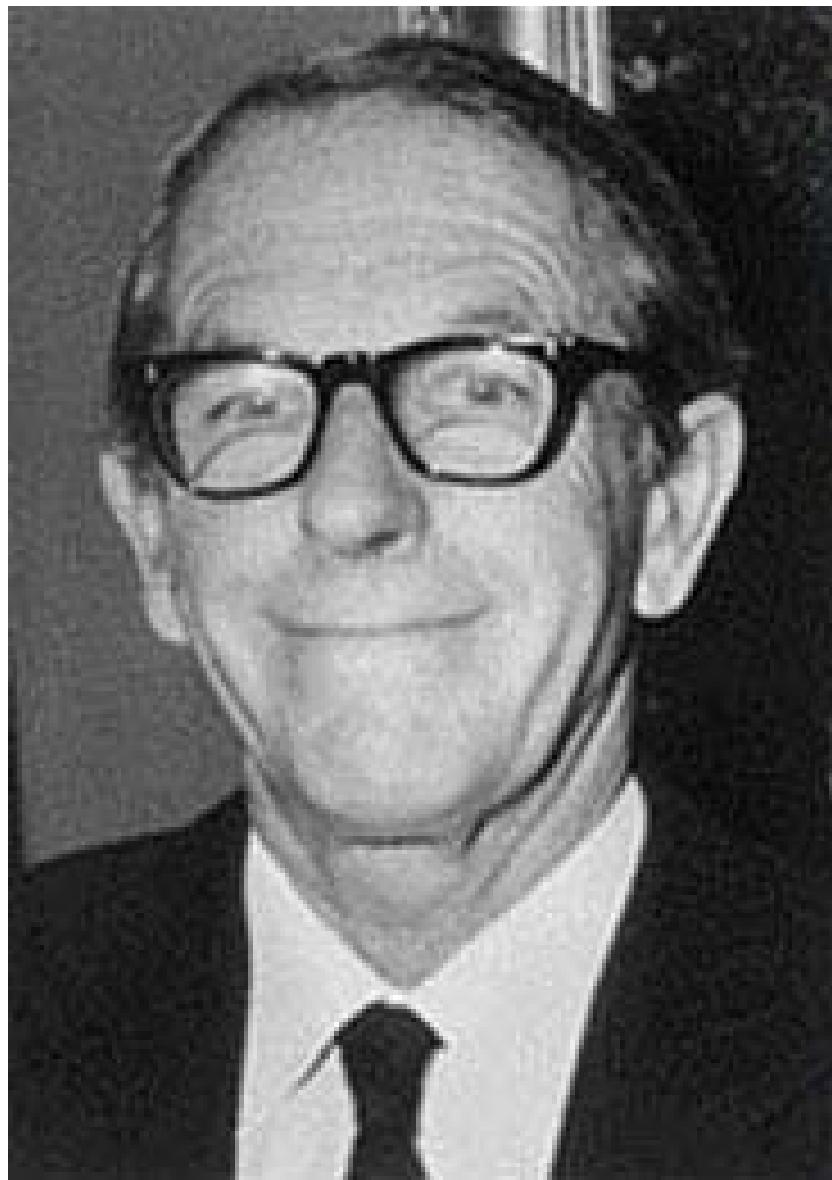


C:\Command.com

	16	32	64	1	2	4	H	D	N	A	B
0x000000:4D5A	7400	B800	0000	2604	0100	FFFF	0000	mZt.,...&...yy..			
0x000010:0000	0000	0001	0000	1E00	0000	0100	0000			
0x000020:0000	0000	0000	0000	0000	0000	0000	0000			
0x000030:0000	0000	0000	0000	0000	0000	0000	0000			
0x000040:2433	2433	454E	5501	00B5	014E	5343	4F00	\$3\$3ENU..u.NSCO.			
0x000050:0306	0016	001A	0001	04FF	FF48	0302	0056yyH...v			
0x000060:0303	0061	0308	006C	0302	01FF	FF7A	0303	...a...l...yyz..			
0x000070:CCEA	0383	03EB	03A4	03EC	03BC	03ED	03D2	i.e.f.e.x.i.x.i.0			
0x000080:03EE	03ED	03EF	0313	04F0	032A	04F1	033C	.i.i.i...d.*.n.<			
0x000090:04F2	034D	04F3	0369	04F4	0380	04F5	03B6	.ò.M.ò.i.ò.ò.ò.¶			
0x0000A0:04F6	03CD	04F7	03D8	04F8	03F8	04F9	031E	.ò.i.÷.ò.ò.ò.ò.ò.			
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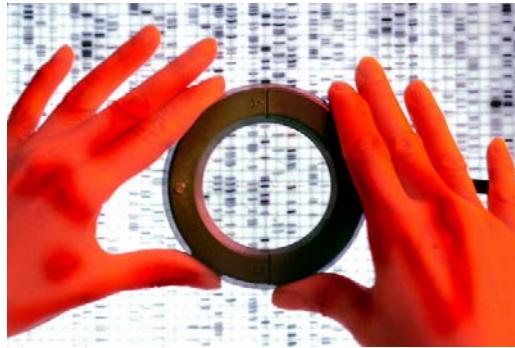
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Size : 93812



Nobel foundation

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GTAATCACTCTTAATACACTGCAAGTTAAAATAGCATTCTTGACCAGAAAAATAAGAA
TCTATGCATTAAAAGTGAAAACAGACTCATATGCTGATGAACATTAGCTATAAAT
TGTAACAATAATTAGCAATTCAATTGAAATTATTTATGTTCTAAATGCGTCGCTCTC
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TGATTCGCGATTTCGCGAACACCCCGCGGATCATAAACATTGCAACAGCTGCCTGT
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1980
500 bp/day (manual)



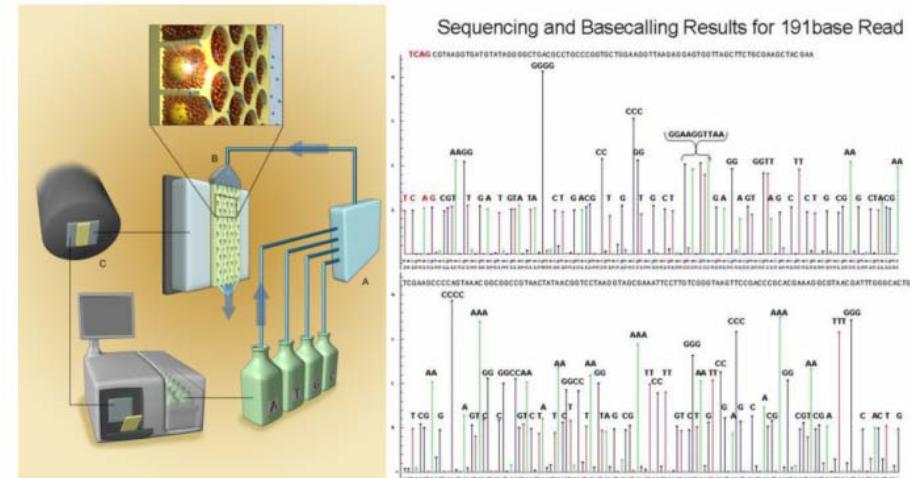
1987
36,000 bp/day (semi-auto)



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



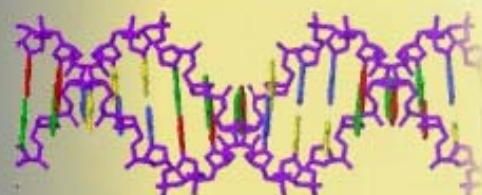
1998
500,000 bp/day (automatic)



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

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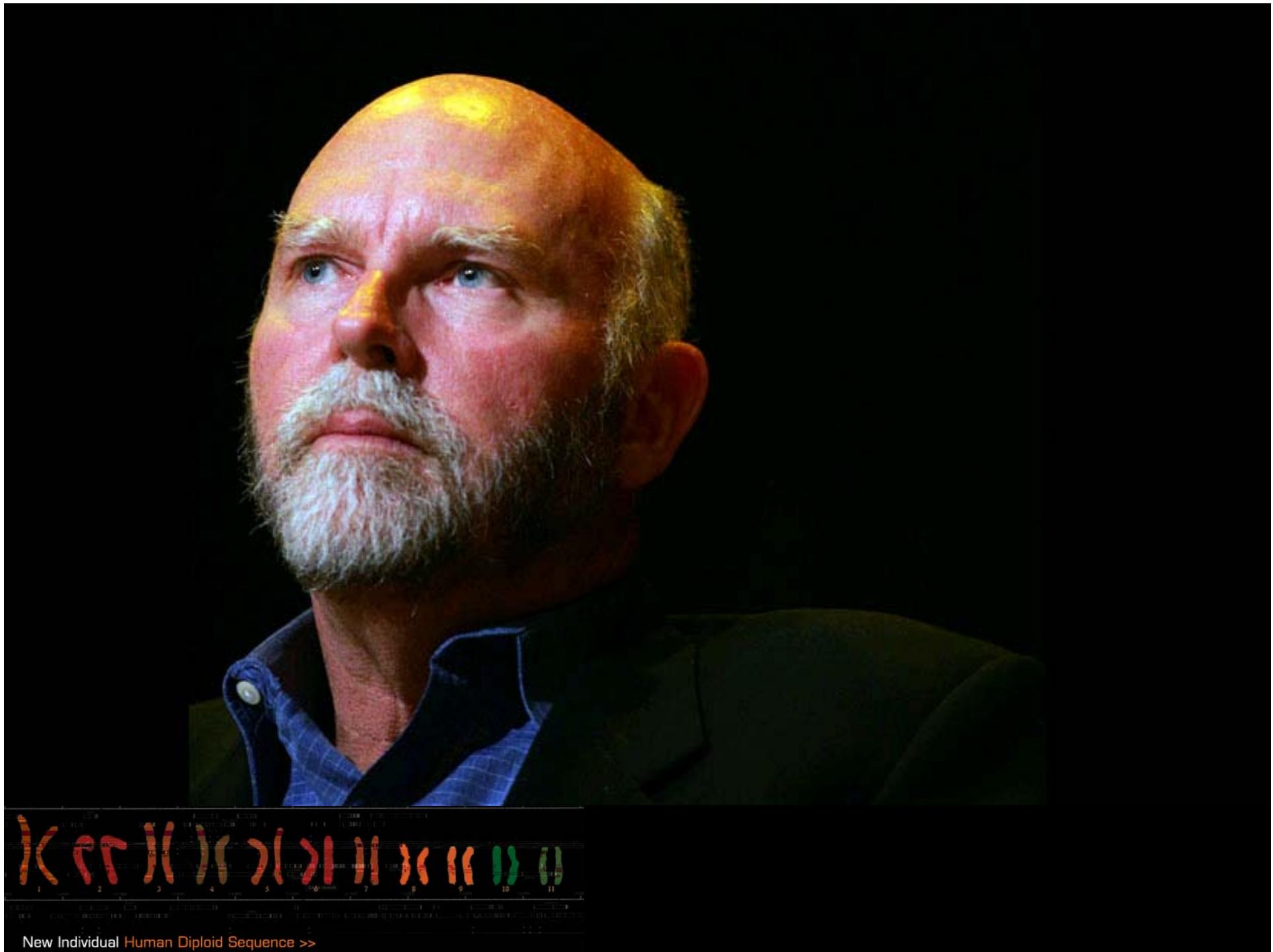
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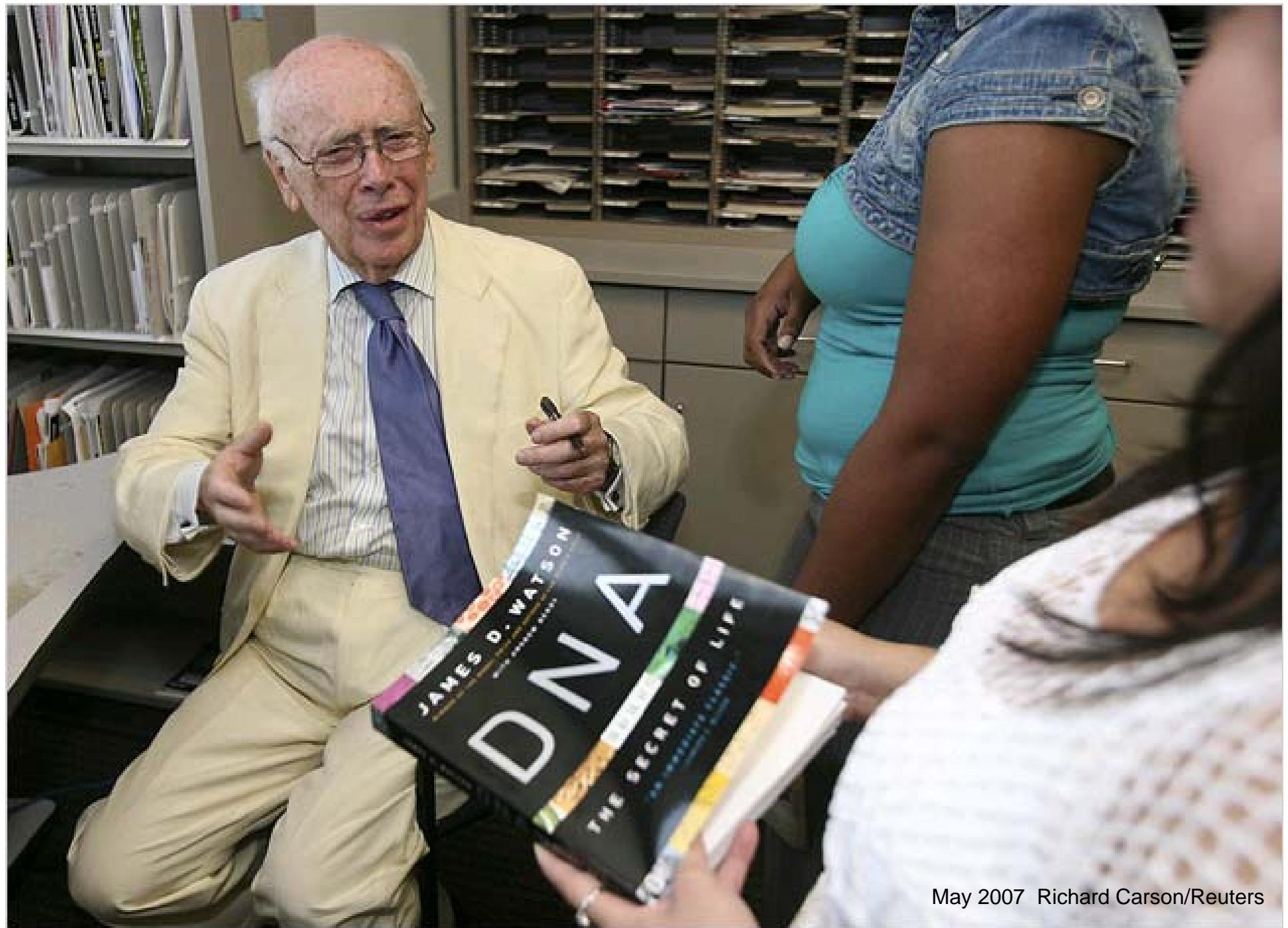
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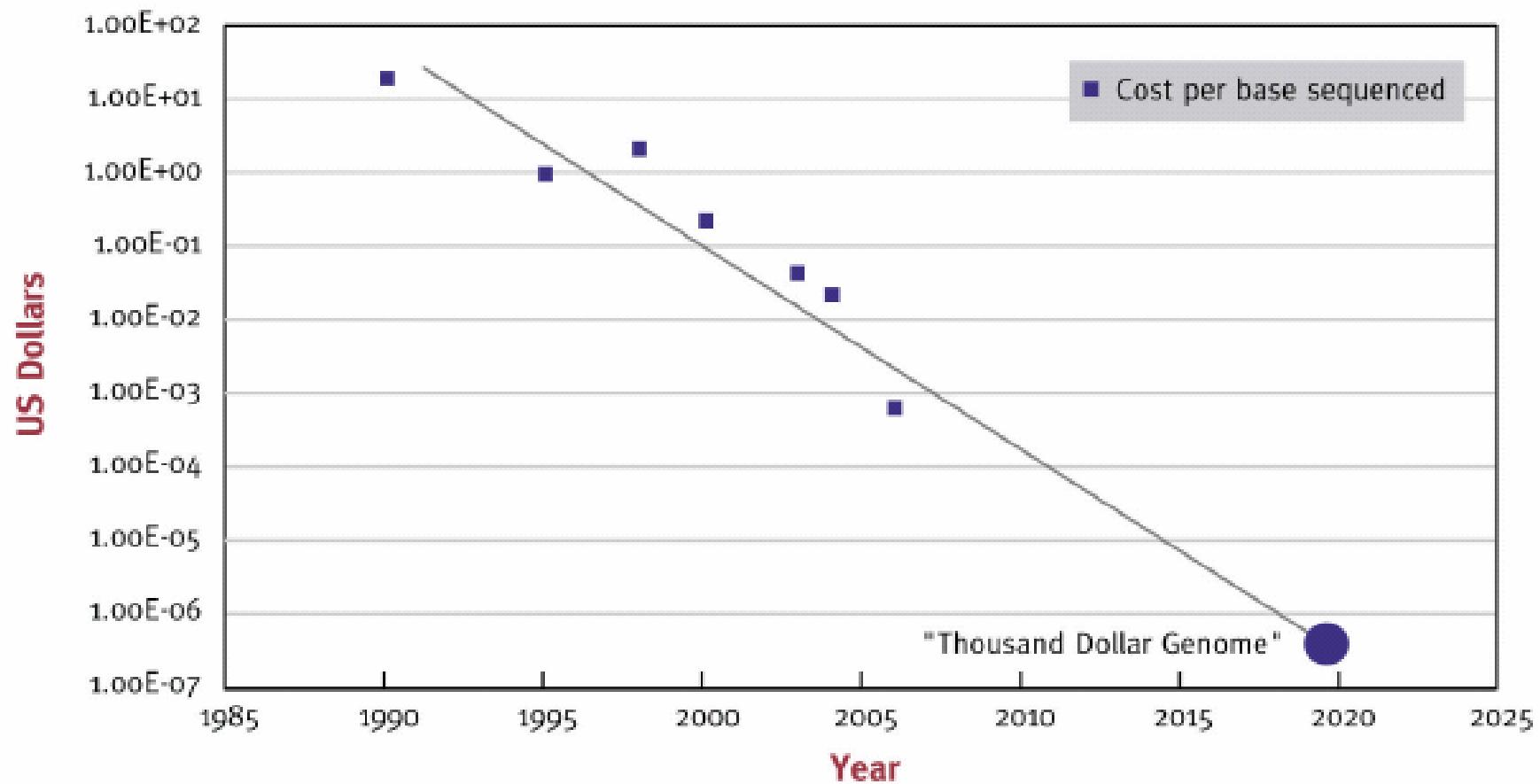
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New Individual Human Diploid Sequence >>

