

# Synthetic Biology

*Risks, rewards, and opportunities*

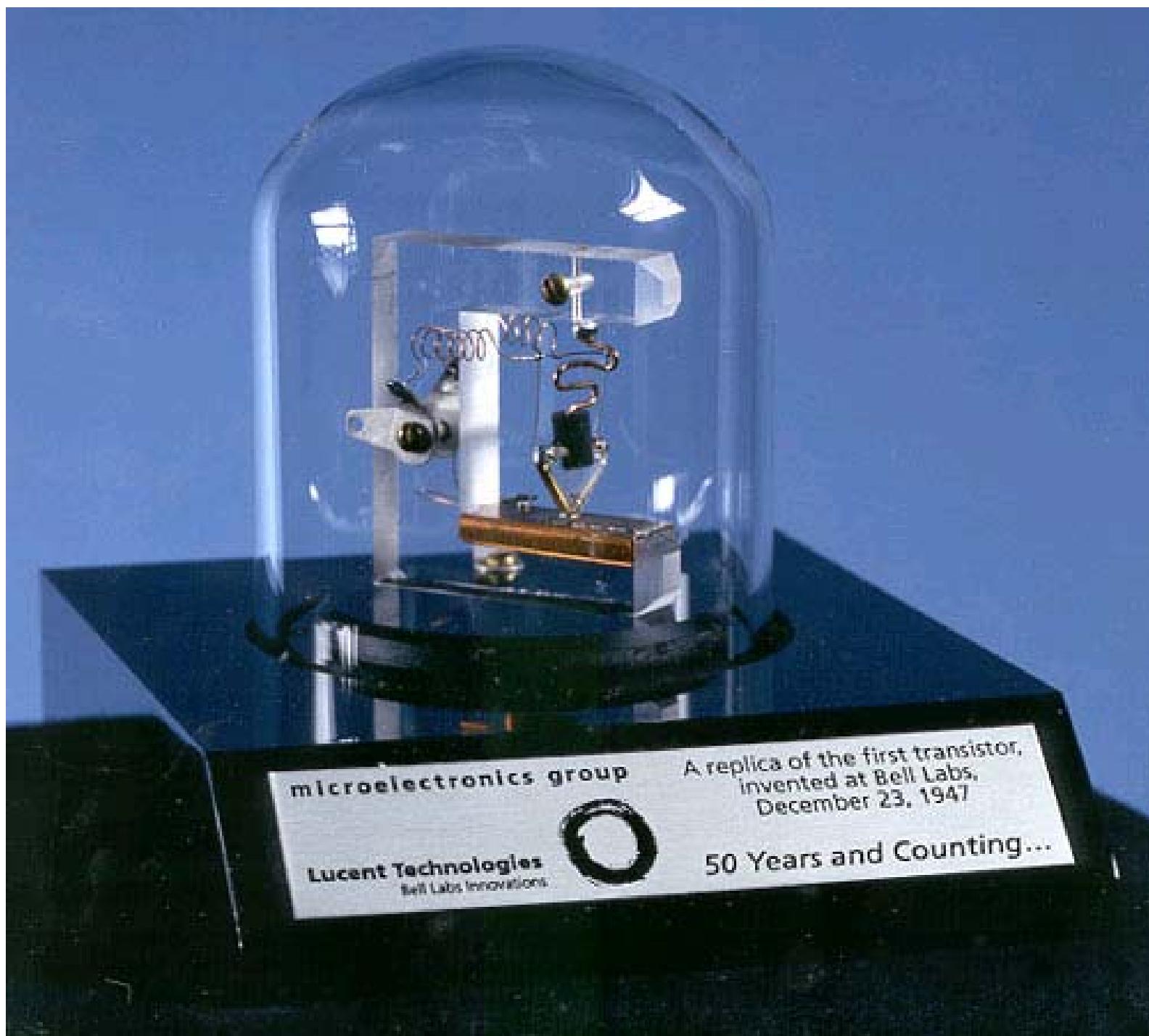
Andrew Hessel

[ahessel@gmail.com](mailto:ahessel@gmail.com)

Cross Cancer Institute, October 23 2007

**Synthetic biology is a basket of technologies that facilitate the engineering of living organisms**

**Potentially the single most important technology of this century...**

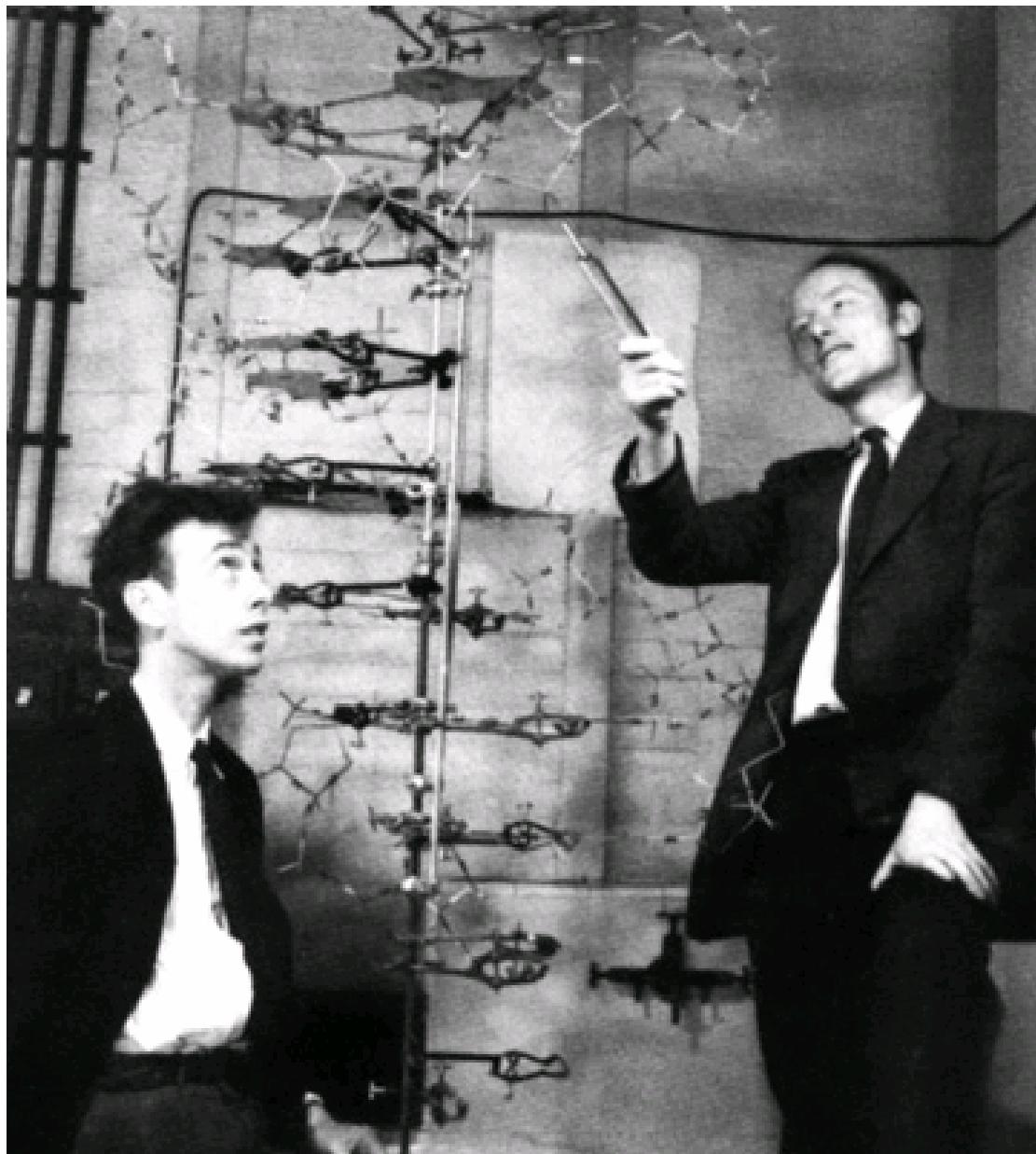


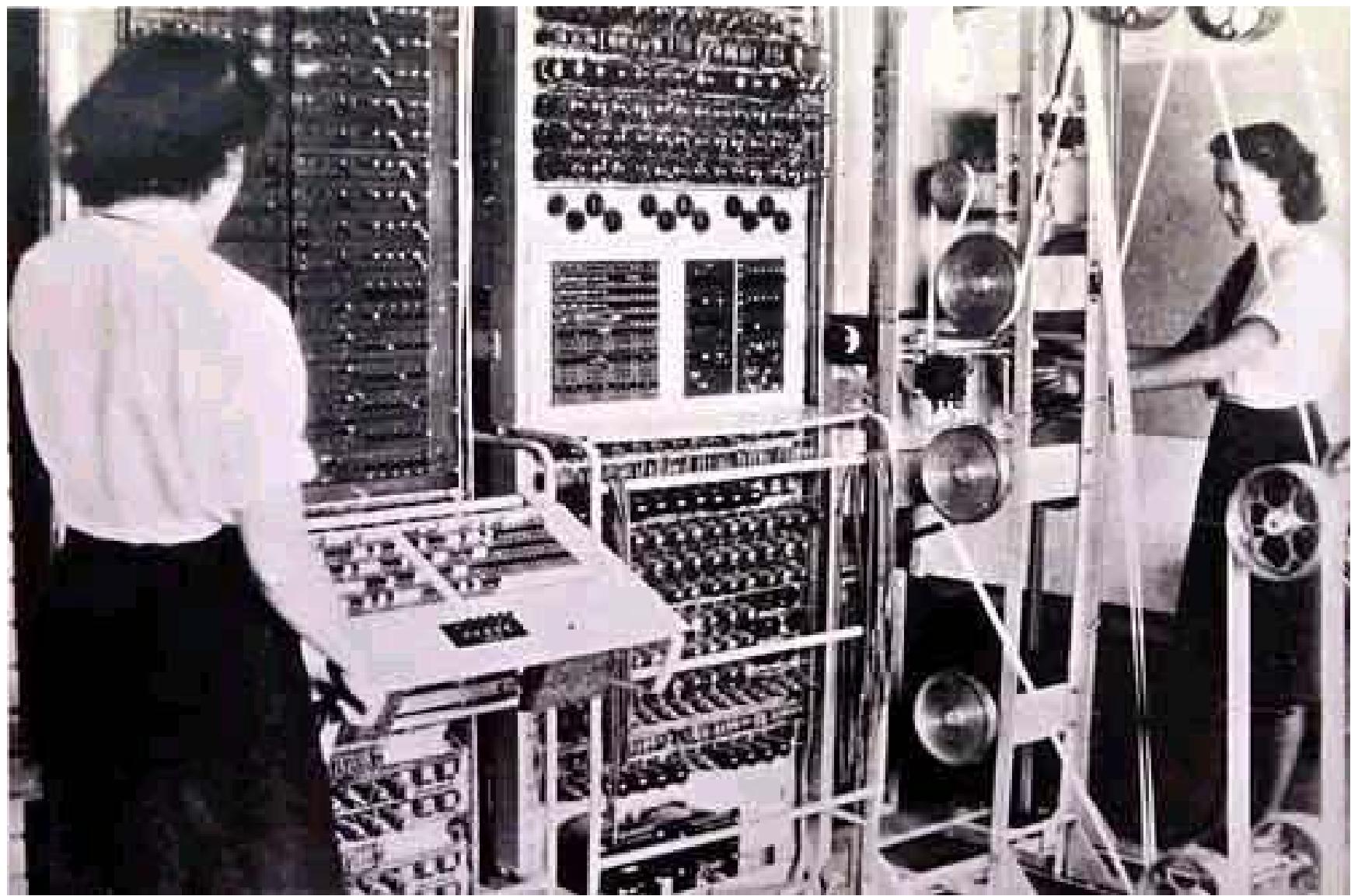
microelectronics group

Lucent Technologies  
Bell Labs Innovations

A replica of the first transistor,  
invented at Bell Labs,  
December 23, 1947

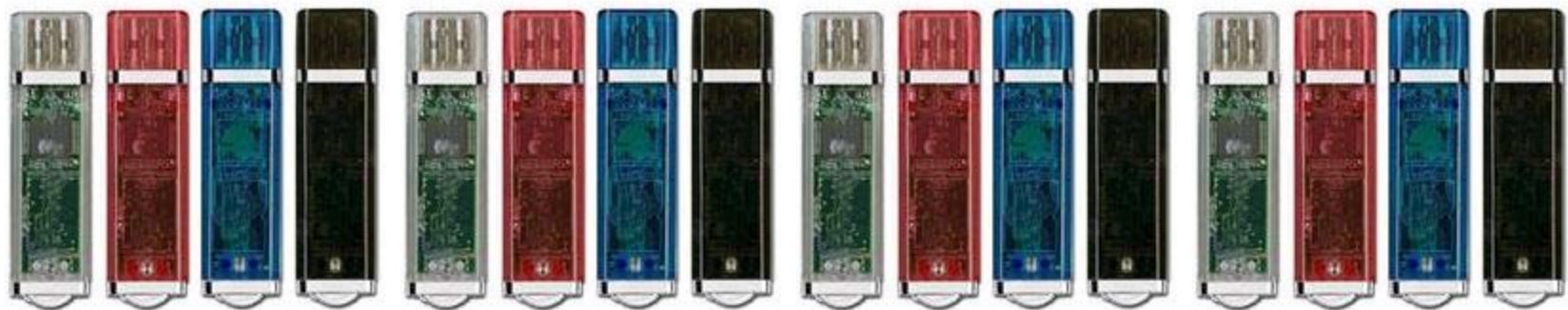
50 Years and Counting...

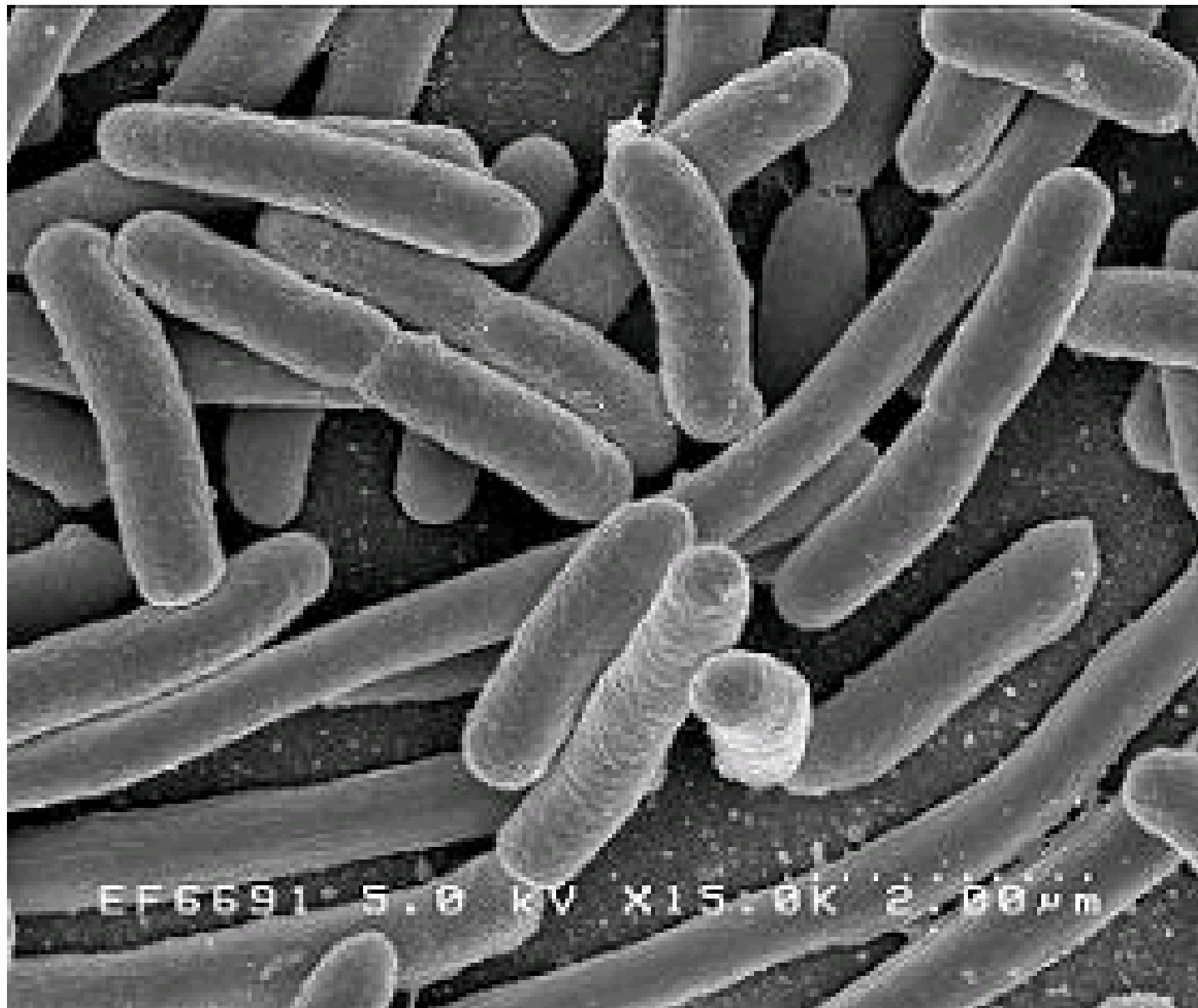




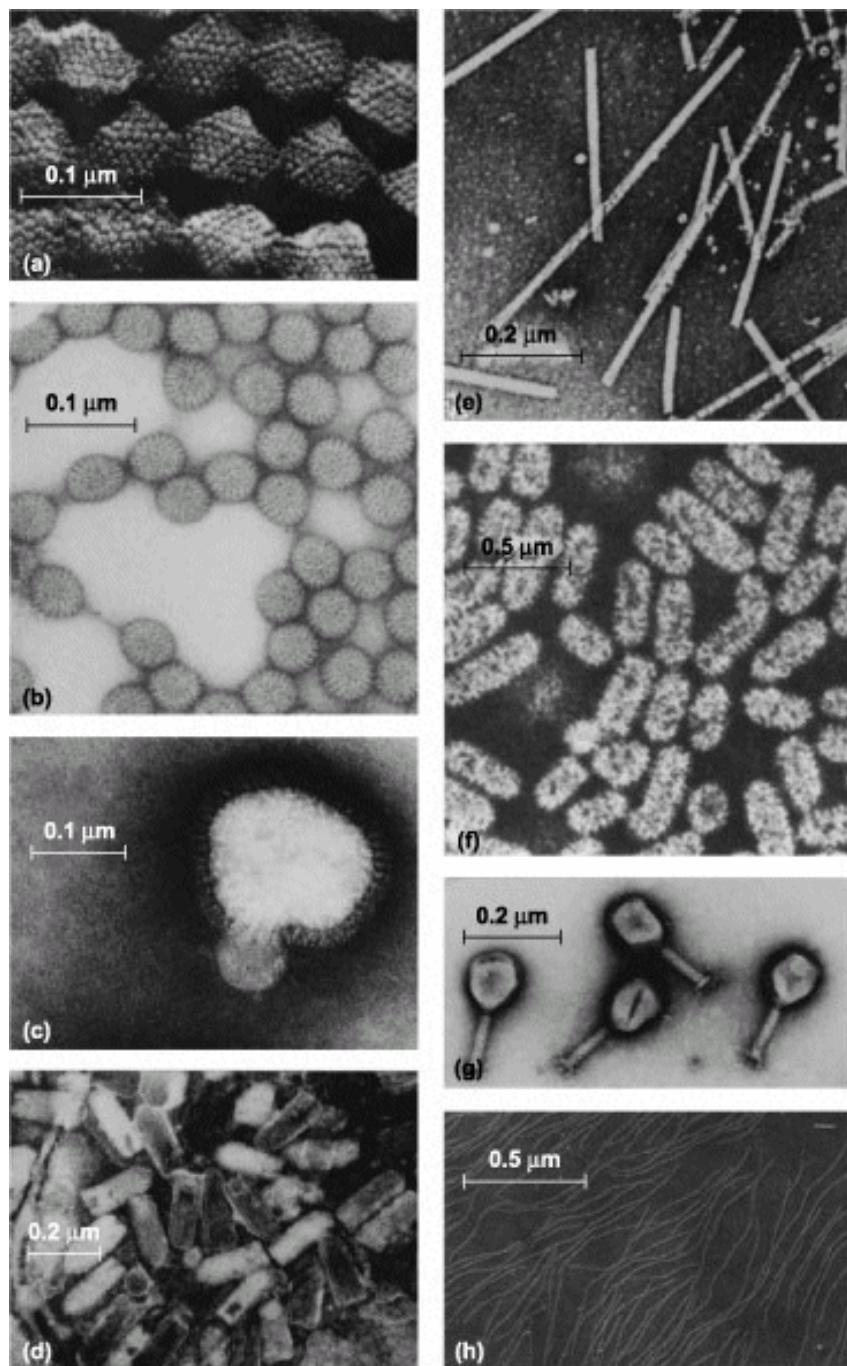








EF6691 5.0 kV X15.0K 2.00μm



Bits (0s,1s) encode information for digital electronic processors (computers)

