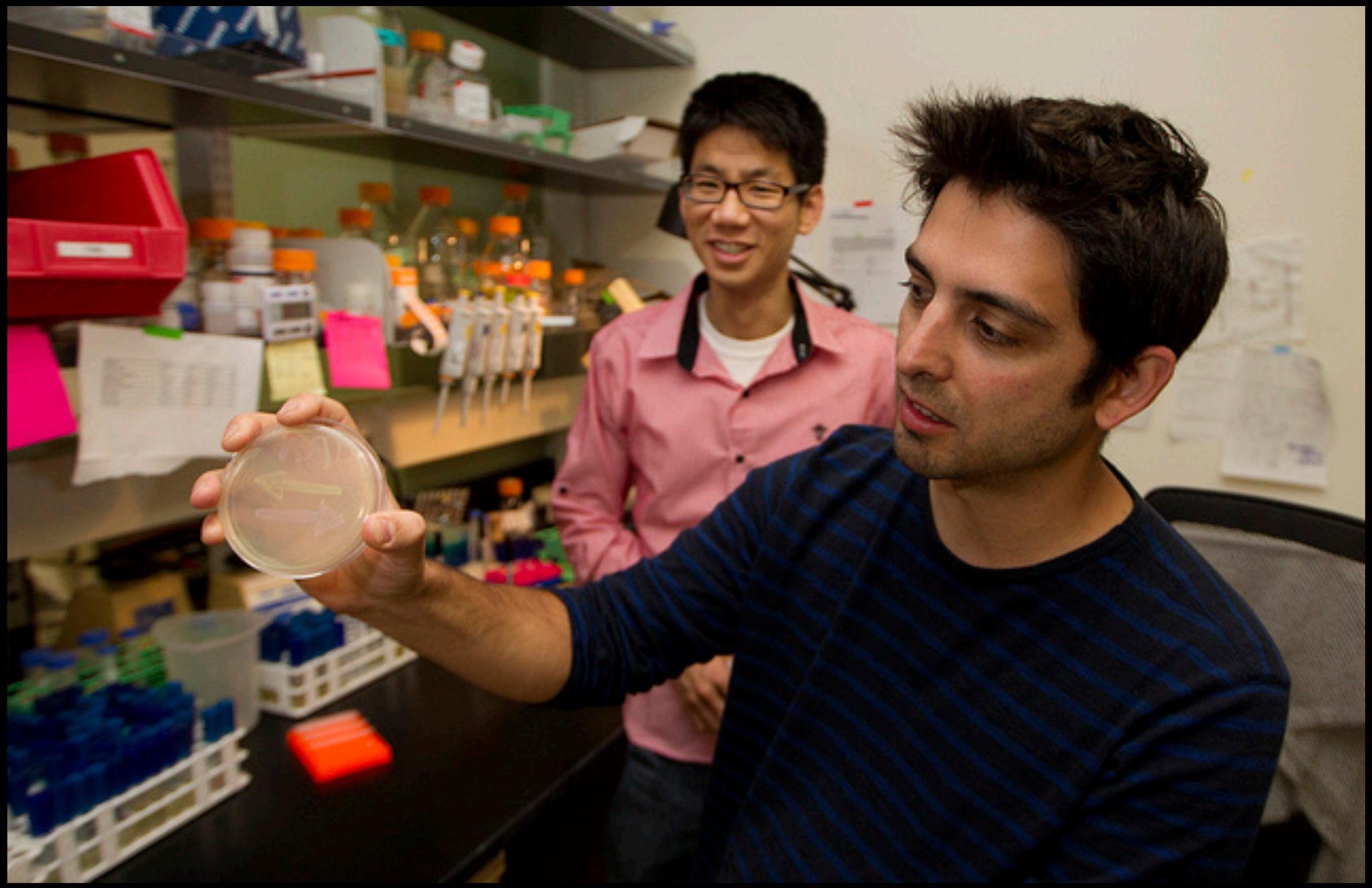
Integrases, Aliens, & Bill Joy

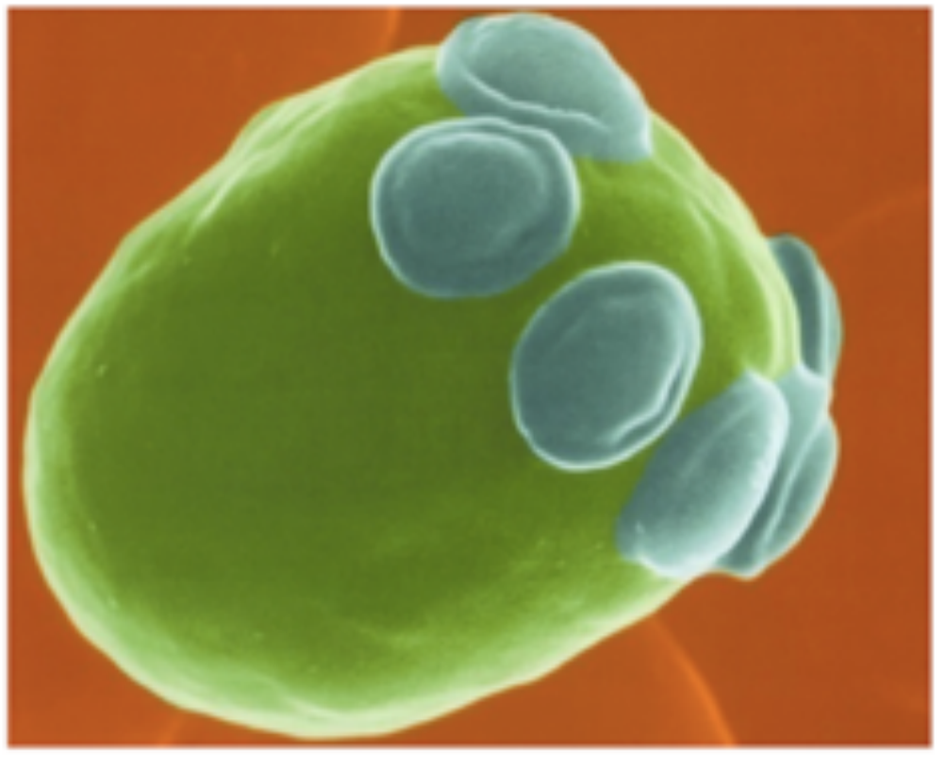
Drew Endy
Stanford Bioengineering
The BioBricks Foundation

24 September 2012
SBWG Cambridge MA



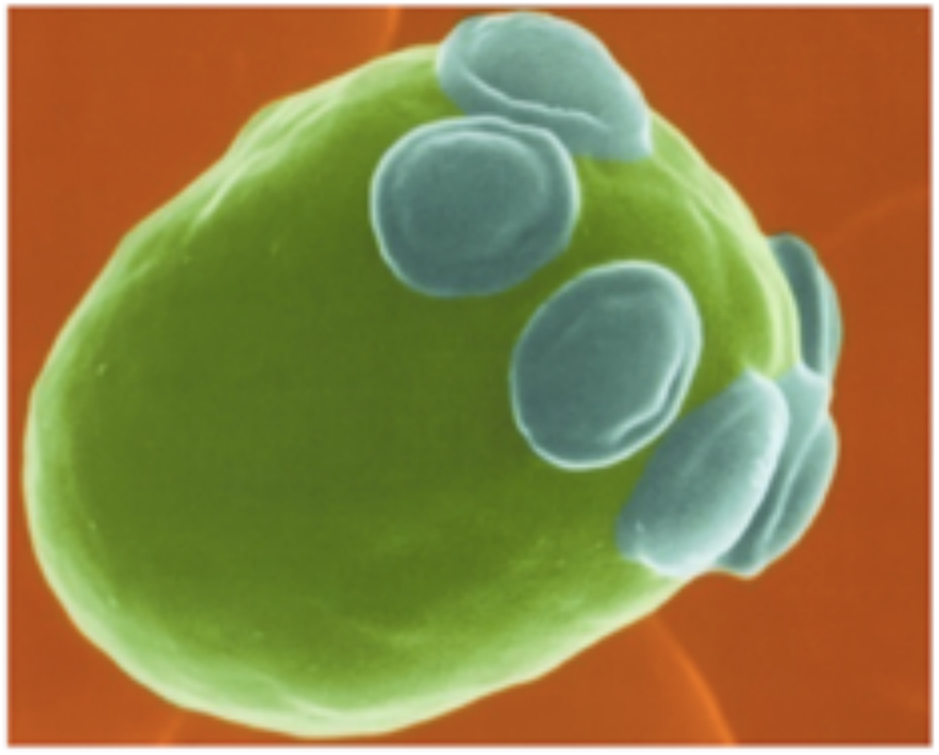
Ton & Jerome want 8 bio. bits

Aging

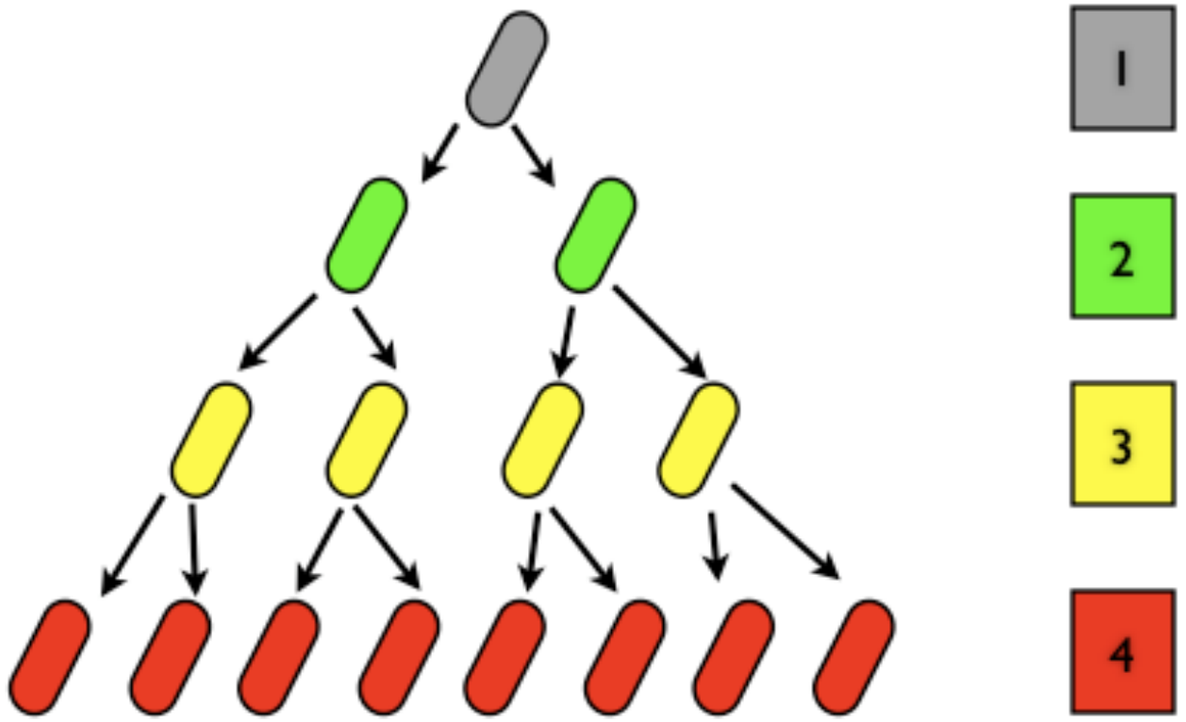


Anna Cosney and John Forsdyke

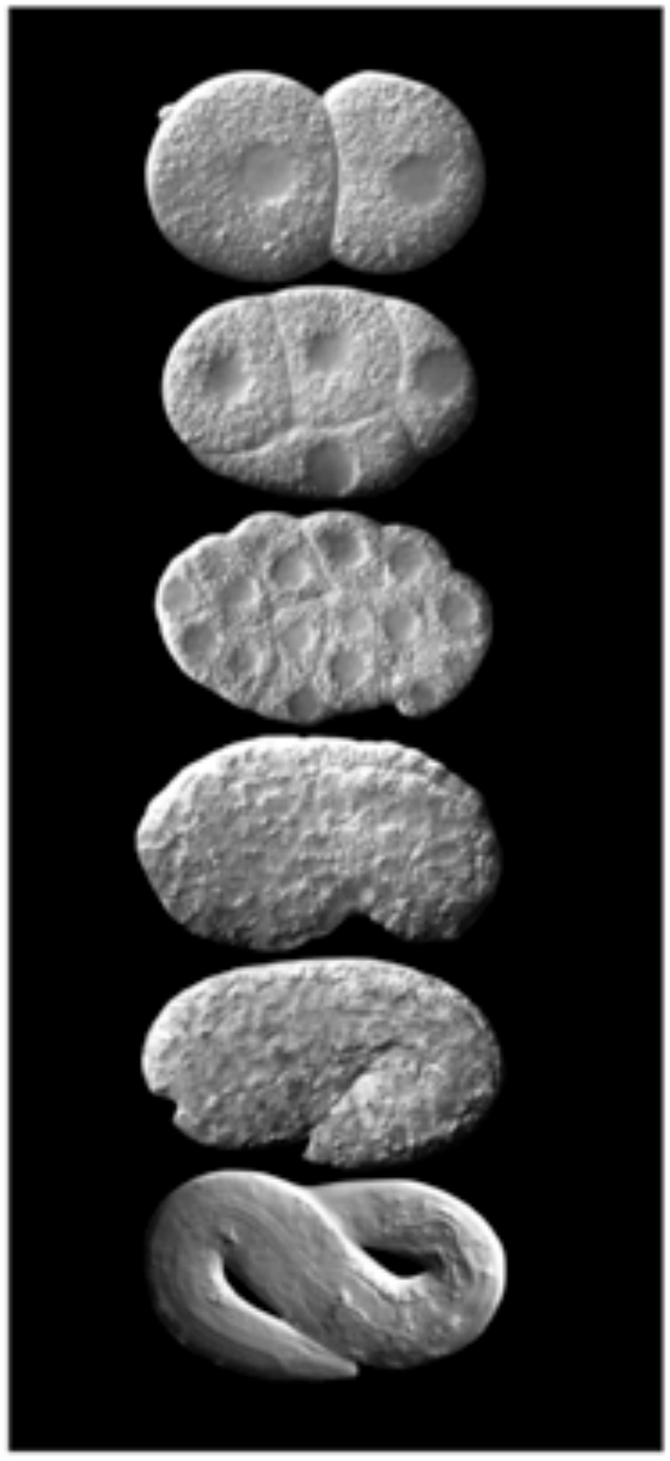
Aging



Anna Cosney and John Forsdyke

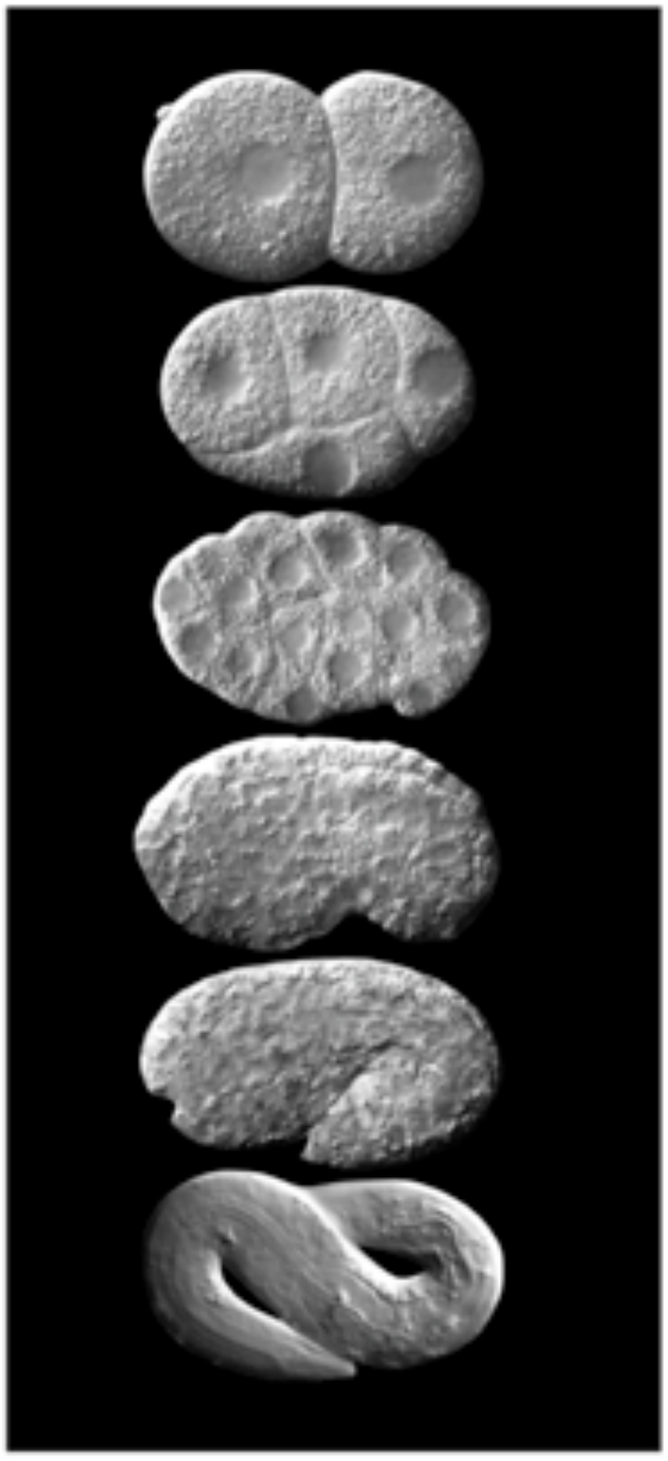


Development

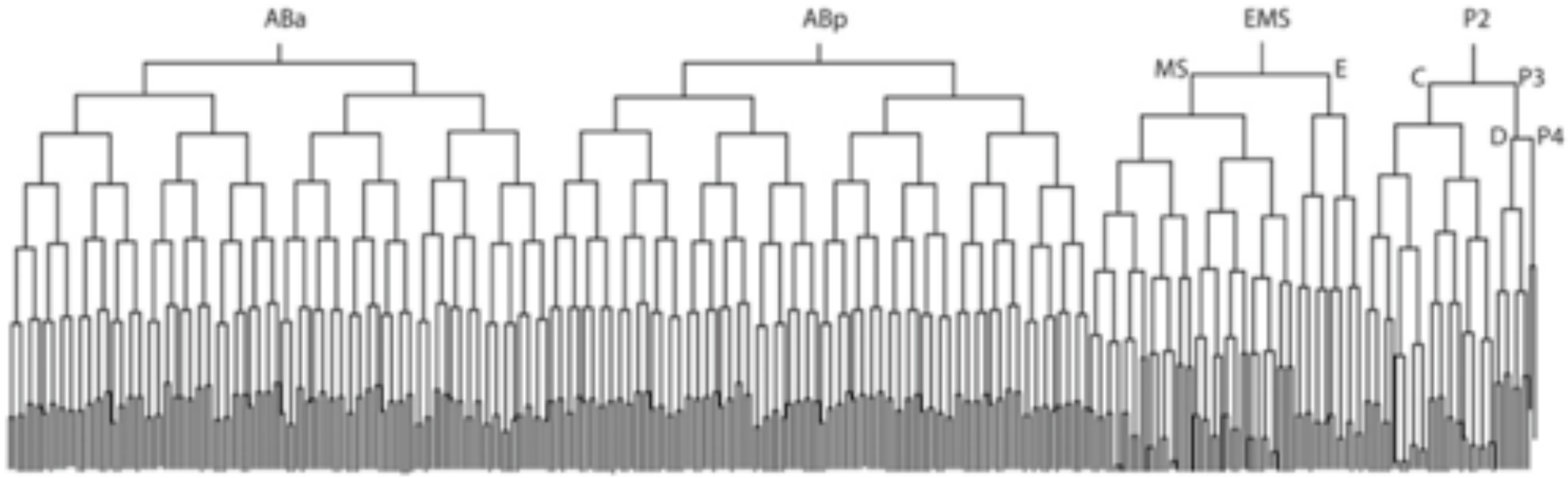


Bruce W. Draper.

Development



Bruce W. Draper.



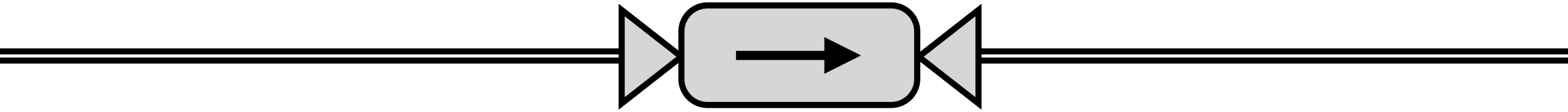
http://waterston.gs.washington.edu/lineaging.htm

But really we are working on this type of stuff because it challenges us to get better at...

(i) composition of molecular parts
(ii) reliability of performance ("noise", evolution)

BONNET et al., PNAS May 2012

***please see Nash & Pollock (1981, 1983) thru Friedland & Lu et al. (2010+) for prior work on flipping DNA and data storage*



“flipee”

BONNET et al., PNAS May 2012

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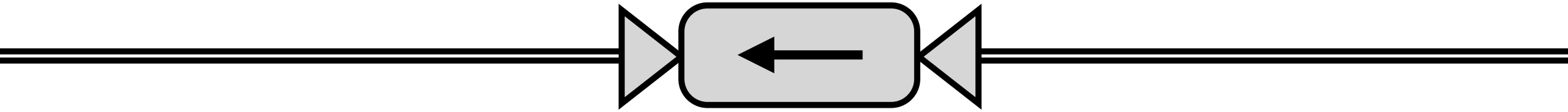

“flipee”

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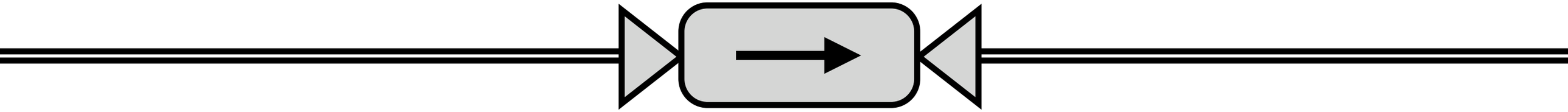

“flipee”

BONNET et al., PNAS May 2012

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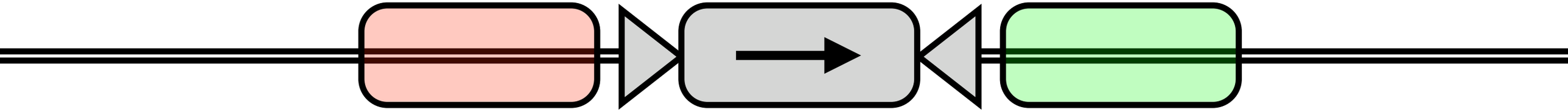
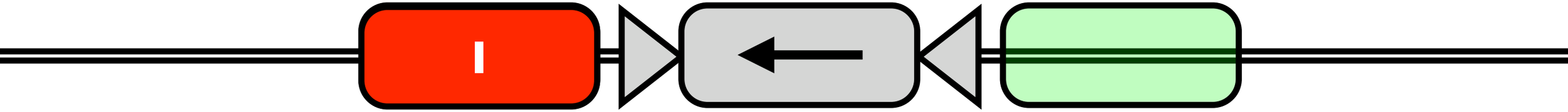


"flipee"

BONNET et al., PNAS May 2012

***please see Nash & Pollock (1981, 1983) thru Friedland & Lu et al. (2010+) for prior work on flipping DNA and data storage*



"flipee"

BONNET et al., PNAS May 2012

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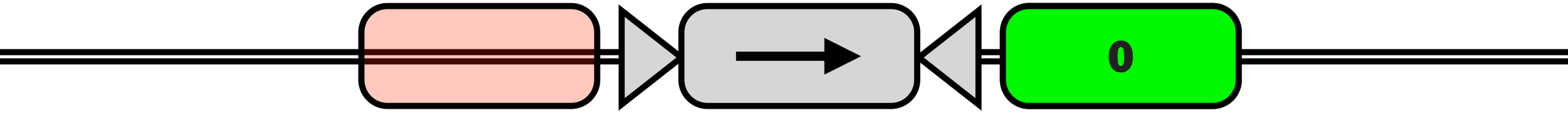

“flipee”

BONNET et al., PNAS May 2012

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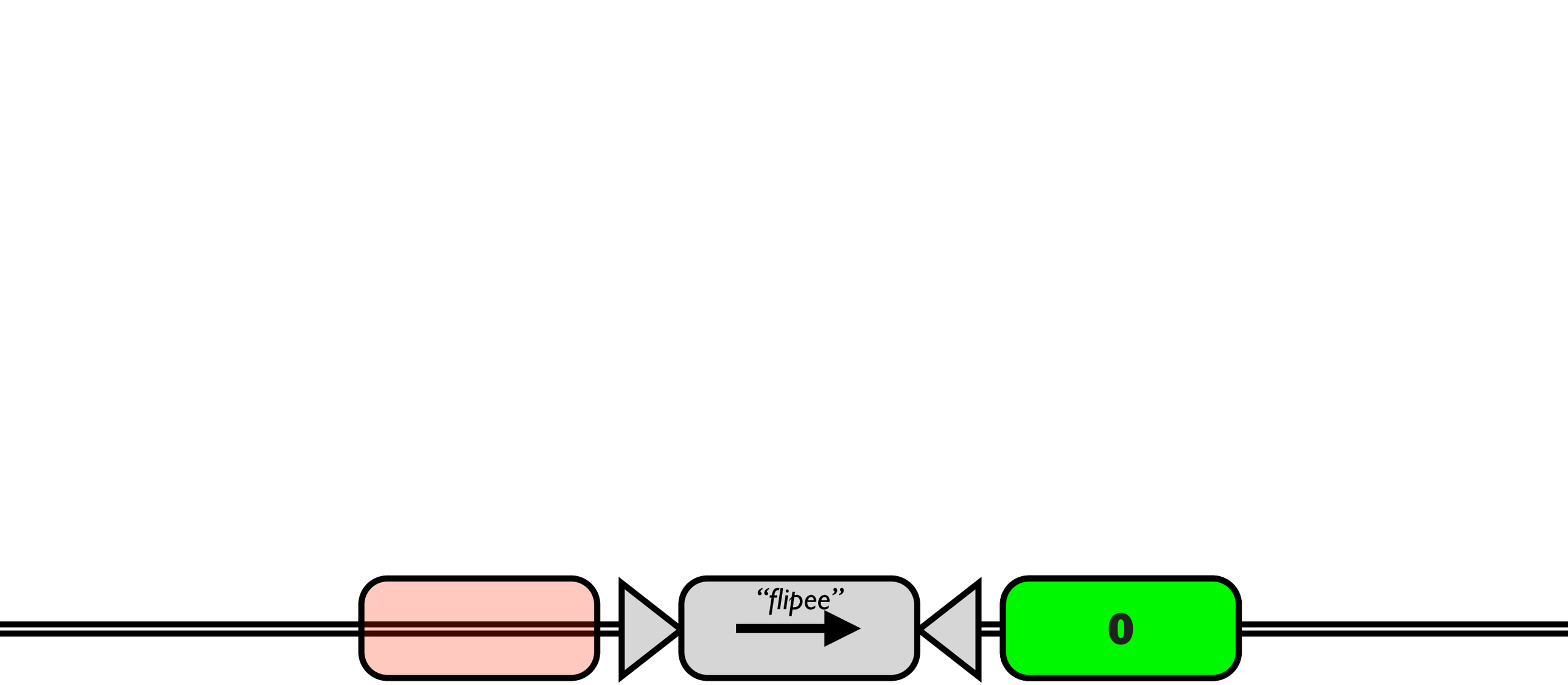

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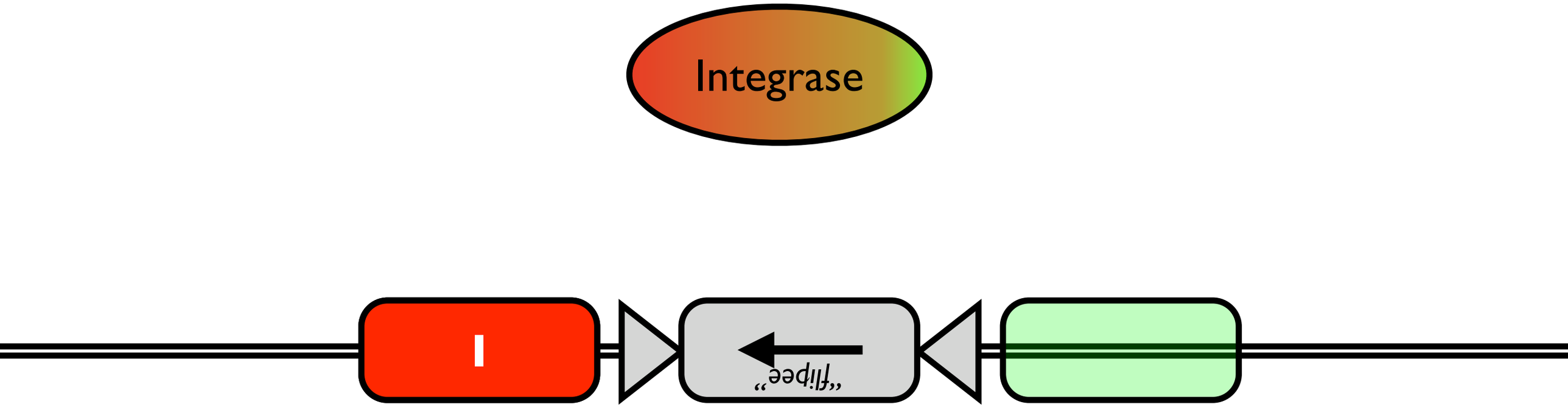