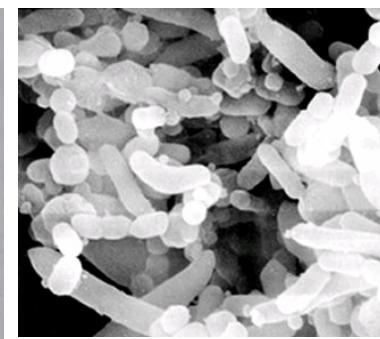


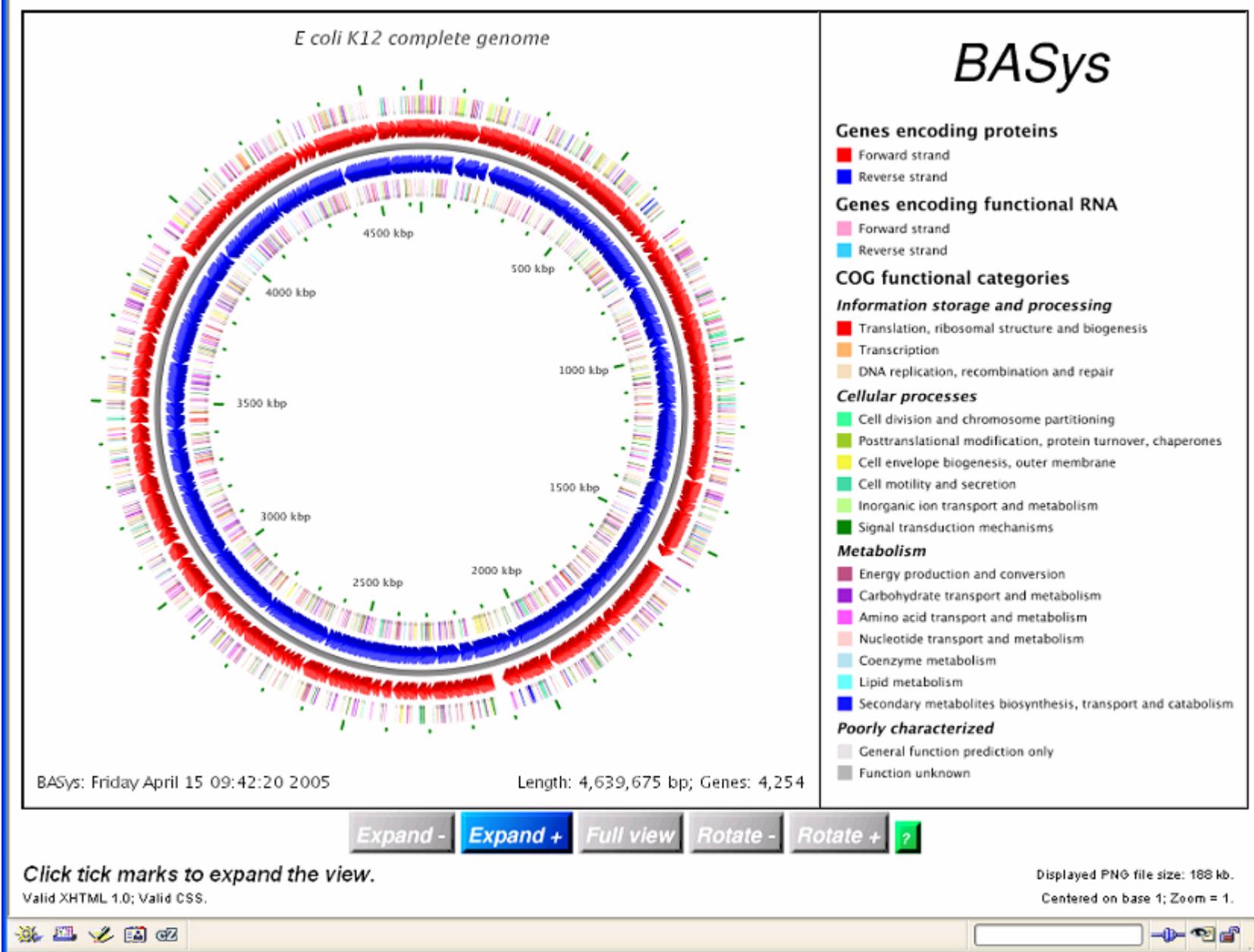
May 2007 Richard Carson/Reuters

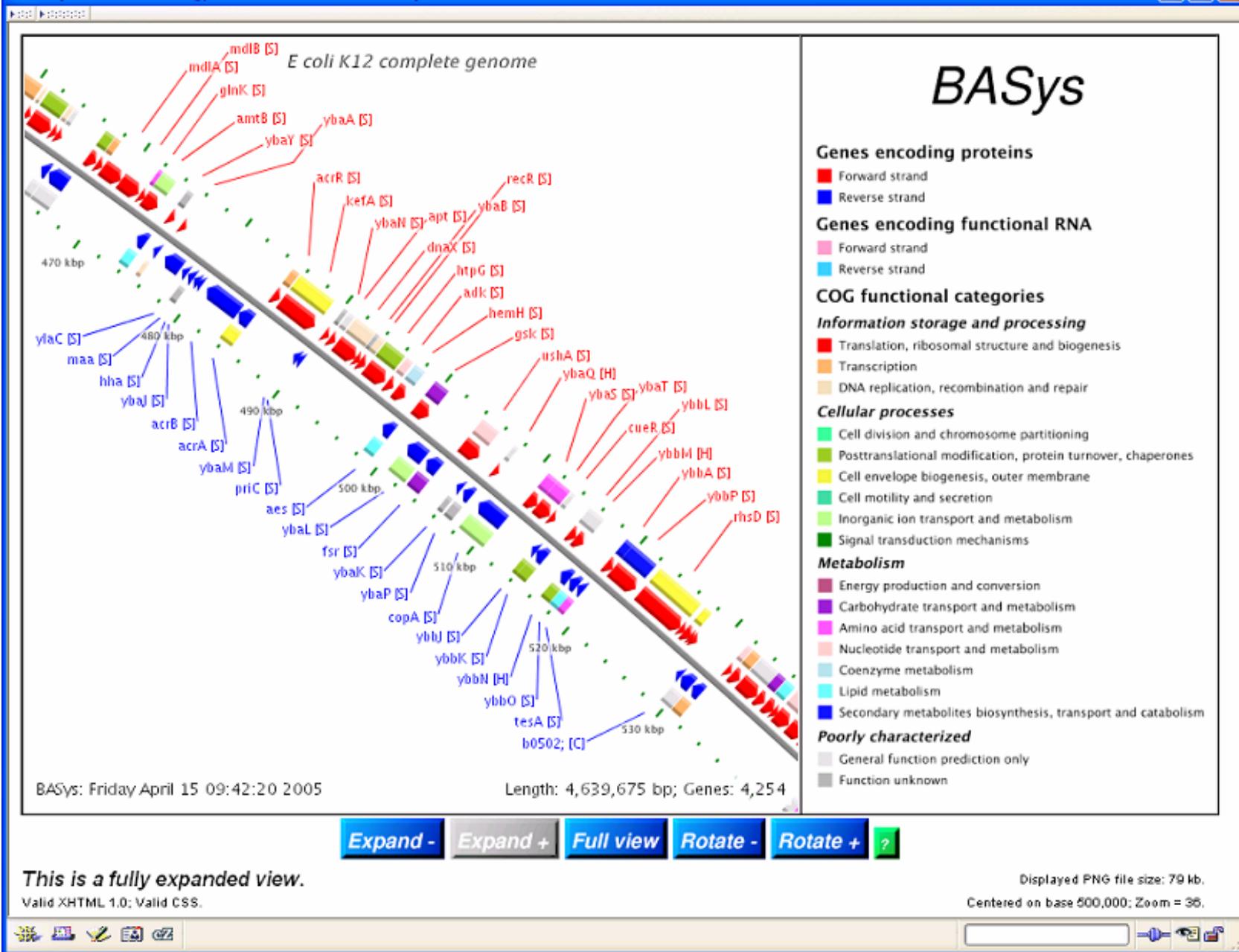


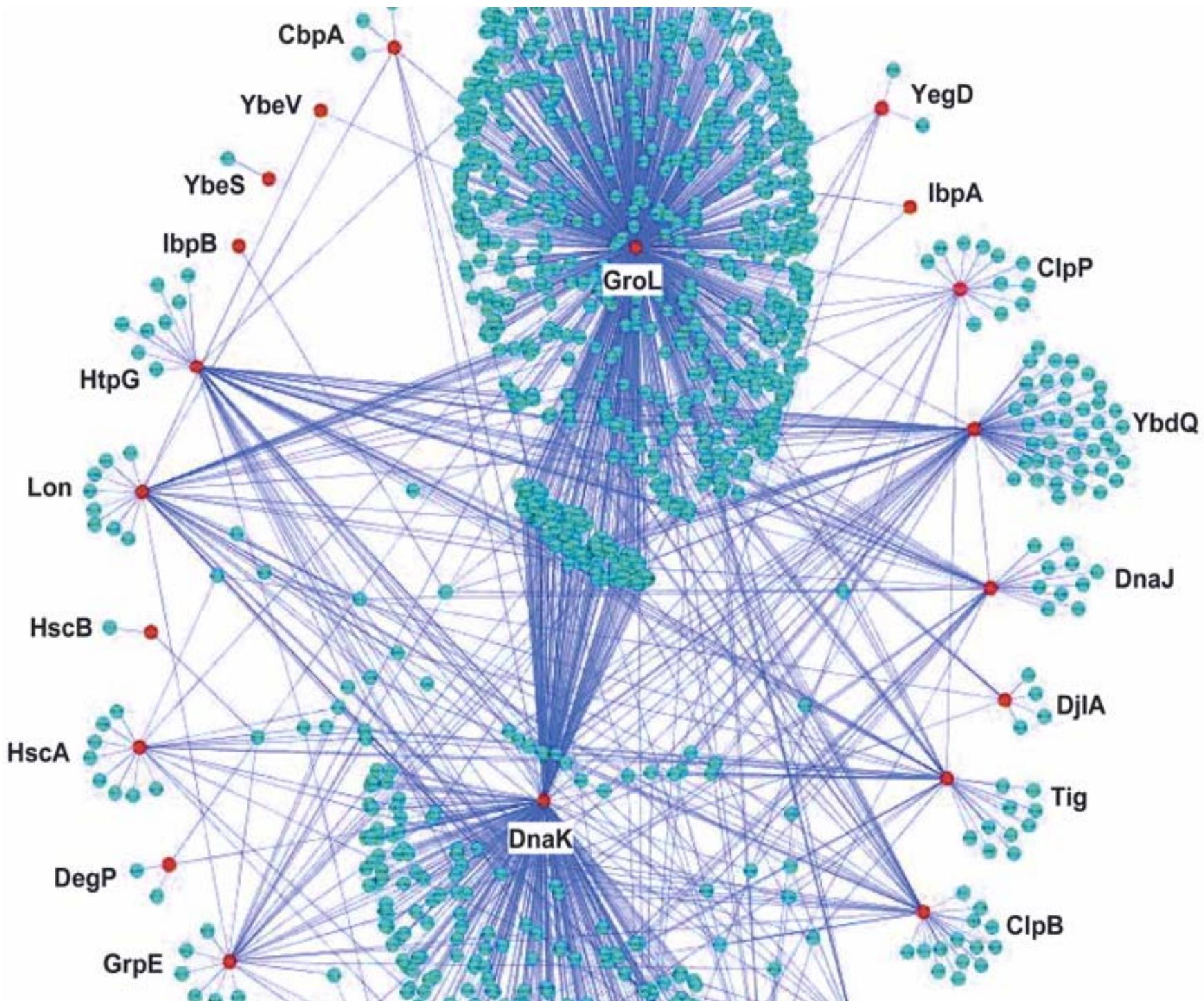
Source: R. Carlson, Bio-era

Environmental Shotgun Sequencing: Its Potential and Challenges for Studying the Hidden World of Microbes