DNA encodes information for analog biochemical processors (cells)

DNA is source code for biological systems

**Change the code, change metabolism**

# Genomes

are special programs that encode:

- Instructions for biochemical processors
- Machinery to duplicate the processor and install the program onto processors

*Equivalent in computing not to an operating system but to all the software it would take to run a production line at Apple or Dell Inc.*



danielig 072006 - S3is

C:\Command.com

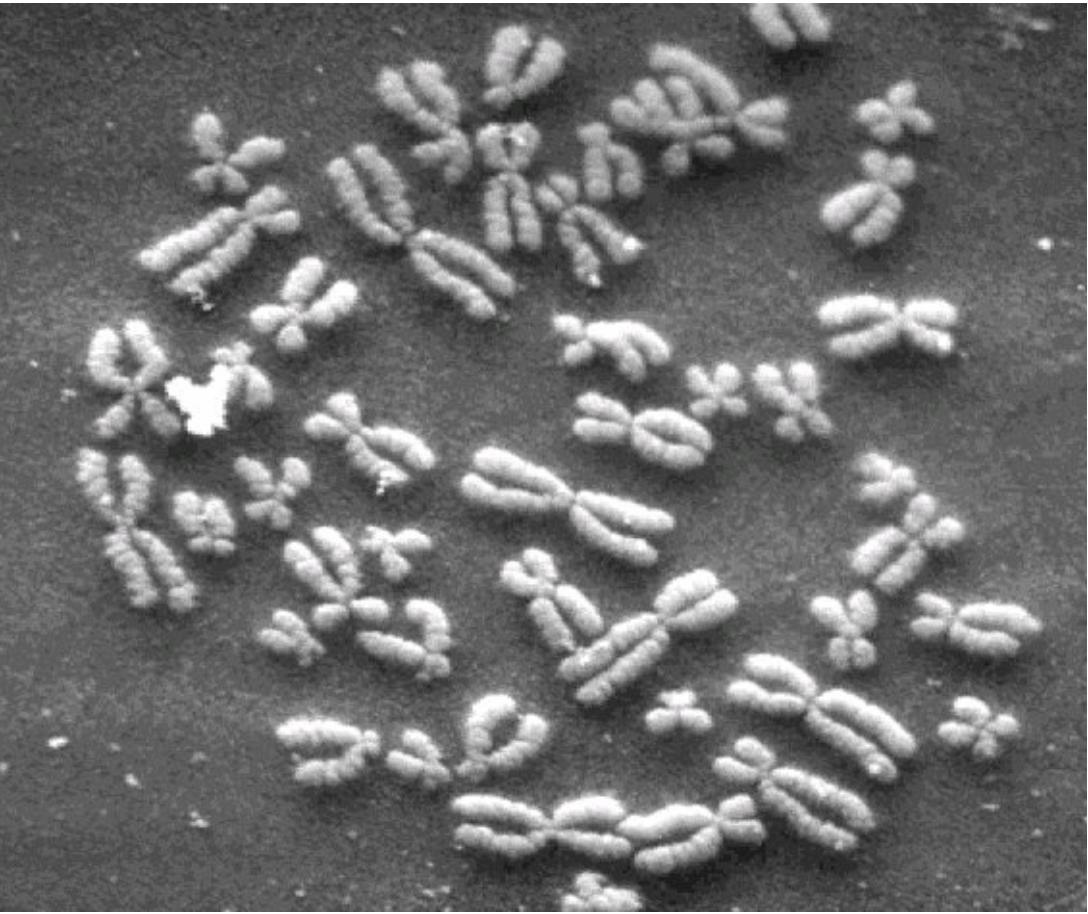
File Edit View Insert Options Window Help

16 32 64 1 2 4 H D N

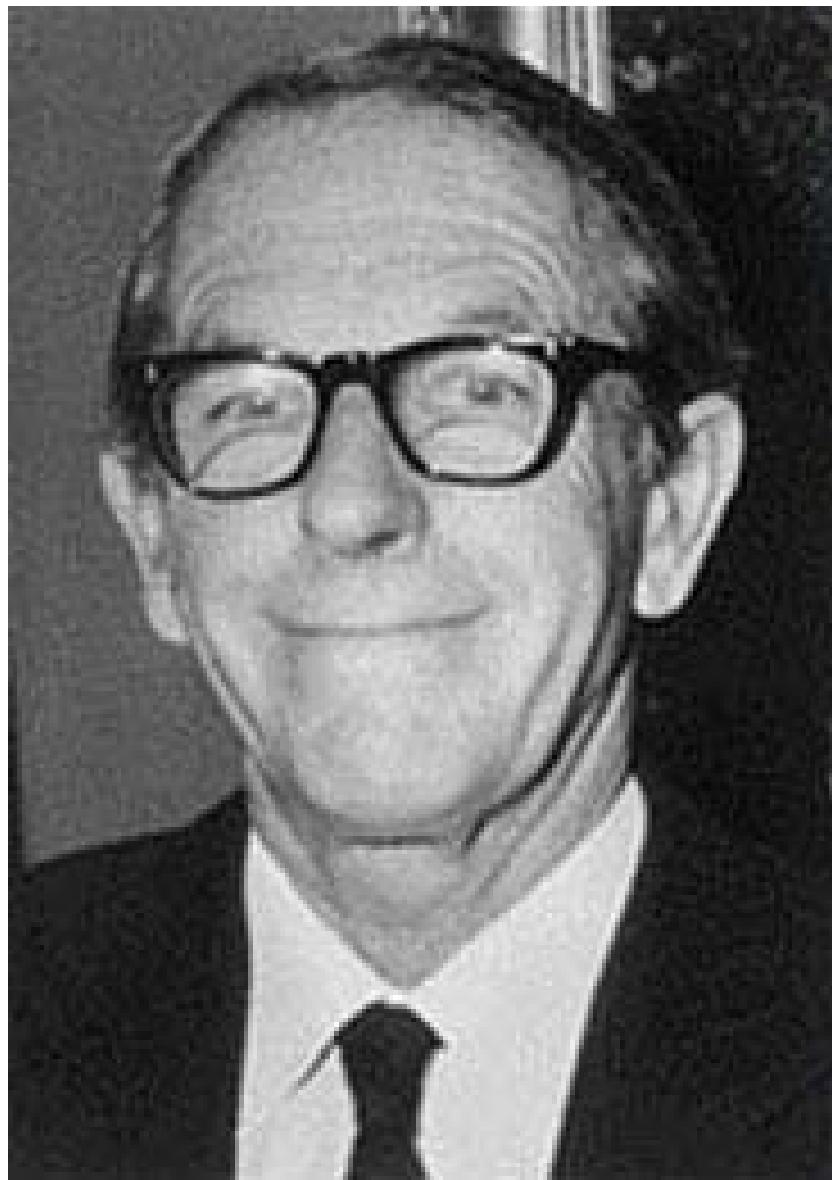
Address	Value	Hex	ASCII
0x000000	4D5A	7400 B800 0000 2604 0100 FFFF 0000	MZt.,...&...ÿÿ..
0x000100	0000 0001	0000 1E00 0000 0100 0000	.....
0x000200	0000 0000	0000 0000 0000 0000 0000	.....
0x000300	0000 0000	0000 0000 0000 0000 0000	.....
0x000400	2433 2433	454E 5501 00B5 014E 5343 4F00	\$3\$3ENU..µ.NSC0.
0x000500	0306 0016	001A 0001 04FF FF48 0302 0056	.....ÿÿH...v
0x000600	0303 0061	0308 006C 0302 01FF FF7A 0303	...a...l...ÿÿz..
0x000700	CCEA 0383	03EB 03A4 03EC 03BC 03ED 03D2	íê.f.ë.¤.i.¤.i.º
0x000800	03EE 03ED	03EF 0313 04F0 032A 04F1 033C	.í.i.i...ð.*.ñ.<
0x000900	04F2 034D	04F3 0369 04F4 0380 04F5 03B6	.ò.M.ó.i.ó.□.ð.¶
0x000A00	04F6 03CD	04F7 03D8 04F8 03F8 04F9 031E	.ð.Í.÷.§.§.§.ù..
0x000B00	05FA 033F	05FB 034F 05FC 0357 05FD 0363	.ú.?..û.0.û.º.ý.c

Pos : 0

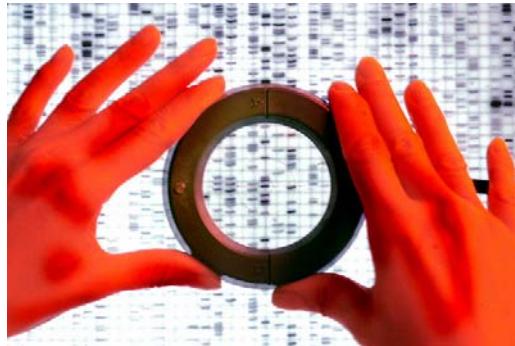
Size : 93812



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TTA-GGA-CGC-ATT-GCA-ACT-CAA-AAT-CAG-AAT-ATA-AAT-ATC-GAA-AAG-AAT-TCT-AGC-TAT-  
TAC-GTA-GTT-GAG-AAA-TCT-TGG-AGT-ACA-TTA-TCG-GAT-CTT-GAA-AAA-GAA-AAA-TAT-ACA-  
AAA-AGT-GCA-ATT-GCT-GGT-ATC-AAT-CTT-ATA-ACA-AGC-TTA-GAG-CCA-ATA-ATA-GAA-GAT-  
GGT-AAT-GGT-GTA-TTA-AAC-TTA-AAA-ATA-CAA-GCT-GAT-AAT-AAA-GGT-GAA-TTA-GGC-GAT-  
ATT-AGA-GAT-ATT-TTA-ATT-CAA-AGA-GAA-AAT-ATT-AAT-TGG-GAA-ATT-GGT-TTA-AGT-TTA-  
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CAT-AAT-GCT-TCT-ACT-ATT-GAA-CCG-AGC-TTG-AAA-TTT-GAT-ATA-AAA-CTT-ATT-GGT-  
GTT-CCT-GCC-ACA-ATA-ATT-TGT-TTA-GAG-ACC-CCT-TGG-GAA-GAA-TGA



Nobel foundation



1980  
500 bp/day (manual)



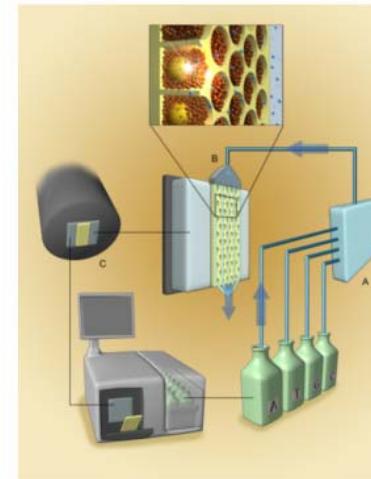
**1987**  
36,000 bp/day (semi-auto)



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

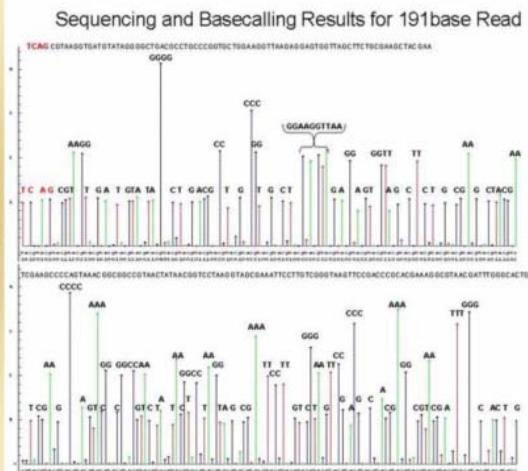


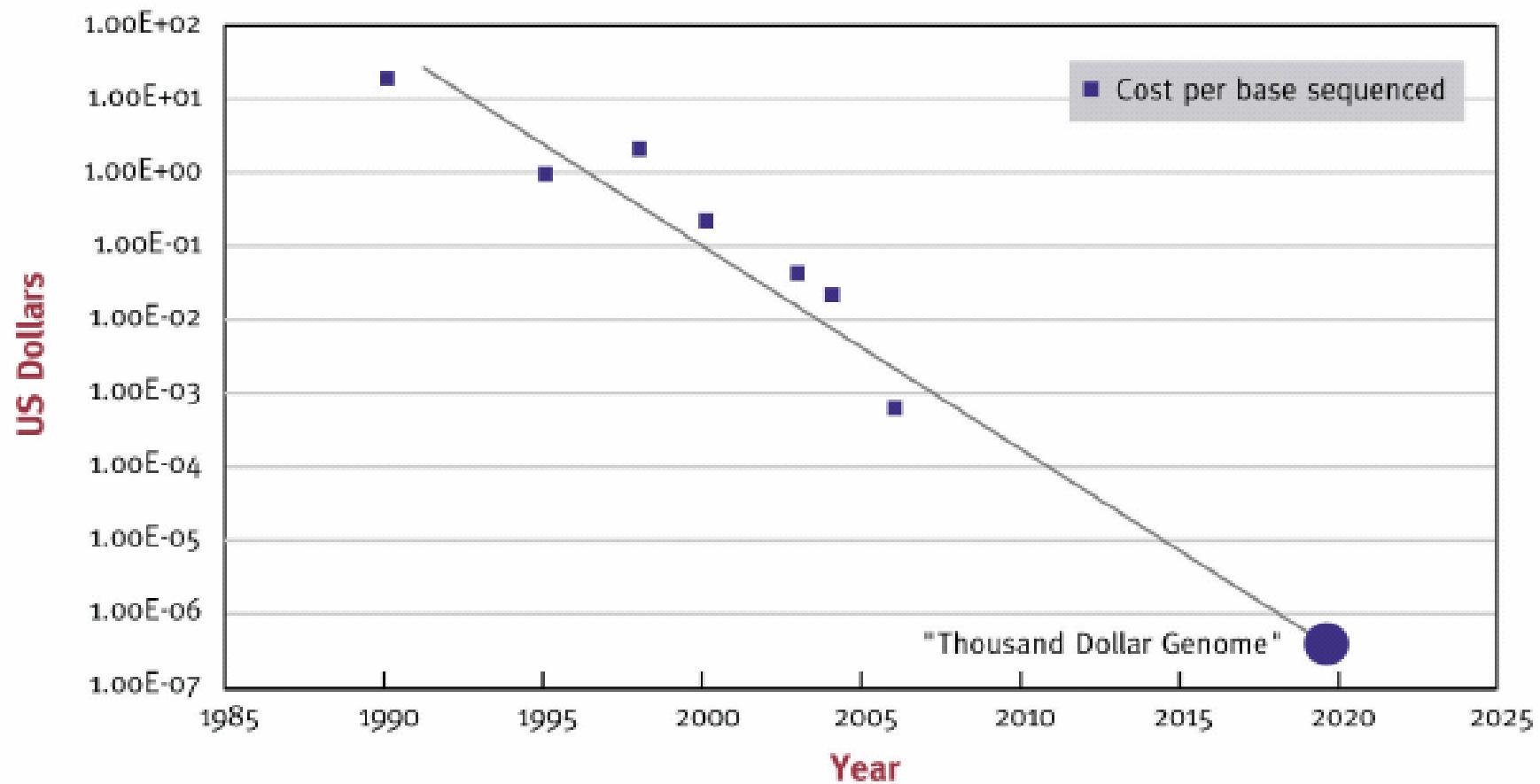
**1998**  
500,000 bp/day (automatic)



# 2007 – Sequencing by Synthesis

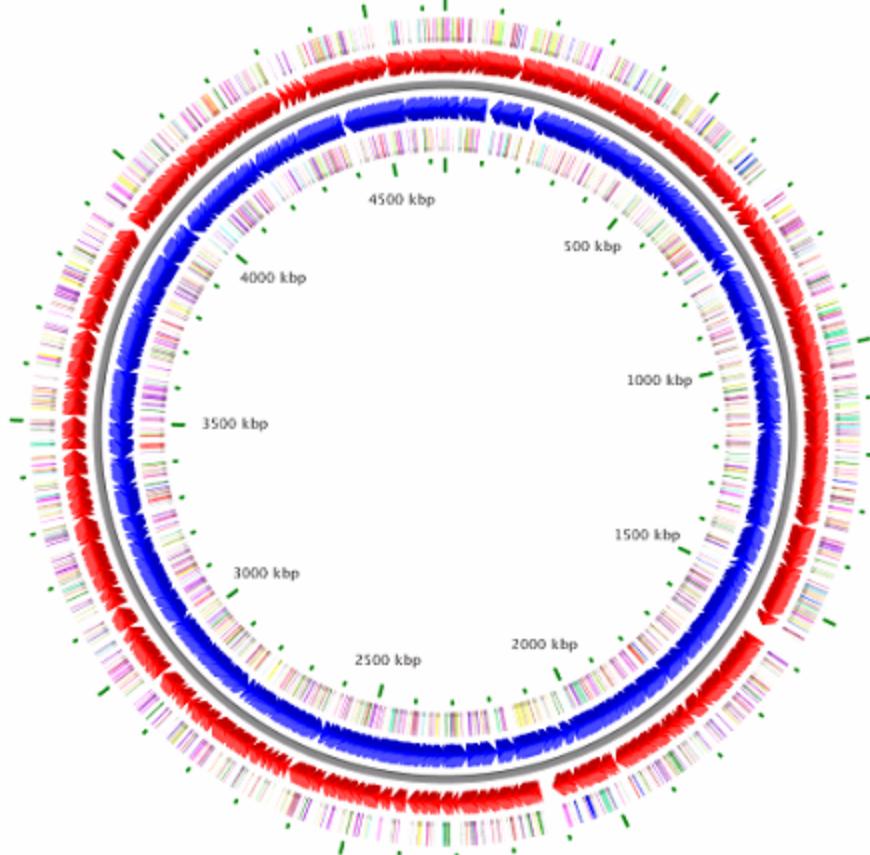
1GB bp/day (automatic)





Source: R. Carlson, Bio-era

*E. coli* K12 complete genome



BASys: Friday April 15 09:42:20 2005

Length: 4,639,675 bp; Genes: 4,254

# BASys

## Genes encoding proteins

- Forward strand (red)
- Reverse strand (blue)

## Genes encoding functional RNA

- Forward strand (pink)
- Reverse strand (cyan)

## COG functional categories

### Information storage and processing

- Translation, ribosomal structure and biogenesis
- Transcription
- DNA replication, recombination and repair

### Cellular processes

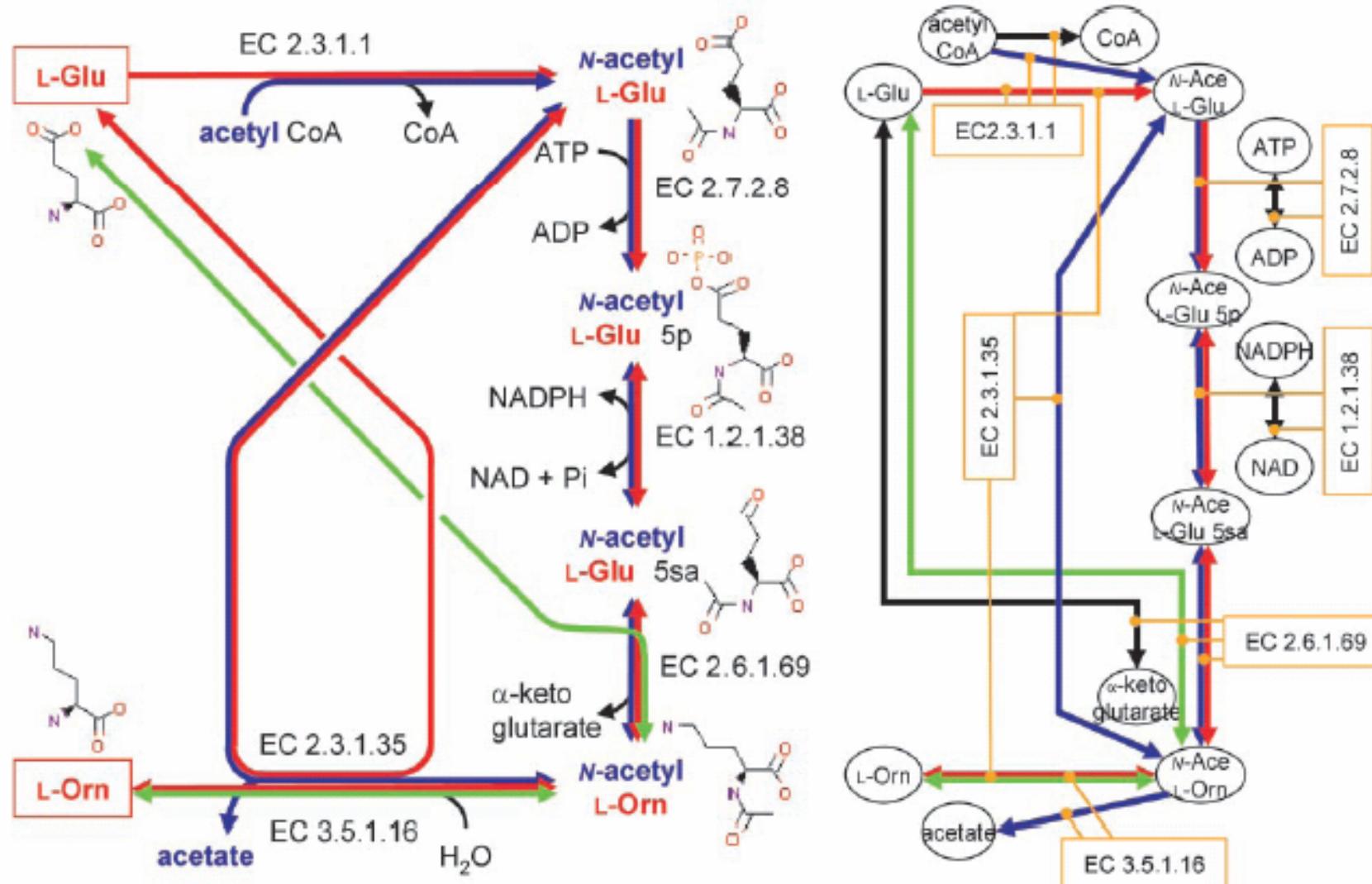
- Cell division and chromosome partitioning
- Posttranslational modification, protein turnover, chaperones
- Cell envelope biogenesis, outer membrane
- Cell motility and secretion
- Inorganic ion transport and metabolism
- Signal transduction mechanisms