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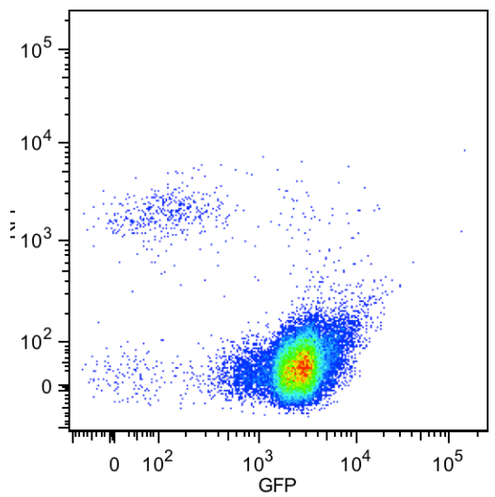
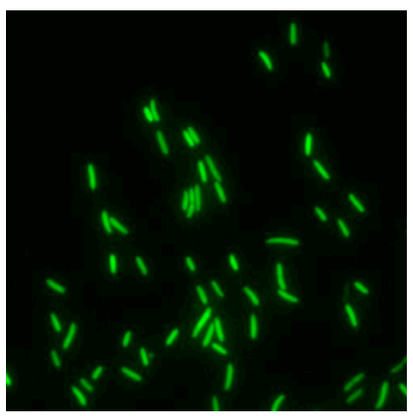
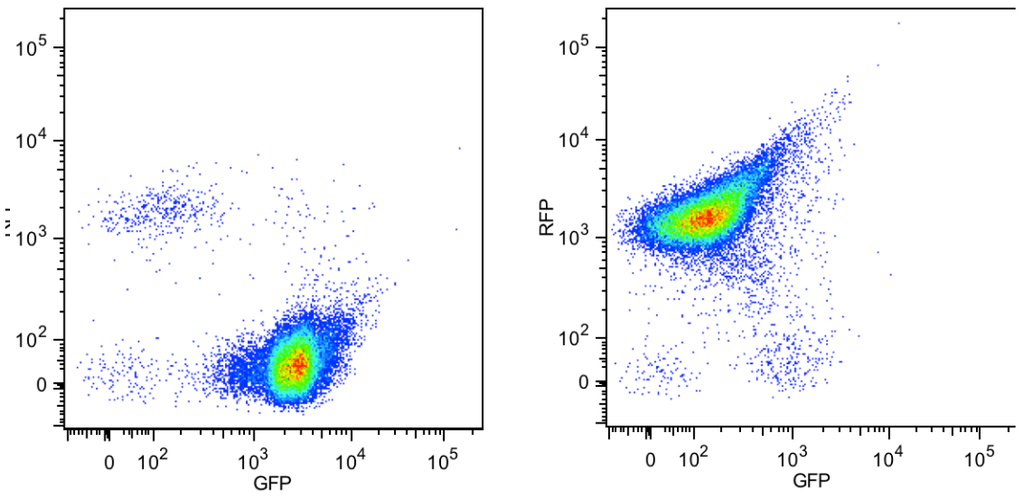
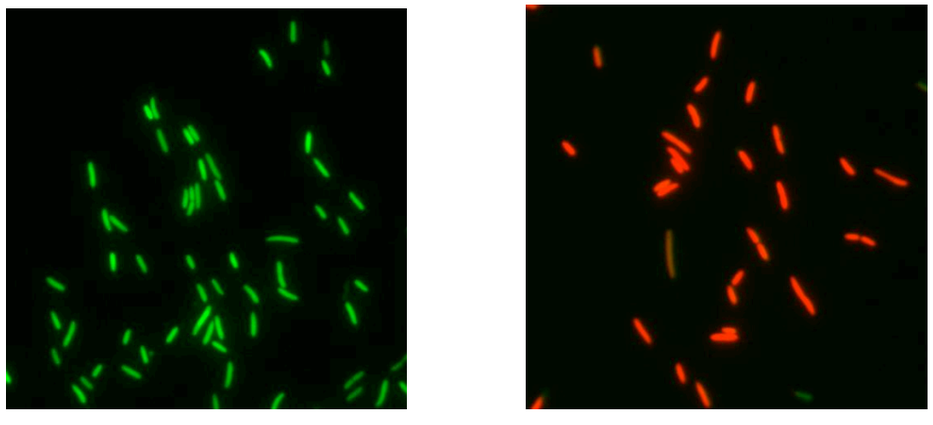


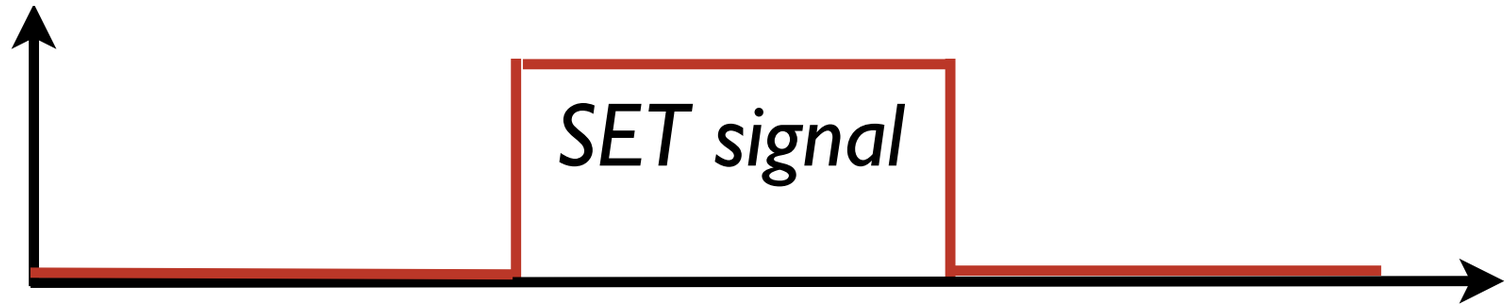


Pre "O"

Switch







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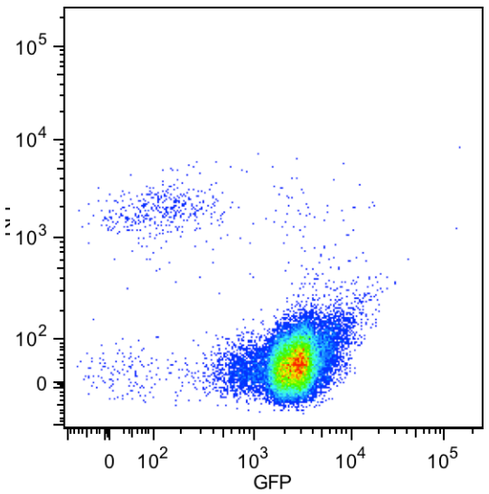

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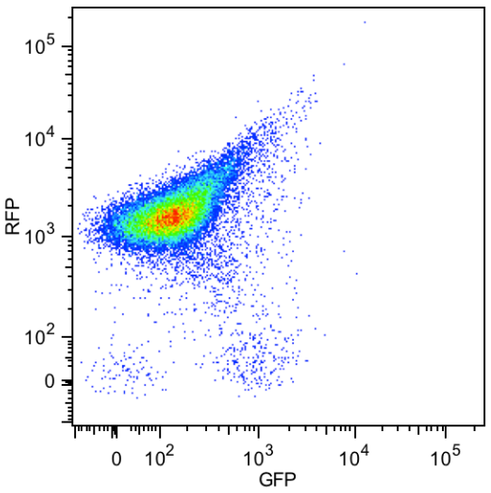

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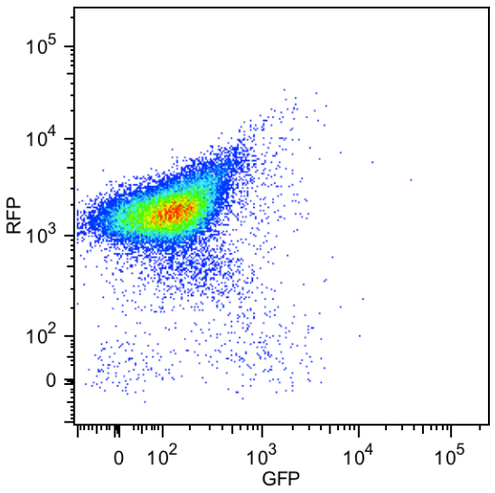
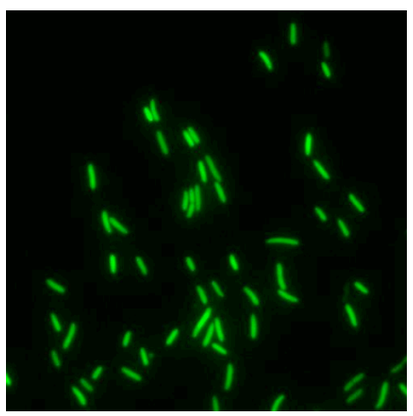
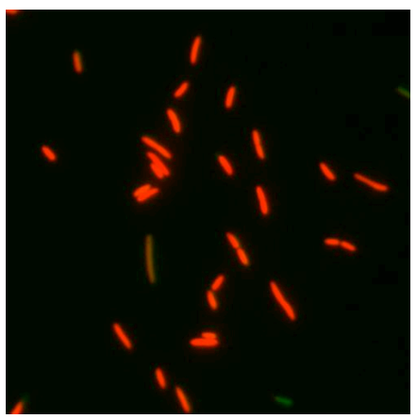
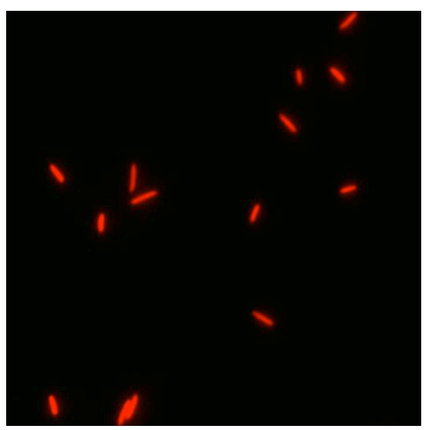
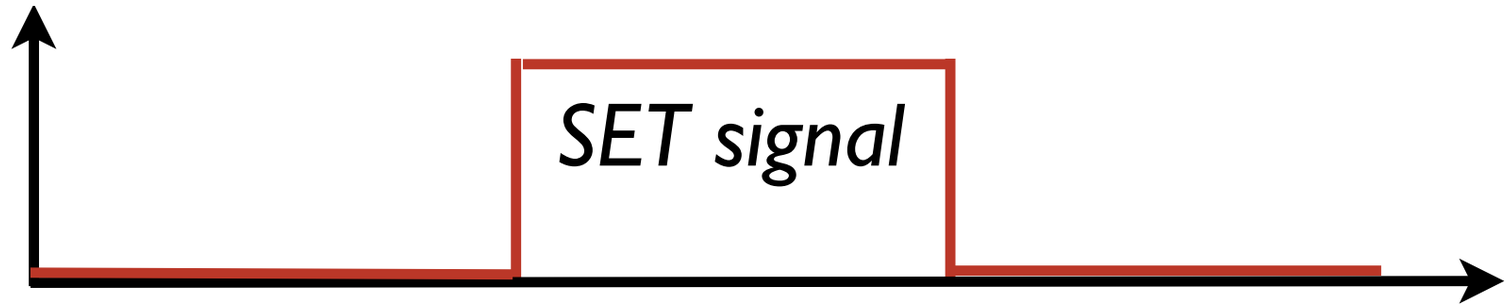








We can write one "memory"



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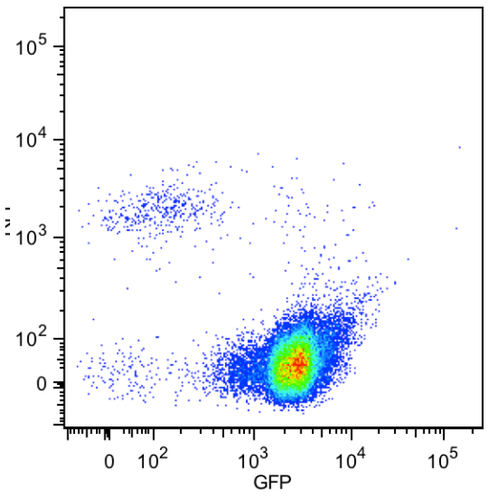

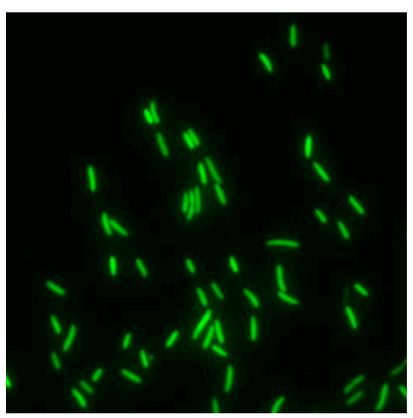

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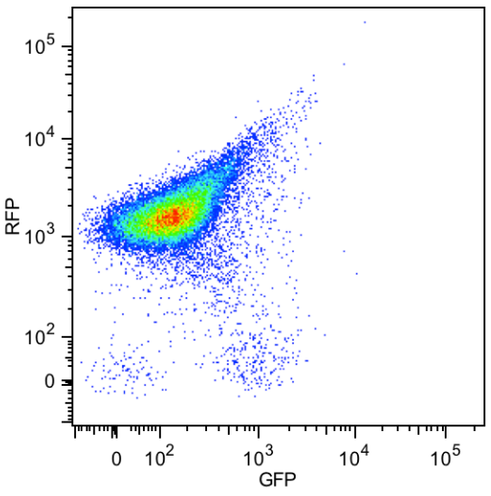

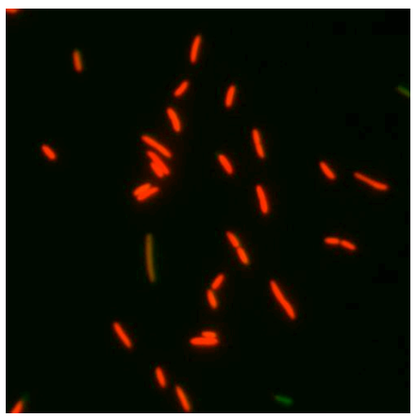

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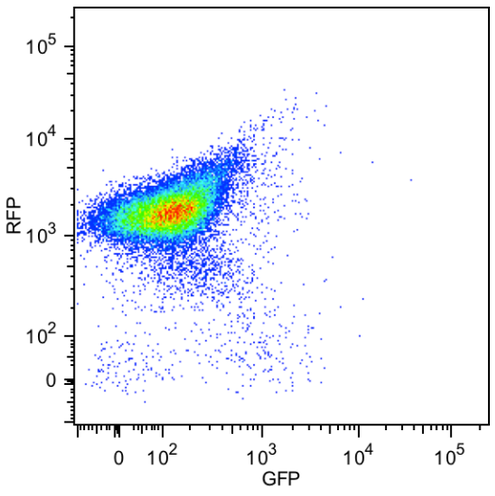
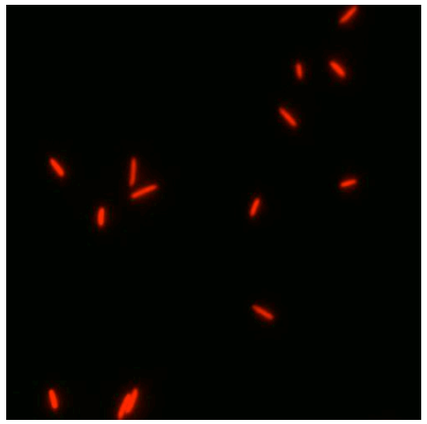
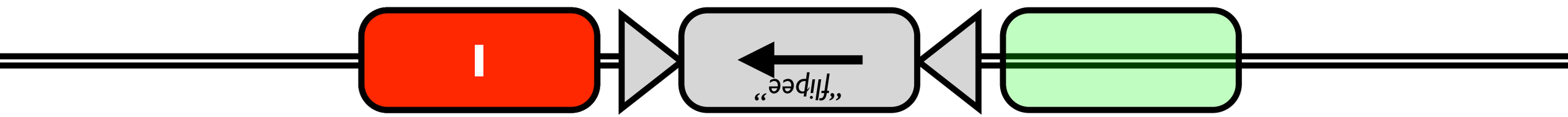
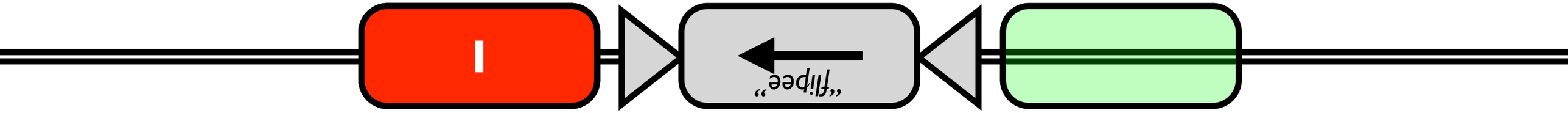
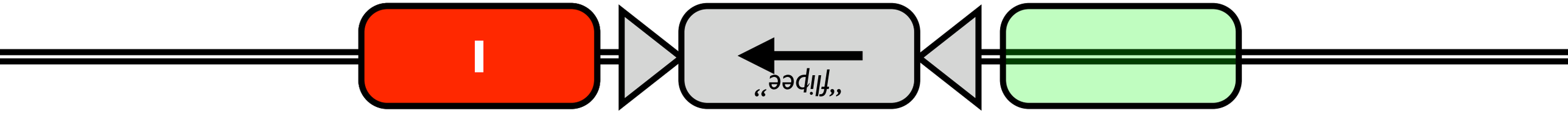


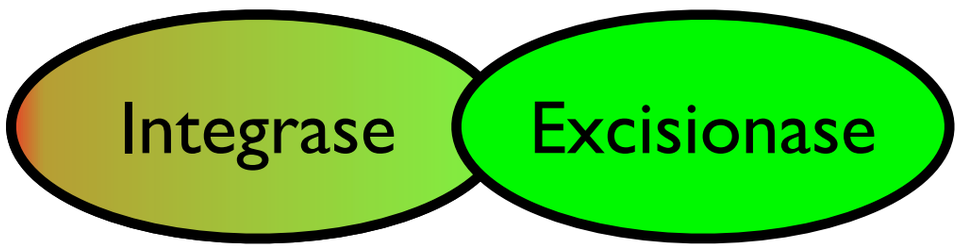






Integrase





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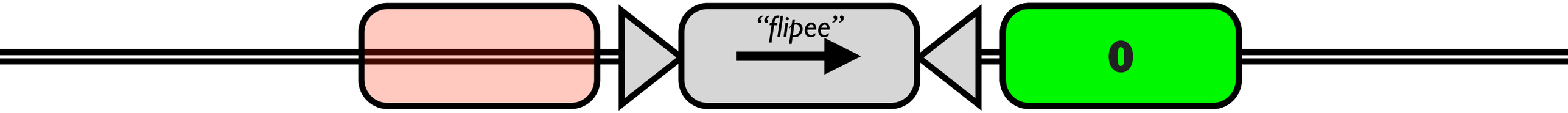

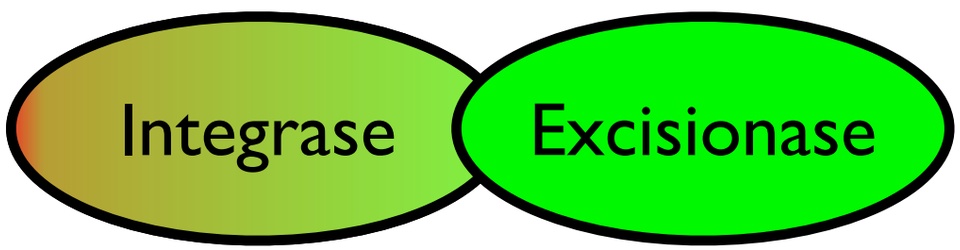

RESET "flipper"

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Control of Phage Bxb1 Excision by a Novel Recombination Directionality Factor

Pallavi Ghosh, Laura R. Wasil, Graham F. Hatfull*

Pittsburgh Bacteriophage Institute and Department of Biological Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America

Mycobacteriophage Bxb1 integrates its DNA at the *attB* site of the *Mycobacterium smegmatis* genome using the viral *attP* site and a phage-encoded integrase generating the recombinant junctions *attL* and *attR*. The Bxb1 integrase is a member of the serine recombinase family of site-specific recombination proteins and utilizes small (<50 base pair) substrates for recombination, promoting strand exchange without the necessity for complex higher order macromolecular architectures. To elucidate the regulatory mechanism for the integration and excision reactions, we have identified a Bxb1-encoded recombination directionality factor (RDF), the product of gene *47*. Bxb1 gp47 is an unusual RDF in that it is relatively large (~28 kDa), unrelated to all other RDFs, and presumably performs dual functions since it is well conserved in mycobacteriophages that utilize unrelated integration systems. Furthermore, unlike other RDFs, Bxb1 gp47 does not bind DNA and functions solely through direct interaction with integrase–DNA complexes. The nature and consequences of this interaction depend on the specific DNA substrate to which integrase is bound, generating electrophoretically stable tertiary complexes with either *attB* or *attP* that are unable to undergo integrative recombination, and weakly bound, electrophoretically unstable complexes with either *attL* or *attR* that gain full potential for excisive recombination.

Citation: Ghosh P, Wasil LR, Hatfull GF (2006) Control of phage Bxb1 excision by a novel recombination directionality factor. PLoS Biol 4(6): e186. DOI: 10.1371/journal.pbio.0040186

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Pittsburgh Bacteriophage Institute and Department of Biological Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America

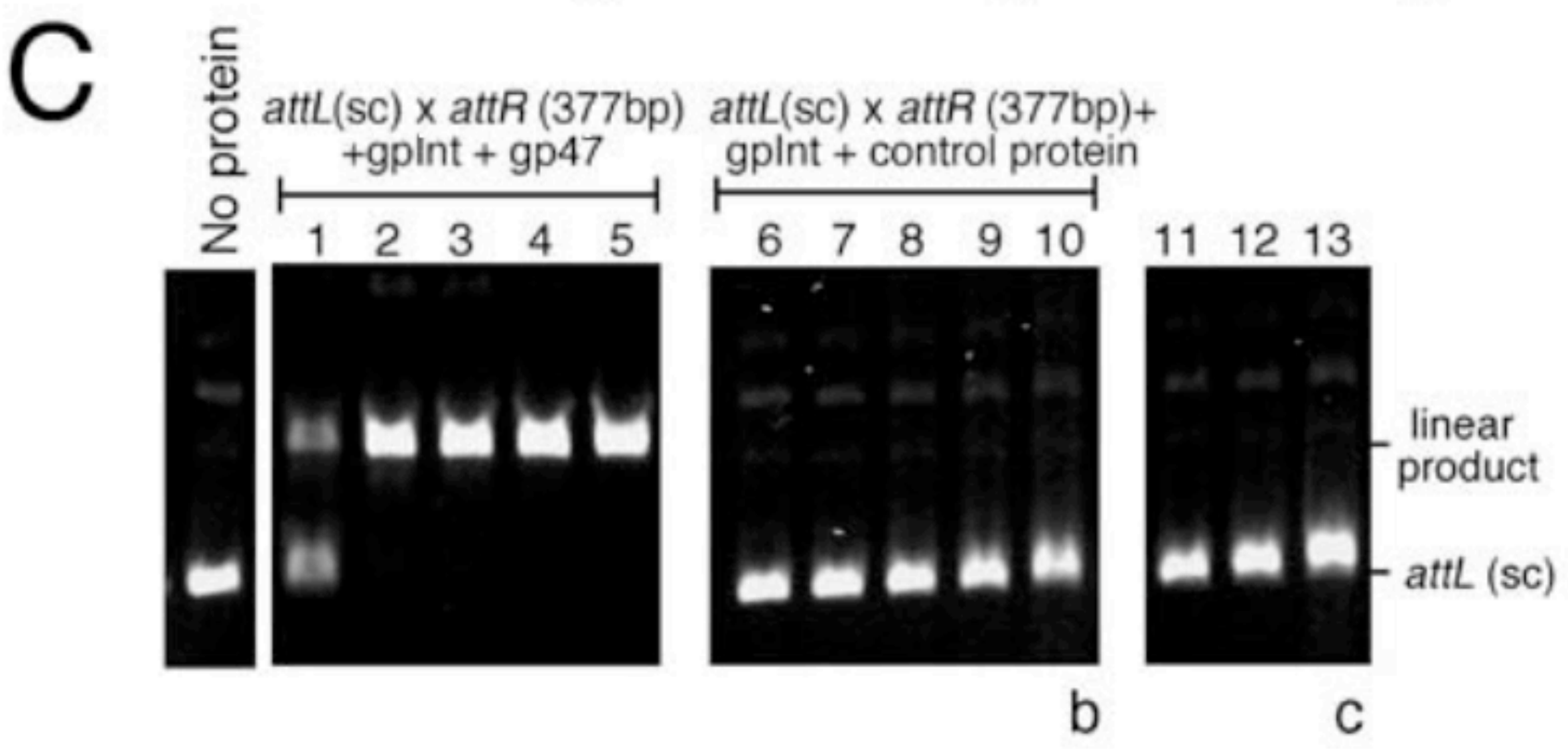

Figure 5. In Vitro Excisive Recombination Using gp47

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Control of Phage Bxb1 Excision by a Novel Recombination Directionality Factor

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Pittsburgh Bacteriophage Institute and Department of Biological Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America

