BIOE.44

Synthetic Biology Lab

11 May 2010 Lecture / Discussion notes

http://openwetware.org/wiki/Stanford/BIOE44

GOALS FOR TODAY's CLASS

1. Might changing technologies / tools impact ownership, sharing, and innovation frameworks underlying genetic and biological engineering?

Property Rights are Important

X000001
July 31, 1790

The United States.

To all to whom these Presents shall come. Greeting.

Whereas Samuel Hopkins of the City of Philadelphia and State of Pensylvania hath discovered an Improvement, not known or used before such Discovery, in the making of Pot ash and Pearl ash by a new Apparatus and Process, that is to say, in the making of Pearl ash 1st. by burning the raw Ashes in a Furnace, 2d. by dissolving and boiling them when so burnt in Water, 3rd. by drawing off and settling the ley, and 4th. by boiling the ley into salts which then are the true Pearl ash; and also in the making of Pot ash by fluxing the Pearl ash so made as aforesaid; which Operation of burning the raw Ashes in a Furnace, preparatory to their Dissolution and boiling in Water, is new, leaves little Residuum; and produces a much greater Quantity of Salt: These are therefore in pursuance of the Act, entitled "An Act to promote the Progress of useful Arts", to grant to the said Samuel Hopkins, his Heirs, Administrators and Assigns, for the Term of fourteen Years, the sole and exclusive Right and Liberty of using, and vending to others the said Discovery, of burning the raw Ashes previous to their being dissolved and boiled in Water, according to the true Intent and Meaning of the Act aforesaid. In Testimony whereof I have caused these Letters to be made patent, and the Seal of the United States to be hereunto affixed. Given under my Hand at the City of New York this thirty first Day of July in the Year of our Lord one thousand seven hundred & Ninety.

G. Washington

City of New York July 31st. 1790.

I do hereby Certify that the foregoing Letters patent were delivered to me in pursuance of the Act, entitled "An Act to promote the Progress of useful Arts", that I have examined the same, and find them conformable to the said Act.

Edm: Randolph Attorney General for the United States.

The first U.S. patent, issued to Samuel Hopkins on July 31, 1790, for an innovative way of making "pot ash and pearl ash" -- source, Wikipedia

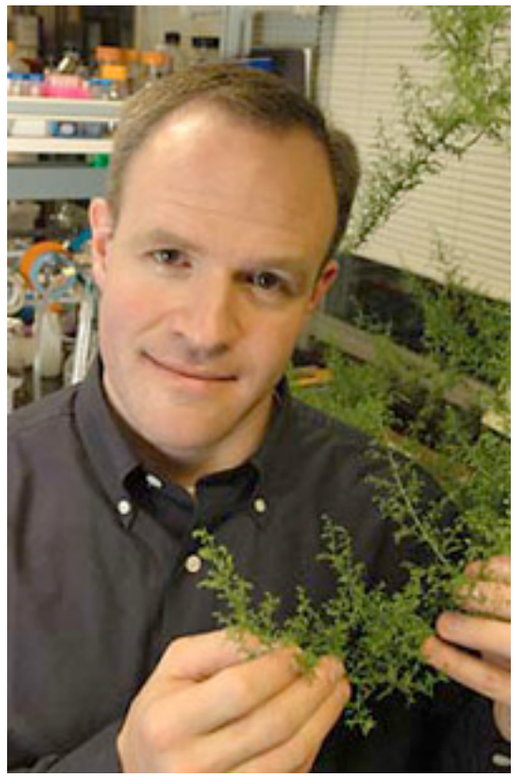
1. Define and scale relationships among parties

2. Support investment and returns

3. Rights frameworks change over time

What About Biotech Today?

Example: UC Berkeley, Amyris Inc., & One World Health team up against malaria!