### Metabolism

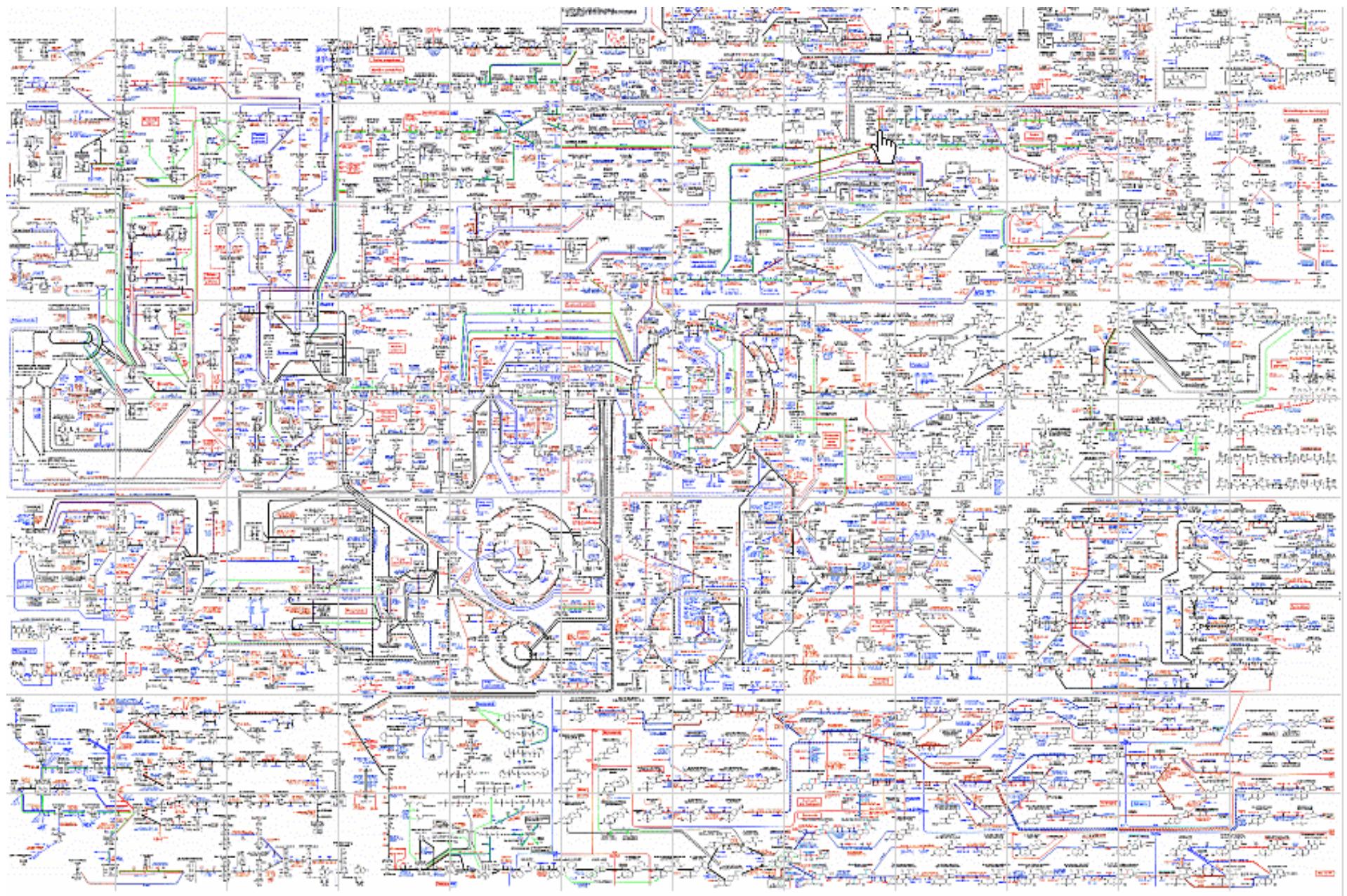
- Energy production and conversion
- Carbohydrate transport and metabolism
- Amino acid transport and metabolism
- Nucleotide transport and metabolism
- Coenzyme metabolism
- Lipid metabolism
- Secondary metabolites biosynthesis, transport and catabolism

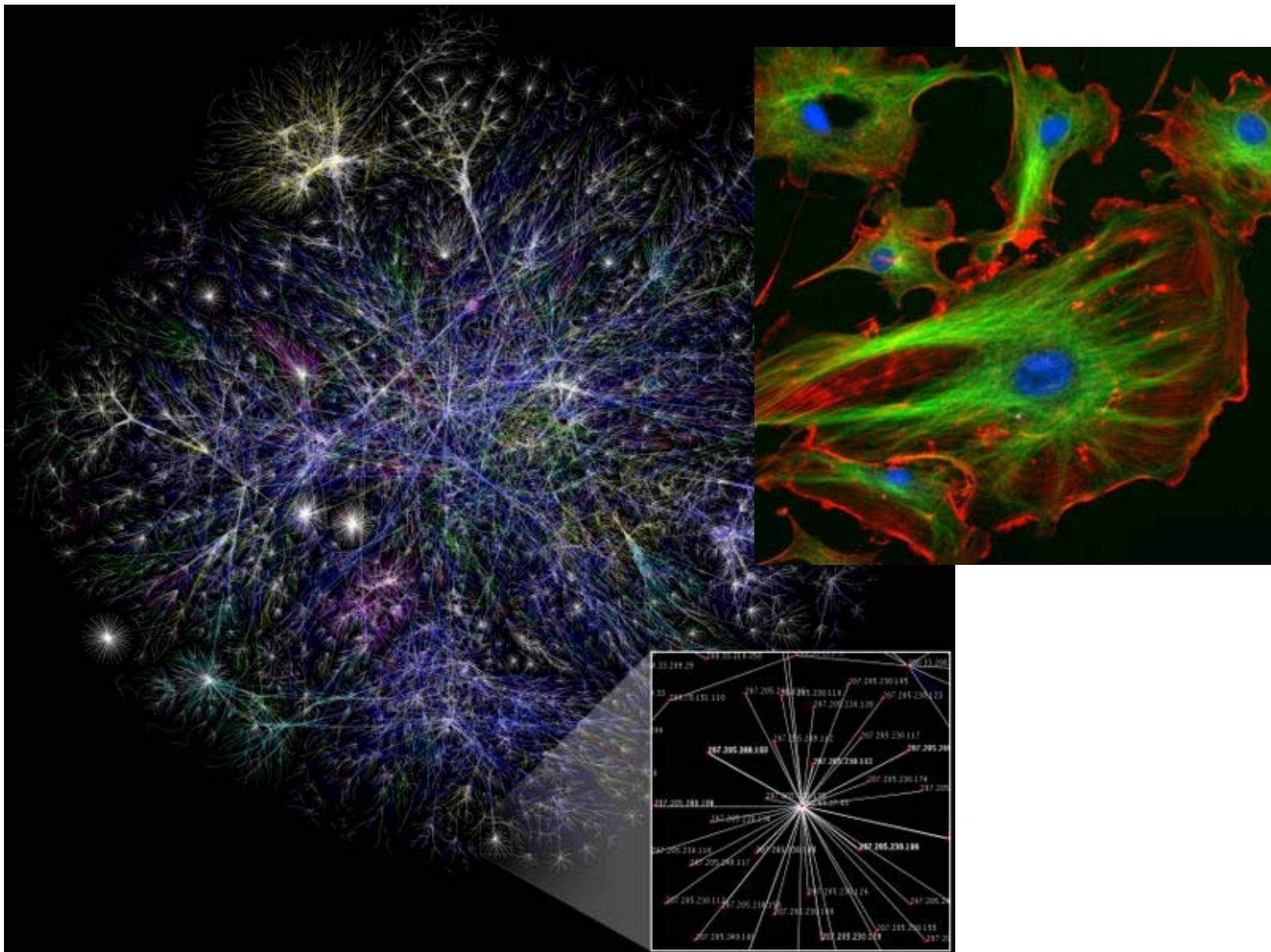
### Poorly characterized

- General function prediction only
- Function unknown



Ornithine biosynthesis





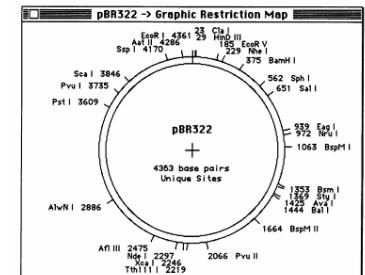
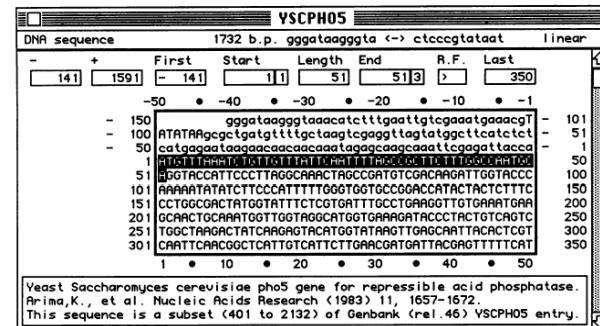


'DNA Strider': a 'C' program for the fast analysis of DNA and protein sequences on the Apple Macintosh family of computers

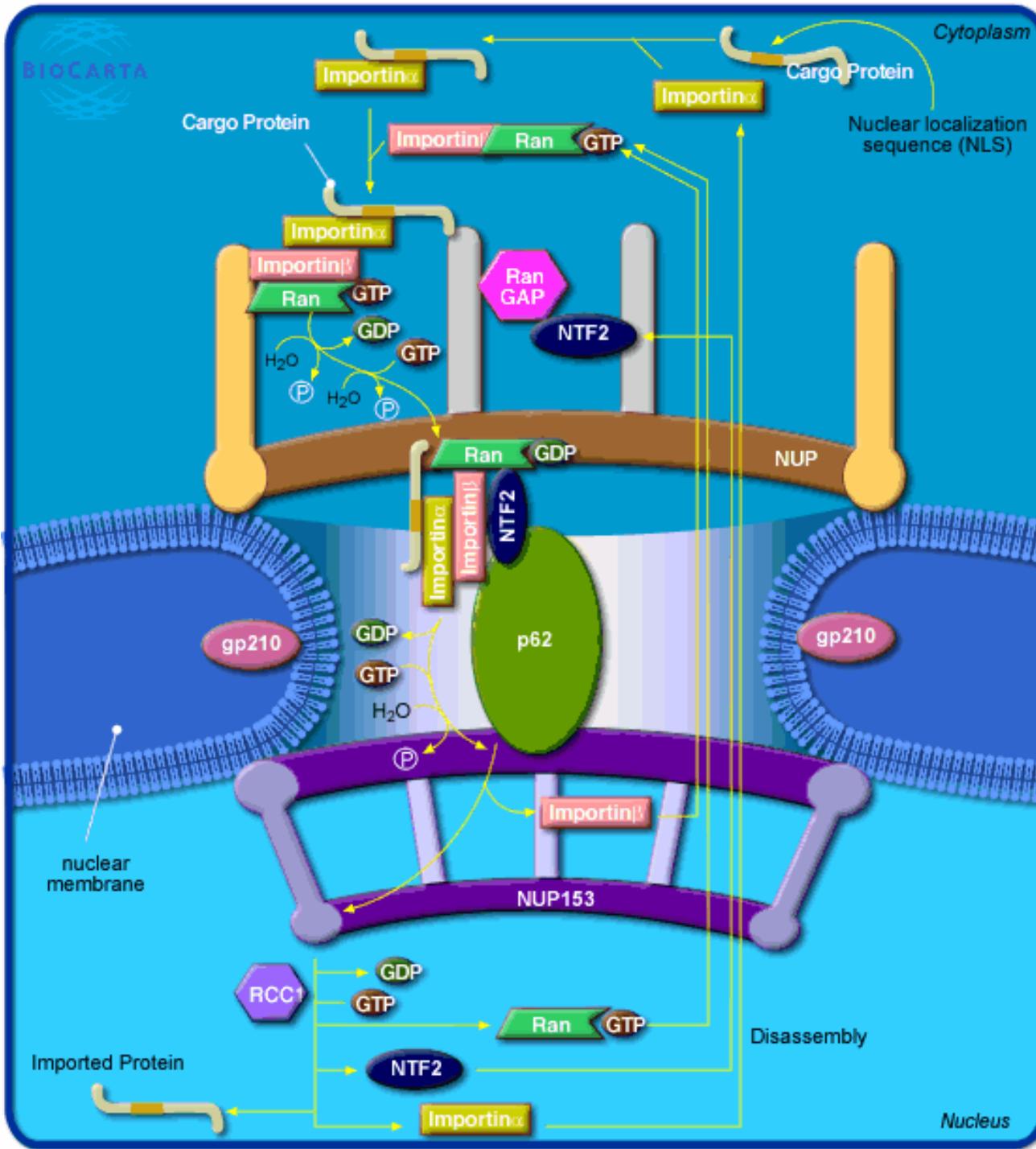
Christian Marck

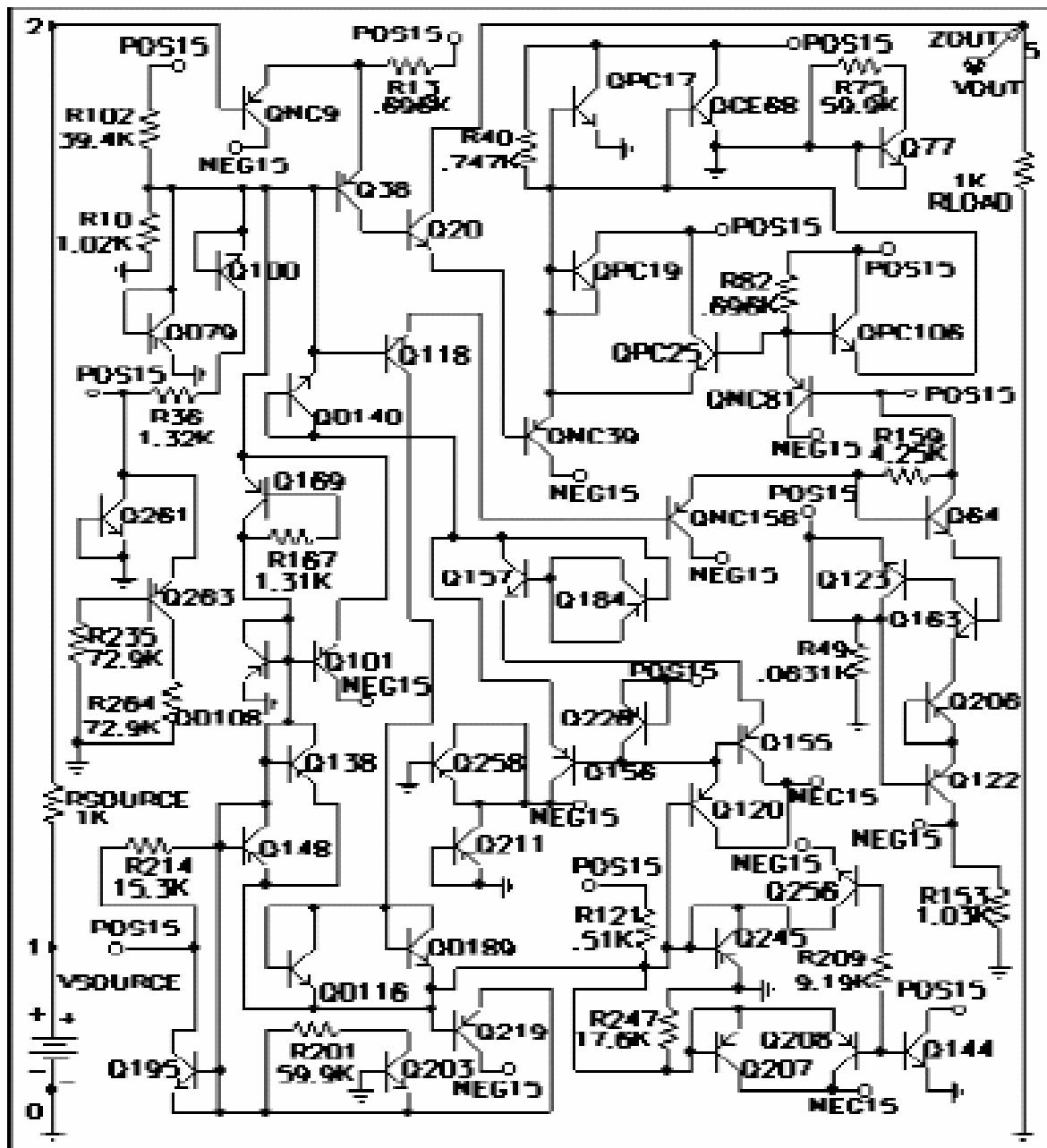
Service de Biochimie, Bâtiment 142, Département de Biologie, Centre d'Etudes Nucléaires de Saclay  
91191 Gif-sur-Yvette Cedex, France

