

Design of Asynchronous Genetic Circuits

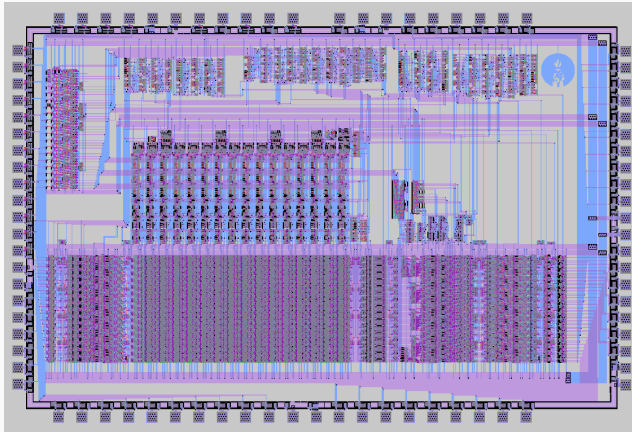
Chris J. Myers

CE Junior Seminar

August 27, 2019

University of Utah

ASYNCHRONOUS DESIGN AT CALTECH



The first fully asynchronous microprocessor
(Designed by Alain Martin's group at Caltech in 1989)



Academia

Timing ignored

Complex-gates

Systematic methods

Verified correct

Conservative designs



Industry

Timing critical

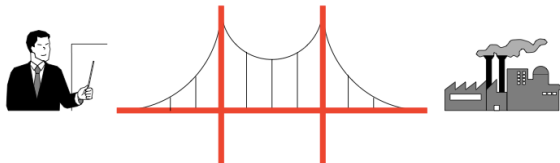
Semi-custom

Adhoc methods

Extensive simulation

Unreliable designs

TIMED ASYNCHRONOUS CIRCUITS



Utilize explicit timing information

Semi-custom

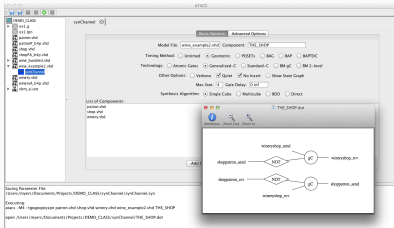
Systematic methods

Verified correct

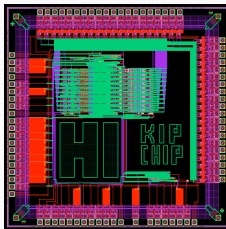
Efficient and reliable designs

(ICCD 1992, IEEE TVLSI 1993, CAV 1994, IEEE TCAD 1999)

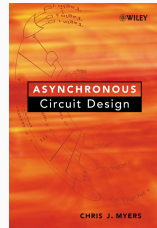
TIMED ASYNCHRONOUS CIRCUIT DESIGN AND VERIFICATION



ATACS Software



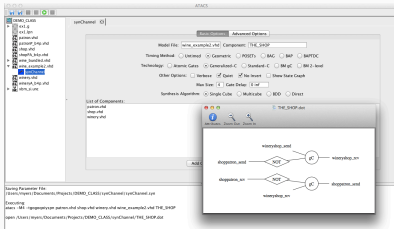
Self-timed Multiplier



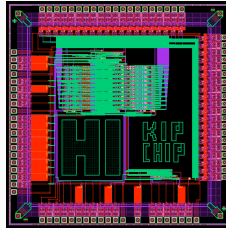
Textbook

- 20 journal papers, 4 patents, and 45 conference/workshop papers (including 10 published at this conference).
- 1 postdoc, 5 MS students, and 6 PhD students (3 tenured faculty).

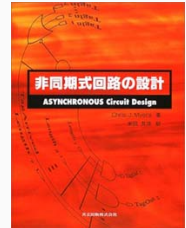
TIMED ASYNCHRONOUS CIRCUIT DESIGN AND VERIFICATION



ATACS Software



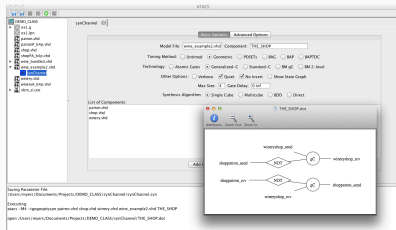
Self-timed Multiplier



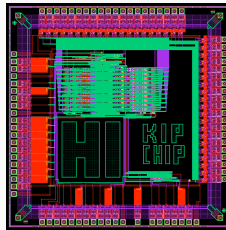
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TIMED ASYNCHRONOUS CIRCUIT DESIGN AND VERIFICATION



ATACS Software



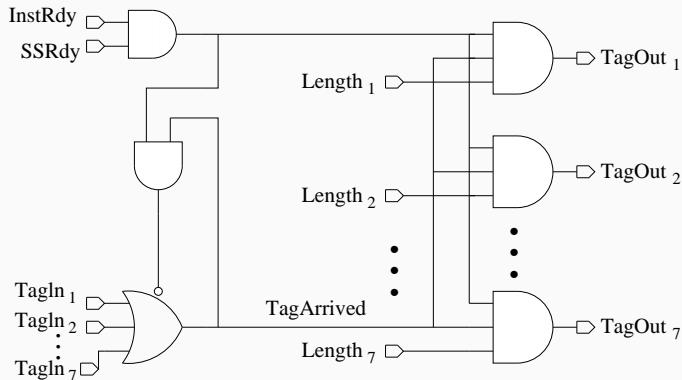
Self-timed Multiplier



Textbook

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INTEL RAPPID PROJECT



ASYNC 1999 (Best Paper Award), IEEE JSSC 2001,
US Patents 5,978,899, 5,948,096, 5,941,982, and 5,931,944.

- Test chip fabricated in May 1998 using a 0.25 μm process.
- Three times faster while consuming half the power of the comparable synchronous design.

TOP 10 REASONS TO HIRE AN ASYNCHRONOUS DESIGNER



Manpreet Khaira

Fifth International Symposium on Advanced Research in
Asynchronous Circuits and Systems
Barcelona (Spain), 18-21 April 1999

TOP 10 REASONS TO HIRE AN ASYNCHRONOUS DESIGNER

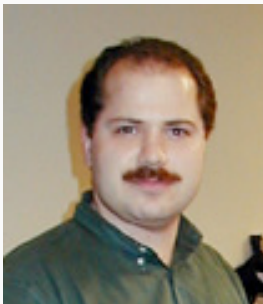


Manpreet Khaira

No. 1 - They are really smart, and we can teach them to do something real.

Fifth International Symposium on Advanced Research in
Asynchronous Circuits and Systems
Barcelona (Spain), 18-21 April 1999

ASYNCHRONOUS GENETIC CIRCUITS

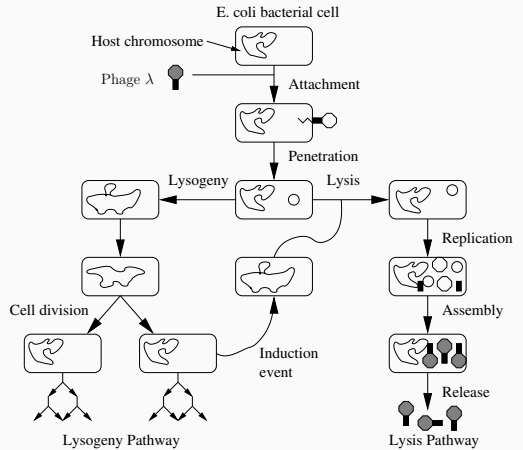
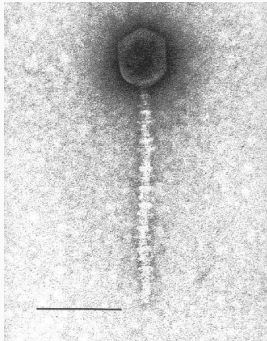


Michael Samoilov

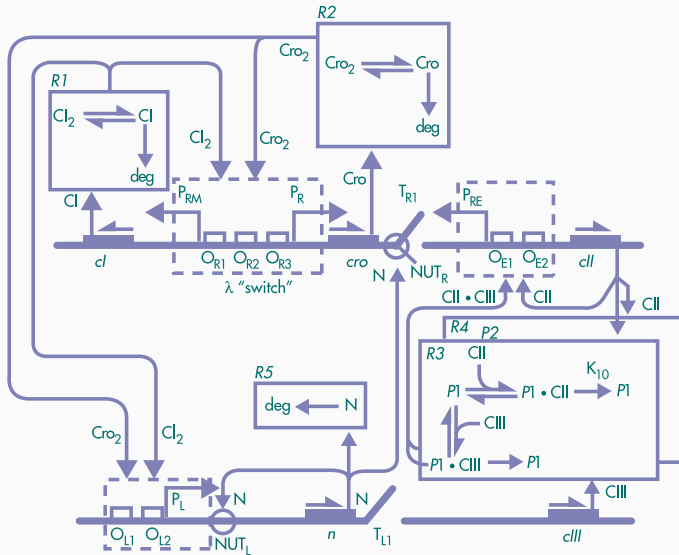


Adam Arkin

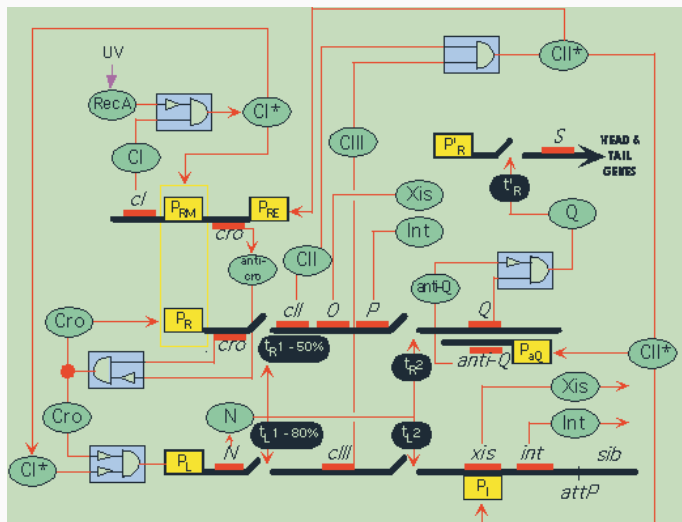
PHAGE λ VIRUS



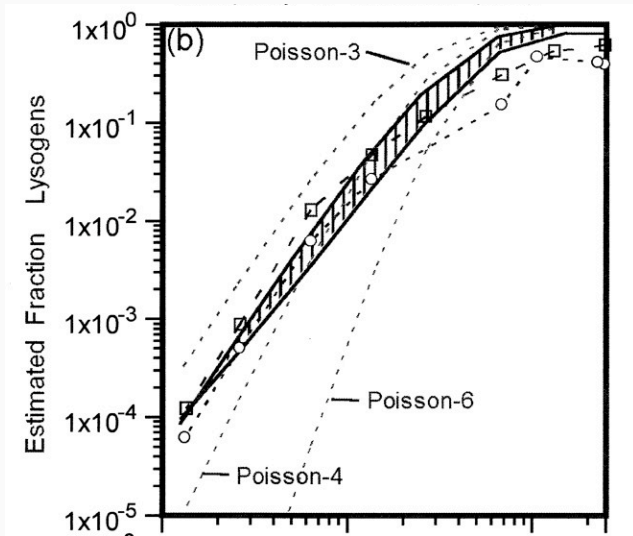
PHAGE λ DECISION CIRCUIT



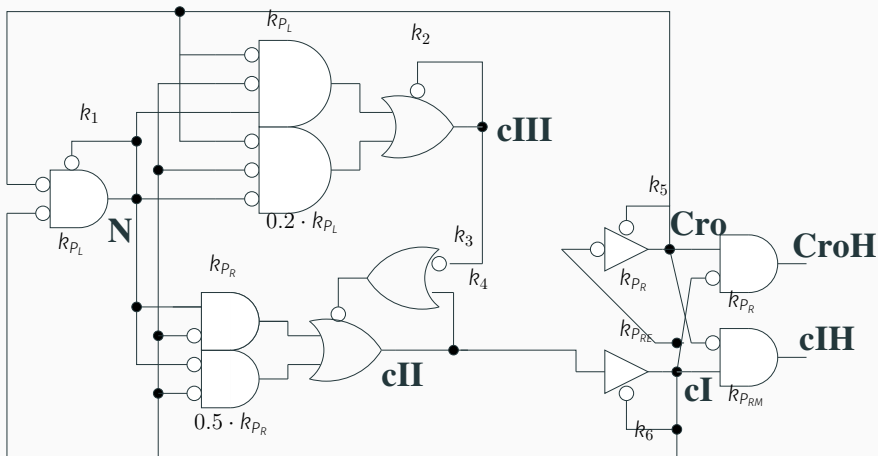
ASYNCHRONOUS CIRCUIT?