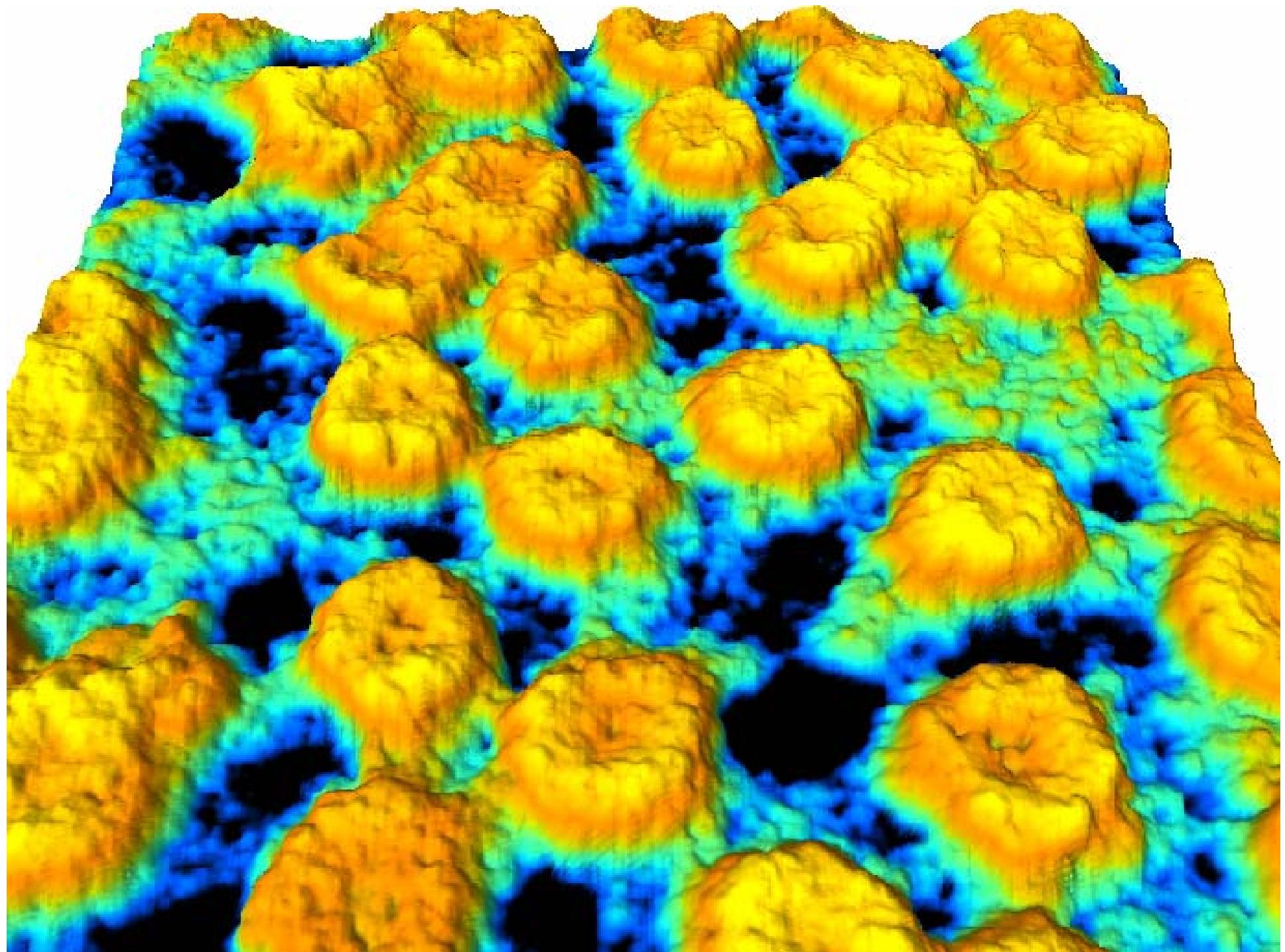


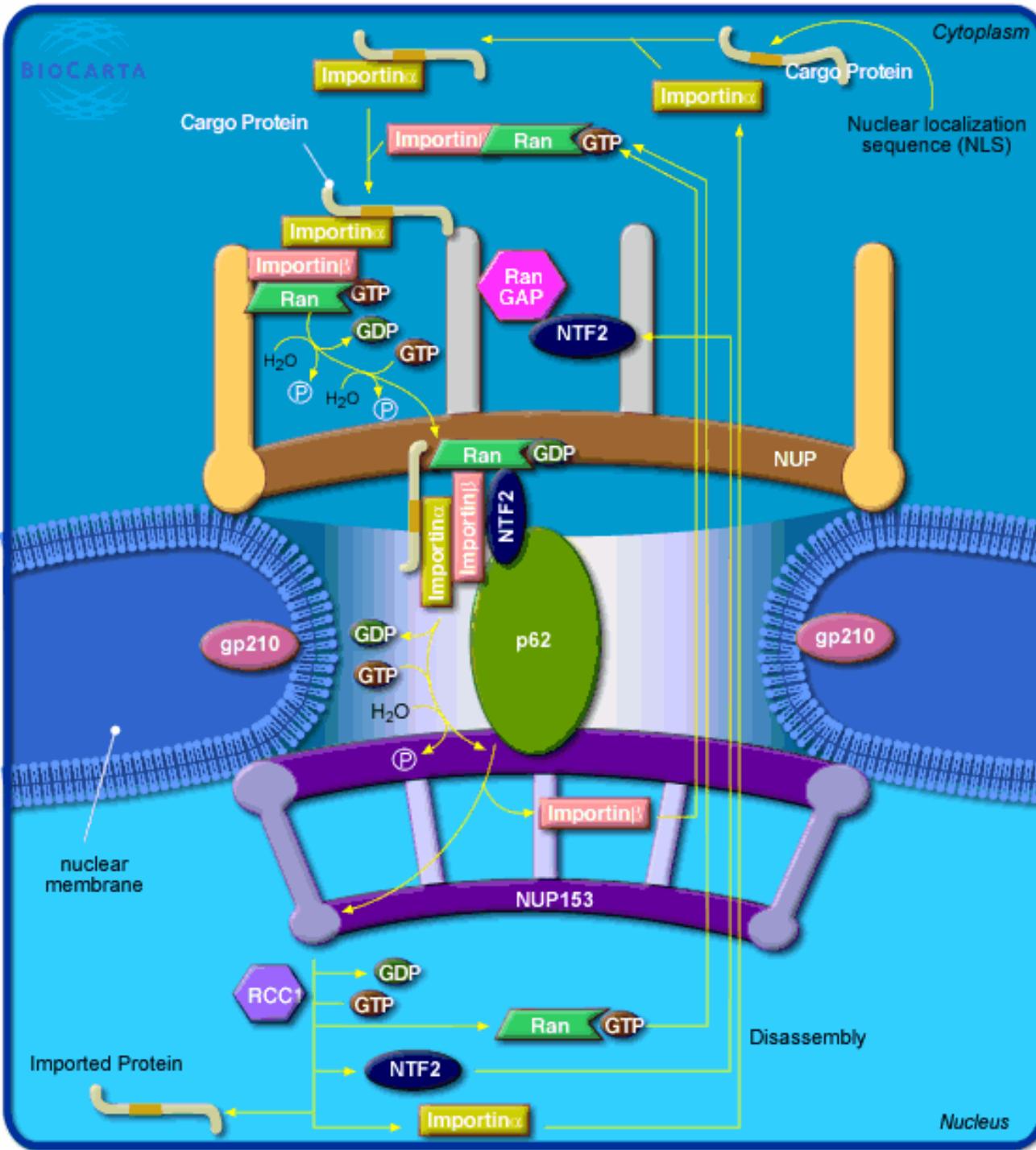


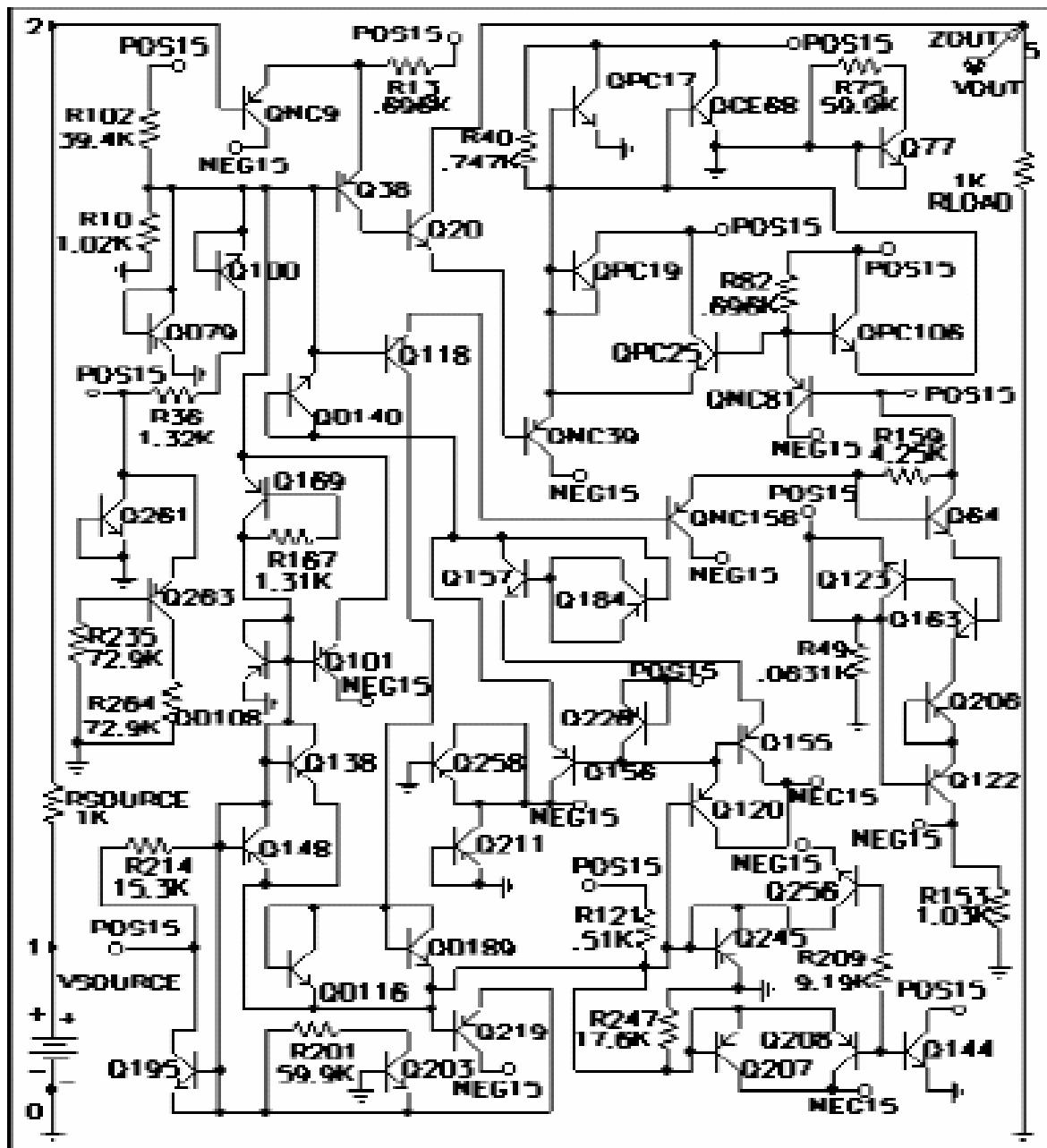
IBM's BlueGene/L: world's fastest supercomputer, 3 years running



596 TFLOPS (trillion floating point operations per second)







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

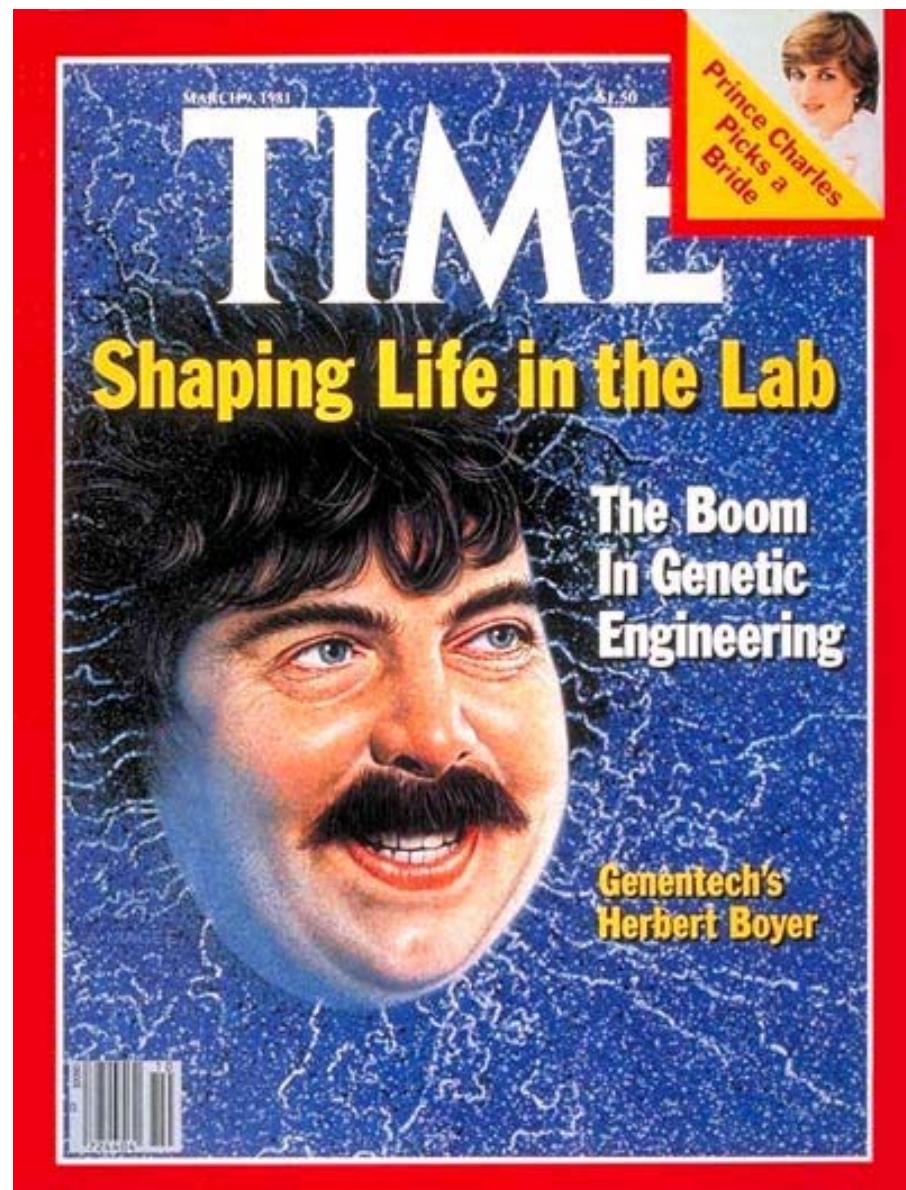
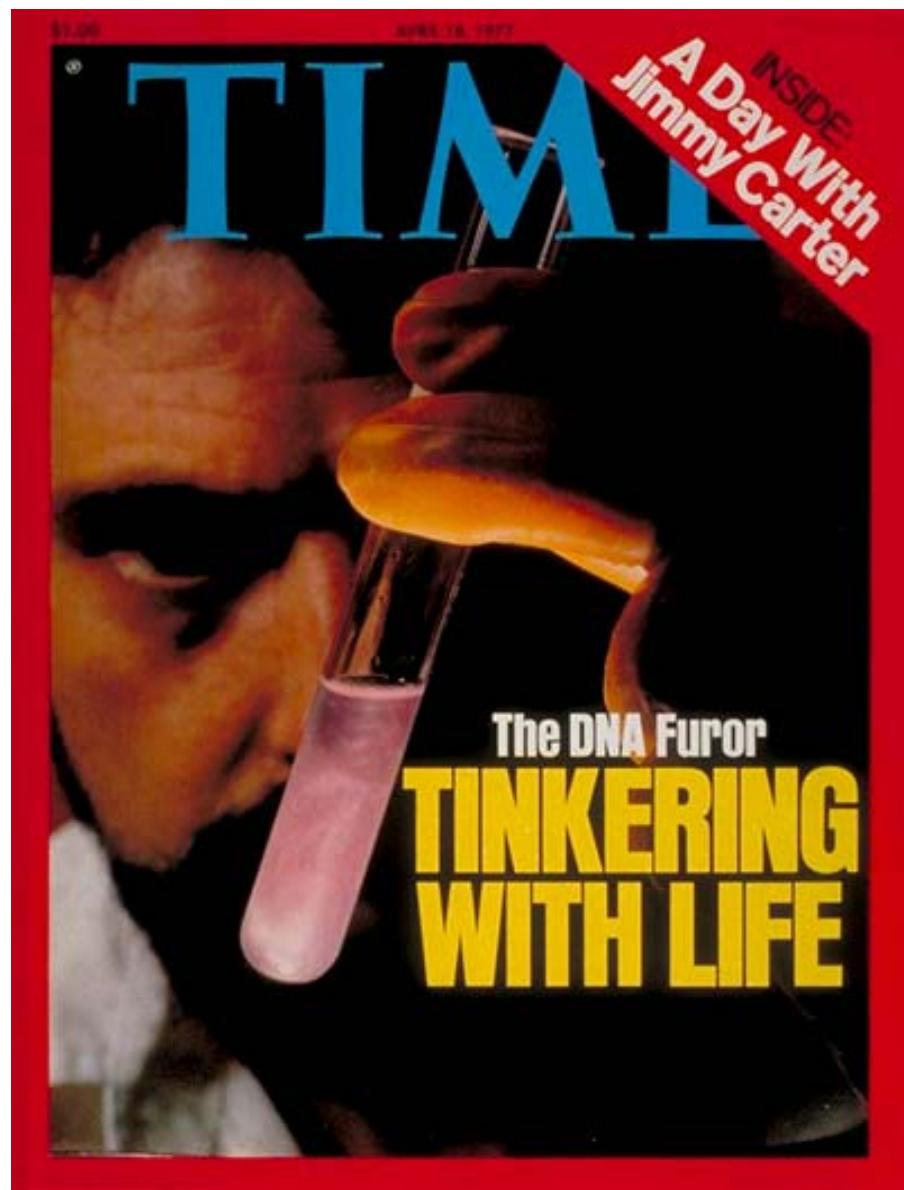
REDUCTION | COMPLEXITY

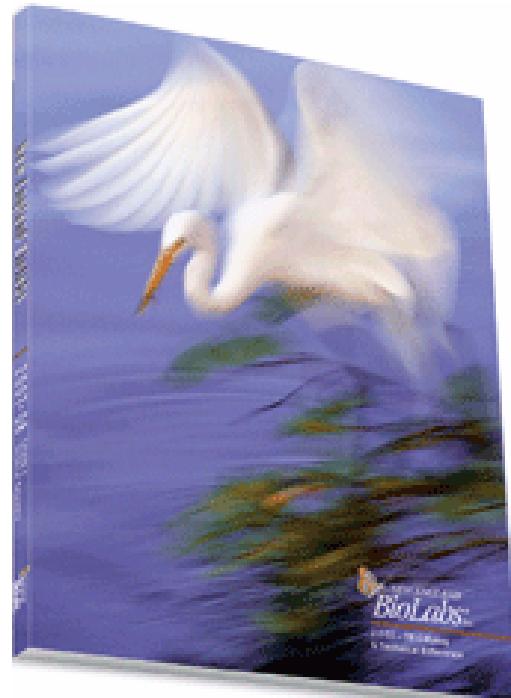


If we didn't build it, we may not be able to fully understand it.

