CENTRO DE CIENCIAS DE BENASQUE PEDRO PASCUAL

Fronteras de la Computación

Advances in Synthetic Biology toward Biological Computers

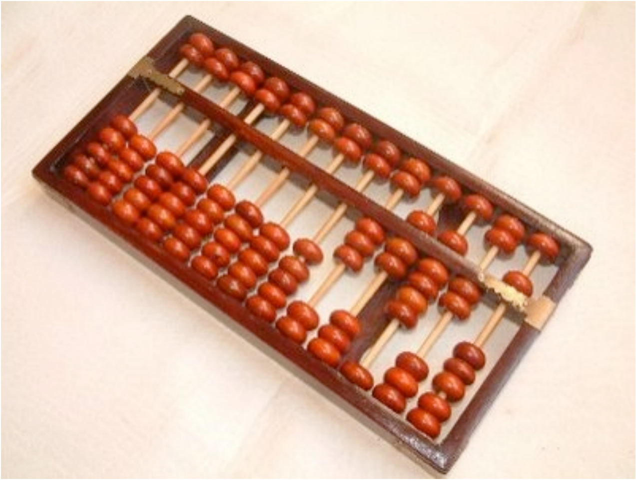
UNIVERSITAT POMPEU FABRA

Javier Macía Santamaría

Laboratorio de Sistemas Complejos.

Benasque 2011.

Computation with different devices



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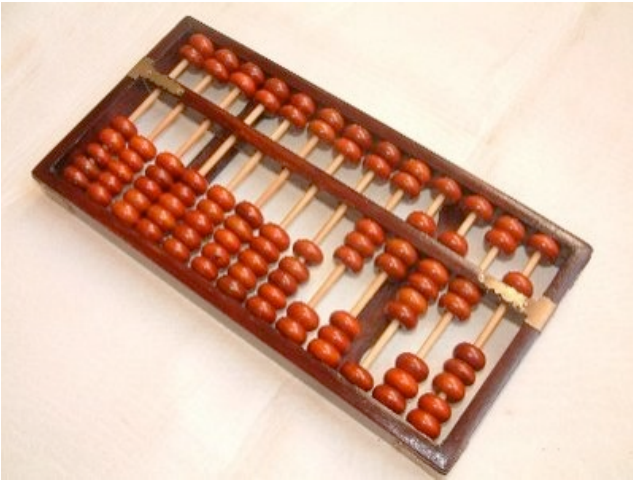

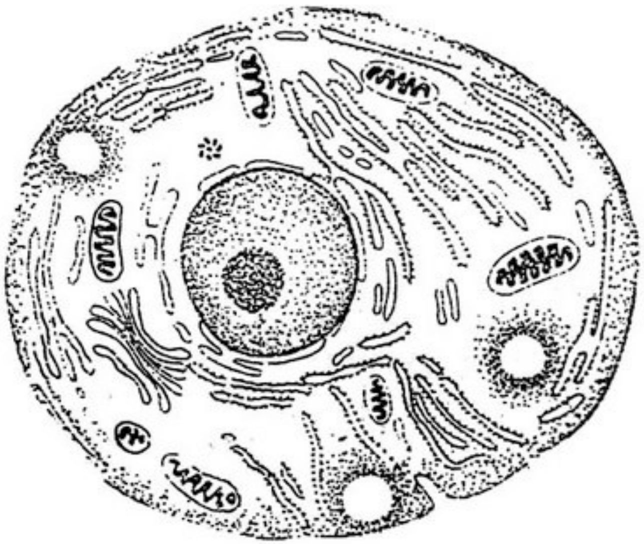

What is a Biological Computer?

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The Free Encyclopedia

Main page
Contents

Biocomputers

From Wikipedia, the free encyclopedia

Biocomputers use systems of biologically derived molecules, such as DNA and proteins, to perform computational calculations involving storing, retrieving, and processing data.

Applications of Cellular Computation

- Clean hazardous waste

RESEARCH REVIEW

INTERNATIONAL MICROBIOLOGY (2005) 8:213-222
www.im.microbios.org

INTERNATIONAL MICROBIOLOGY

Ildefonso Cases[1]
Víctor de Lorenzo[1,2*]

[1]National Center for Biotechnology, CSIC, Madrid, Spain
[2]Center for Astrobiology, INTA-CSIC, Madrid, Spain

Genetically modified organisms for the environment: stories of success and failure and what we have learned from them

Summary. The expectations raised in the mid-1980s on the potential of genetic engineering for in situ remediation of environmental pollution have not been

Applications of Cellular Computation

- Clean hazardous waste
- Use plants to sense chemicals

Letters

Cultivating plant synthetic biology from systems biology

Tessa A. Bowen†, Jeffrey K. Zdunek† and June I. Medford*
Department of Biology, 1878 Campus Delivery, Colorado State University, Fort Collins, CO 80523-1878, USA