VS

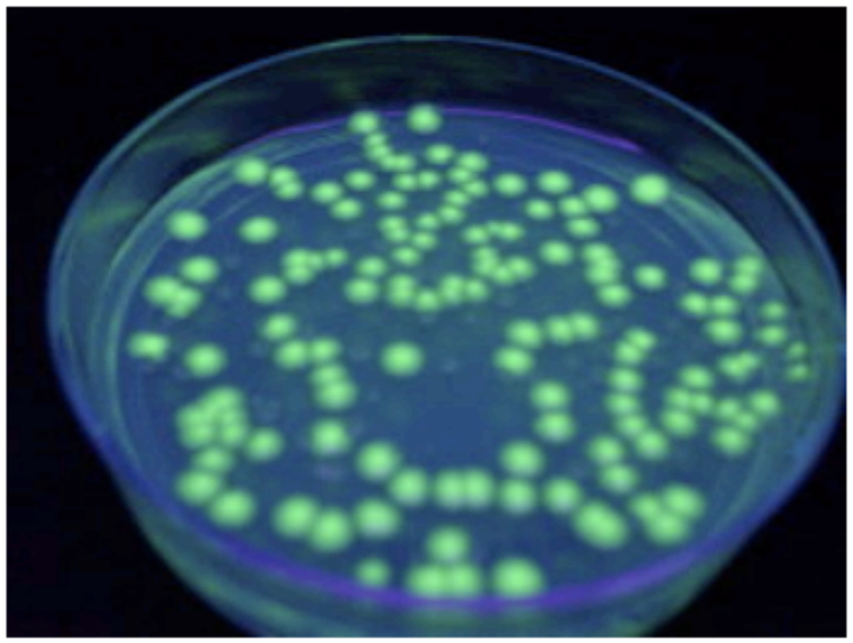
1. ~10 step biosynthesis project leading to artemisinin

2. ~$25 million research and development budget

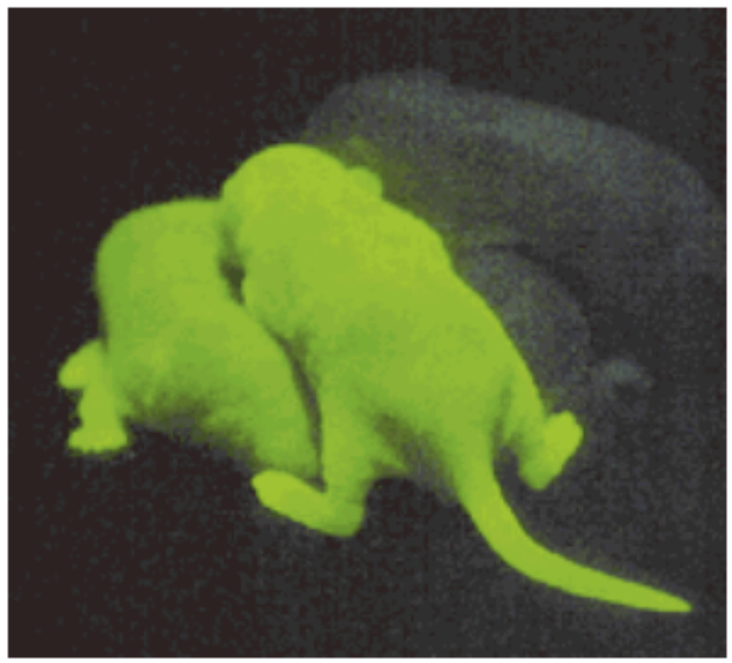
3. Strong, traditional patent-based property rights program

4. Enable and preserve freedom to operate

http://www.yildizindunyasi.net/bilim%20dunyasi/gfp.htm



http://homepage3.nifty.com/nature_of_minamino/



http://www.brown.edu/Courses/BI0105_Miller/read/optical.html

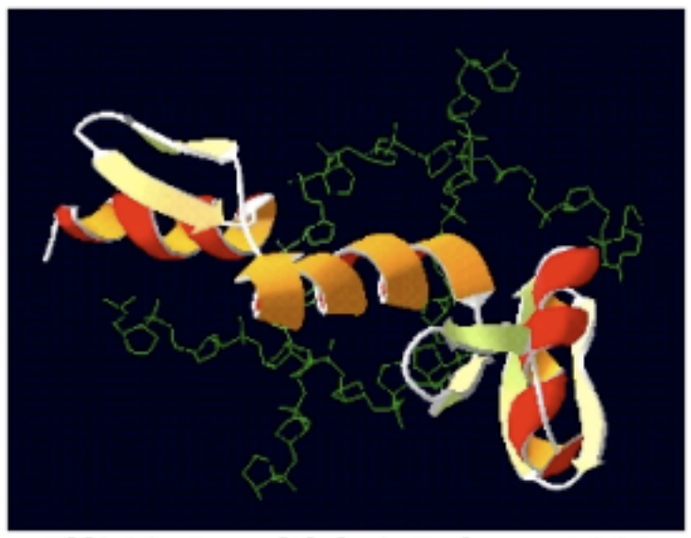
United States Patent *5,491,084*
Chalfie , et al. **February 13, 1996**