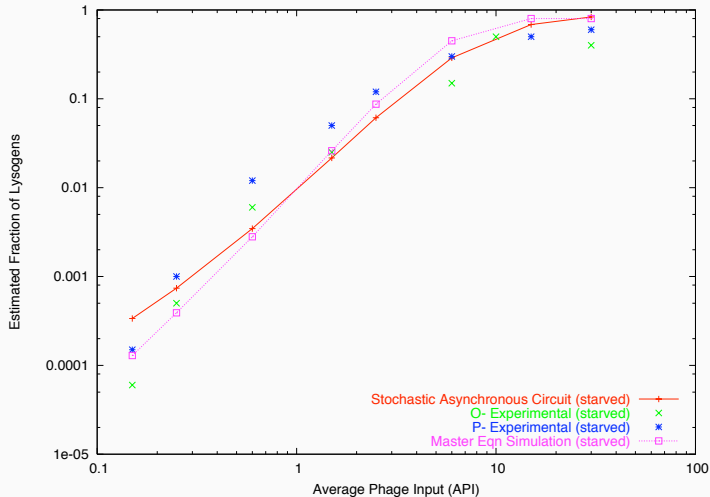
STOCHASTIC CIRCUIT?



STOCHASTIC ASYNCHRONOUS CIRCUIT?



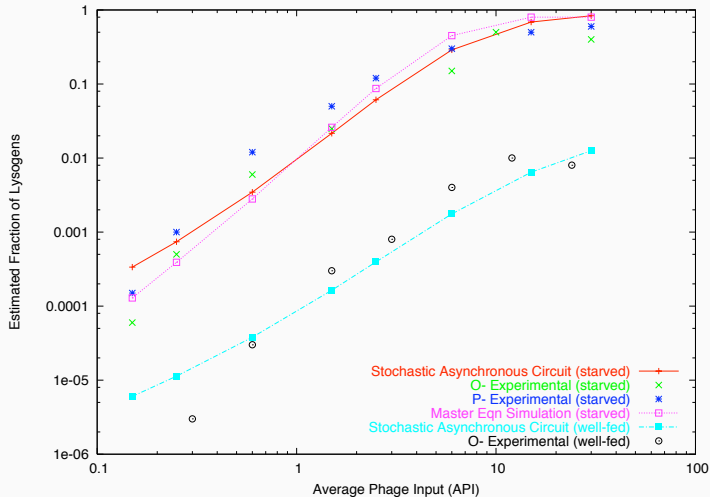
STOCHASTIC ASYNCHRONOUS CIRCUIT RESULTS



SAC results generated in only 7 minutes.

Kuwahara et al., Trans. on Comp. Sys. Bio. (2006)

STOCHASTIC ASYNCHRONOUS CIRCUIT RESULTS



SAC results generated in only 7 minutes.
Kuwahara et al., Trans. on Comp. Sys. Bio. (2006)

SYSTEMS BIOLOGY VERSUS SYNTHETIC BIOLOGY



Drew Endy

SYSTEMS BIOLOGY VERSUS SYNTHETIC BIOLOGY



Drew Endy

Synthetic biology applications:

- Produce drugs and bio-fuels.
- Consume toxic waste.
- Destroy tumors.

SYSTEMS BIOLOGY VERSUS SYNTHETIC BIOLOGY



Drew Endy

Synthetic biology applications:

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- Synthetic biology adds *standards, abstraction, and decoupling* to genetic engineering practice.

SYSTEMS BIOLOGY VERSUS SYNTHETIC BIOLOGY



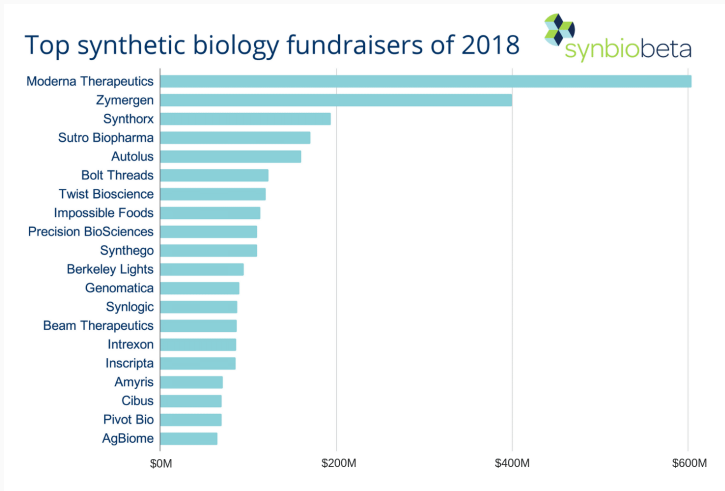
Drew Endy

Synthetic biology applications:

- Produce drugs and bio-fuels.
- Consume toxic waste.
- Destroy tumors.

- Synthetic biology adds *standards*, *abstraction*, and *decoupling* to genetic engineering practice.
- Since *genetic circuits* are inherently asynchronous, seems appropriate to leverage asynchronous design and verification methodologies.

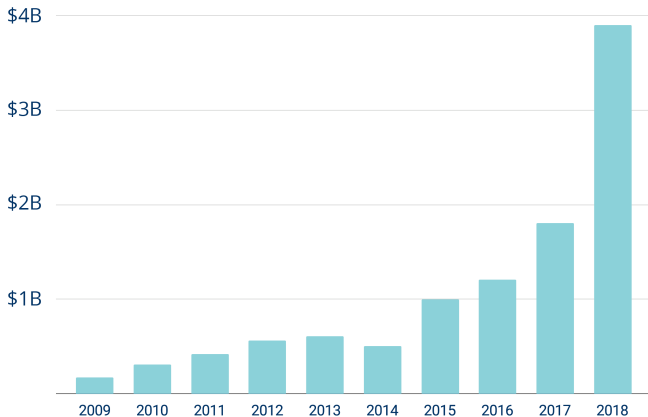
SYNTHETIC BIOLOGY STARTUPS



98 Synthetic Biology Companies
Raised More Than \$3.8 Billion in 2018

SYNTHETIC BIOLOGY STARTUPS

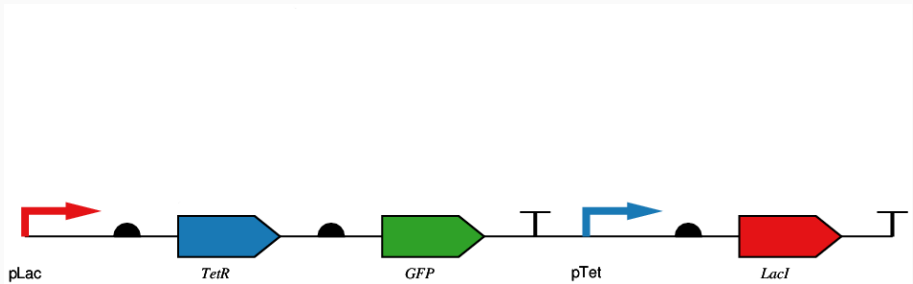
Funding for synthetic biology companies, 2009-2018



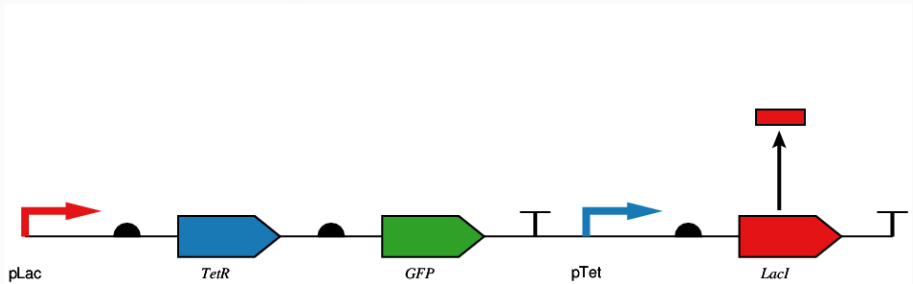
GENETIC CIRCUIT DESIGNS

- Genetic circuits are created from biological components that mimic the behavior of Boolean logic gates.
- Genetic circuits can be built inside of a living organism (*in vivo*) or in a test tube (*in vitro*).
- Most genetic circuits that have been built are *combinational circuits*.
- Some *sequential memory circuits* have been constructed.

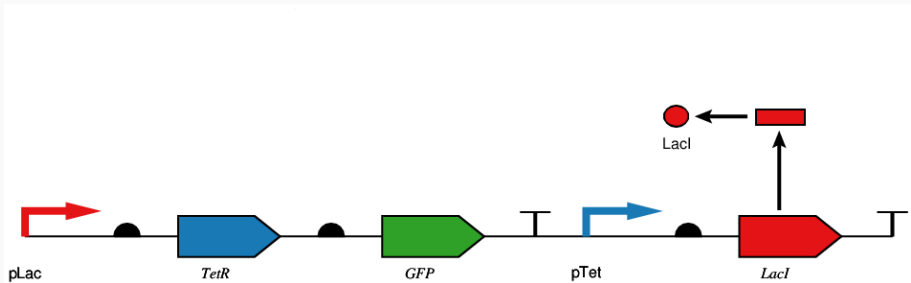
GENETIC TOGGLE SWITCH (GARDNER ET AL. 2000)



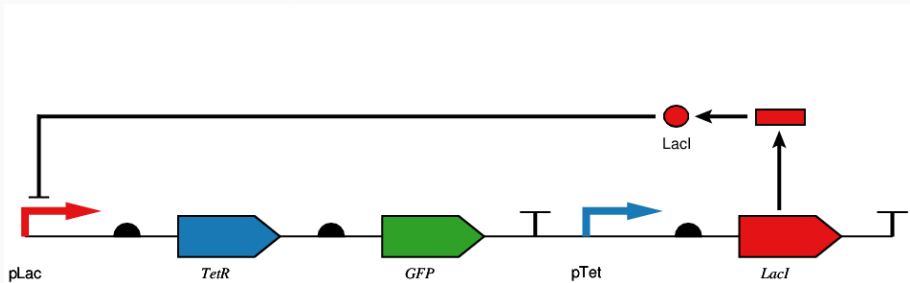
GENETIC TOGGLE SWITCH (GARDNER ET AL. 2000)



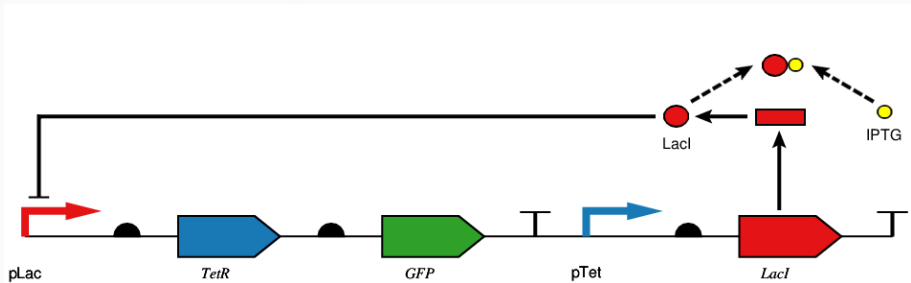
GENETIC TOGGLE SWITCH (GARDNER ET AL. 2000)