(*Author for correspondence: tel +1 970 491 7865; fax +1 970 491 0649; email June.Medford@colostate.edu)

†These authors contributed equally to this work

Applications of Cellular Computation

- Clean hazardous waste
- Use plants to sense chemicals
- Clean fuel

Defossiling Fuel: How Synthetic Biology Can Transform Biofuel Production

David F. Savage[†], Jeffrey Way[‡], and Pamela A. Silver[†,*]

[†]Department of Systems Biology, Harvard Medical School, Boston, Massachusetts 02115 and [‡]EMD Serono Lexigen Research Center, Billerica, Massachusetts 01821

Applications of Cellular Computation

- Clean hazardous waste
- Use plants to sense chemicals
- Clean fuel
- Recognize and destroy tumors

doi:10.1016/j.jmb.2005.10.076

J. Mol. Biol. (2006) 355, 619–627

JMB

Available online at www.sciencedirect.com

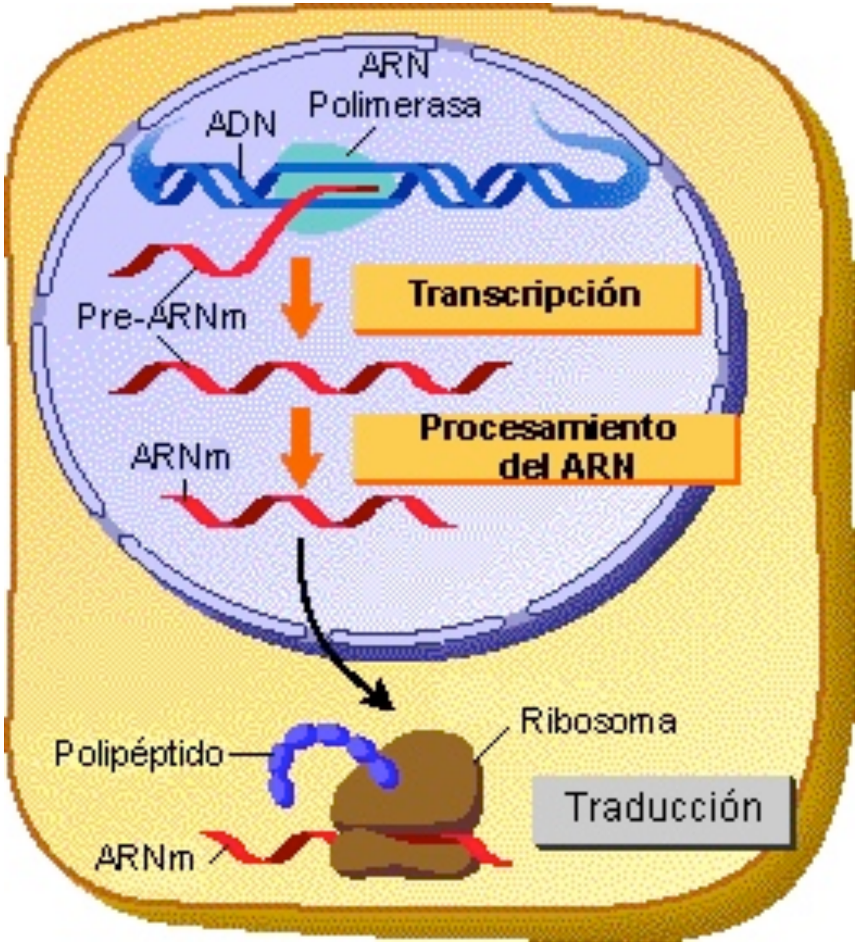
SCIENCE DIRECT

ELSEVIER

Environmentally Controlled Invasion of Cancer Cells by Engineered Bacteria

J. Christopher Anderson[1,3], Elizabeth J. Clarke[3], Adam P. Arkin[1,2*] and Christopher A. Voigt[2,3]

Gene Transcription Mechanisms



Gene Transcription manipulations

- **Transcriptional regulations**: Activation and inhibition using Transcription Factors (TF).

Gene Transcription manipulations

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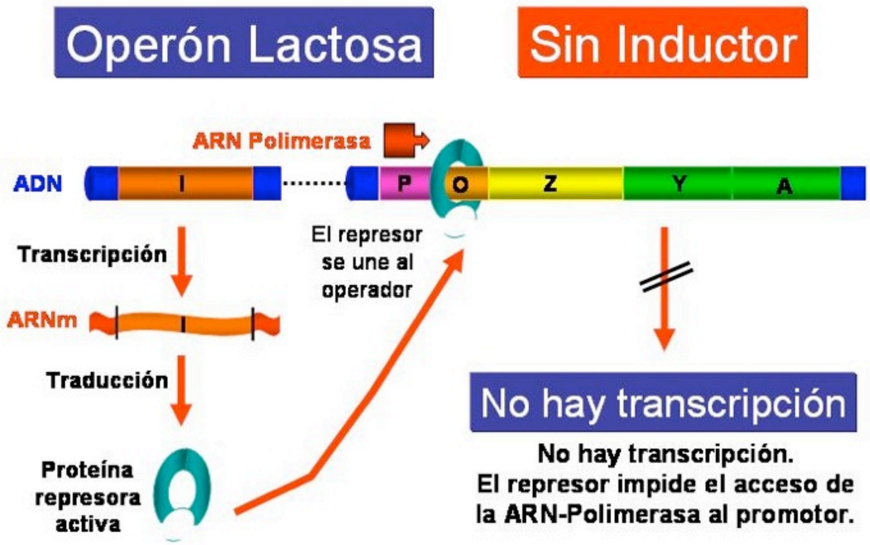