Uses of green-fluorescent protein

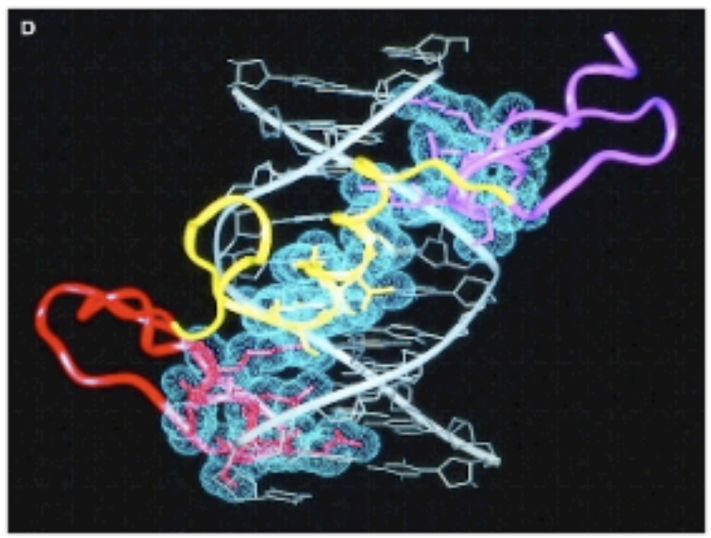
Abstract

This invention provides a cell comprising a DNA molecule having a regulatory element from a gene, other than a gene encoding a green-fluorescent protein operatively linked to a DNA sequence encoding the green-fluorescent protein. This invention also provides a method for selecting cells expressing a protein of interest which comprises: a. introducing into the cells a DNAI molecule having DNA sequence encoding the protein of interest and DNAII molecule having DNA sequence encoding a green-fluorescent protein; b. culturing the introduced cells in conditions permitting expression of the green-fluorescent protein and the protein of interest; and c. selecting the cultured cells which express green-fluorescent protein, thereby selecting cells expressing the protein of interest. Finally, this invention provides various uses of a green-fluorescent protein.

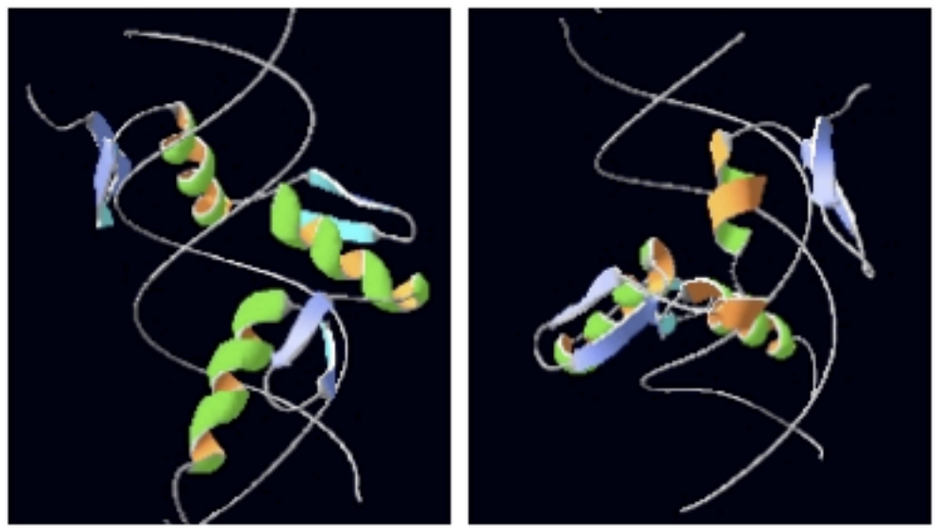
Inventors: **Chalfie; Martin** (New York, NY); **Prasher; Douglas** (East Falmouth, MA)
Assignee: **The Trustees of Columbia University in the City of New York** (New York, NY); **Woods Hole Oceanographic Institution** (Woods Hole, MA)
Appl. No.: **119678**
Filed: **September 10, 1993**



Zif268, Paveltich & Pabo c. 1991



Random Zif268s, Greisman & Pabo c. 1997



$TATA_{ZF-6}$ & $TATA_{ZF-2'}$ Wolfe et al. c. 2001

United States Patent **6,903,185**
Kim , et al. **June 7, 2005**

Poly ***zinc*** finger proteins with improved linkers

Abstract

Chimeric proteins, and methods for their production and use are disclosed. The chimeric proteins comprise a flexible linker between two ***zinc*** finger DNA-binding domains, wherein the linker comprises eight or more amino acids between the second conserved histidine residue of the carboxy-terminal ***zinc*** finger of the first domain and the first conserved cysteine residue of the amino-terminal ***zinc*** finger of the second domain.