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



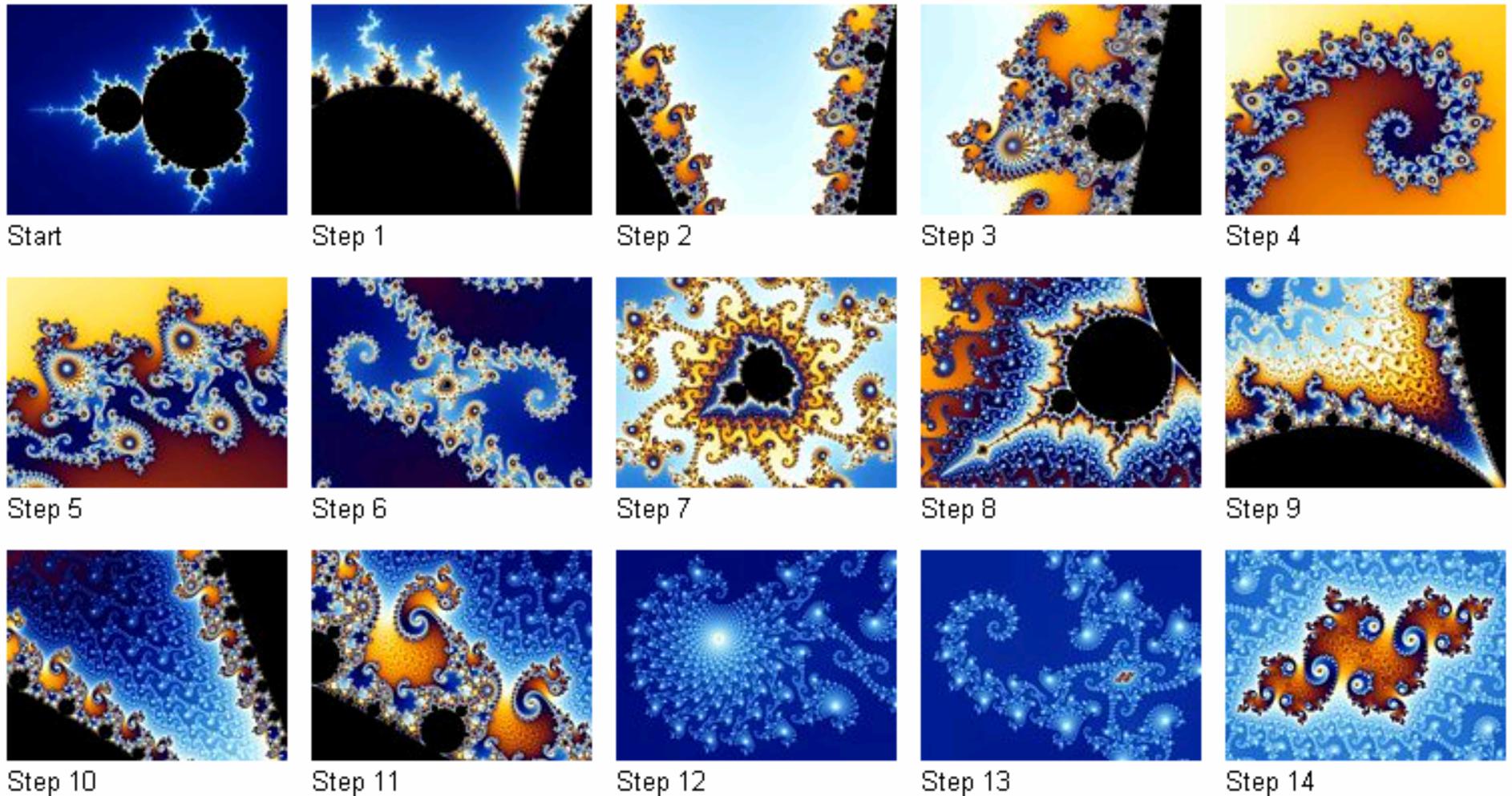
280.6 TFLOPS with 131072 nodes



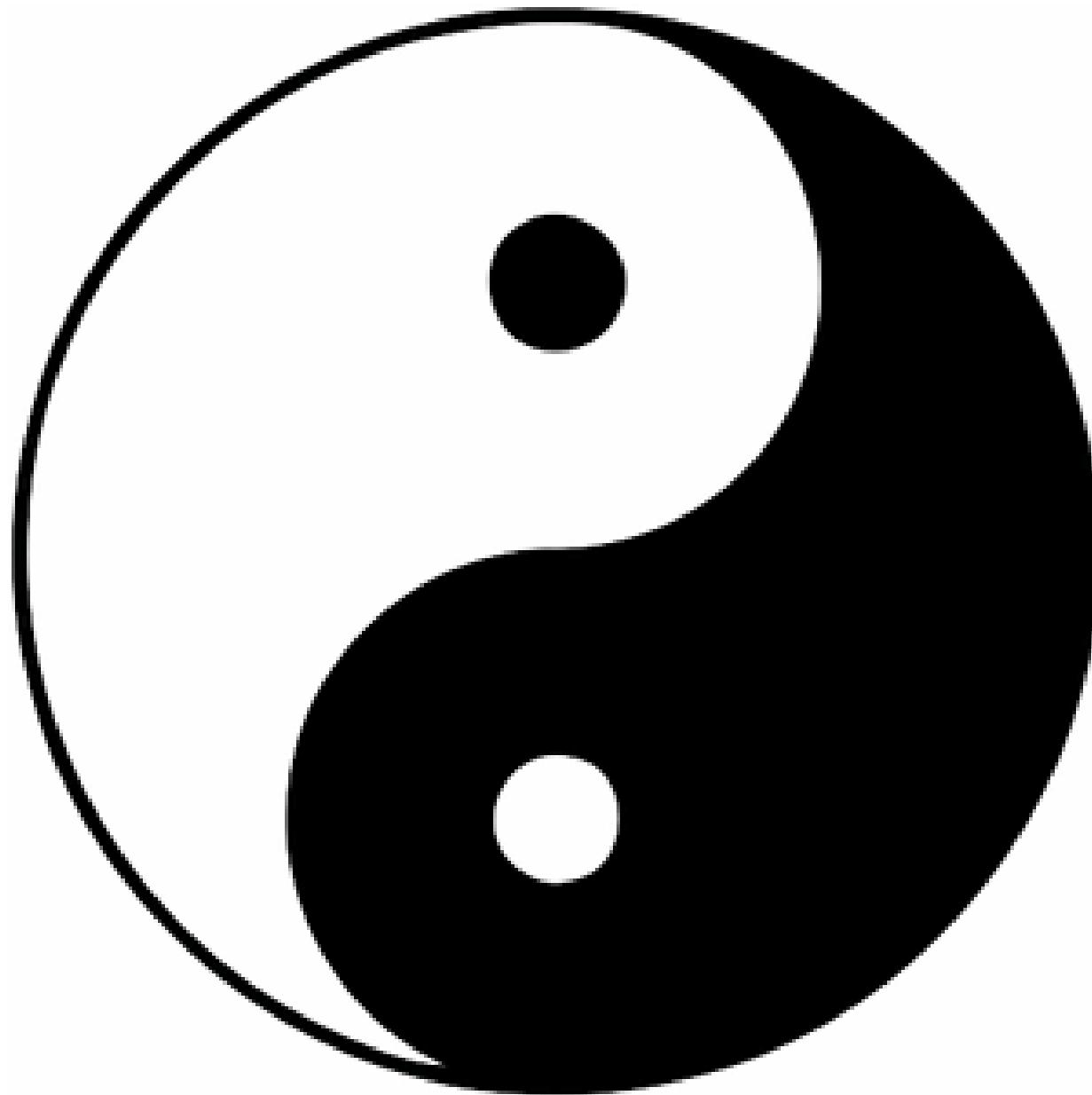


J.R. Koza et al.  
Automatic creation of computer  
programs for designing  
electrical circuits using genetic  
programming.

$$M = \left\{ c \in \mathbb{C} : \sup_{n \in \mathbb{N}} |f_c^n(0)| < \infty \right\}.$$



Reduction | Complexity



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

Genetic “Engineering”

Writing code

**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*

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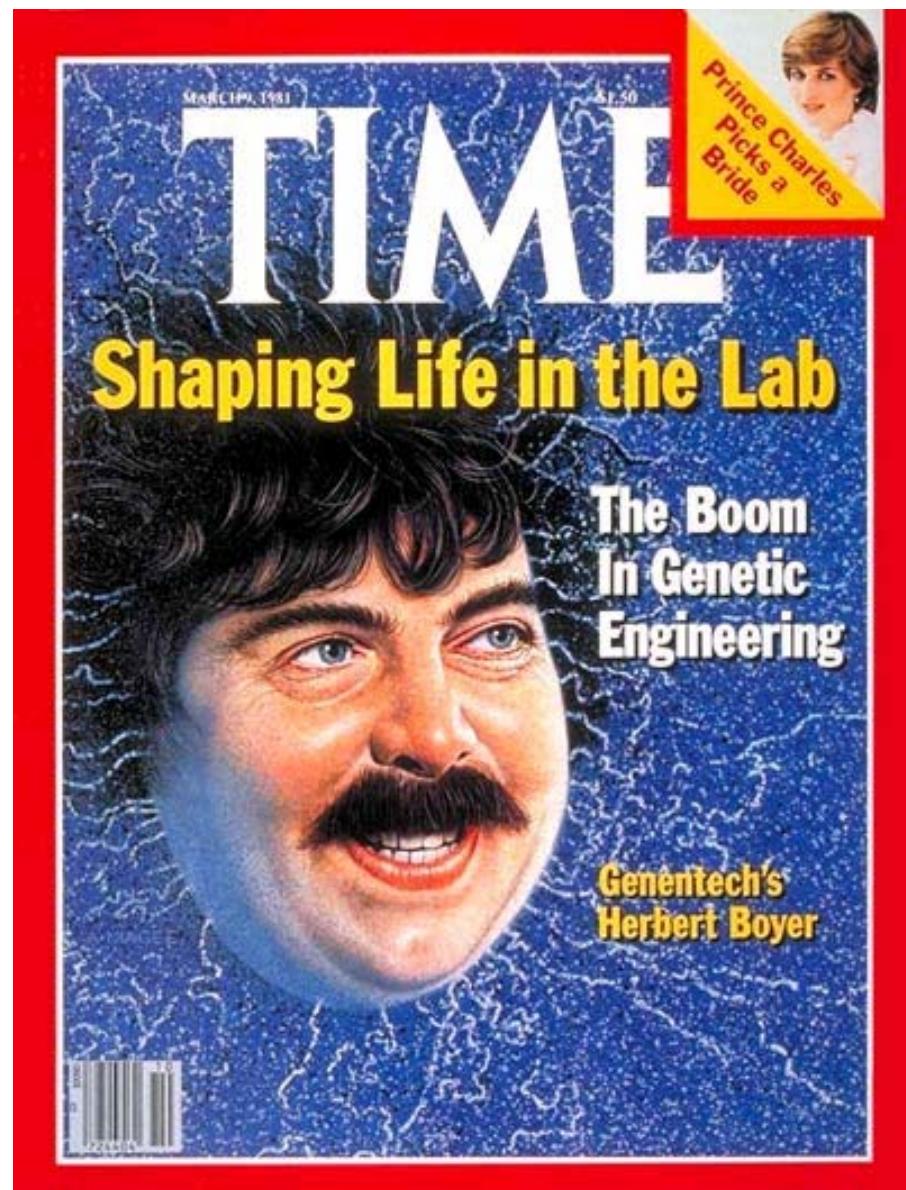
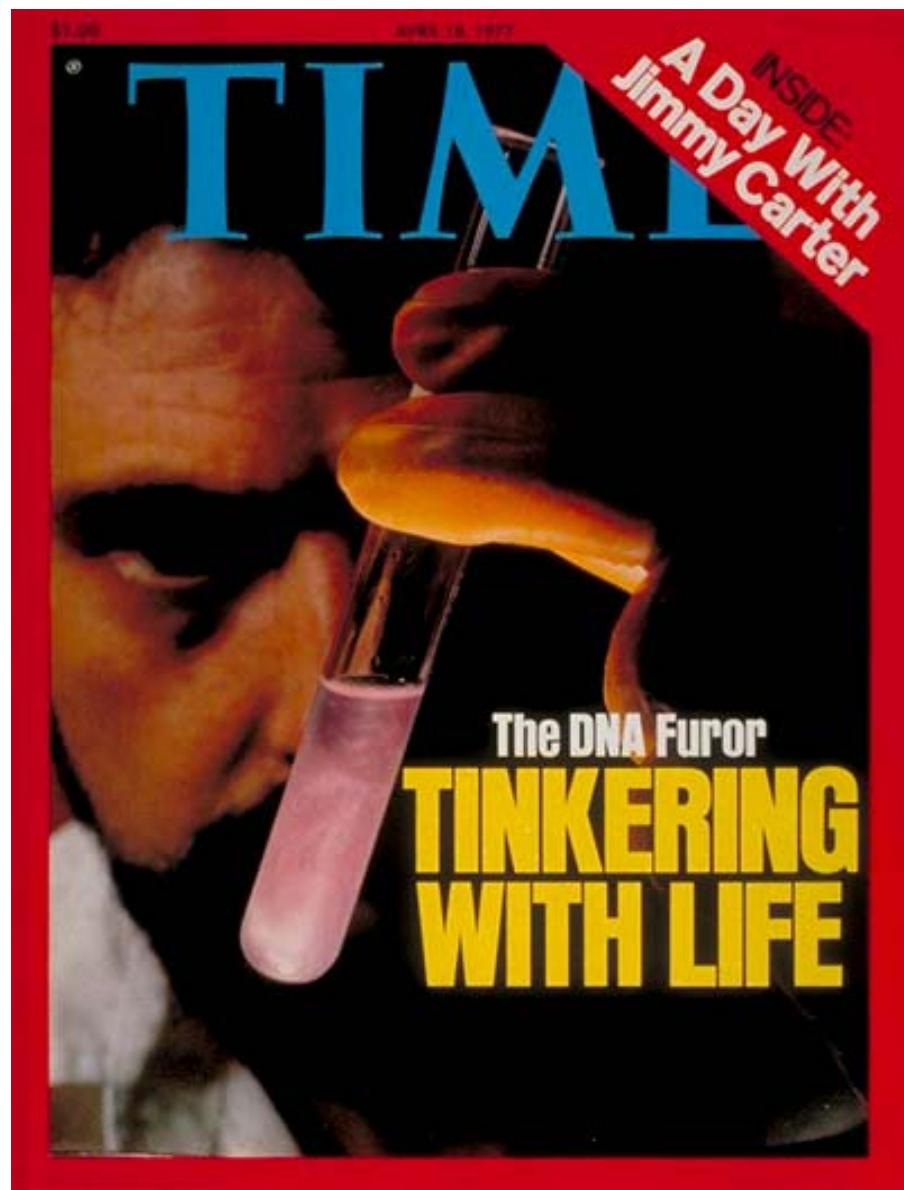
**Construction of Biologically Functional Bacterial Plasmids *In Vitro***

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

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

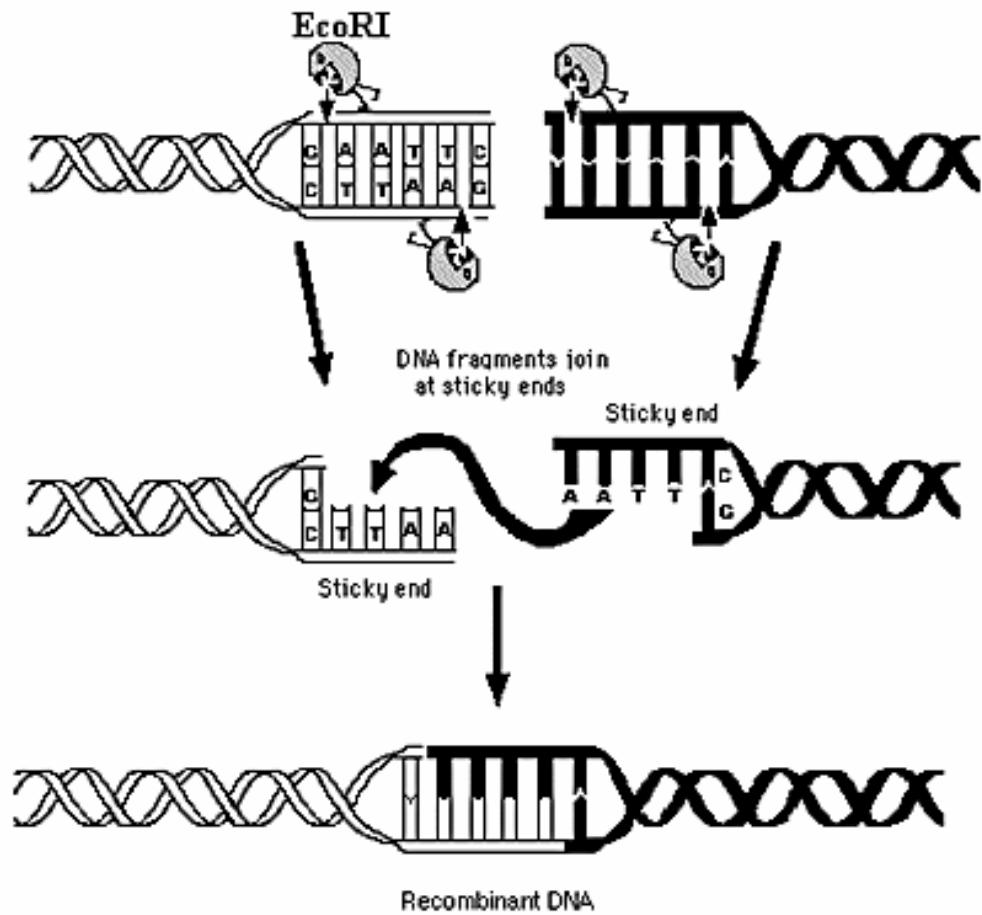
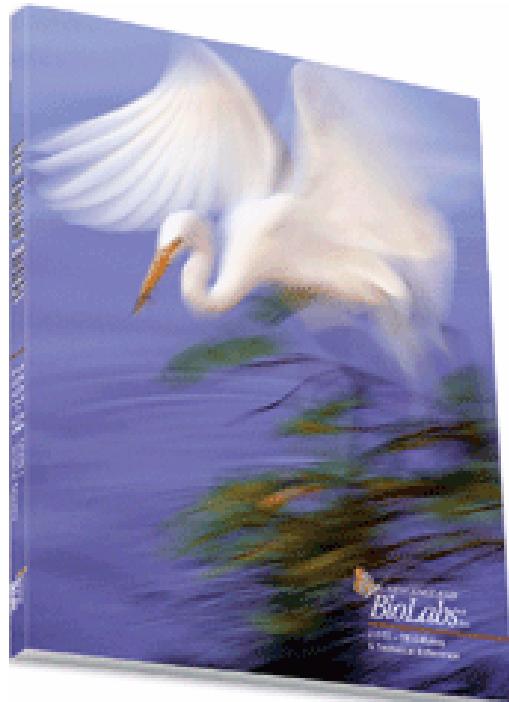
\* Department of Medicine, Stanford University School of Medicine, Stanford, California 94305; and † Department of Microbiology, University of California at San Francisco, San Francisco, Calif. 94122

*Communicated by Norman Davidson, July 18, 1973*





home page...  
[rebase.neb.com](http://rebase.neb.com)

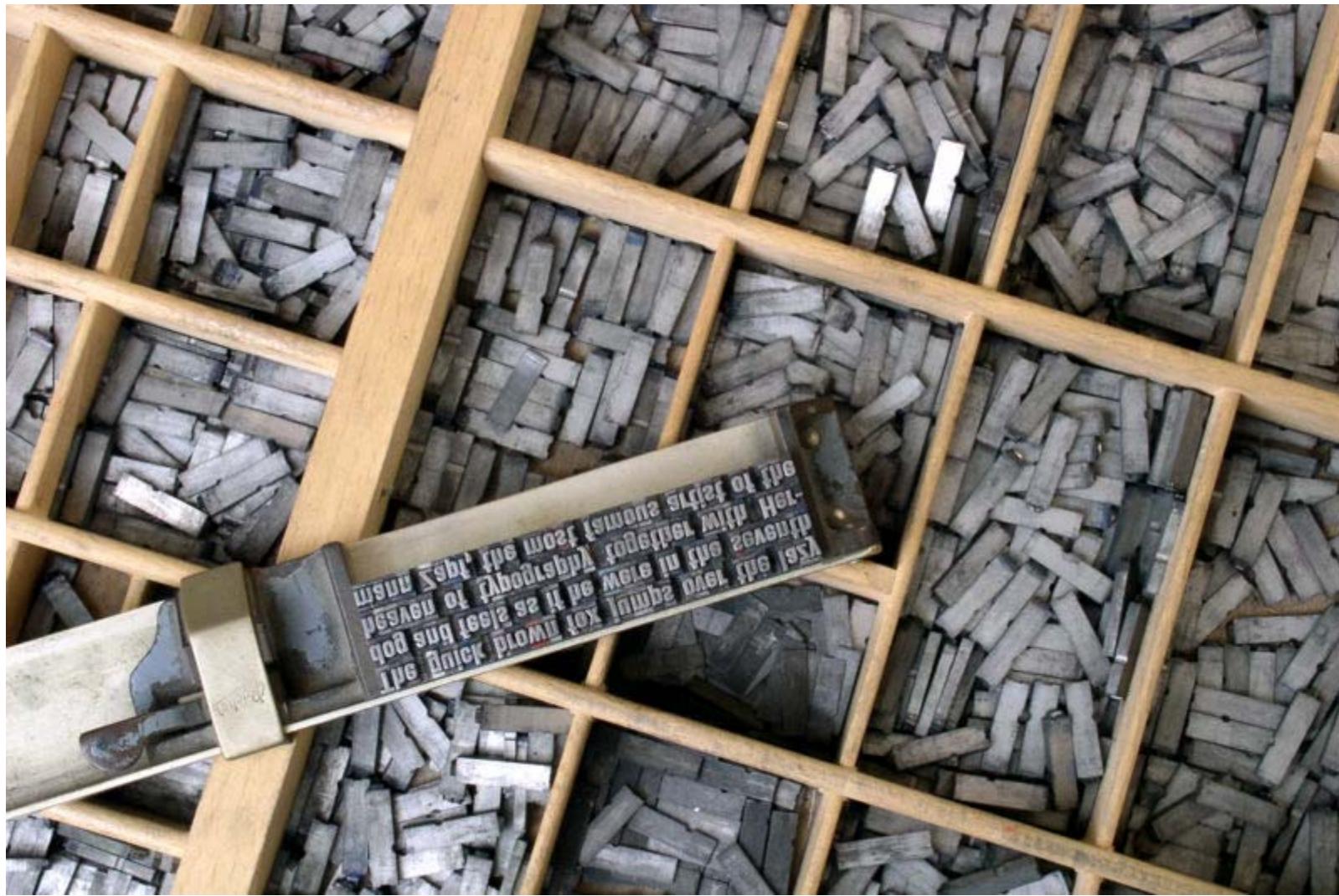


## Restriction Enzyme Action of EcoRI

if you can WRITE DNA,

You're no LONGER liMITED

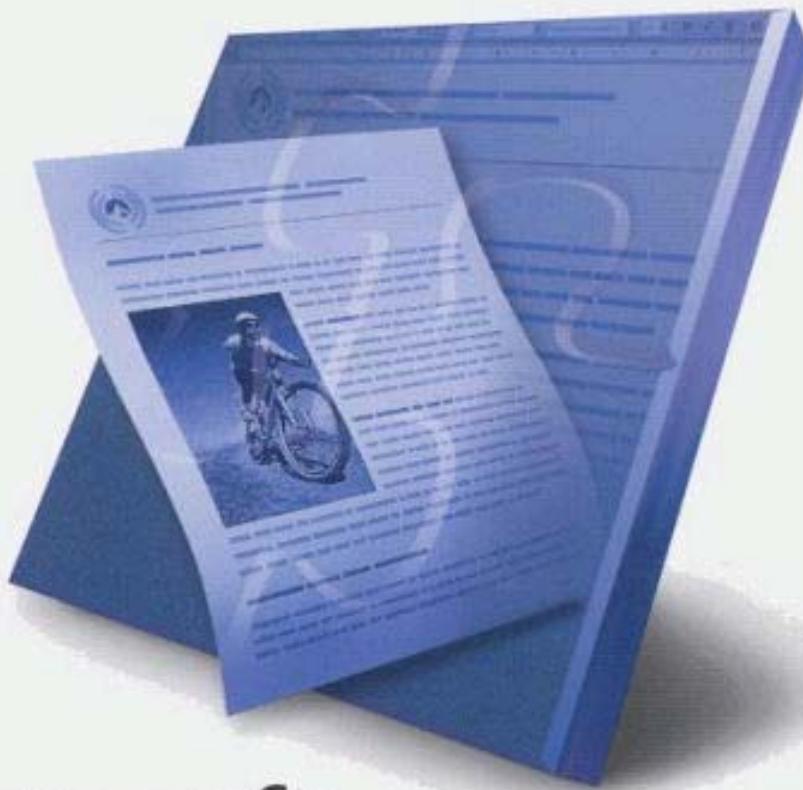
to "What IS IT" but TO what you could MAKE •