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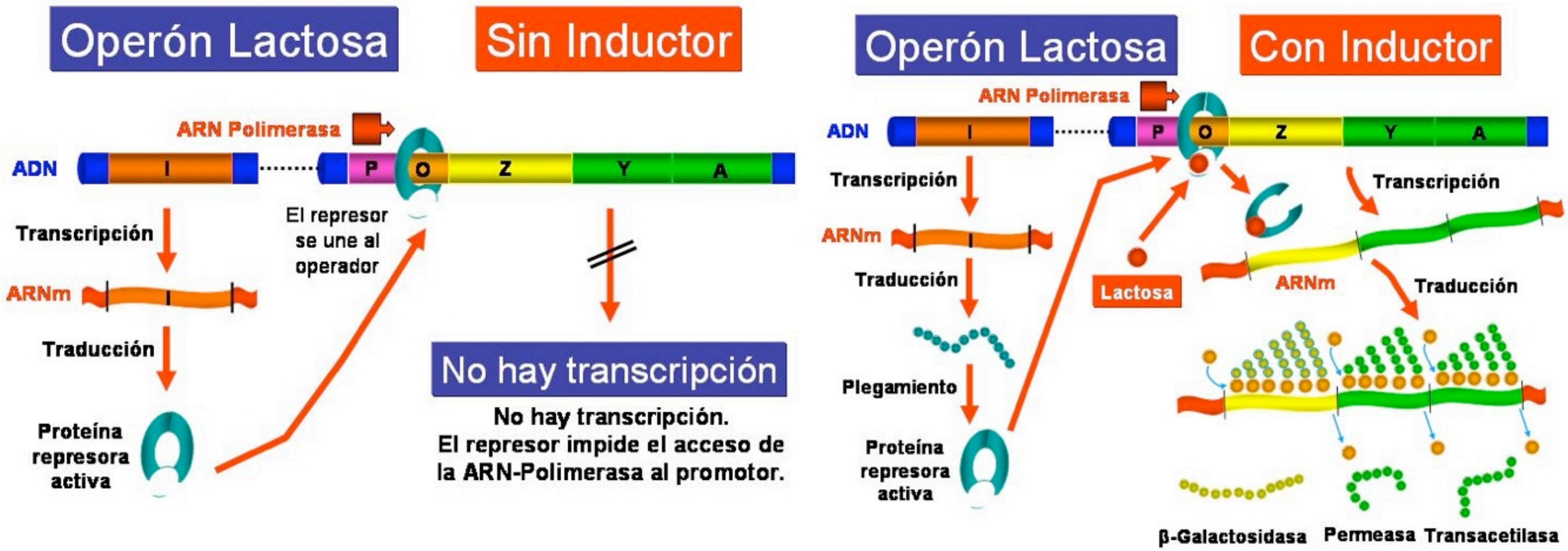
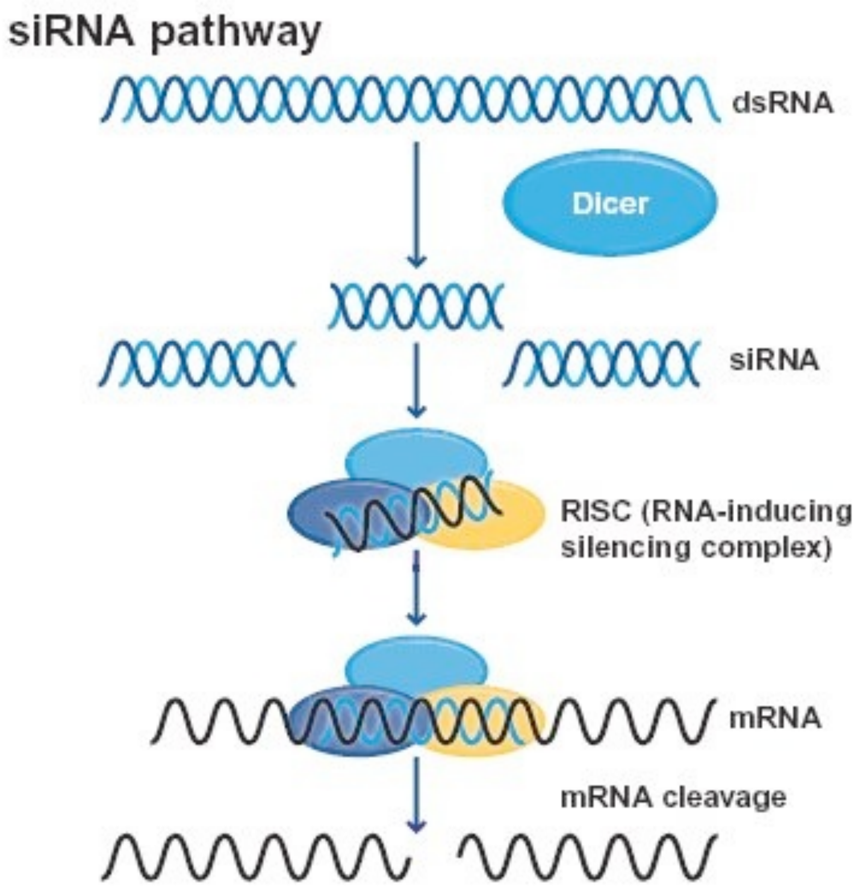