Inventors: **Kim; Jin-Soo** (Inchon, KR); **Pabo; Carl O.** (Newton, MA)
Assignee: **Massachusetts Institute of Technology** (Cambridge, MA)
Appl. No.: **146221**
Filed: **May 13, 2002**

United States Patent Application **20050112615**
Kind Code **A1**
***Davies*, Stephen William ; et al.** **May 26, 2005**

Genetic circuit inverting amplifier

Abstract

We describe methods and compositions for setting the level of gene expression in a cell. The instant invention is of an amplifier, an analog circuit. It is directly analogous to the inverting amplifier commonly used in electronics. This circuit produces an output wherein an increase in the input signal leads to a proportional decrease in the output. Similarly, a decrease in the input leads to an increase in the output signal. Here the

United States Patent Application **20040235101**
Kind Code **A1**
Maclsaac, Kenzie D. ; et al. **November 25, 2004**

Genetic circuit clocked latch

Abstract

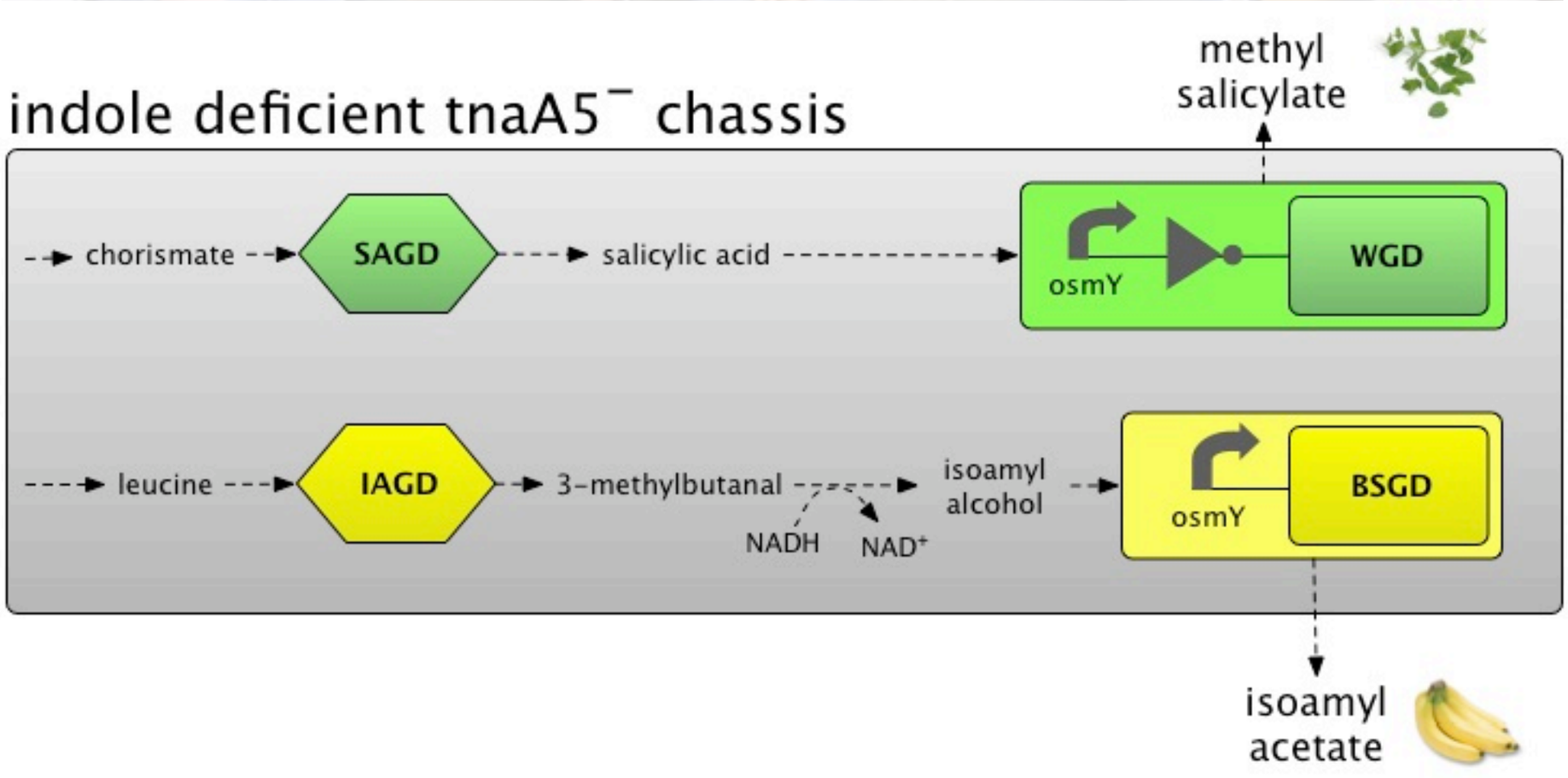
We describe methods and compositions for setting and maintaining the state of gene expression in a cell. The genetic circuit clocked latch has two states with each state corresponding to a different pattern of gene expression. The genetic circuit clocked latch allows one to set the state of