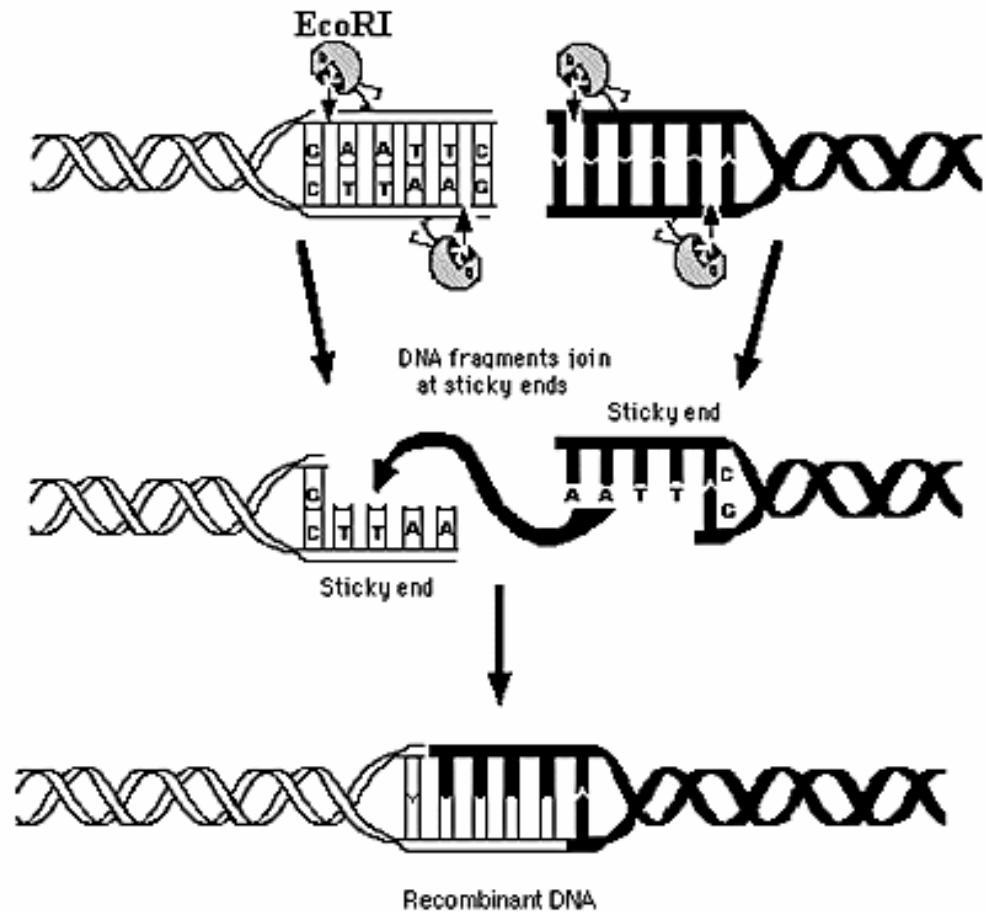
Genetic “Engineering”

Writing code





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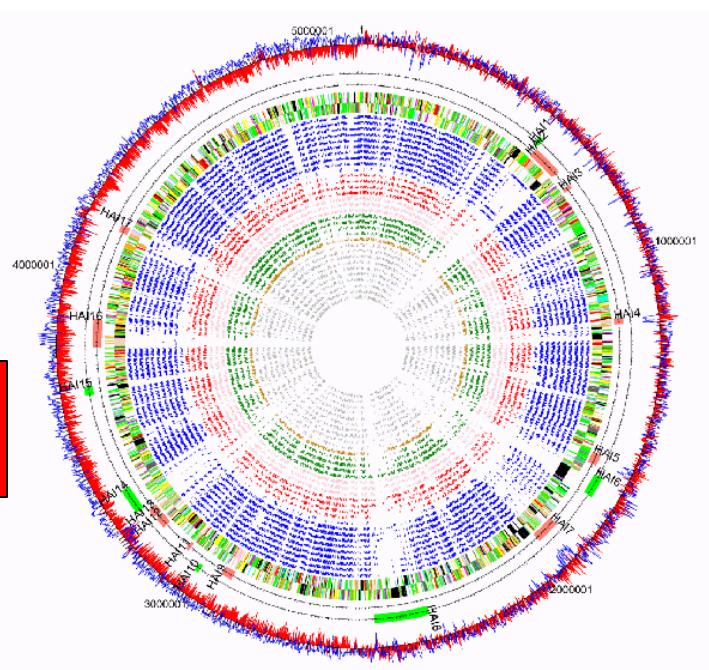
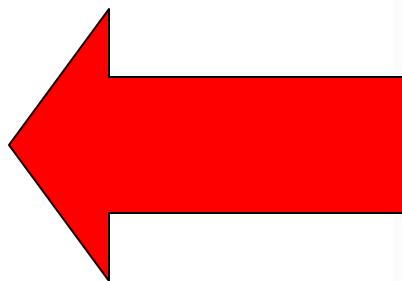
http://en.wikipedia.org/wiki/Image:Metal_movable_type.jpg



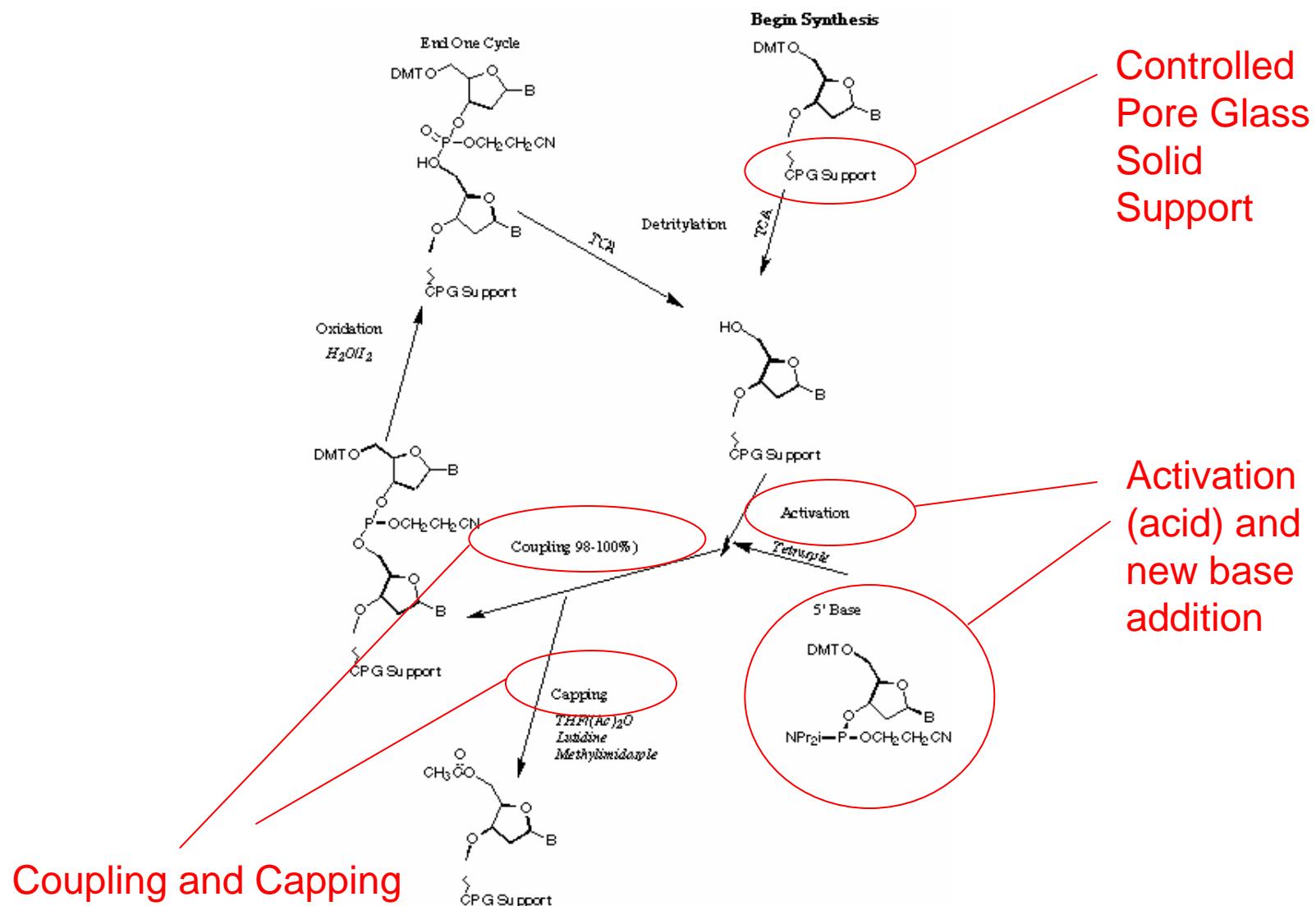


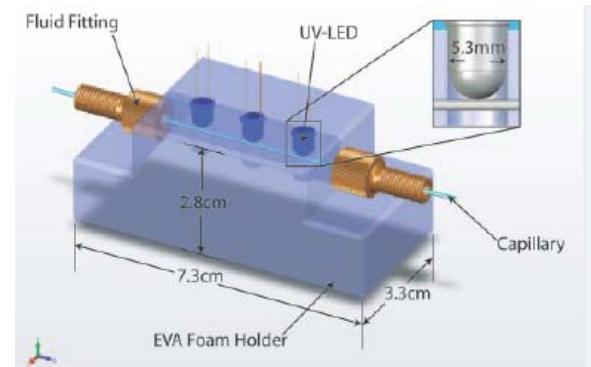
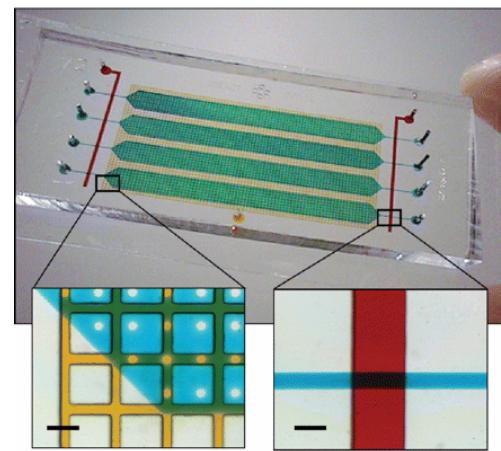
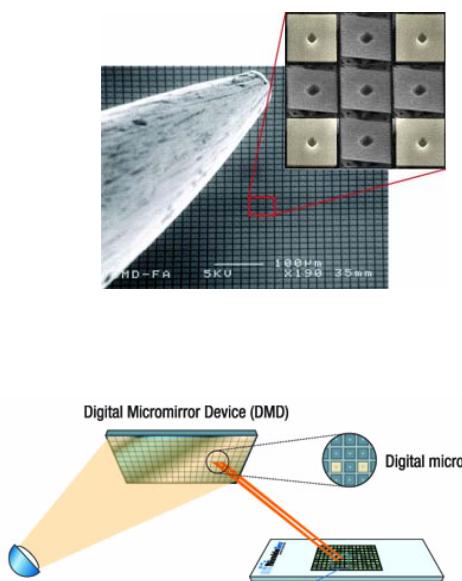
Physical DNA

sequencing



Digital DNA





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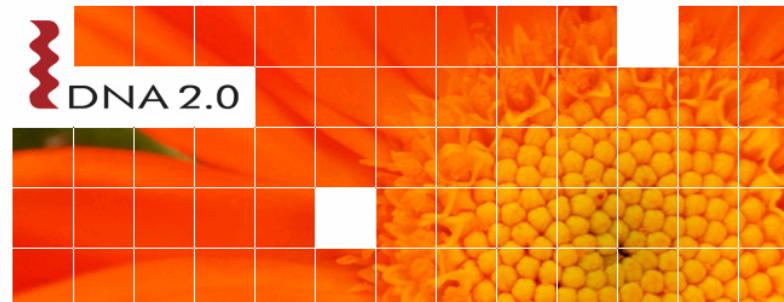
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Sources: Source: R. Carlson, G. Epstein, A. Yu (2005)

Cost per Base of DNA Sequencing and Synthesis

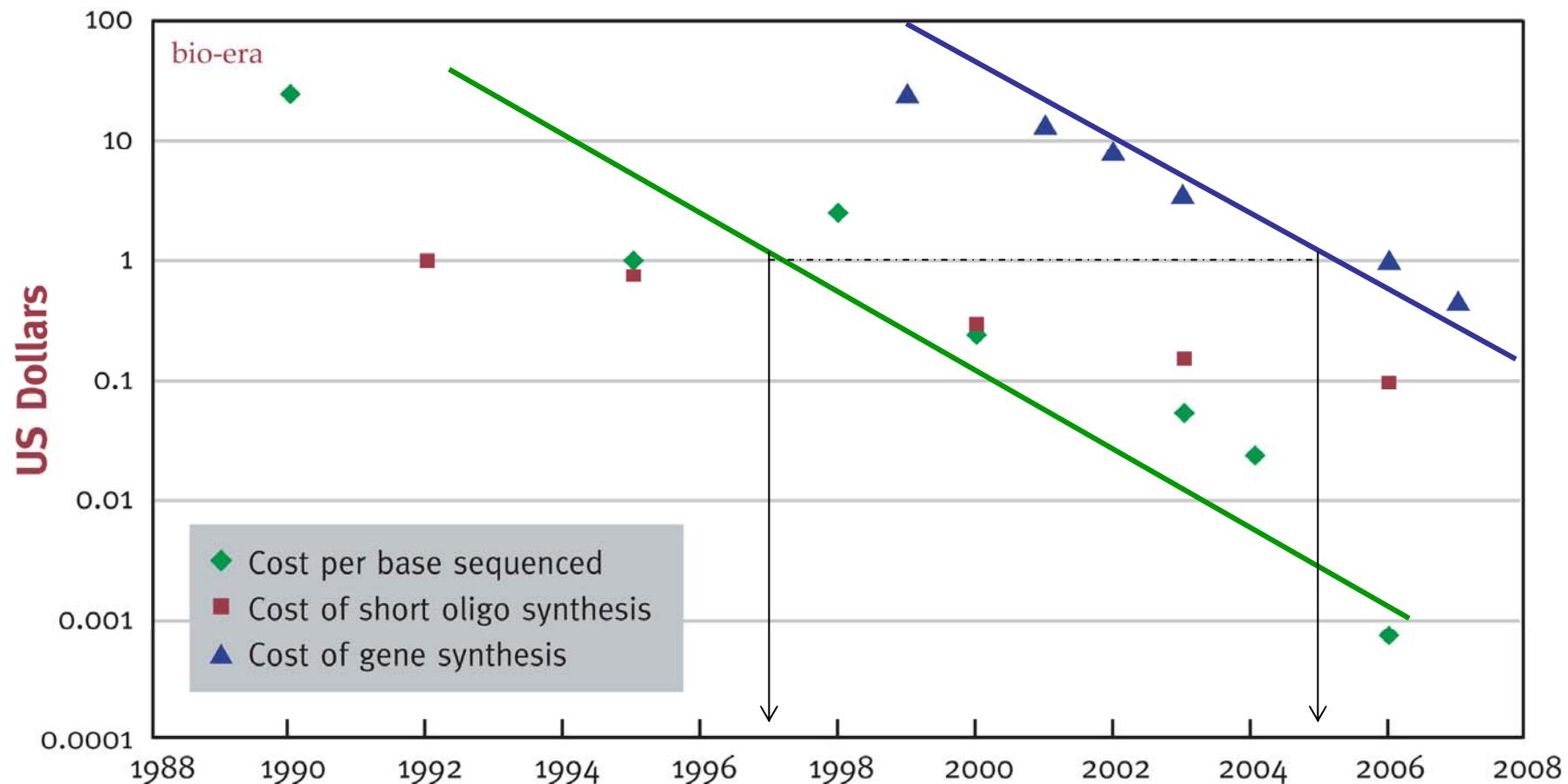


Figure from *Genome Synthesis and Design Futures*, Bio Economic Research Associates, © 2007. www.bio-era.net