[http://en.wikipedia.org/wiki/Image:Metal\\_movable\\_type.jpg](http://en.wikipedia.org/wiki/Image:Metal_movable_type.jpg)

Designed for  
  
Microsoft®  
Windows NT®  
Windows®98

**Microsoft®**



Microsoft®  
**Word 2000**   
Microsoft Office Application

The Microsoft Office Word Processor

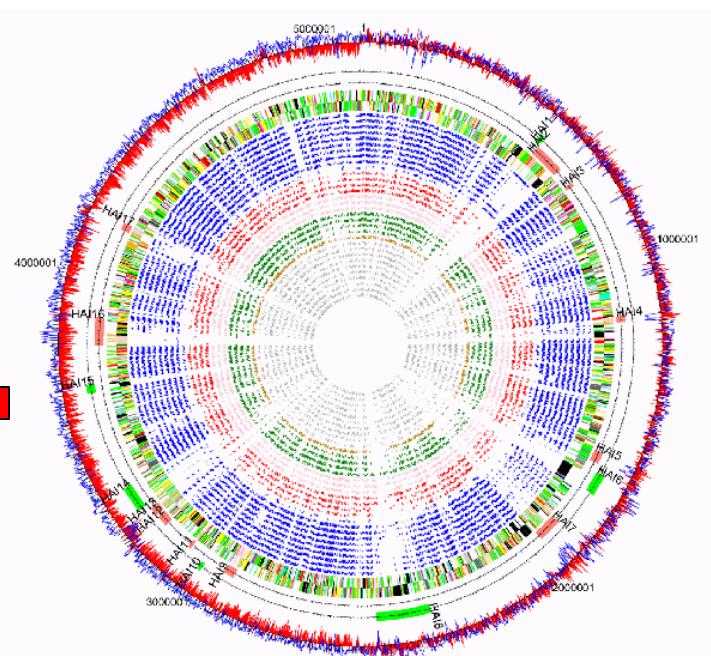


## Physical DNA

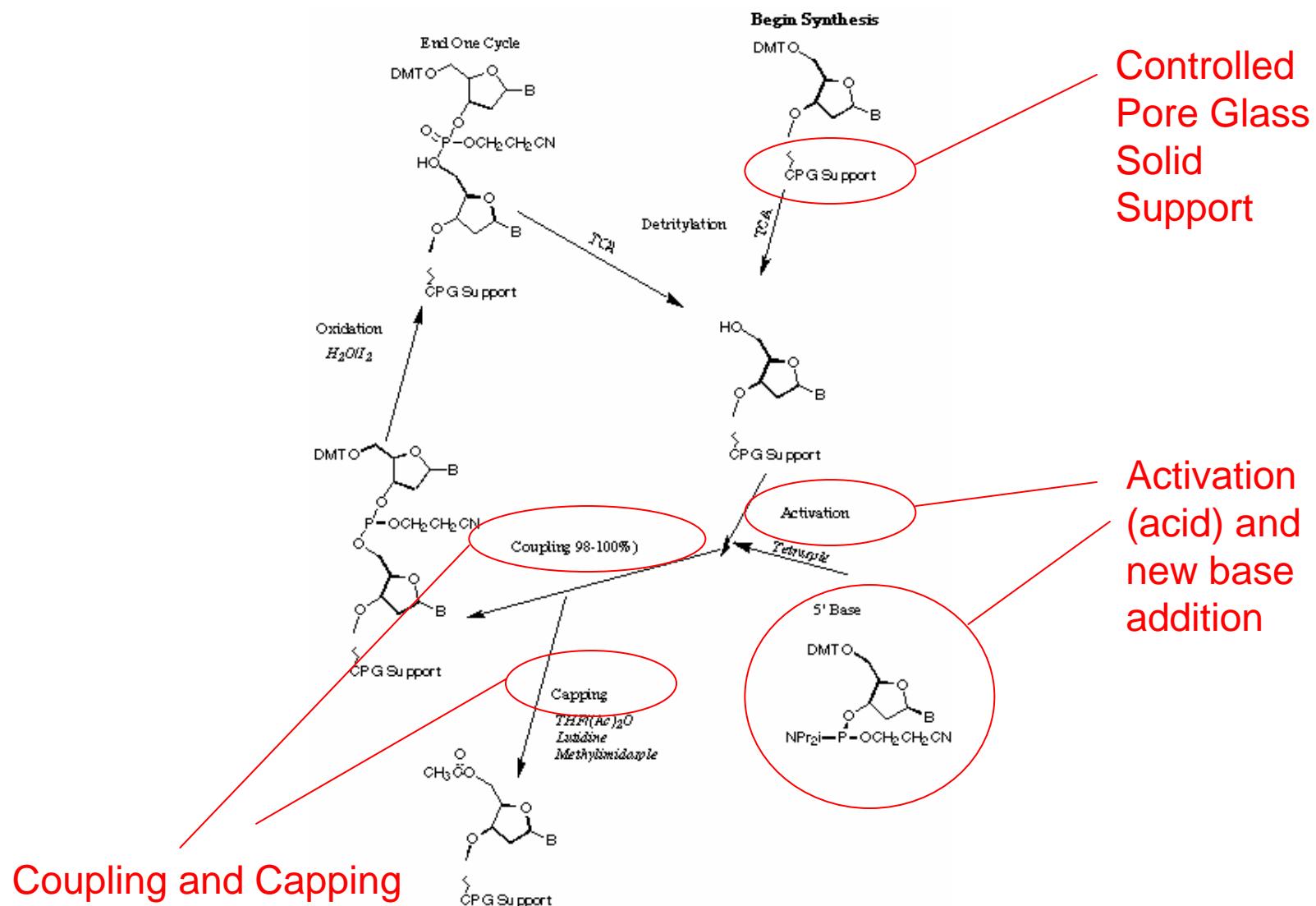
## sequencing

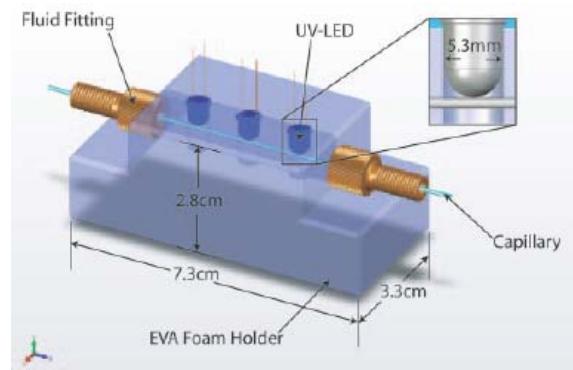
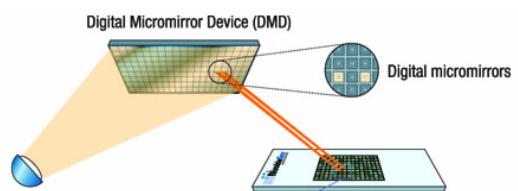
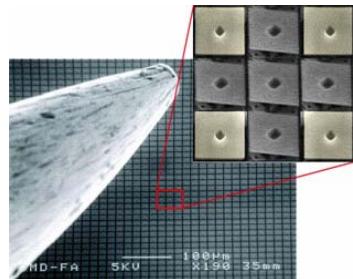
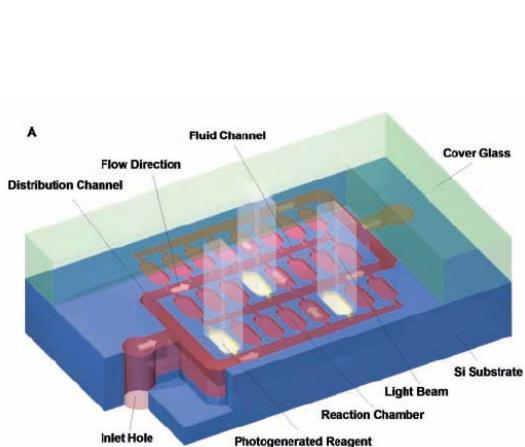


## synthesis



# Digital DNA





# 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

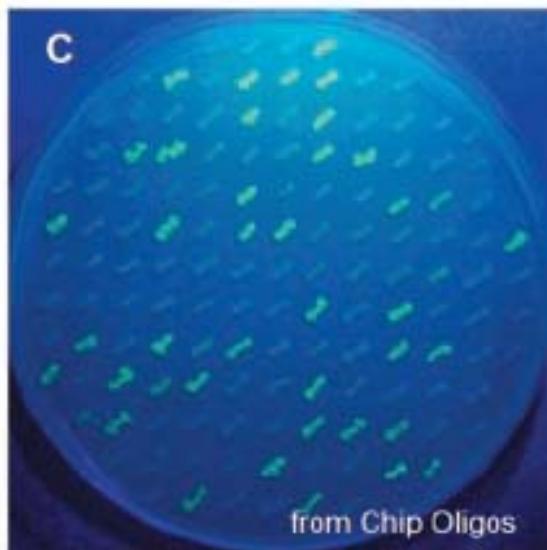
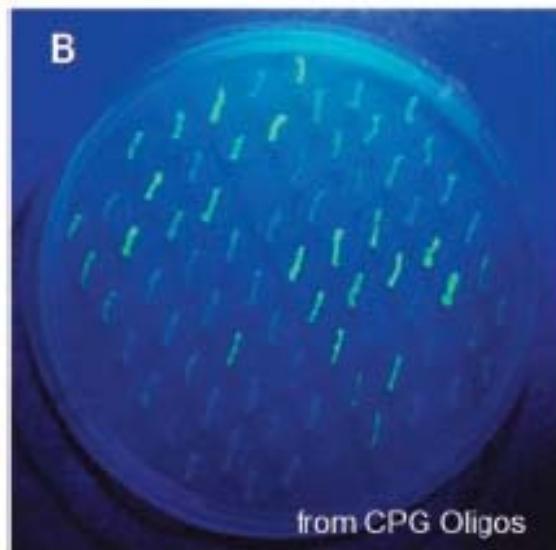
Item location: Saint Louis, Missouri, United States

History: [0 bids](#)

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[Email to a friend](#)



EGFP gene 714 bp

**D**

Oligonucleotide set 1

Oligonucleotide set 2

↓ ligation

Construct I

Construct II

↓ PCR

DNA Construct

## Sponsored Links

## Gene Synthesis \$0.59/bp

Dependable Service @ Low Price:  
Come on Down and Save Your Budgets!  
[www.epochbiolabs.com](http://www.epochbiolabs.com)

## Bio S&T Gene Synthesis

Low price, free LB stab  
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## Gene Synthesis - \$0.69/bp

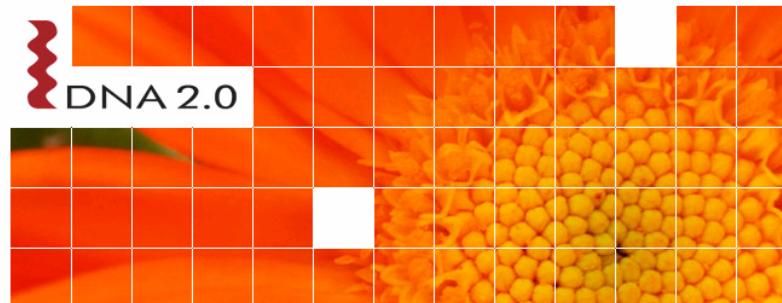
All purpose **gene synthesis**.  
Speed up R&D. Save money, time.  
[www.codondevices.com](http://www.codondevices.com)

## Custom Gene Synthesis

For small, large & difficult genes.  
Free codon optimization services  
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## Gene Synthesis

## OligoMix - Oligonucleotide Mixture **gene construction / synthesis**



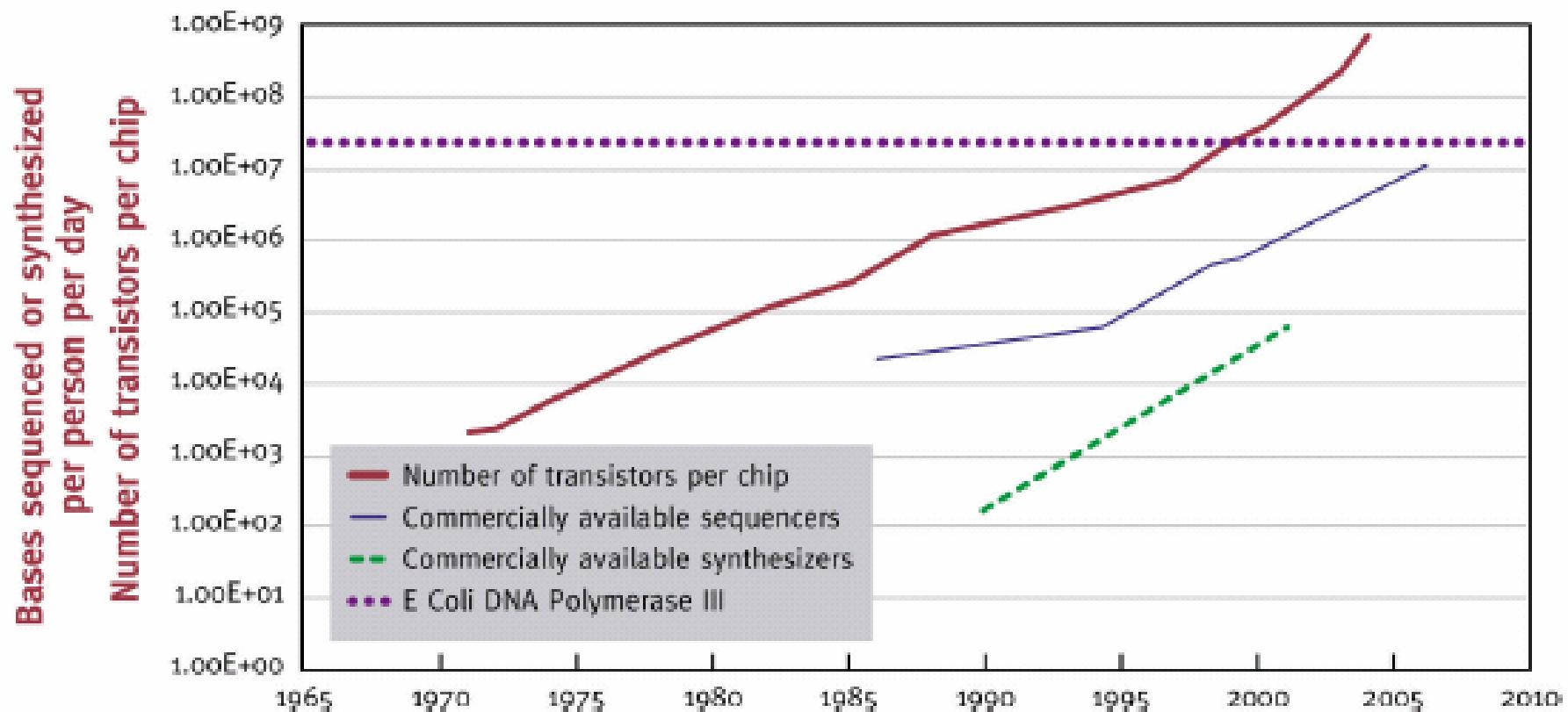
THE BUILDING BLOCKS OF LIFE. BUILT FOR YOU.



