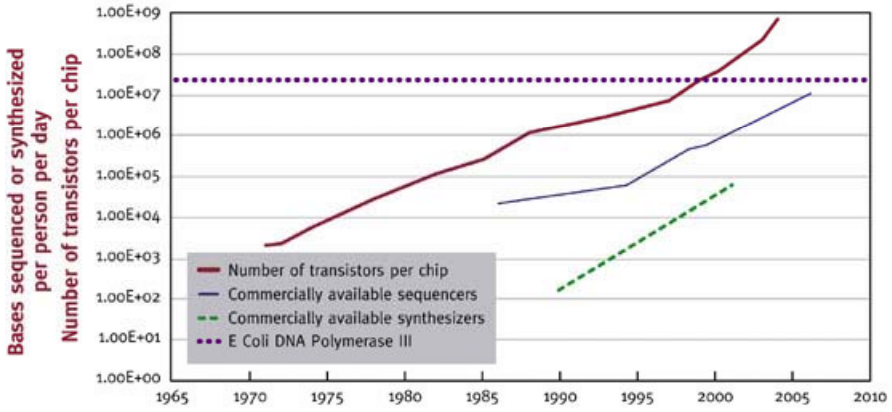
Design of Synthetic Genetic Systems

Closing the Design Automation Loop

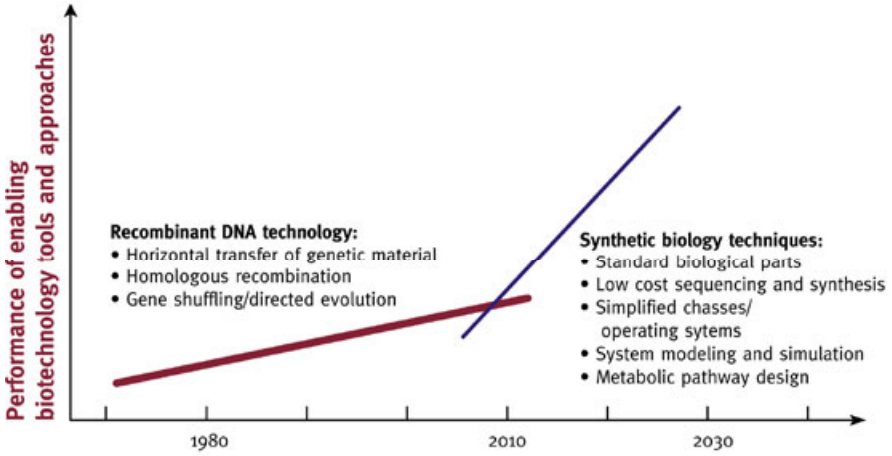
Jean Peccoud
Virginia Bioinformatics Institute
Virginia Tech

Moore's law of synthetic genomics

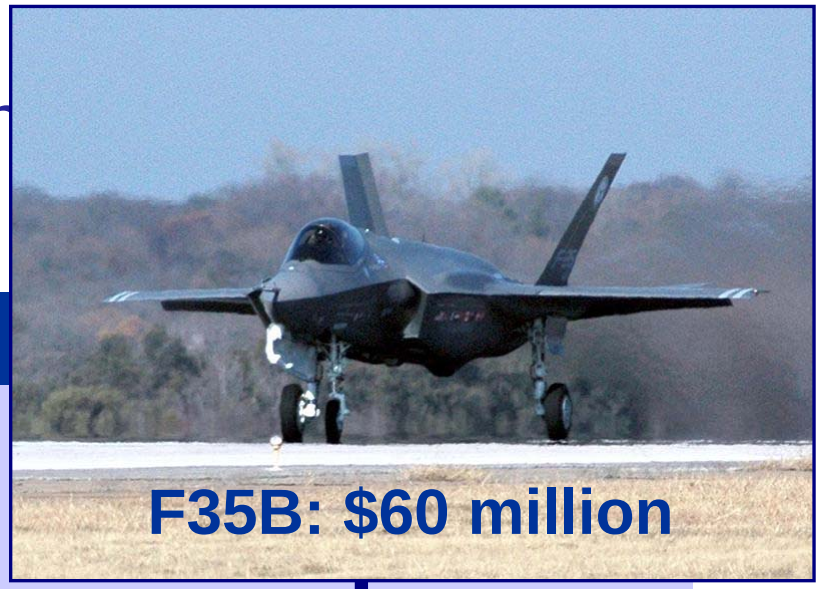
- **The productivity of DNA sequencing has increased more than 500-fold over the past decade. At this rate, productivity is doubling every 24 months.**
- **Over the same period, the costs of sequencing have declined by more than three orders of magnitude from $1.00 per base pair to less than $0.001 per base pair.**
- **Productivity of DNA synthesis technologies has increased 700-fold over the past decade, doubling every 12 months.**
- **Costs of gene synthesis have fallen from approximately $30 per base pair to less than $1 per base pair over the same period.**



Source: R. Carlson, Bio-era

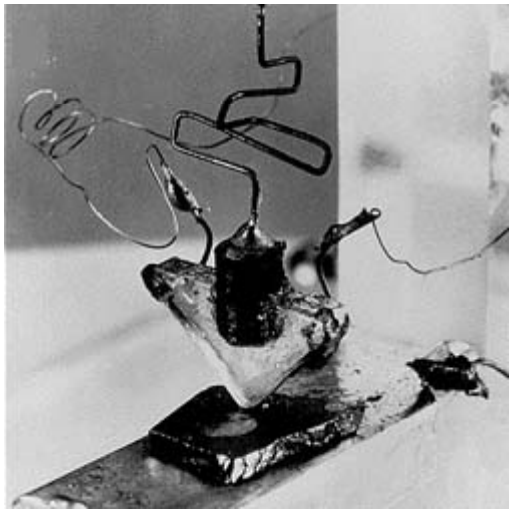


It is affordable to synth



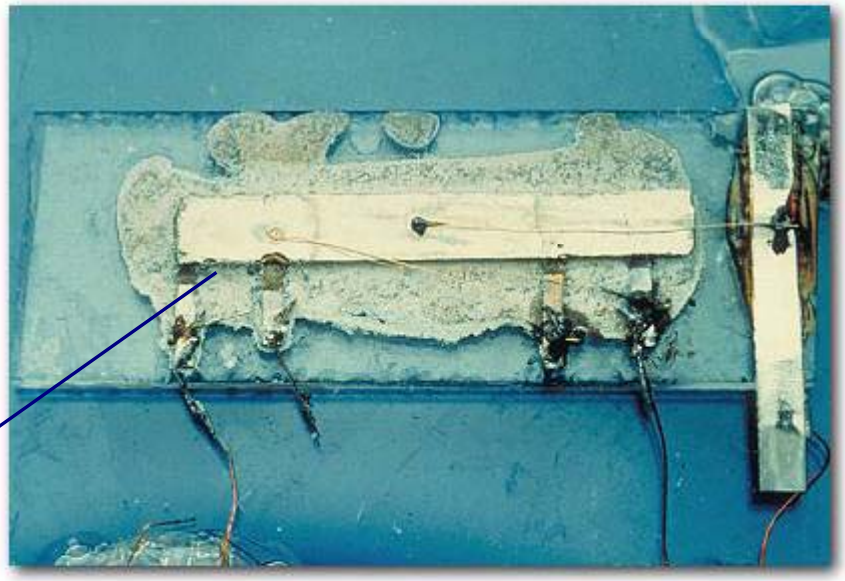
Organism	
Virus, Bacteriophage MS2	
Virus, SV40	
Virus, Phage Φ-X174;	
Filoviruses, Ebola	1.9×10^{4}
Bacterium, *Carsonella ruddii*	1.6×10^{5}
Bacterium, *Escherichia coli*	4×10^{6}
Nematode, *Caenorhabditis elegans*	9.8×10^{7}
Insect, *Drosophila melanogaster* aka Fruit Fly	1.3×10^{8}
Mammal, *Homo sapiens*	3.2×10^{9}

50 years ago



First tr
Bell La

Complexity of current artificial gene networks



First Integrated circuit.

Five components

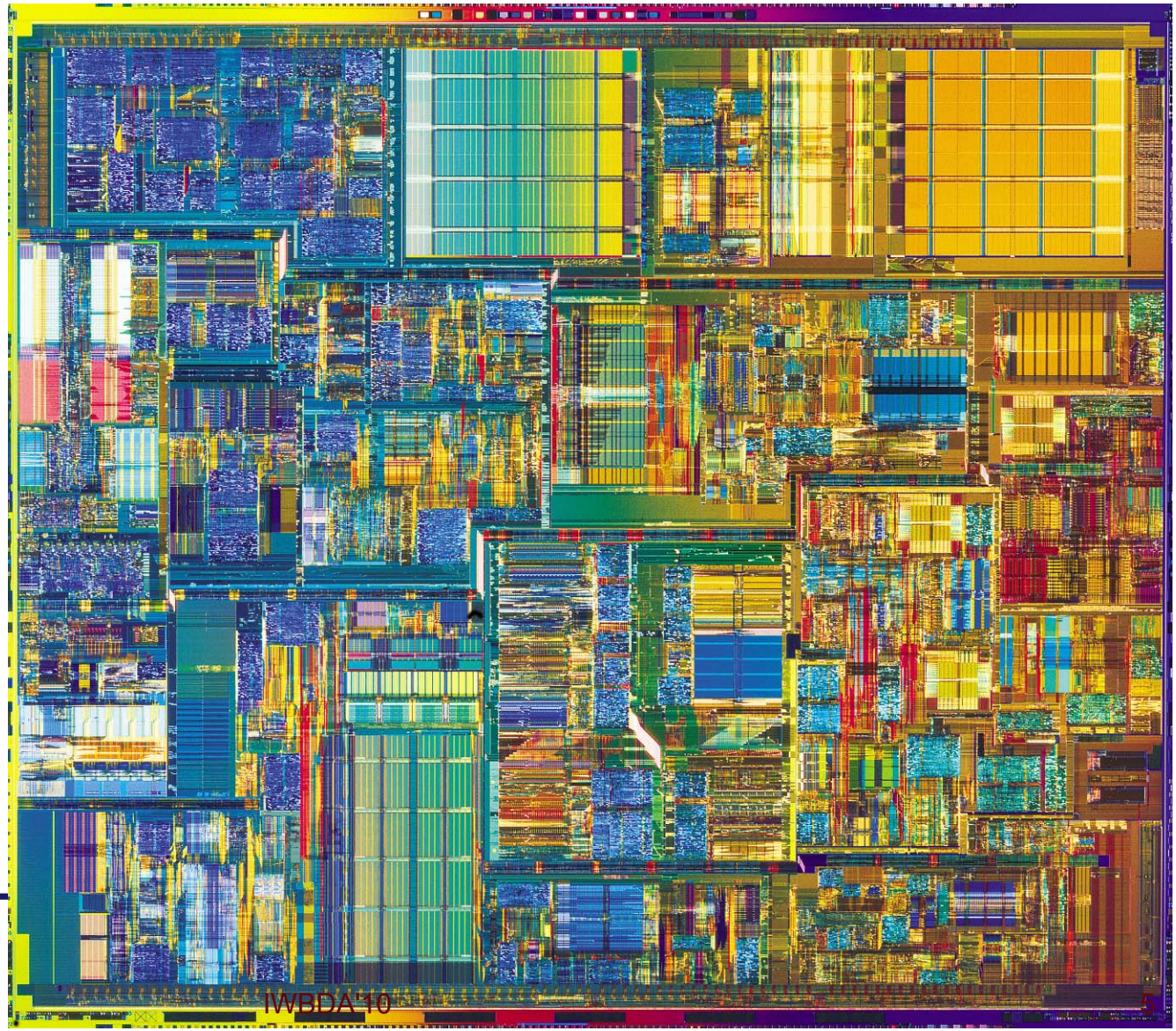
Texas Instruments 1958

2012?

~~2040~~: 55 mb of synthetic DNA?

Pentium 4 (2000)

55 million transistors



June 11, 2010

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RELIGION

Catholic Church: synth… good development but …

Published May 21, 2010 | Associated Press

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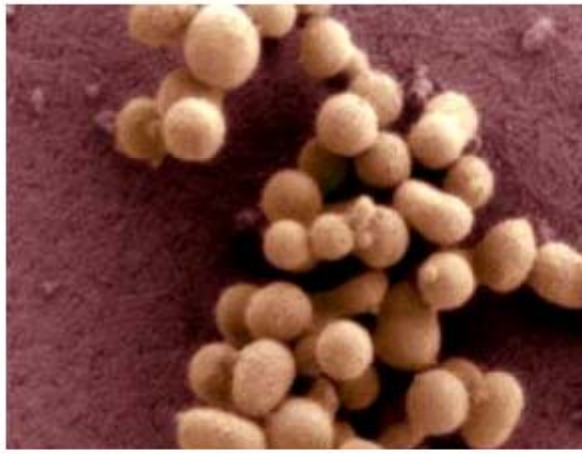

A scanning electron micrograph image of the synthetic bact… JCVI-syn1.

EDITION: U.S. | INTERNATIONAL | MÉXICO

Set edition preference

CNN Health

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Vatican calls synthetic cell creation 'interesting'

By the CNN Wire Staff

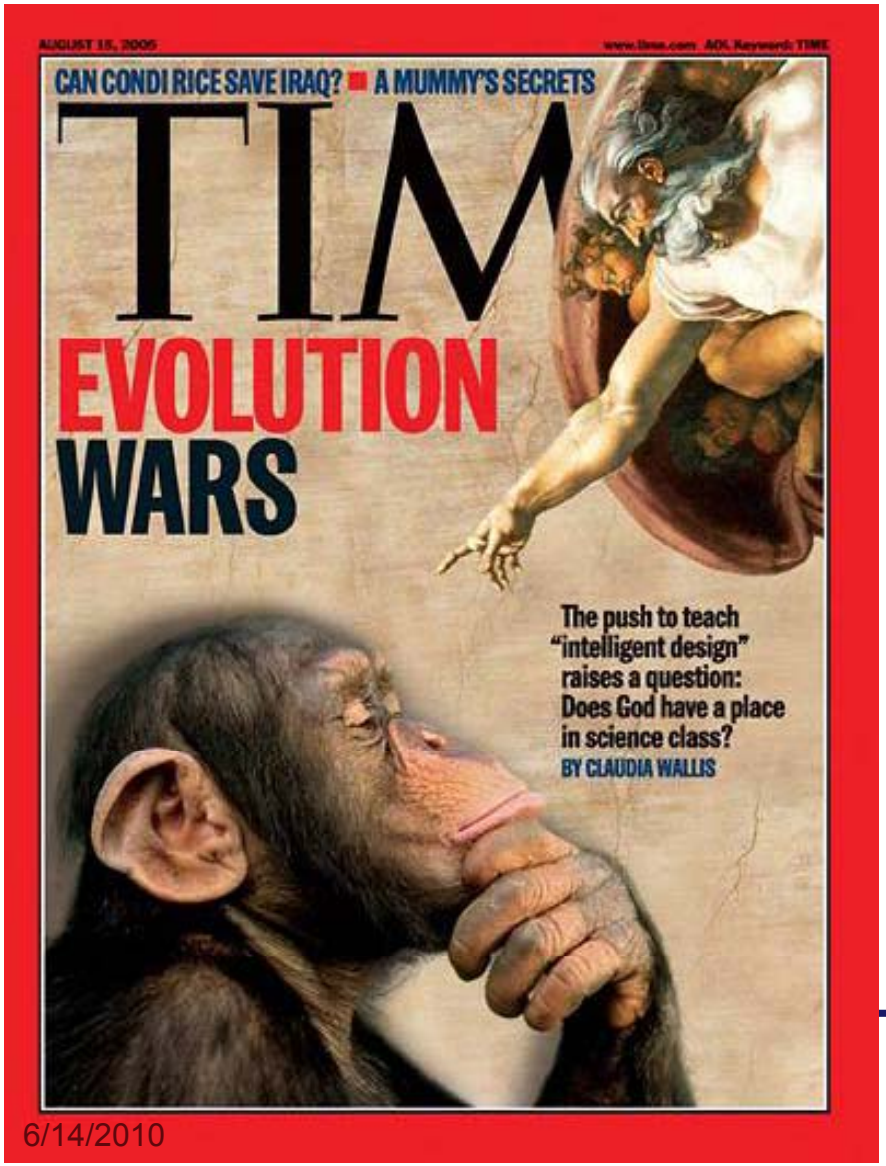
May 22, 2010 9:58 a.m. EDT

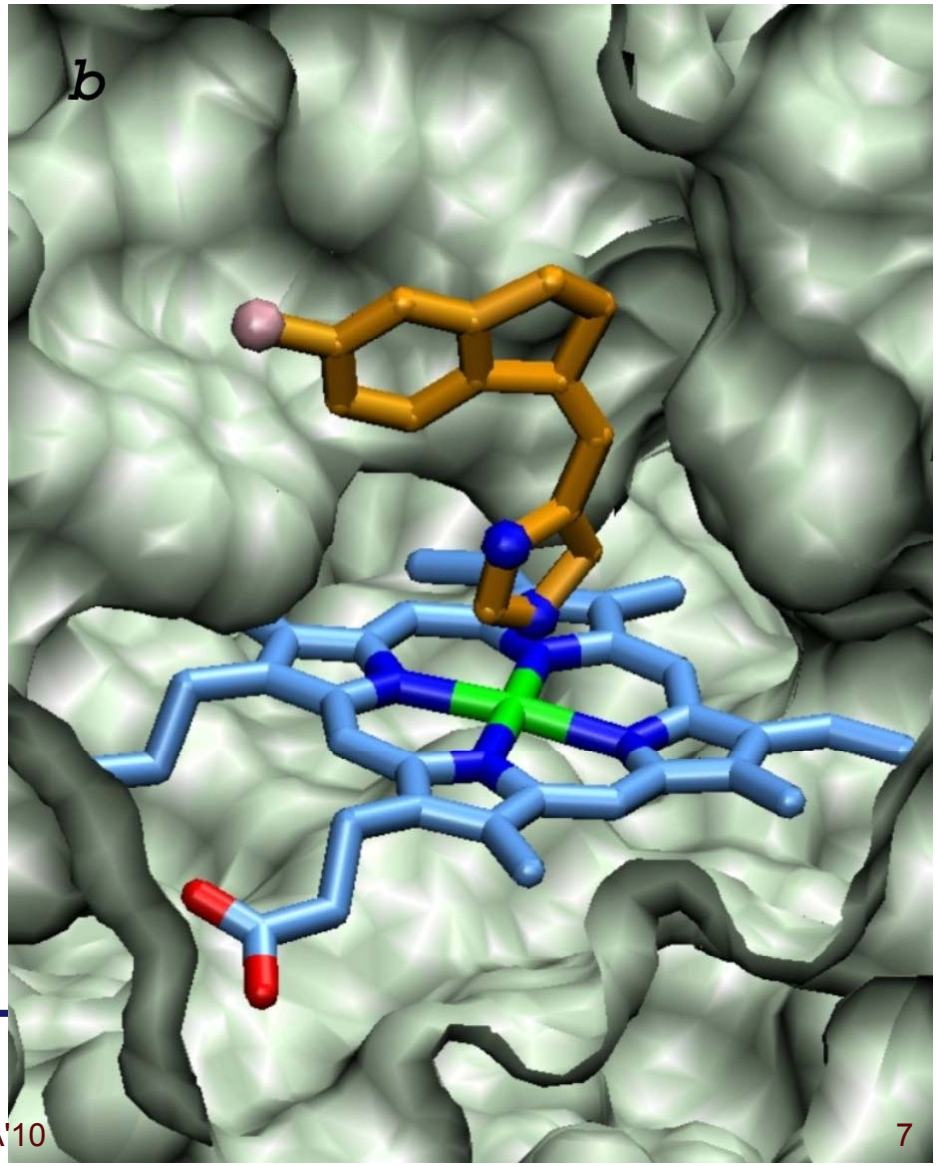
J. Craig Venter Venter says synthetic cells will help give science new tools for creating new food and vaccines.