United States Patent ***6,774,222***
Schneider , et al. **August 10, 2004**

Molecular computing elements, gates and flip-flops

Abstract

This invention relates to novel molecular constructs that act as various logic elements, i.e., gates and flip-flops. The constructs are useful in a wide variety of contexts including, but not limited to, computation and control systems. The basic functional unit of the construct comprises a nucleic acid having at least two protein binding sites that cannot be simultaneously occupied by their cognate binding protein. This basic unit can be assembled in any number of formats providing molecular constructs that act like traditional digital logic elements (flips-flops, gates, inverters, etc.).


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

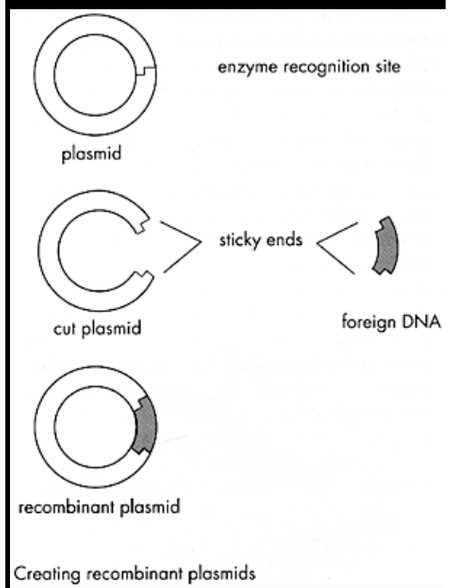
```
;;; Scheme code for Twenty-One Simulator [PS2 Fall '90]

(define (twenty-one player-strategy house-strategy)
  (let ((house-initial-hand (make-new-hand (deal))))
    (let ((player-hand
           (play-hand player-strategy
                      (make-new-hand (deal))
                      (hand-up-card house-initial-hand))))
      (if (> (hand-total player-hand) 21)
          0                                ; ``bust'': player loses
          (let ((house-hand
                 (play-hand house-strategy
                            house-initial-hand
                            (hand-up-card player-hand))))
            (cond ((> (hand-total house-hand) 21)
                   1)                      ; ``bust'': house loses
                  ((> (hand-total player-hand)
                      (hand-total house-hand))
                   1)                      ; house loses
                  (else 0))))))            ; player loses
```

Synthetic Biology as Tools Revolution

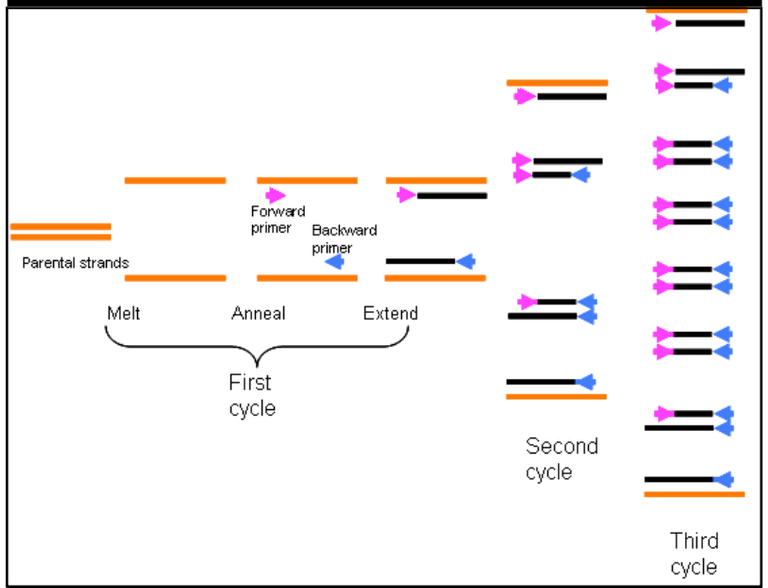
First Gen. Biotech =

Recombinant DNA



Basic "Cut" & "Paste"