Gene Transcription manipulations

Post-transcriptional regulations: siRNA

Gene Transcription manipulations

Post-transcriptional regulations: siRNA



Part I: Review of Synthetic Biology achievements

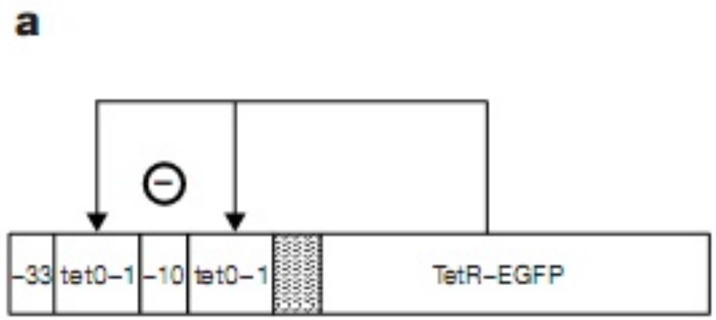
Prokaryotes

2000
Becskei i Serrano (CRG)
Engineering stability in gene networks by autoregulation

2000
Gardner et al.
Construction of a genetic toggle switch in *Escherichia coli*

2000
Elowitz et al.
A synthetic oscillatory network of transcriptional regulators

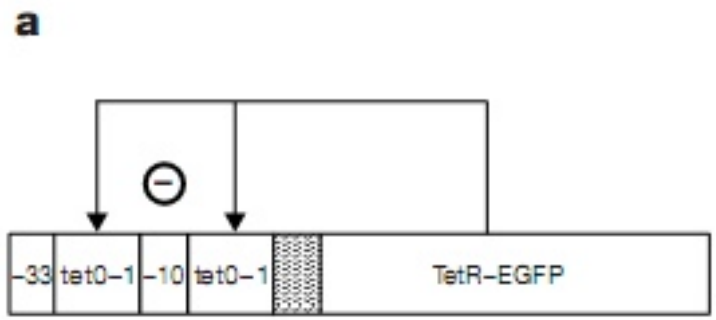
Mono-stability (negative feedback)



$$\frac{dtetR}{dt} = ks * pL + km * tetR_2 - kd * tetR^2 - kdeg * tetR$$

Becskei i Serrano (2000). Engineering stability in gene networks by autoregulation. *Nature* **405**, 590-593

Mono-stability (negative feedback)



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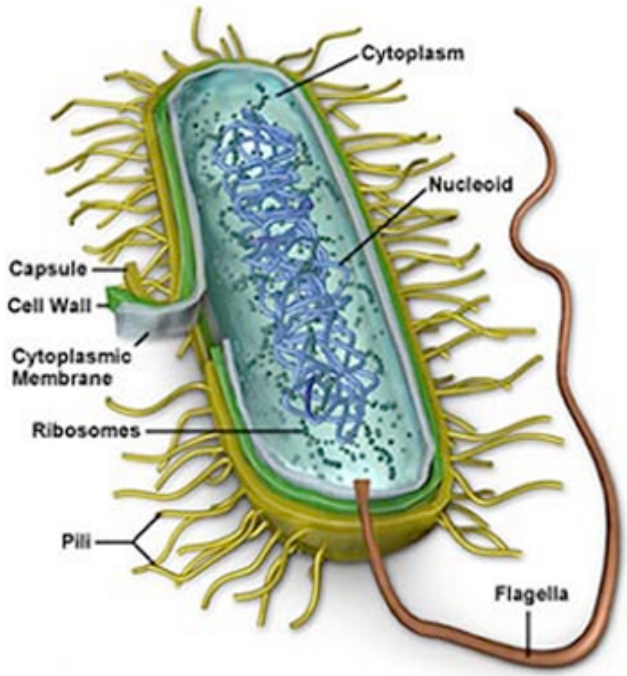