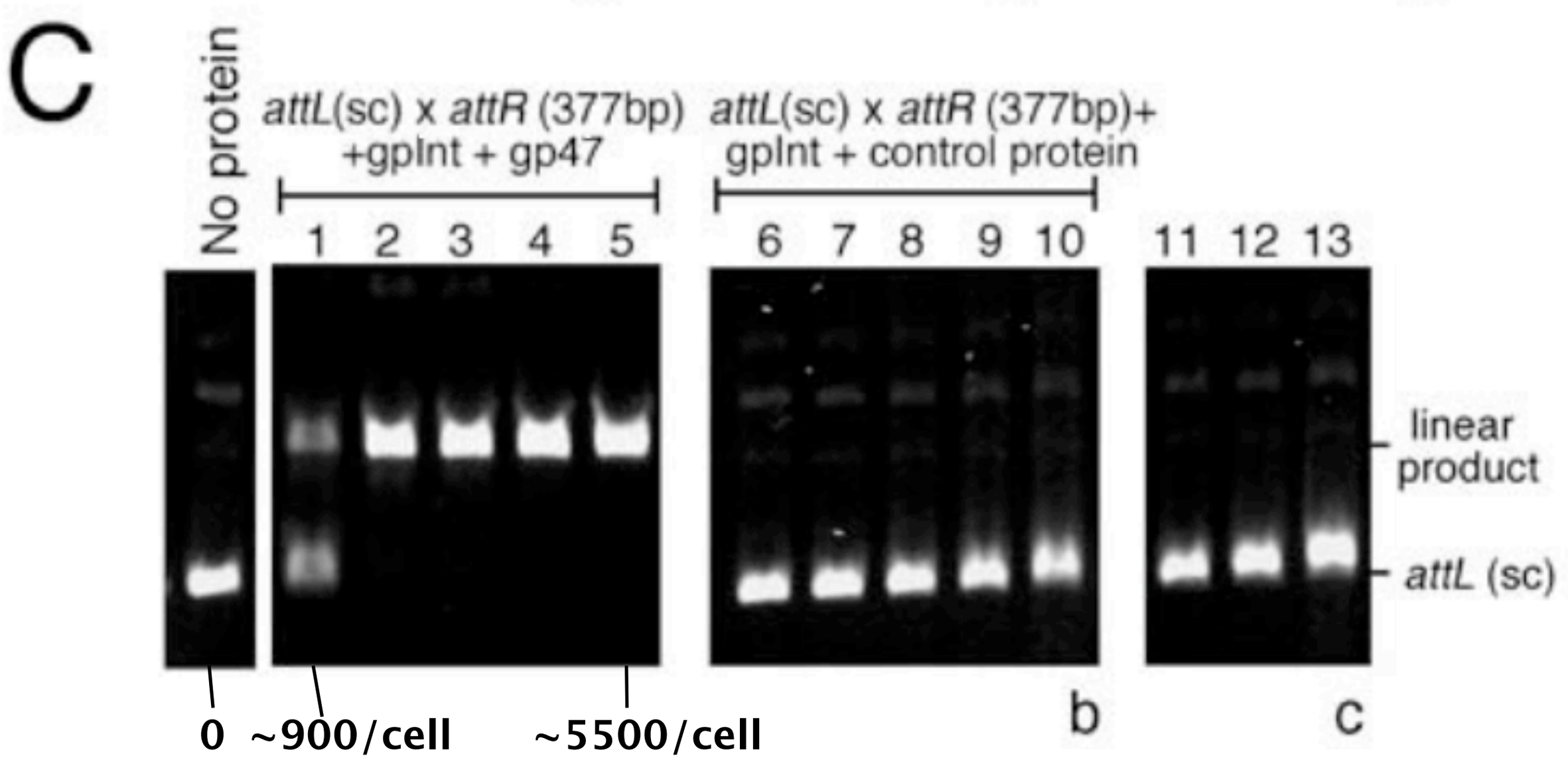
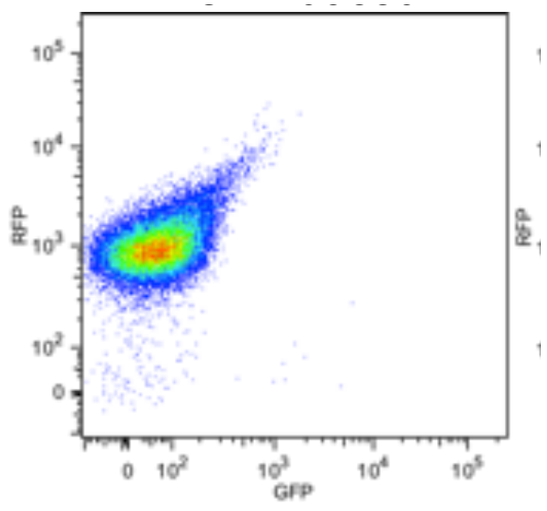
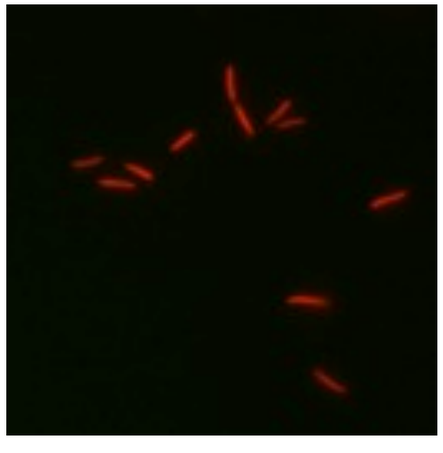
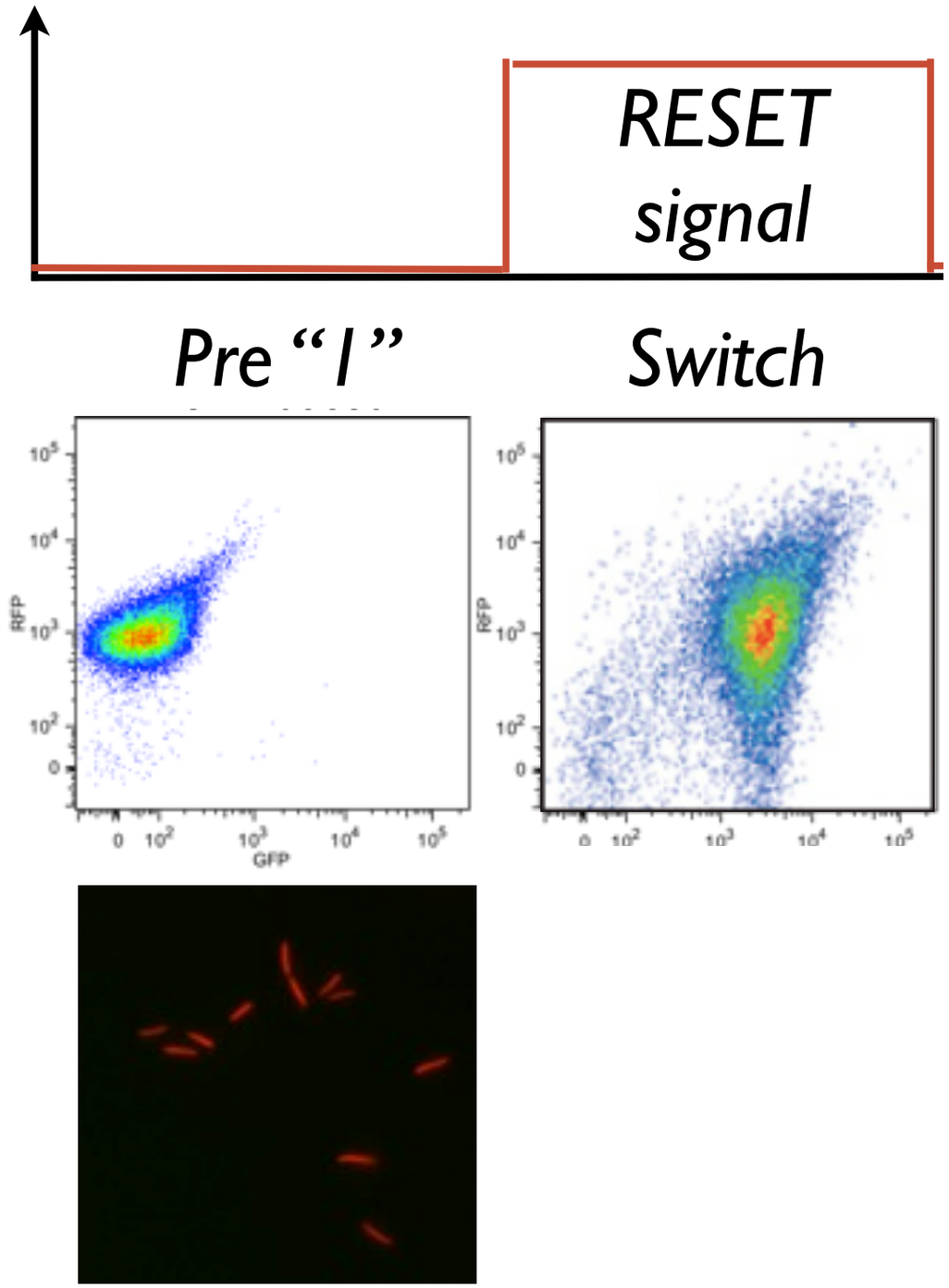


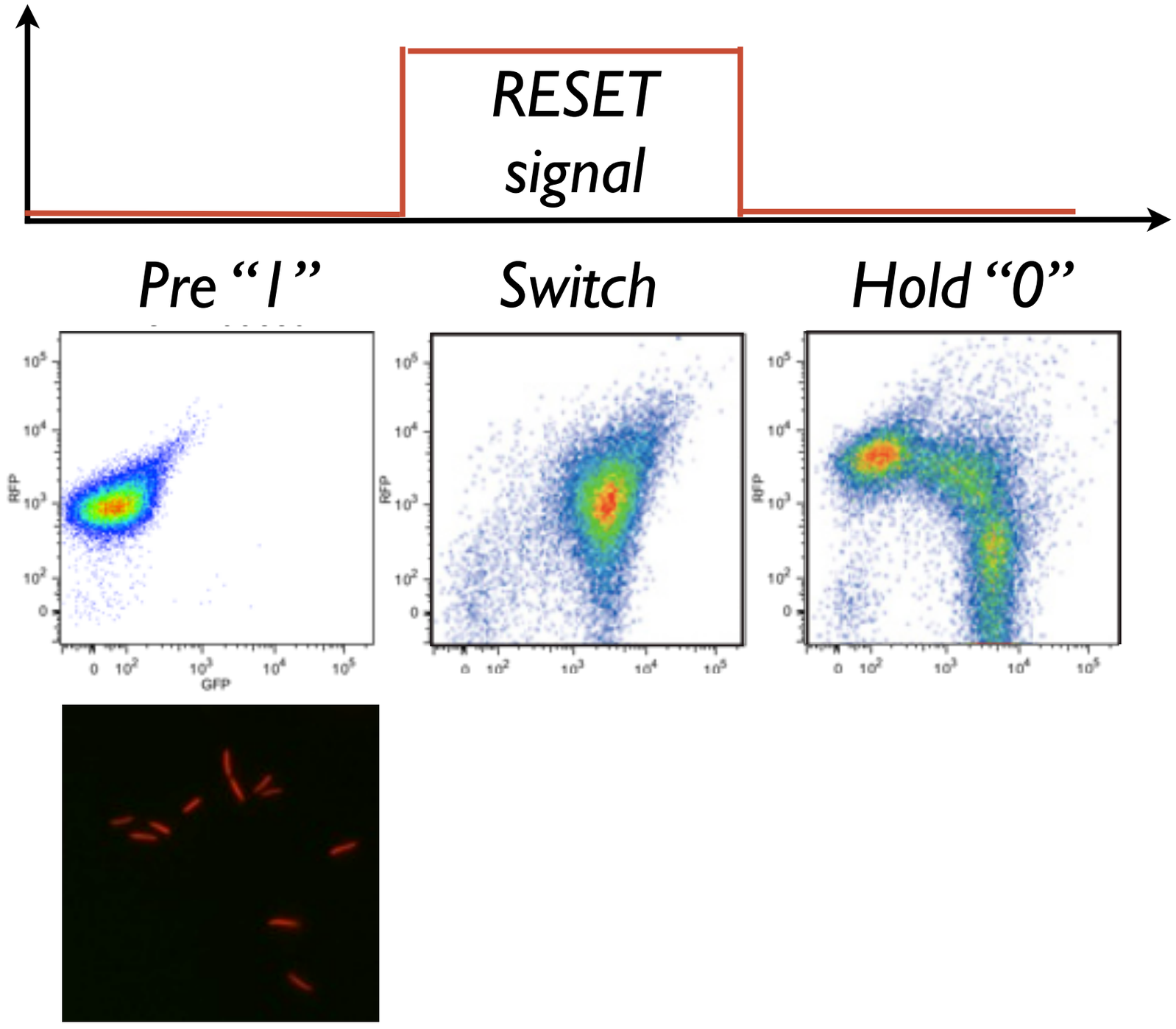
Figure 5. In Vitro Excisive Recombination Using gp47

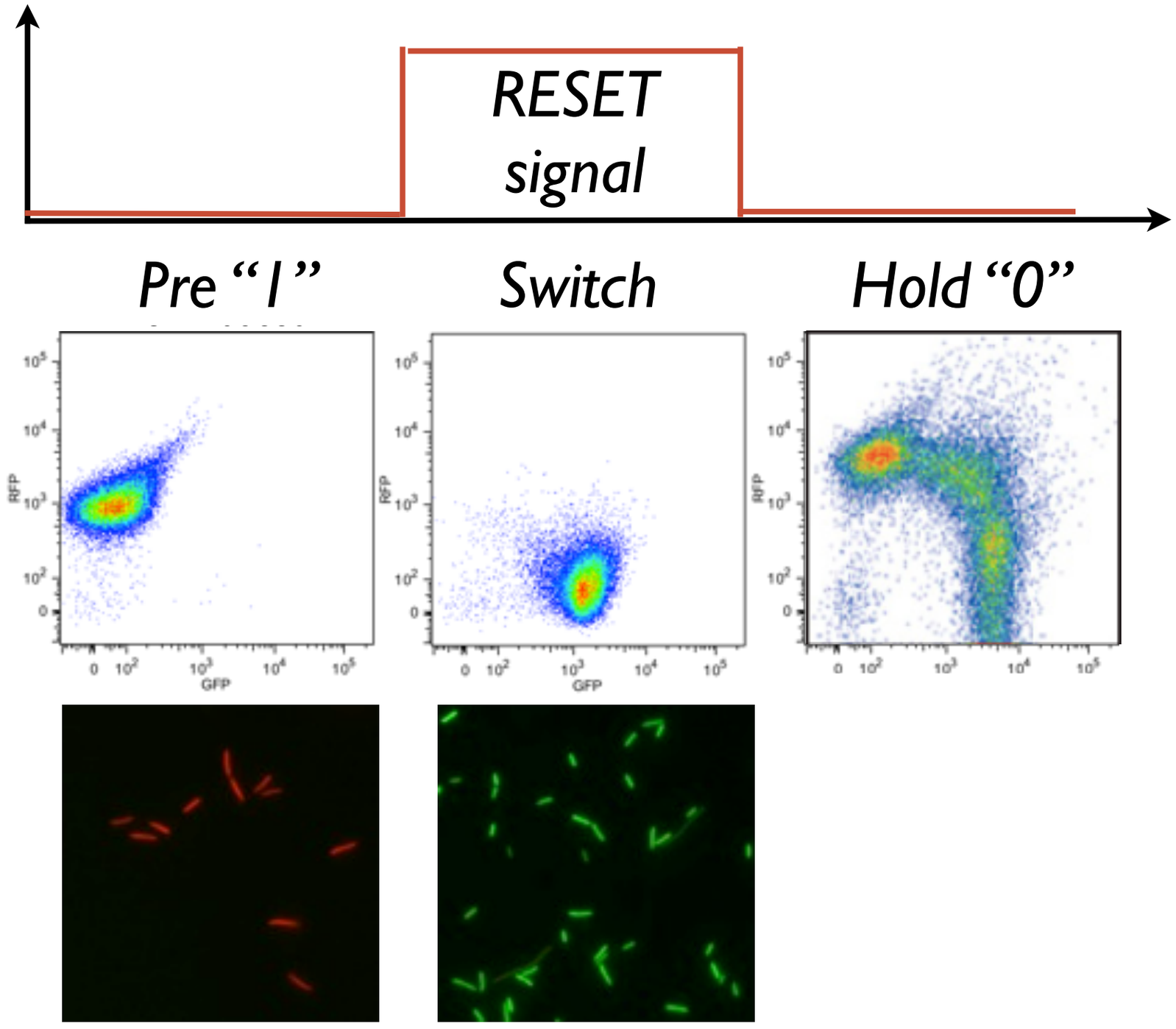
Pre "I"

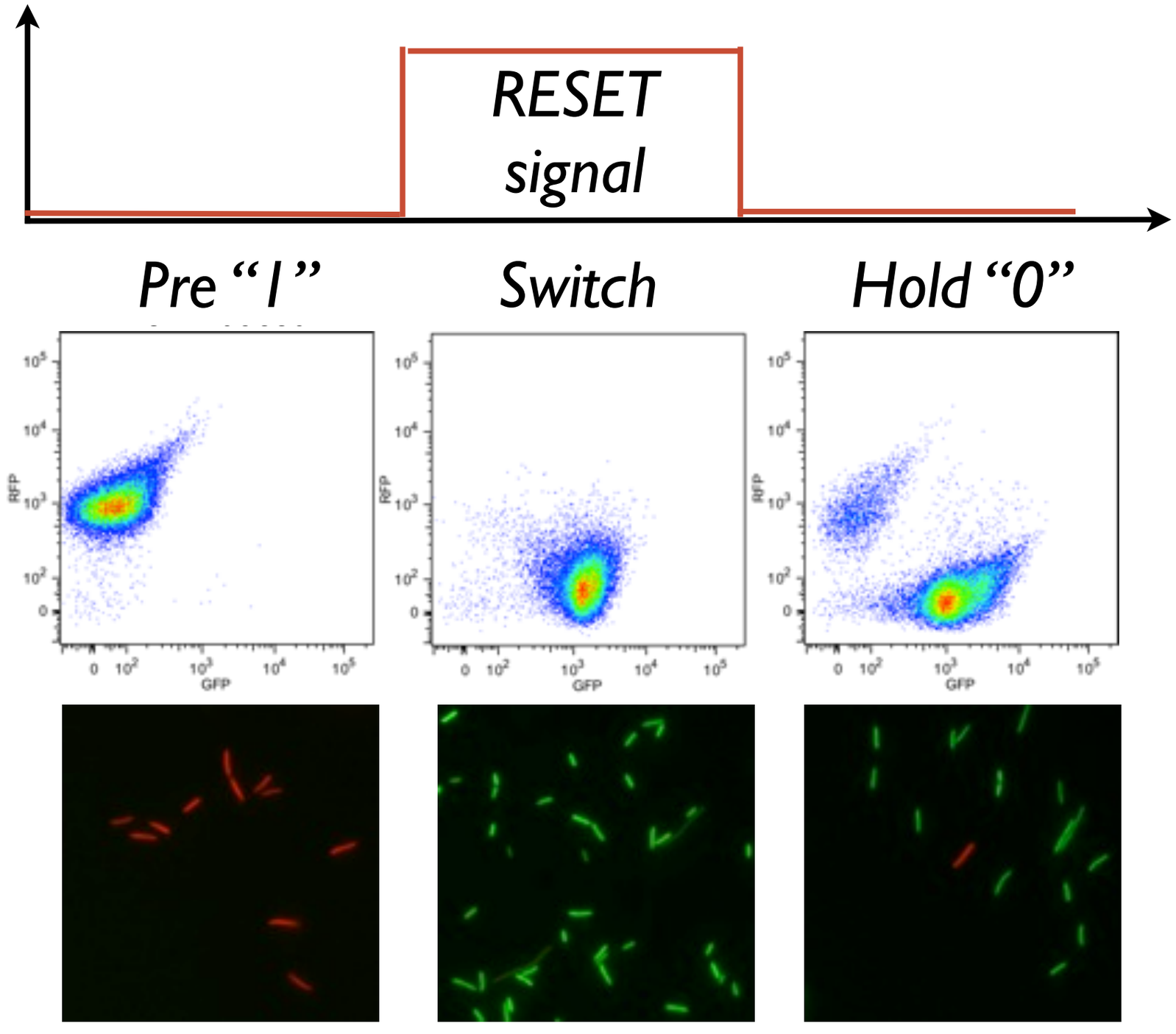




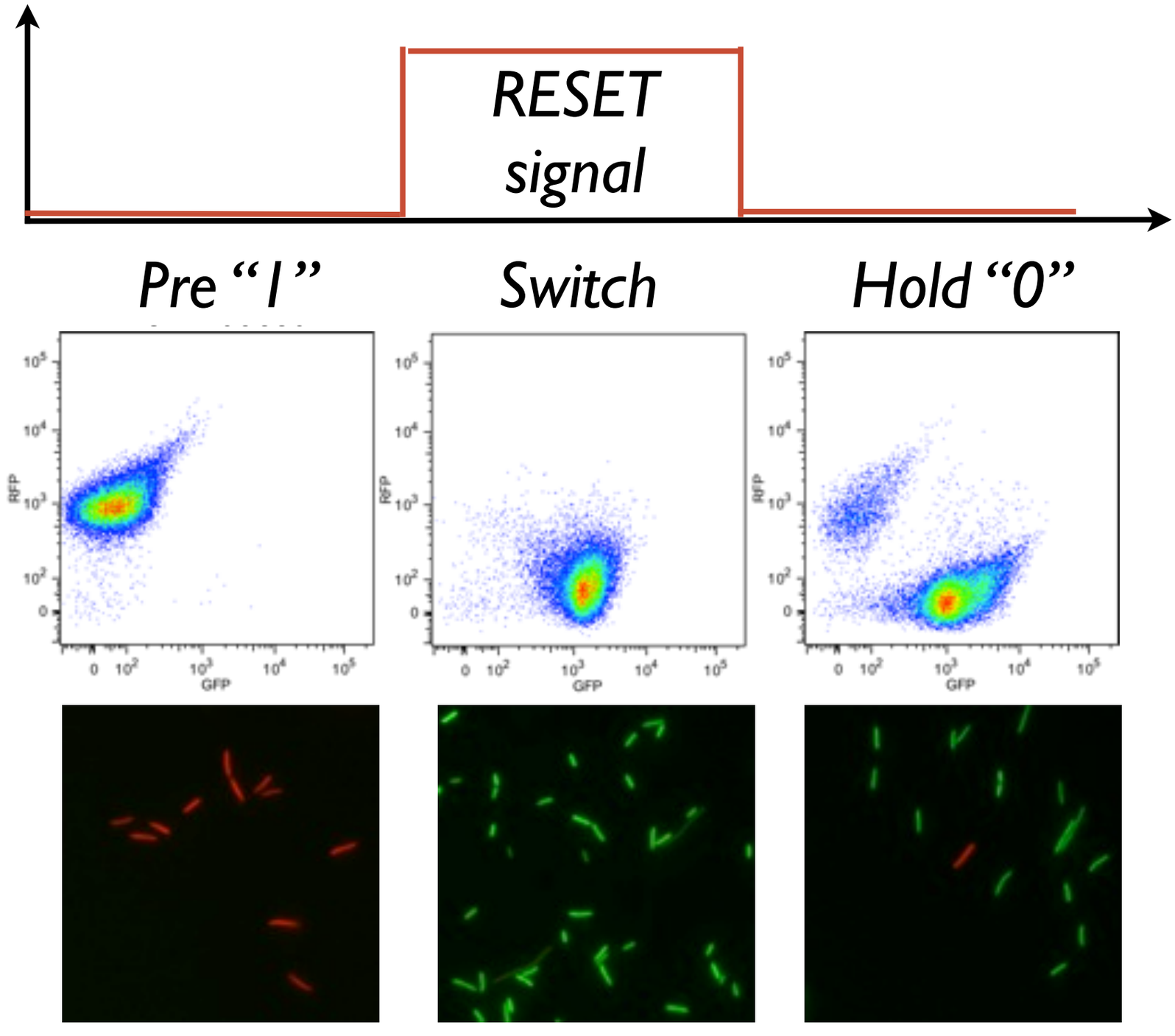

RESET
signal
Pre "I"
Switch
RFP
GFP
0
10^2
10^3
10^4
10^5



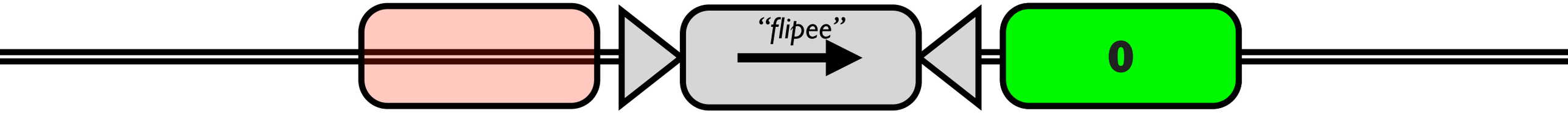


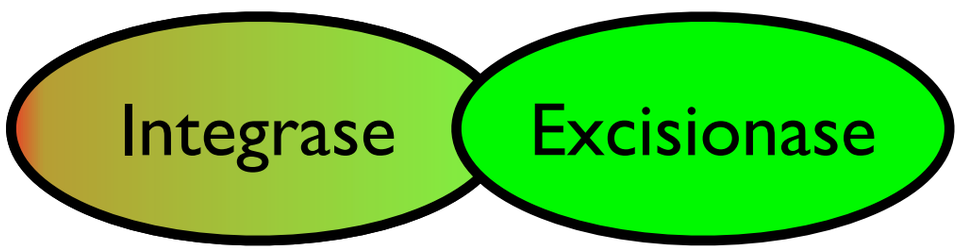


We can mostly erase a memory!



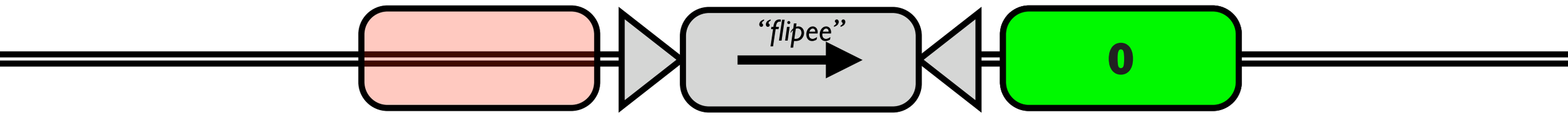
Even bigger problems putting together

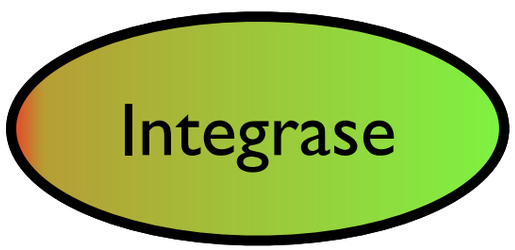




RESET "flipper"

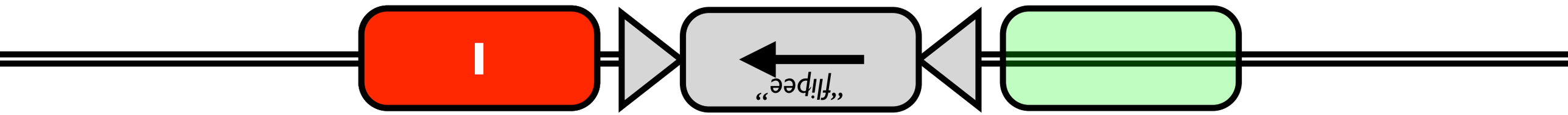
Even bigger problems putting together





RESET "flipper"

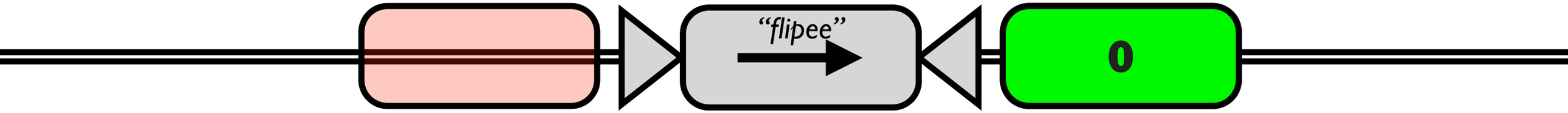
Even bigger problems putting together

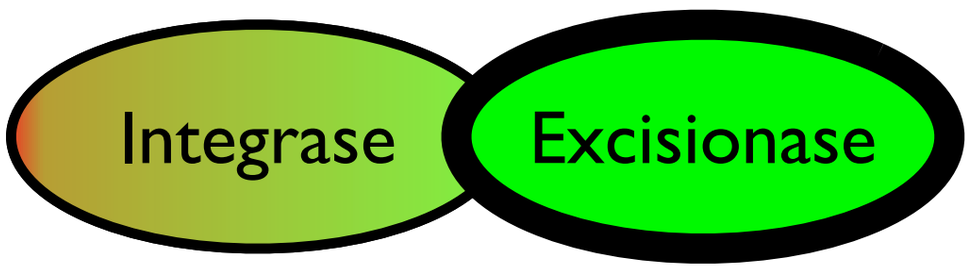


Integrase

SET "flipper"

Even bigger problems putting together

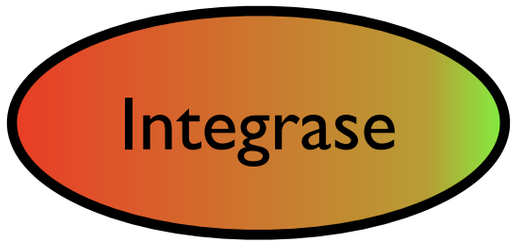


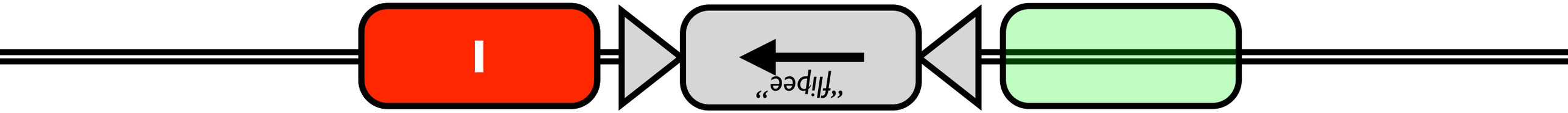


RESET "flipper"

Even bigger problems putting together

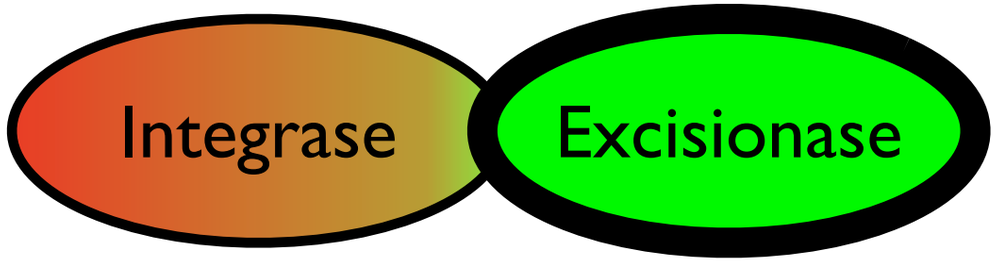
SET "flipper"

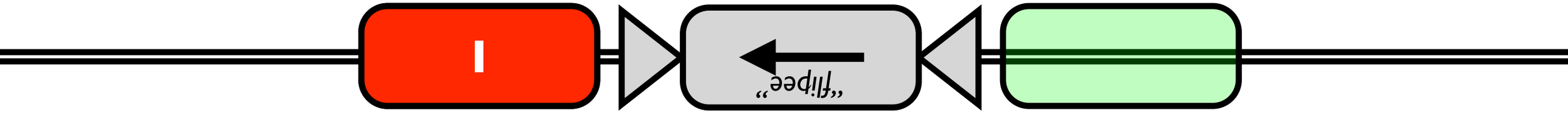




Even bigger problems putting together

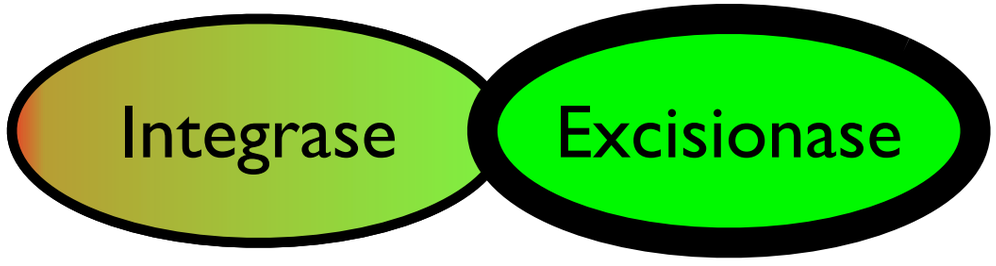
SET "flipper"