Synthetic trend lags by about 8 years

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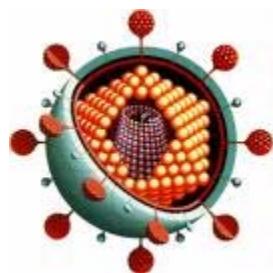
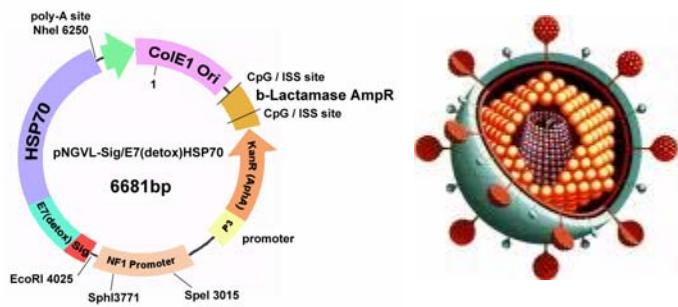
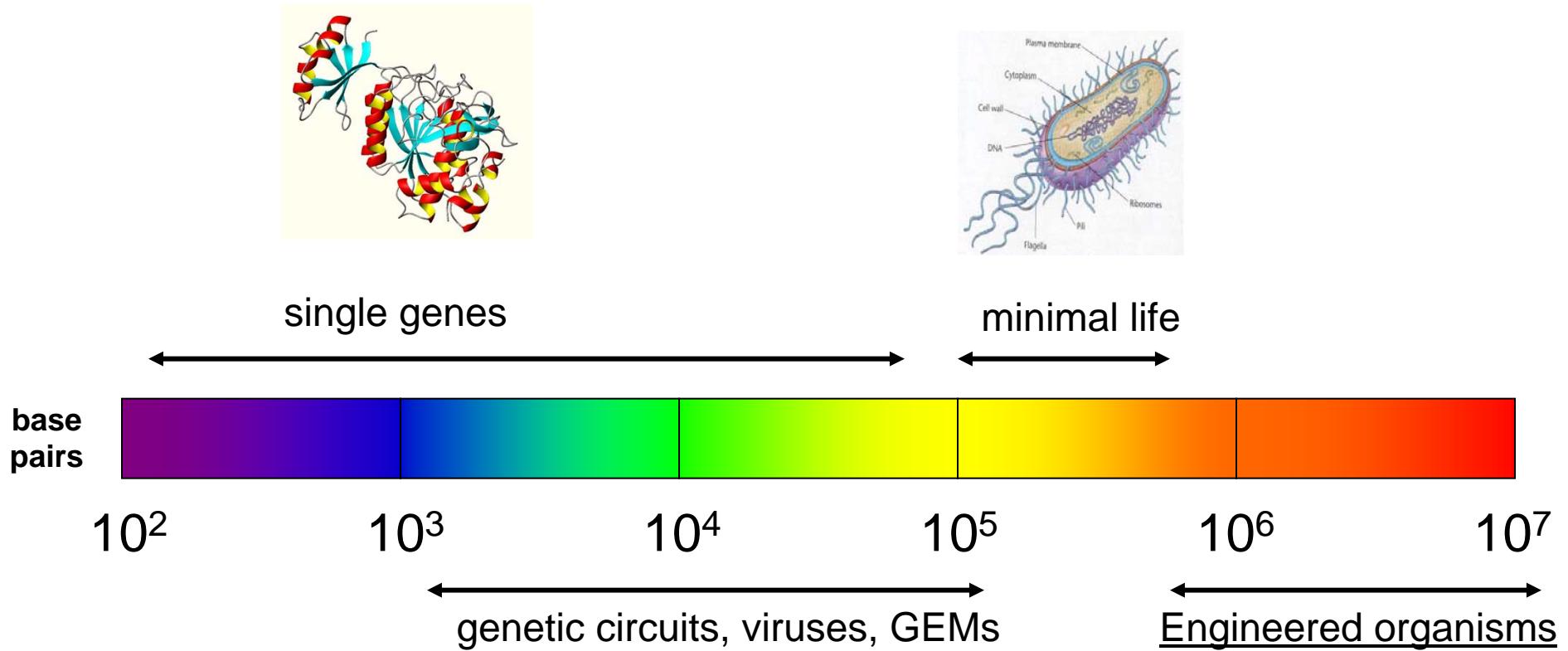
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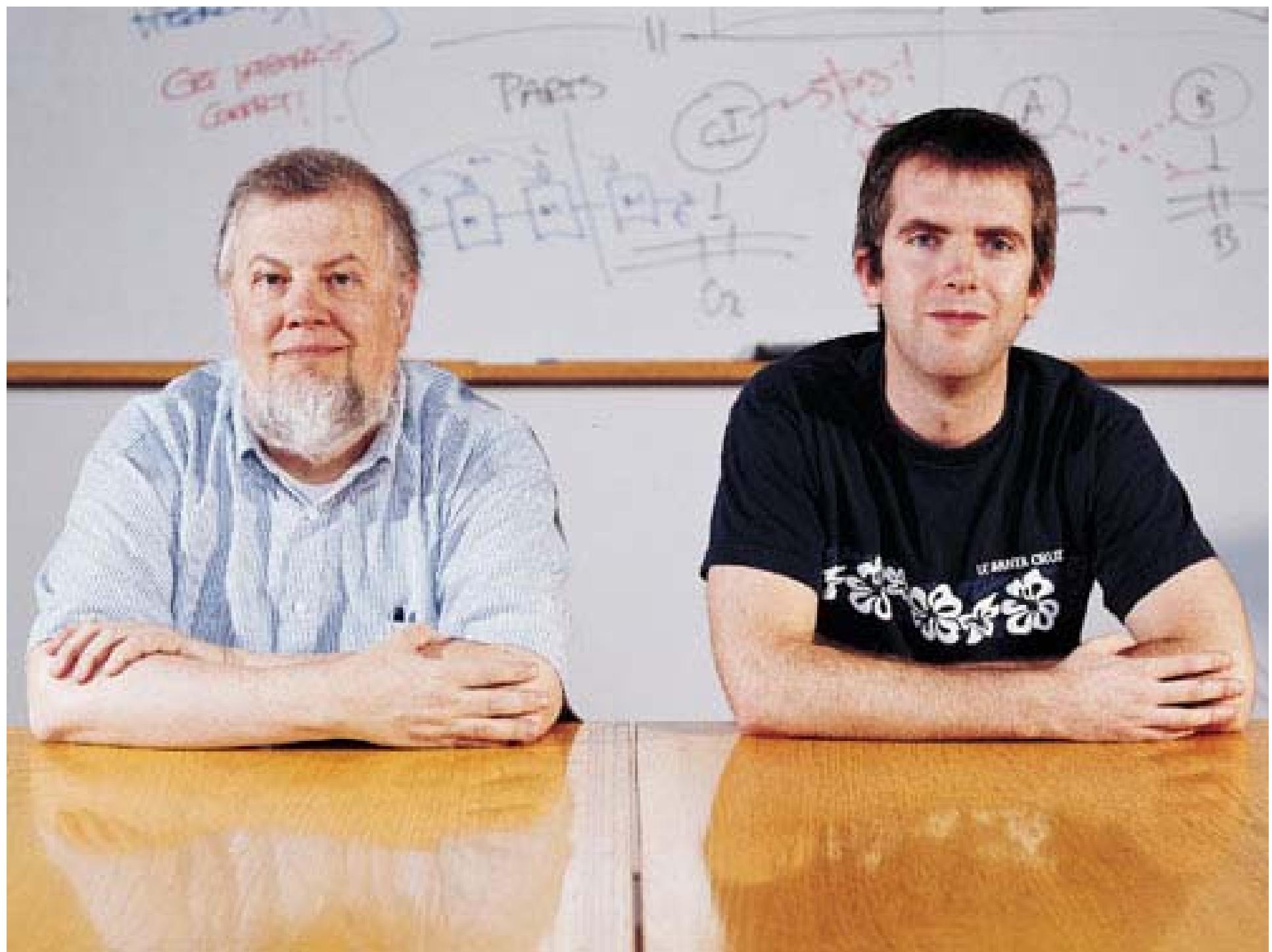
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Applications dependent on synthetic capabilities and \$







F1760

Sender Device

B0015

terminator

Name: B0015

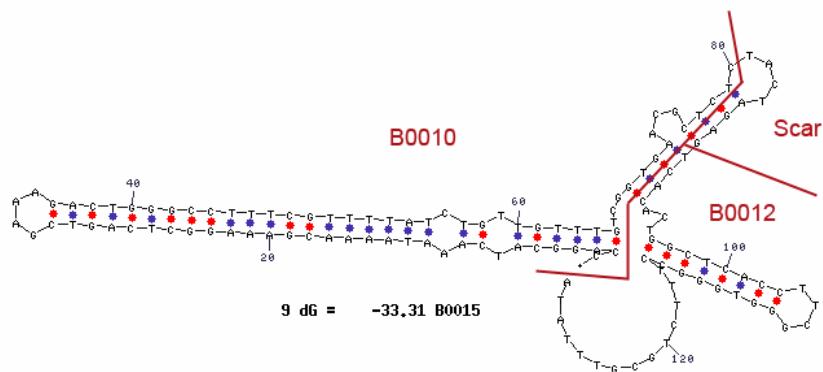
Type: Double terminator

Length 129 bp

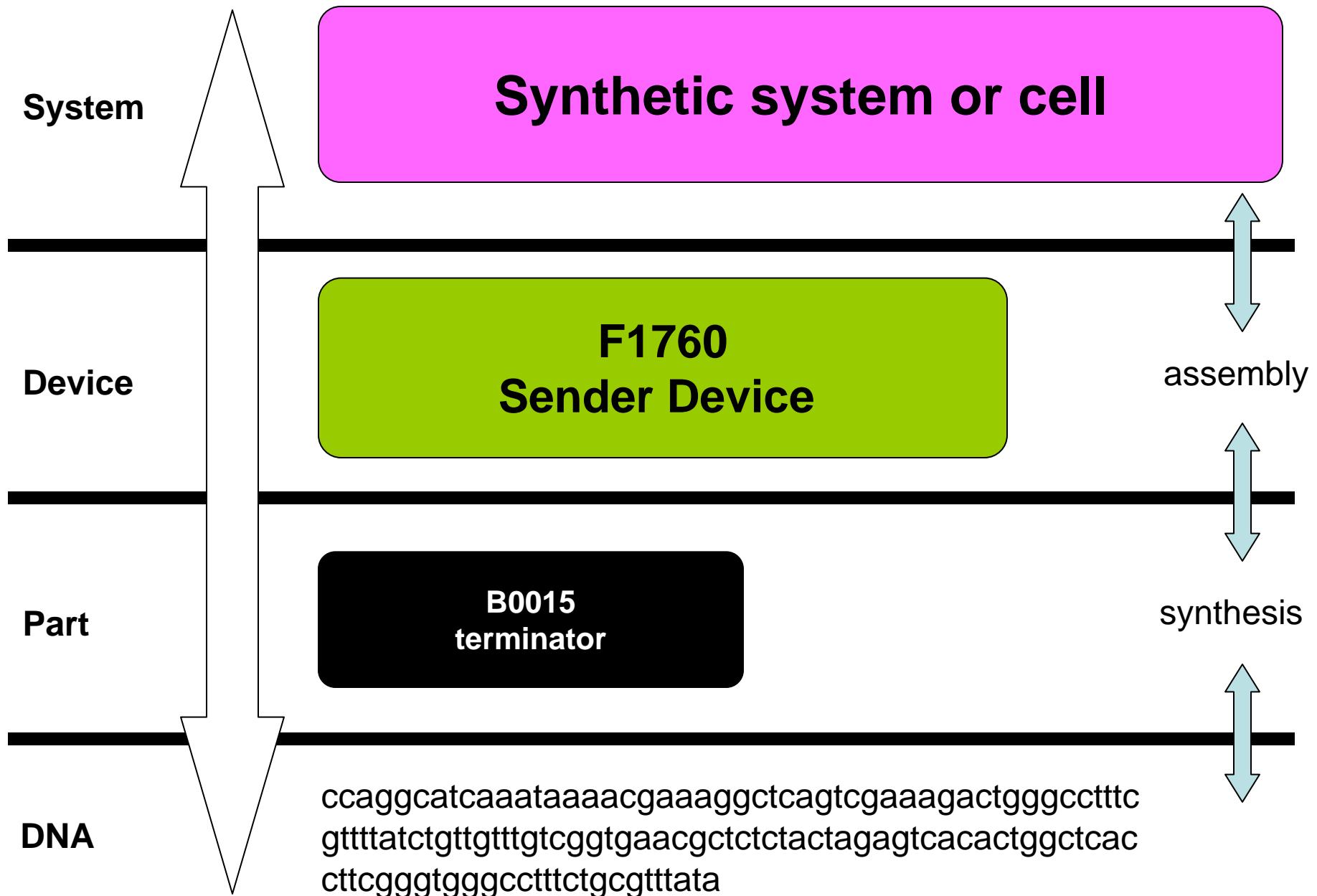
Designed by: Reshma Shetty

Forward efficiency: 0.984

Reverse efficiency: .295



STANDARDIZED DATA




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Transcriptional Regulators

Available repressible regulators (normally ON) [-?](#)
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-?	Name	Description	Direction	Control -?	Output Low High	Length
A	W BBa_I14032	promoter P(Lac) IQ	Forward			37
A	W BBa_R0040	promoter (tetR, negative)	Forward	aTc, tetracycline		54
A	W BBa_R0051	promoter (lambda cl regulated)	Forward	lambda cl		49

Available inducible regulators (normally OFF) [-?](#)
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-?	Name	Description	Direction	Control -?	Output Low High	Length
A	BBa_I12007	Modified lambda Prm promoter (OR-3 obliterated)	Forward	cl		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](#)
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-?	Name	Description	Direction	Control -?	Output Low 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

3OC₆HSL → PoPS Receiver

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



Authors:

Barry Canton [bcanton@mit.edu]

Anna Labno [alabno@mit.edu]

Last Update: 15 January 2007

Description

A transcription factor (LuxR, BBa_C0062) that is active in the presence of cell-cell signalling molecule 3OC₆HSL is controlled by a TetR-regulated operator (BBa_R0040). Device Input is 3OC₆HSL. 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 3OC₆HSL, exogenous