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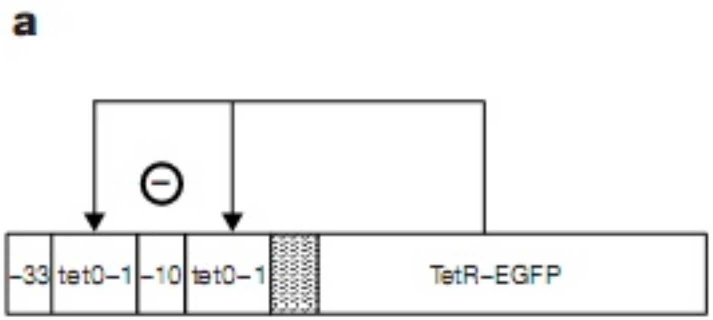
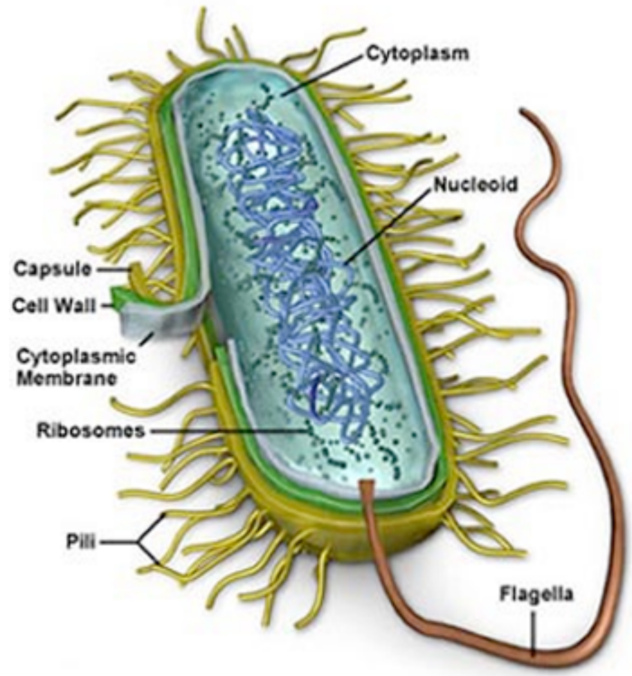


$$\frac{dtetR}{dt}=ks*pL+km*tetR_2-kd*tetR^2-kdeg*tetR$$

$$\frac{dtetR_2}{dt}=kd*tetR^2-km*tetR_2$$

$$\frac{dpL}{dt}=ku*pO-kb*pL*tetR_2$$



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Mono-stability (negative feedback)

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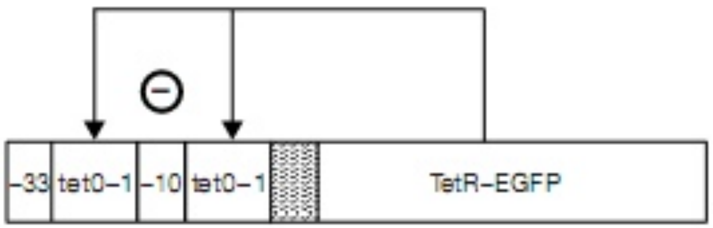

$$\frac{dtetR}{dt} = ks*pL + km*tetR_2 - kd*tetR^2 - kdeg*tetR$$

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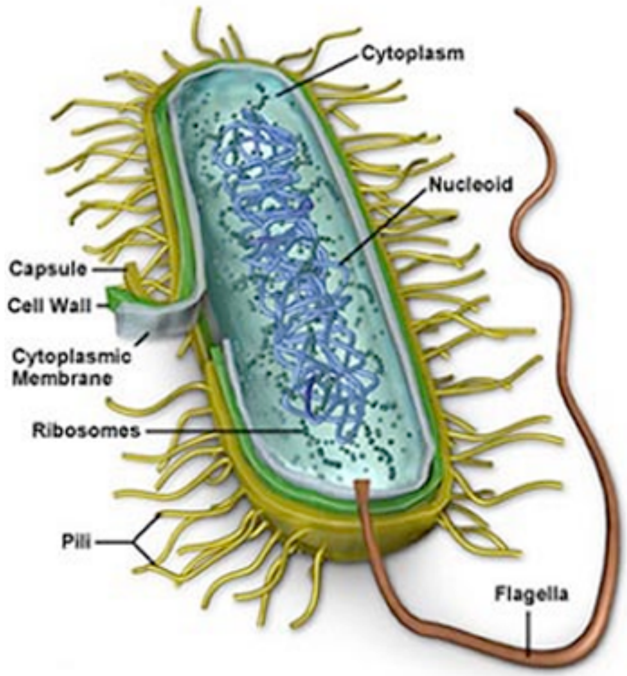