Rome, Italy (CNN) -- The Vatican had praise Saturday for this week's announcement that scientists had created the world's first synthetic cell, calling it an "interesting result" that could help cure disease.

In an article Saturday, the Vatican newspaper L'Osservatore Romano called it "important research" and "the work of high-quality genetic engineering." But it said the scientists who created the cell had not

Design:
A controversial notion in biology





Design:
a transformative notion in biology

Biology is still a science

- Still in "**discovery**" mode
  - Drug discovery
  - Plant breeding, genetic selection
  - Directed evolution….
- Trial and error is still the dominant mode of investigation

An engineering counterpart to biology

- Still searching for a name
  - Synthetic biology, genetic engineering, bioengineering…
- Main characteristics
  - **Specify**: Assume ownership of what we build
  - **Simplify**: Simple designs easy to simulate and fabricate
  - **Abstract**: Simple language closer to needs than solutions
  - **Divide**: Division of labor to increase productivity, size of projects

Outline

Design of biological systems

- *Controversial and transformative*

Lessons from 40 years of EDA

- **Shrinking the size of the design space**

The genetic code and beyond

- DNA as a second language

CAD meets CAM

- Recoupling design and fabrication

Design evaluation

- Coupling design and data acquisition

Co-design of biological systems

- Beyond the proof of concept design

A shifting intellectual property landscape

- Unleashing the business potential of open source

47 Years of Design Automation

Key to success

1964-1978

- Research don
- Main topics
  - Circuit s
  - Logic si
  - Wire rou

1979-1993

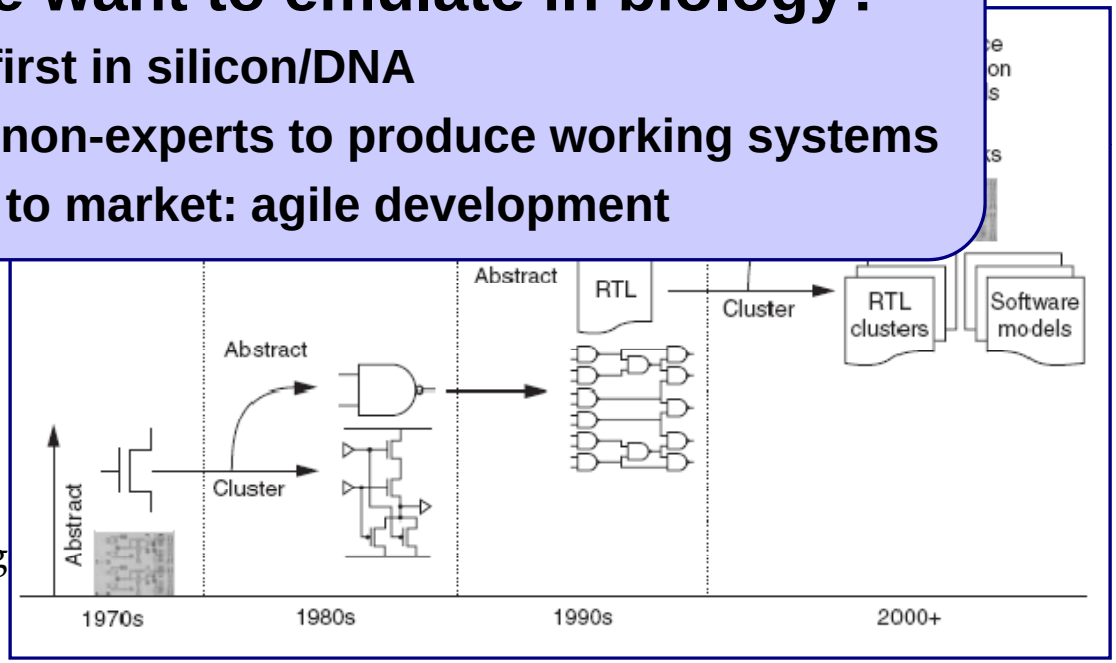
- Emergence of academic research
- Main topics
  - Verification and testing
  - Layout
  - Logic synthesis (design optimization)
  - Hardware description languag

1994-present

- Dominated by academic research
- Major contributions…

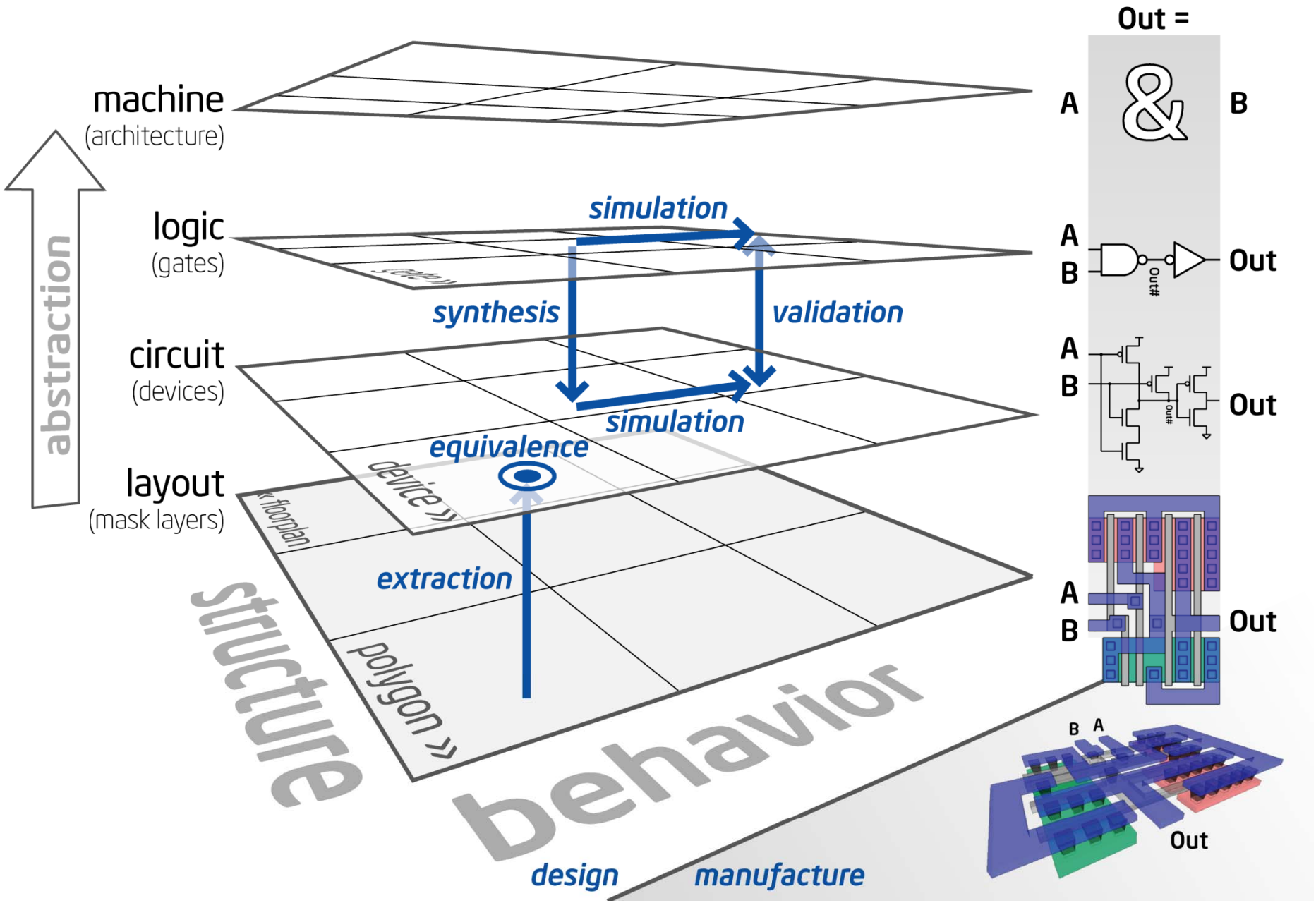
What do we want to emulate in biology?

- **Working first in silicon/DNA**
- **Ability of non-experts to produce working systems**
- **Fast time to market: agile development**

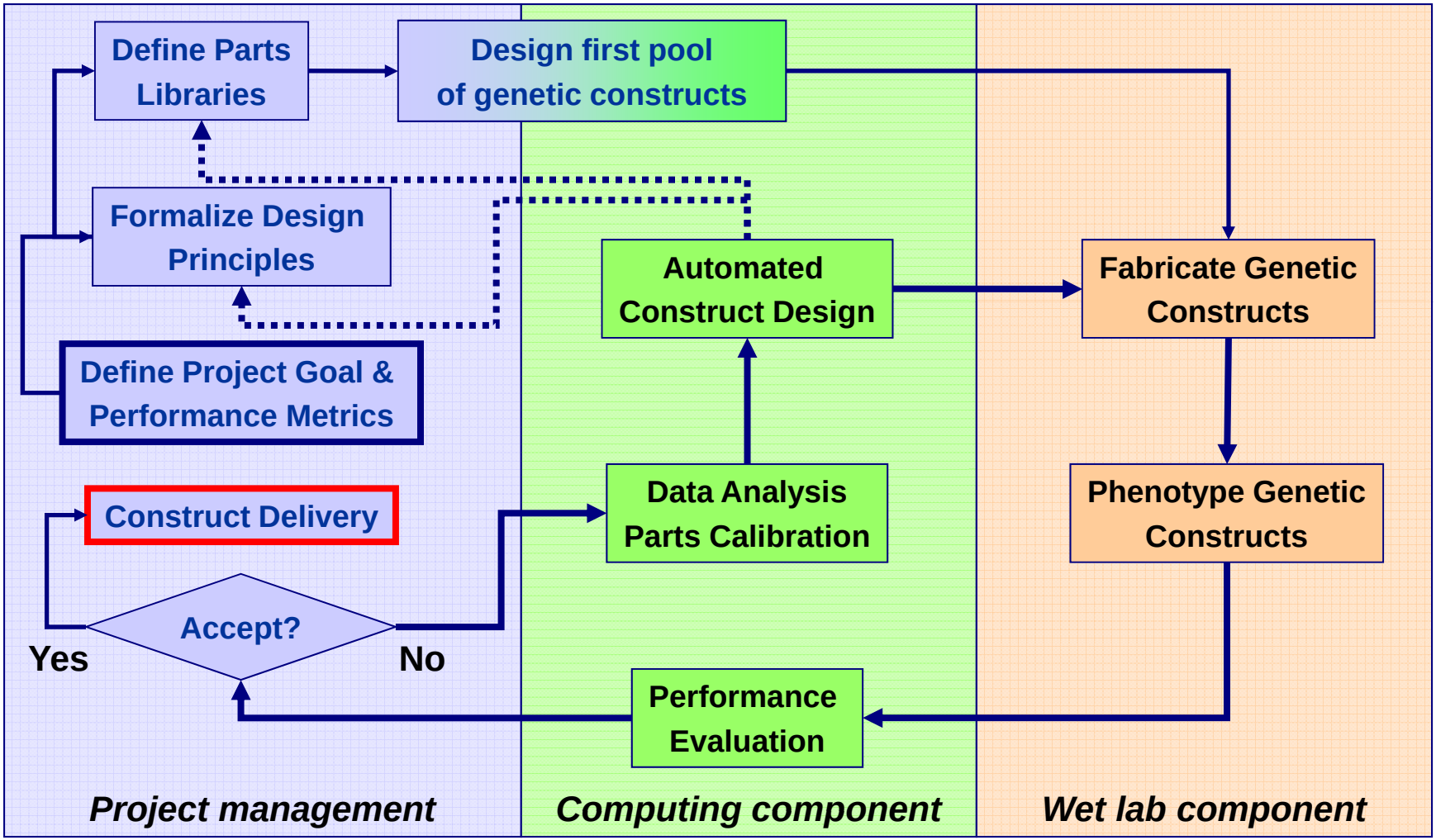


Steadily raising the level of abstraction

Alberto Sangiovanni-Vincentelli, 2003


machine
(architecture)
logic
(gates)
circuit
(devices)
layout
(mask layers)
abstraction
simulation
synthesis
validation
simulation
equivalence
extraction
« floorplan
« device
« polygon
structure
behavior
design
manufacture
Out =
A
B
&
Out
Out#

Integrated workflow of parts-based biology



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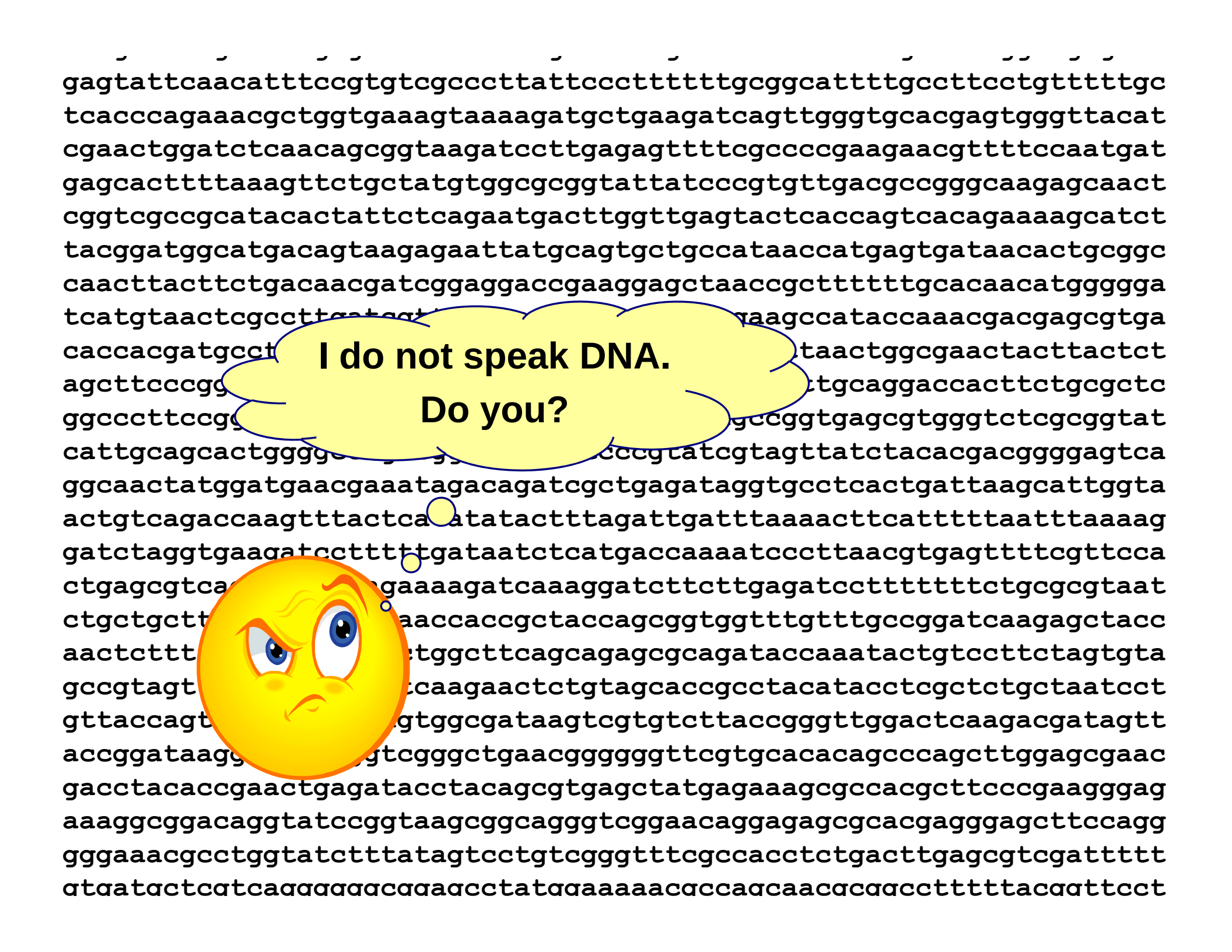
Who can read this?

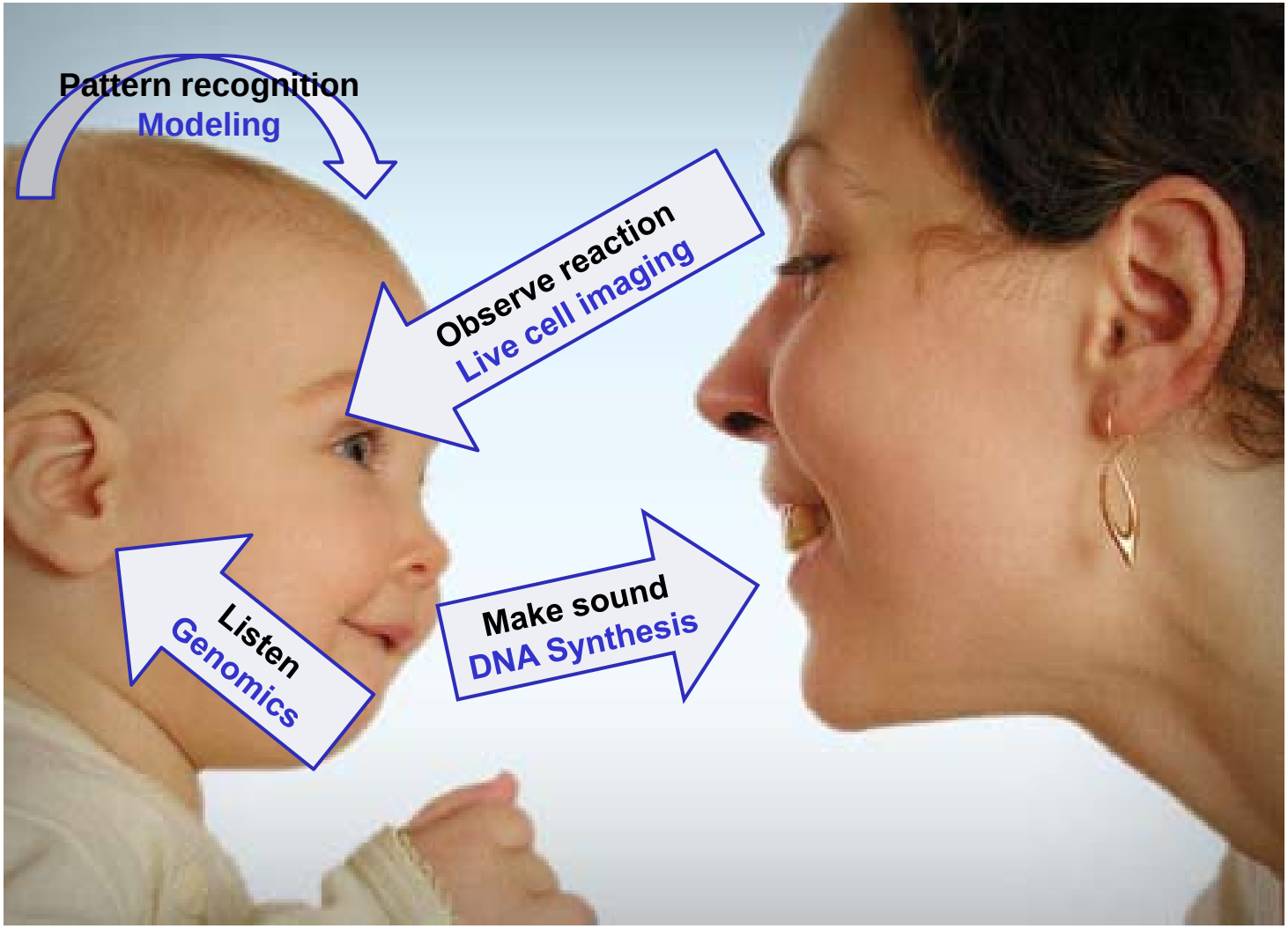
Virginia Bioinformatics Institute (VBI) is a research institute dedicated to the study of the biological sciences. The research platform of VBI is "Bioinformatics" of VBI ... biological.