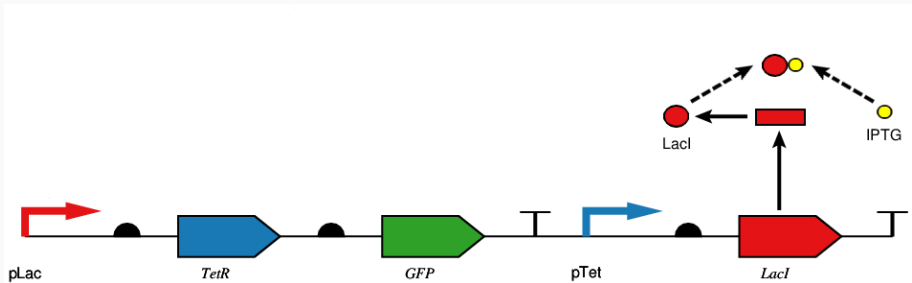
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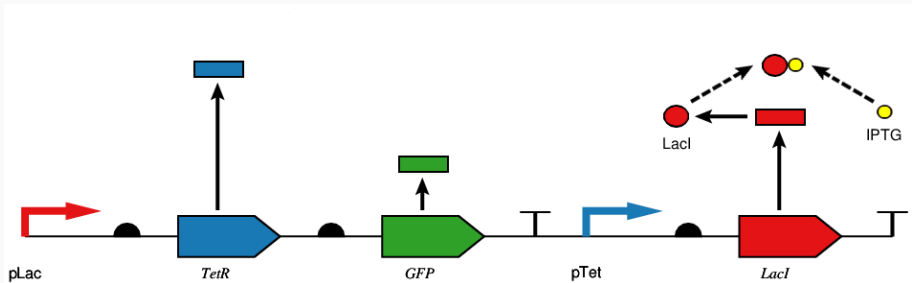
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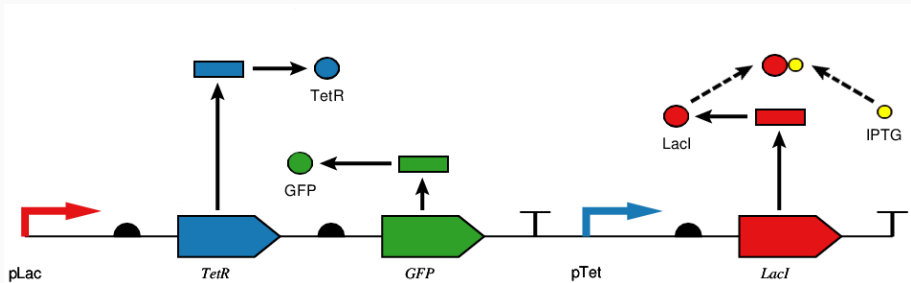
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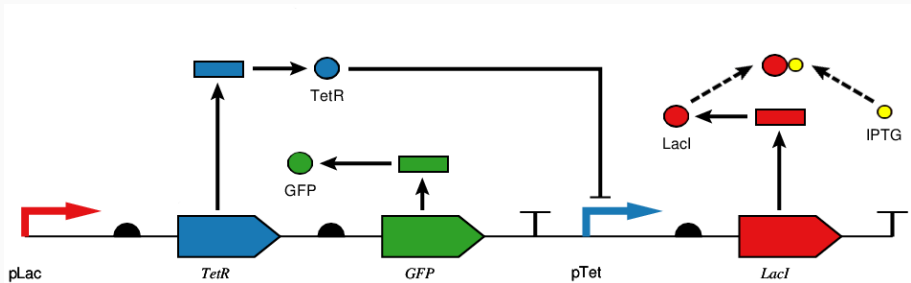
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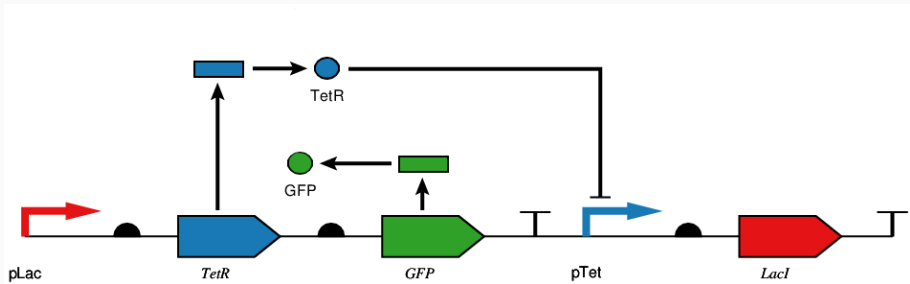
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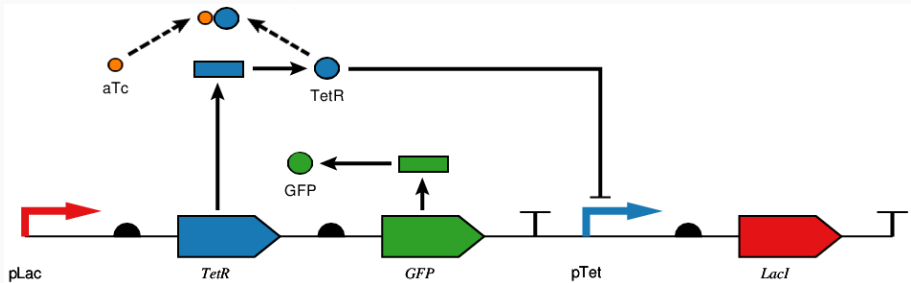
GENETIC TOGGLE SWITCH (GARDNER ET AL. 2000)



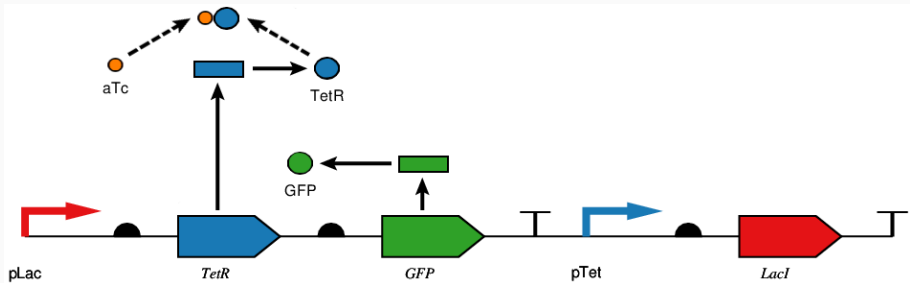
GENETIC TOGGLE SWITCH (GARDNER ET AL. 2000)



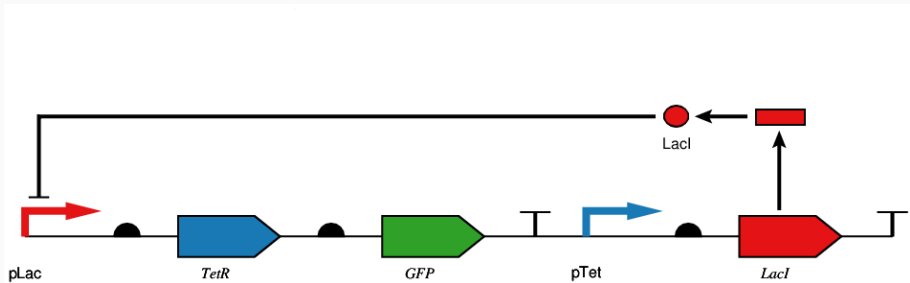
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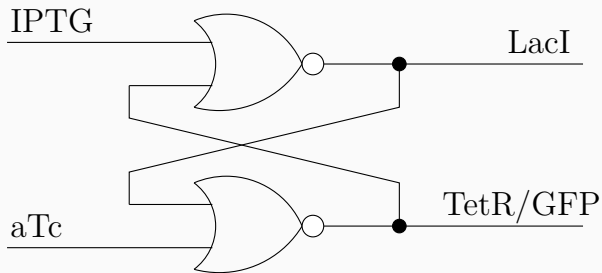
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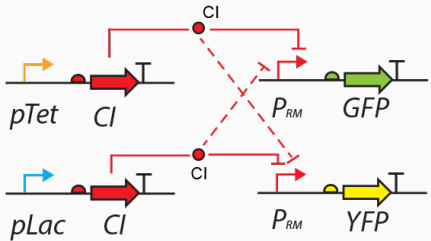
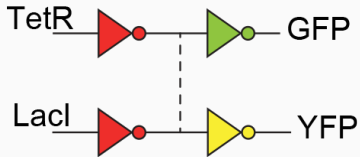
GENETIC TOGGLE SWITCH (SR LATCH) LOGIC DIAGRAM