Polymerase Chain Reaction



Amplify & Make Simple Changes

DNA Sequencing

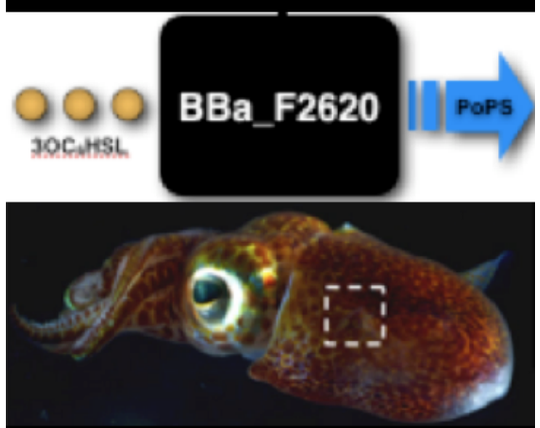
Read Out the Genetic Code

Next Gen. Biotech Adds New Tools =

Synthesis

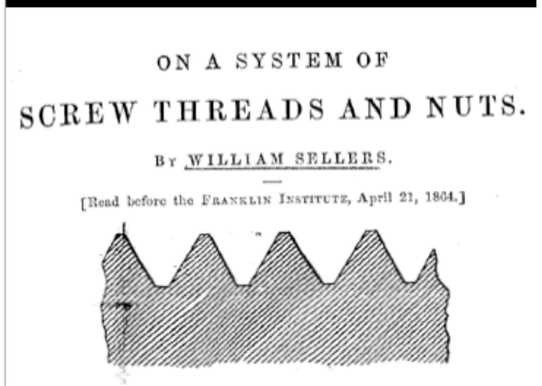
Decoupling of design & fabrication, leading to CAD and EDA.

Abstraction



Engineered simplicity enabling many component systems.

Standardization


ON A SYSTEM OF
SCREW THREADS AND NUTS.
By WILLIAM SELLERS.
[Read before the Franklin Institute, April 21, 1864.]

Refined genetic components supporting "off the shelf" reuse.