By using bioinformatics, which combines transdisciplinary approaches to information technology and biology, researchers at VBI interpret and apply vast amounts of biological data generated from basic research to some of today's key challenges in the biomedical, environmental and agricultural sciences. Work at VBI involves collaboration in diverse disciplines such as mathematics, computer science, biology, plant pathology, biochemistry, systems biology, statistics, economics and synthetic biology.

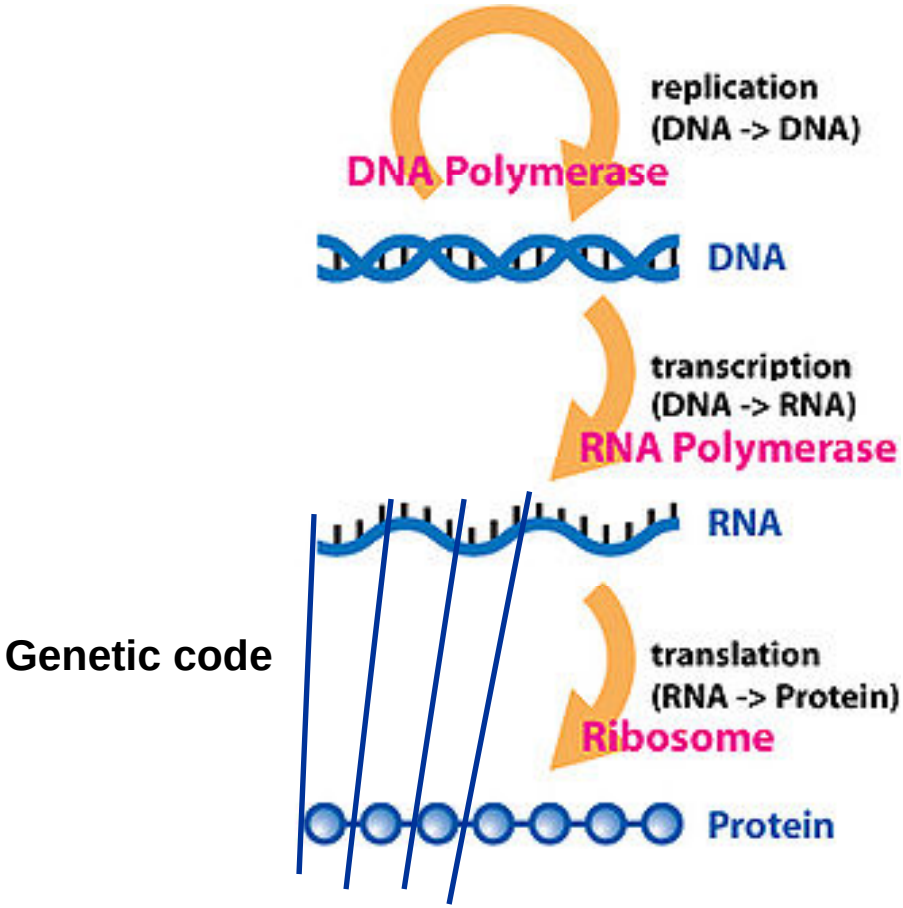
The institute develops genomic, proteomic and bioinformatic tools that can be applied to the study of infectious diseases as well as the discovery of new vaccine, drug and diagnostic targets.


I do not speak DNA.
Do you?

Learning DNA as a second language…



The central dogma: a linguistic metaphor



nature Vol 442|17 August 2006|doi:10.1038/nature04979

ARTICLES

A genomic code for nucleosome positioning

Eran Segal[1], Yvonne Fondufe-Mittendorf[2], Lingyi Chen[2], AnnChristine Thåström[2], Yair Field[1], Irene K. Moore[2], Ji-Ping Z. Wang[3] & Jonathan Widom[2]

Vol 465|6 May 2010|doi:10.1038/nature09000 nature

ARTICLES

Deciphering the splicing code

Yoseph Barash[1,2]*, John A. Calarco[2]*, Weijun Gao[1], Qun Pan[2], Xinchen Wang[1,2], Ofer Shai[1], Benjamin J. Blencowe[2] & Brendan J. Frey[1,2,3]

Formal Grammars

R1: Sentence → Subject + Predicate

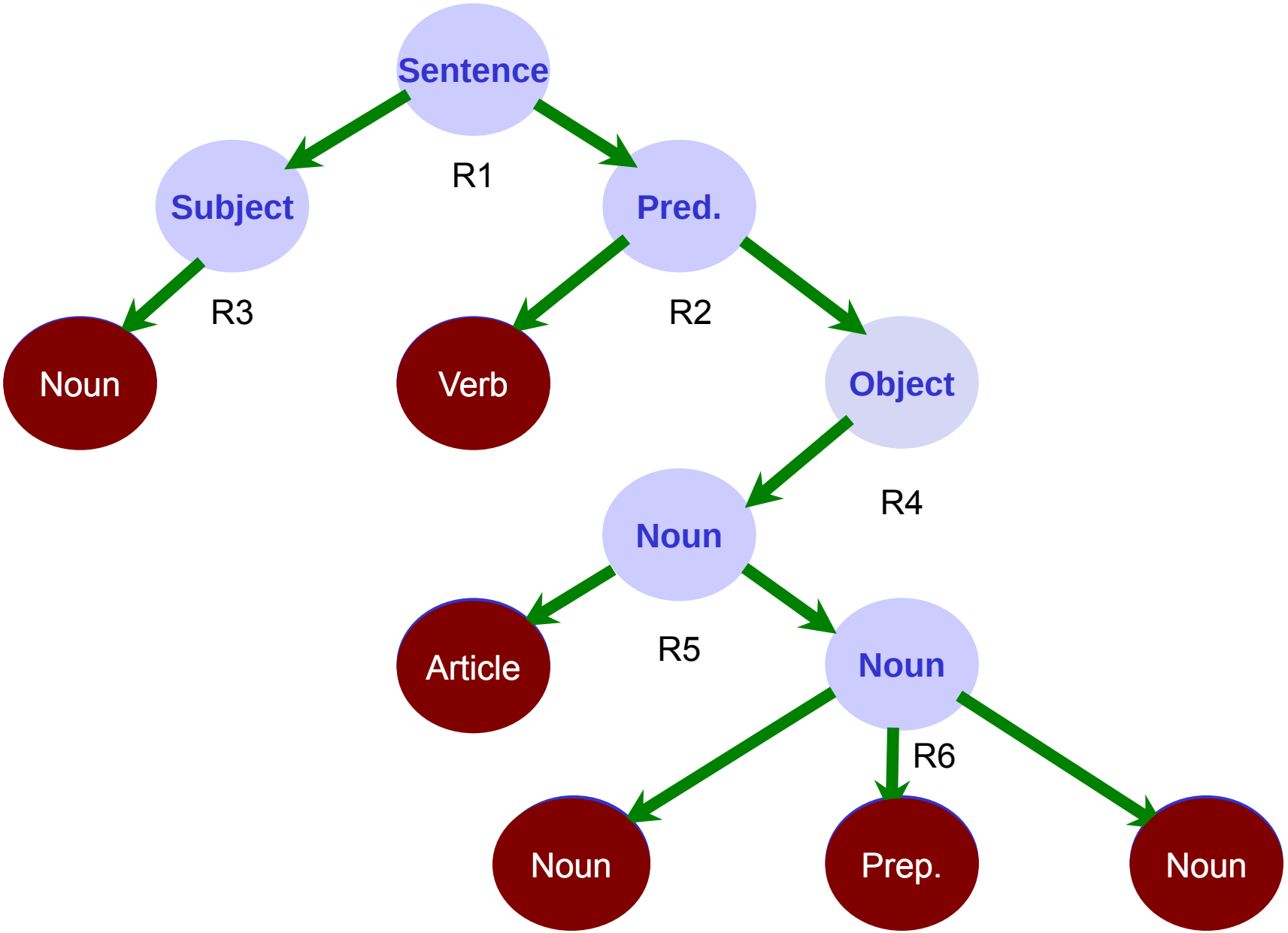
R2: Predicate → Verb + Object

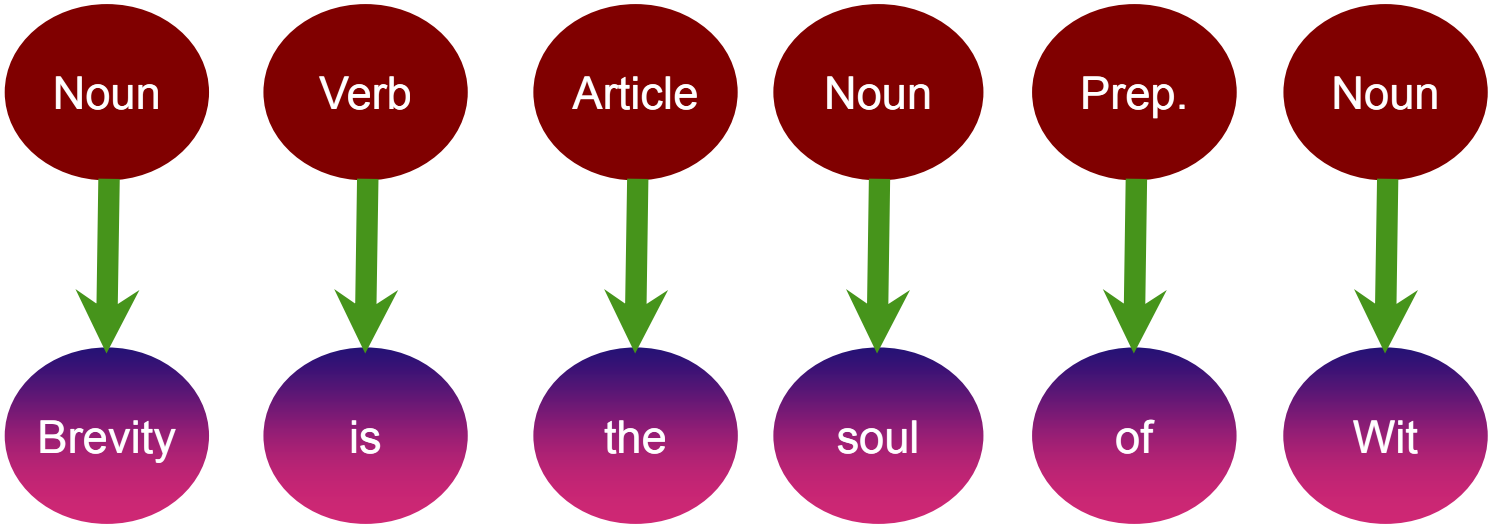
R3: Subject → Noun

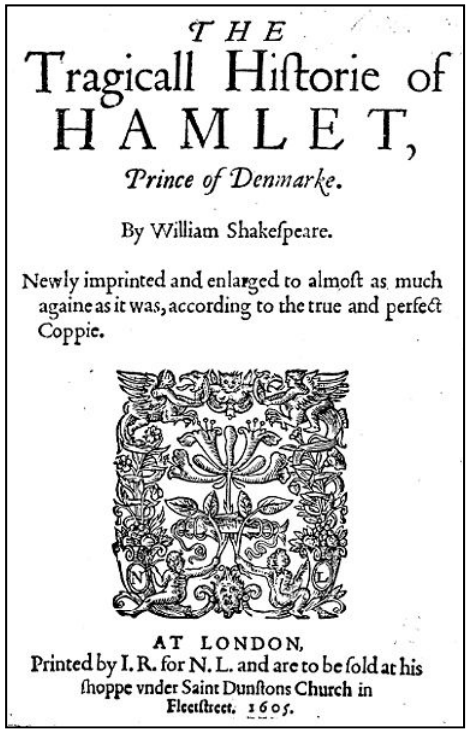
R4: Object → Noun

R5: Noun → Article + Noun

R6: Noun → Noun + Preposition + Object


Sentence
R1
Subject
Pred.
R3
R2
Noun
Verb
Object
R4
Noun
Article
R5
Noun
R6
Noun
Prep.
Noun





THE
Tragicall Hiſtorie of
HAMLET,
Prince of Denmarke.

By William Shakeſpeare.

Newly imprinted and enlarged to almoſt as much againe as it was, according to the true and perfect Coppie.

AT LONDON,
Printed by I. R. for N. L. and are to be ſold at his ſhoppe vnder Saint Dunſtons Church in Fleetſtreet. 1605.

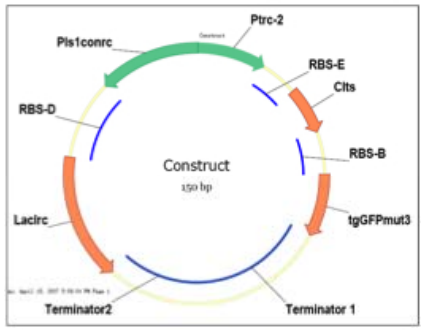
~Shakespeare

BIOINFORMATICS ORIGINAL PAPER
Vol. 23 no. 20 2007, pages 2760–2767
doi:10.1093/bioinformatics/btm446

Systems biology

A syntactic model to design and verify synthetic genetic constructs derived from standard biological parts

Yizhi Cai[1], Brian Hartnett[1], Claes Gustafsson[2] and Jean Peccoud[1,*]