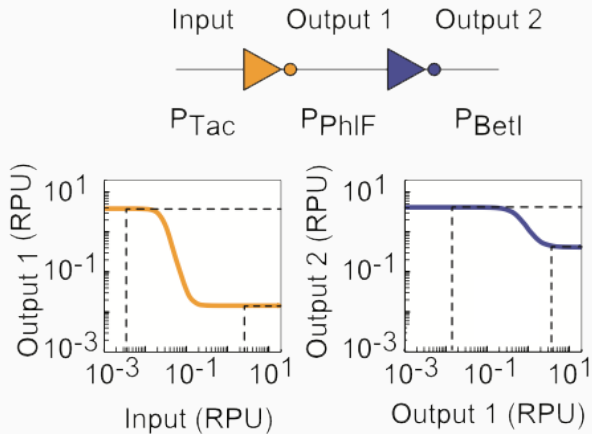
GENETIC DESIGN CONSTRAINTS

- Crosstalk
- Signal Mismatch
- Roadblocking
- Context Effects

CROSSTALK

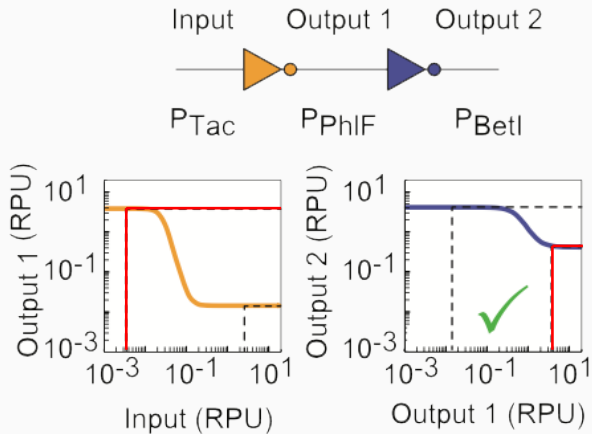


SIGNAL MISMATCH



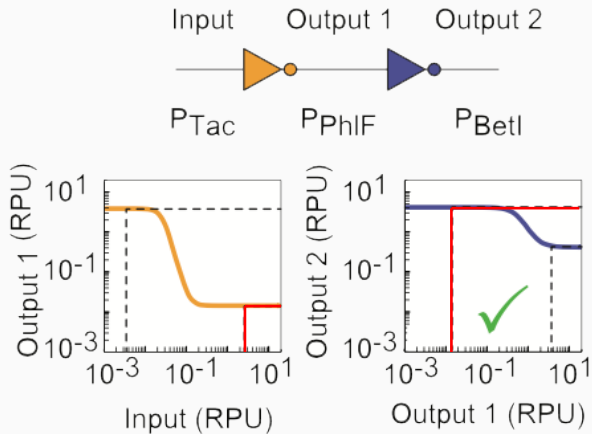
Nielsen et al., *Science*, 2016

SIGNAL MISMATCH



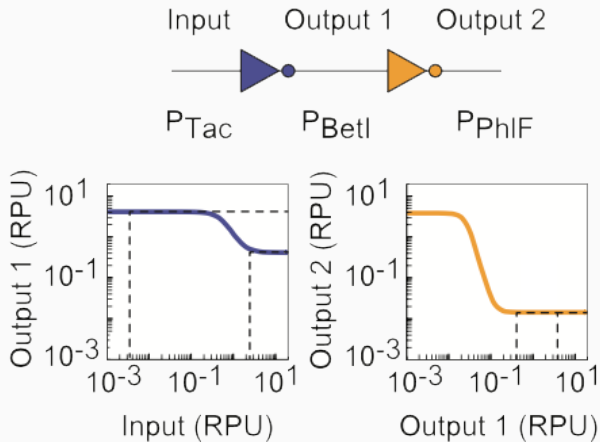
Nielsen et al., *Science*, 2016

SIGNAL MISMATCH



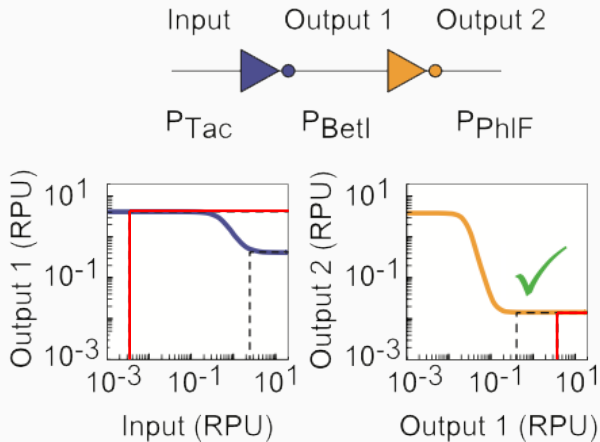
Nielsen et al., *Science*, 2016

SIGNAL MISMATCH



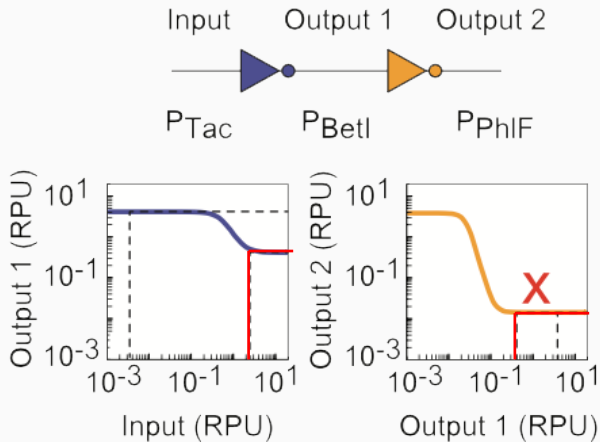
Nielsen et al., *Science*, 2016

SIGNAL MISMATCH



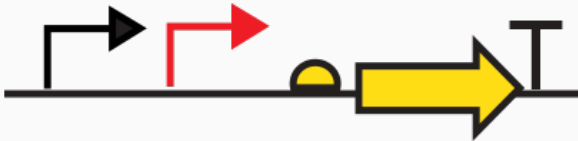
Nielsen et al., *Science*, 2016

SIGNAL MISMATCH



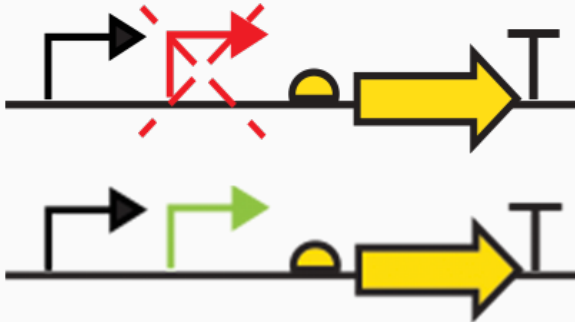
Nielsen et al., *Science*, 2016

ROADBLOCKING



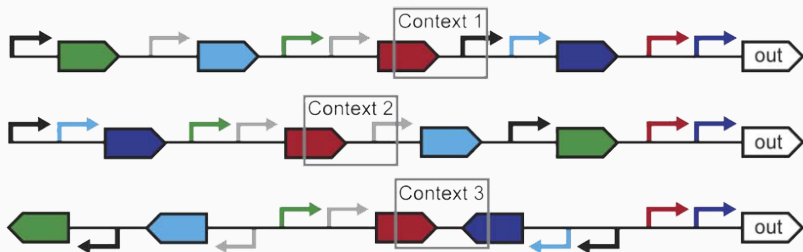
Nielsen et al., *Science*, 2016

ROADBLOCKING



Nielsen et al., *Science*, 2016

CONTEXT EFFECTS



Vaidyanathan et al., *IEEE*, 2015

GENETIC DESIGN AUTOMATION (GDA)

- Building a complex circuit that operates correctly under the genetic design constraints is time consuming.
- *Genetic design automation* (GDA) can help refine the design space before building a circuit in the laboratory.
- Models can be generated programatically and analysis of these models can help evaluate design alternatives on a computer (*in silico*).



Professor David Donoho
Stanford University

An article about computational science in a scientific publication is not the scholarship itself, it is merely advertising of the scholarship. The actual scholarship is the complete ... set of instructions [and data] which generated the figures.

Essential information for synthetic DNA sequences

To the Editor:

Following a discussion by the workgroup for Data Standards in Synthetic Biology, which met in June 2010 during the Second Workshop on Bioscience Automation in Anaheim, California, we wish to highlight a problem relating to the reproducibility of the synthetic biology literature. In particular, we have noted the very small number of articles reporting synthetic gene networks that disclose the complete sequence of all the constructs they describe.

To our knowledge, there are only a few examples where full sequences have been released. In 2005, a patent application¹ disclosed the sequences of the toggle switches published four years earlier in a paper by Gardner *et al.*². The same year, Basu *et al.*³ deposited their construct sequences for programmed pattern formation into GenBank³. Examples of synthetic DNA sequences derived from standardized parts that have been made available in GenBank include the refactored genome of the bacteriophage

gaps between key components are almost never reported, presumably because they are not considered crucial to the report. Yet, synthetic biology relies on the premise that synthetic DNA can be engineered with base-level precision.

Missing sequence information in papers hurts reproducibility, limits reuse of past work and incorrectly assumes that we know fully which sequence segments are important. For example, many synthetic biologists are currently realizing that translation initiation rates are dependent on more than the Shine-Dalgarno sequence⁴. Sequences upstream of the start codon are crucial for translation rates, yet are underreported. Similarly, it has been demonstrated that intron length can affect the dynamics of genetic oscillators⁵. Many more such examples are likely to emerge.

Because full sequence disclosure is critical, we wonder why the common requirement by many journals to provide GenBank entries for genomes and natural sequences has

and welcome contributions from the greater community.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

Jean Peccoud¹, J Christopher Anderson², Deepak Chandran³, Douglas Densmore⁴, Michal Galdzicki⁵, Matthew W Lux¹, Cesar A Rodriguez⁶, Guy-Bart Stan⁷ & Herbert M Sauro³

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³Department of Bioengineering, University of Washington, Seattle, Washington, USA.

⁴Department of Electrical and Computer Engineering, Boston University, Boston, Massachusetts, USA. ⁵Biomedical and Health Informatics, University of Washington, Seattle, Washington, USA. ⁶BIOFAB, Emeryville, California, USA. ⁷Department of Bioengineering and Centre for Synthetic Biology and Innovation, Imperial College London, London, UK. e-mail: peccoud@vt.edu

1. Gardner, T.S. & Collins, J.J. US patent 6,841,376 (2005).
2. Gardner, T.S., Cantor, C.R. & Collins, J.J. *Nature* **403**, 339–342 (2000).
3. Basu, S., Gerchman, Y., Collins, C.H., Arnold, F.H. & Woicik, D. *Nature* **434**, 112–115 (2006).



SYNTHETIC BIOLOGY OPEN LANGUAGE (SBOL)

VERSION 1 RELEASED IN 2011

nature
biotechnology

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NATURE BIOTECHNOLOGY | COMPUTATIONAL BIOLOGY | PERSPECTIVE



日本語要約

The Synthetic Biology Open Language (SBOL) provides a community standard for communicating designs in synthetic biology

Michal Galdzicki, Kevin P Clancy, Ernst Oberortner, Matthew Pocock, Jacqueline Y Quinn,
Cesar A Rodriguez, Nicholas Roehner, Mandy L Wilson, Laura Adam, J Christopher Anderson,
Bryan A Bartley, Jacob Beal, Deepak Chandran, Joanna Chen, Douglas Densmore, Drew
Endy, Raik Grünberg, Jennifer Hallinan, Nathan J Hillson, Jeffrey D Johnson, Allan Kuchinsky,
Matthew Lux, Goksel Misirli, Jean Peccoud, Hector A Plahar, Evren Sirin, Guy-Bart Stan, Alan
Villalobos, Anil Wipat, John H Gennari, Chris J Myers & Herbert M Sauro

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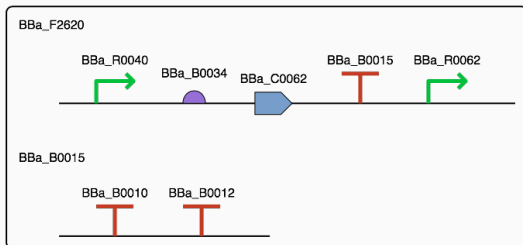
[Affiliations](#) | [Contributions](#) | [Corresponding author](#)

Nature Biotechnology 32, 545–550 (2014) | doi:10.1038/nbt.2891
Received 09 November 2013 | Accepted 20 December 2013 | Published online 06 June 2014

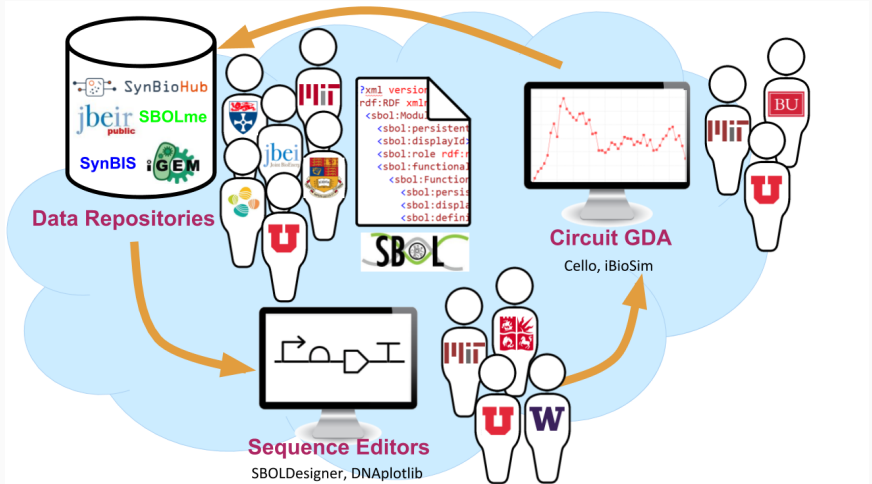
COMMUNITY PAGE

SBOL Visual: A Graphical Language for Genetic Designs

Jacqueline Y. Quinn¹, Robert Sidney Cox III², Aaron Adler³, Jacob Beal³, Swapnil Bhatia⁴, Yizhi Cai⁵, Joanna Chen^{6,7}, Kevin Clancy⁸, Michal Galdzicki⁹, Nathan J. Hillson^{6,7}, Nicolas Le Novère¹⁰, Akshay J. Maheshwari¹¹, James Alastair McLaughlin¹², Chris J. Myers¹³, Umesh P¹⁴, Matthew Pocock^{12,15}, Cesar Rodriguez¹⁶, Larisa Soldatova¹⁷, Guy-Bart V. Stan¹⁸, Neil Swainston¹⁹, Anil Wipat¹², Herbert M. Sauro^{20*}



SYNTHETIC BIOLOGY WORKFLOW USING SBOL



Myers et al., *Biochemical Society Transactions* (2017).

INTERNATIONAL GENETICALLY ENGINEERED MACHINE (IGEM) COMPETITION



Started in 2004 with 5 teams and 31 participants.
In 2017: 310 teams with nearly 5400 participants from 44 countries.

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IGEM REGISTRY OF STANDARD BIOLOGICAL PARTS (BIOBRICKS)

Registry of Standard Biological Parts



tools catalog repository assembly protocols help search



Adding Parts to the Registry

The Registry's Repository contains thousands of documented parts with available DNA samples. Last year, iGEM teams submitted samples for over 2000 parts.

Be sure to add your parts and send samples to the Registry so that they can be made available to the community!