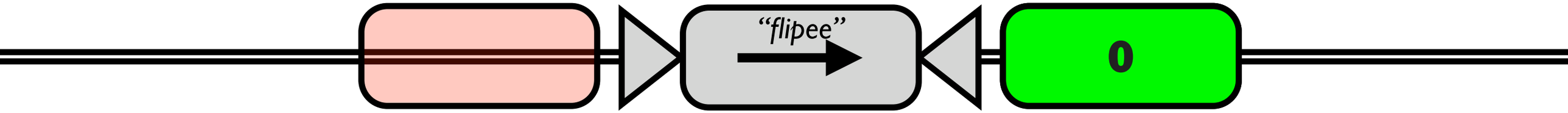




Even bigger problems putting together

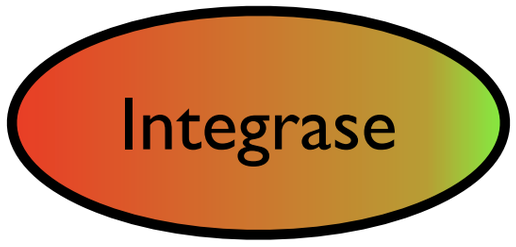
RESET "flipper"

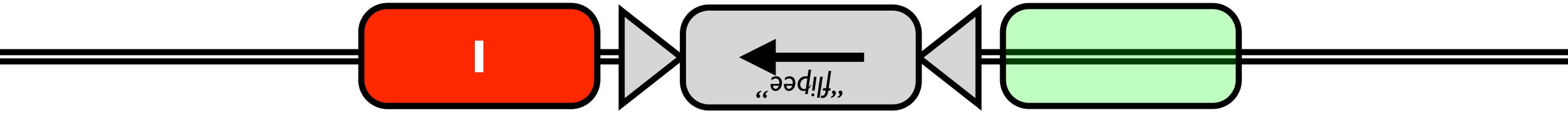




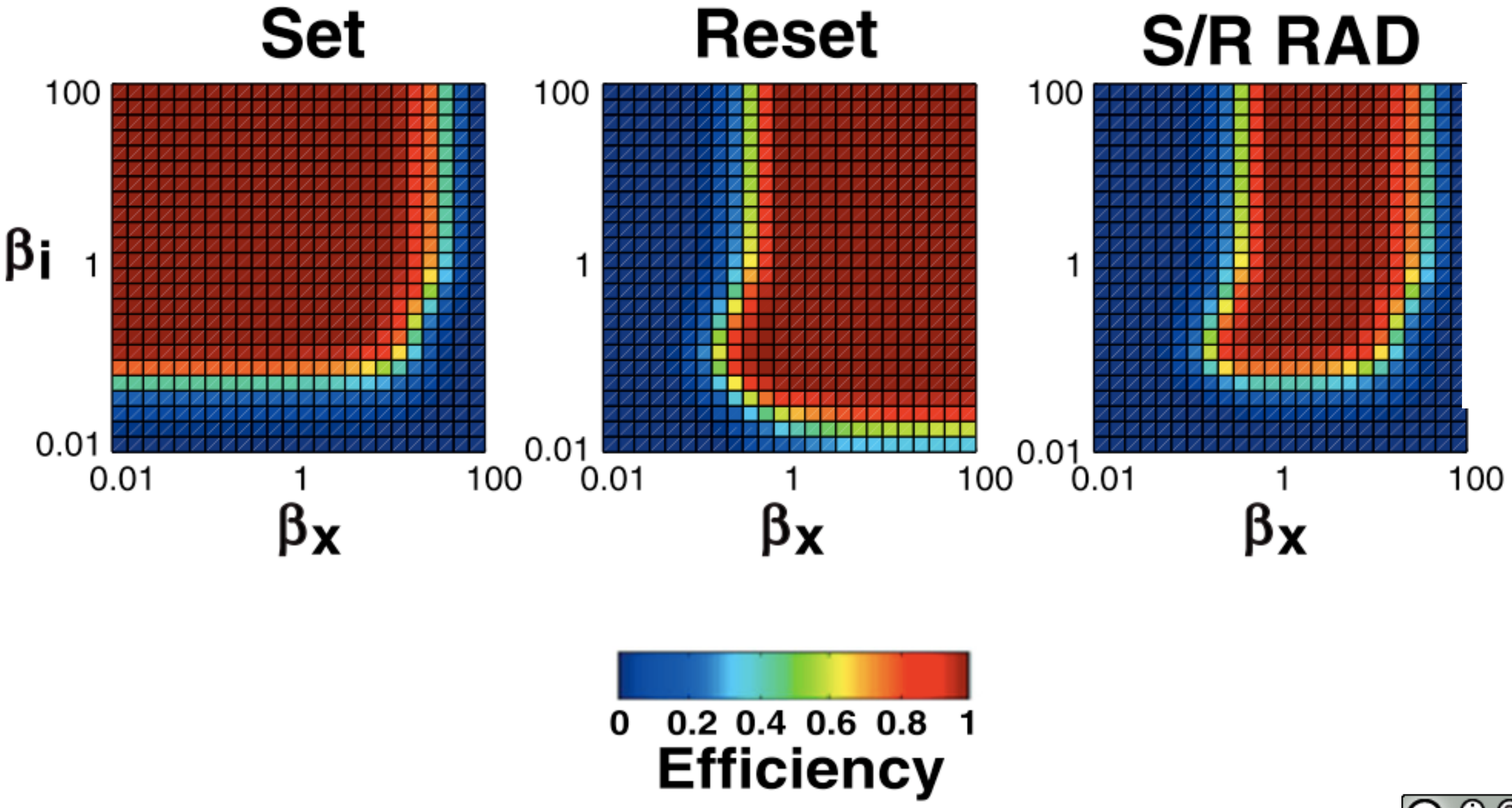
Even bigger problems putting together

SET "flipper"

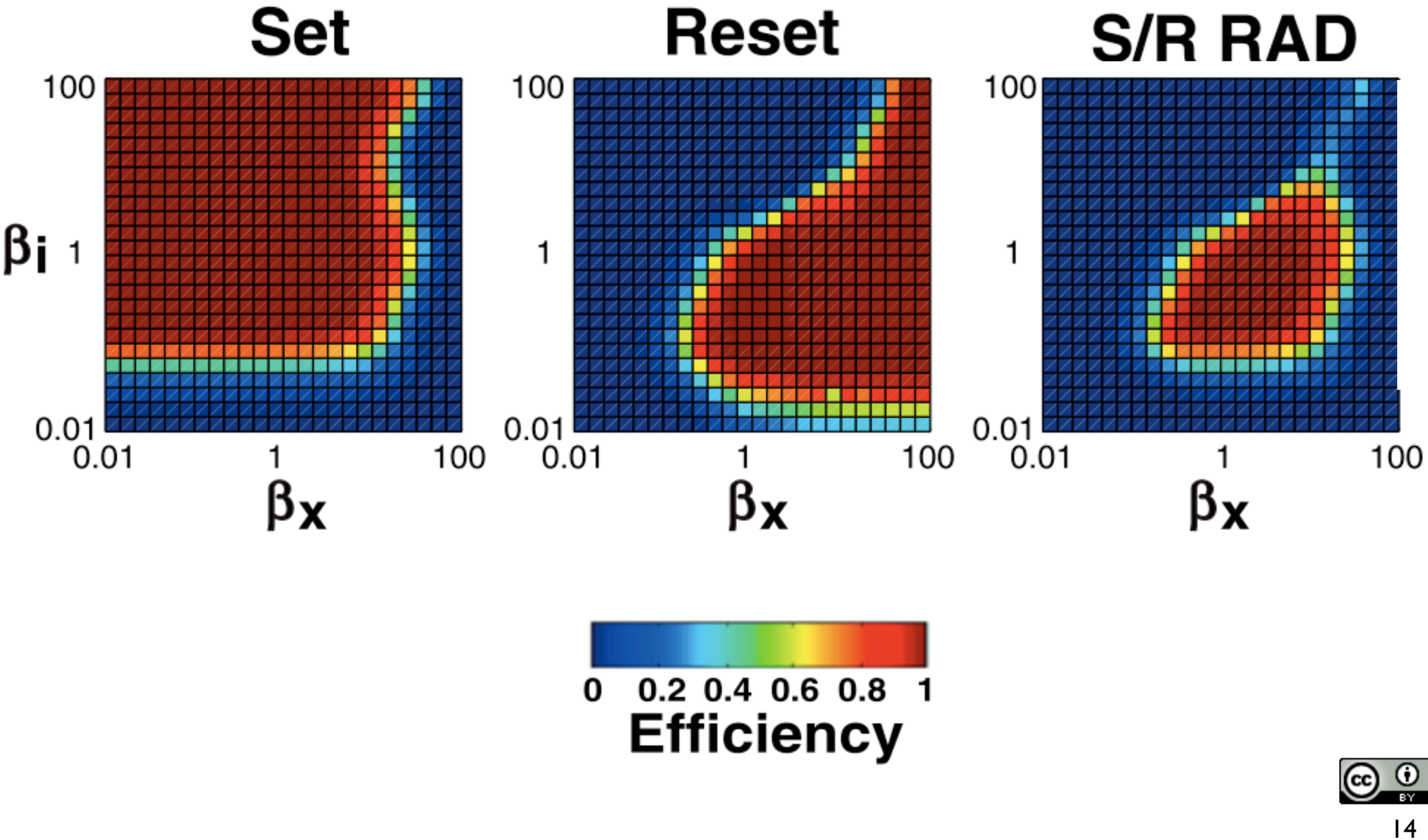




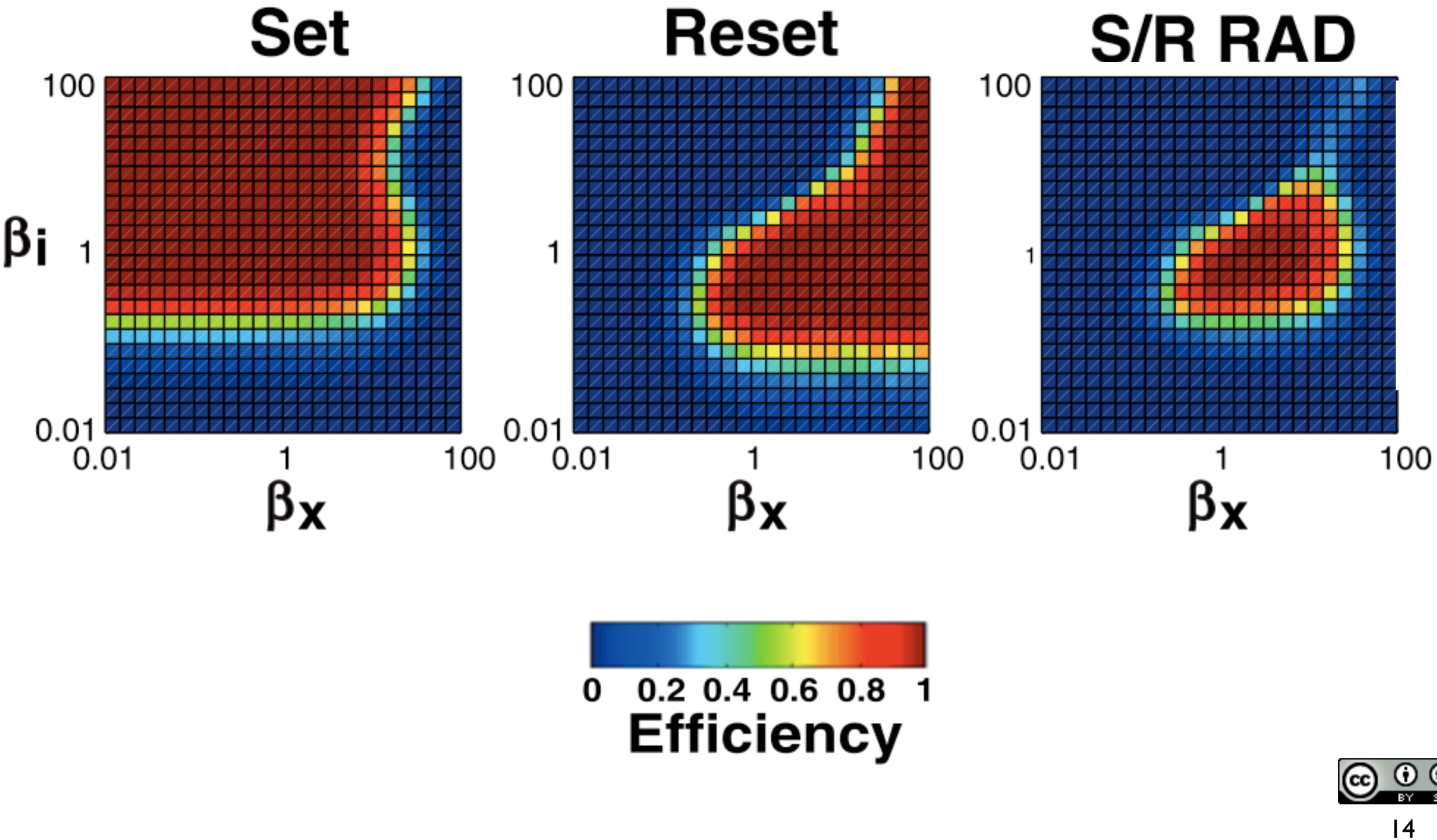
Switch given sustained input pulses



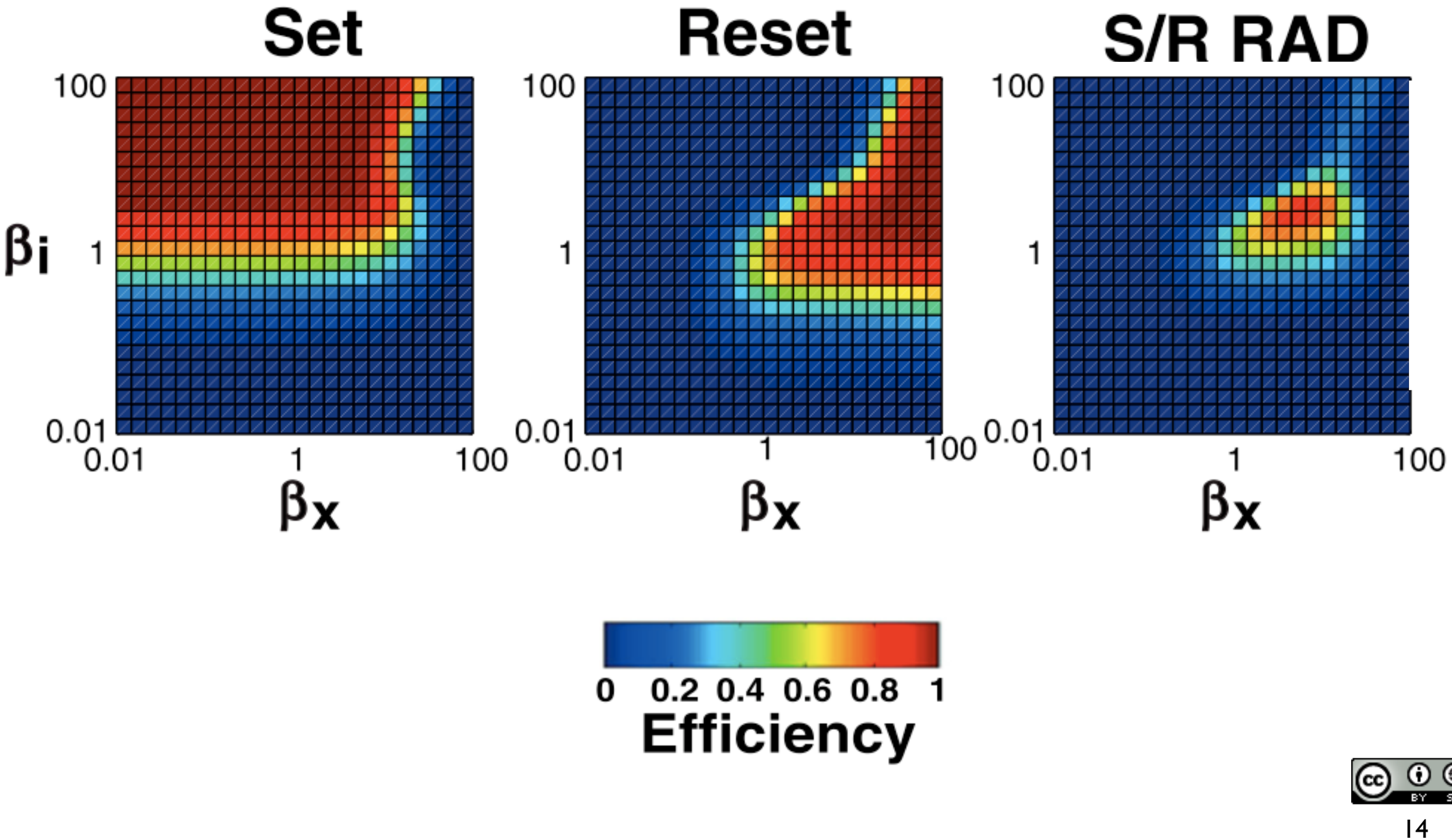
Switch & hold given 2000’ input pulses



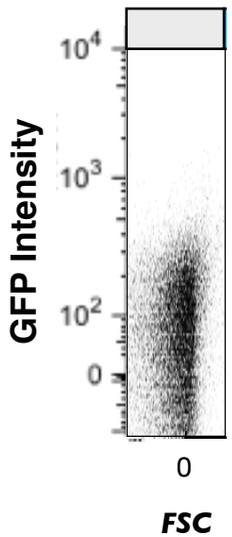
Switch & hold given 200’ input pulses



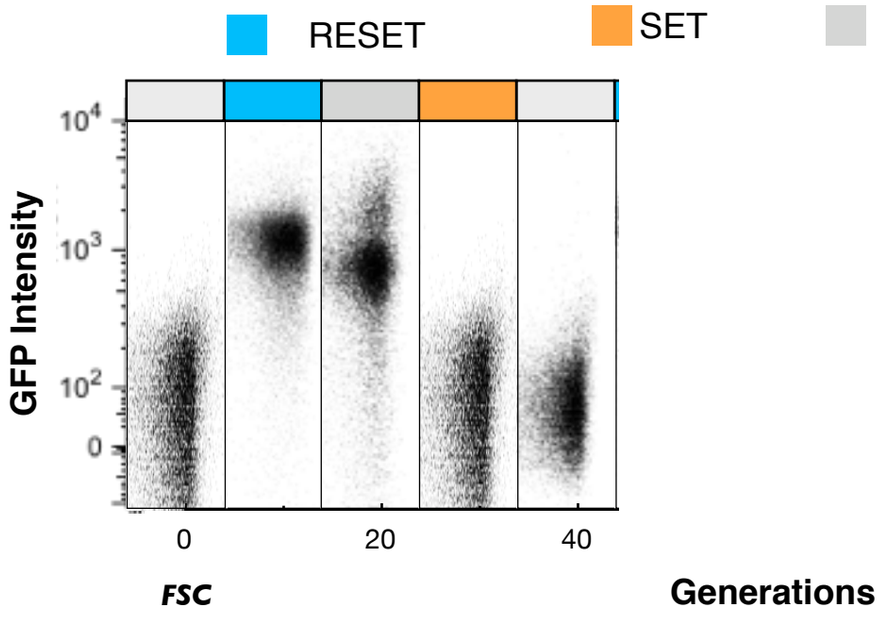
Switch & hold given 20’ input pulses



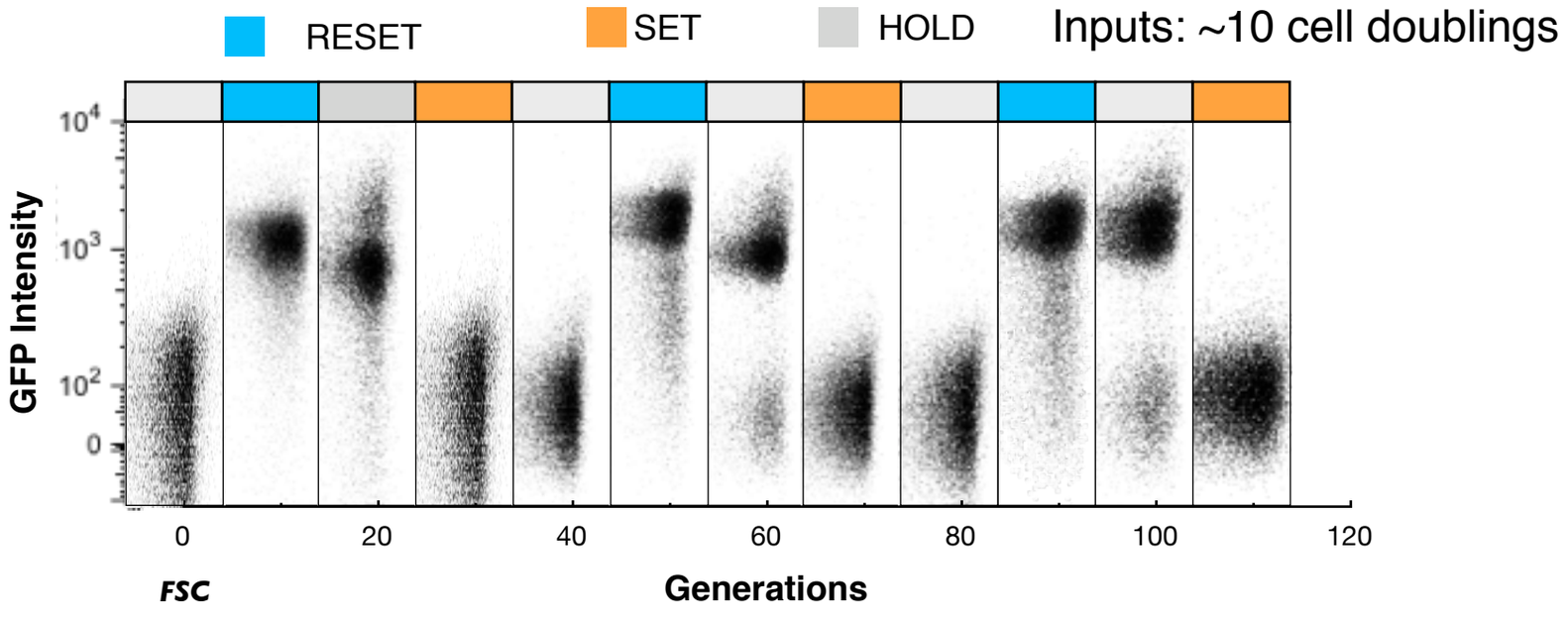
RESET SET HOLD Inputs: ~10 cell doublings

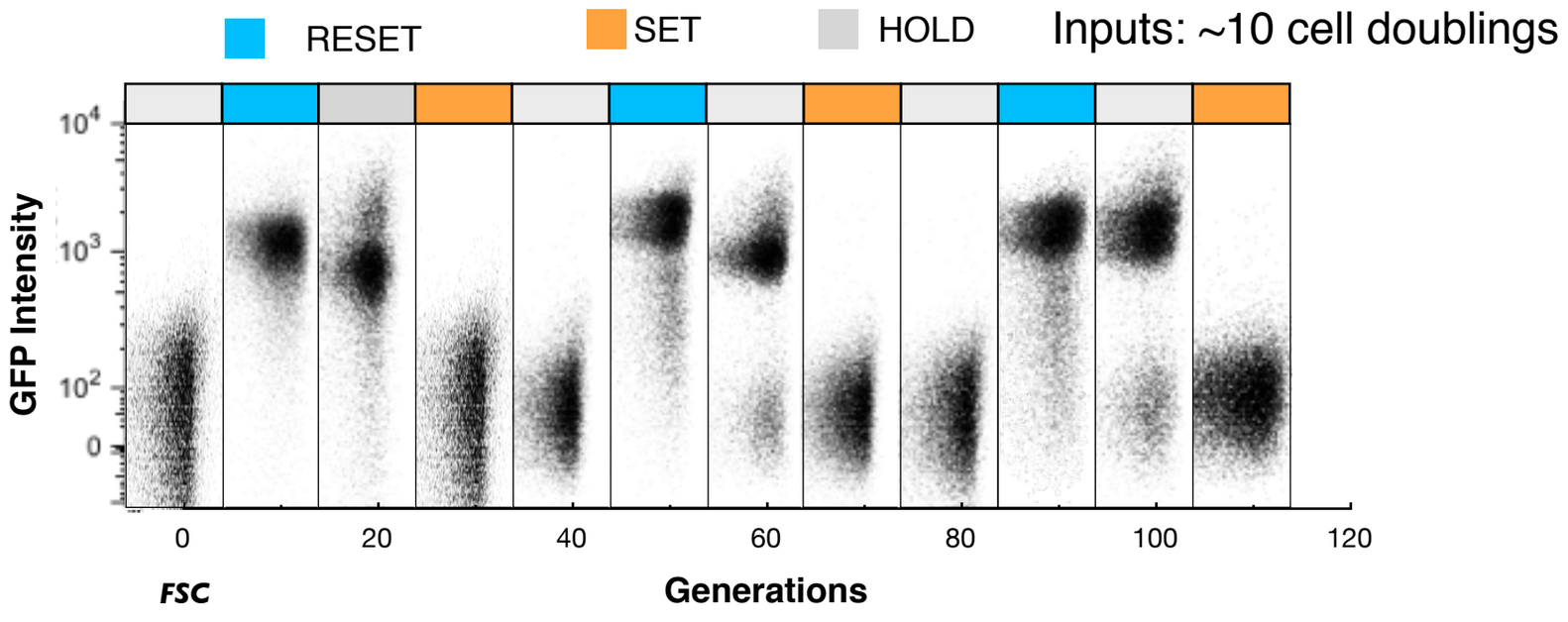


Generations

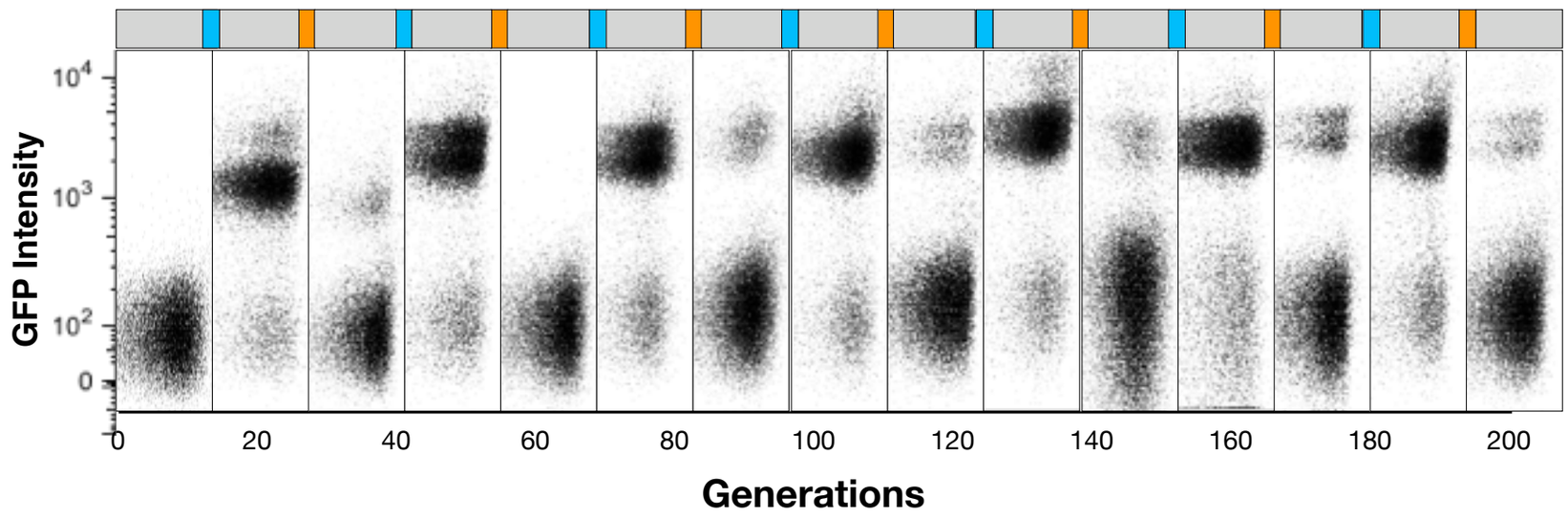


Inputs: ~10 cell doublings

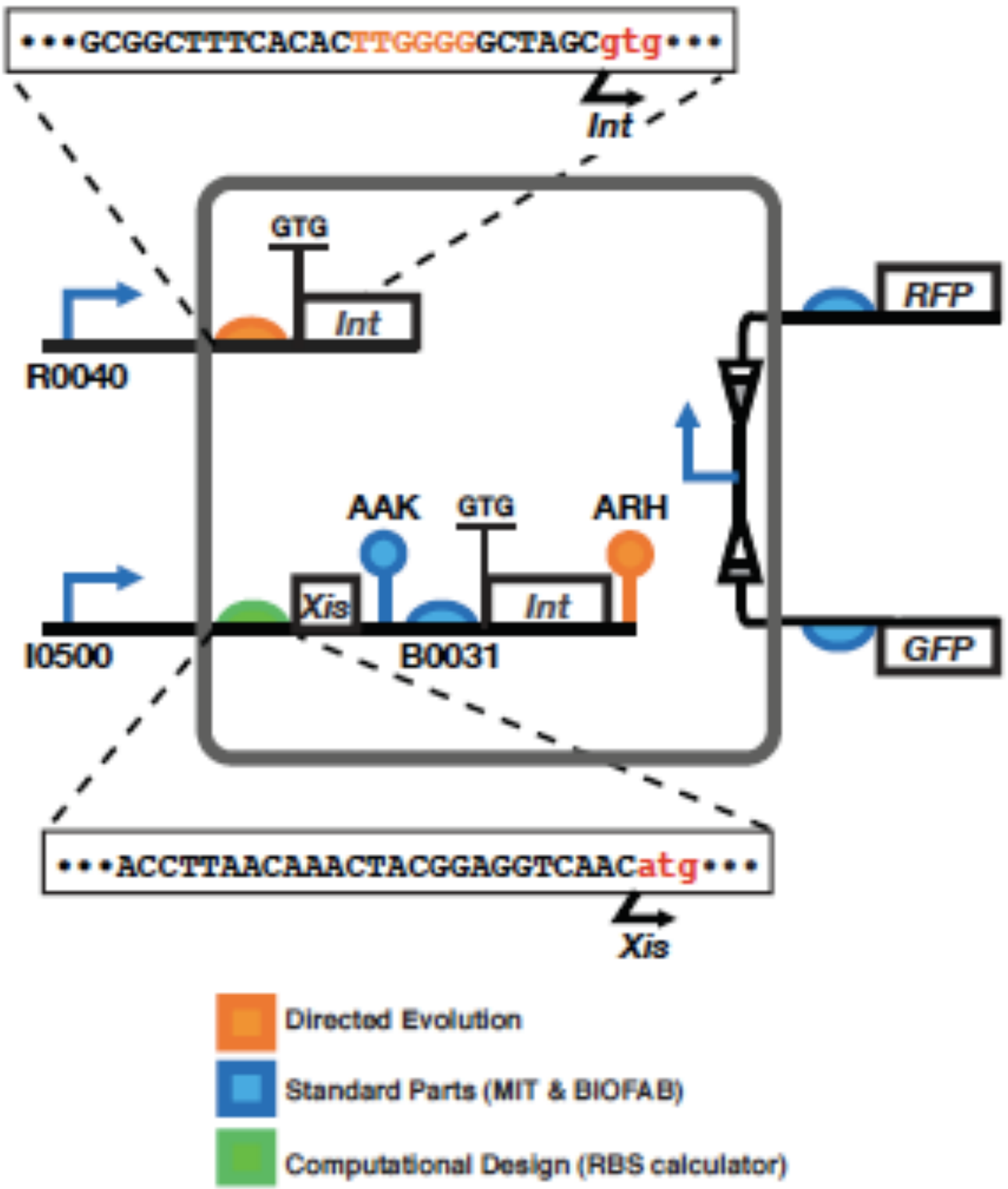

RESET
SET
HOLD
Inputs: ~10 cell doublings
GFP Intensity
10^4
10^3
10^2
0
0
20
40
60
80
100
120
FSC
Generations



Shorter Inputs: ~2.5 cell doublings



~3 years and ~750 attempts...