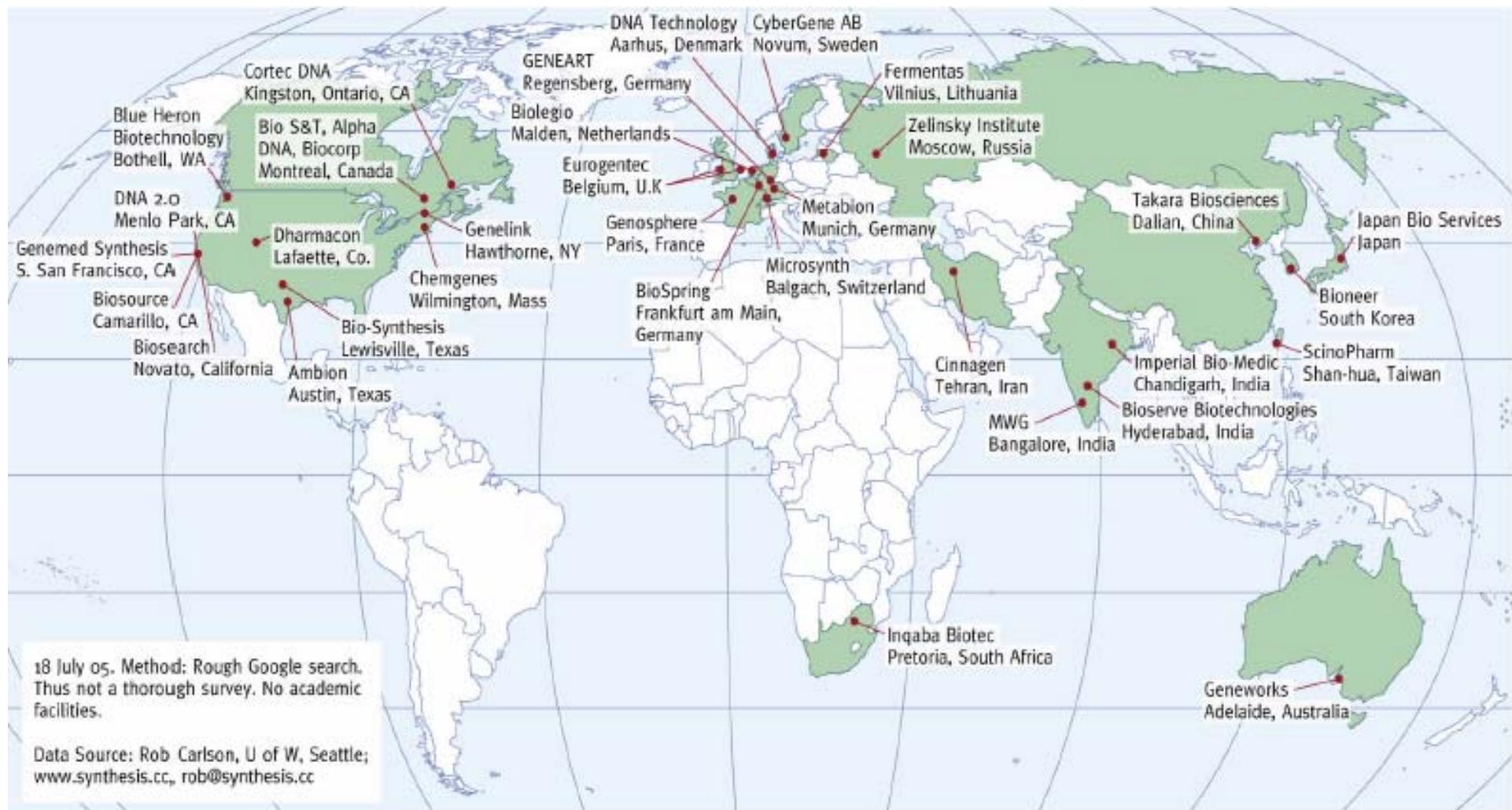
the constructive biology company™

# BLUEHERON®

## BIOTECHNOLOGY

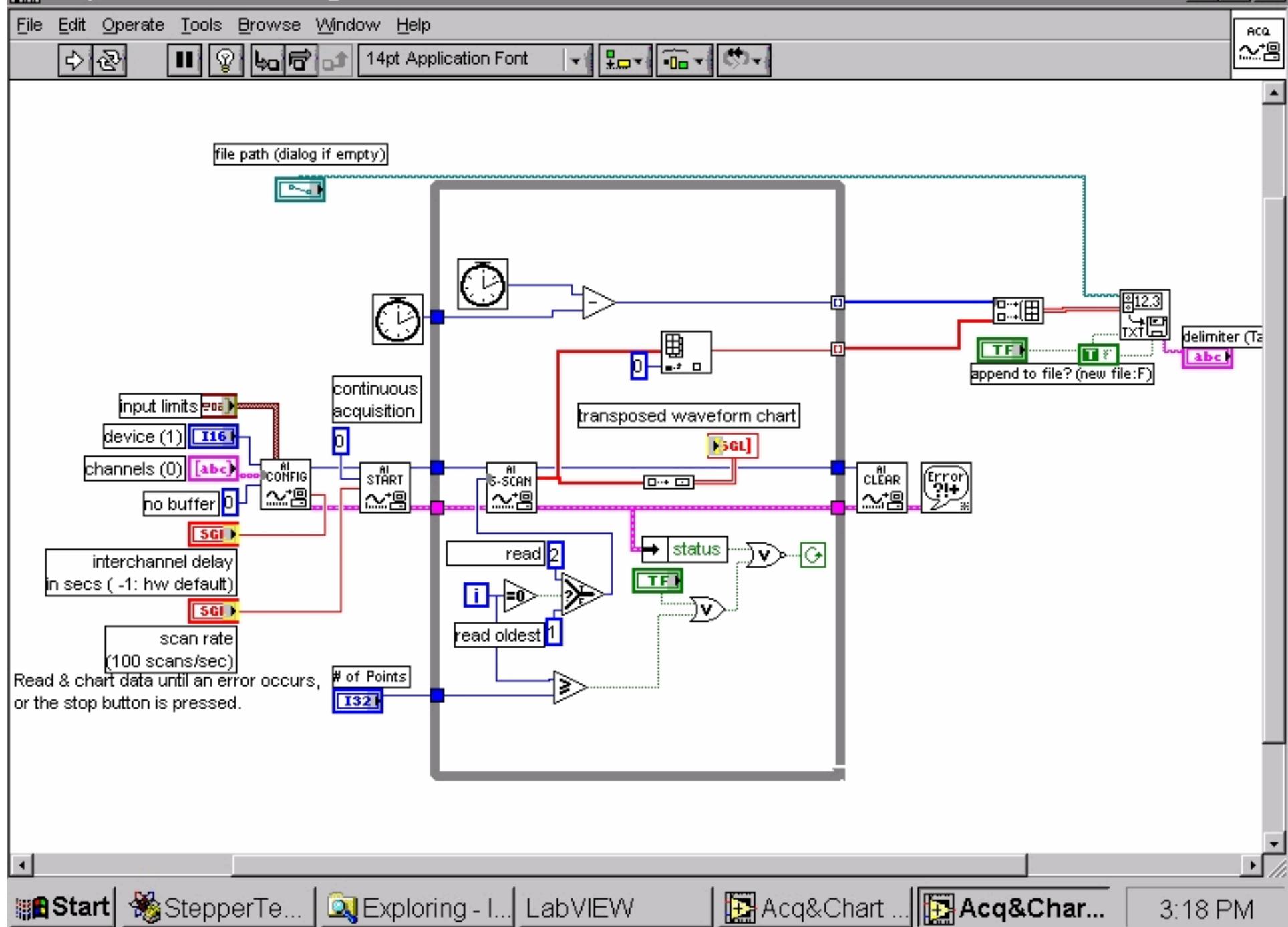


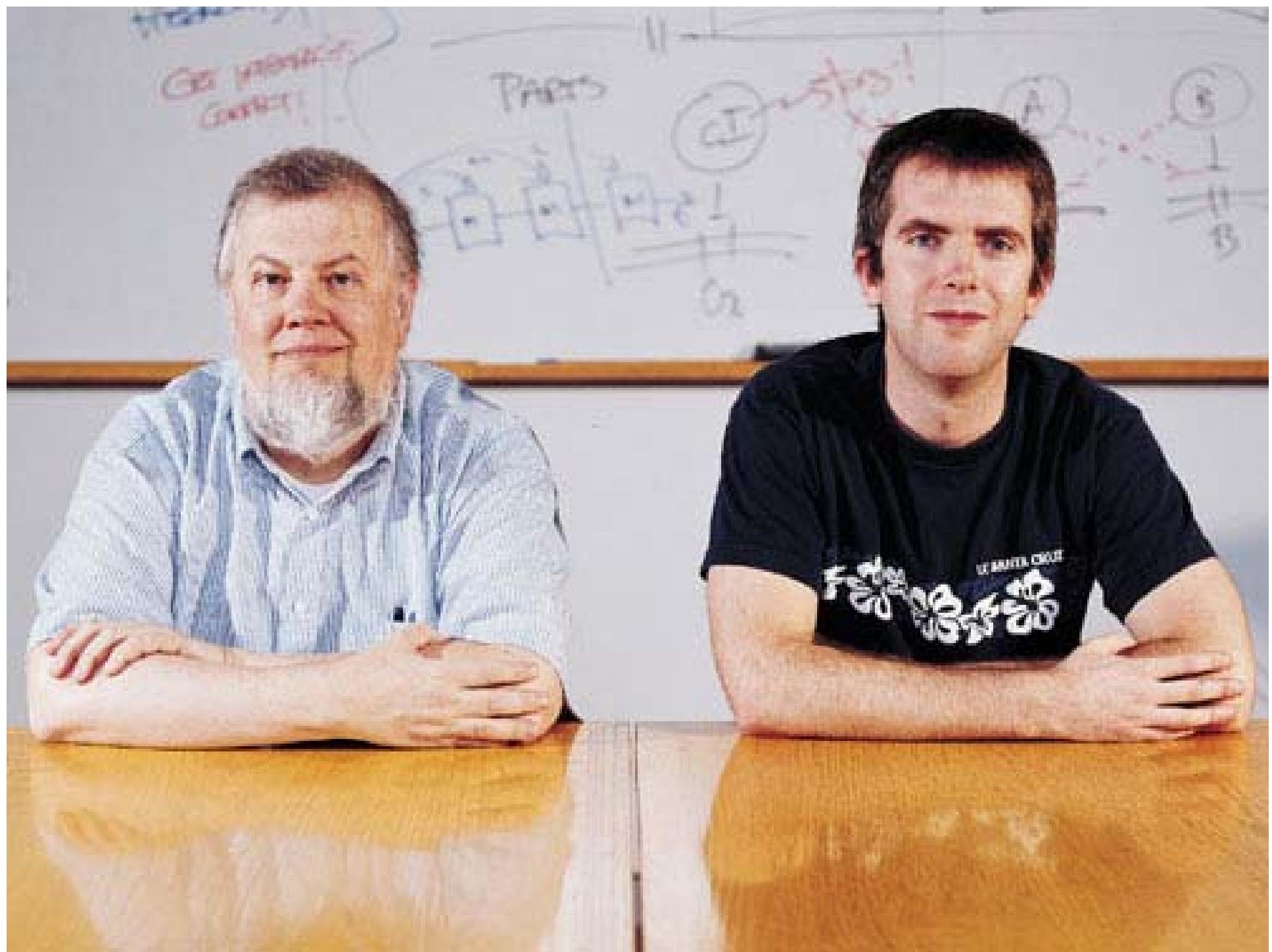
Source: R. Carlson, Bio-era.



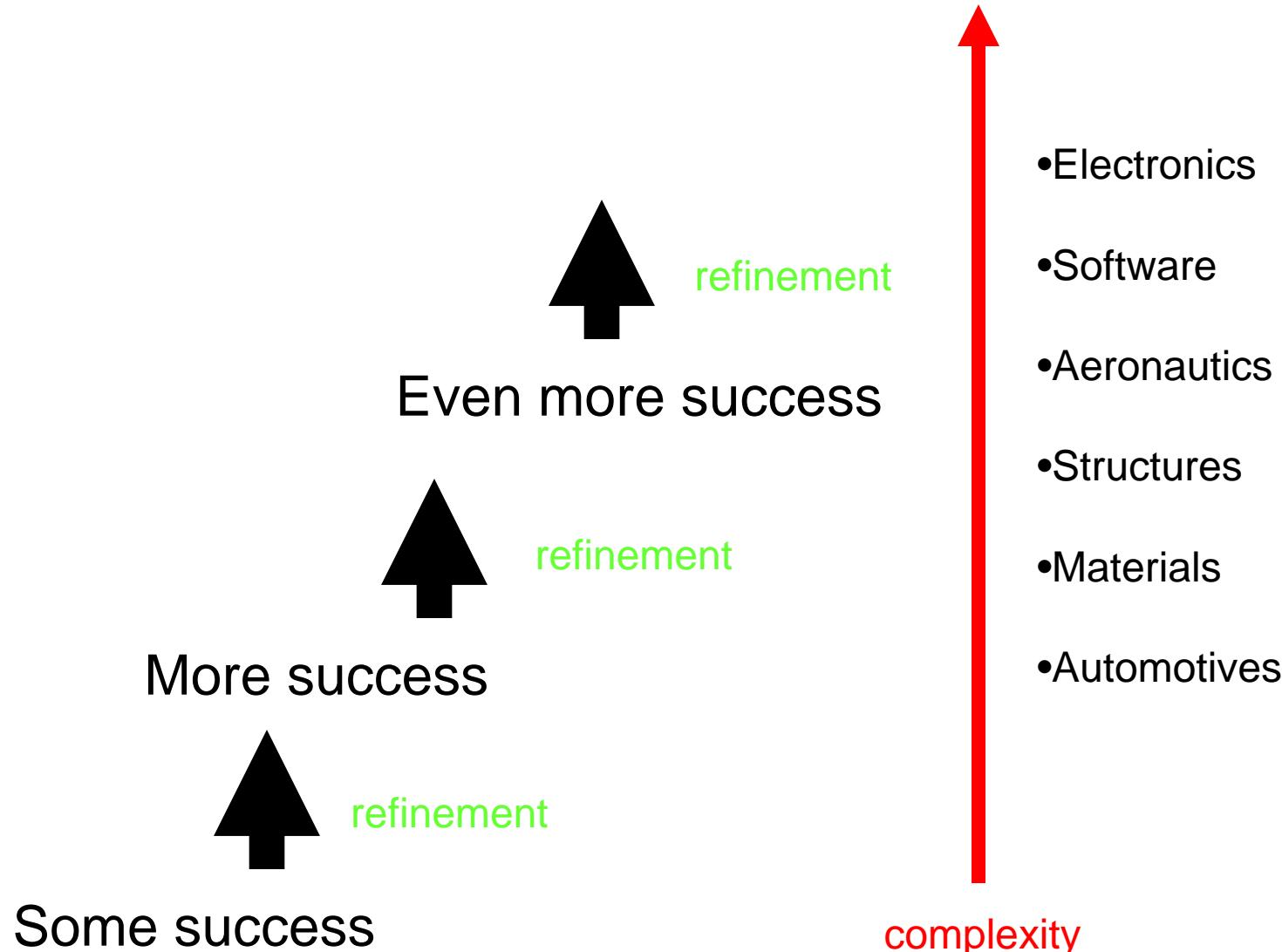
Sources: Source: R. Carlson, G. Epstein, A. Yu (2005)

Acq&Chart to xls.vi Diagram \*





# Engineering process...



# F1760

Sender Device

# B0015

terminator

Name: B0015

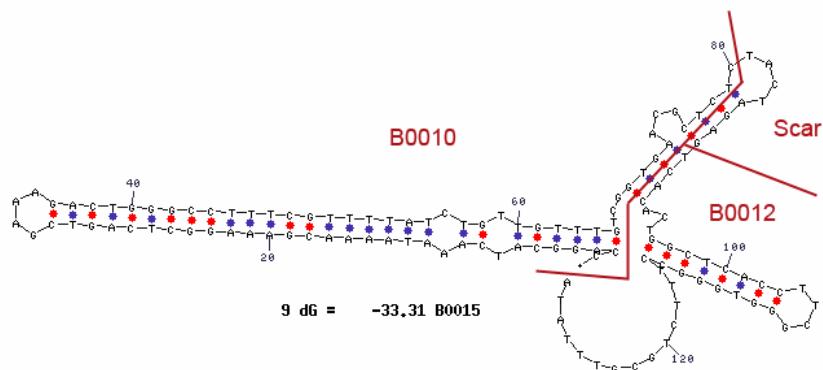
Type: Double terminator

Length 129 bp

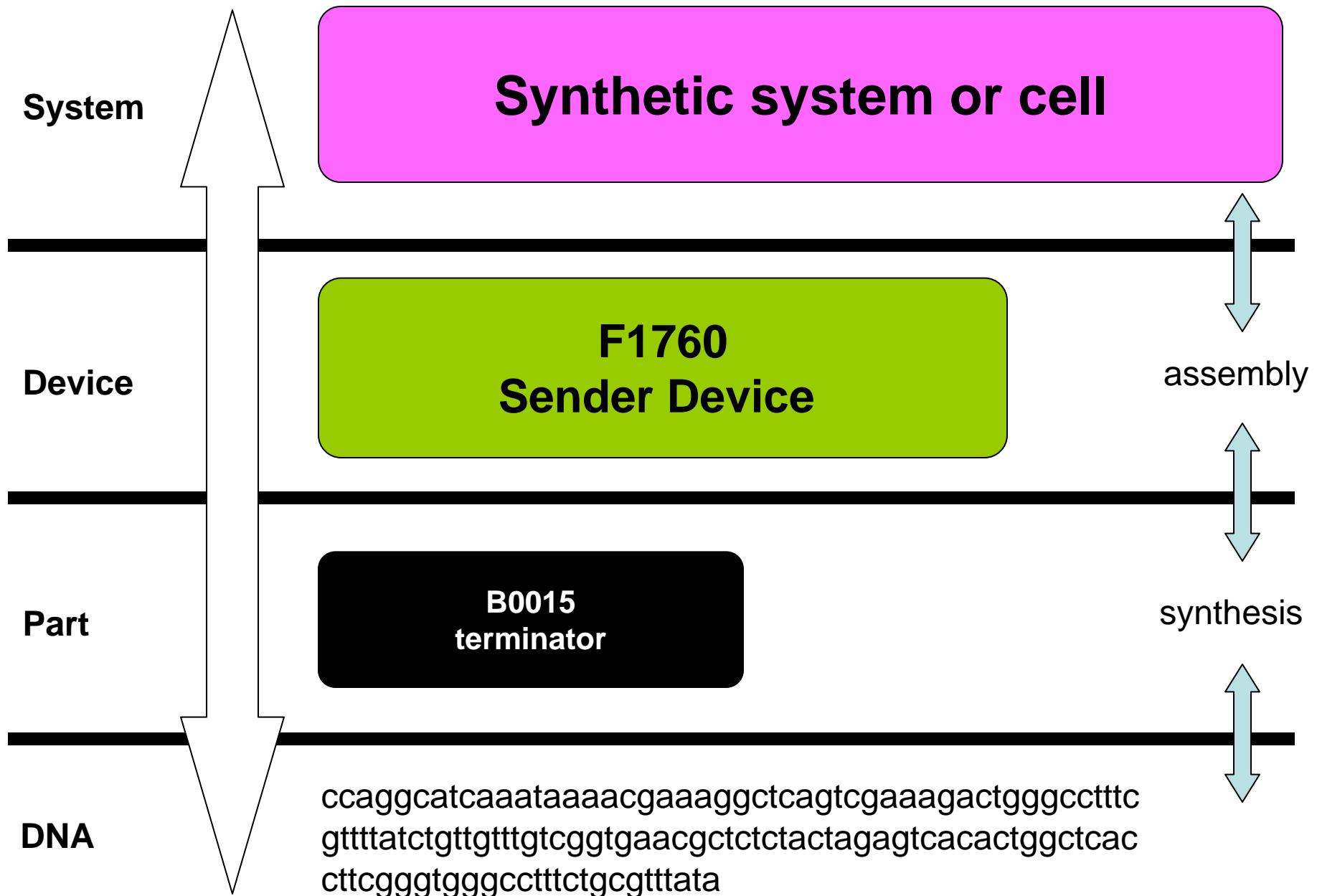
Designed by: Reshma Shetty

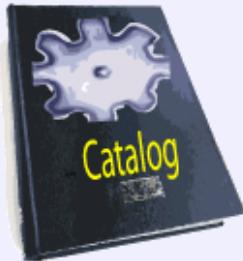
Forward efficiency: 0.984

Reverse efficiency: .295



## STANDARDIZED DATA




[jump to part](#)
[BBa\\_](#)
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# Transcriptional Regulators

**Available repressible regulators (normally ON) [-?](#)**
[Show 0 more parts](#)
[Edit](#)

-?	Name	Description	Direction	Control <a href="#">-?</a>	Output Low High	Length
A W	<a href="#">BBa_I14032</a>	promoter P(Lac) IQ	Forward			37
A W	<a href="#">BBa_R0040</a>	promoter (tetR, negative)	Forward	aTc, tetracycline		54
A W	<a href="#">BBa_R0051</a>	promoter (lambda cl regulated)	Forward	lambda cl		49

**Available inducible regulators (normally OFF) [-?](#)**
[Show 0 more parts](#)
[Edit](#)

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

**Available other regulators**
[Show 172 more parts](#)
[Edit](#)

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





## Shares:

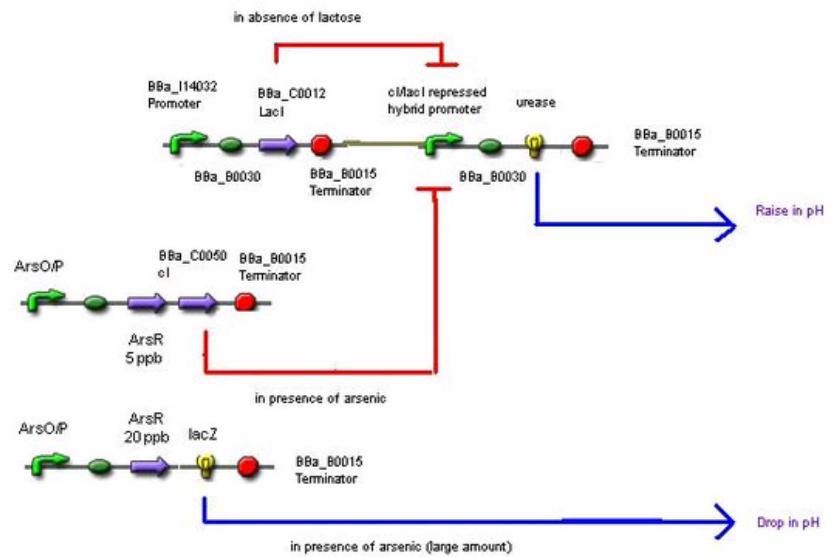
- DNA parts
- DNA code
- Protocols
- Experience
- Publications
- One big rule: share back!





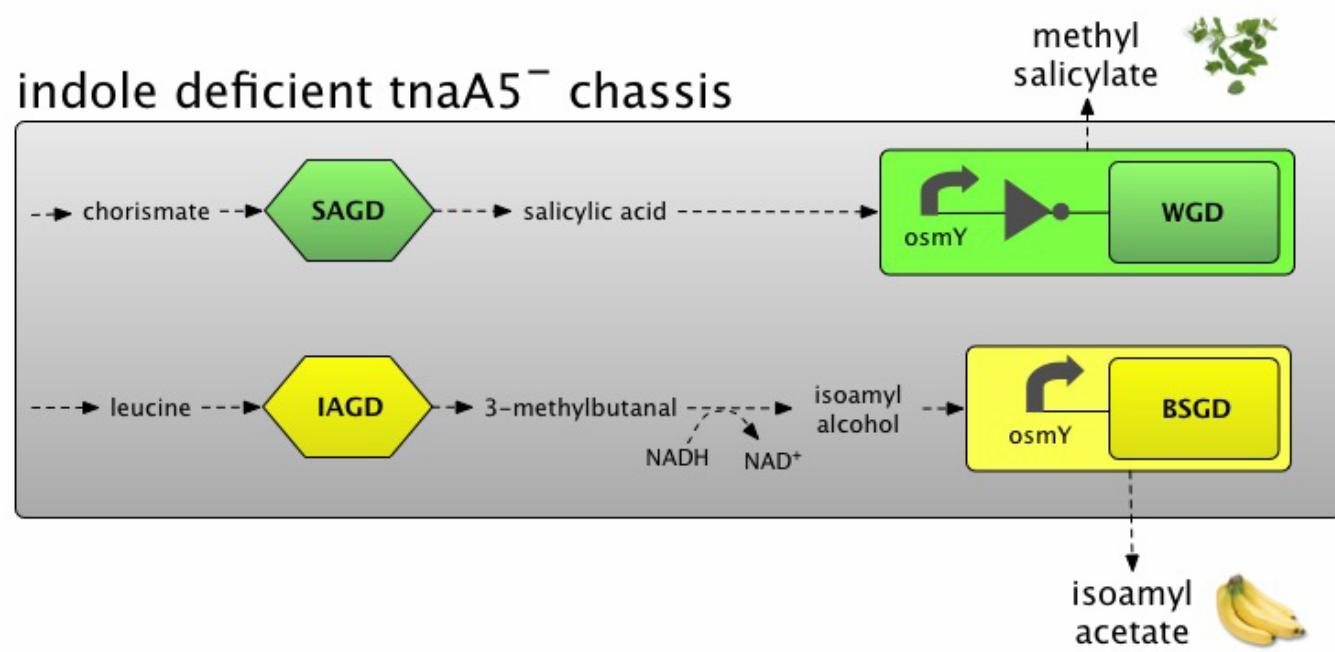
2006 Jamboree – 400 gengineers







## indole deficient *tnaA5*<sup>-</sup> chassis





# iGEM 2007 Wiki

International Genetically Engineered Machine Competition

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## The University of Ljubljana

They became the reigning champion of iGEM last year after winning the Grand Prize and returning to Slovenia with the coveted BioBrick trophy. This year they are building synthetic defender cells for the immune system.