[Add a Part Sample Submission](#)

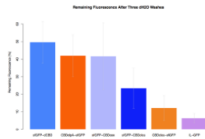
Featured Part

Cellulose Collection

Group: Team Imperial 2014, and others

The 2014 Imperial iGEM team created a bacterial cellulose filter for their **Aqualose** project. They wanted to produce flexible, and pollution-specific filters to aid in water sanitation. They created a set of well-documented cellulose binding domains, paired with reporter genes (GFP) and metal binding domains.

Many other teams have also worked with cellulose, so check out the cellulose related parts collection.



Catalog

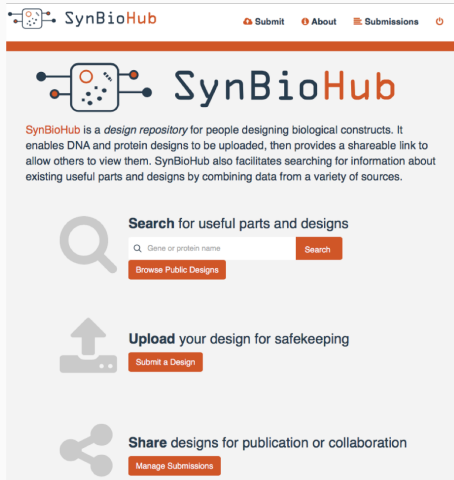
The iGEM Registry has over 20,000 documented parts. The Catalog organizes many of these parts by part type, chassis, function, and more. Browse for parts through the Registry Catalog or use the search menu.

2017 DNA Distribution

The iGEM 2017 DNA Distribution has started shipping! We've added some new material this year, so be sure to read through the 2017 Distribution Handbook for storage instructions and how to use your kit!

<http://parts.igem.org>

DATA REPOSITORIES (SYNBIOHUB)




James McLaughlin
Anil Wipat



Zach Zundel
Chris Myers

Version 1.0 released
June 14, 2017


REFERENCE INSTANCE

 SynBioHub

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Bacillus subtilis Collection
version 1




This collection includes information about promoters, operators, CDSs and proteins from *Bacillus subtilis*. Functional interactions such as transcriptional activation and repression, protein production and various protein-protein interactions are also included.

IGEM Parts Registry
version 1




The IGEN Registry is a growing collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems. As part of the synthetic biology community's efforts to make biology easier to engineer, it provides a source of genetic parts to IGEN teams and academic labs.

IGEM 2017 Distribution
version 1





Distribution of parts for the 2017 IGEN competition

SBOL Compliant Software
version 1




A collection of software that supports the Synthetic Biology Open Language (SBOL) standard

 **ACS Synthetic Biology**
version current





<https://synbiohub.org>

NSF EXPEDITIONS LIVING COMPUTING PROJECT



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PhoenixReduced
version 1
PhoenixReduced

 Phoenix 



Cello Parts
version 1
These are the Cello parts

 CELLO 



LCP Collection
version 1
Designs created as part of the NSF Expeditions Living Computing Project.

AlphaSample
version 1
Sample parts used in Phoenix

 Phoenix 

Cello_VPRGeneration_Paper
version 1
A collection containing 52 Cello circuits that were reconstructed by VPR model generation. Each circuit that was generated from VPR were converted into the SBML data model for verification of the design. The simulation result is plotted from iBiosim and a plot of the result is also found in each circuit's collection.

 CELLO 

<https://synbiohub.programmingbiology.org>

DARPA SYNERGISTIC DATA & DISCOVERY (SD2) PROJECT

SD2 Synbiohub (prod)

Q Search SD2 Synbiohub (prod) Search

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Private Submissions

You currently have 62 private submission(s)

experiment_collection (SD2 Experiments)

version 1

This collection contains all experiments carried out as part of the DARPA SD2 (Synergistic Discovery and Design) program, as well as sub-collections for each challenge problem in the program.

Remove

Copy

PRIVATE

biofab_yeast_gates_q0_aq_10827_collection (yeast-gates_q0_1_biofab_c7090cf3-0b36-4a9d-98c8-81342b81d011_Plan)

version 1

This collection contains metadata for an experiment carried out as part of an SD2 challenge problem.

Remove

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biofab_yeast_gates_q0_10545_collection (yeast-gates_q0_1_biofab_c990c35f-ad2b-444f-9f60-8f0f794121c7_Plan)

version 1

This collection contains metadata for an experiment carried out as part of an SD2 challenge problem.

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Public Submissions

You currently have 0 public submission(s)

<https://hub.sd2e.org>

Q Search

Q promoter regulated by LacI

Search

Advanced Search | SPARQL
Showing 1 - 50 of 7172 result(s)
1 2 3 4 5 Next

LacI

BBa_R0010 Version 1 (Component)
promoter (lacI regulated)

REMOTE

lacI+pL

BBa_R0011 Version 1 (Component)
Promoter (lacI regulated, lambda pL hybrid)

REMOTE

p(tetR)

BBa_R0040 Version 1 (Component)
TetR repressible promoter

REMOTE

lacI

BBa_C0012 Version 1 (Component)
lacI repressor from E. coli (+LVA)

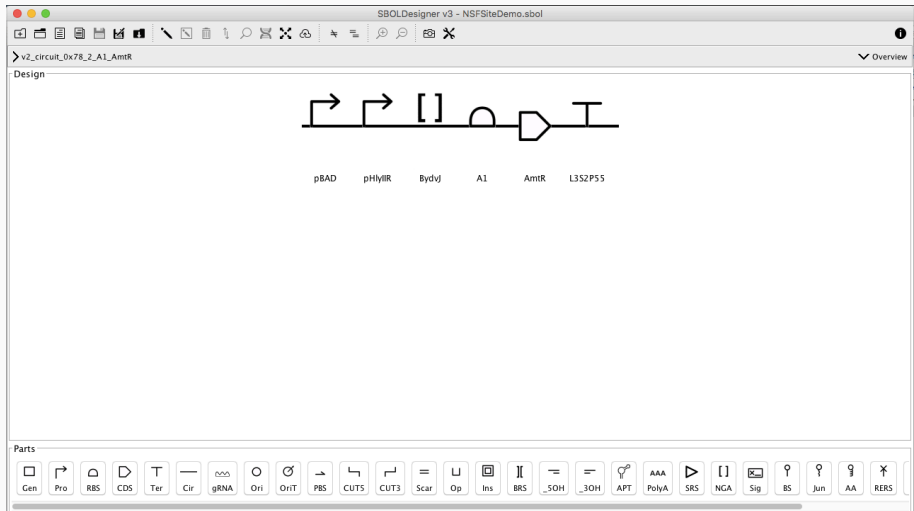
REMOTE

lux pR

BBa_R0062 Version 1 (Component)
Promoter (luxR & HSL regulated -- lux pR)

REMOTE

SEQUENCE EDITORS (SBOLDESIGNER)



SEQUENCE EDITORS (BENCHLING)

Projects

SynBioHub Transfers

NOTEBOOK INVENTORY

- ☐ A1_AmR
Last modified 2 days ago
- ☐ AmtR
Last modified 5 hours ago
- ☐ Test
Last modified 2 days ago
- ☒ The Best
Last modified 3 days ago

SEQUENCE MAP

— +

Create Copy BLAST PDF

LINEAR MAP DESCRIPTION METADATA

— +


PDF

The Best (899 bp)

Other sequence editors that support SBOL:

DeviceEditor, J5, VectorEditor (JBEI), DNAPlotLib (MIT/UW/Bristol), Eugene (Boston), GenoCAD (VBI), BOOST (JGI), etc.

SEQUENCE EDITORS (BENCHLING)


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ACS Synthetic Biology
version currentACS
SyntheticBiology
PUBLIC

 **JBEI Public Registry**
version current



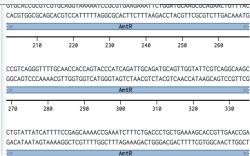
 **Benchling**
version current

Benchling collection of parts



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CIRCUIT GDA TOOLS (CELLO)

Cello

Verilog

Options

Results

About

You are logged in as **myers** [Logout](#)

Verilog

choose

```
1 module A(output out1, input in1, in2);
2   always@(in1,in2)
3   begin
4     case{(in1,in2)}
5       2'b00: {out1} = 1'b0;
6       2'b01: {out1} = 1'b0;
7       2'b10: {out1} = 1'b0;
8       2'b11: {out1} = 1'b1;
9     endcase
10    end
11  endmodule
12
```

design name

Run

Inputs

choose

clear

Index	name	low RPU	high RPU	DNA sequence
1	pTac	0.0034	2.8	AACGATCGTTGGCTGTGTTGACAA
2	pTet	0.0013	4.4	TACTCCACCGTTGGCTTTTTCCC

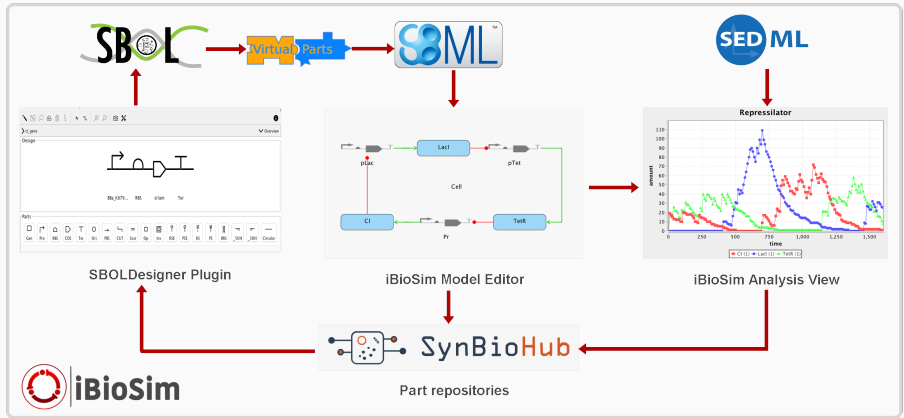
Outputs

choose

clear

Index	name	DNA sequence
1	YFP	CTGAAGCTGTACCGGATGTGCTTCCGGTCTGATGAGTCCGT

CIRCUIT GDA TOOLS (iBIOsim)

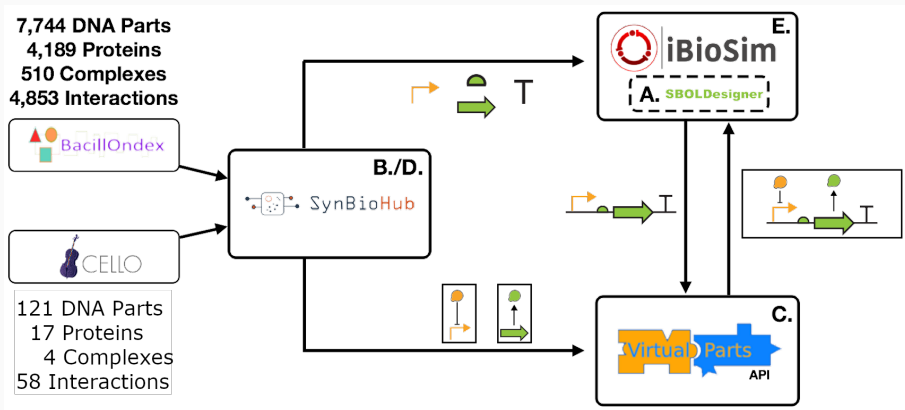


Myers et al., *Bioinformatics* (2009)

Madsen et al., *IEEE Design & Test* (2012)

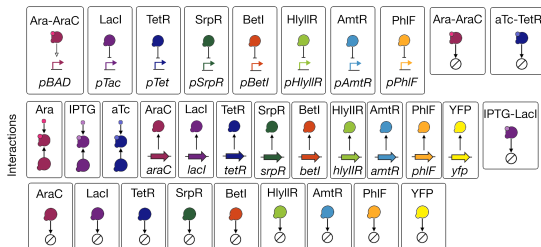
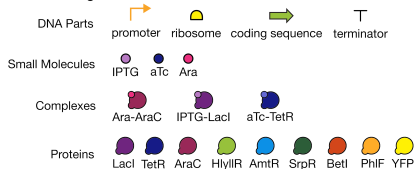
Watanabe et al., *ACS Synthetic Biology* (2018)