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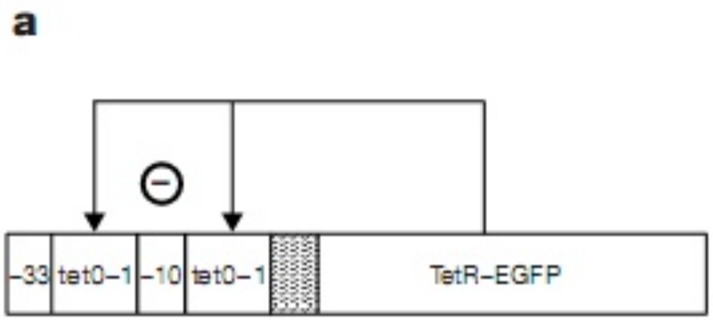

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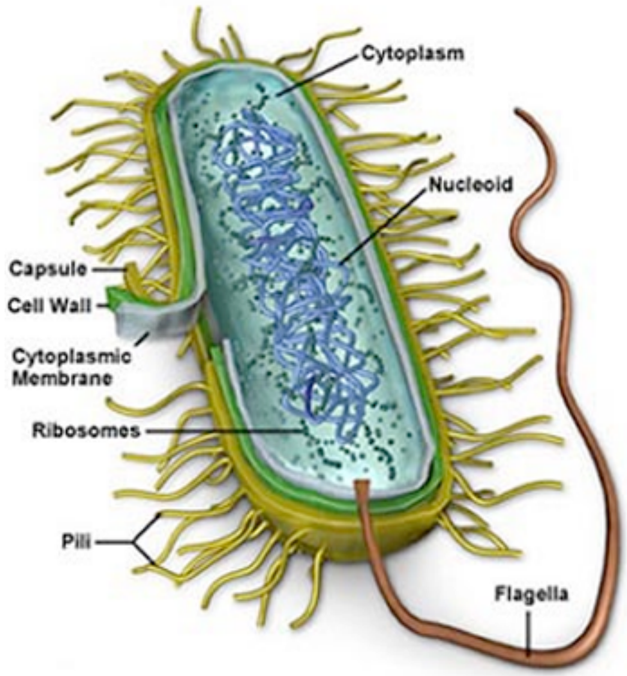
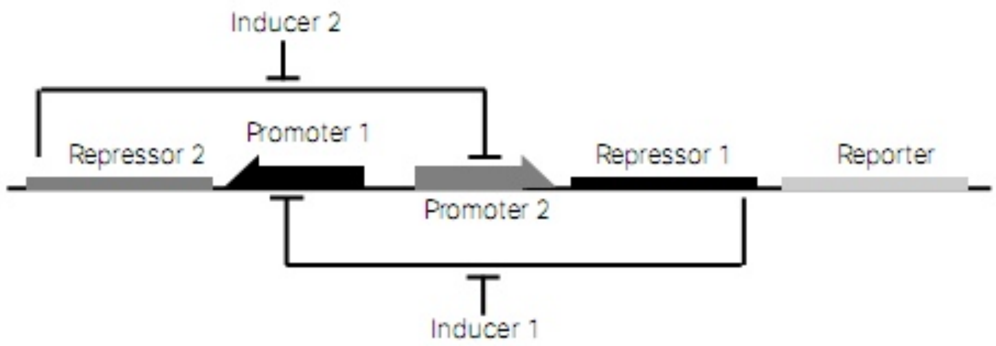


$$\frac{dtetR}{dt} = \frac{ks * n}{(1 + keq * keq_2 * tetR^2)} - kdeg * tetR$$

$$keq = \frac{kd}{km} \quad keq_2 = \frac{kb}{ku}$$

Becskei i Serrano (2000). Engineering stability in gene networks by autoregulation. *Nature* **405**, 590-593

Bi-stability (two negative feedbacks)



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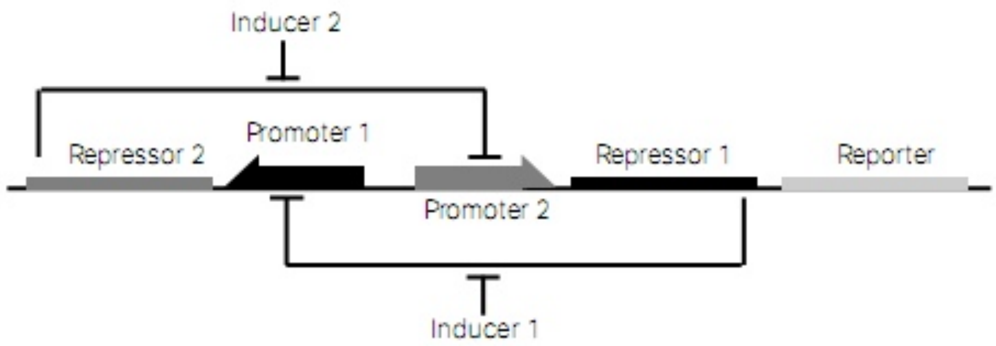