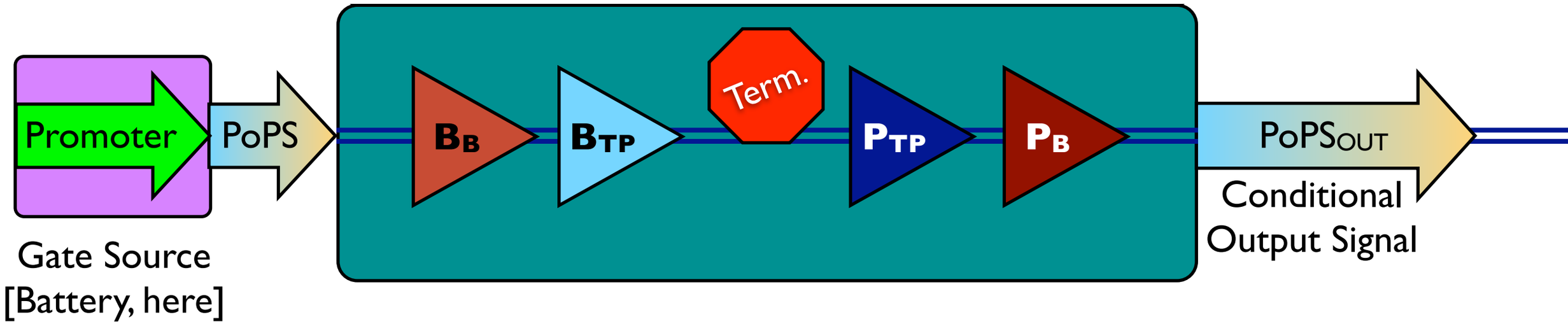
Note, not a formally bistable system

Works b/c we have two relatively nice A-to-D converters.

What else could you make with A-to-D converters?

Boolean Integrase Logic: OR

INPUT		OUTPUT
A	B	A OR B
0	0	0
0	1	1
1	0	1
1	1	1

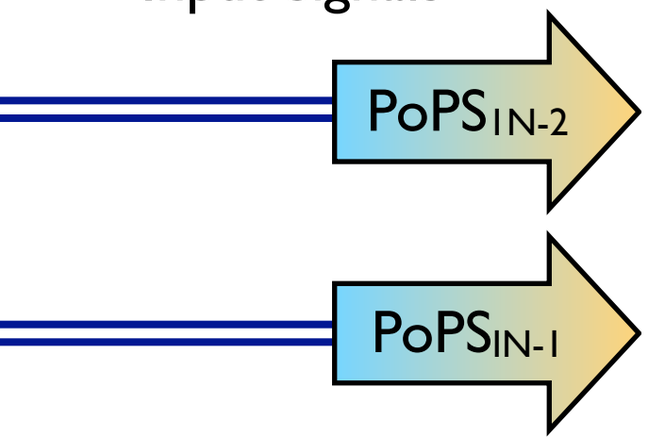


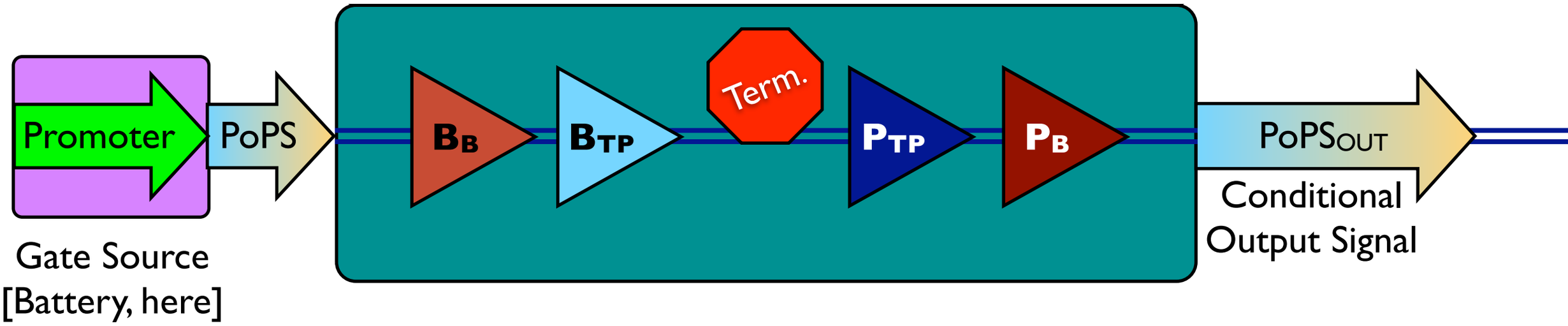
Bonnet & Yin, unpublished

Boolean Integrase Logic: OR

INPUT		OUTPUT
A	B	A OR B
0	0	0
0	1	1
1	0	1
1	1	1

Conditional
Input Signals

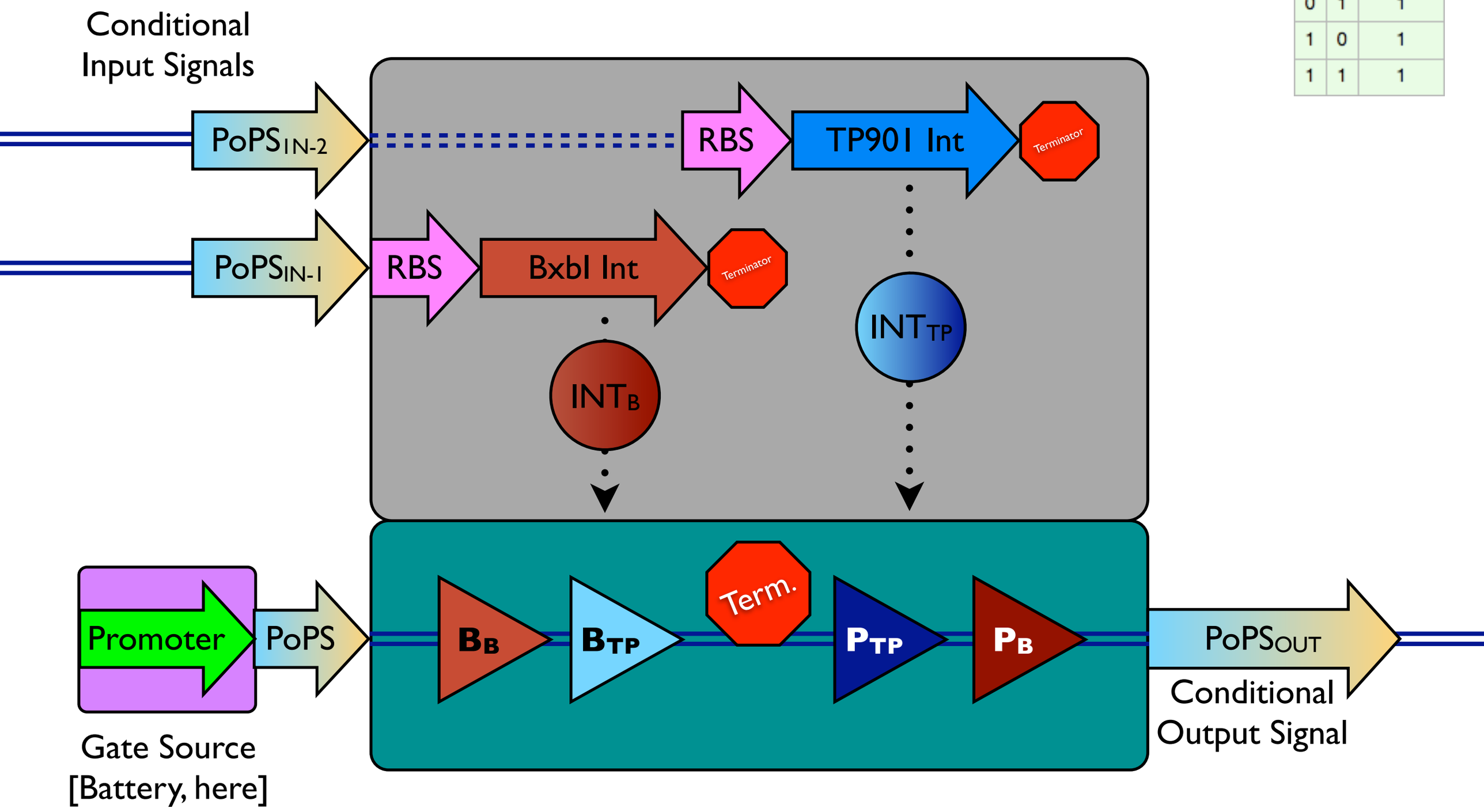




Bonnet & Yin, unpublished

Boolean Integrase Logic: OR

INPUT		OUTPUT
A	B	A OR B
0	0	0
0	1	1
1	0	1
1	1	1



Bonnet & Yin, unpublished

Boolean Integrase Logic: XOR

INPUT		OUTPUT
A	B	A XOR B
0	0	0
0	1	1
1	0	1
1	1	0

Conditional
Input Signals

PoPS$_{IN-2}$

PoPS$_{IN-1}$

RBS

TP901 Int

Terminator

RBS

BxbI Int

Terminator

INT$_{TP}$

INT$_{B}$

Promoter

PoPS

B_B

B_{TP}

Term.

P_{TP}

P_B

PoPS$_{OUT}$

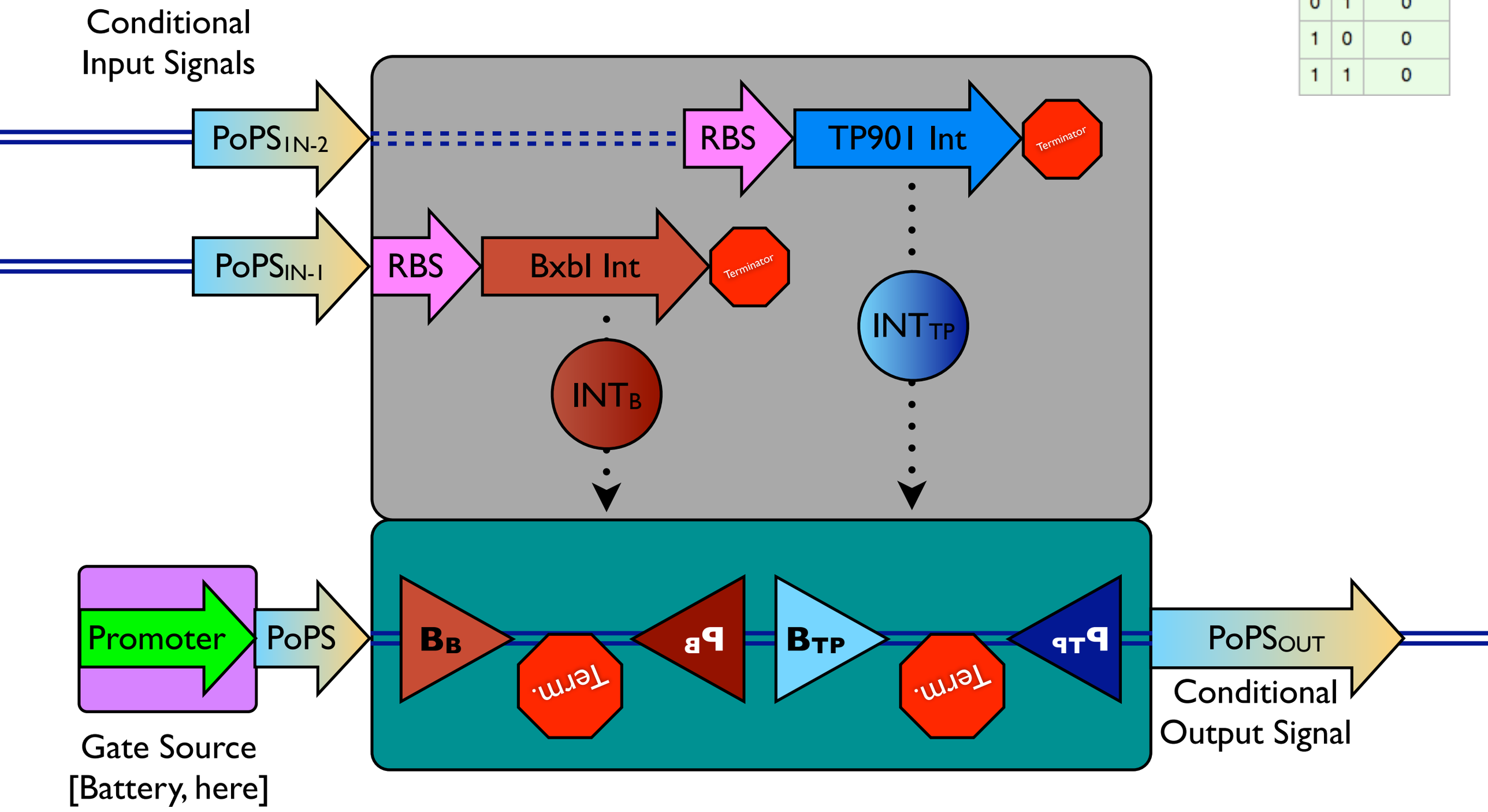
Conditional
Output Signal

Gate Source
[Battery, here]

Bonnet & Yin, unpublished

Boolean Integrase Logic: NOR

INPUT		OUTPUT
A	B	A NOR B
0	0	1
0	1	0
1	0	0
1	1	0



Bonnet & Yin, unpublished

Boolean Integrase Logic: XNOR

INPUT		OUTPUT
A	B	A XNOR B
0	0	1
0	1	0
1	0	0
1	1	1

Conditional
Input Signals

$PoPS_{IN-2}$

$PoPS_{IN-1}$

RBS

TP901 Int

Terminator

RBS

BxbI Int

Terminator

INT_{TP}

INT_B

Promoter

PoPS

B_B

B_{TP}

Term.

P_{TP}

P_B

$PoPS_{OUT}$

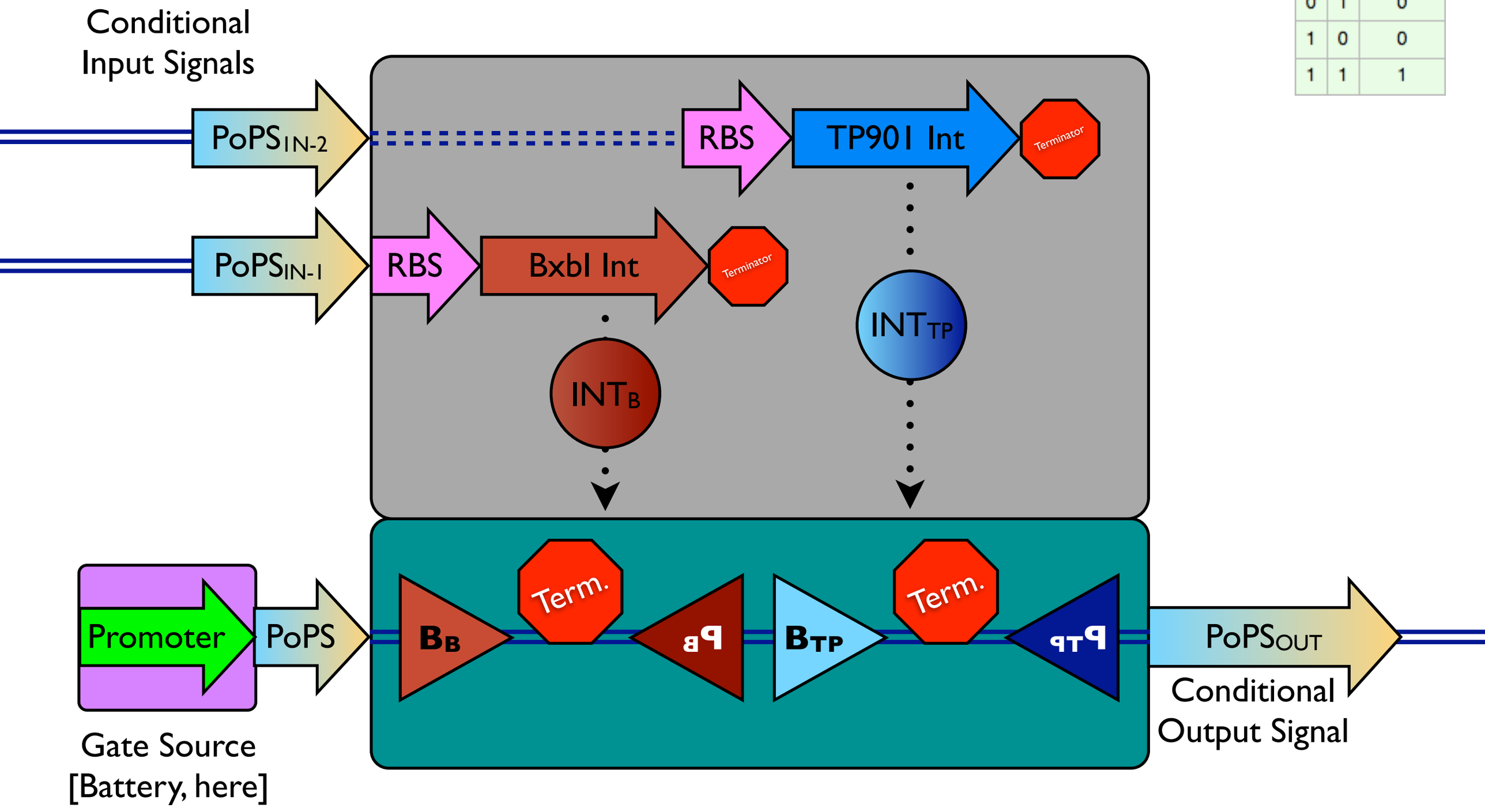
Conditional
Output Signal

Gate Source
[Battery, here]

Bonnet & Yin, unpublished

Boolean Integrase Logic: AND

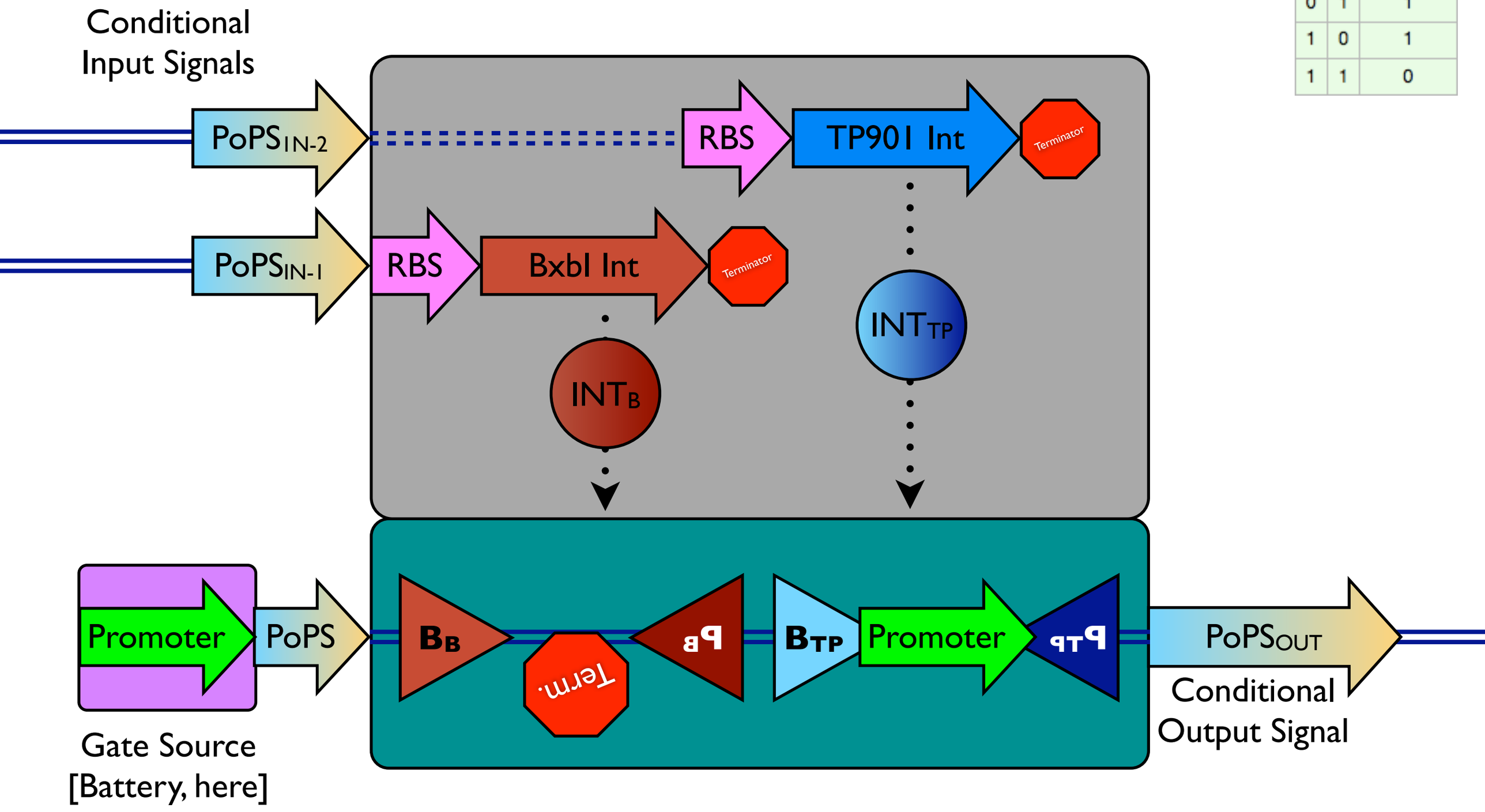
INPUT		OUTPUT
A	B	A AND B
0	0	0
0	1	0
1	0	0
1	1	1



Bonnet & Yin, unpublished

Boolean Integrase Logic: NAND

INPUT		OUTPUT
A	B	A NAND B
0	0	1
0	1	1
1	0	1
1	1	0



Bonnet & Yin, unpublished

Boolean Integrase Logic Gates

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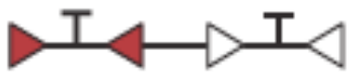
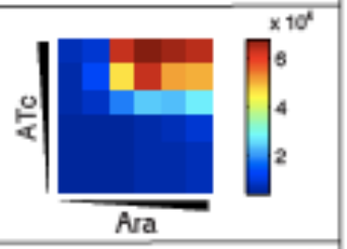
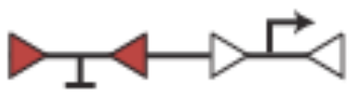
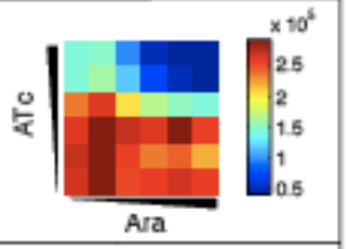
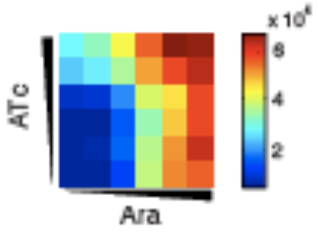
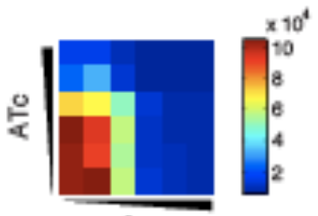
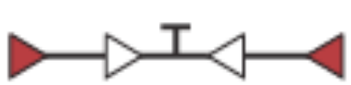
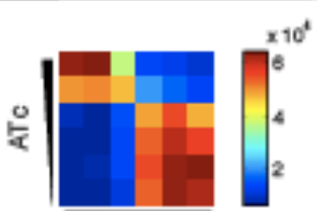
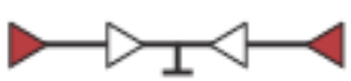
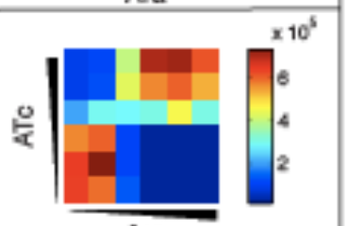
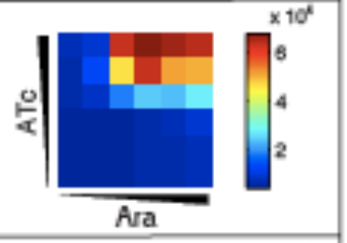
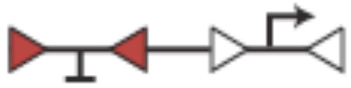
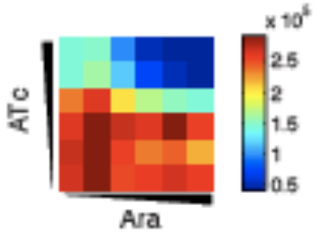
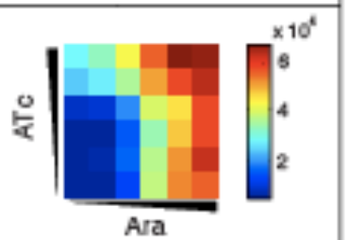
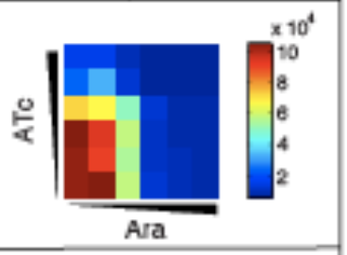
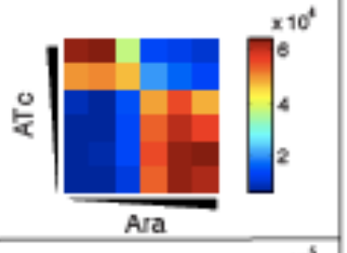
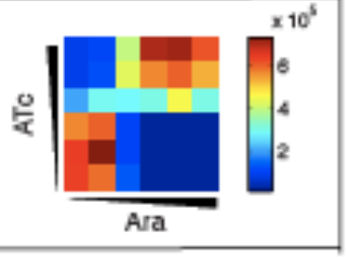
Boolean Integrase Logic Gates