MODEL GENERATION WORKFLOW

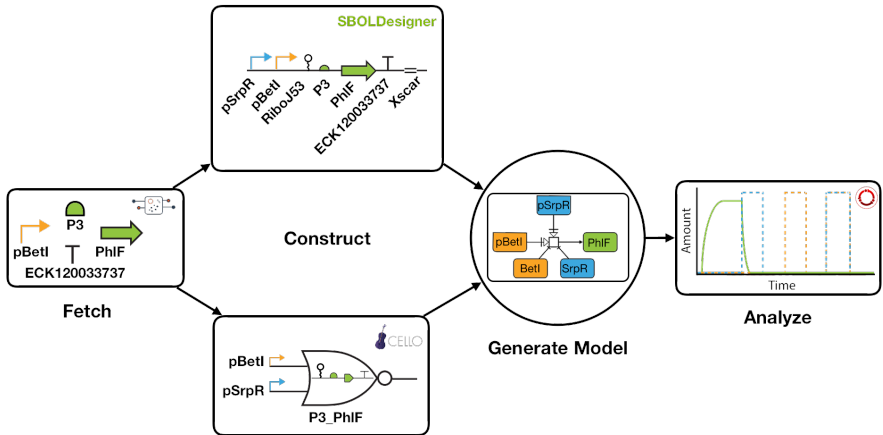


DATA INTEGRATION: CELLO PART LIBRARY

A. Data Integration

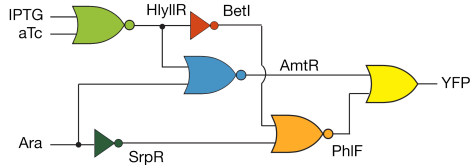


GENETIC CIRCUIT CONSTRUCTION

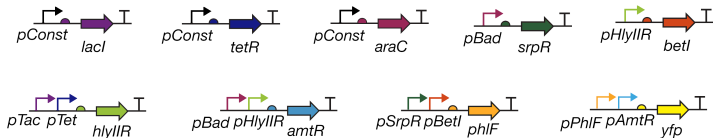


GENETIC CIRCUIT CONSTRUCTION: RULE 30 EXAMPLE

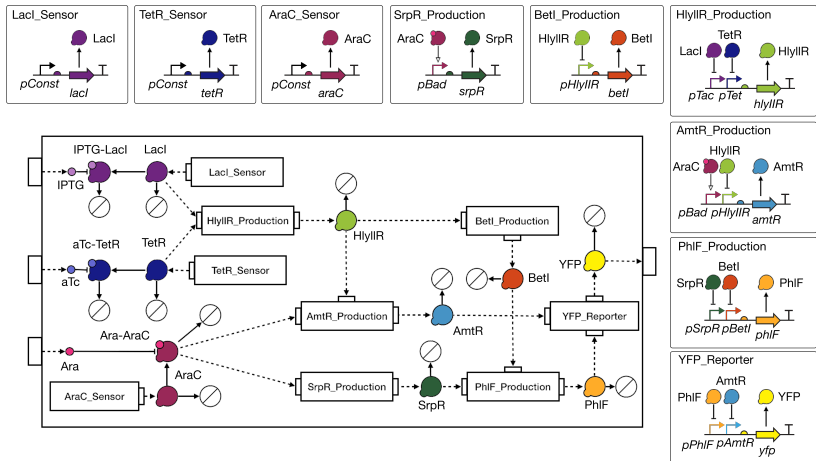
B. Rule 30



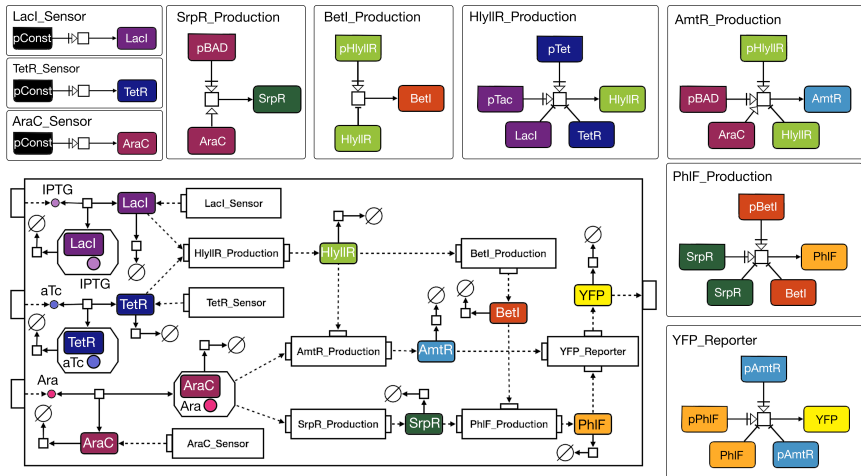
C. Genetic Circuit Construction



ENRICHED SBOL REPRESENTATION: RULE 30 EXAMPLE

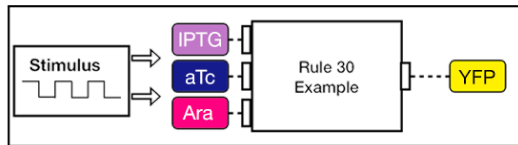


DYNAMIC SBML MODEL: RULE 30 EXAMPLE

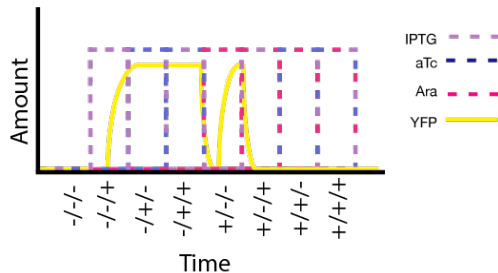


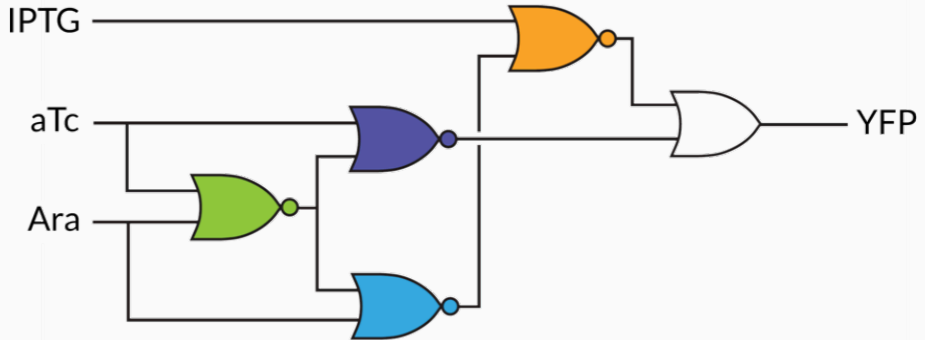
SIMULATION: RULE 30 EXAMPLE

A. Testing Environment

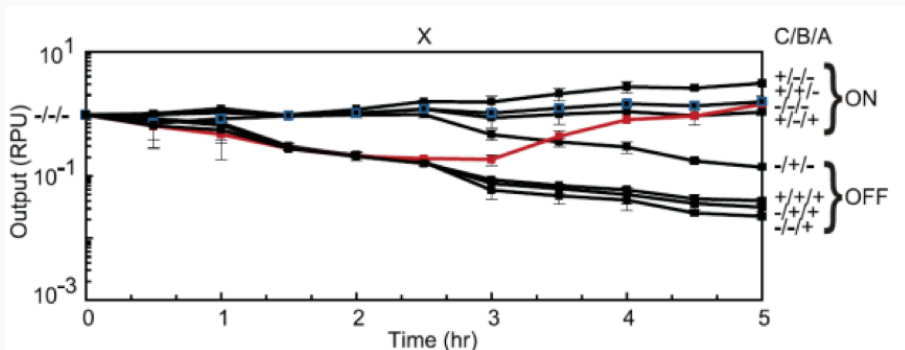


B. Simulation



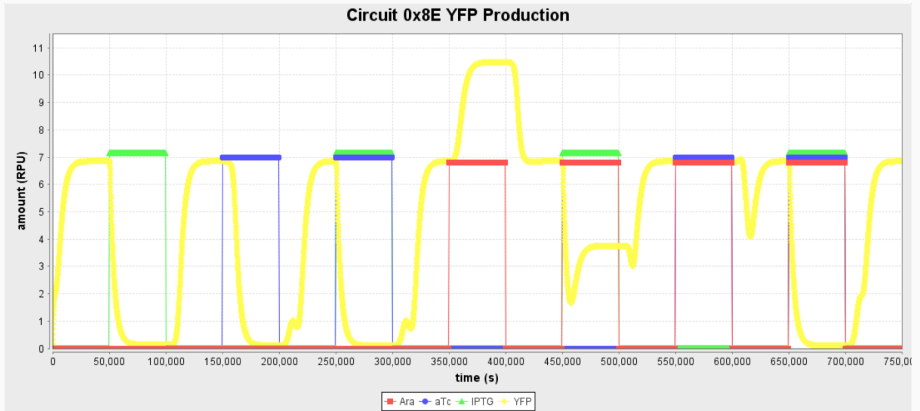
0x8E

CIRCUIT0X8E: EXPERIMENTAL RESULTS



Nielsen et al, *Science* (2016).

CIRCUIT0X8E: SIMULATION



Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, "Analyzing Genetic Circuits for Hazards and Glitches", in preparation for *ASC Synthetic Biology*.

CIRCUIT0x8E: LOGIC FUNCTION

Truth Table for circuit 0x8E:

Ara	IPTG	aTc	YFP
0	0	0	1
0	0	1	0
0	1	0	0
0	1	1	0
1	0	0	1
1	0	1	1
1	1	0	1
1	1	1	0

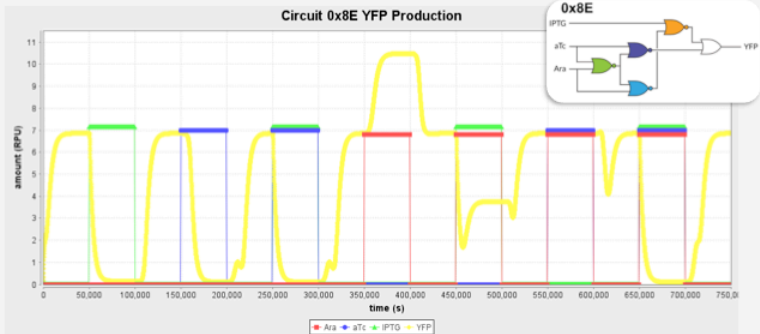
Karnaugh map for circuit 0x8E:

Ara \ IPTG aTc	0 0		0 1		1 1		1 0	
	0	1	0	1	0	1	0	1
0	1	0	0	0	0	0	0	0
1	1	1	1	0	0	1	1	0

Fontanarrosa, Hosseini, Borujeni, Dorfman, Voigt, and Myers, "Analyzing Genetic Circuits for Hazards and Glitches", in preparation for *ASC Synthetic Biology*.