•••

Registry of Standard Biological Parts

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

Browse Parts by Type

Browse Parts by School

Featured Parts

Help & Documentation

Users & Groups

Registry Toolbox

Add a part

Search Parts

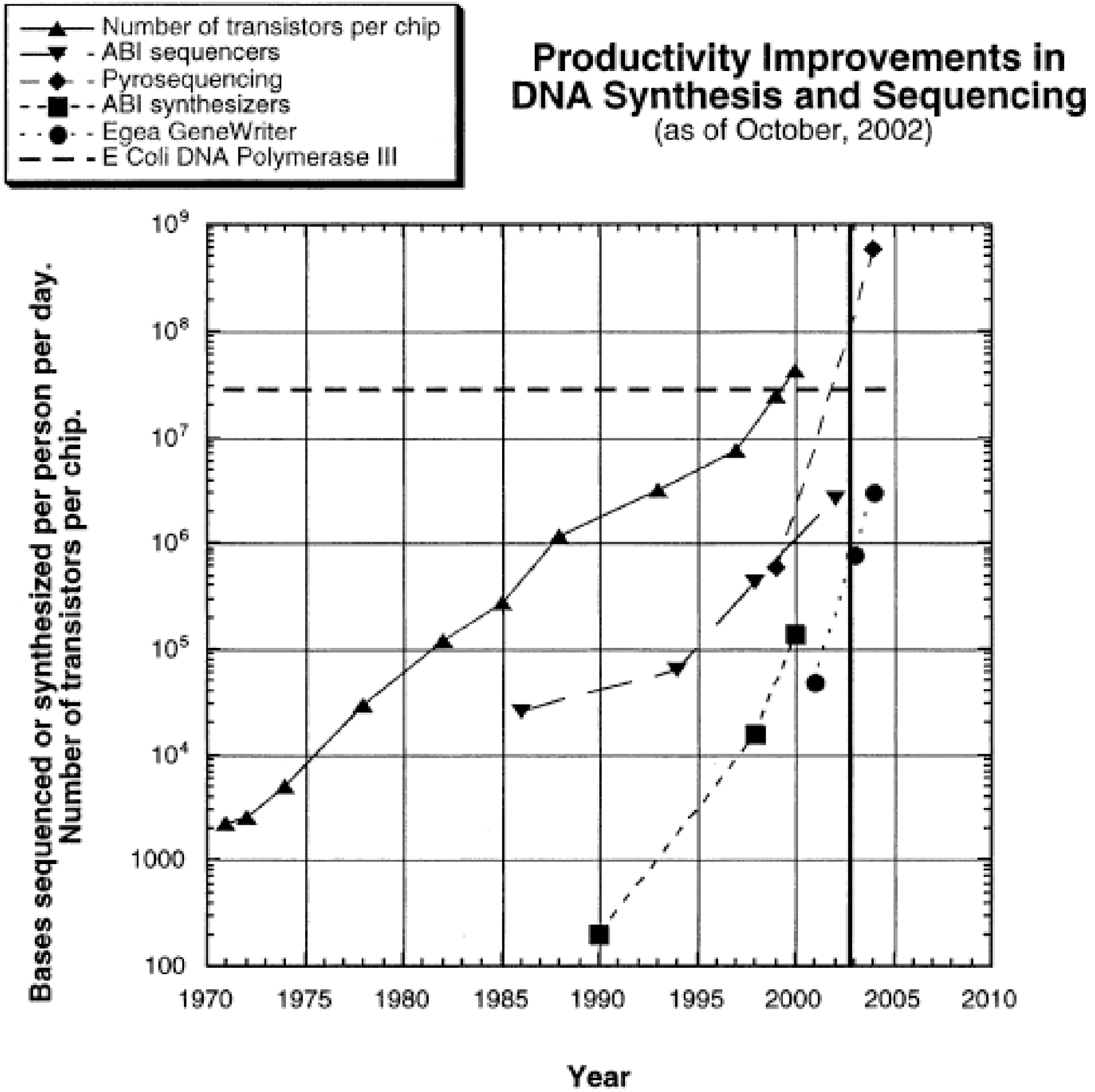
DNA Repositories

Sequence Analysis

Latest News

- [8/01/06] We have contact information for the creators of parts. You can access this information when you access "Hard Information" of a part.
- [8/01/06] A table made for yeast parts is now available on the Part Types page

Report any bugs here | Request new features here | See new features here



Carlson, Pace & Proliferation of Biological Technologies, Biosec. & Bioterror. 1(3):1 (2003)


PATENT
PENDING
THE CHRISTIAN SCIENCE MONITOR
Bennett

Evolution of Property Rights

The Copyright Act of 1976 stipulates (section 102):

(b) In no case does copyright protection for an original work of authorship extend to any idea, procedure, process, system, method of operation, concept, principle, or discovery, regardless of the form in which it is described, explained, illustrated, or embodied in such work.

Congress attempted to clarify the situation for computer programs (Rep. No. 473, 94th Cong., 1st Sess. 54 (1975)):

Section 102(b) is intended, among other things, to make clear that the expression adopted by the programmer is the copyrightable element in a computer program, and that the actual processes or methods embodied in the program are not within the scope of the copyright law.

and the National Commission on New Technological Uses of Copyrighted Works (CONTU), wrote in its final report (1978):

Where could a meaningful line of demarcation be drawn? Between flow chart and source code? Between source code and object code? . . . The Commission believes that none of these is appropriate. The line which must be drawn is between the expression and the idea, between the writing and the process which is described.

From MIT Course 6.805/STS085: Software and copyright law

E.g., copyright law was extended to cover software decades ago. More recently software patents have been pursued.

Connection or Collision?

(synthetic biology meets property rights)

Example:

2008 iGEM competition resulted in 1,500 new BioBrick Parts being developed last year, produced by students across 30 countries.

1. 2008 iGEM budget worldwide ~$4 million

2. Commercial freedom to operate unclear

3. Patent filings on all new 2008 parts would cost up to $37.5 million

4. iGEM and the parts collections continue to grow (geometric)

Connection or Collision?

(synthetic biology meets property rights)

Second Example:

1. DNA sequencing and synthesis technologies make genetic information and material interconvertible

2. Material transfer agreements are thus becoming less relevant

3. Sequencing and synthesis tools improving geometrically

Collision!!!

OPEN ACCESS Freely available online

PLoS BIOLOGY

Essay

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

Arti Rai*, James Boyle

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

In the same way that electrical engineers rely on standard

DNA, its developers believe that, as DNA synthesis technology becomes increasingly inexpensive [7], the registry will be composed largely of information and specifications that can be executed in synthesizers just as semiconductor chip designs are executed by fabrication firms.