Output Swing: 0±1 to 503±1 GFP molecules cfu⁻¹ s⁻¹

Switch Point: 7±1 nM 3OC₆HSL, exogenous

LH Response: 9 min (t_{50%}), 27 min (t_{90%})

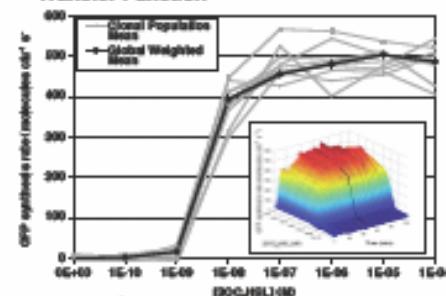
Key Parts

BBa_R0040: TetR-regulated operator

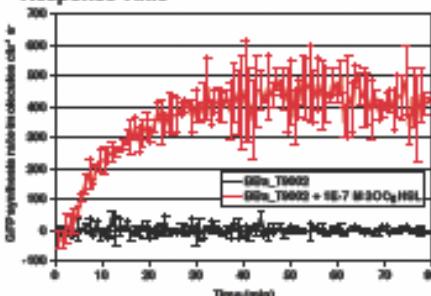
BBa_C0062: luxR ORF

BBa_R0002: LuxR-regulated operator

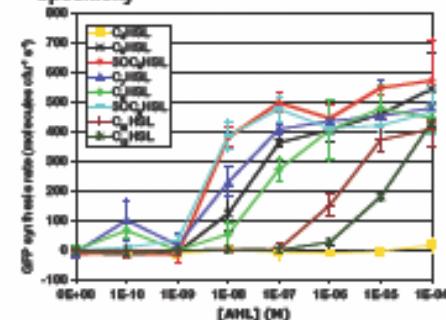
Transfer Function*



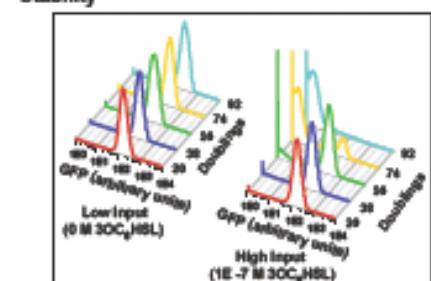
Response Time*



Specificity*



Stability**



Signaling Devices

Demand (low/high Input)

Translational: 256/8048 ribosomes cfu⁻¹
3.8E3/1.2E5 charged tRNA cfu⁻¹ s⁻¹

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 3OC₆HSL

Stability (low/high Input)

Genetic: >92/74 replication events**

Performance: >92/74 replication events**

Conditions (abridged)

Output: Indirect via BBa_E0240

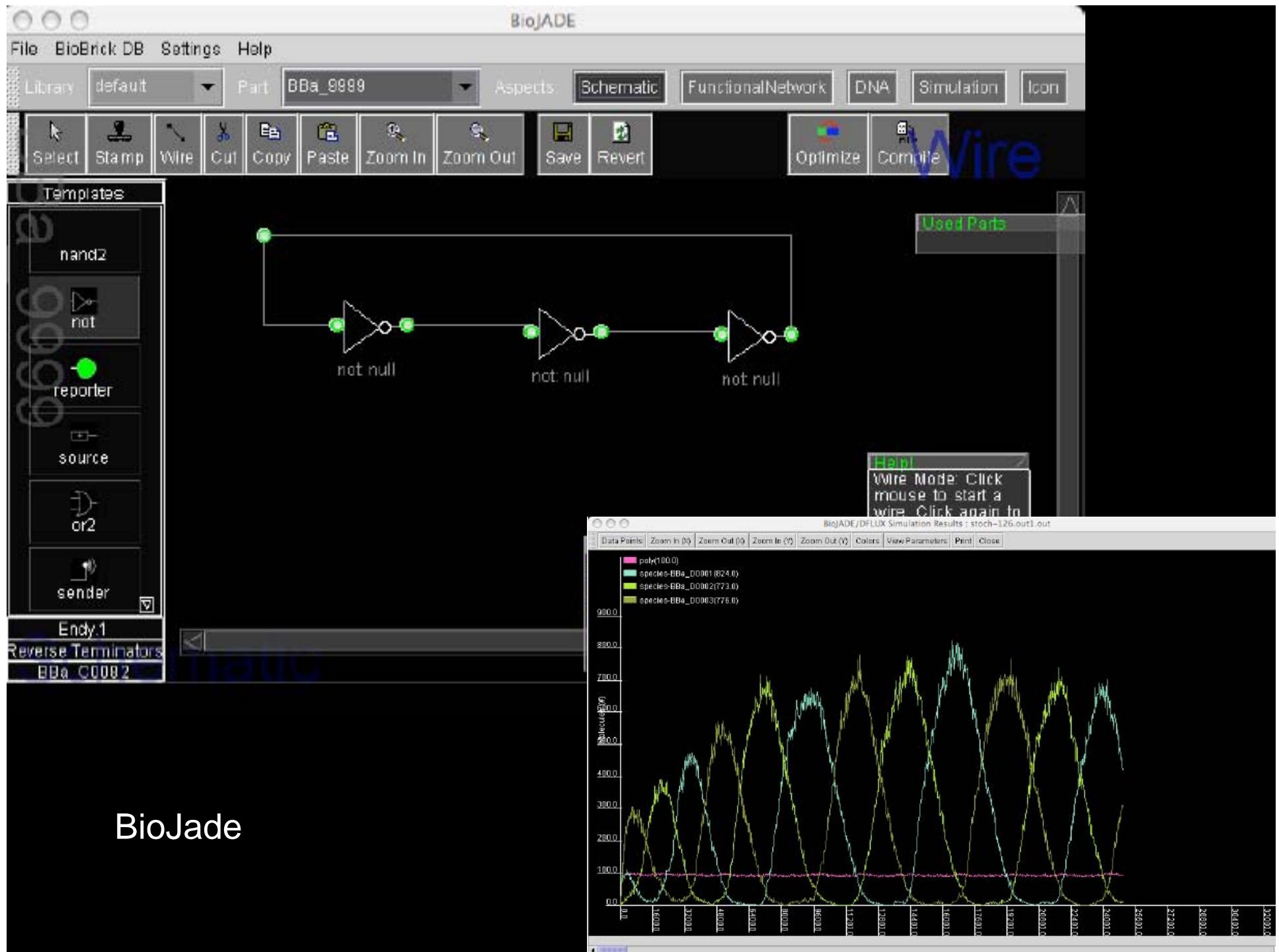
Vector: pSB3K3

Chassis: MG1655

Culture: Supplemented M9, 37°C

*Equipment: PE Victor3 plate reader

**Equipment: BD FACScan cytometer



BioJade



Training DNA programmers

Synthetic biology requires an unprecedented level of interdisciplinary cooperation, fewer laboratory skills, and less overhead than conventional genetic engineering.

Cooperative yet competitive

Open education format...

Shares:

- DNA parts
- DNA code
- Protocols
- Experience
- Publications
- One big rule: share back!





iGEM 2007 Wiki

International Genetically Engineered Machine Competition

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Results of the Jamboree



sat & sun, nov 3-4

iGEM 2007 is now officially concluded! Congratulations to all!

- [Results](#)
- [See the medal winners](#)
- [Media](#) (including links to videos and [flickr™ photo gallery](#))
- [Learn about iGEM 2008](#)

iGEM?

Hundreds of undergraduates all over the world spend their summer making Synthetic Biology a reality by participating in the annual International Genetically Engineered Machine competition.

iGEM through the years

- [2008](#)
- [2007](#)
- [2006](#)

[Learn More](#)

calendar

Jamboree roster + fees due *fri 12 Oct 12*

iGEM wiki frozen + parts *fri postmarked 26 Oct 07*

Jamboree! *sat-sun 3-4 nov 07*

Registry + BioBrick foundation workshops *sun-tue 4-6 nov 07*

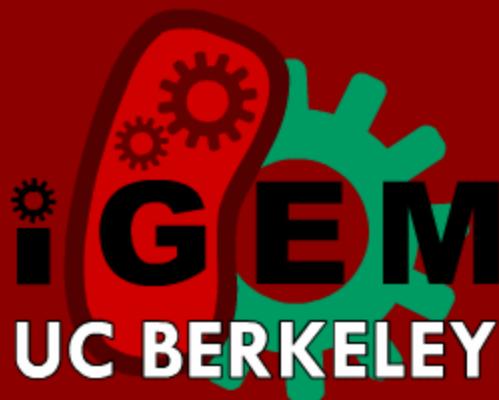




Open source biology ...



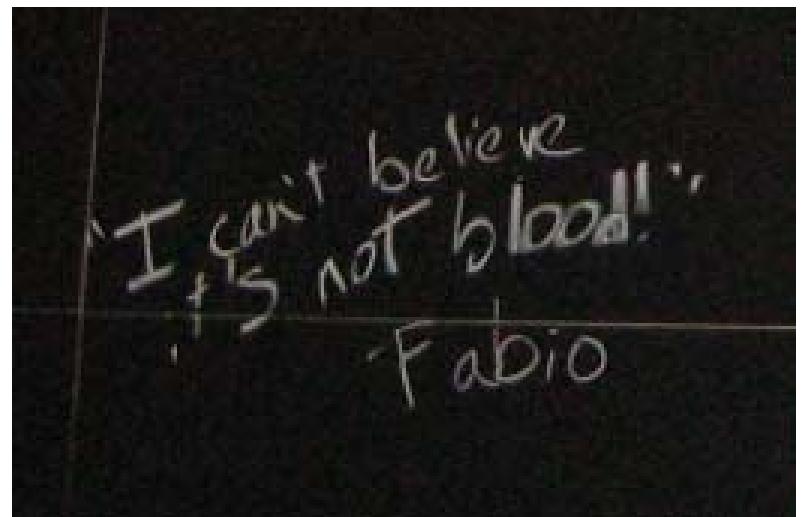
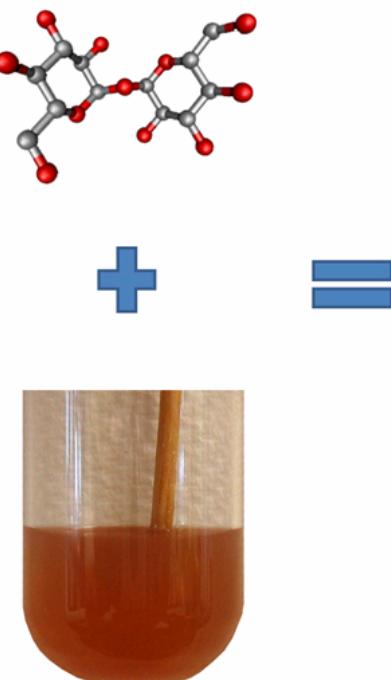
- Maximizes innovation
- Empowers communities
- Generates expertise
- Legal and technical standards

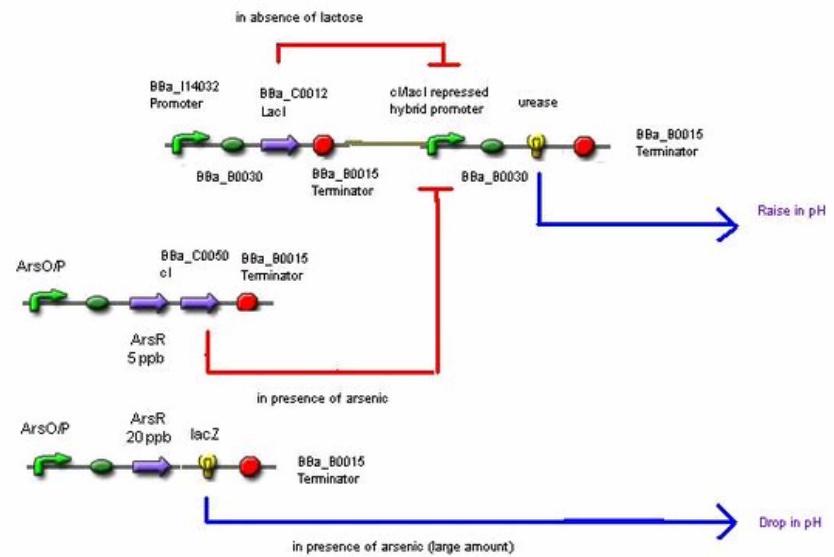


BACTOBLOOD

The necessity of inexpensive, disease-free, and universally compatible blood substitutes is undisputed. There are currently no blood substitutes approved for use in the US or the UK, and whole blood is almost always in short supply. Developing countries have the greatest need for blood transfusions, yet many lack the necessary donation and storage infrastructure and the required pool of healthy donors. To address this problem, we are developing a cost-effective red blood cell substitute constructed from engineered *E. coli* bacteria. Our system is designed to safely transport oxygen in the bloodstream without inducing sepsis, and to be stored for prolonged periods in a freeze-dried state.

Support for Berkeley iGEM 2007 was generously provided by SynBERC and The Camille and Henry Dreyfus Foundation, Inc.







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Sci-Tech



Under a magnification of 6836x, this scanning electron micrograph (SEM) depicts a number of Gram-negative Escherichia coli bacteria of the strain O157:H7. (Courtesy of Centers of Disease Control and Prevention)

Alberta team trying to turn E. coli into fuel

Updated Mon. Nov. 5 2007 8:12 AM ET

The Canadian Press

CAMBRIDGE, Mass. -- A University of Alberta team trying to turn E. coli into fuel has earned a first place finish in the energy category at an international genetic engineering competition at MIT.

Andrew Hessel, a consultant with the Alberta Ingenuity Fund who has helped teams from three Alberta universities compete, says while none of the teams from the University of Calgary, the University of Lethbridge or the U of A made it to the final competition, he calls it a fantastic educational experience.



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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.

The New York Times

English, Algebra, Phys Ed ... and Biotech



Jim Wilson/The New York Times

George Cachianes, left, formerly of Genentech, teaches biotechnology at Lincoln High School in San Francisco.