## Jamboree



[sat & sun, nov 3-4](#)

The Jamboree is the culmination of iGEM. Lots of information is on the [Jamboree Page](#), or jump right to:

- [schedule](#)
- [Jamboree Registration](#)
- [hotels](#)
- [compete](#)
- [dna submission](#)

## 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.

[Learn More](#)

## calendar

[Jamboree roster + fees due](#) *fri 12 oct 07*

[iGEM wiki frozen + parts postmarked](#) *fri 26 Oct 07*

[Jamboree!](#) *sat-sun 3-4 nov 07*

[Registry + BioBrick foundation workshops](#) *sun-tue 4-6 nov 07*

## iGEM Press







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[Landscape and Culture: The Social Meaning of Place](#)  
  
[Who Protects the Protectors? Health, War & Society Film Series](#)

## U of A team building a better bacterium

By [Ileiren Poon](#), ExpressNews Staff

October 22, 2007 - Edmonton - A group of University of Alberta students have spent the summer working on building a new kind of bacteria - one that might hold some answers to the planet's diminishing supply of fossil fuels.

The team members - who call themselves the Buta-nerds - have been working on a way to create an organism that will produce butanol fuel for an annual competition hosted by



Members of the U of A Buta-nerds team are collecting data for a Nov. competition at MIT.

[Print story](#) | [Email story](#)

 [U of A team prepares for MIT competition in November:](#)

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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.

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™

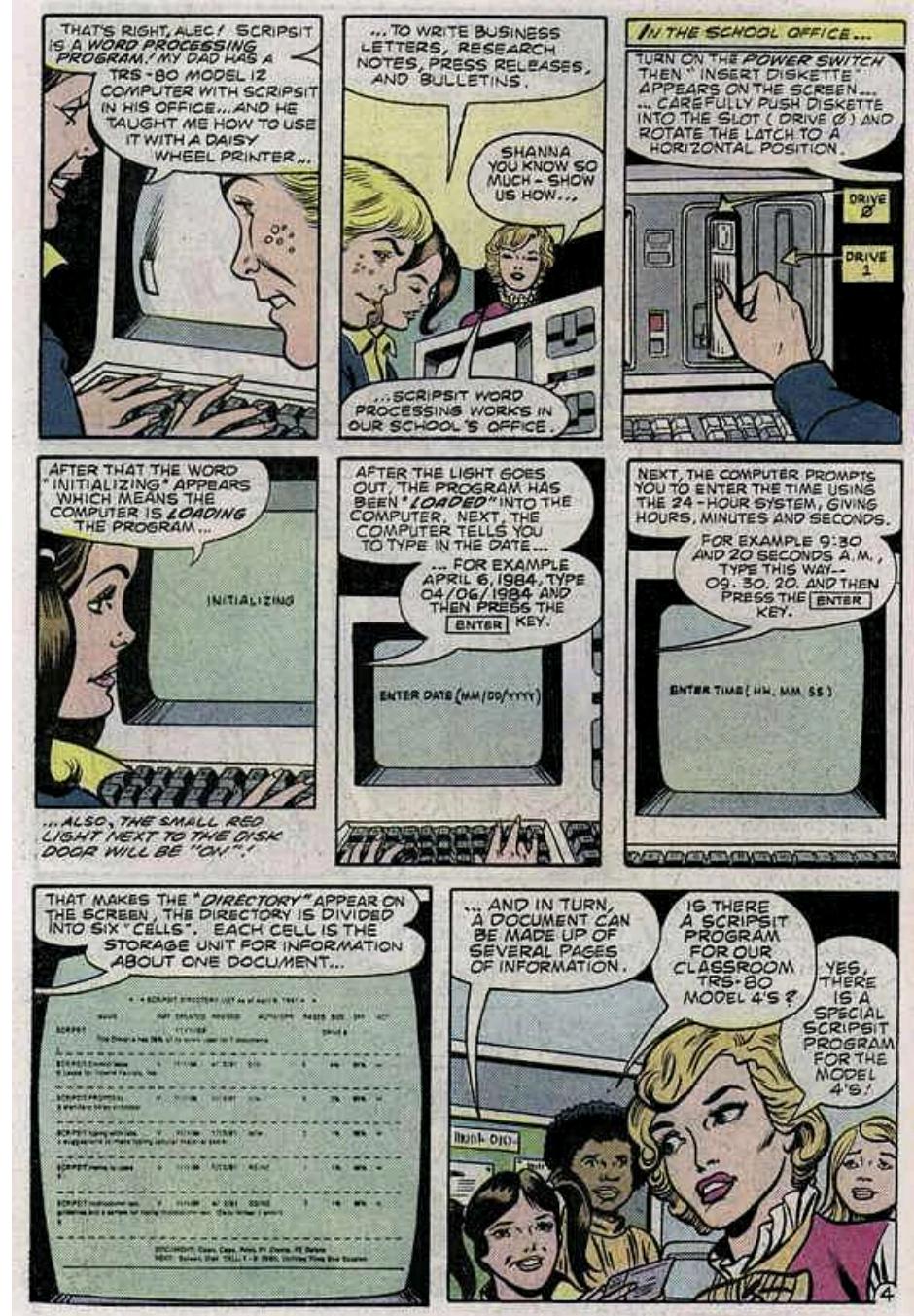
ALEC AND  
SHANNA  
STARRING IN

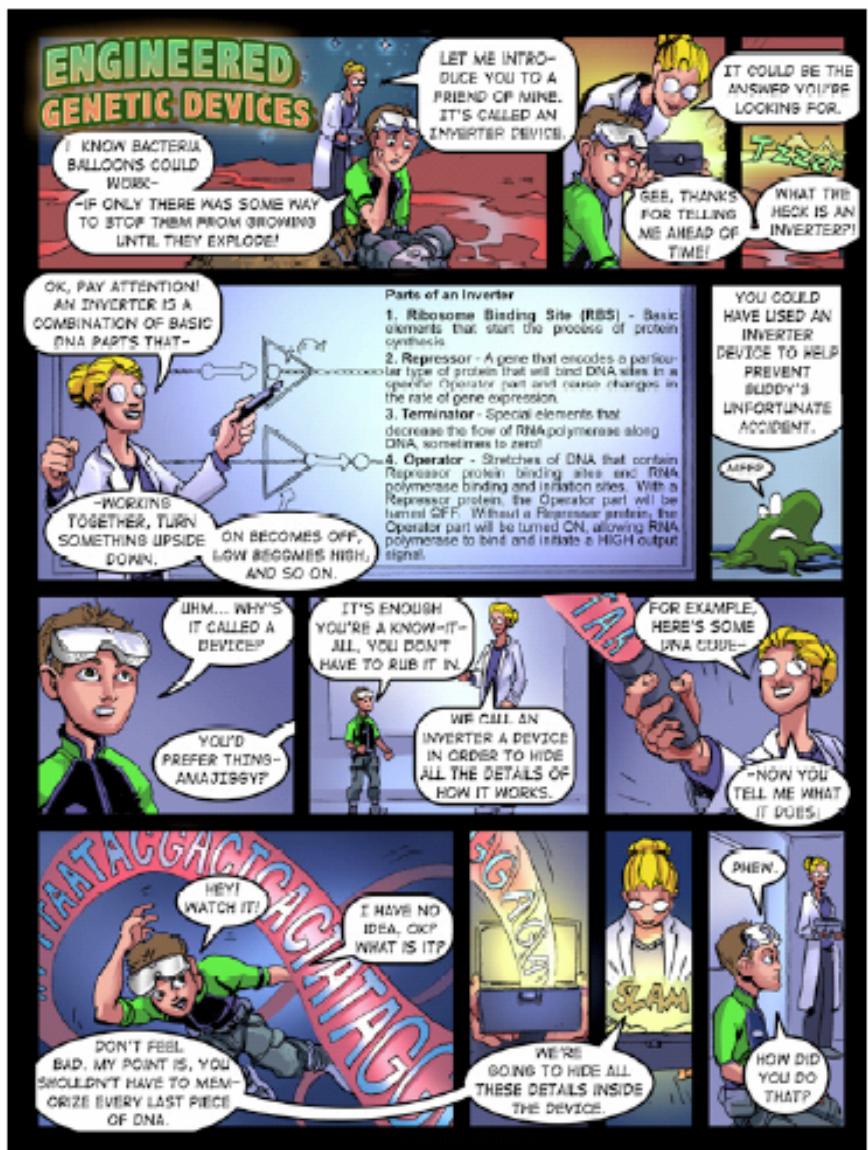
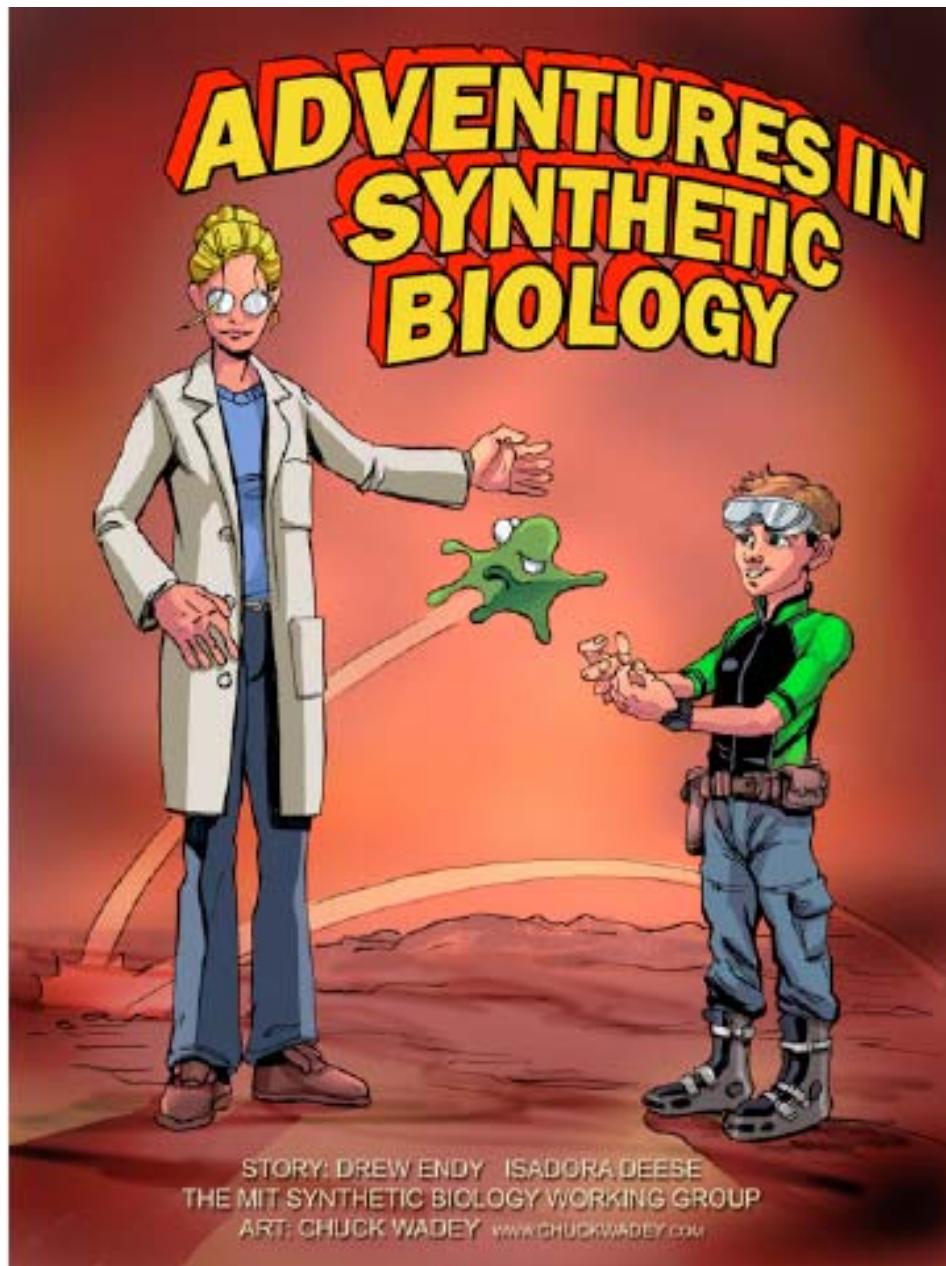
# THE COMPUTER TRAP

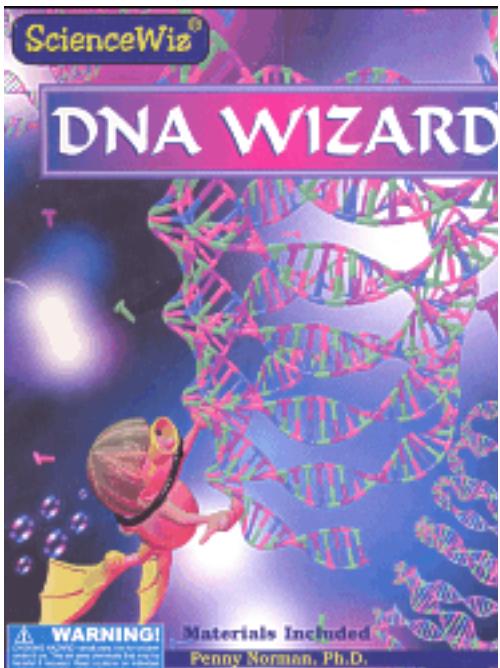
A comic book illustration of four people on a boat deck at night. A man in a green sweater is on the right, another man in a brown jacket is in the center, a woman in a purple sweater is on the left, and a man in a blue shirt is partially visible behind the woman. They are working with ropes and equipment. 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". A small speech bubble from the man in the green sweater says "I'm not afraid of sharks!".

COMPLIMENTS OF  
**RadioShack®**  
The Name in Classroom Computing™

DICK  
AYERS  
AND  
CHIC  
STONE







# 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?

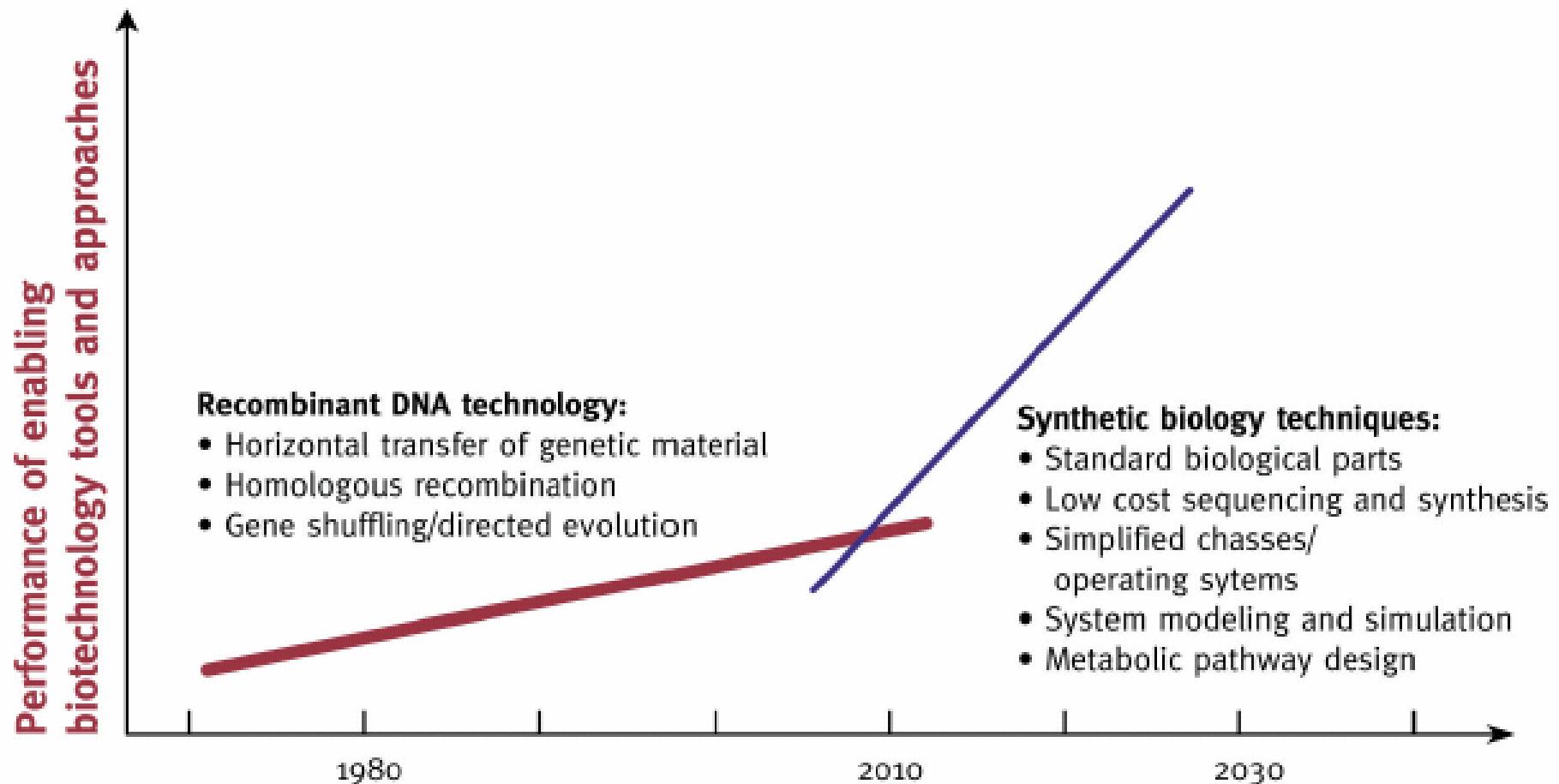
Ooey, Gooey, DNA!

Dress up for sterile techniques.

Quality time, quality learning, quality play.

Solve the chromosome puzzle.

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?

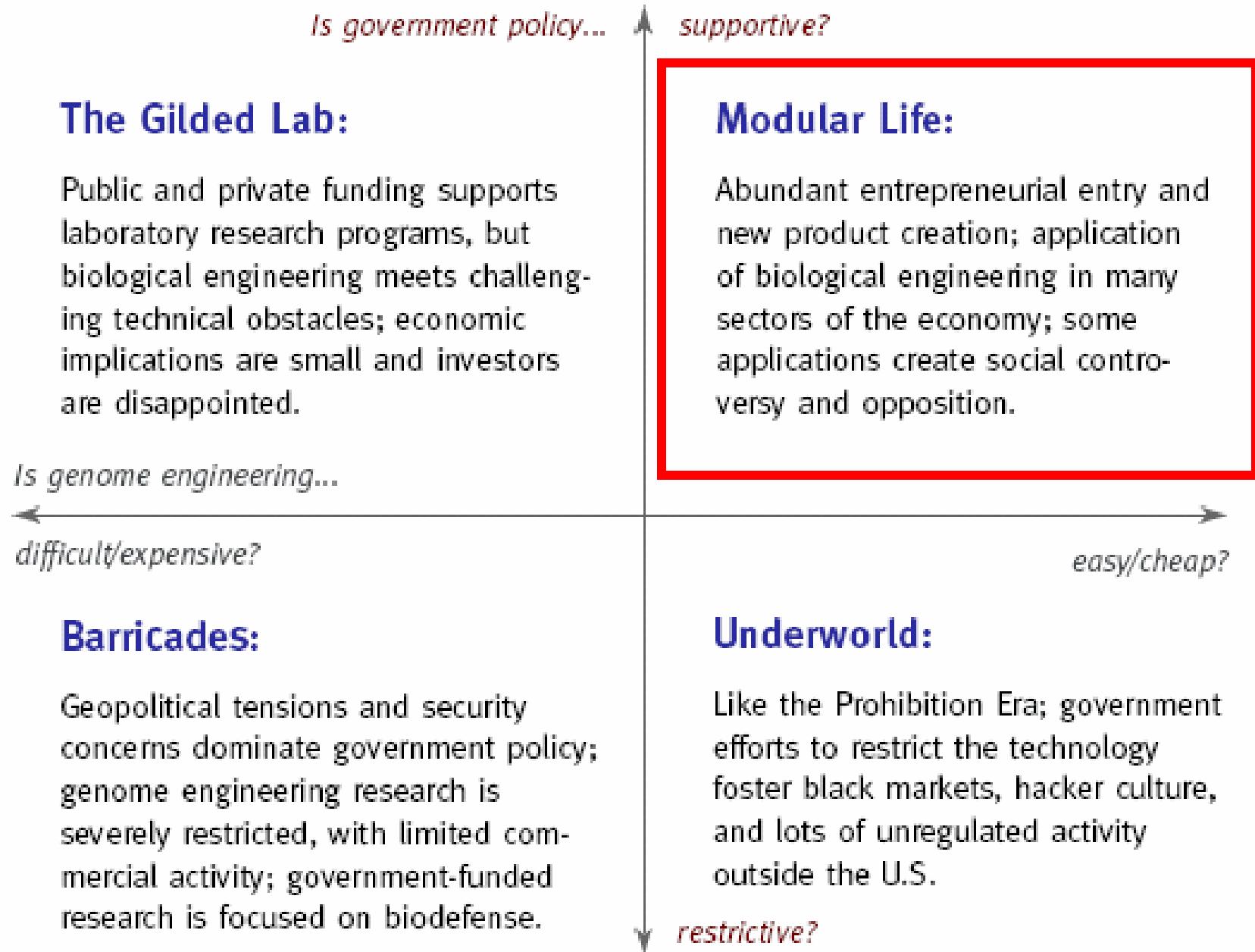
## Predetermined Elements

- 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

### Genome Transplantation in Bacteria: Changing One Species to Another

Carole Lartigue, John I. Glass, \* Nina Alperovich, Rembert Pieper, Prashanth P. Parmar, Clyde A. Hutchison III, Hamilton O. Smith, J. Craig Venter

The J. Craig Venter Institute, Rockville, MD 20850, USA.