terminator- cistron- promoter-

gene- RBS-

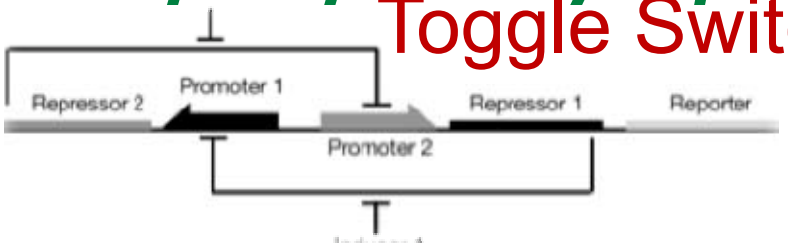
Operon

promoter cistron terminator

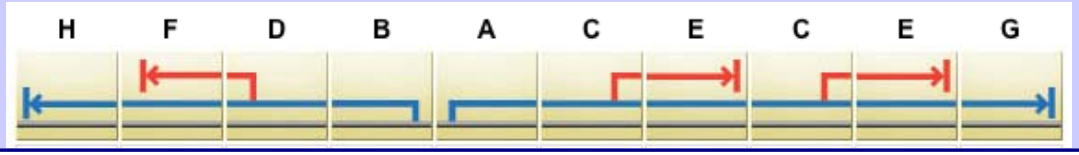
cistron cistron

RBS gene RBS gene

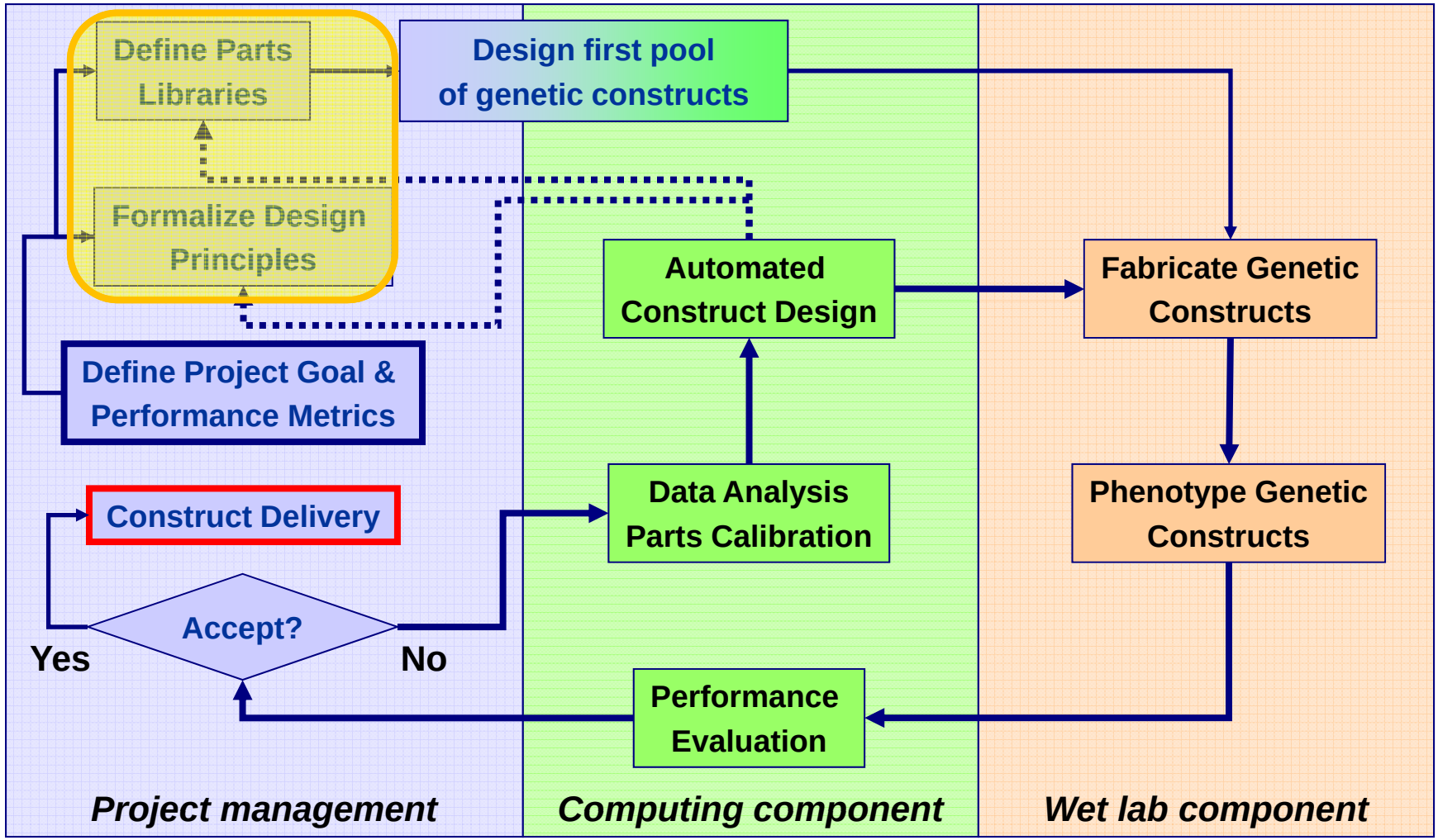
Toggle Switch



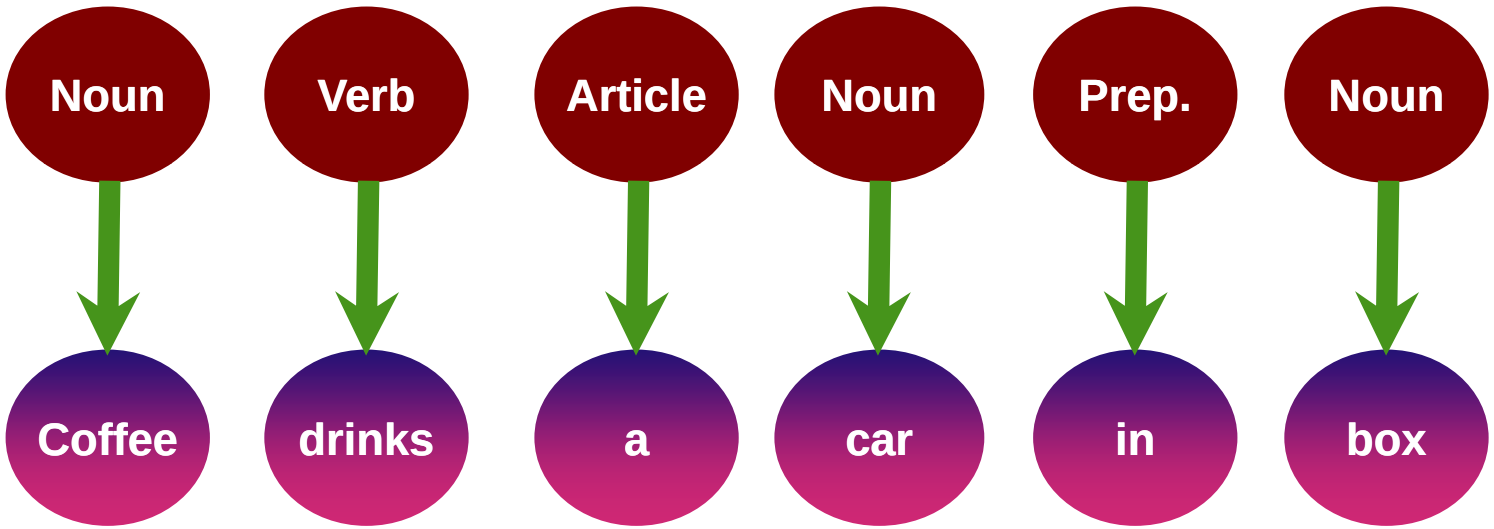
ter2- tetR- RBS-C- PI-s1con- Ptrc RBS-A lacI RBS-B cI ter1



Integrated workflow of parts-based biology

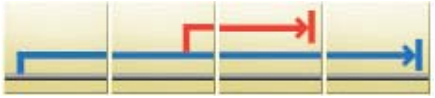


A correct structure is not enough...



Words have no meaning! (by themselves)

Bear Claw



Green Fluorescent Protein

Context-dependencies: RBS ORF

Coding-Sequence Determinants of Gene Expression in *Escherichia coli*

Grzegorz Kudla,[1]* Andrew W. Murray,[2] David Tollervey,[3] Joshua B. Plotkin[1]†

doi:10.1006/jmbi.2001.5040 available online at http://www.idealibrary.com on IDEAL® *J. Mol. Biol.* (2001) **313**, 215–228

JMB

Anatomy of *Escherichia coli* Ribosome Binding Sites

Ryan K. Shultzaberger[1,2], R. Elaine Bucheimer[3], Kenneth E. Rudd[4] and Thomas D. Schneider[2]*

Automated design of synthetic ribosome binding sites to control protein expression

Howard M Salis[1], Ethan A Mirsky[2] & Christopher A Voigt[1]

Attribute Grammars

Add semantic layer to a syntax

Attribute grammar=

- Context-free grammar +
- Attributes +
- Semantic actions

Attribute

- Property associated with a part
- Notation
  - ptrc2.transcription_rate
- Two types of attributes
  - Inherited attribute: gets value from its parental node
  - Synthesized attribute: gets value from its children nodes

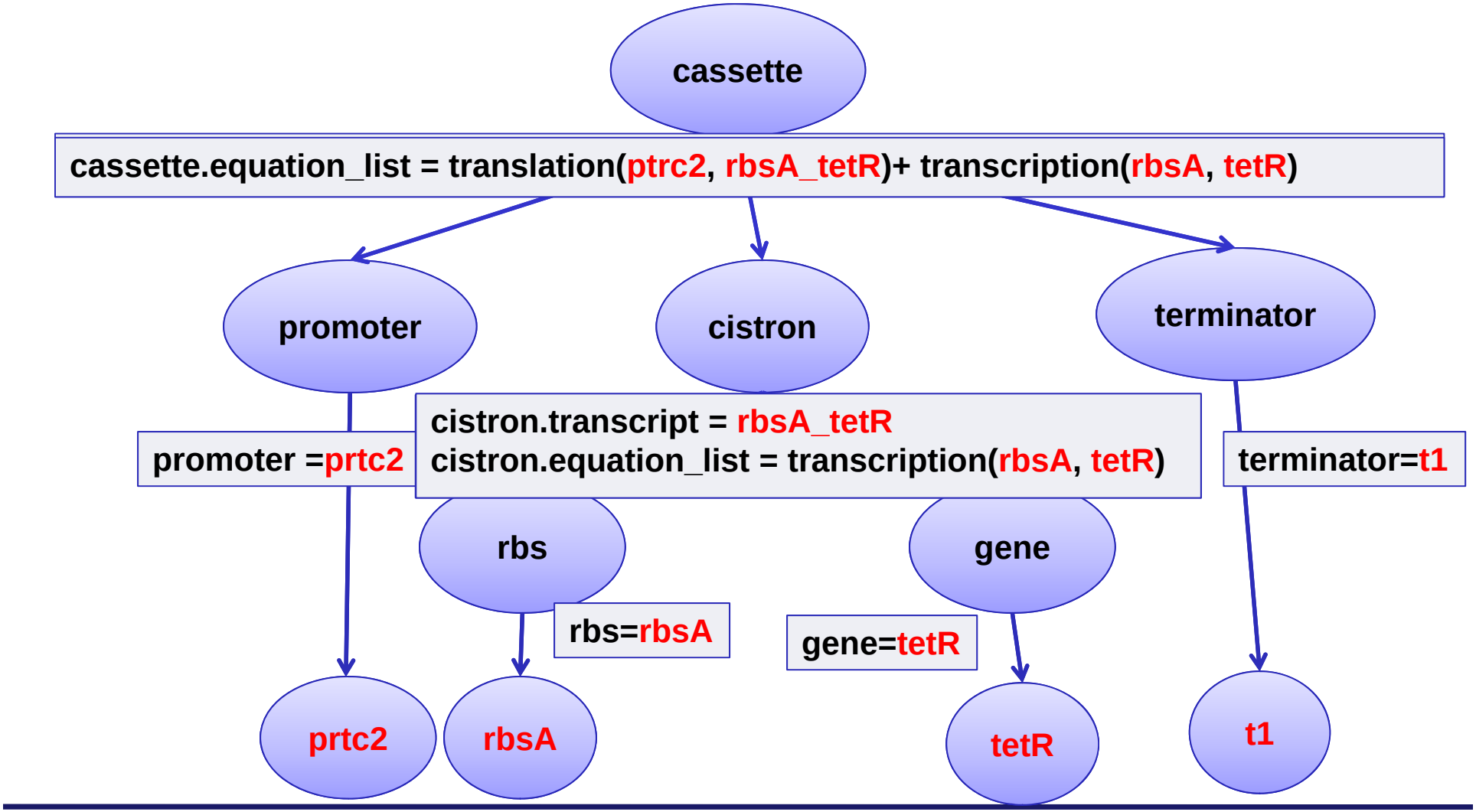
Semantic actions

- Functions updating the attributes of the language objects.
- Associated with production rules

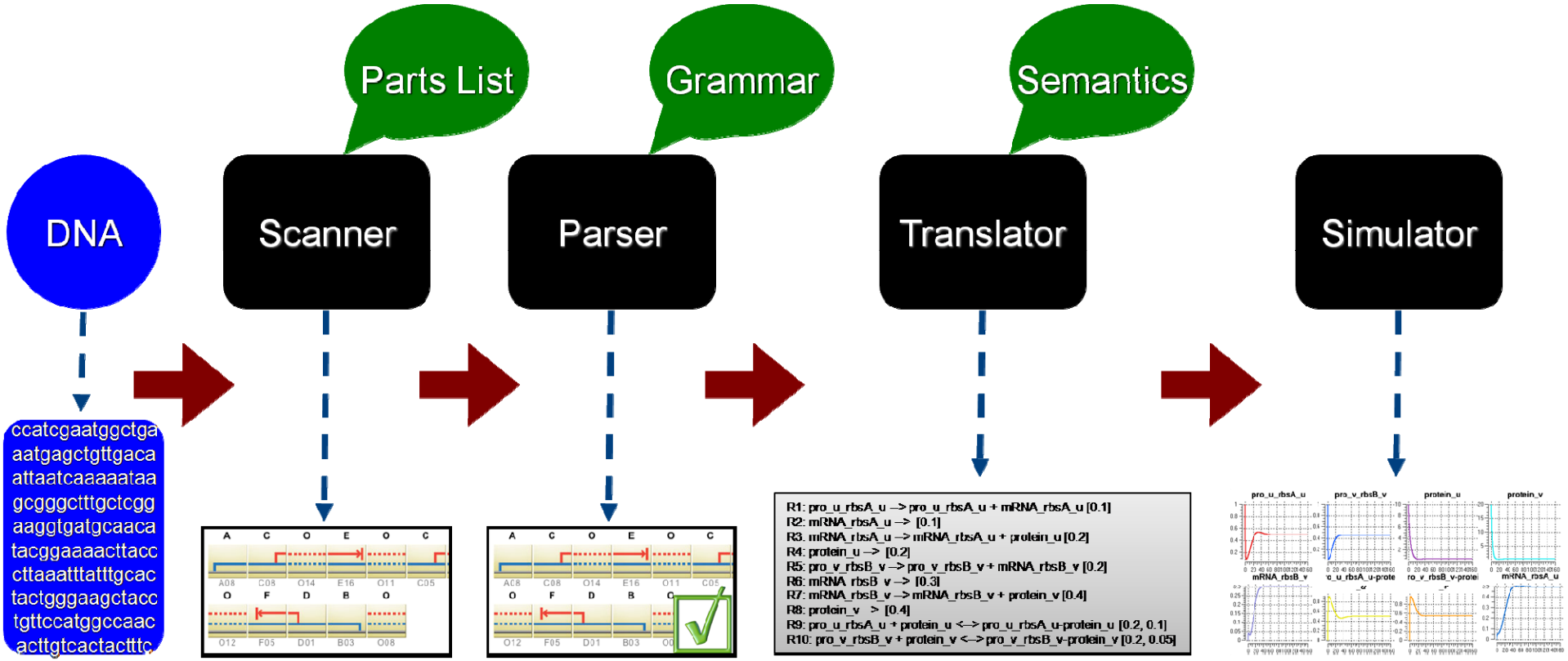
Attribute	Value
Name	ptrc2
Sequence	ccatcgaatggctgaaat…
transcription_rate	25
repressor_list	[lacI, 4, 0.001, 1]

```
cistron → rbs, gene
{
cistron.transcript =
        rbs.name + gene.name;
cistron.equation_list =
        transcription(rbs, gene);
}
```

Synthesizing the attributes: a simple example



Compiling parts-based DNA sequences



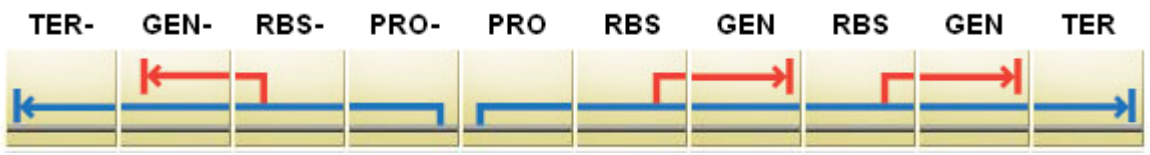
OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Modeling Structure-Function Relationships in Synthetic DNA Sequences using Attribute Grammars

Yizhi Cai, Matthew W. Lux, Laura Adam, Jean Peccoud*

Design optimization



41,472 possible designs

82,944 SBML files

41,472 stability analyses

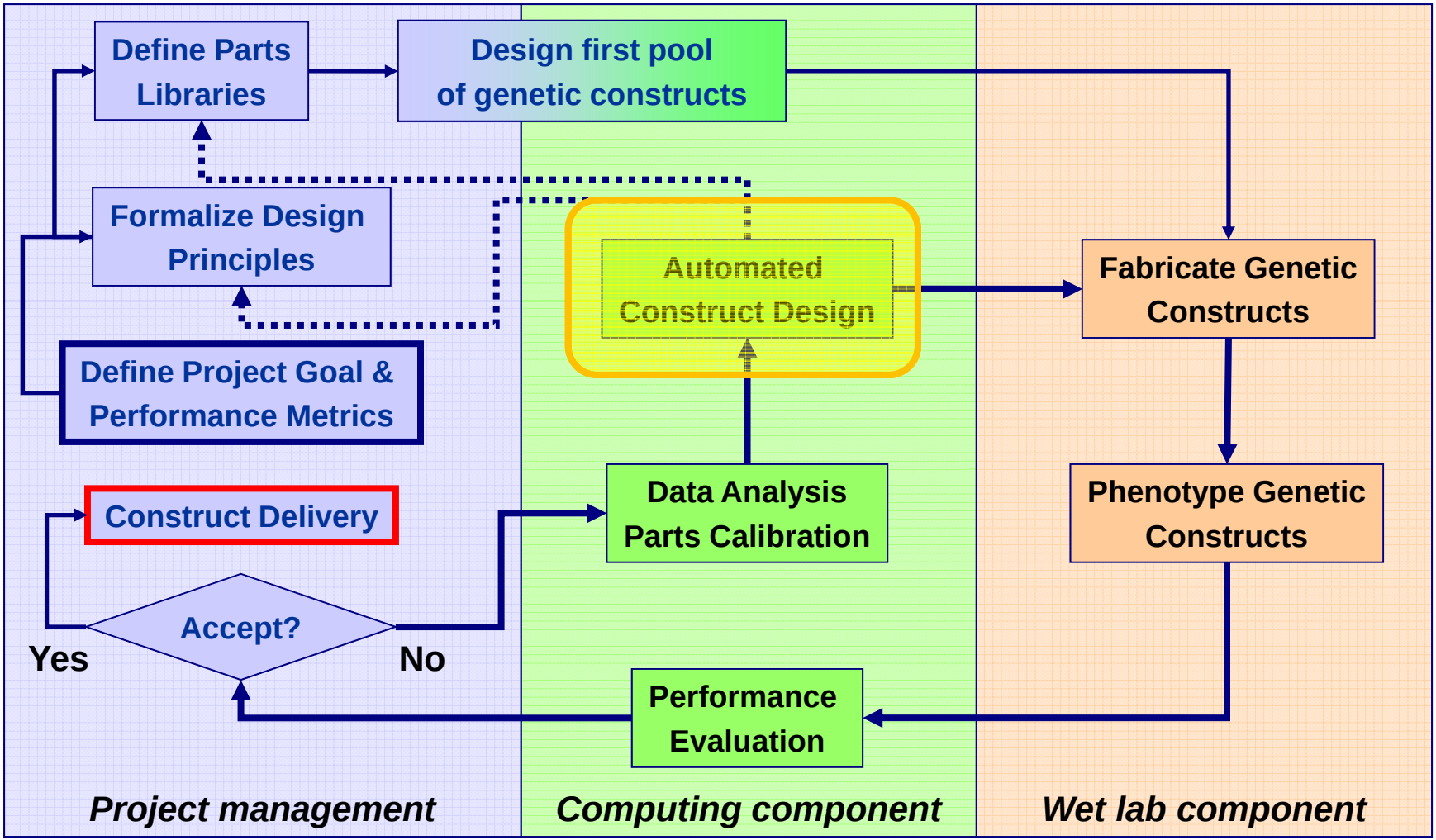
Robustness and detectability of 384 potential switch designs

Genes →	lacI | cI•GFP								cI | tetR•GFP								tetR | lacI•GFP							
RBS →	H	G	E	F	C	D	A	B	H	G	E	F	C	D	A	B	H	G	E	F	C	D	A	B
B	1	337	227	184	94	61	16	1	1	1	1	1	1	1	1	31	1	1	1	1	1	1	1	1
A	1358	348	231	187	95	61	1	1	1	1	1	1	1	74	67	33	1	1	1	1	1	1	1	1
D	1382	348	231	187	94	61	1	1	1	93	94	94	92	89	66	1	1	1	1	1	1	1	1	1
C	1381	348	231	187	94	60	1	1	1	96	96	95	92	89	64	1	1	1	1	1	1	3	1	1
F	1381	348	231	187	93	1	1	1	96	97	96	96	92	87	54	1	1	1	1	1	8	1	1	1
E	1381	348	231	187	91	1	1	1	97	97	96	95	91	86	1	1	1	1	1	1	8	1	1	1
G	1383	348	231	186	84	1	1	1	98	97	96	95	90	84	1	1	1	1	38	29	1	1	1	1
H	1383	343	204	1	1	1	1	1	98	87	1	1	1	1	1	1	98	61	38	25	1	1	1	1
B	1	1	1	1	1	1	1	1	1	1	1	1	1	1	87	18	1	1	1	1	1	1	1	1
A	1	1	1	1	1	1	1	77	1	1	1	713	476	332	89	1	1	1	1	1	1	1	1	1
D	1	1	1	1	98	99	98	76	1	1278	1014	876	505	341	65	1	1	1	1	1	2	1	1	1
C	1	94	98	99	100	100	98	76	1	1320	1031	886	506	339	1	1	1	1	4	4	1	1	1	1
F	1	100	100	100	100	100	98	75	1	1352	1044	894	504	332	1	1	28	7	1	1	1	1	1	1
E	94	100	100	100	100	100	98	74	1	1358	1046	895	502	328	1	1	28	7	1	1	1	1	1	1
G	99	100	100	100	100	100	98	72	1430	1365	1048	894	496	316	1	1	29	1	1	1	1	1	1	1
H	100	100	100	100	100	100	95	1	1677	1356	1017	850	1	1	1	1	29	1	1	1	1	1	1	1
RBS →	H	G	E	F	C	D	A	B	H	G	E	F	C	D	A	B	H	G	E	F	C	D	A	B
Genes →	cI | lacI•GFP								tetR | cI•GFP								lacI | tetR•GFP							