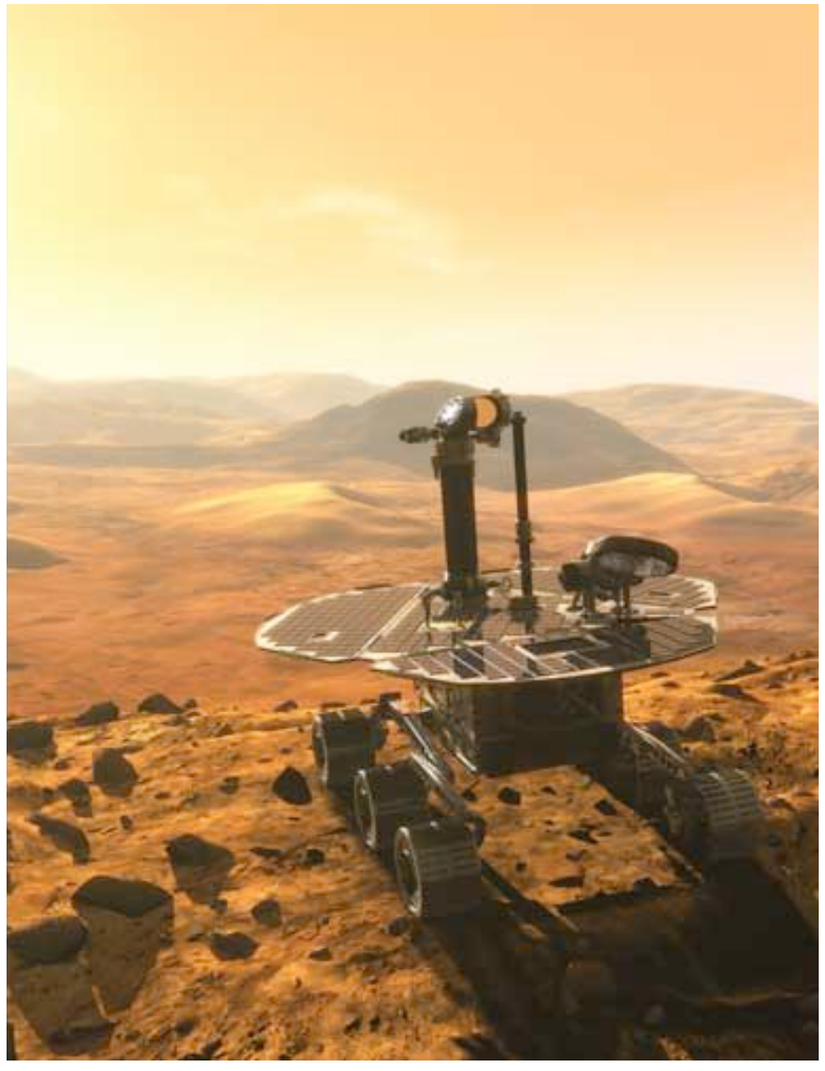
Synthetic biology has already produced important results, including more accurate AIDS tests and the possibility of unlimited supplies of previously scarce drugs for malaria [8]. Proponents hope to use synthetic organisms to produce not only medically relevant chemicals but also industrial materials, including biofuels such as hydrogen and ethanol [9]. At the same time, synthetic biology has engendered numerous policy concerns. From its inception, commentators have raised issues ranging from bioethical and environmental worries to fears of bioterrorism—indeed, the US Central

tension between different methods of creating "openness." On the one hand, one standard mechanism for creating openness has involved putting material in the public domain, outside the world of property. On the other, synthetic biology researchers may want to use intellectual property rights to create a "commons," just as developers of free and open source software use the leverage of software copyrights to impose requirements of openness on future programmers, requirements greater than those attaching to a public domain work. But synthetic biology, unlike software, is not necessarily protected by copyright. Should we rethink the boundary lines between intellectual property and the public domain as a result?

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

Intellectual property law in the US has

Challenge or Opportunity?



Experiments and advancements in the business models and ownership, sharing, and innovation frameworks will be at least as important to our future biotechnology successes and competitiveness as will be the advancements of our educational programs and research laboratories.

Past Lessons & Inspirations

Early 1970s

"The first Unix application would be a word-processing program to be used by AT&T's patent-writing group."

http://www.spectrum.ieee.org/print/1571

Mid 70s to Mid 90s

"Who can afford to do professional work for nothing? ... Nothing would please me more than being able to hire ten programmers and deluge the hobby market with good software."
Bill Gates, Microsoft, Inc.

http://www.time.com

"Proprietary software divides the users and keeps them helpless, and that is wrong."
Richard Stallman, Free Software Foundation

http://www.boycottnovell.com/2009/03/14/

Today

Google™ E*TRADE The New York Times

MySQL®

Free, Open Tools

Patents:	Standard practice	Slow & expensive
Copyright:	Cheap, easy to Use	Could be too strong. Not used today
Contracts:	Defined agreements	Leaky
Public Domain:	Cheap, fast	May not offer protection. Hard to build community
Sui Generis:	Could be exactly right	Expensive & political

Is a new prop. right needed?

What features would you want?