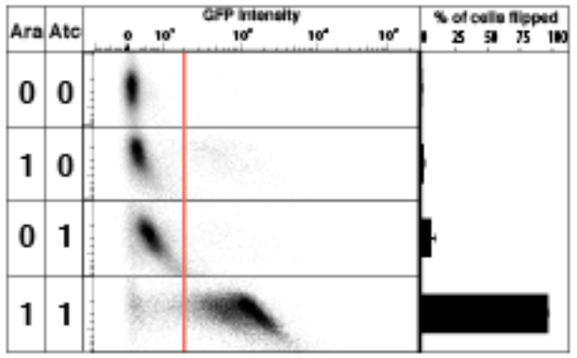
Function	Truth Table	Architecture	Measured
AND	ARA ATC OUT 0 0 0 1 0 0 0 1 0 1 1 1		
NAND	ARA ATC OUT 0 0 1 1 0 1 0 1 1 1 1 0		
OR	ARA ATC OUT 0 0 0 1 0 1 0 1 1 1 1 1		
NOR	ARA ATC OUT 0 0 1 1 0 0 0 1 0 1 1 0		
XOR	ARA ATC OUT 0 0 0 1 0 1 0 1 1 1 1 0		
XNOR	ARA ATC OUT 0 0 1 1 0 0 0 1 0 1 1 1		

Bonnet & Yin, unpublished

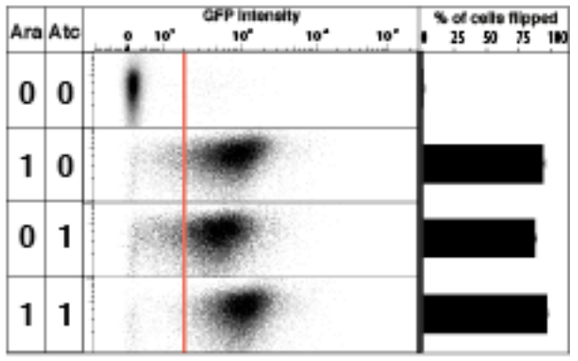
Boolean Integrase Logic Gates

Function	Truth Table ARA	ATC	OUT	Architecture	Measured
AND	0	0	0		
	1	0	0		
	0	1	0		
	1	1	1		
NAND	0	0	1		
	1	0	1		
	0	1	1		
	1	1	0		
OR	0	0	0		
	1	0	1		
	0	1	1		
	1	1	1		
NOR	0	0	1		
	1	0	0		
	0	1	0		
	1	1	0		
XOR	0	0	0		
	1	0	1		
	0	1	1		
	1	1	0		
XNOR	0	0	1		
	1	0	0		
	0	1	0		
	1	1	1		

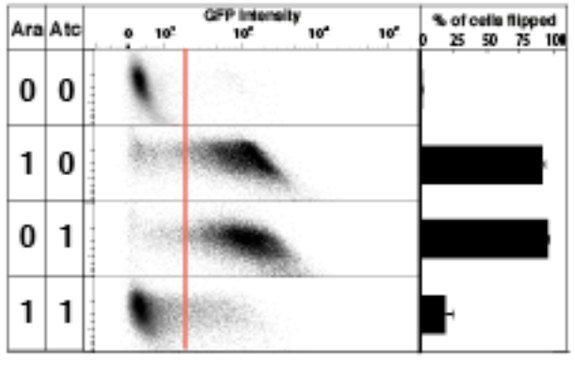
AND



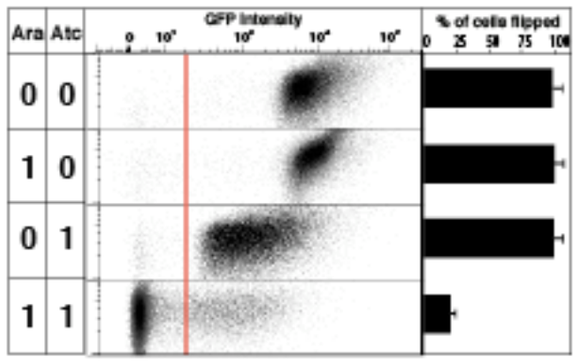
OR



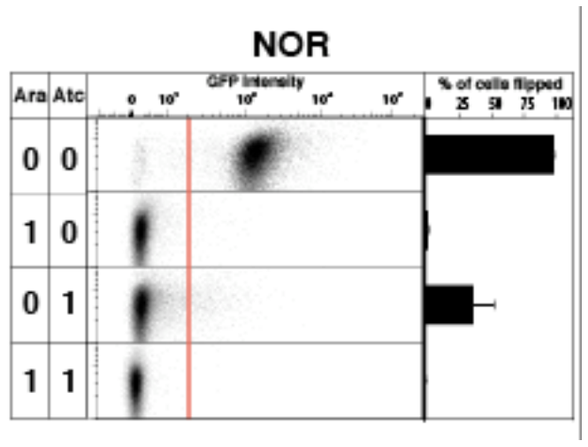
XOR



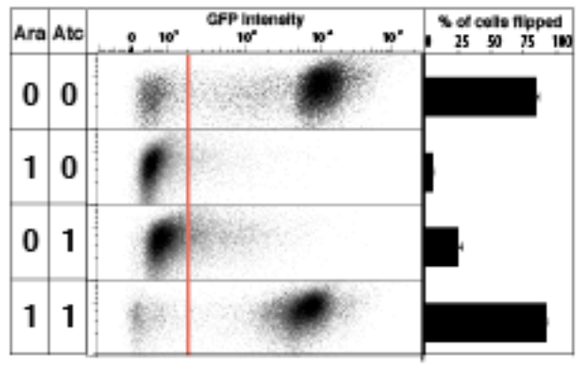
NAND



NOR



XNOR



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Research

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Engineered cell-cell communication via DNA messaging

Monica E Ortiz and **Drew Endy**

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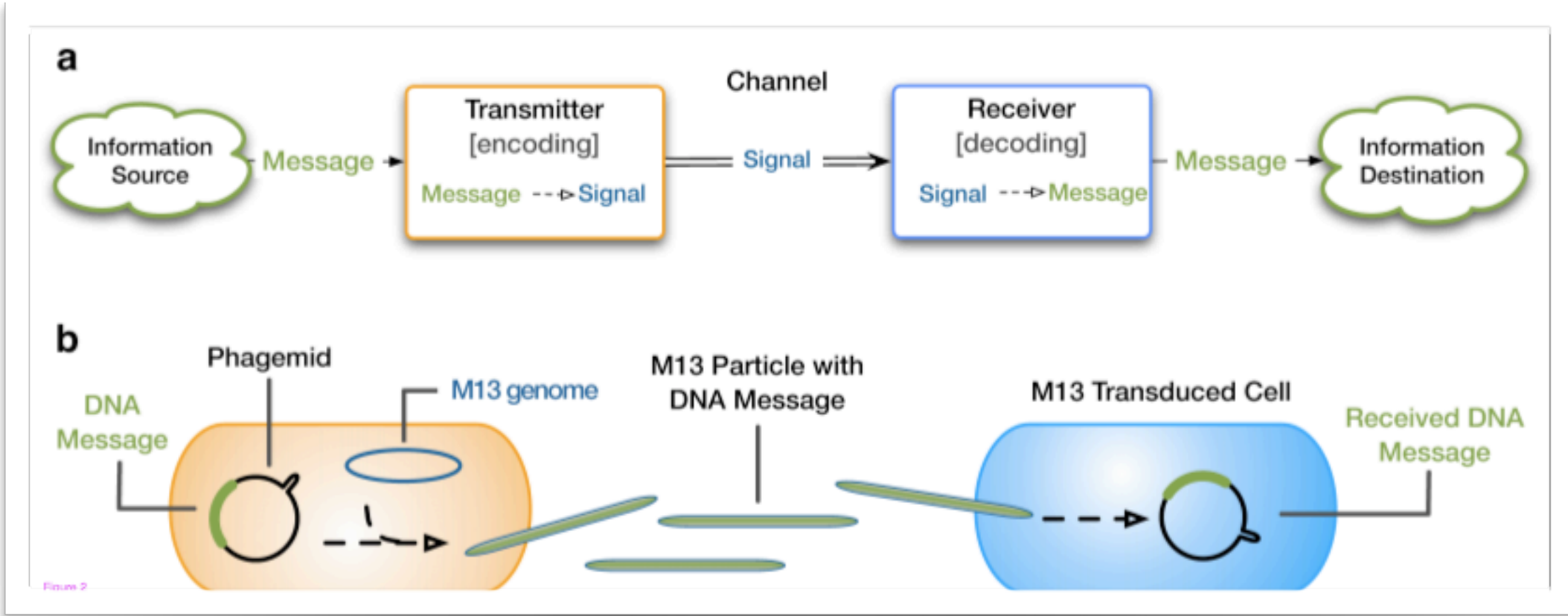
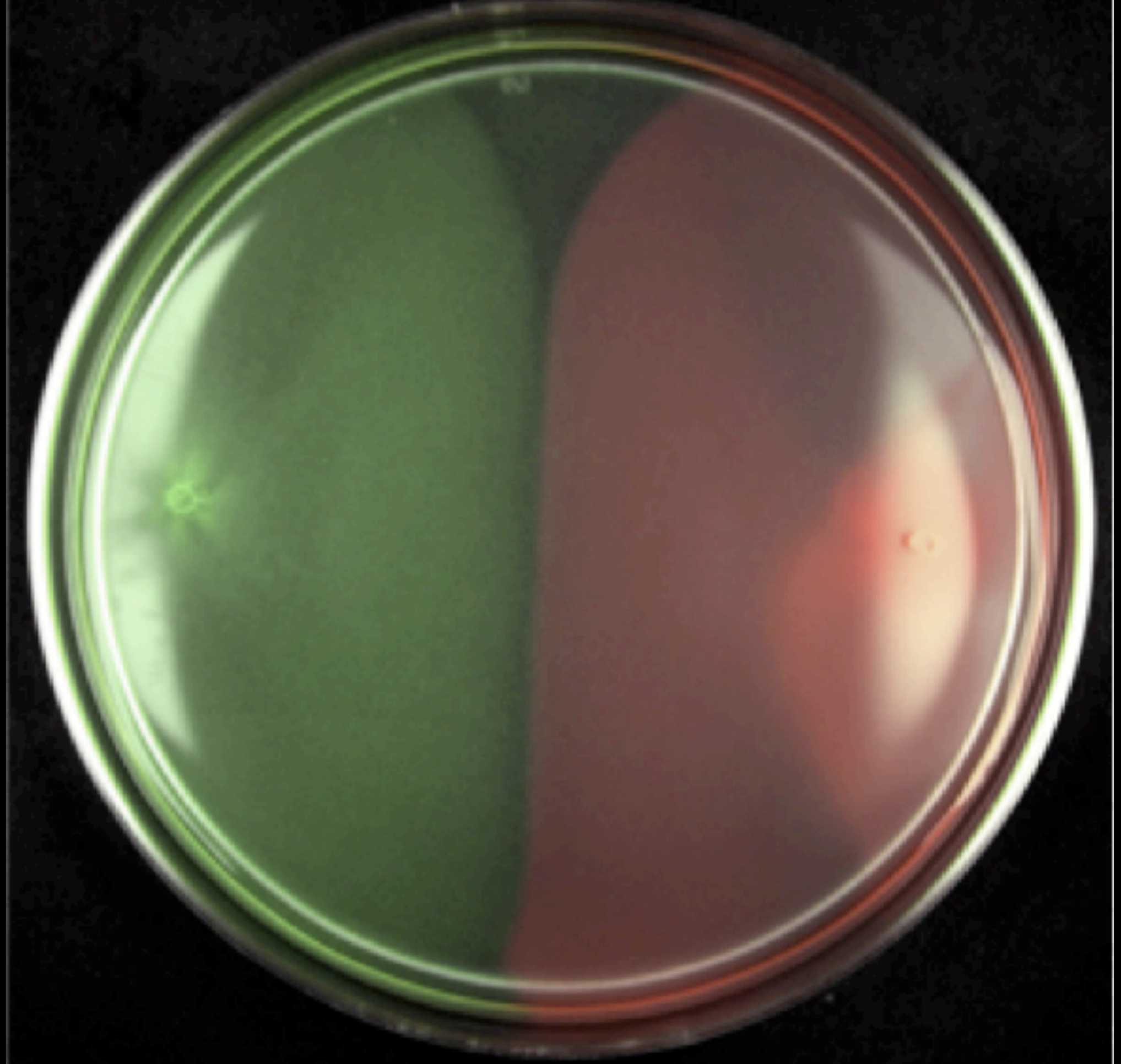
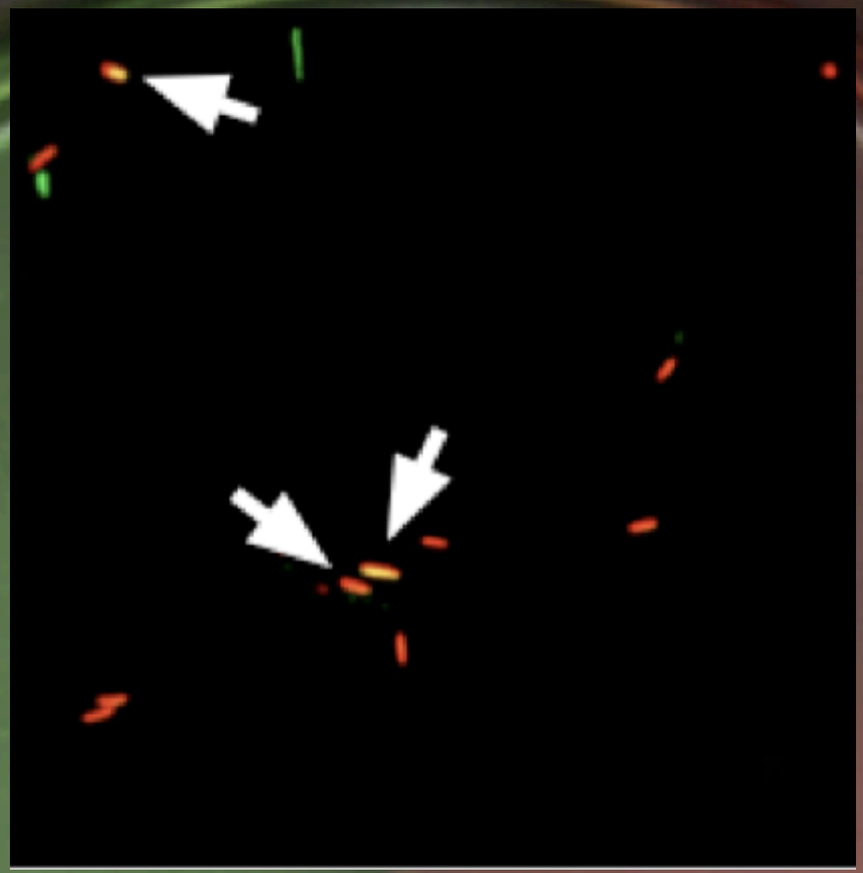
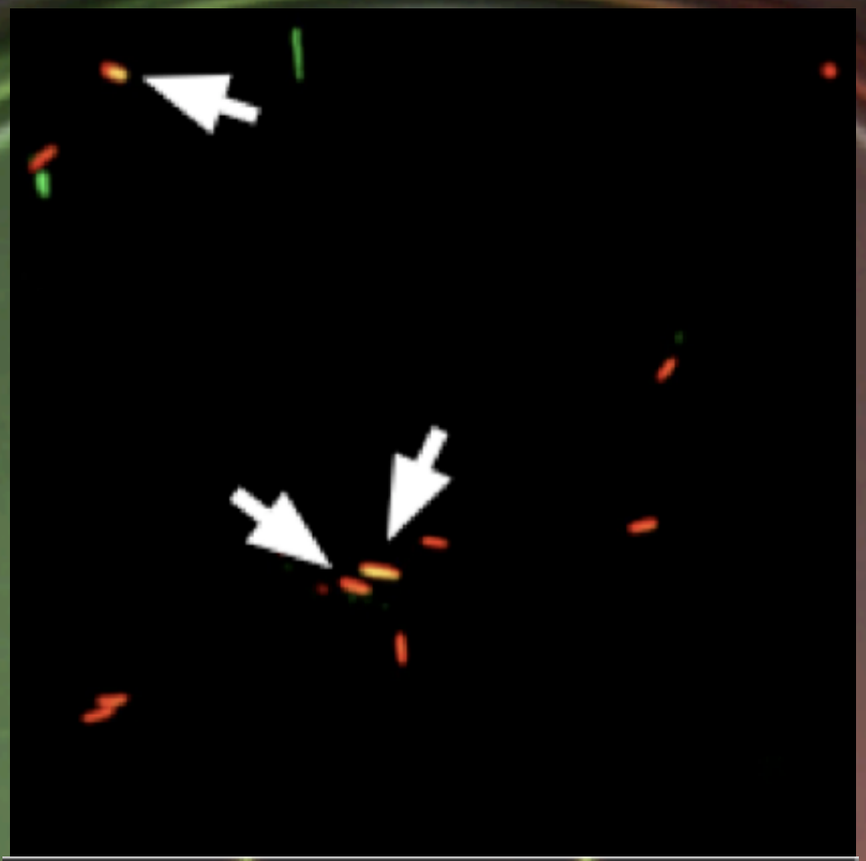
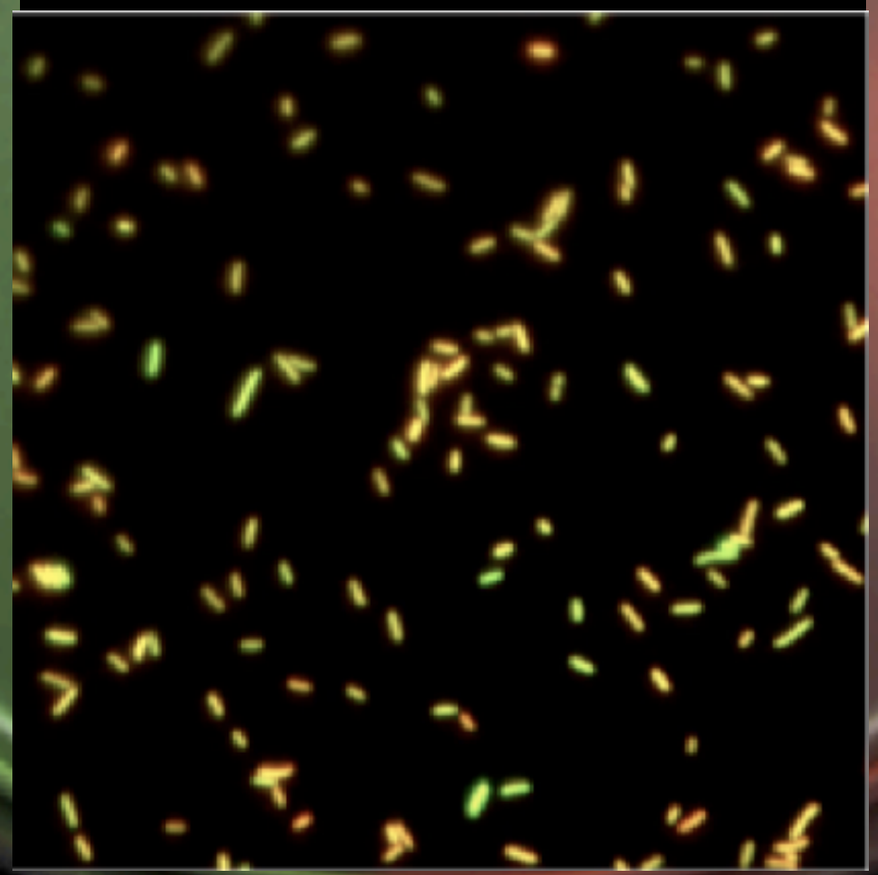










Scientists Examine Tiny Viruses For Messages From Outer Space

By WALTER SULLIVAN

A search for messages from other worlds is focusing not on the heavens but on certain bacterial viruses.

The search, in Japan, is for special meaning in the coded genetic signals within the viruses. It was prompted by the discovery that the genetic sequence of one virus seems more contrived than natural.

Two Japanese scientists have suggested that part of the genetic sequence is a message encapsulated in virus particles to survive prolonged space journeys and dispatched into the universe by one or more highly advanced civilizations. According to the hypothesis, the viruses, with their encoded messages, may now infect bacteria within the intestines of virtually every human being.

In 1973 Dr. Francis H. C. Crick, co-discoverer of the structure of the molecule within which the genetic messages are encoded (deoxyribonucleic acid, or DNA), suggested that such a process might have been used by advanced civilizations to disperse the seeds of life throughout the universe.

Article in Icarus

He and Dr. Leslie E. Orgel of the University of California at San Diego published this proposal in the journal Icarus under the title "Directed Panspermia." Dr. Orgel is an internationally recognized investigator of the origins of life.

The possibility that such viruses might carry messages is suggested in the current issue of Icarus by Hiromitsu Yokoo of Kyorin University and Tairo Oshima of the Mitsubishi-Kasei Institute of Life Sciences, both in Tokyo. Their attention is focused on the bacteria-infecting virus, or phage, known as PhiX-174.

DNA information is in the form of three-letter "words," or nucleotides, using an "alphabet" that consists of only four "letters" (chemical units known as bases). In 1977 British scientists, in the first complete dissection of such a phage's DNA, were able to spell out all 5,375 words of its message. Those words, grouped into "sentences" — that is genes — not only specify the chemical composition and structure of the virus but also control all its functions.

A surprising discovery was that overlapping portions of the message could be read in three different ways, each of them meaningful, depending on where the reading began.

'Difficult to Explain'

This can be compared to a telegram with no spacing between the letters that says one thing if the reader begins with the first letter and something completely different if he or she starts with the second or third letter.

As noted by the Japanese authors, "It is quite difficult to explain the origin and evolution of overlapping genes in terms of molecular evolution." For this reason ent happens to be aiming an antenna at the sender at the correct time and radio frequency. A phage, if it dropped into a suitable environment, would replicate. In this way, the Japanese say, "biological messages can be automatically copied and cover the entire planet."

They would persist until the evolution of intelligent life and, finally, of investigators interested in the genetics of phages. A phage like PhiX-174 would be one of the first deciphered because it is one of the simplest. Even such primitive organisms as bacteria depend on DNA messages that may run to millions of nucleotides.

Drawbacks as Messengers

The authors concede drawbacks to viruses as messengers. They must reach a planet whose biochemical environment is suited to the virus. Furthermore, the encoded message must survive numerous replications without becoming so altered by mutation as to destroy the message.

PhiX-174 replicates only through infection of intestinal bacteria (Escherichia coli), but it is structurally similar to other phages, all of which, the two Japanese suggest, may have evolved from a common ancestor of extraterrestrial origin.

The Japanese analysis has been based on a communication strategy favored by a number of American scientists interested in the problem and used in demonstration transmissions from the giant antenna at Arecibo, P.R.

This consists of using two signals to transmit a message whose total number of signals is a multiple of two prime numbers, such as 31 and 41. The recipient is expected to guess that the message should be displayed like a television picture made up of 31 rows, each formed of 41 dots or spaces (as specified by the signals), or of 41 lines of 31 signals.

One or the other of these arrangements would form a meaningful picture.

Various Arrangements Tried

In the overlapping sequences of PhiX-174 the investigators have found one of 121 three-letter units — a multiple of 11 times 11. They have tried various arrangements consisting of 11 lines of 11, displaying the four letters of the DNA alphabet as four colors. This, they hoped, would produce some clearly artificial signal, such as a cross, that might have survived long-term changes in the DNA sequence.

"Unfortunately," they report, "no significant pattern was observed." However, they add, "Further speculation is irresistible." Other coding sequences in PhiX-174 add up to the products of prime numbers, such as one of 91 units (7 times 13), which so far has proved uninstructive, and another of 533 letters (13 times 41) which has not yet been tested.

"We consider this exercise a prototype

HENRY SCHULTZ DIES; HEADED CIVIC GROUP

Leader of Anti-Defamation League in Era of Senator McCarthy

Henry E. Schultz, a retired national chairman of the Anti-Defamation League of B'nai B'rith and a former member of the New York City Board of Higher Education, died Saturday at the Miami Heart Institute in Miami. He was 72 years old and lived in Miami Beach.

Mr. Schultz had been recently employed as a consultant to the J. B. Williams Company, where he was legal counsel from 1960 until 1975. Prior to 1960 he maintained a private practice as an attorney.

As chairman of the Anti-Defamation League from 1952 until 1963, Mr. Schultz was in charge of its affairs during the tense years of public debate over the question of Communism in American institutions. He was credited with maintaining a necessary centrist policy for the organization, according to Nathan C. Belth, a writer and a league staff member during Mr. Schultz's tenure.

As a member of the Board of Higher Education from 1941 to 1969, Mr. Schultz "had been through the Communist wars on City College campuses," Mr. Belth said.

Questioned Senator McCarthy

"He put the question of anti-Semitism" to Senator Joseph R. McCarthy "directly in a personal meeting and came away with the feeling that the Senator was not an anti-Semite," Mr. Belth said. But, he added, Mr. Schultz " noted the Senator's methods injured many of our Democratic institutions."

Mr. Schultz presided over the league in 1953 when it presented the Democratic Legacy Award to President Eisenhower. It was during that dinner, held in Washington, that the Mr. Eisenhower made his famous speech citing the "right of every man to meet his accuser face to face." The speech was considered a signal event in an eventual campaign against Senator McCarthy's tactics.

Mr. Belth said, however, that Mr. Schultz "was concerned about the extreme left, too."

In October 1947, during his membership on the Board of Higher Education, Mr. Schultz was strongly opposed by deans, administrators and faculty members of the city's four city colleges for his role in proposing an amendment to bar so-called subversive groups from speaking on campuses.

Mr. Schultz, who was born in New York City, earned his legal degree from New York Law School in 1928. An honorary doctorate in the humanities was presented to him in 1961 by West Virginia State College.

He was a member of the executive

Bernard Leach, 92, Noted Potter; Briton Learned From Japanese

Special to The New York Times

LONDON, May 6 — Bernard Leach, an internationally renowned potter, died at his home in St. Ives, Cornwall, today. He was 92 years old.

Much of his work was infused with an Oriental delicacy. The quiet simplicity of form of his pieces are nowhere more appreciated than in Japan, where for years he lived and worked.

He was conscious of his debt to the Oriental potters; to him, the greatest compliment was to have his work compared to the Chinese pottery of the Sung dynasty of 700 years ago.

Mr. Leach was born in Hong Kong, the son of a colonial judge, and studied art at the Slade School in London. His father, he recalled, looked askance at his artistic ambitions, but did nothing to discourage them.

Mr. Leach traveled widely in China and Japan in his early 20's. In Japan he studied under Ogata Kenzan, a famous potter who had inspired him to take up the art.

Initial Enthusiasm Recalled

When in his 80's and almost blind, Mr. Leach, a tall, amiable man, recalled his initial enthusiam, "My first child was born and I was torn between my first child and my first kiln," he said

The first pots he made sold for the equivalent of 25 cents. He progressed artistically and materially fairly quickly and he recalled how his prices increased with each of his exhibitions.

On his return to England from Japan in 1920, he settled in St. Ives, a small seaside resort, and with the help of a gifted Japanese potter, Shoji Hamada, founded The Leach Pottery there. It is still producing pots with Mr. Leach's son David in charge. Mr. Hamada, described by Mr. Leach as "my perfect friend," died in Japan in January 1978 at the age of 83.

In the pottery at St. Ives only 10 percent of the first year's production of 2,000 to 3,000 pieces survived. Twenty percent, Mr. Leach recalled, was broken in the kiln and the rest was scrapped because it was below his standard.

At the height of his endeavors, about 30,000 pieces a year were produced by Mr. Leach and his workers. Most were of the 60 to 70 shapes he used for objects such as casseroles, jugs and jam pots.

Honored for His Work

In "A Potter's Book" published in 1940, one of several books he wrote on pottery, he complained that English collectors were quick to reject work with minor blemishes even when the artistic merit was not affected. "It is a pity people in England are so fussy about technical imperfections," he wrote, observing that a blot from a quill on a Rembrandt drawing would not cause it to be cast aside.

The Times of London summed up a comprehensive collection of Mr. Leach's work by saying, "Ultimately his productions are to be judged not as objects of some utility or even as so many agreeable pieces of decoration with technical felicities of glaze, color and shape (though these are certainly to be found) but fundamentally as a translation of 'familiar virtues' into stoneware or porcelain."

He was honored for his work in the United States, Japan and Britain. In 1973 Queen Elizabeth II made him a Companion of Honor "for services to the art of pottery."

The following year when he won a $14,000 prize awarded by the Japan Foundation, Hidemi Kon, the foundation's president, described him as "the most distinguished ceramics artist the world has today."

Mr. Leach is survived by three sons and three daughters. His third wife is the American-born Janet Darnell, one of the leading potters in Britain.

Camera Press

Bernard Leach

Col. Robert Heinl Jr.; Columnist and Author Of History of Marines

Special to The New York Times

WASHINGTON, May 6 — Robert D. Heinl Jr., a retired colonel in the United States Marine Corps and a former syndicated columnist and author, died of a heart attack yesterday in Saint Barthélemy, a Caribbean island. He was 62 years old.

Colonel Heinl was appointed chief of the United States naval mission to Haiti in January 1959 and served until he was ordered to leave the country by former Haitian President, François Duvalier, on Feb. 20, 1963. The dictator's order came

MARY LOUISE GILLERAN

Mary Louise Gilleran, an administrative assistant to the Metropolitan New York Chapter of the American Red Cross, died Thursday at Roosevelt Hospital at the age of 61.