MAY 3, 1982

\$1.50

TIME

COMPUTER GENERATION A New Breed of Whiz Kids

1.3%
INFLATION VANISHES!
At Least for
A Month



TRS-80 COMPUTER

CAT. NO. 68-2030

whiz kids™

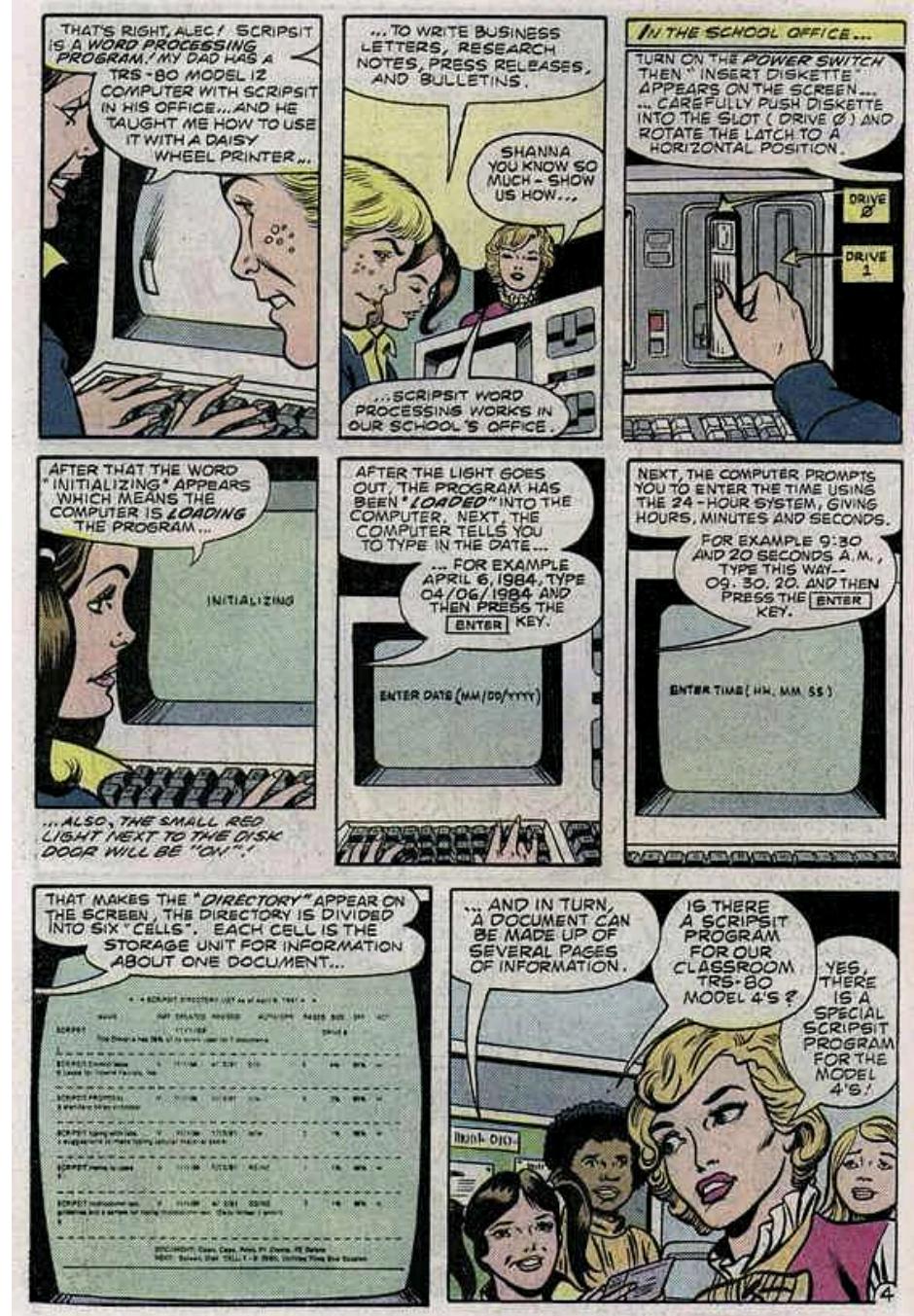
ALEC AND
SHANNA
STARRING IN

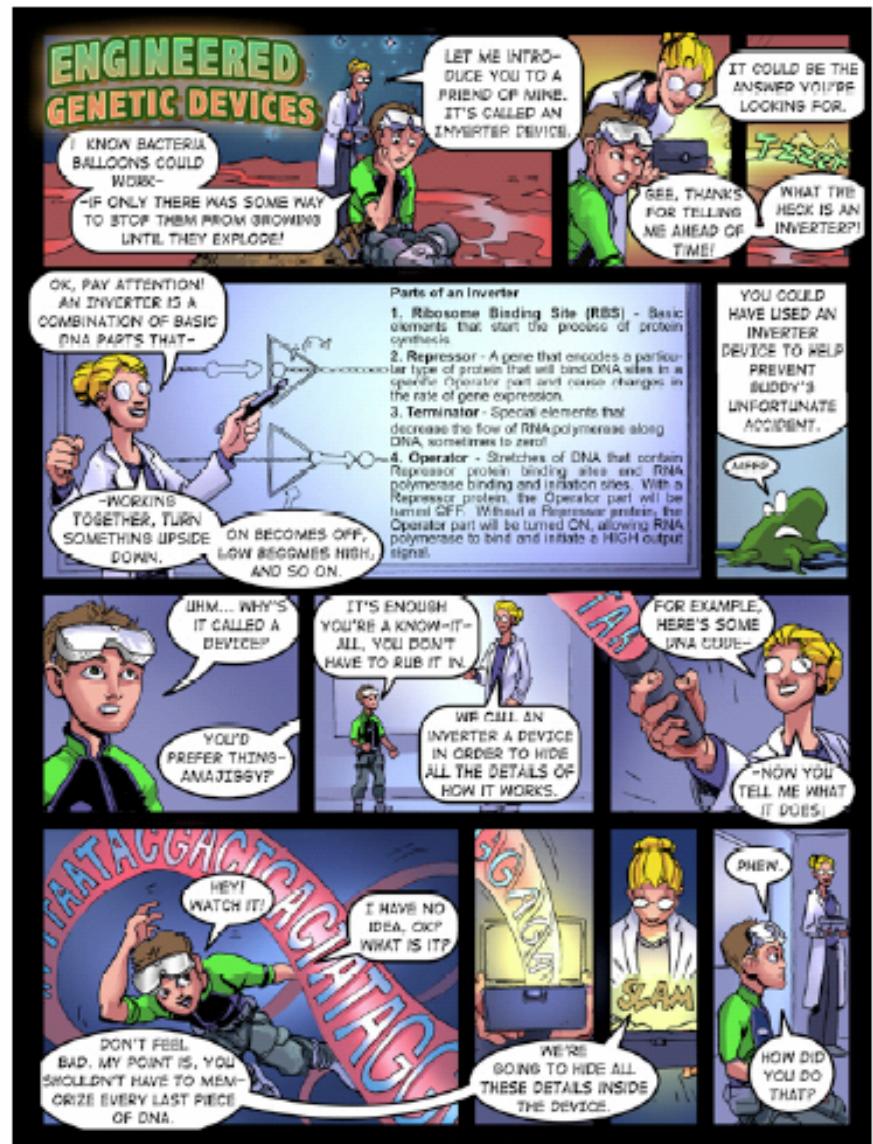
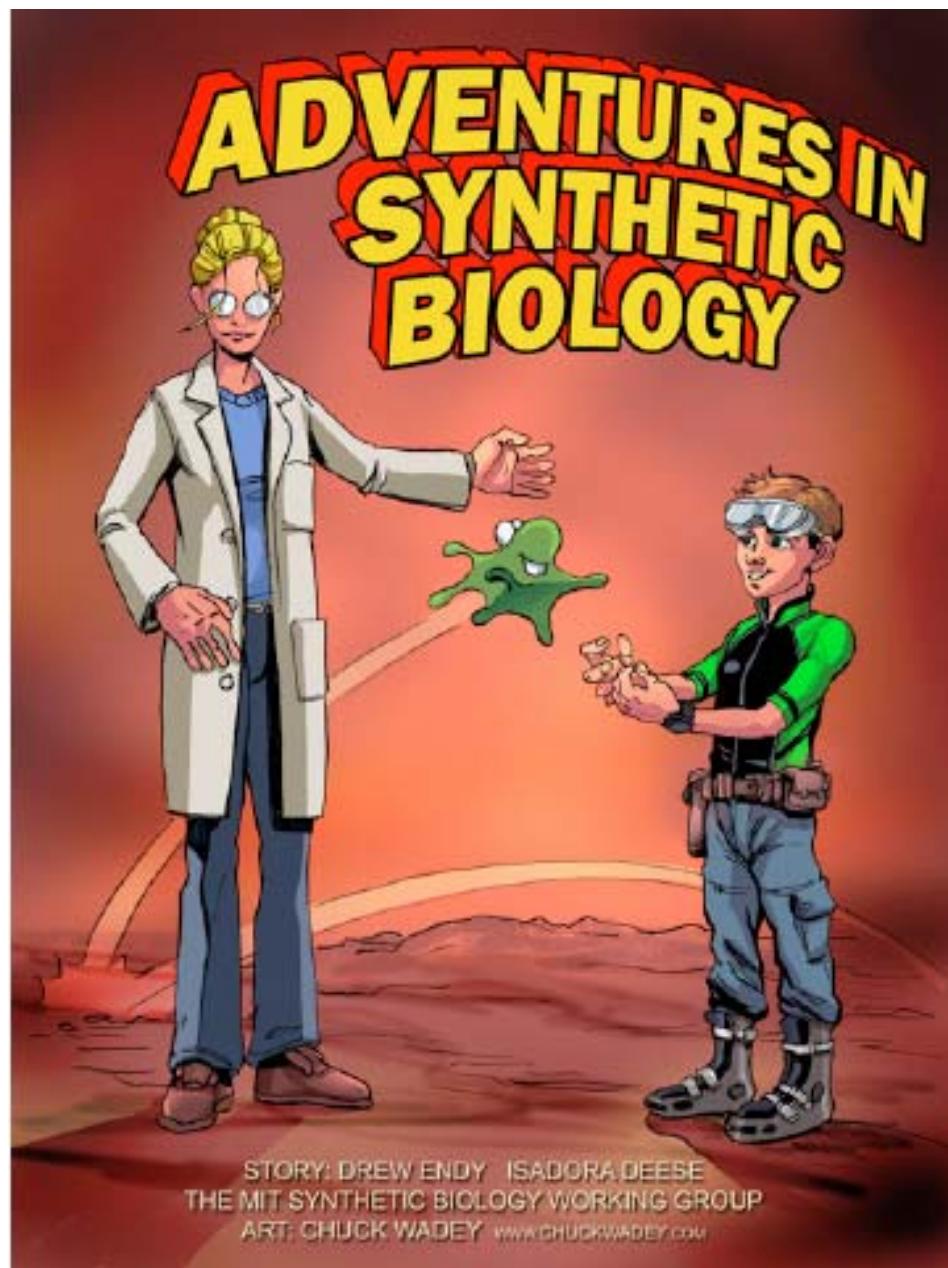
THE COMPUTER TRAP

A comic book illustration of four people on a boat deck at night. A man in a green sweater is on the right, another man in a brown jacket is in the center, a woman in a purple sweater is on the left, and a man in a blue shirt is partially visible behind the woman. They are working with ropes and equipment. The background shows a city skyline across the water. A yellow starburst in the bottom left contains the text "COMPLIMENTS OF Radio Shack® The Name in Classroom Computing™" and "DICK AYERS AND GENE STONE".

COMPLIMENTS OF
RadioShack
The Name in Classroom Computing™

DICK
AYERS
AND
CHIC
STONE







ELECTRONICS LAB



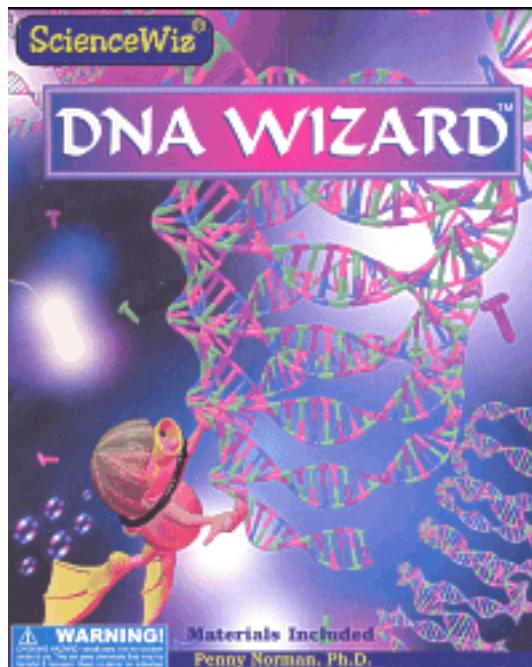
- Start a great hobby in electronics
- No prior knowledge needed to assemble
- Spring-coil connections make it safe and easy for anyone to use
- Includes detailed step-by-step illustrated manual for easy project construction
- Build a radio, AM broadcast station, electronic organ, kitchen timer, logic circuits and more
- Comes with built-in speaker, 7-segment LED display, two fully integrated circuits and rotary controls

130 in 1

THE FUN WAY TO LEARN ABOUT ELECTRONICS
AND STUDY THE WONDERS OF SCIENCE

ELECTRONIC
130 in 1
LAB

ITEM NO. MX905
Requires 6 "AA" batteries (not included)
For ages 10 and up



Projects with DNA

For ages 8 and up
Adult Supervision Required

Materials included except for the items listed.
Through play, hands-on projects, patterns and puzzles
this book and kit explores the amazing DNA story.

Build a DNA ladder.

Extract DNA

Heat SHOCK!

Decode the code of life

Grow glowing cells

Is it a boy or girl?

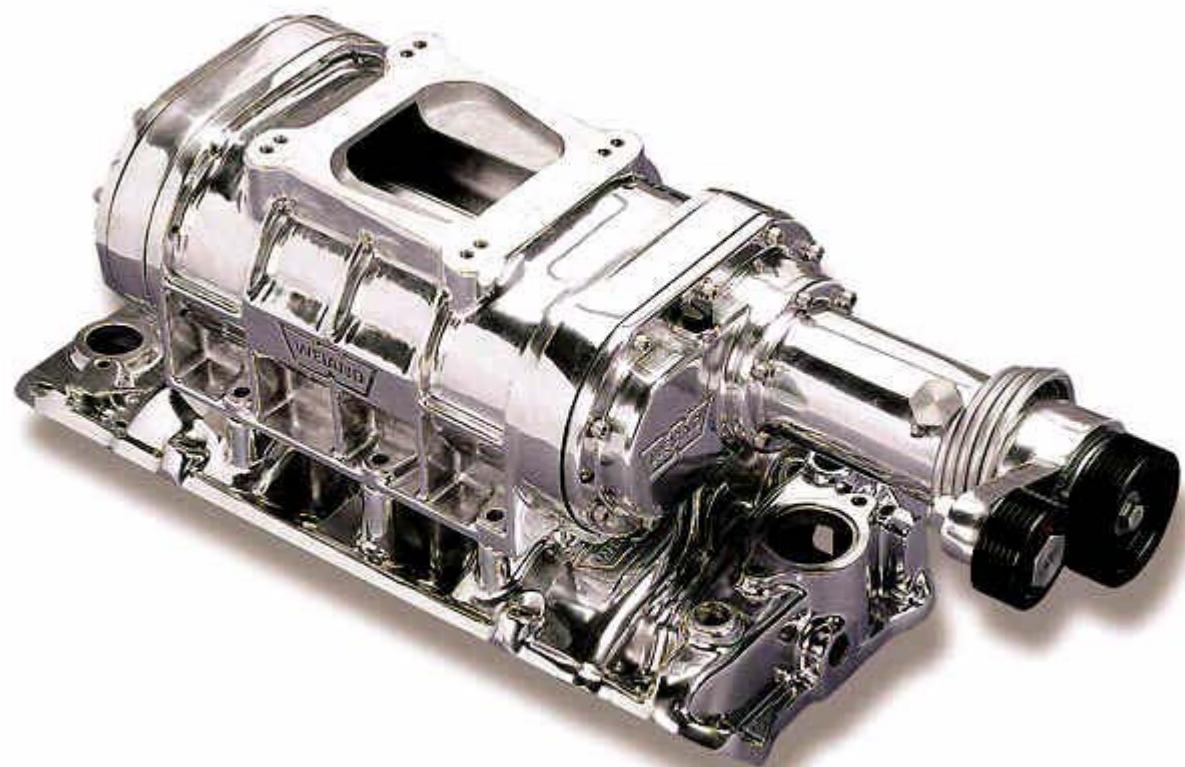
Solve the chromosome puzzle.