$$\frac{du}{dt} = \frac{\alpha_1}{1 + v^{\beta}} - u$$

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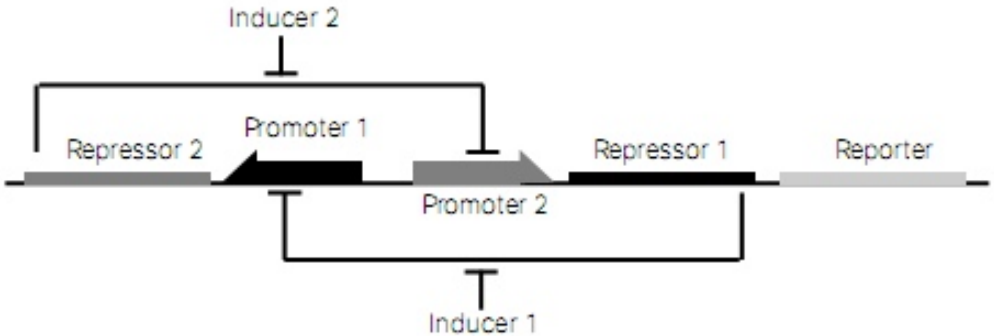

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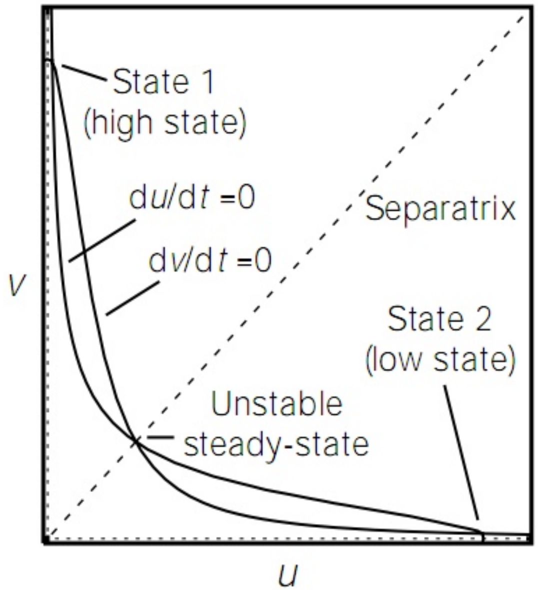

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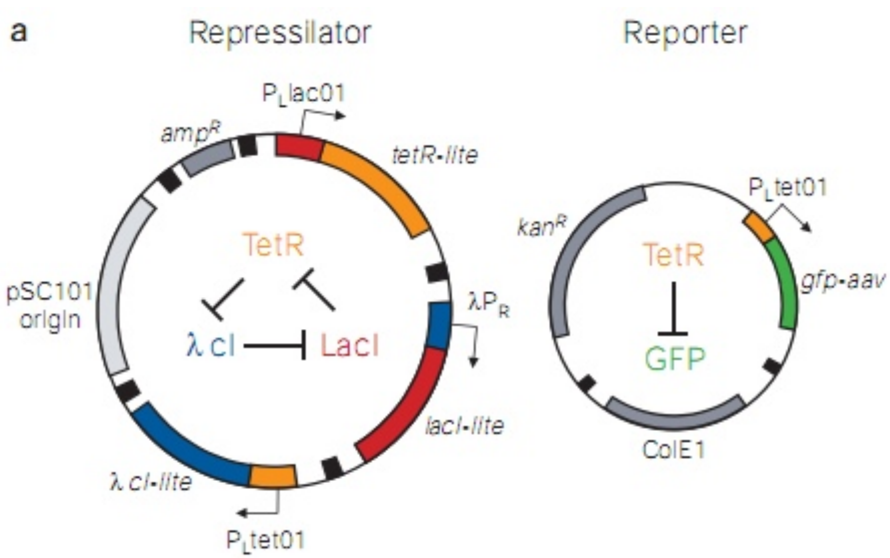
Oscillators (delay)



Elowitz et al. (2000) A synthetic oscillatory network of transcriptional regulators. *Nature* **403**, 335-338

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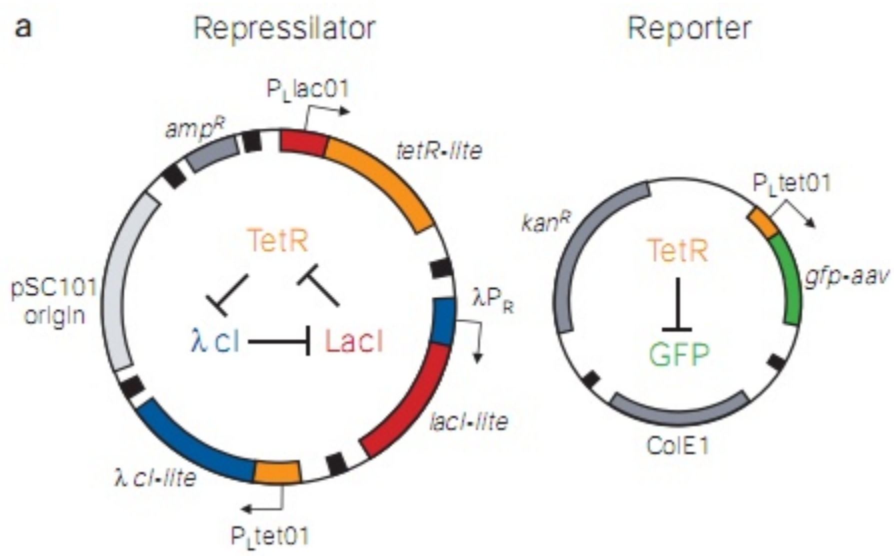