High Ratio

Ratio=1

Integrated workflow of parts-based biology



XCell Description Languages

Generation 1

- DNA
- Mol. Biol.
- MIT Registry

Generation 2

- Formal syntax
- Structural
- Application-specific
- GenoCAD

Generation 3

- Portable language
- Abstract representation
- Compilable into DNA for different targets organisms

First Generation

Machine code

```
8E542408 83FA0077 06E80000
0000C383 FA027706 E8010000
00C353BB 01000000 E9010000
```

DNA Sequence

```
ccatcgaatggctgaaatgagctgttgacaattaatca
tccggctcgtataatgtgtggaattgtgagcggataac
aatttcacacaggaaaccggttatga
```

Second Generation

Assembly Language

```
fib:
      mov edx, [esp+8]
      cmp edx, 0
      Ja @f
      mov eax, 0
      re t
      @@:
      push ebx
      mov ebx, 1
      mov ecx, 1
      @@:
            lea eax,[ebx+ecx]
```

XDL v1

```
Parts
      PROMOTER pro1 = "ccatcgaat…";
      PROMOTER pr:02 = "gcatgctcc… ";
      RES rbsl = "aggaatttaa…";
      RES rbs2 = "aggaaaccggtt…";
      GENE gene1 = "atggtgaat…";
      GENE gene2 = "atgcgtaaa…";
      GENE gene2 = "atgagcaca…";
      TERMINATOR ter= "ctagcataa…";
EndOfParts;
Construct
[pro1, rbsl, gene1, ter]-;
[pro2, rbs2, gene2, rbs2, gene3, ter];
EndOfConstruct
```

Third Generation

C

```
#include<stdio.h>
#include<malloc.h>
int main ()
{
      unsigned char huge
```

XDL v2

```
include coli. lib
include boolean. Lib

LIGAND x = aTc;
LIGAND y = IPTG;
REPORTER g = GFP;

switch (LIGAND x, LIGAND y,
      REPORTER g)
```

Opinion

Cell PRESS

Genetic design: rising above the sequence

Jonathan A. Goler[1], Brian W. Bramlett[2] and Jean Peccoud[3]

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- Coupling design and data acquisition

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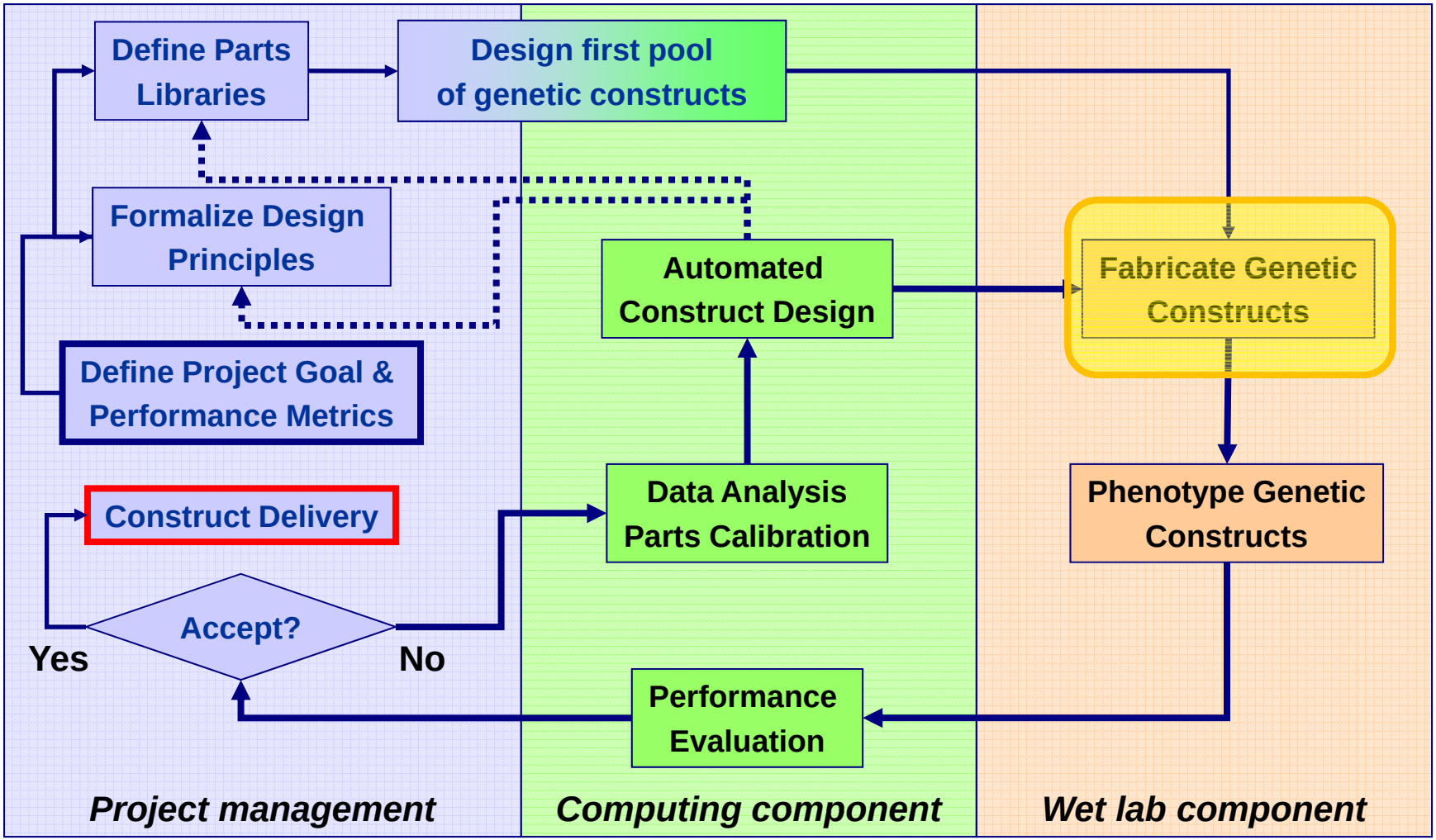
- Unleashing the business potential of open source

Integrated workflow of parts-based biology



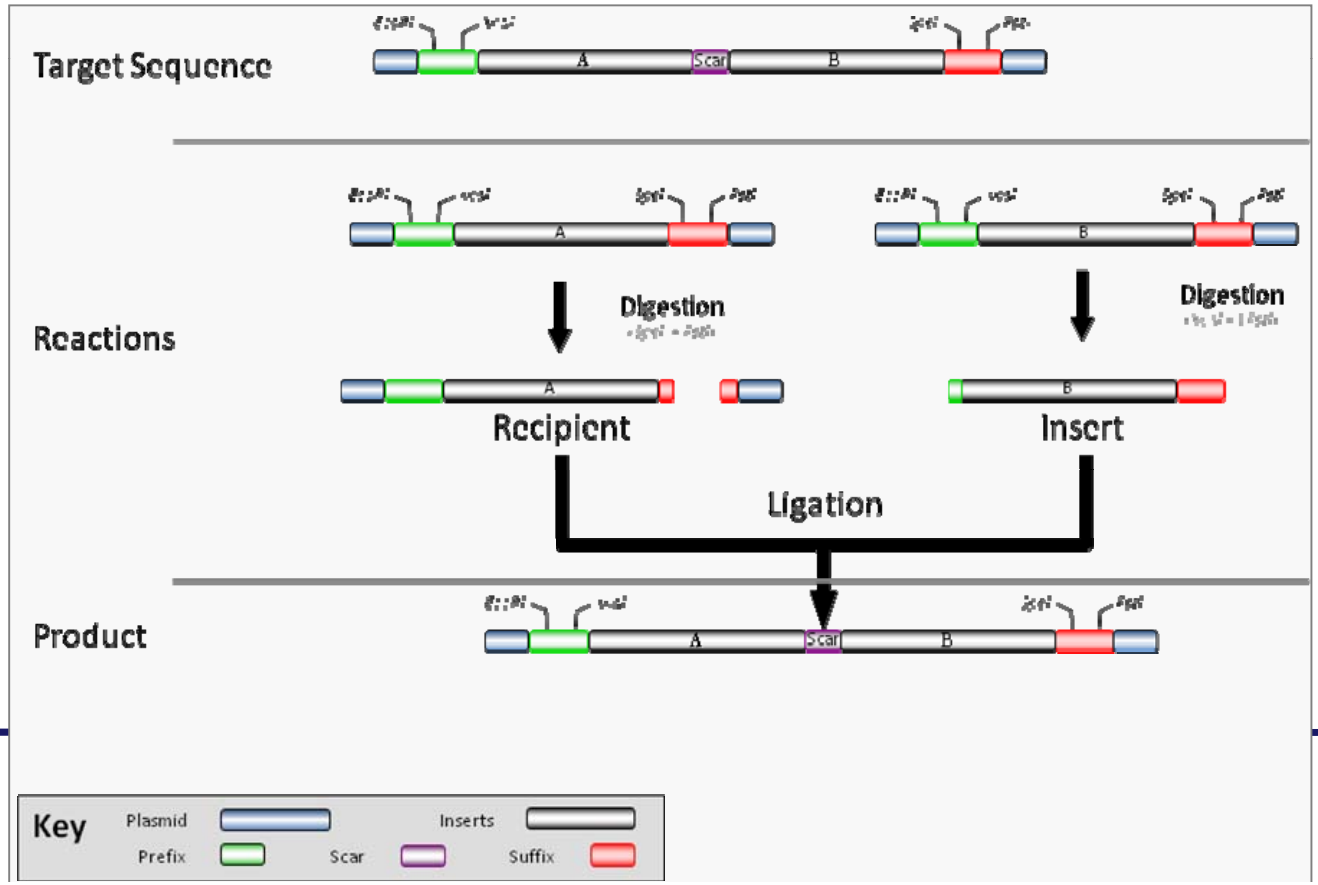
BioBrick Assembly

BioBrick™ standards

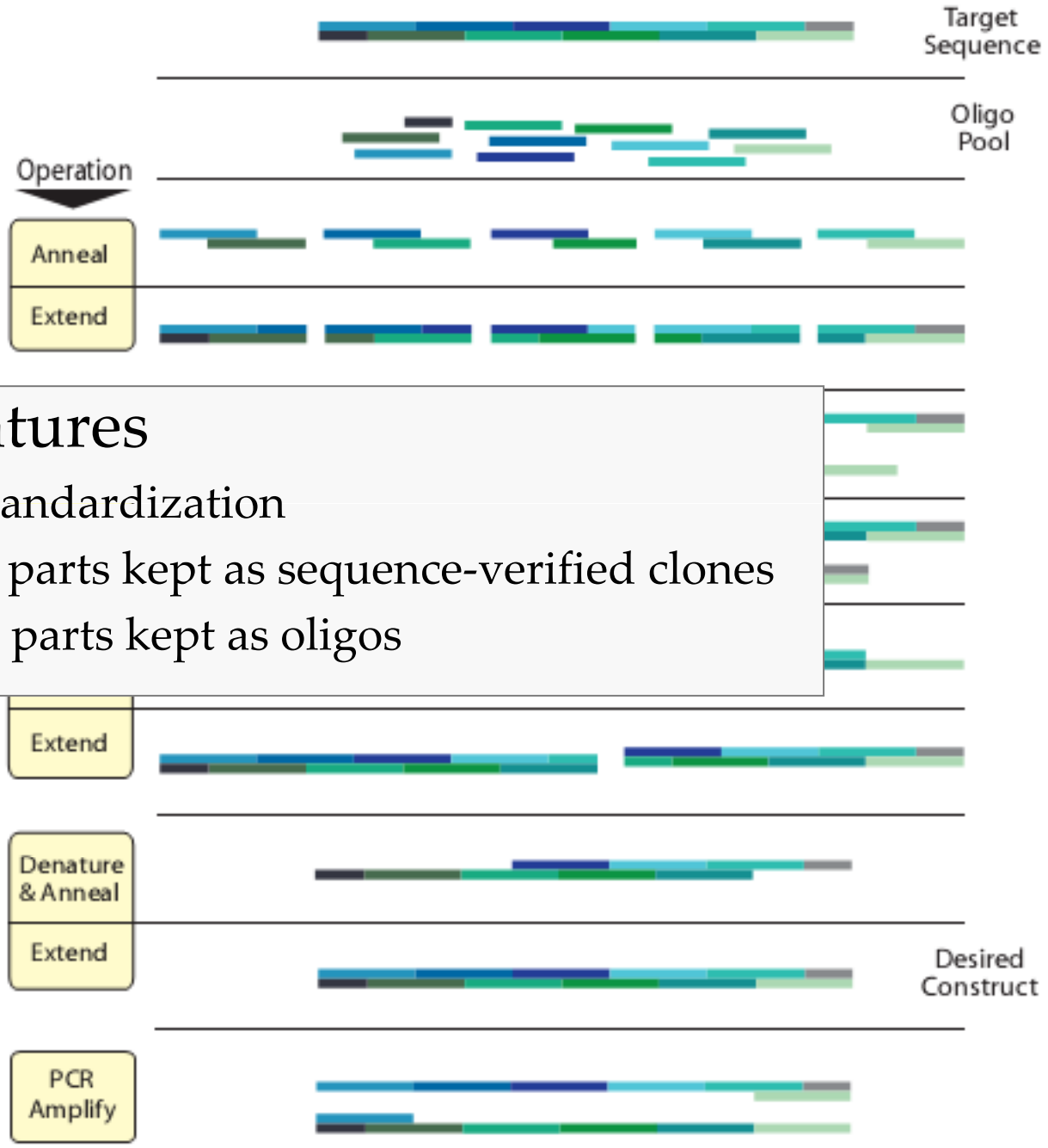
- Assembly of two BB parts is streamlined
- Composition: assembly of two BB parts is BB compliant

Limitations

- Restriction sites
- Scar
- Proliferation of standards



Parts-based fabrication: parts-synthesis



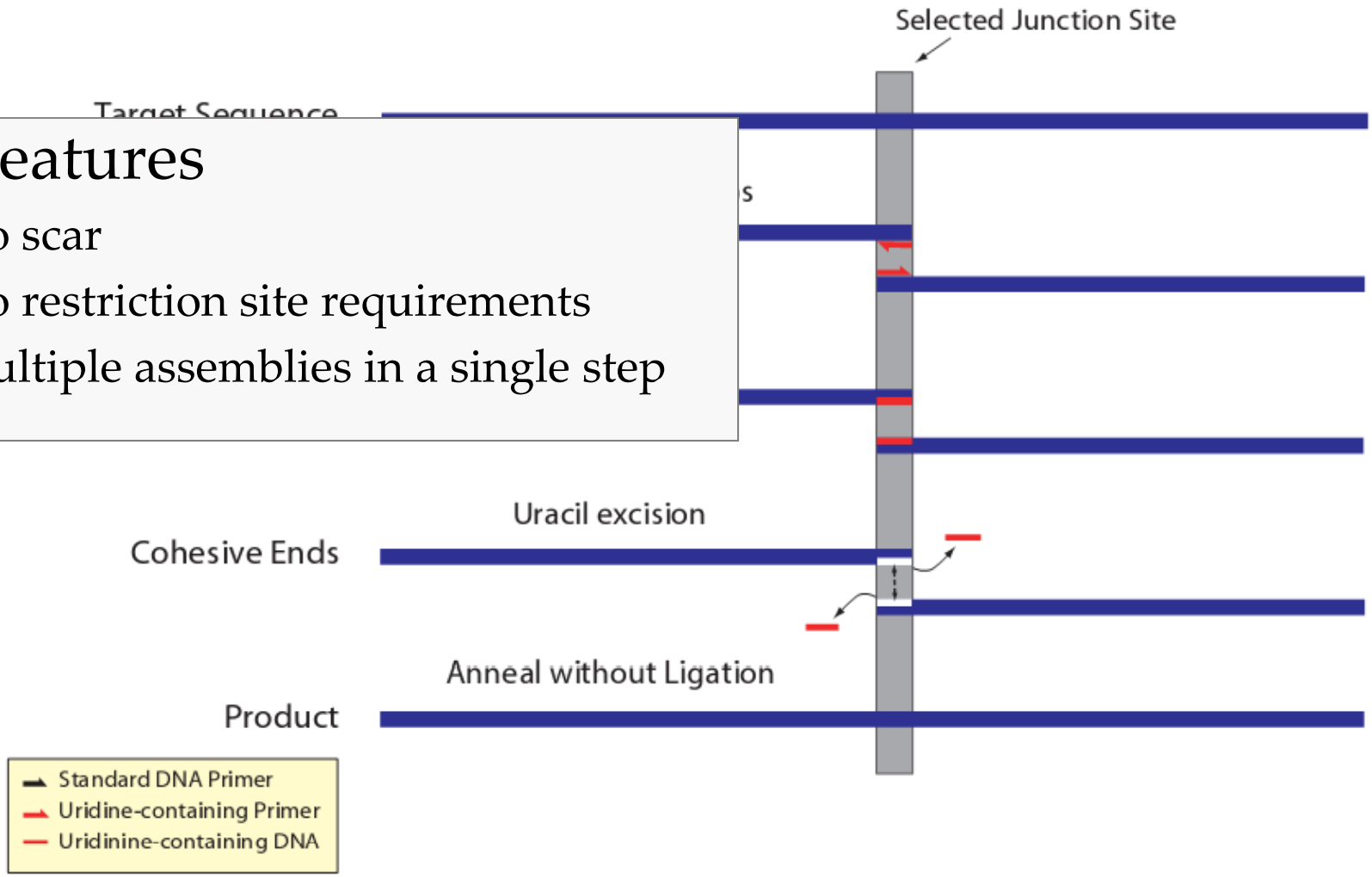
Main features

- No standardization
- Long parts kept as sequence-verified clones
- Short parts kept as oligos