CIRCUIT0x8E: HAZARD ANALYSIS

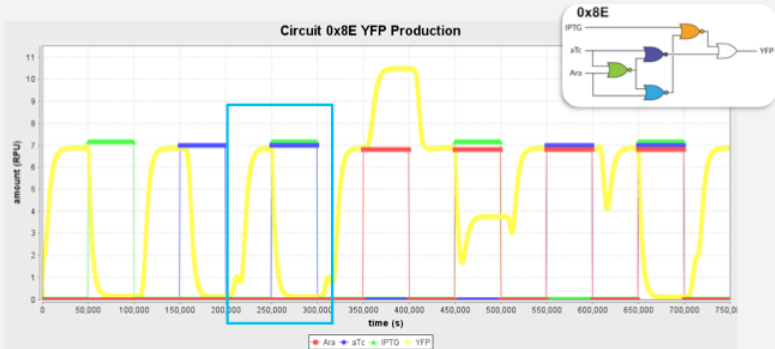
Ara \ IPTG aTc	0 0	0 1	1 1	1 0
0	1	0	0	0
1	1	1	0	1



Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0x8E: HAZARD ANALYSIS

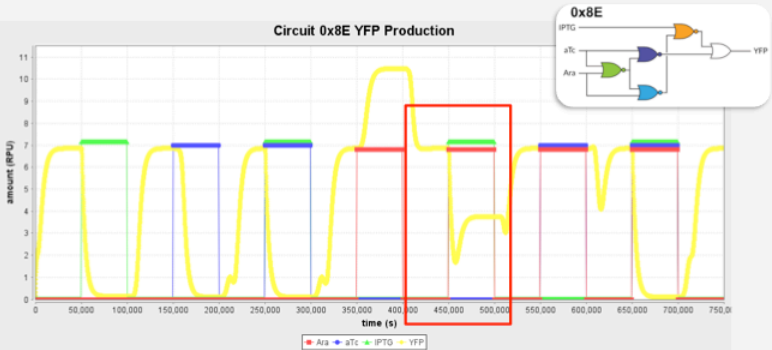
Ara \ IPTG aTc	00	01	11	10
0	1	0	0	0
1	1	1	0	1



Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0x8E: HAZARD ANALYSIS

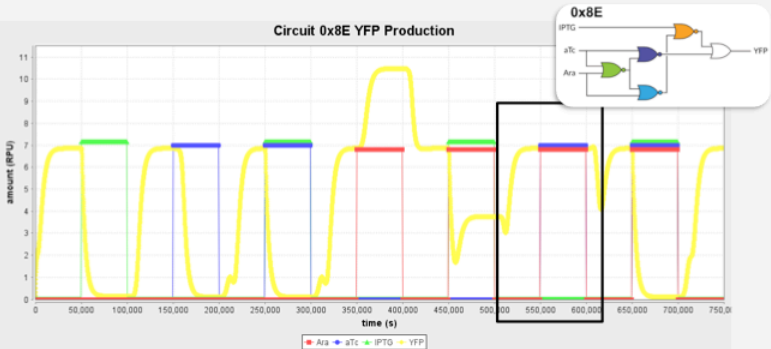
Ara	IPTG	aTc	00	01	11	10
0	1	0	1	0	0	0
1	0	1	1	1	0	1



Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0x8E: HAZARD ANALYSIS

Ara \ IPTG aTc	0 0	0 1	1 1	1 0
0	1	0	0	0
1	1	1	0	1



Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

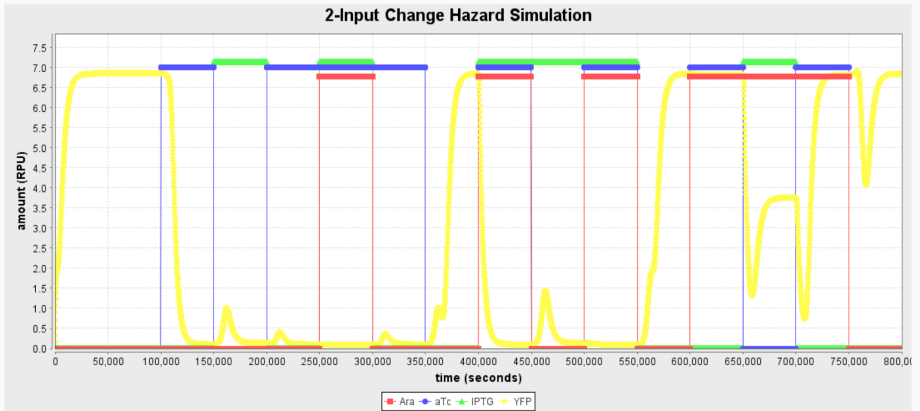
CIRCUIT0X8E: 2-INPUT FUNCTION HAZARDS

IPTG aTc Ara	00	01	11	10
	0	0	0	0
	1	1	0	1

2 input change hazards				
Case 1-2	IPTG	0	1	0
	aTc	1	1	1
	Ara	0	1	0
Case 3-4	IPTG	0	1	0
	aTc	1	0	1
	Ara	0	0	0
Case 5-6	IPTG	1	1	1
	aTc	1	0	1
	Ara	1	0	1
Case 7-8	IPTG	0	1	0
	aTc	1	0	1
	Ara	1	1	1

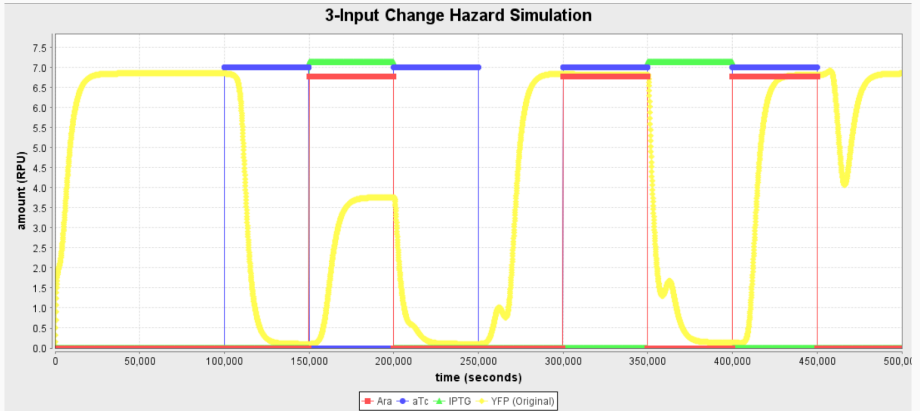
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: 2-INPUT FUNCTION HAZARDS



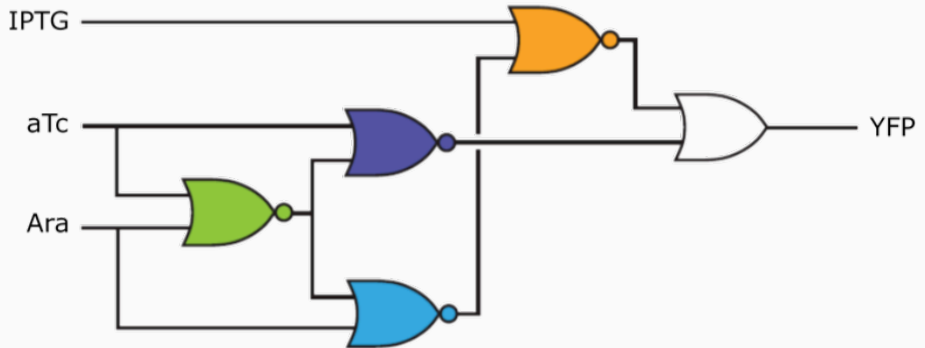
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: 3-INPUT FUNCTION HAZARDS



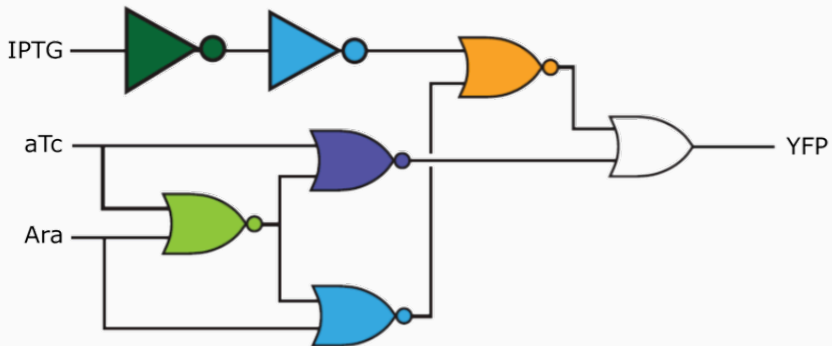
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: REDUNDANT LOGIC



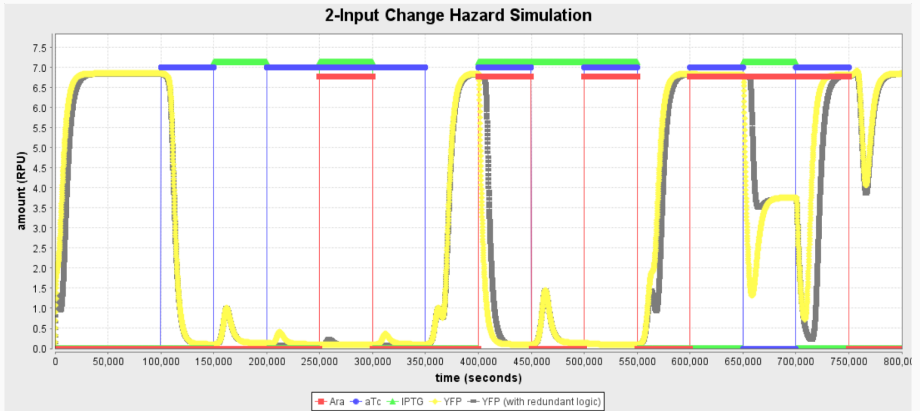
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, "Analyzing Genetic Circuits for Hazards and Glitches", in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: REDUNDANT LOGIC



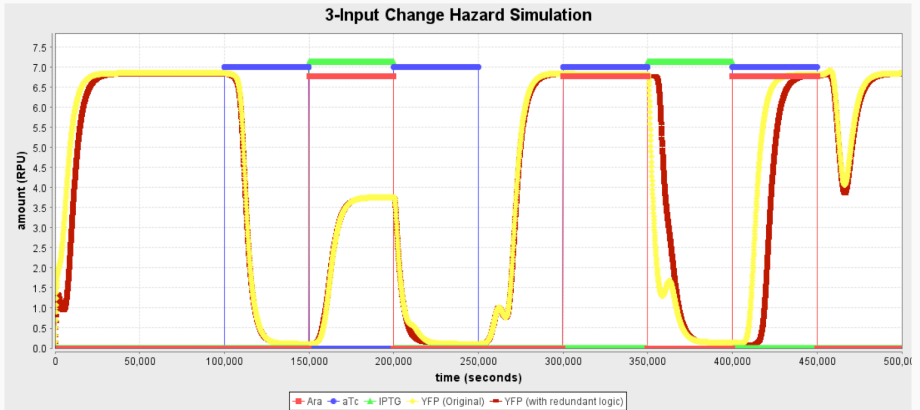
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, "Analyzing Genetic Circuits for Hazards and Glitches", in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: REDUNDANT LOGIC



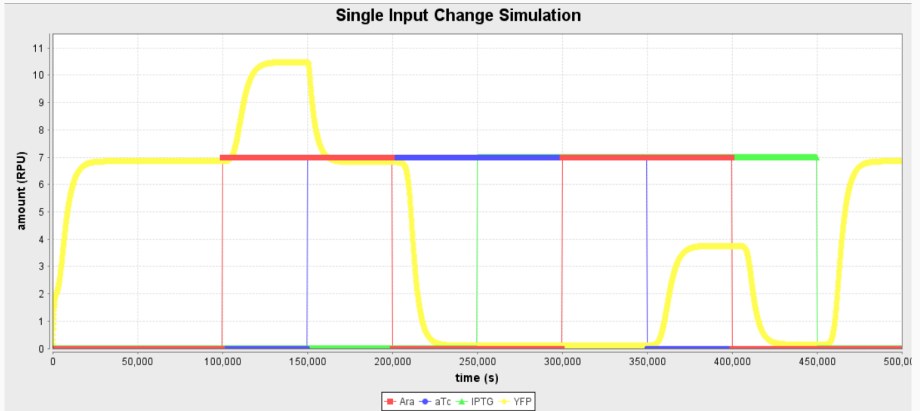
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: REDUNDANT LOGIC



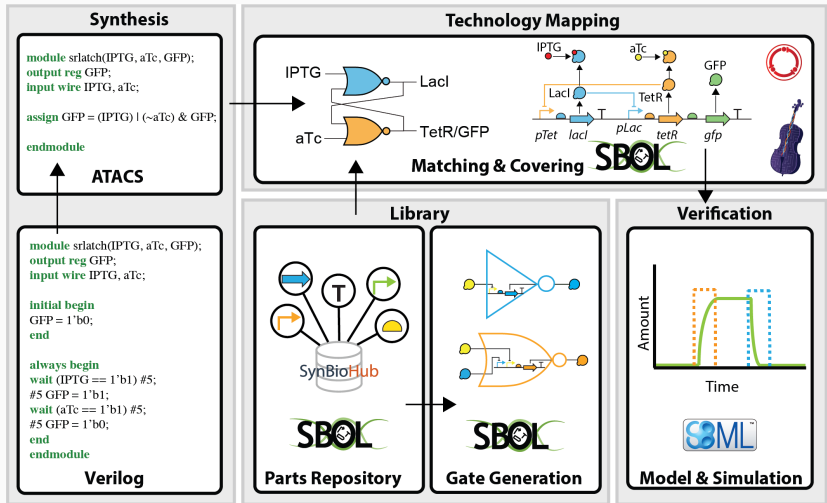
Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

CIRCUIT0X8E: GRAY CODE



Fontanarrosa, Hosseini, Borujeni, Dorfan, Voigt, and Myers, “Analyzing Genetic Circuits for Hazards and Glitches”, in preparation for *ASC Synthetic Biology*.