## science theguardian

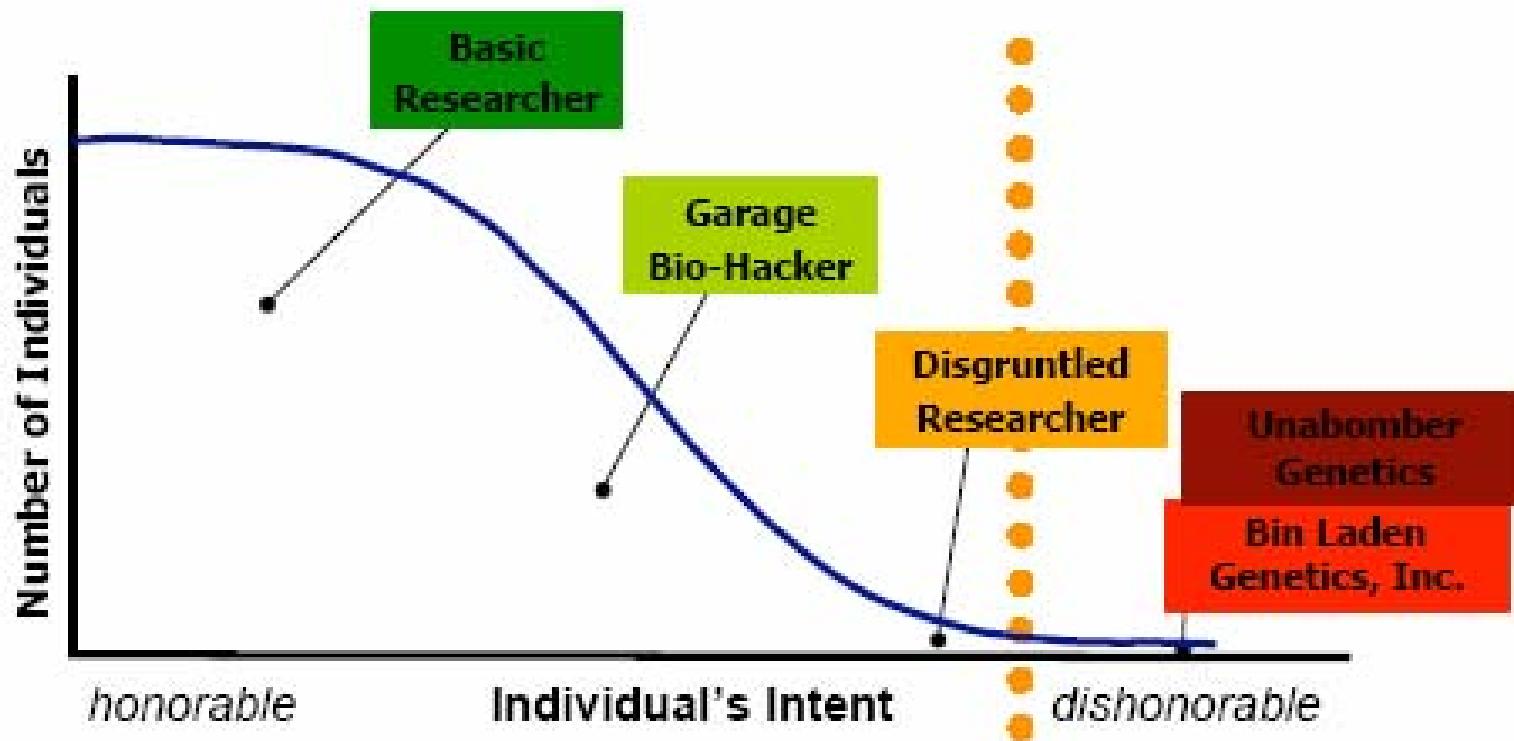
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## I am creating artificial life, declares US gene pioneer

- Scientist has made synthetic chromosome
- Breakthrough could combat global warming

## *Suite of solutions*

---



## SYNTHETIC GENOMICS | *Options for Governance*

---

Michael S. Gartland, The J. Craig Venter Institute, Rockville, Maryland; Drew Endy, Massachusetts Institute of Technology, Cambridge, Massachusetts; Gerald L. Epstein, Center for Strategic and International Studies, Washington, District of Columbia and Robert M. Friedman, The J. Craig Venter Institute, Rockville, Maryland

October 2009

J. Craig Venter®  

dicaprio

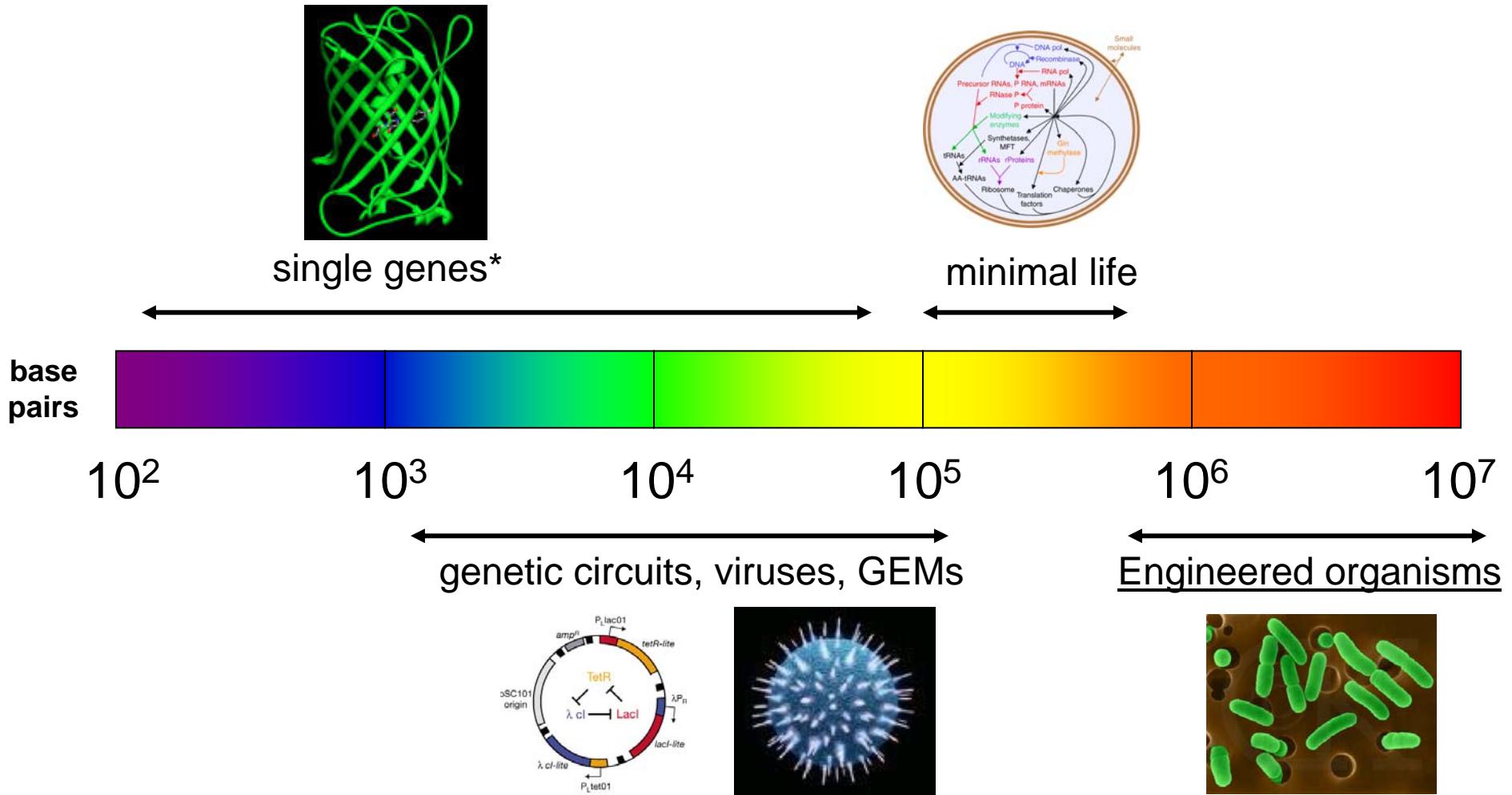
hanks



## Q&A: Former fraudster Frank Abagnale offers IT security advice

Next generation biotechnology

# Applications dependent on synthetic capabilities





# LS9, INC.

the renewable petroleum company™





Realizing the Promise of Synthetic Biology

COMPANY PROFILE

TECHNOLOGY

CURRENT PROJECTS

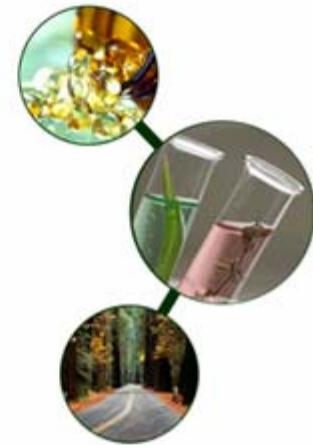
NEWS

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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## Stop Cloning Genes SYNTHESIZE THEM!

Rapid, high-quality,  
low-cost gene synthesis



Gene  
Synthesis



Constructed  
Variant  
Libraries



Constructed  
Operons &  
Operon Variant  
Libraries



Genomic  
Engineering





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## Investors

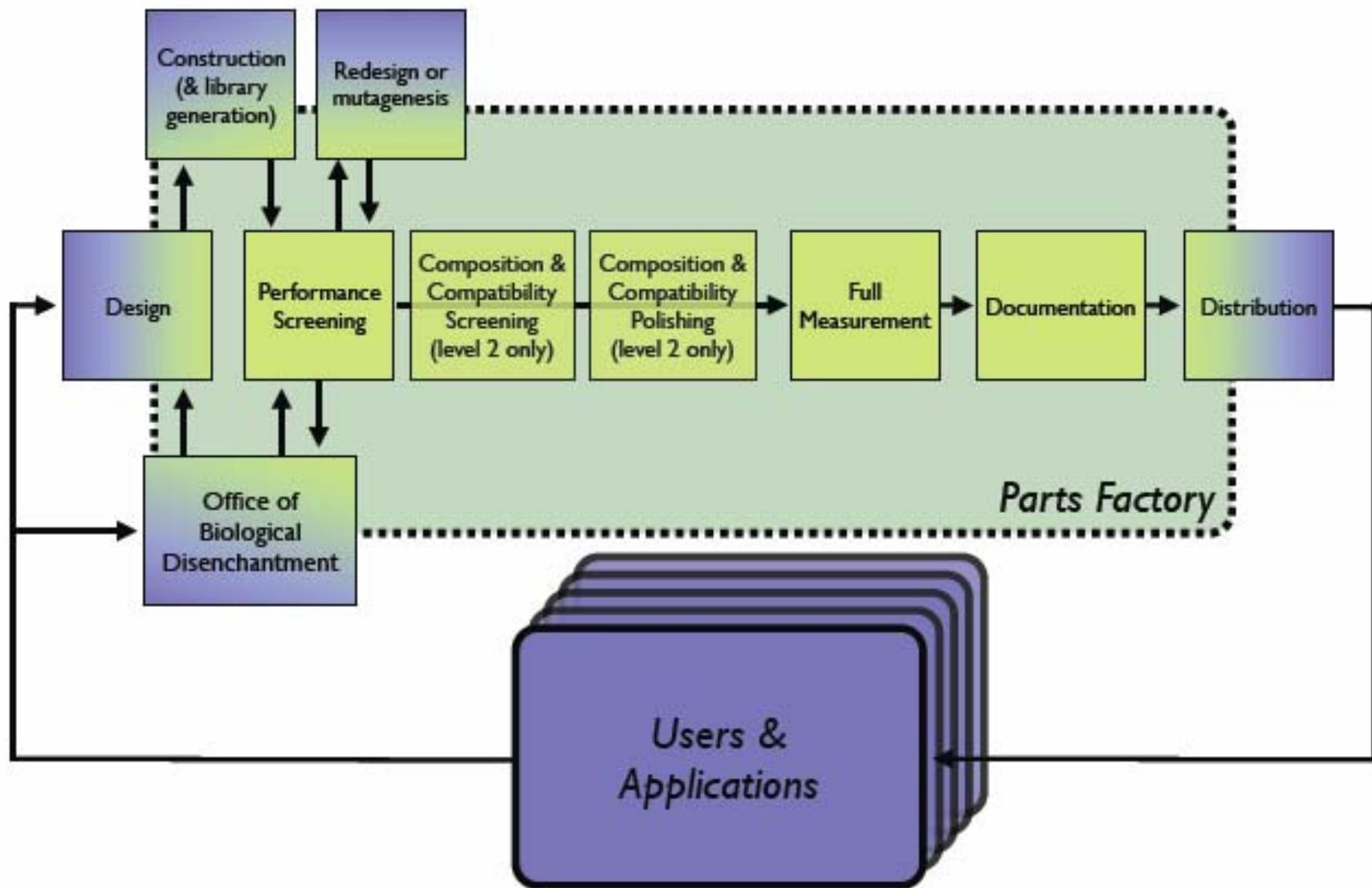
**Funded by a syndicate of well-respected, top-tier venture capital firms, Archemix has raised over \$100 million to date.**

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.

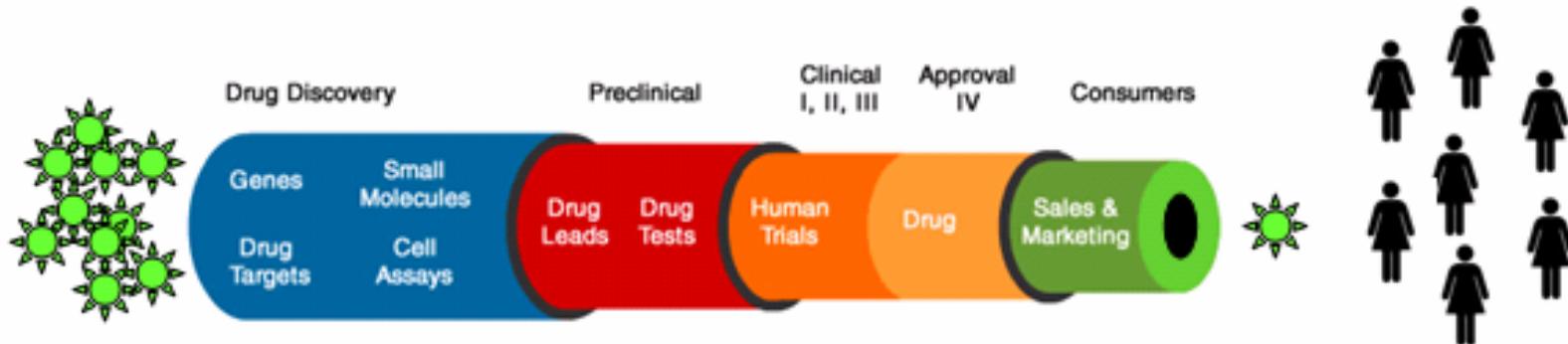
## Archemix and Merck KGaA Sign Strategic Alliance

*Collaboration to Focus Primarily on Cancer Therapeutics Using Novel Aptamer Technology*



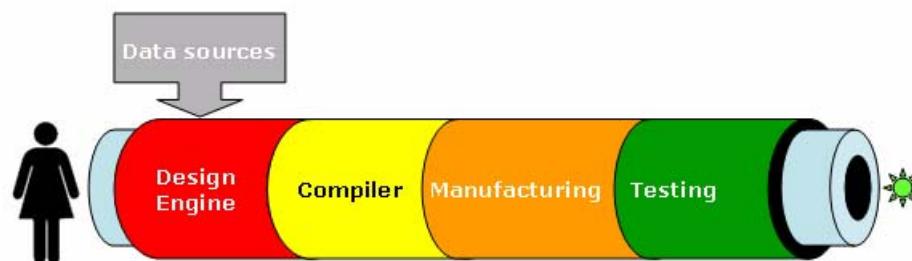


## Toward a New Drug Development Pipeline Suitable for Personalized Cancer Therapeutics

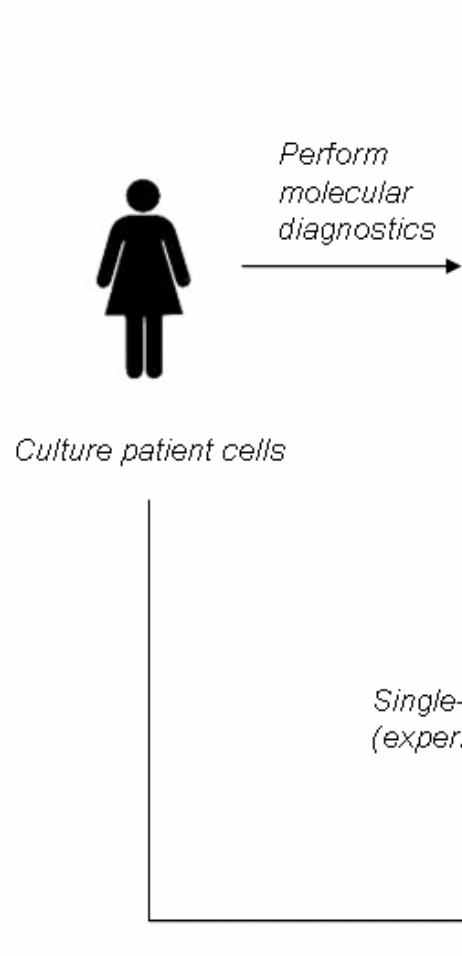


Ideally, a next-generation pipeline for effective cancer drugs would:

- As an output, produce personalized medicines
- Be able to produce a targeted medicine for every cancer, newly diagnosed or recurring
- Allow for rapid and sustainable development of these outputs
- Have favorable drug development economics, ie. the cost of producing drugs decreases over time
- Make a failure of any drug in the pipeline a trivial event
- Be able to grow in output capacity to satisfy the needs of a global market
- Continuously incorporate the latest understanding and data from molecular biology, oncology, and related sciences, plus growing clinical experience with personalized medicines
- And, finally, ensure the highest possible standards of safety and oversight



## Clinical presentation



## Open Bio-Fabrication

## Shared knowledge base

*in vitro testing should show drug affects only cancer cells, otherwise failures analyzed and design process repeated*

**Pinkarmy.org**



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## Google Health Wants to Digitize Your Medical Records

Google Health, Mayer says, wants to digitize your health records—x-rays, immunization records, every surgery, every doctor visit, everything. And she wants you to be able to take it with you anywhere in the world, perhaps on some kind of external device. That information will be protected by a password, but you will also be able to share it with your friends and family.



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# GENETICS IS ABOUT TO GET PERSONAL

don't panic, we're here to help

23andMe is a privately held company developing new ways to help you make sense of your own genetic information.

# Opportunities for Alberta if..

- Can think ***BIG*** and move ***Fast***
- Tear down barriers between professions and institutions and think global in scale
- Move aggressively to educate!
- Develop core resources (informational and physical)
- Choose exciting and valuable applications
- Support next-generation industry



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Alberta Ingenuity operates  
the Alberta Heritage Foundation for Science and Engineering Research,  
a \$1 billion endowment to support research.

# Ingenuity

NEWS

**Ingenuity launches bold new \$100 million research program**  
October 10, 2007 - Ingenuity Accelerators focus on ensuring future prosperity of the province.