Mrs. Gilleran had worked for the agency for nearly a year and was previously employed as an administrator for the American Field Service. Born in Chicago, she attended Southern Seminary in Buena Vista, Va. She had been a New York City resident for the past 40 years.

Mrs. Gilleran is survived by her husband, Robert J. Gilleran, circulation manager for Family Circle magazine, and her daughter, Marianne.

Deaths

AHRENS—Jane M., on Sunday, May 6, 1979, beloved wife of the late Walter, devoted mother of Diane N. Marino, Mary J. Hibbard, the late Dennis M., Ellen E., Anne F. Delgado, J. Eileen Zane and Lucy L. Ahrens. Loving sister of James G. Murray. Also survived by 16 grandchildren. Reposing at the Macken Mortuary, 92 Clinton Ave., Rockville Centre, N.Y. Mass of the Resurrection St. Agnes Cathedral, Tuesday, May 8, 8 PM. Interment Holy Rood Cemetery, Westbury, N.Y., private. Family will receive friends Monday, 2-5 and 7-9 PM, and Tuesday, 2-5 PM.

BALANOFF—Mischa, husband of the late Nina Balanoff, father of Barbara Pasternack and the late Sonia Goodman, grandfather of Steven Arcane, Michael and Jonathan Pasternack, great-grandfather of Alex and Anthony Arcane. Services at the Gramercy Park Chapel, 2nd Ave. and 9th St., Tuesday, May 8, 1 PM.

BERTELL—Rae. Beloved wife of John (Sam), adored sister of Irene Walters, William, Teddy, and Joe Sieves, dearest aunt and great aunt. Services Monday 2:30 P.M. Schwartz Brothers "Forest Park Chapels" Queens Boulevard and 76th Road, Forest Hills.

BULLARD—Annie Adams Sharpes. In Fairfield, Connecticut, May 3, 1979. Of 482 Mill Plain Road. Mother of

Deaths

Ahrens, Jane
Balanoff, Mischa
Bertell, Rae
Bullard, Annie
Burden, James
Chasen, Robert
Diamond, Max
Feig, Minnie
Gleichenhaus, B.
Godnick, Richard
Green, Leo
Grishaver, A.
Gruen, Margaret
Homelsky, Frank
Jacobs, Beatrice
Kasfein, Julius
Katz, Charles
Katz, Nina
Koppel, Helen
Lagazio, Kate
Langsner, Ann
Meizer, Morris
Moseley, Mary
Moss, Ethel
Newmark, Estelle
O'Brien, Richard
Perryman, Curtis
Polk, Lois
Pollitt, Leanore
Reckeweg, George
Rizzi, Juliette
Ryan, Mary
Savedoff, A.
Schultz, Henry
Sheeler, Charles
Smith, Walter
Sze, Deson
Weinberger, Viola
Ziegler, Belle

JACOBS—Beatrice Edith Moore, passed away at State University Hospital of Downstate Medical Center, Saturday, May 5, 1979. A solemn Mass of the Resurrection in thanksgiving of her life will be offered at St. Augustine's Episcopal Church,

Deaths

POLLITT—Leanore Levine. Our deepest expression of sympathy to Basil and Katha Pollitt, Belle and Joseph Levine and Zeena Kaswel, wife of our President, on the untimely death of Lee, beloved wife, mother, daughter, and sister. To the family we extend our heartfelt condolences.
Management Flushing-Zeger, Inc.

RECKEWEG—George Otto, 71 years old, died at his residence on Sunday morning May 6th. Was a native of Germany and a retired building manager in NYC, a member of the Daniel Carpenter Lodge F&AM, NYC, and the Building Managers Assoc. NYC. Survived by wife Mary Stoddart Reckeweg, one daughter, Mrs. Gerrit Schroeder, also two grandchildren. Funeral will be at 8 PM Monday May 7th at the Highlands Funeral Home, Louisville, Ky. Cremation will follow.

RIZZI—Juliette Medved, on May 5, 1979, wife of Charles A., mother of Charles Andrew and Alfred Anthony, sister of Mrs. Helen M. Krinka and Mrs. D. Marguerite Sarracino, aunt of niece and nephews. Interment and services private. Kindly make contributions to the New York Medical College, Valhalla, N.Y.

RYAN—Mary. Reposing at Williams Funeral Home, Broadway at 233 St., Bronx, until Tuesday, 10:30 AM.

Directed Panspermia

F. H. C. CRICK

Medical Research Council, Laboratory of Molecular Biology, Hills Road, Cambridge, England

AND

L. E. ORGEL

The Salk Institute for Biological Studies, P.O. Box 1809, San Diego, California 92112

Received June 22, 1972; revised December 20, 1972

It now seems unlikely that extraterrestrial living organisms could have reached the earth either as spores driven by the radiation pressure from another star or as living organisms imbedded in a meteorite. As an alternative to these nineteenth-century mechanisms, we have considered Directed Panspermia, the theory that organisms were deliberately transmitted to the earth by intelligent beings on another planet. We conclude that it is possible that life reached the earth in this way, but that the scientific evidence is inadequate at the present time to say anything about the probability. We draw attention to the kinds of evidence that might throw additional light on the topic.

Introduction

It was not until the middle of the nineteenth century that Pasteur and Tyndall completed the demonstration that spontaneous generation is not occurring on the Earth nowadays. Darwin and a number of other biologists concluded that life must have evolved here long ago when conditions were more favourable. A number of scientists, however, drew a quite different conclusion. They supposed that if life does not evolve from terrestrial nonliving matter nowadays, it may never have done so. Hence, they argued, life reached the earth as an "infection" from another planet (Oparin, 1957).

resistant spore would receive so large a dose of radiation during its journey to the Earth from another Solar System that it would be extremely unlikely to remain viable. The probability that sufficiently massive objects escape from a Solar System and arrive on the planet of another one is considered to be so small that it is unlikely that a single meteorite of extrasolar origin has ever reached the surface of the Earth (Sagan, private communication). These arguments may not be conclusive, but they argue against the "infective" theories of the origins of life that were proposed in the nineteenth century.

It has also been argued that "infective"

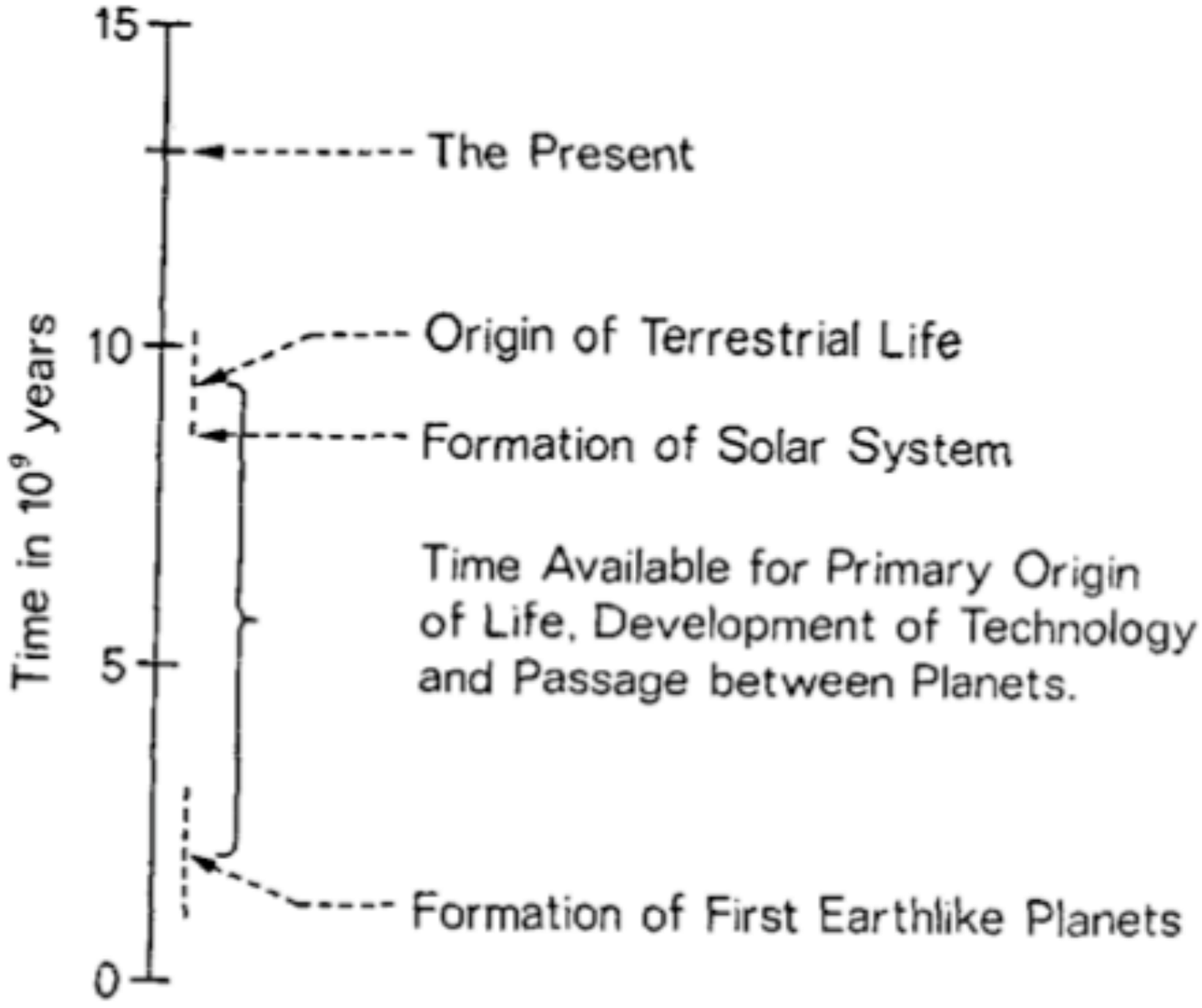


FIG. 1. An approximate time-scale for the events discussed in the paper. To simplify illustration the age of the galaxy has been somewhat arbitrarily taken as 13×10^9 yr.

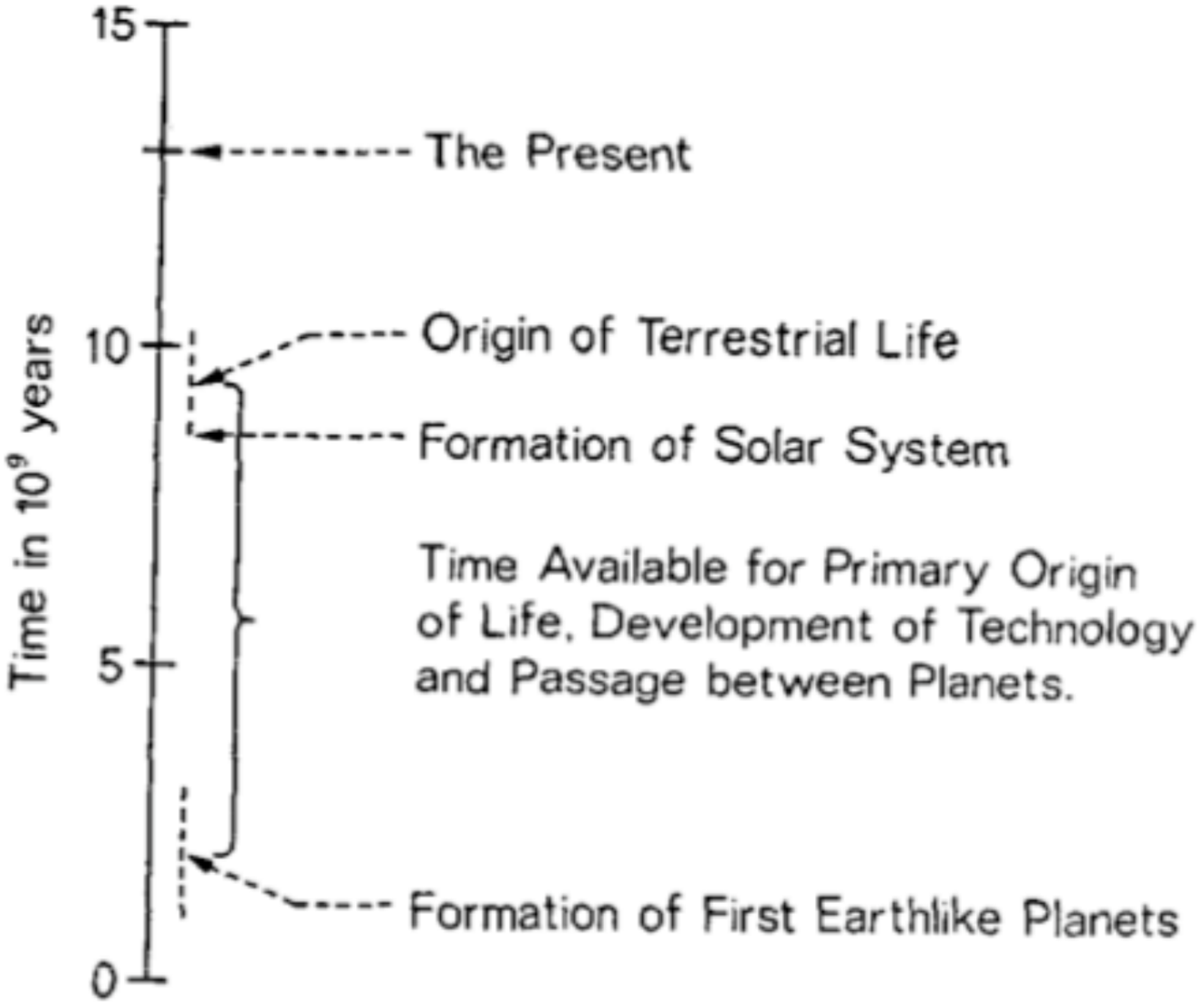
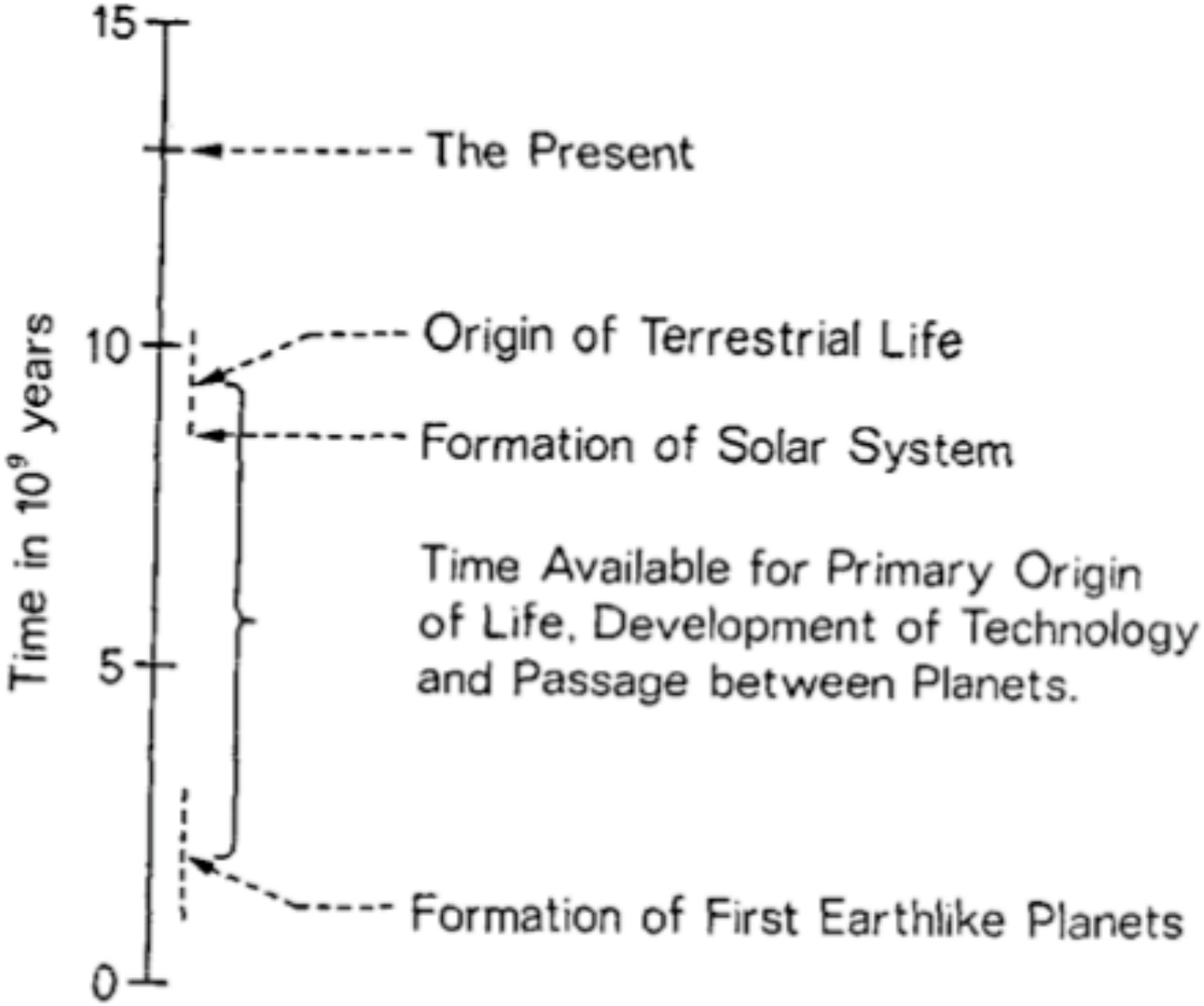


FIG. 1. An approximate time-scale for the events discussed in the paper. To simplify illustration the age of the galaxy has been somewhat arbitrarily taken as 13×10^9 yr.

THE PROPOSED SPACESHIP

The spaceship would carry large samples of a number of microorganisms, each having different but simple nutritional requirements, for example blue-green algae, which could grow on CO_2 and water in "sunlight." A payload of 1000 kg might be made up of 10 samples each containing 10^{16} microorganisms, or 100 samples each of 10^{15} microorganisms.



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It would not be necessary to accelerate the spaceship to extremely high velocities, since its time of arrival would not be important. The radius of our galaxy is about 10^5 light years, so we could infect most planets in the galaxy within 10^8 yr by means of a spaceship traveling at only one-thousandth of the velocity of light. Several thousand stars are within a hundred light years of the Earth and could be reached within as little as a million years by a spaceship travelling at only 60,000 mph, or within 10,000 yr if a speed of one-hundredth of that of light were possible.

ICARUS 38, 148–153 (1979)

Is Bacteriophage ϕX174 DNA a Message from an Extraterrestrial Intelligence?

HIROMITSU YOKOO* AND TAIRO OSHIMA†

*Department of Physics, School of Medicine, Kyorin University Hachioji, Tokyo 192, Japan and
†Mitsubishi-Kasei Institute of Life Sciences, Machida, Tokyo 194, Japan

Received May 22, 1978; revised August 30, 1978

We speculate that a simple biological system carrying a message and capable of self-replication in suitable environments may be one possible channel for interstellar communication. A preliminary experiment was performed to test the hypothesis that phage ϕX174 DNA carries a message from an advanced civilization.

Electromagnetic waves are generally accepted as the best medium for interstellar communication (Cocconi and Morrison, 1959; Bracewell, 1960; Drake, 1961; Cameron, 1963; Shklovskii and Sagan, 1966; Oliver and Billingham, 1971; Ponnamperuma and Cameron, 1974; Black *et al.*, 1977), and little attention has been paid to other information transfer systems. So far, 13 projects have been devoted to the search for radio signals which might be transmitted to us by other civilizations (Black *et al.*, 1977). Numerous discussions have also been devoted to the appropriate receiving systems and frequencies to be used. However no scientific attempt seems to have been made to search for messages from extraterrestrial intelligence (ETI) by media other than electromagnetic radiations.

The purpose of this paper is to stress that biological media should not be neglected as possible information exchange systems between interstellar civilizations, and to encourage the examination of certain living systems. A preliminary effort has been made to investigate whether or not phage ϕX174 DNA carries a message

A BIOLOGICAL MEDIUM

It might be possible that a civilization more advanced than ours prepares an artificial or artificially modified phage (or bacterial) DNA which is capable of proliferating actively under suitable conditions and at the same time carries an intelligent message encoded in its base sequence. Biochemistry on our planet is still not advanced enough to synthesize such sophisticated biomolecules, but, judging from the recent progress in biological sciences, it is most likely that our civilization will gain enough information to carry out such a project within a few decades. It has already been suggested that there is no technical difficulty in sending a phage or microorganism to other stars (Crick and Orgel, 1973). The message-carrying particles encapsulated for safety can easily be launched to other stars directionally or isotropically by a civilization such as ours.

Biological media have certain advantages over electromagnetic waves. The phage or microorganism carrying the message can self-replicate after arriving on an appropriate planet. Unlike long distance tele-

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Hmm....
~1E31 phage per Earth...

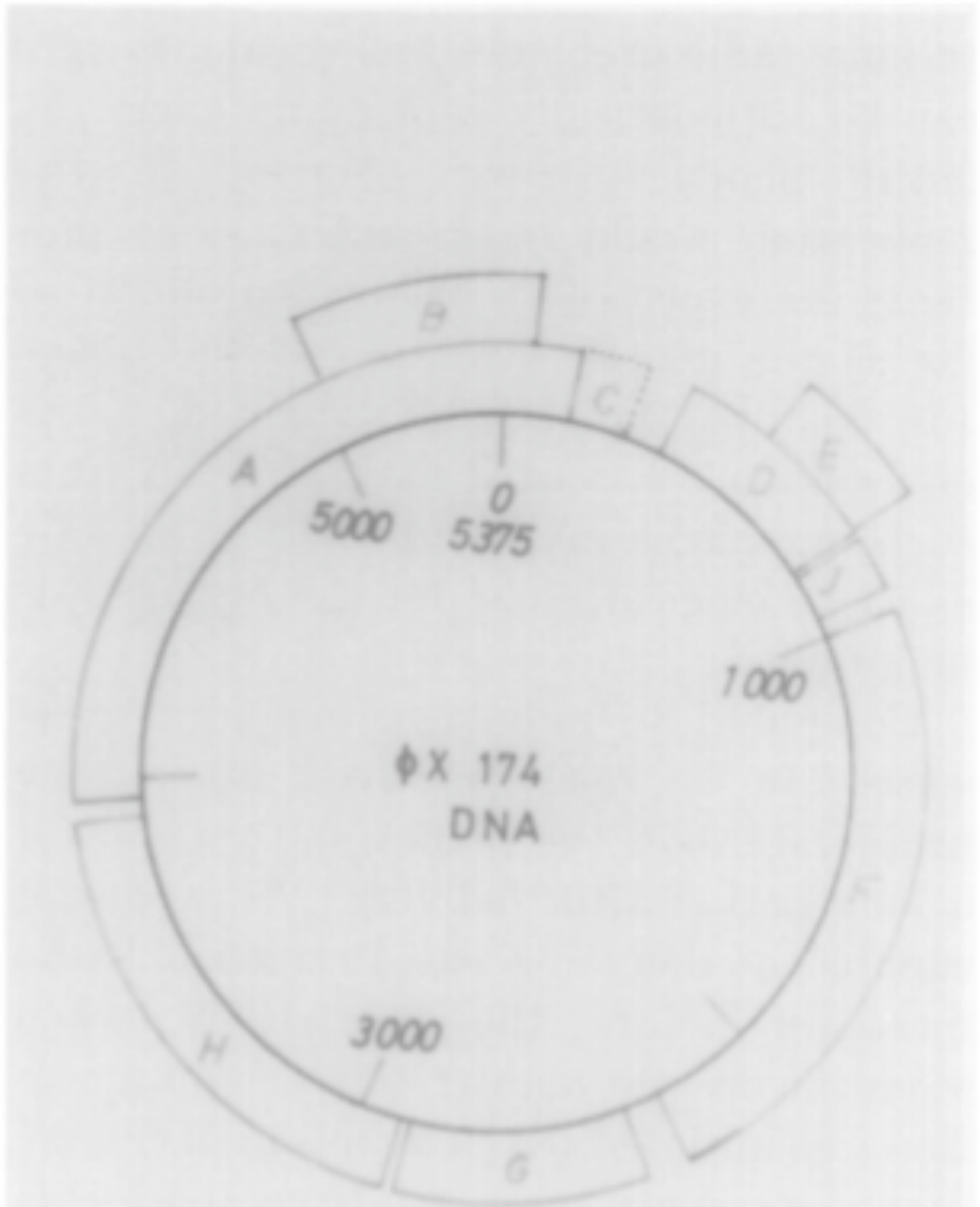
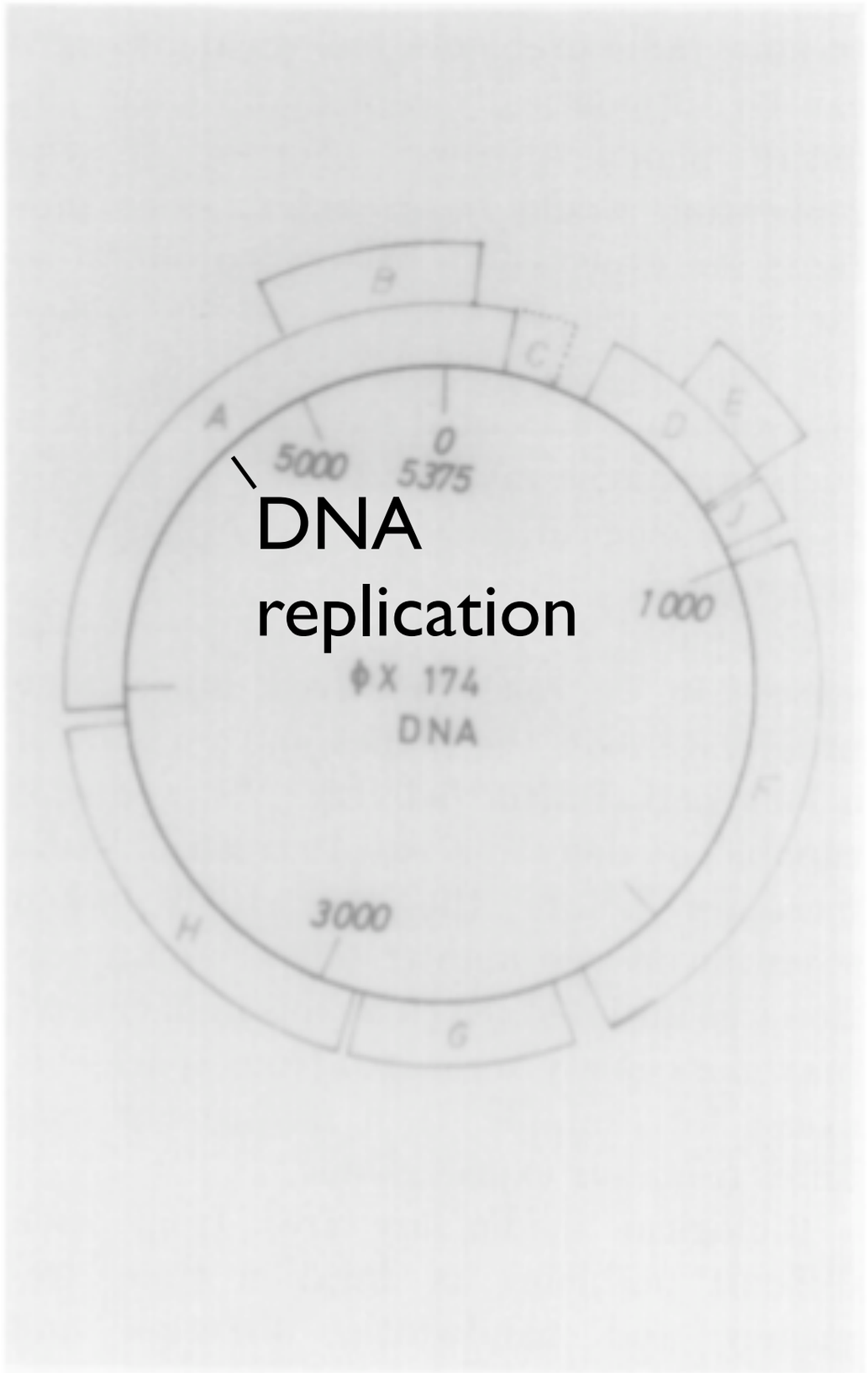


FIG. 1. Genetic structure of ϕ174 DNA, modified after a figure appearing in Sanger *et al.*, (1977).