ASYNCHRONOUS GENETIC CIRCUIT DESIGN METHODOLOGY

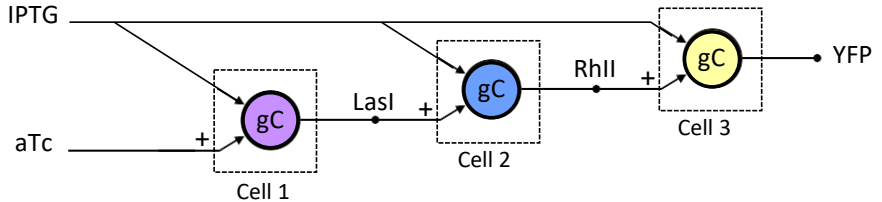


GENETIC SENSOR SPECIFICATION

```
module async_sensor(Start, Sensor, Actuator);  
    input wire Start, Sensor;  
    output reg Actuator;  
    initial begin  
        Actuator = 1'b0;  
    end  
    always begin  
        wait (Start == 1'b1 && Sensor == 1'b1);  
        #5 Actuator = 1'b1;  
        wait (Sensor == 1'b0);  
        #5 Actuator = 1'b0;  
    end  
endmodule
```

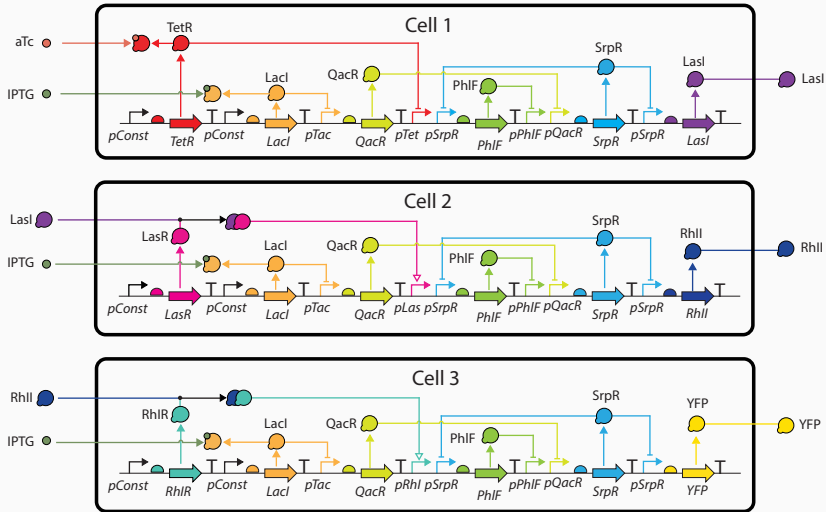
Nguyen, Jones, Vaidyanathan, Densmore, and Myers, “Design of Asynchronous Genetic Circuits”, in *Proceedings of the IEEE* (2019).

GENETIC SENSOR DESIGN



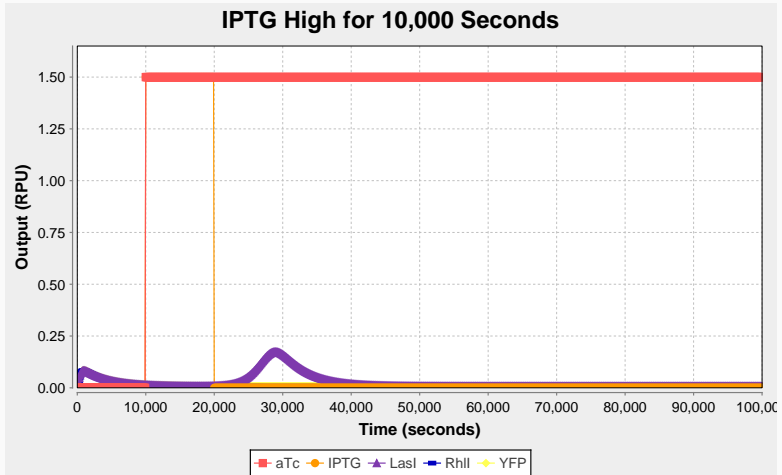
Nguyen, Jones, Vaidyanathan, Densmore, and Myers, "Design of Asynchronous Genetic Circuits", in *Proceedings of the IEEE* (2019).

GENETIC SENSOR DESIGN



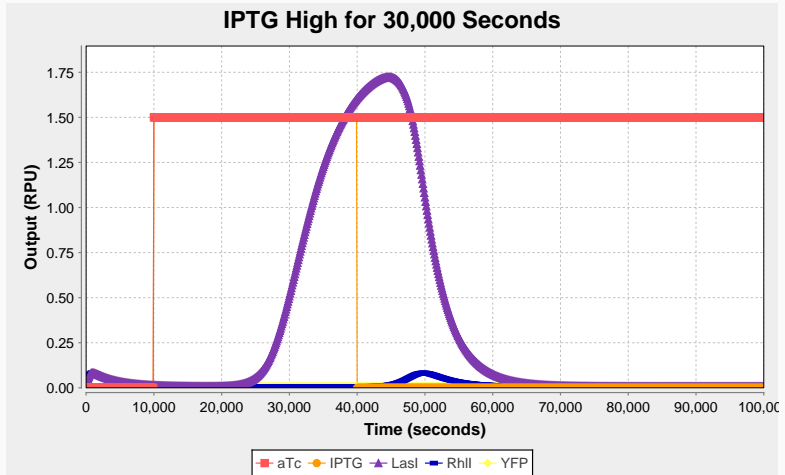
Nguyen, Jones, Vaidyanathan, Densmore, and Myers, "Design of Asynchronous Genetic Circuits", in *Proceedings of the IEEE* (2019).

GENETIC SENSOR SIMULATION



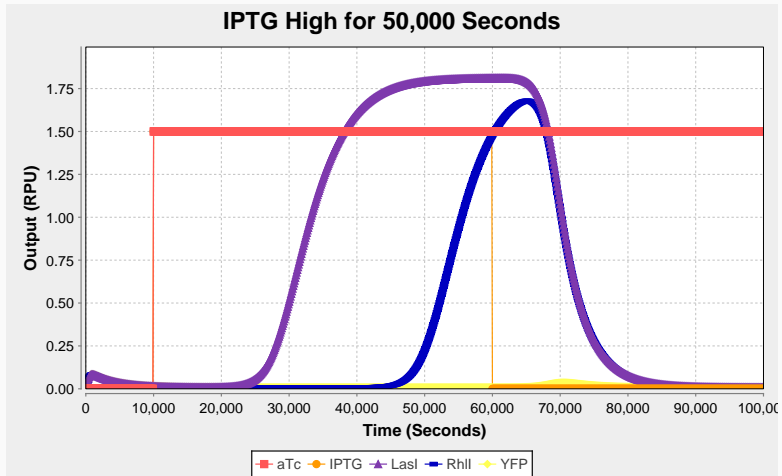
Nguyen, Jones, Vaidyanathan, Densmore, and Myers, "Design of Asynchronous Genetic Circuits", in *Proceedings of the IEEE* (2019).

GENETIC SENSOR SIMULATION



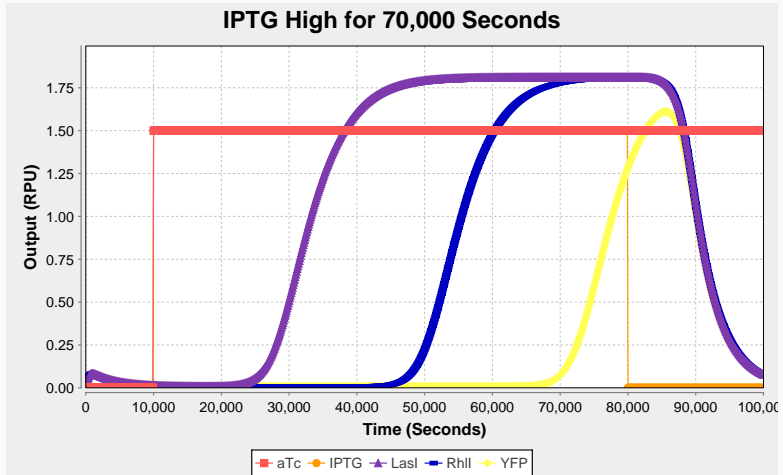
Nguyen, Jones, Vaidyanathan, Densmore, and Myers, "Design of Asynchronous Genetic Circuits", in *Proceedings of the IEEE* (2019).

GENETIC SENSOR SIMULATION

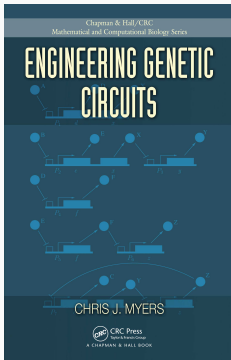


Nguyen, Jones, Vaidyanathan, Densmore, and Myers, "Design of Asynchronous Genetic Circuits", in *Proceedings of the IEEE* (2019).

GENETIC SENSOR SIMULATION



Nguyen, Jones, Vaidyanathan, Densmore, and Myers, "Design of Asynchronous Genetic Circuits", in *Proceedings of the IEEE* (2019).



Textbook

- ECE/CS/BioEn 6760
Offered in Fall 2020
- Our research work:
<http://www.async.ece.utah.edu>
- SBOL standard:
<http://sbolstandard.org>
Checkout our Youtube channel for demos
- SynBioHub Repository:
<https://synbiohub.org>



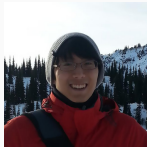
Adam Arkin

Since the engineering principles by which such circuitry is constructed in cells comprise a super-set of that used in electrical engineering, it is, in turn, possible that we will learn more about how to design asynchronous, robust electronic circuitry as well.

ACKNOWLEDGEMENTS (UNIVERSITY OF WASHINGTON)



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Kiri Choi



Dr. Herbert Sauro

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(Now with Keele University)



Dr Angel Goni-Moreno



Prof. Anil Wipat

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(Now with BBN/Raytheon)



Prashant Vaidyanathan



Prof. Douglas Densmore

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(University of Bristol)



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(KAUST)



Dr. Ernst Oberortner
(Joint Genome Institute)

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Nathan Barker (SUU/Chair CS)



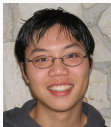
Scott Glass (BS/CE)



Hiroyuki Kuwahara (KAUST)



Curtis Madsen (Sandia)



Nam Nguyen (UCSD/Postdoc)



Tyler Patterson (BS/CE)



Nicholas Roehner (BBN/Raytheon)



Meher Samineni (Amazon)



Jason Stevens (UWash/PhD)



Leandro Watanabe (Google)



Michael Zhang (Google)



Zhen Zhang (Utah State U.)



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Tramy Nguyen (PhD/ECE)



James Scholz (BS/CS)



Zach Zundel (BS/CS/BioEn)



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