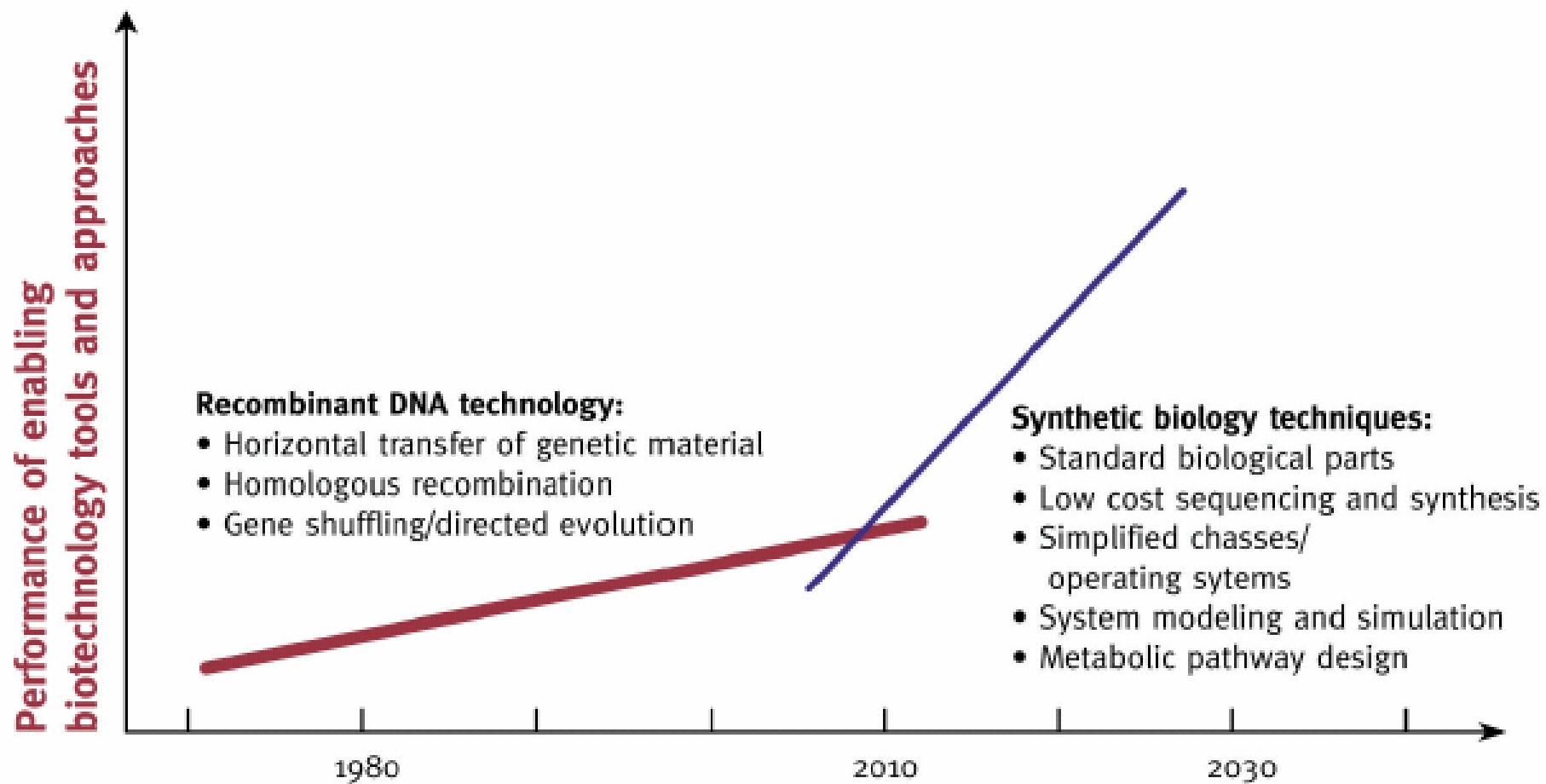
Ooey, Gooey, DNA!

Dress up for sterile techniques.

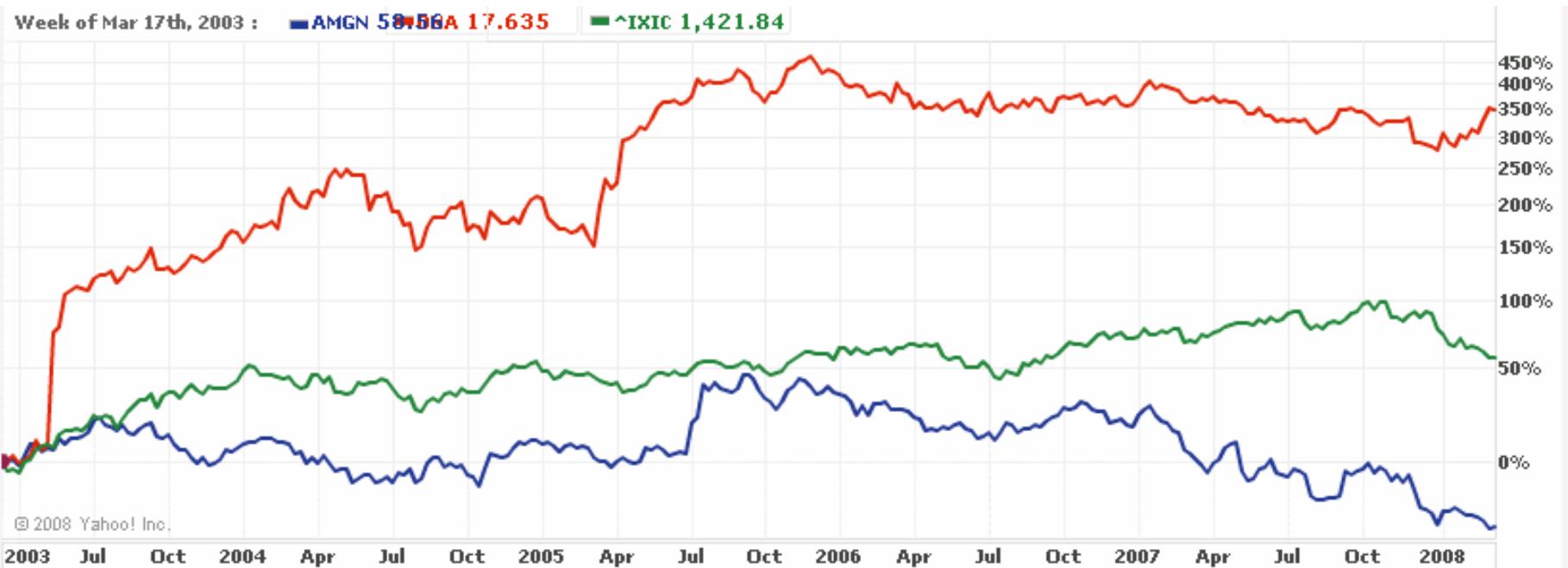
Quality time, quality learning, quality play.

Next generation biotechnology





Source: Bio era





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Stop Cloning Genes SYNTHESIZE THEM!

Rapid, high-quality,
low-cost gene synthesis



Gene
Synthesis



Constructed
Variant
Libraries



Constructed
Operons &
Operon Variant
Libraries

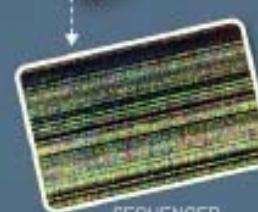
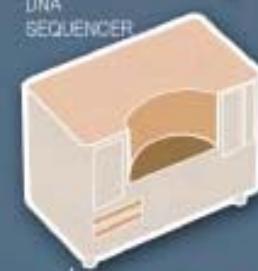


Genomic
Engineering

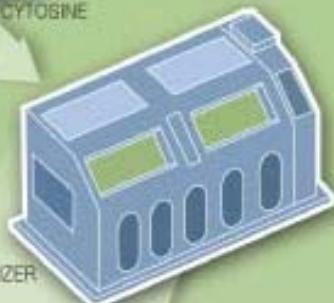


Sequencing

DNA is collected from the world's oceans and the soil.



Programming the Genetic Code



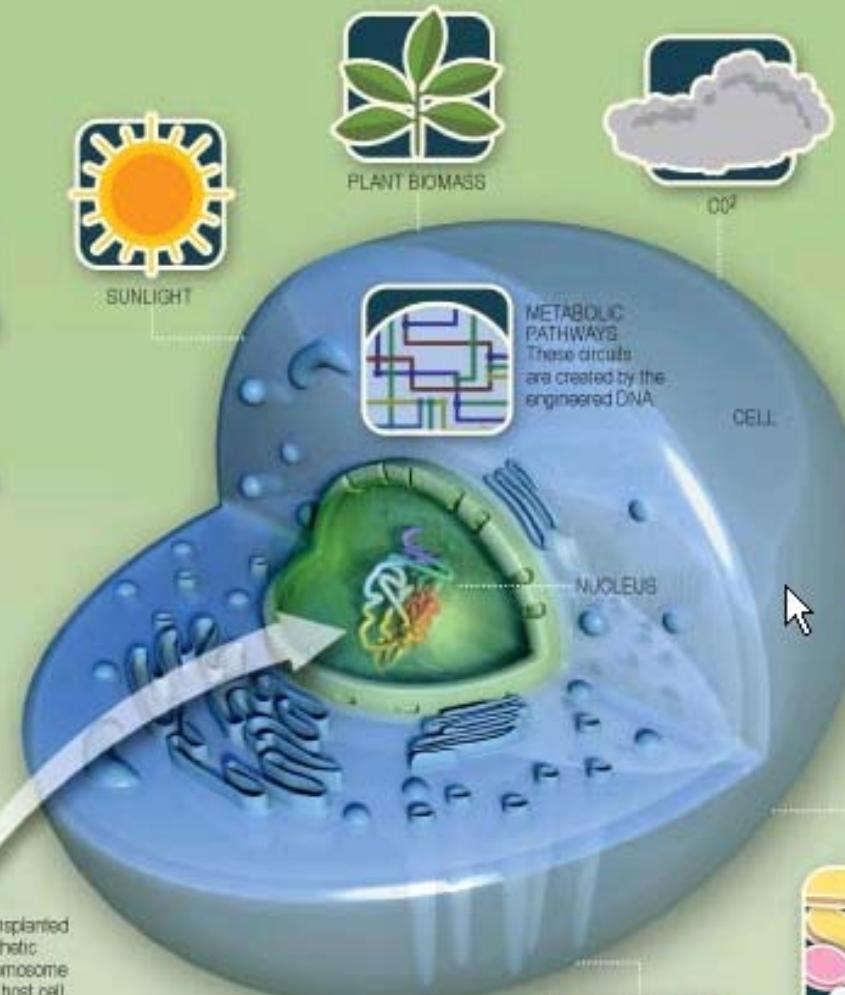
Overlapping synthetic oligonucleotides



Transplanted synthetic chromosome into host cell



Bioenergy or Specific Chemical Production



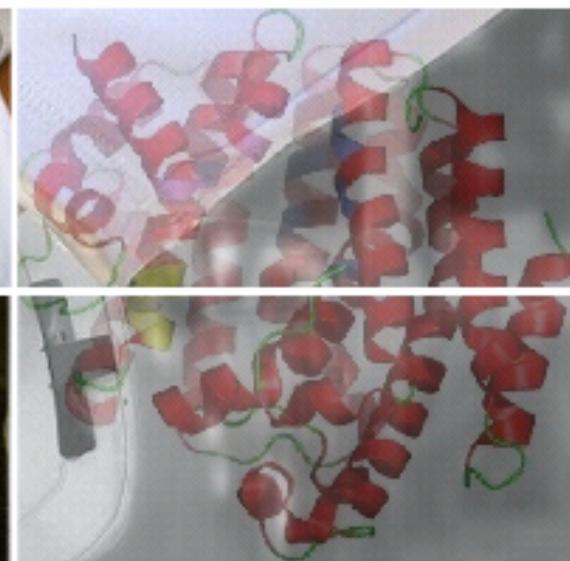
GENE FUNCTIONS

- DNA Replication
- Cell Reproduction
- Protein Synthesis
- Cellular Metabolism
- Cellular Signaling
- Molecule Transport



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Realizing the Promise of Synthetic Biology

COMPANY PROFILE

TECHNOLOGY

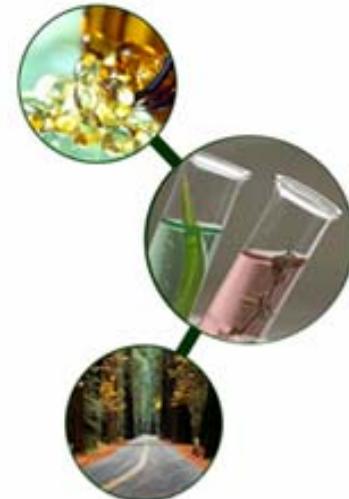
CURRENT PROJECTS

NEWS

CAREERS

Welcome

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



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Investors

Funded by a syndicate of well-respected, top-tier venture capital firms, Archemix has raised over \$100 million to date.

The Series B round (\$53M, completed 1Q 2004) was led by Highland Capital Partners, and included all of the Series A investors and Athenian Venture Partners.

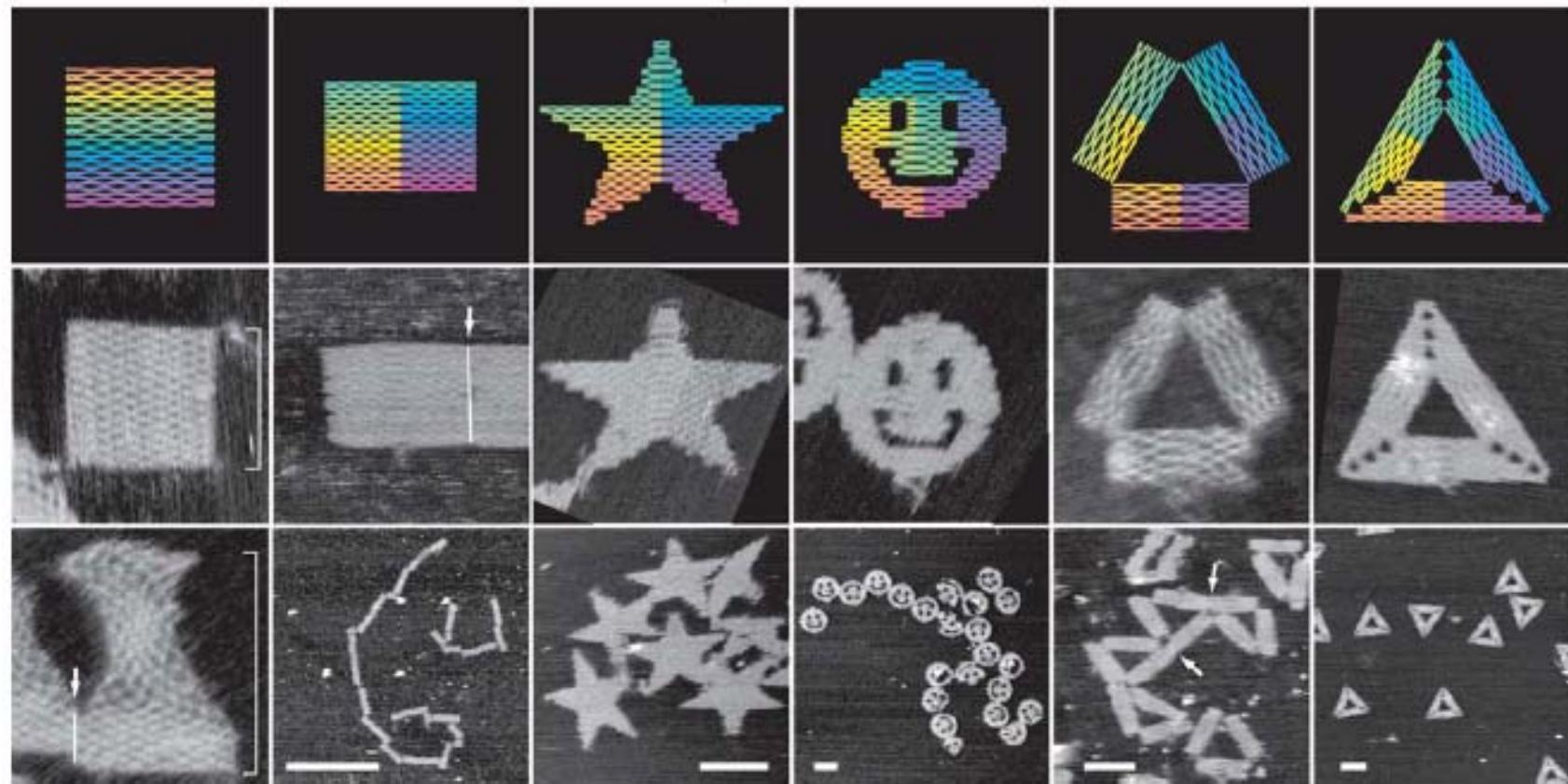
The Series A round (\$52M, completed 3Q 2002) included lead investors Atlas Venture, Prospect Venture Partners and SV Life Sciences. Other investors included Rho Ventures, Care Capital, MDS Capital, POSCO BioVentures, and US Trust Private Equity.

Archemix and Merck KGaA Sign Strategic Alliance

Collaboration to Focus Primarily on Cancer Therapeutics Using Novel Aptamer Technology

Folding DNA to create nanoscale shapes and patterns

Paul W. K. Rothemund¹





Predator-Prey *E. coli* Mol. Sys. Bio

Within 10 years, if present trends continue...

- Synthesis and boot-up will become integrated and practical on the desktop
- 10 MB of DNA synthesis will cost <\$10K
- Drag and drop metabolic design software, and parts libraries, will be open sourced
- A substantially different academic and industry landscape than exists today

Summary

- Synthetic biology transforming life science into an information science
- Multidisciplinary
- Accelerating technology development and globally fueling innovation and competition
- IT industry-type dynamics, but greater ramifications for society
- Open source may play a crucial role