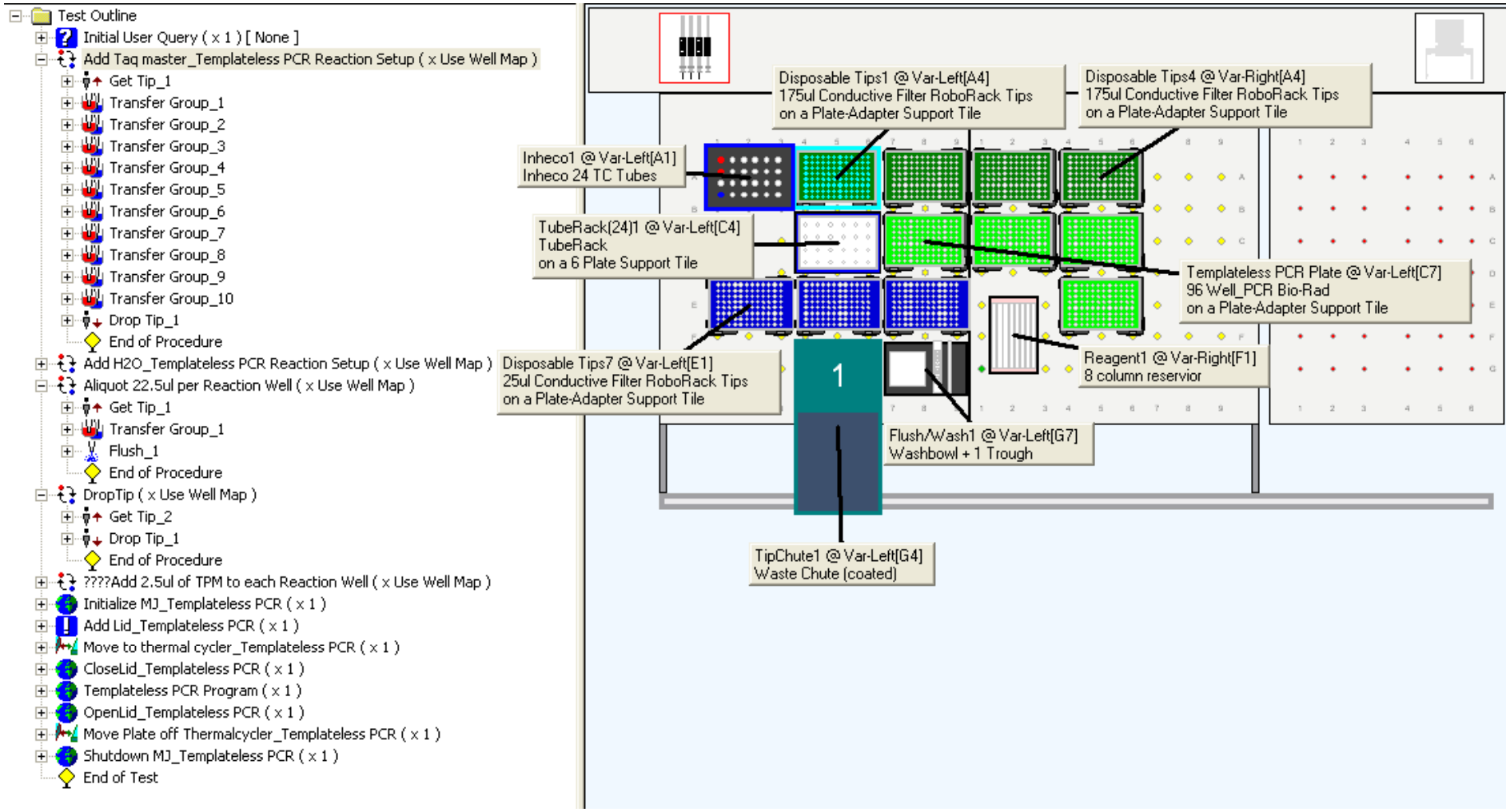
Parts-based fabrication: parts assembly by USER fusion

Main features

- No scar
- No restriction site requirements
- Multiple assemblies in a single step



Automating each of the steps



Optimization of fabrication processes

Published online 23 March 2010 *Nucleic Acids Research, 2010, Vol. 38, No. 8* **2607–2616**
doi:10.1093/nar/gkq165

Algorithms for automated DNA assembly

Douglas Densmore[1,2,*], Timothy H.-C. Hsiau[2], Joshua T. Kittleson[2], Will DeLoache[2,3], Christopher Batten[4] and J. Christopher Anderson[2,5]

[1]Department of Fuel Synthesis, Joint BioEnergy Institute, 5885 Hollis St., Fourth Floor, Emeryville CA 94608, [2]Department of Bioengineering, University of California, Berkeley, CA 94720, [3]Department of Biology, Davidson College, Davidson, NC 28036, [4]School of Electrical and Computer Engineering, Cornell University, Ithaca, NY 14853 and [5]Berkeley National Laboratory, Physical Biosciences Division; QB3: California Institute for Quantitative Biological Research; 327 Stanley Hall, Berkeley, CA 94720, USA

Molecular Systems Biology 4; Article number 191; doi:10.1038/msb.2008.26
Citation: *Molecular Systems Biology* 4:191

www.molecularsystemsbiology.com

molecular systems biology

REPORT

Recursive construction of perfect DNA molecules from imperfect oligonucleotides

Gregory Linshiz[1,2,3], Tuval Ben Yehezkel[2,3], Shai Kaplan[1], Ilan Gronau[1], Sivan Ravid[1], Rivka Adar[2] and Ehud Shapiro[1,2,*]

[1] Department of Computer Science and Applied Mathematics, Weizmann Institute of Science, Rehovot, Israel and [2] Department of Biological Chemistry, Weizmann Institute of Science, Rehovot, Israel
[3] These authors contributed equally to this work
* Corresponding author. Department of Computer Science and Applied Mathematics, and Department of Biological Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel. Tel.: +972 8 9344506; Fax: +972 8 947 1746; E-mail: ehud.shapiro@weizmann.ac.il

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CAD meet CAM

Fabrication strategy can constrain the design space: BioBricks 1.0

- Scar between parts
- Does not allow fusion of protein domains
- Reserved sequences (restriction sites)

Design strategies can facilitate fabrication

- Minimize local GC content: alternative parts, parts design
- Minimize repeats

Tuning the process parameters

- Different protocols for different steps
- Parameters of specific protocols (oligo design, oligo synthesis, etc)
- Complex effects of parameters on the process performance
  - Save on oligo synthesis but may result in higher sequencing costs

Optimization for different figures of merit

- Collect performance statistics to establish a baseline
- Simulate existing process to identify parameter sensitivity
- Simulate revised process to identify possible improvements
- Deploy improved processes customized for specific projects

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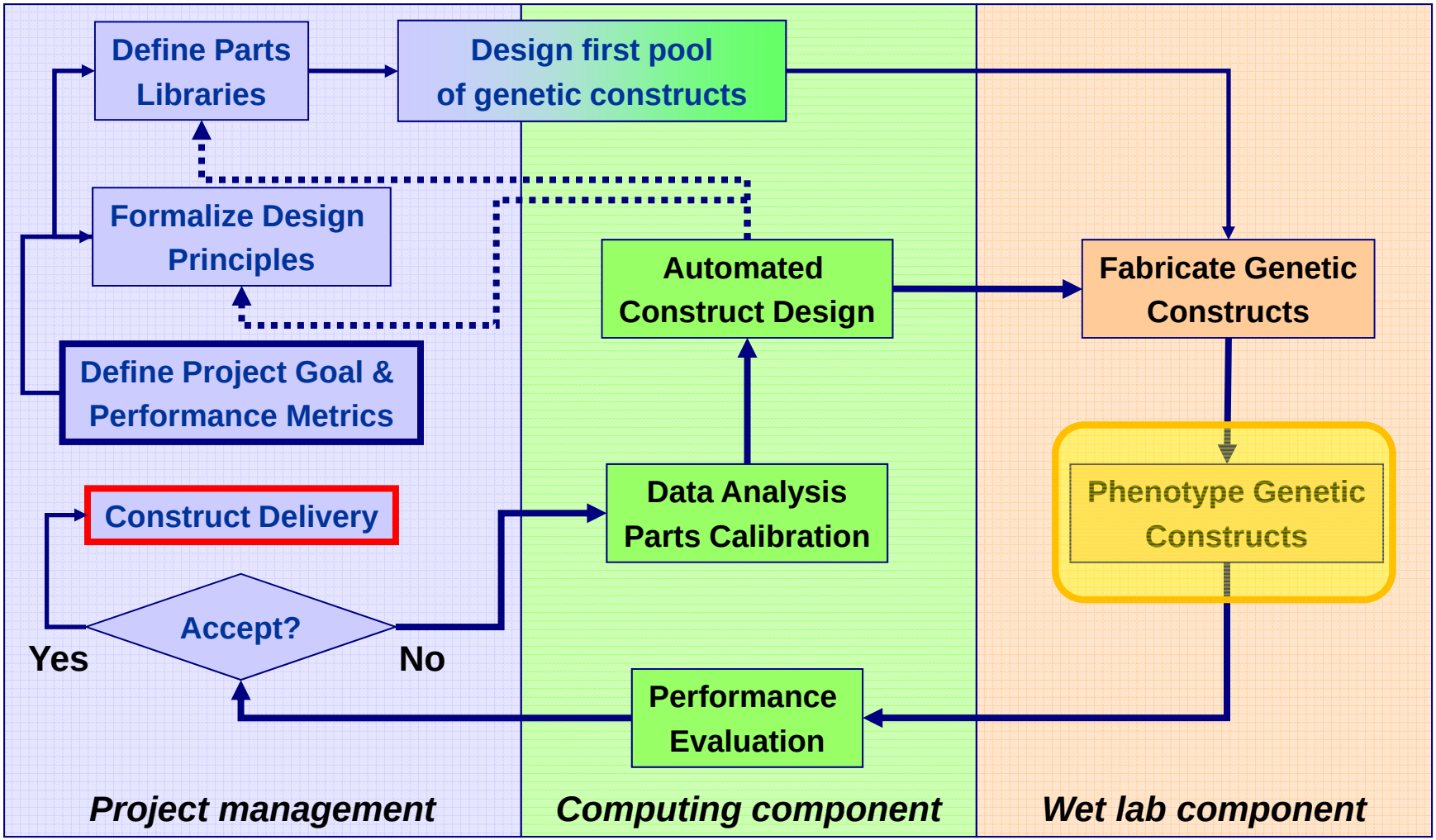


Cell Cycle: Robust yet Sloppy

Robustness of the outcome

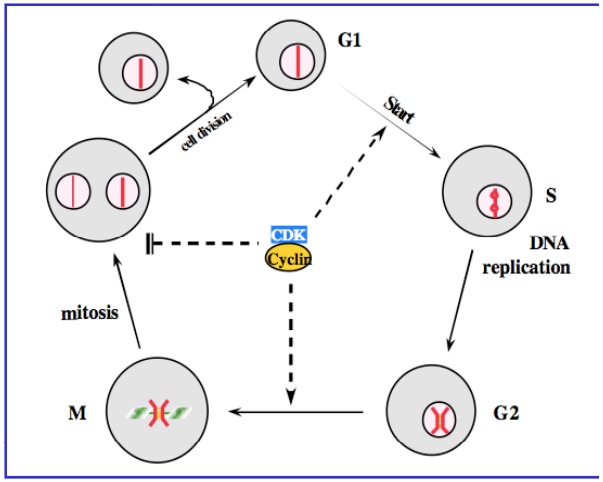
- Sequence of events

Sloppiness of the process

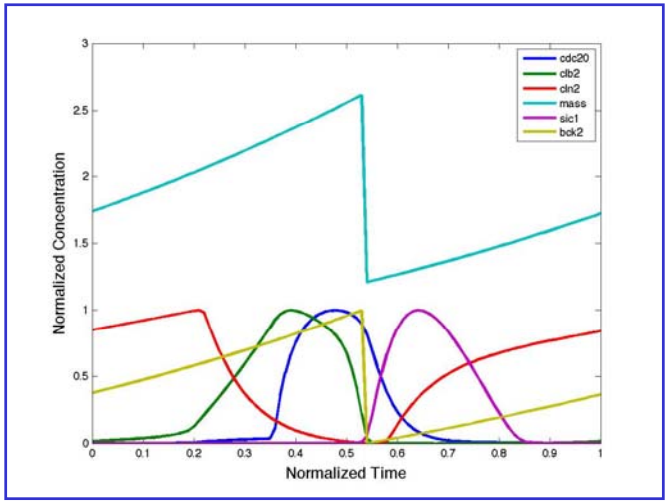
- Time between division (CV 10%-15%)
- Size at cell division (CV 5%-8%)

Sources of fluctuations

- Molecular noise: small molecule numbers
- Fluctuation of the division process



Gene	Average molecules per cell	
	mRNA	**Protein**
CLN2	1.2	1000
CLN3	1.1	110
CLB6	0.4	50
SWI5	0.8	690
CDC28	2.2	6000



Sources: Chen and Tyson

Measuring the stochastic dynamics of gene networks

Requirements

- Fine time-resolution
- Single cell data
- Track individual cells (space, information, cell lineage)

Objectives

- Estimate the dynamics of the statistical distribution of gene expression and product localization

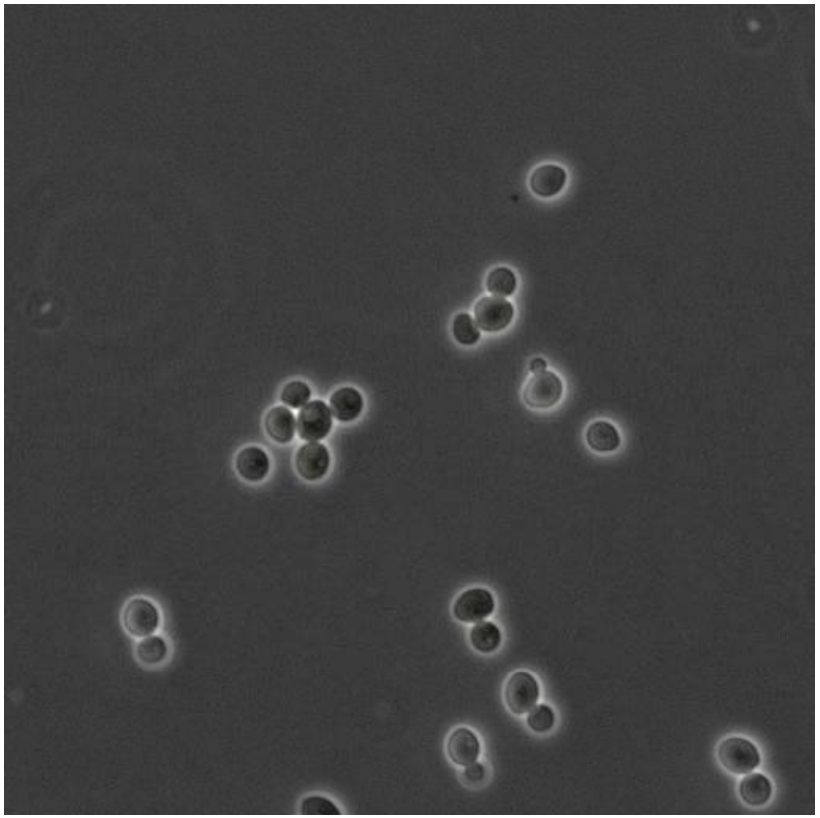
Method

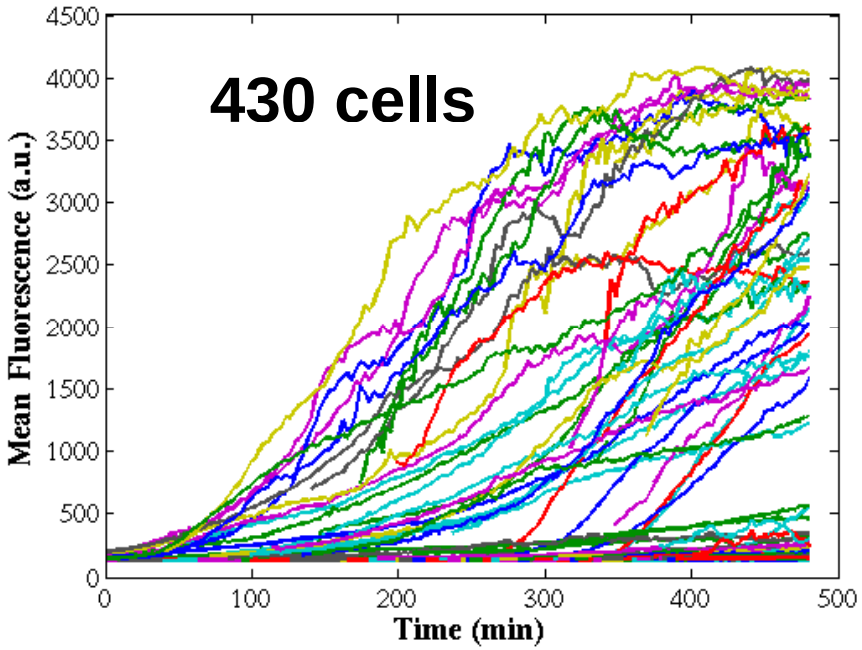
- Custom image processing
- [Custom hardware]
- [Custom control algorithm]

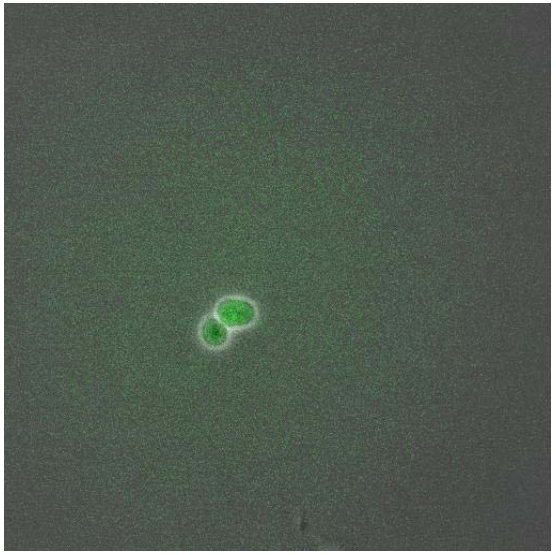
Typical Experiment Size

- 10 hours
- 3 min resolution
- 20 fields of view
- Phase / Fluo.
- 8,000 images
- 4 GB data