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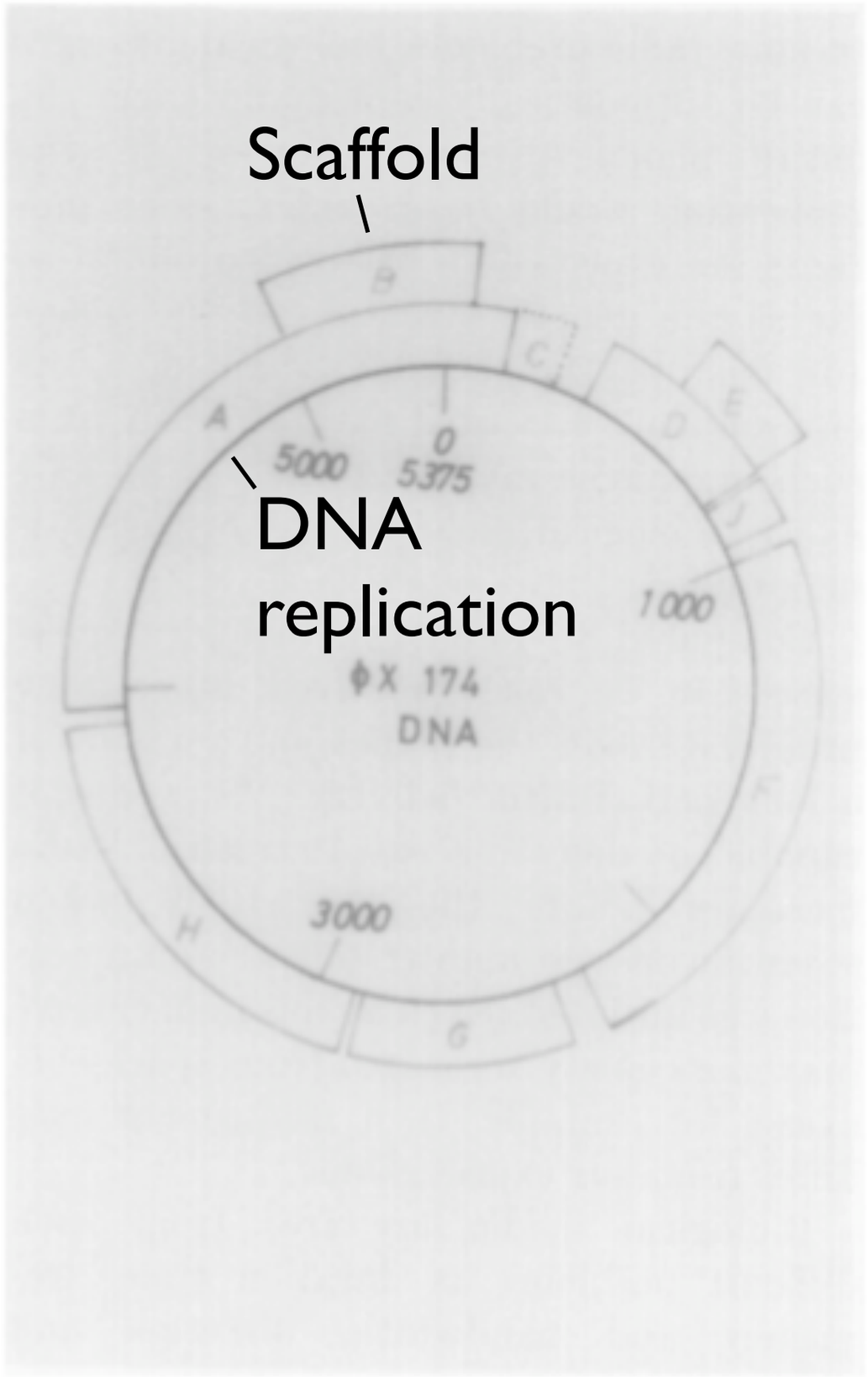

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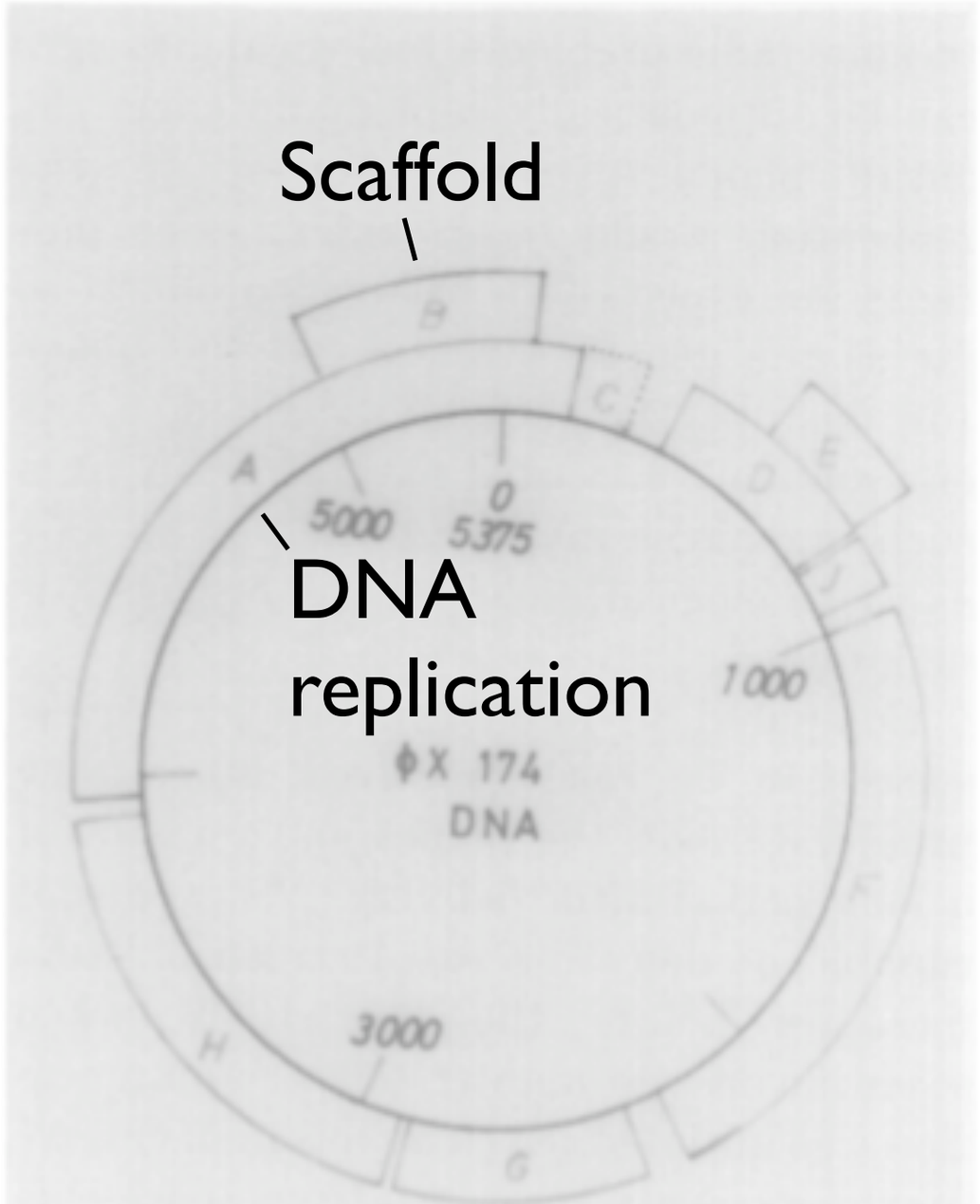

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GAA	TGG	AAC	AAC	TCA	CTA	AAA	ACC	AAG	CTG	TCG
CTA	CTT	CCC	AAG	AAG	CTG	TTC	AGA	ATC	AGA	ATG
AGC	CGC	AAC	TTC	GGG	ATG	AAA	ATG	CTC	ACA	ATG
ACA	AAT	CTG	TCC	ACG	GAG	TGC	TTA	ATC	CAA	CTT
ACC	AAG	CTG	GGT	TAC	GAC	GCG	ACG	CCG	TTC	AAC
CAG	ATA	TTG	AAG	CAG	AAC	GCA	AAA	AGA	GAG	ATG
AGA	TTG	AGG	CTG	GGA	AAA	GTT	ACT	GTA	GCC	GAC
GTT	TTG	GCG	GCG	CAA	CCT	GTG	ACG	ACA	AAT	CTG
CTC	AAA	TTT	ATG	CGC	GCT	TCG	ATA	AAA	ATG	ATT
GGC	GTA	TCC	AAC	CTG	CAG	AGT	TTT	ATC	GCT	TCC
ATG	ACG	CAG	AAG	TTA	ACA	CTT	TCG	GAT	ATT	TCT

FIG. 2. One hundred and twenty one triplet codons from the A protein reading frames, which are utilized in overlap to code the B protein. The B protein, composed of 120 amino acid residues, is coded by this sequence except for the first two and the last nucleotide bases (Sanger *et al.*, 1977). The four DNA nucleotides are represented by their conventional symbols, A, G, C, and T.

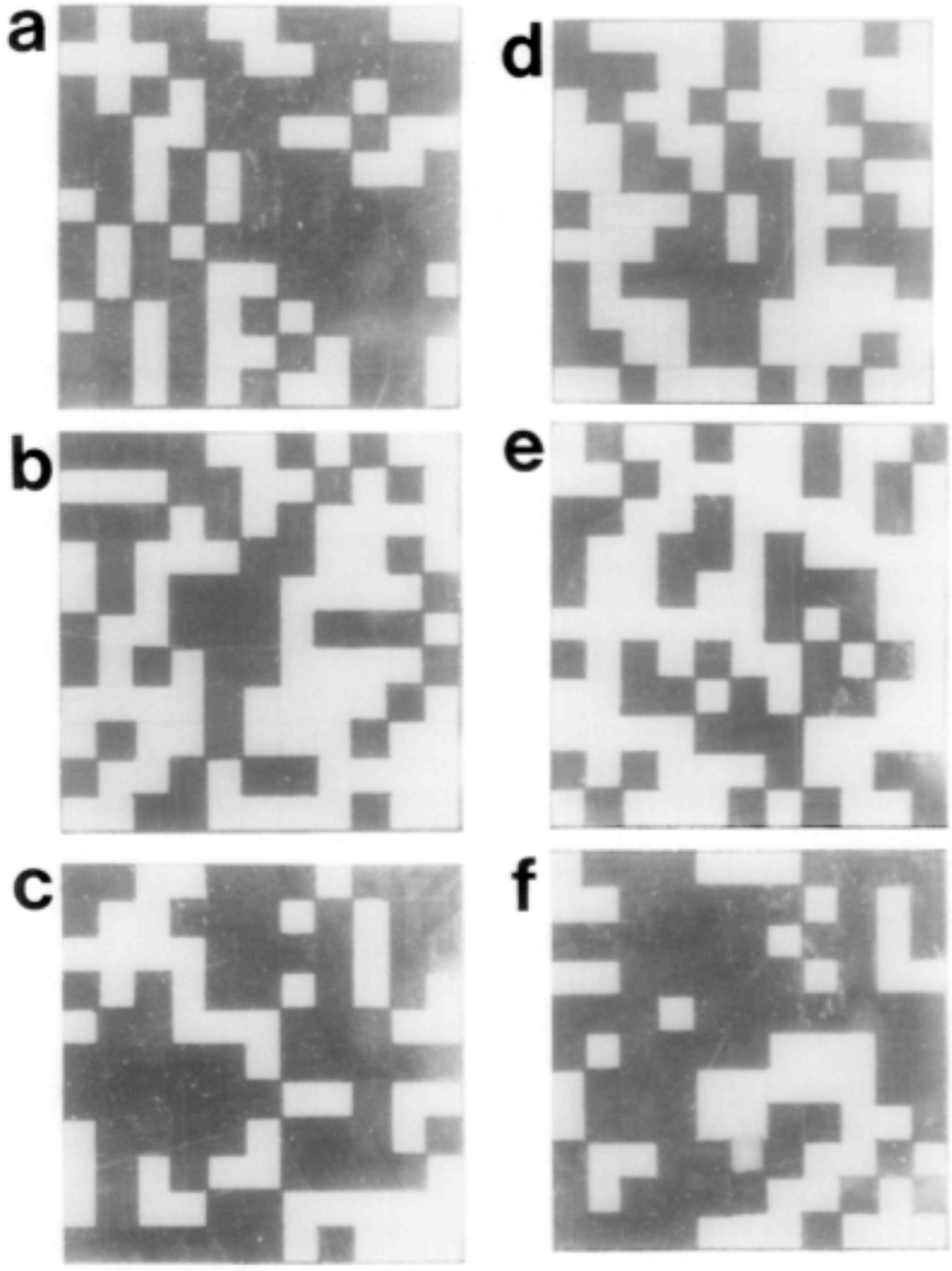
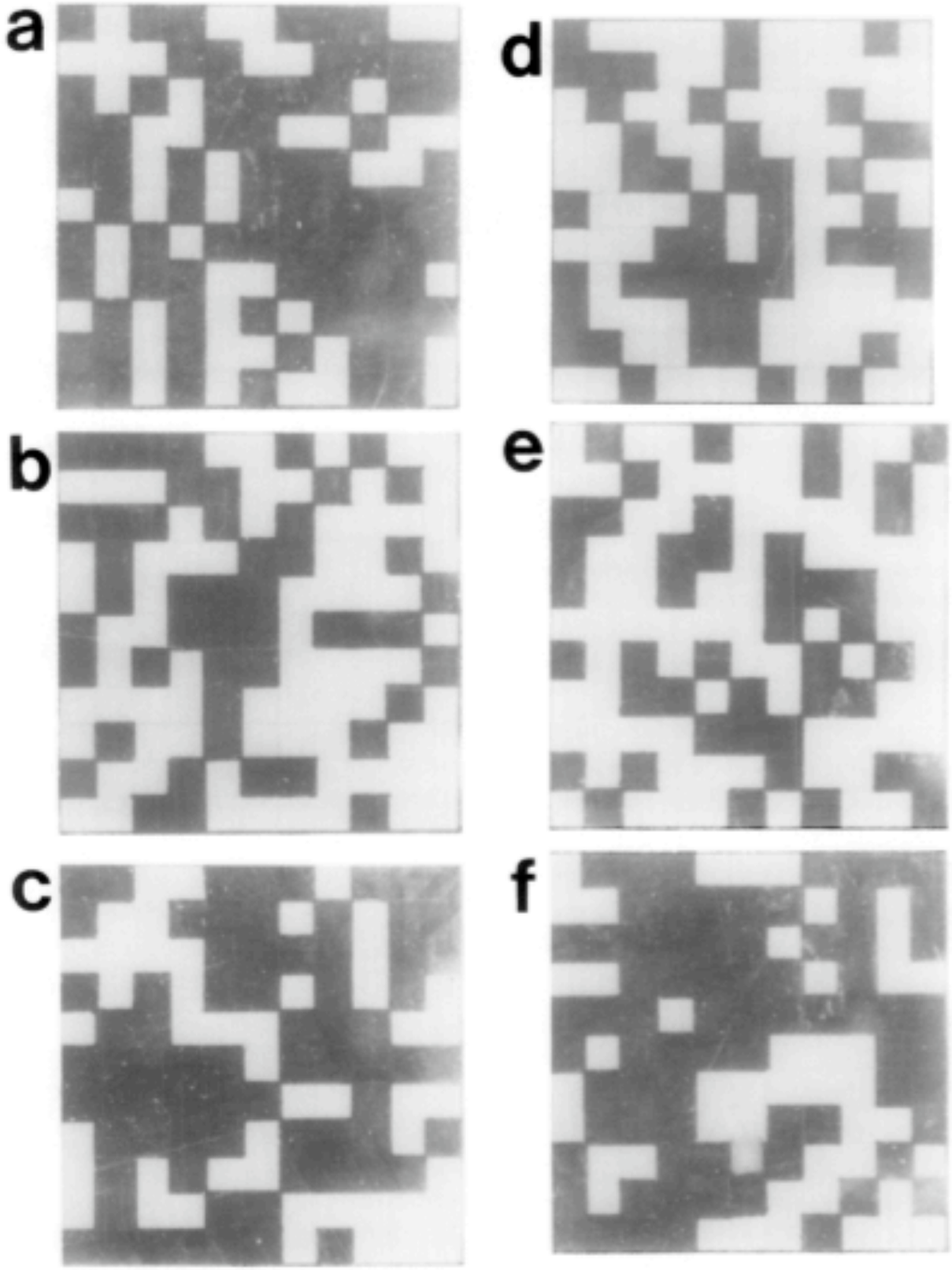


FIG. 3. Possible two-dimensional pictures constructed from the sequence listed in Fig. 2. The first (a, d), second (b, e), and third (c, f) nucleotides were arranged in 11 × 11 arrays, respectively. These letters were put in order from top left to bottom right as in writing an English sentence. In pictures a–c, dark squares were given to purine bases; in d–f, guanine and cytosine were assigned dark squares.



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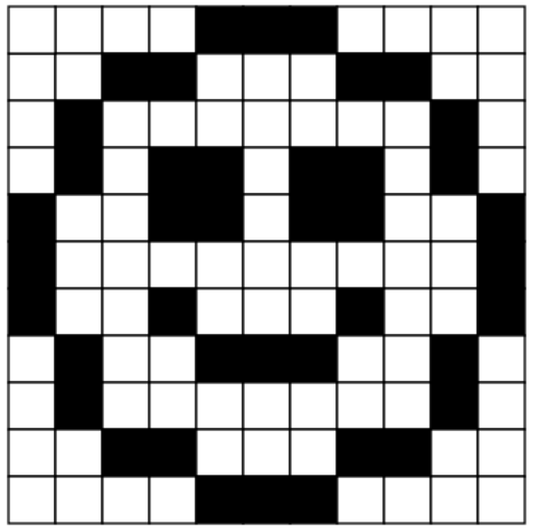
Could you code...



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Article Type: Special Issue: Viruses of Microbes

Section/Category: 10 Genomes & Evolution

Keywords: refactoring; bacteriophage øX174; yeast; recombination; synthetic biology; genome engineering; synthetic genomics; DNA assembly; irreducible complexity; overlapping genes

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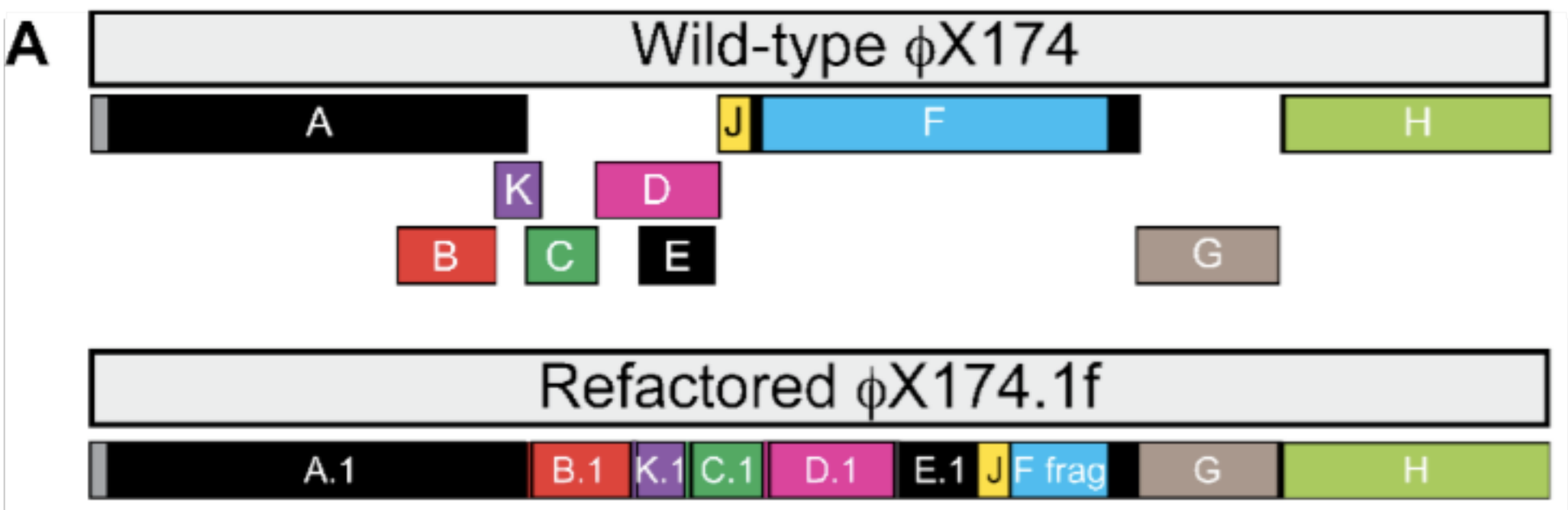
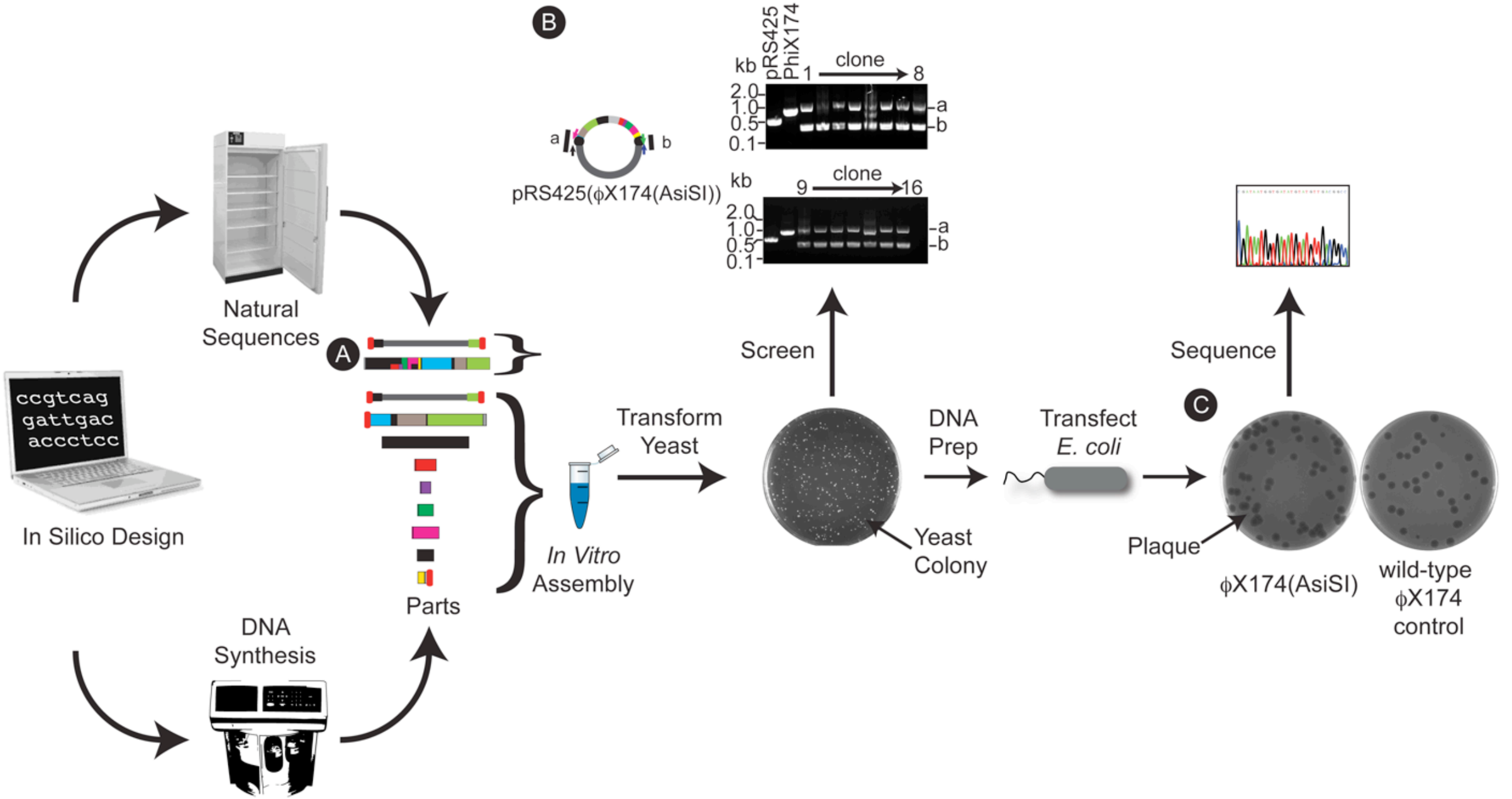
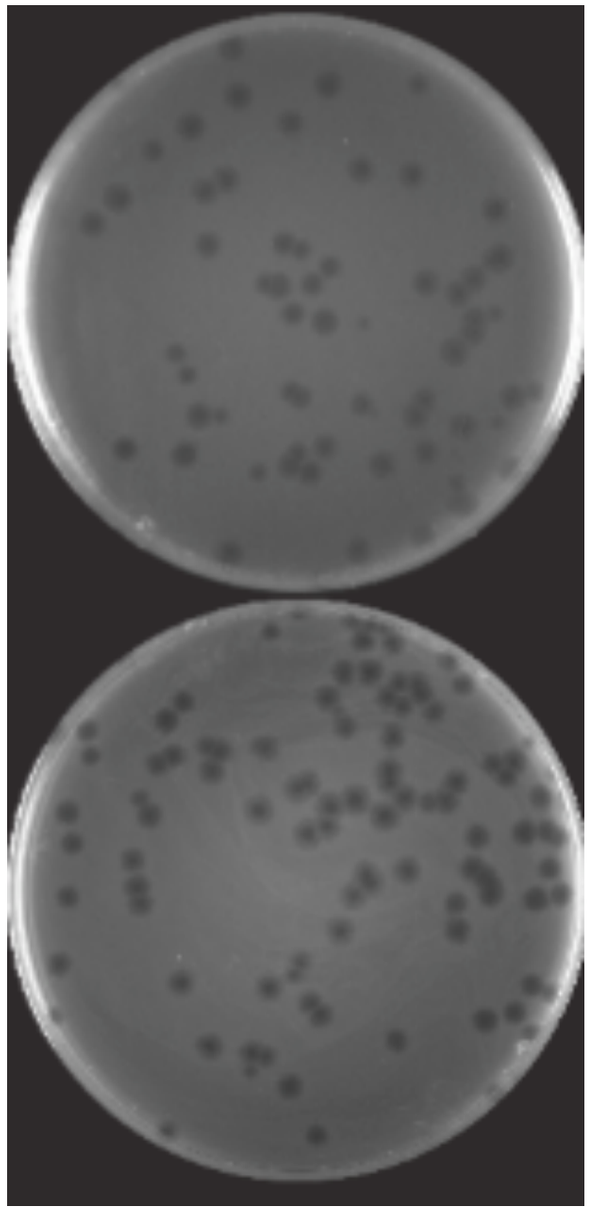


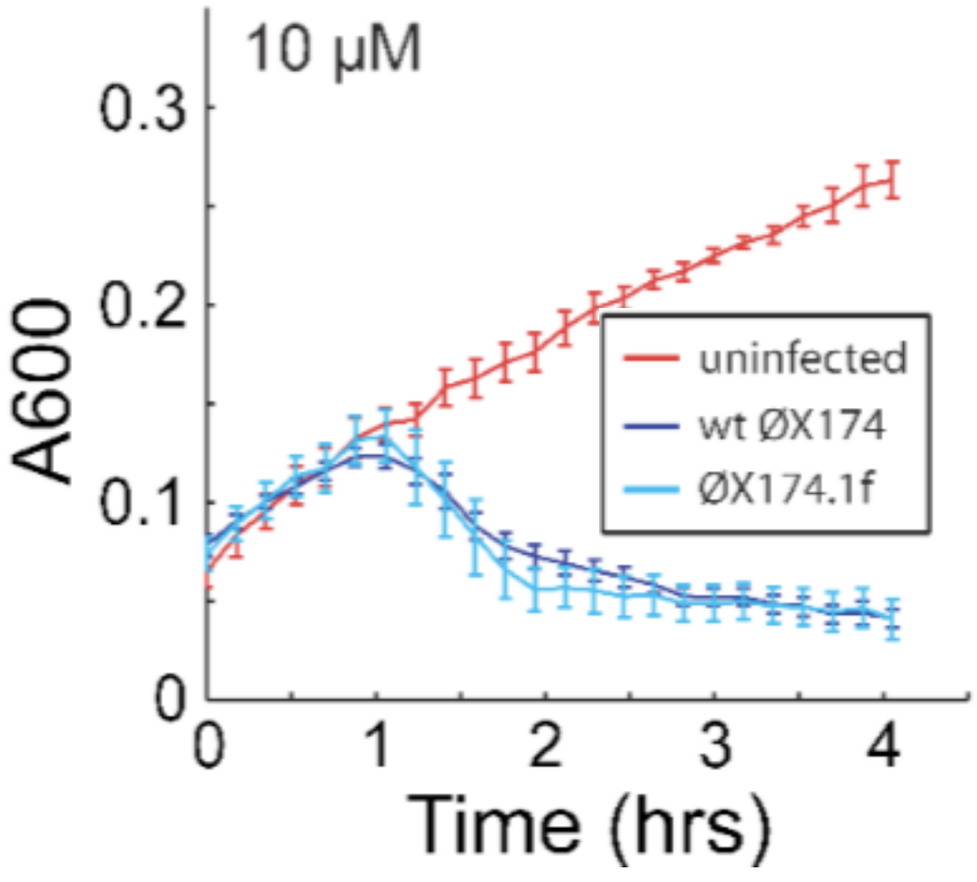


Jaschke et al., in press

wild type
ϕX174

refactored
ϕX174.1f





Jaschke et al., in press

øX174 is known to have 11 CDSs.

However, analysis suggests ~82 ORFs of length 30+ codons with putative RBSs...

Going to try exploring "reverse negative" genomics.

"No matter who you are, most of the smartest people work for someone else" - Bill Joy (?)

http://www.andyross.net/bill_joy.htm

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"No matter who you are, most of the best biotechnology ideas will be imagined and made true by someone else"

So what do you (we) do about it?