Example : GAL1pr-YFP

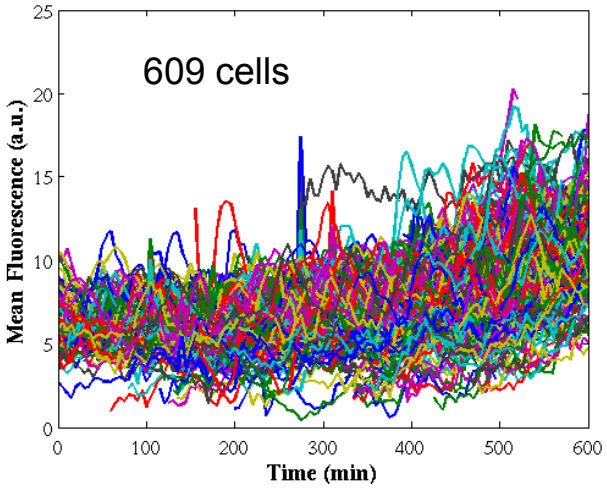




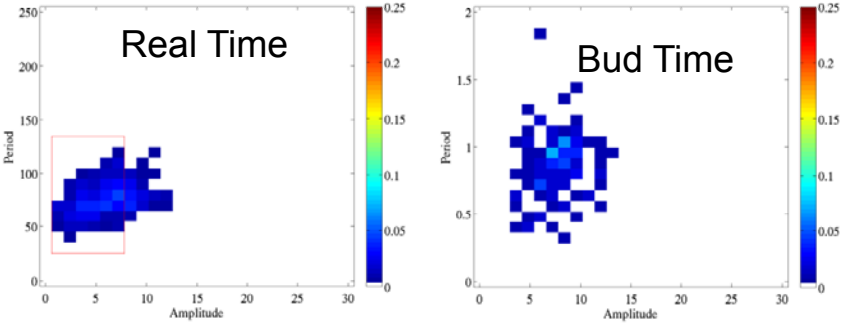


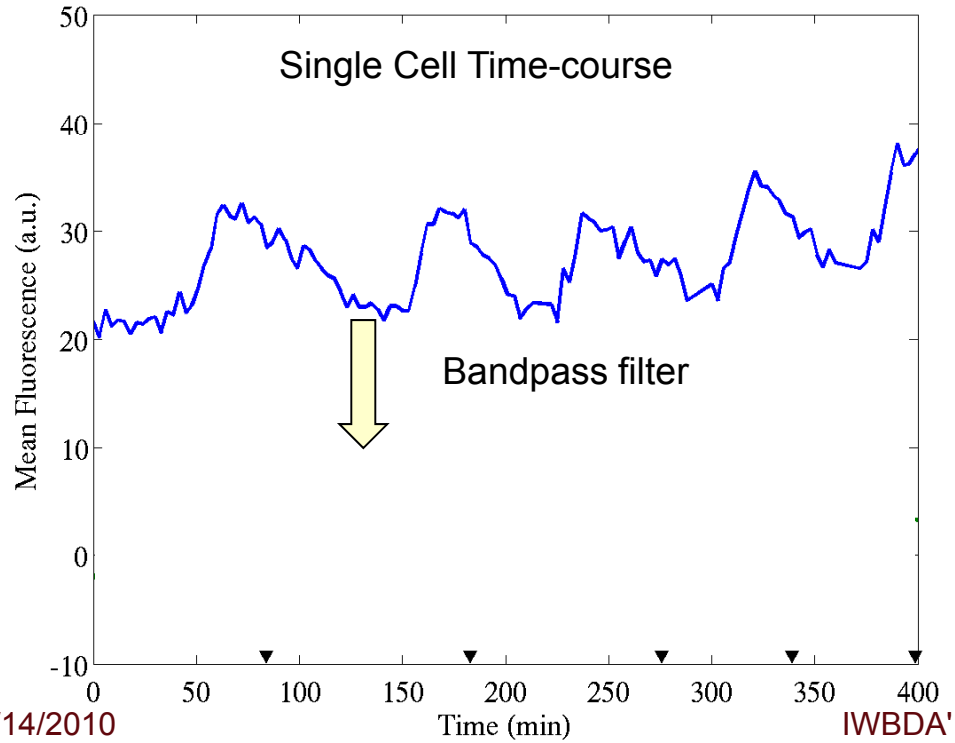
CLN2-GFP

Characterizing the fluctuations of the cell cycle oscillations

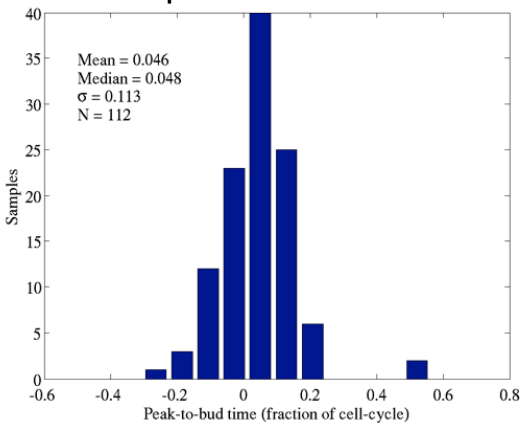


Population Amplitude & Period





Population Phase



Coupling Design and Measurement

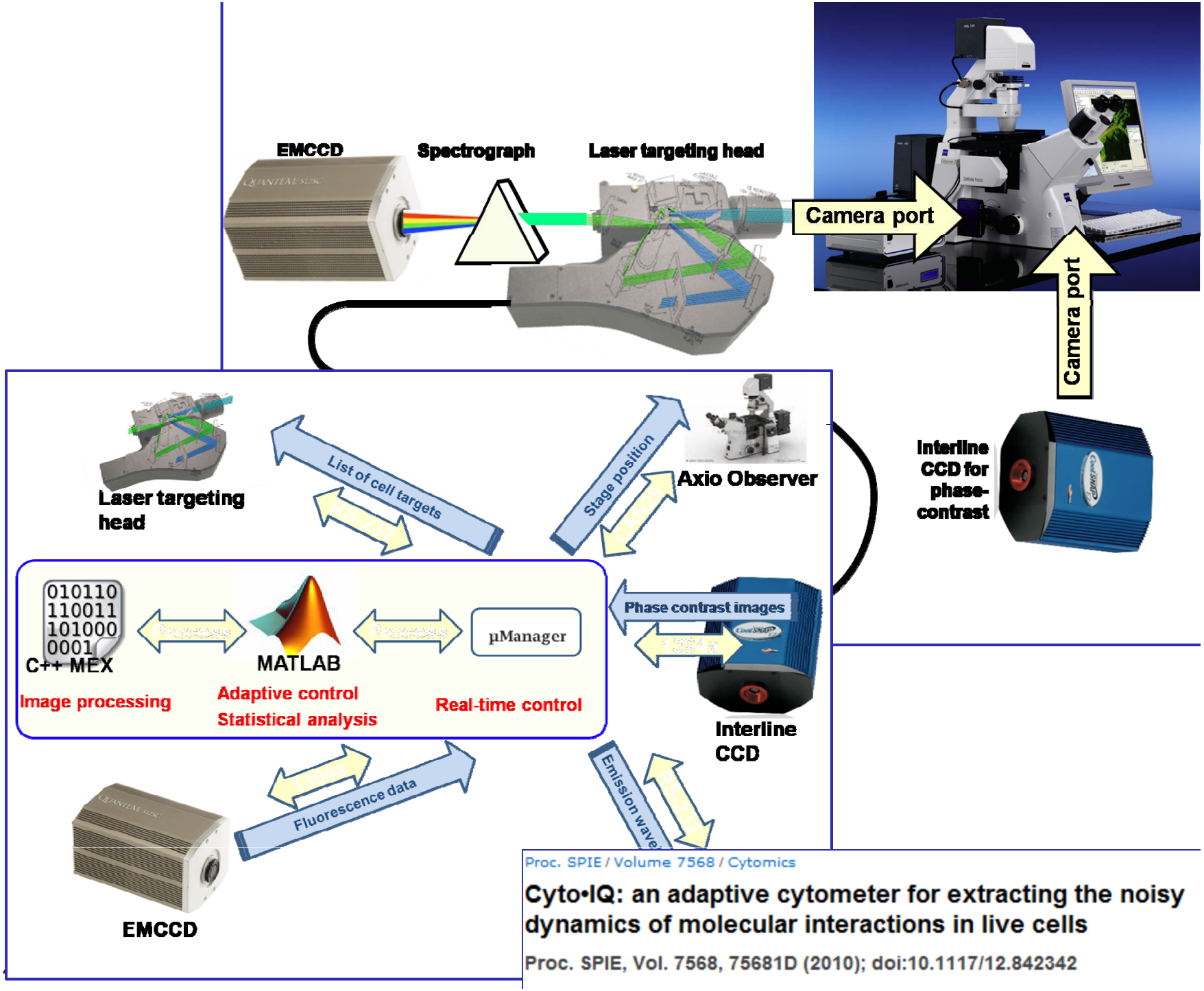
It is difficult to reconcile data with the model

- Stochastic model / single cell data
  - Mean value, first moment, entire distribution, rare events
- Need a model of the measurement system
  - Lack of information about GFP maturation / degradation
  - Error in raw data acquisition and data processing

We have a problem

- Time lapse microscopy is inherently inefficient
- Need real time image processing / data analysis
- Need to adapt the data acquisition to the experiment (not the other way around)
- Will lead to the development of a new generation of T&M instruments

Cyto•IQ HW and SW Architecture



Proc. SPIE / Volume 7568 / Cytomics

Cyto•IQ: an adaptive cytometer for extracting the noisy dynamics of molecular interactions in live cells

Proc. SPIE, Vol. 7568, 75681D (2010); doi:10.1117/12.842342

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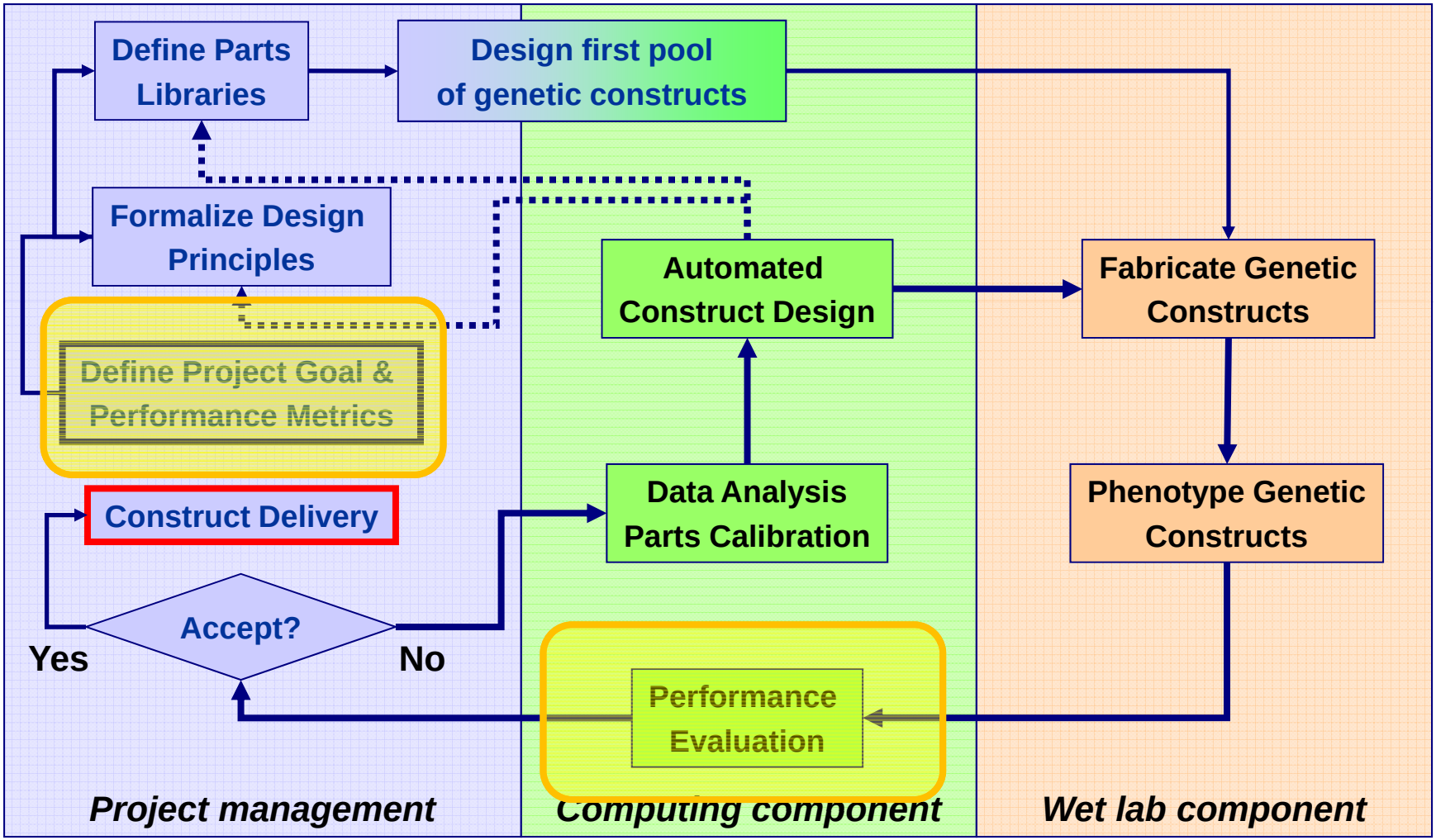
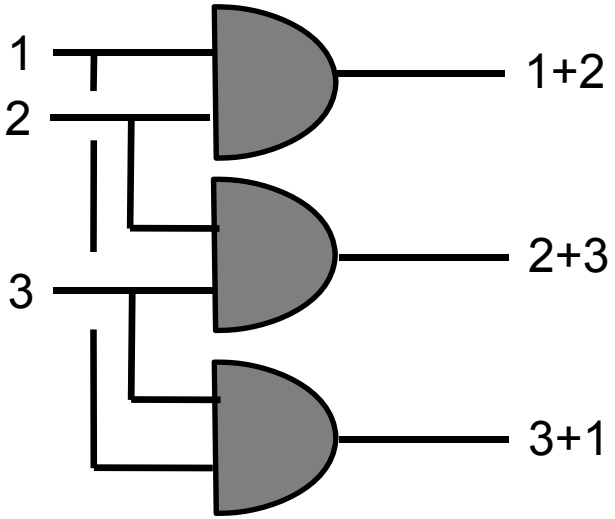


Environmental Sensor: Specification

Defense application

3 Inputs, unique output for any pair on inputs



Input 1	Input 2	Input 3	Output 1	Output 2	Output 3
-	-	-	-	-	-
-	-	+	-	-	-
-	+	-	-	-	-
-	+	+	-	+	-
+	-	-	-	-	-
+	-	+	-	-	+
+	+	-	+	-	-
+	+	+	+	+	+

Co-design of the environmental sensor

Why co-design?

Compare multiple approaches

- Finding the "best" design
- Different design domains
- Some alternative methods

Load on cells generally unknown

- Spread load out
- Transcriptional control somewhat inefficient

Performance metrics

Difficulty of implementation:

- Cost/risk of development
- Number of design cycles

Performance:

- Accuracy
- Signal strength
- Sensitivity
- Response time
- Low "power" consumption

Fieldable application

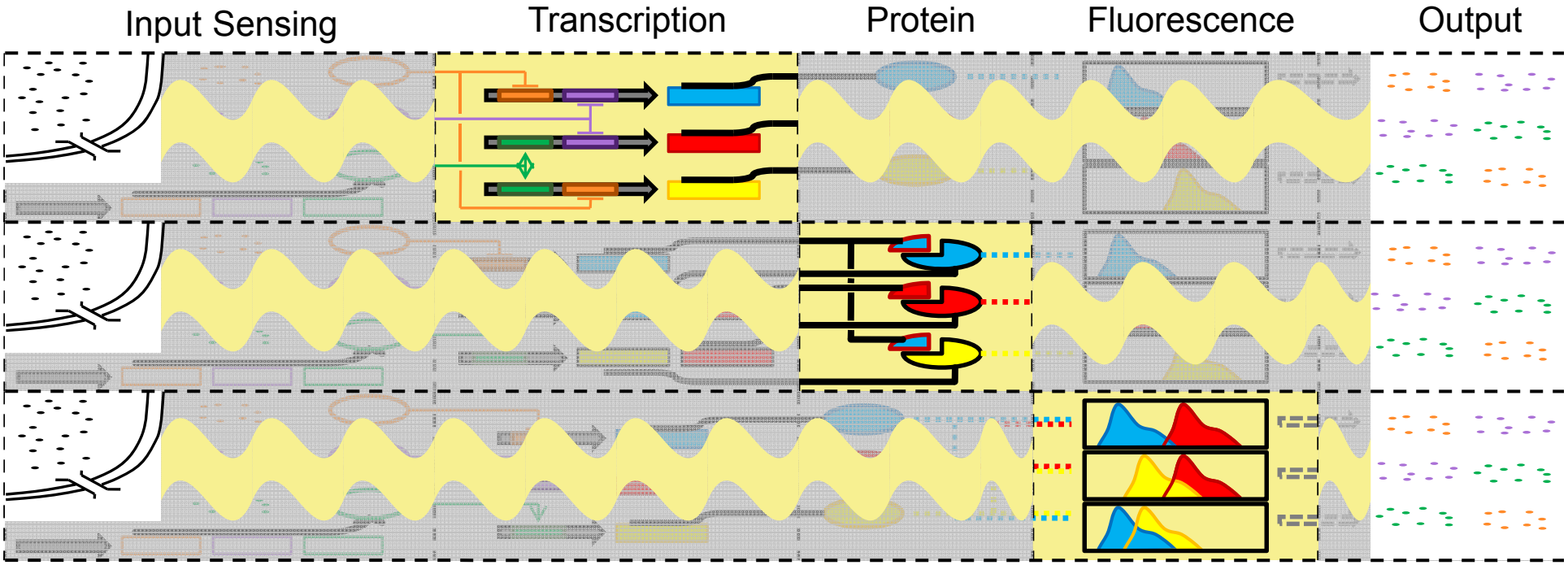
- Cost of manufacturing
- Integration in an IT system

Multiple design domains

Implement at different layers of cellular control

Transcription, translation, post-translation, detection

Similar to the software/hardware codesign problem



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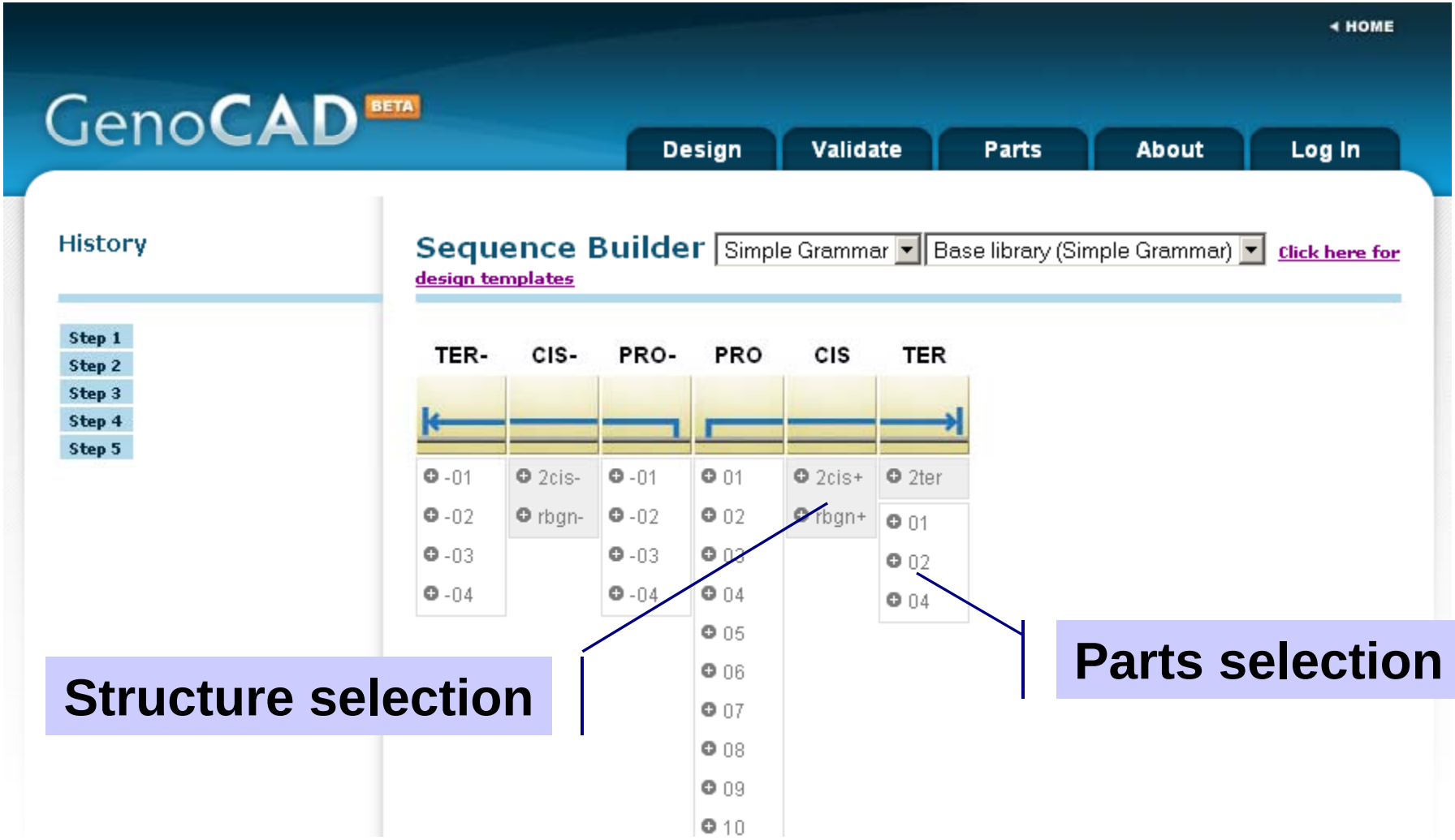
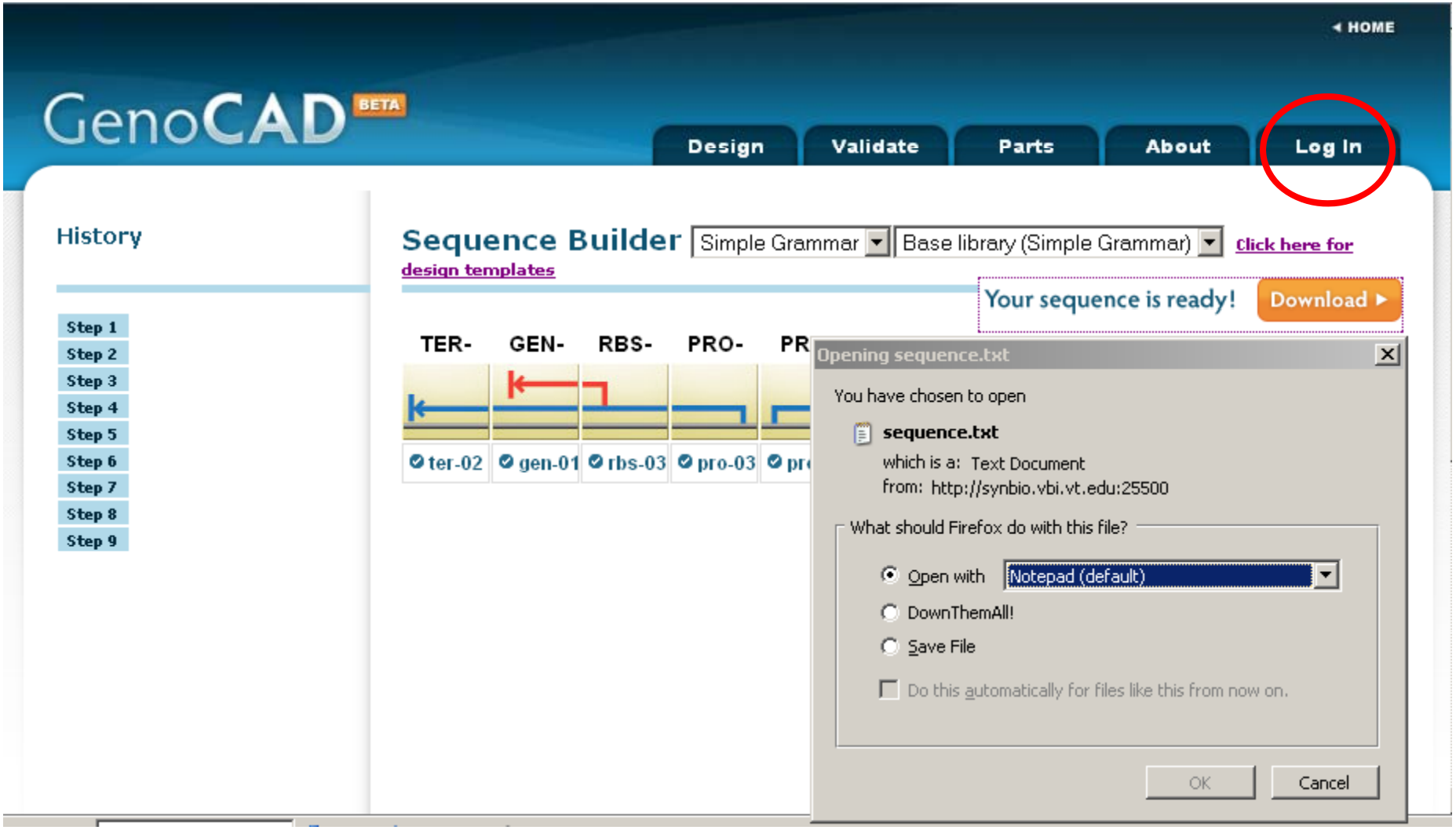
www.genocad.org

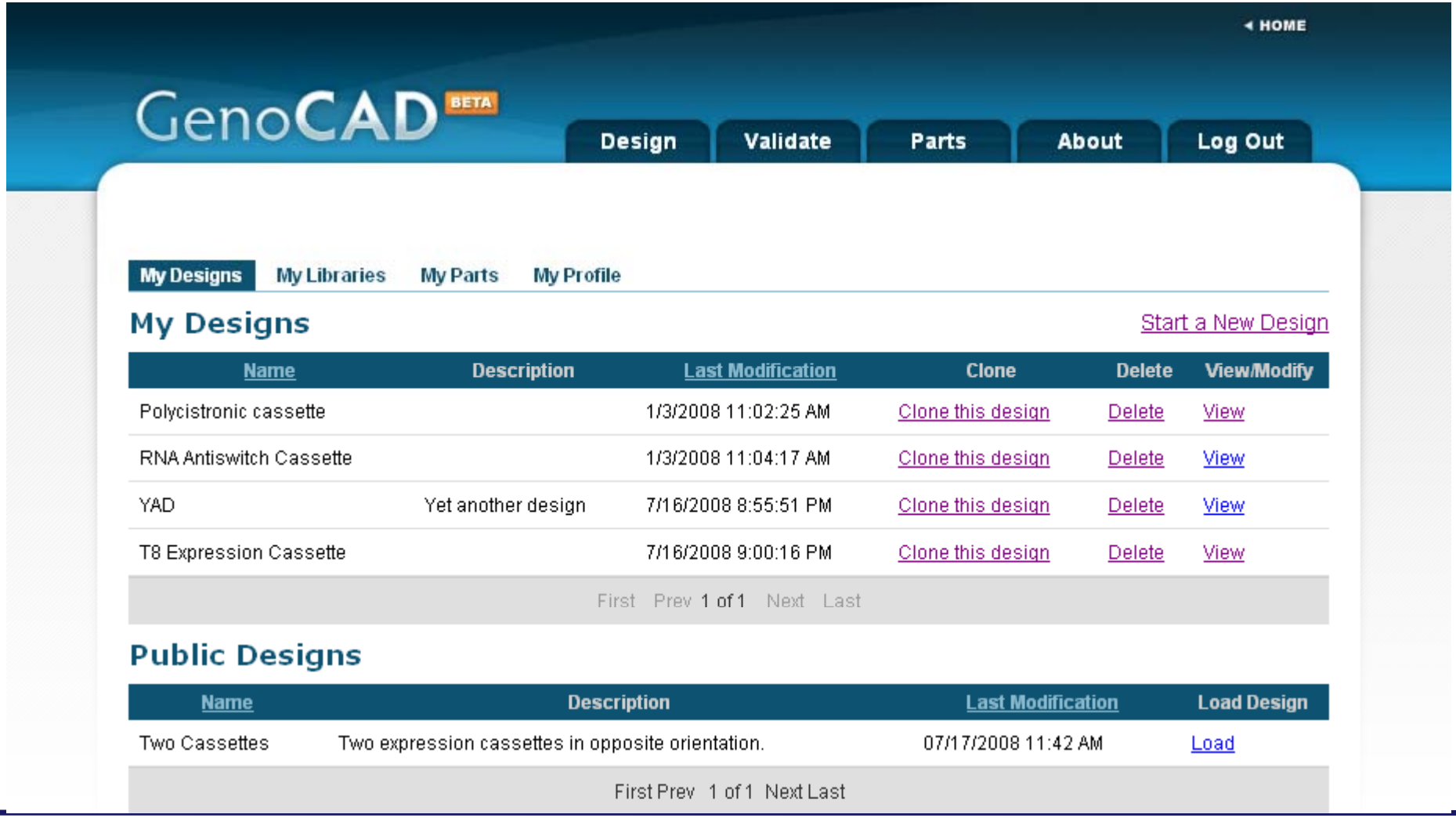
Change structure or select parts



Export the sequence…



My designs


HOME
GenoCAD BETA
Design
Validate
Parts
About
Log Out
My Designs
My Libraries
My Parts
My Profile
My Designs
Start a New Design
Name
Description
Last Modification
Clone
Delete
View/Modify
Polycistronic cassette
1/3/2008 11:02:25 AM
Clone this design
Delete
View
RNA Antiswitch Cassette
1/3/2008 11:04:17 AM
Clone this design
Delete
View
YAD
Yet another design
7/16/2008 8:55:51 PM
Clone this design
Delete
View
T8 Expression Cassette
7/16/2008 9:00:16 PM
Clone this design
Delete
View
First Prev 1 of 1 Next Last
Public Designs
Name
Description
Last Modification
Load Design
Two Cassettes
Two expression cassettes in opposite orientation.
07/17/2008 11:42 AM
Load
First Prev 1 of 1 Next Last

GenoCAD Design Strategy

A collaboration tool

- **Legal**: licensing, parts database, business rules
- **Bioinformatics**: organization central parts library
- **Application specialists**: vector design
- **Molecular biologists**: vector construction

Lightweight client: limit the hassle factor

- No software installation
- Web browser

Graphical user interface

- Familiar workflows: shopping carts
- Understandable by a middle-schooler

GenoCAD Open Source License

From web site to open source software development

"***Don't ask don't tell licensing***" is not open source

- Typical scenario: *faking it*
- Problems:
  - Status of IP unclear
  - Access to software may be terminated

The three faces of Open Source licensing

- Initial code base
- Developer contributions
- End-user

VT partnered with ICSB for licensing GenoCAD

- Inter-institutional agreement
- Apache system of licenses: business friendly
- Protects the community

How to use GenoCAD?
Gene Synthesis

Customize back-end DB

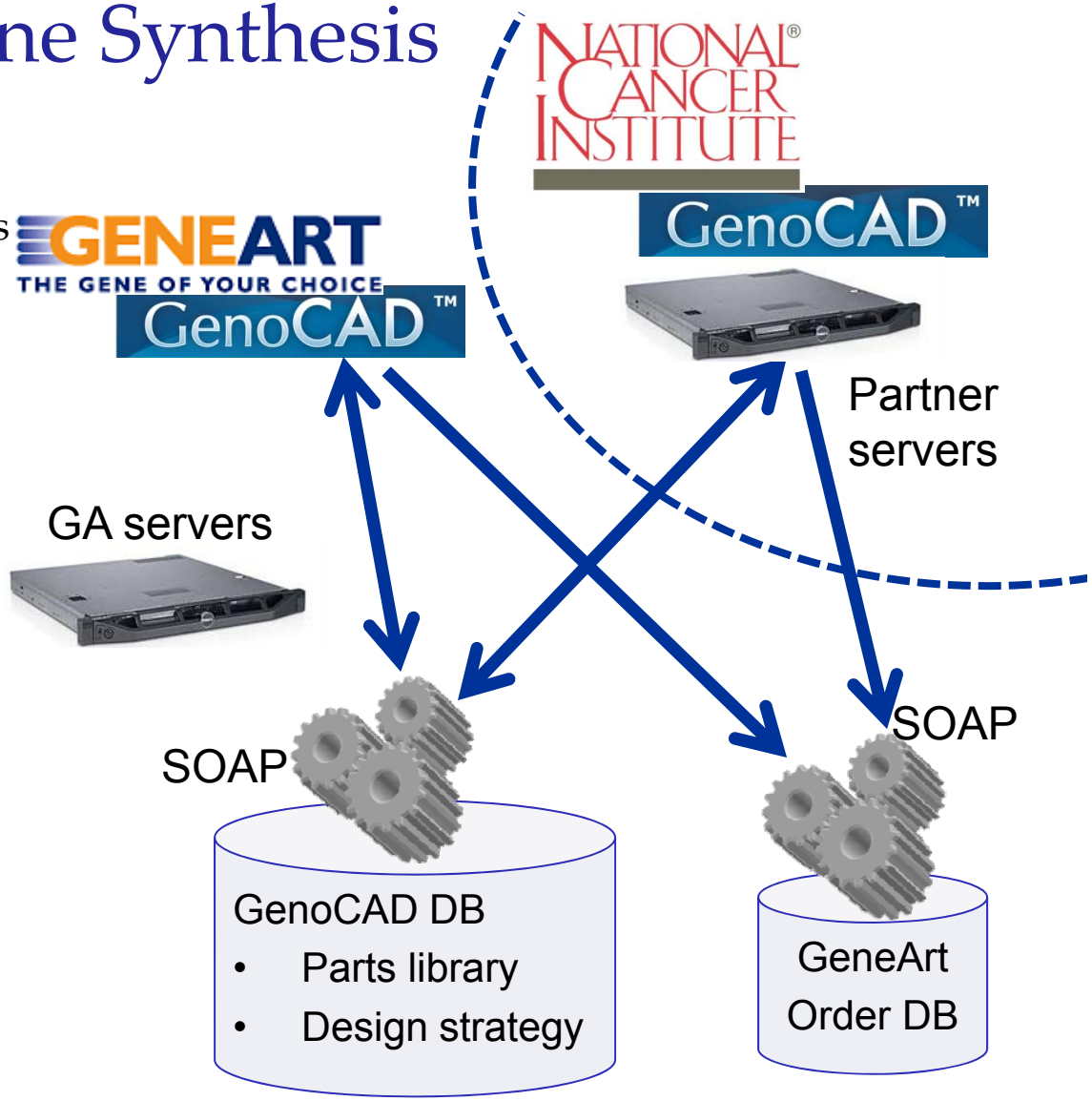
- Modify existing parts libraries
- Create new parts libraries
- Customize design strategies
- Design libraries/strategies for specific customers/projects

Integrate GenoCAD in MyGeneArt.com

- Authentication
- Ordering system

Custom front-end for partners

- Resides on partner servers
- Connects to partner db (auth)
- Connects to GenoCAD db on GA servers



Why use GenoCAD?

Defend / grow market share with value-added services

- Gene synthesis is a commodity
- Create value by providing differentiating services:
  - Helping users design constructs: parts library & design strategies for different domains
  - Seamless ordering process

Reduce costs through knowledge capture

- Reduce the cost of pre-sale support
  - GA spends less time with customers without comprising project success
- Capture company expertise in design strategies

Increase profitability by maximizing parts reuse

- Resale previously synthesized sequences
  - Develop domain-specific parts libraries
- Reduced cost to the customer, increase profit margin

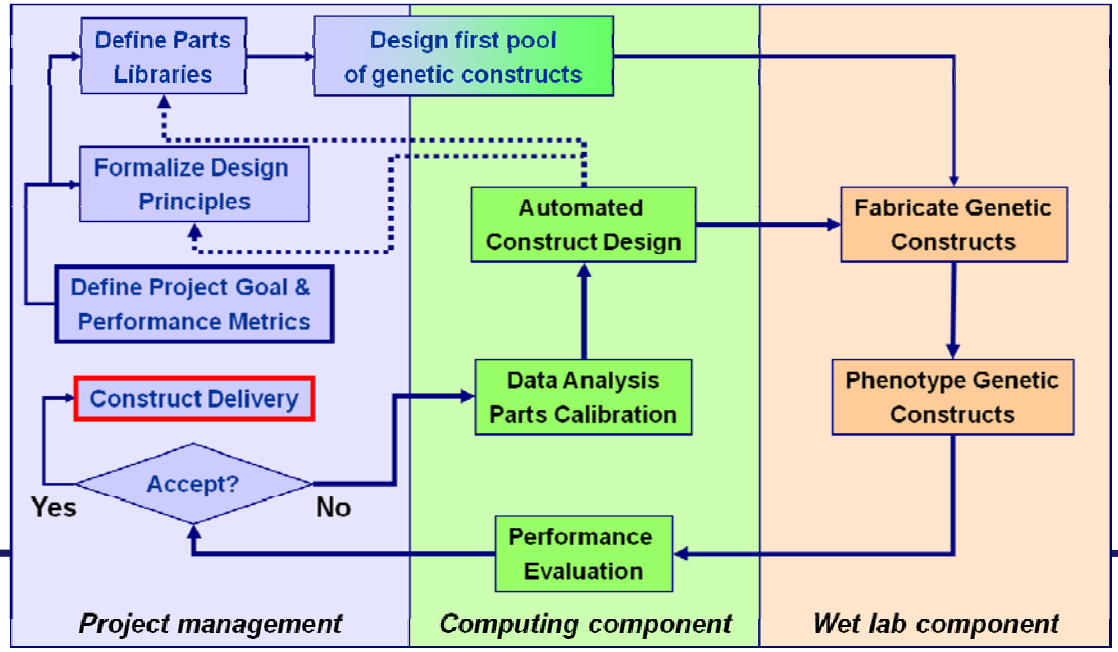
Capturing value by integrating open components

Where is the value?

- Integration of tools and processes to close the DA loop
- Integration will be domain/problem specific
- Integration includes the team

How to capture value?

- Data sets generated by well structured experimental design
- Design strategies for a particular problem
- End product of the design process



digital biology foundation

supporting life sciences software that works together.

Take home messages…

Finding a market to live the vision

- Demonstrate the **value proposition today**
- Test, capture, formalize **existing biological knowledge**
- Find a language to **communicate with potential users**

Reducing the cost of DNA fabrication by several orders of magnitude

- Avenues to rationally **optimize** the process
- **Recoupling** fabrication and design to increase fab efficiency
- Define target **languages describing fab processes**

Expressing and measuring the function of genetic parts

- Imaging: **reduction of raw data** (flow cytometry, microscopy)
- **Context-dependence** of functional parameters
- **Identifiability** of functional parameters

Acknowledgements

Leadership

- VBI : Jean Peccoud, M. Czar, O. Folkerts, M. Wilson

Experiments

- VBI SynBio: J. Marchand, D. Ball, M. Lux, S. Zheng, J. Long
- VT iGEM'07: E. DeLalla, B. Lyons, M. Sweede
- VBI CLF: C. Evans, K. Cooper, M. Blauvelt

Data analysis

- VBI SynBio: Y. Cai, R. Shelton, M. Lux, L. Adams
- VBI CIG: M. Shrinivasrao, O. Crasta

Collaborators

- VBI: S. Hoops, J. Lewis
- Virginia Tech: J. Tyson, W Baumann
- Brandeis: J. Cohen
- JHU: J. Boeke, J. Bader
- Boston U.: J. Collins
- Berkeley: J.C. Anderson, J. Goler
- UIUC: W. Sanders
- MIT : R. Rettberg, R. Weiss
- Lux Bio Group: B.W. Bramlett
- DNA2.0: C. Gustafsson
- SAIC: G. Doyle
- MITRE: J. Dileo, M. Petersen

Funding

Questions?

CAD Model of VBI

Photo of VBI