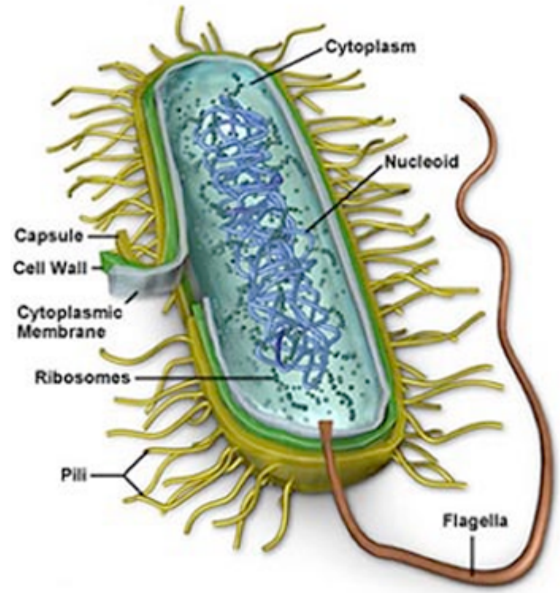

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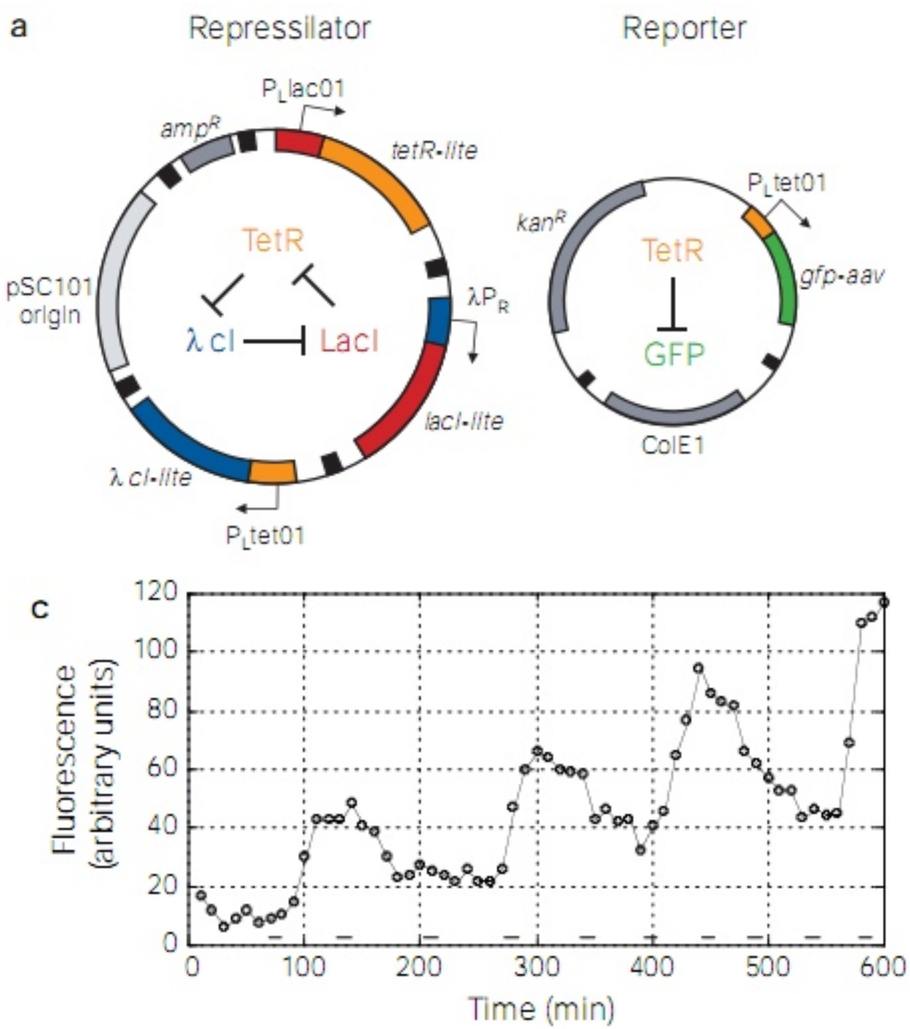

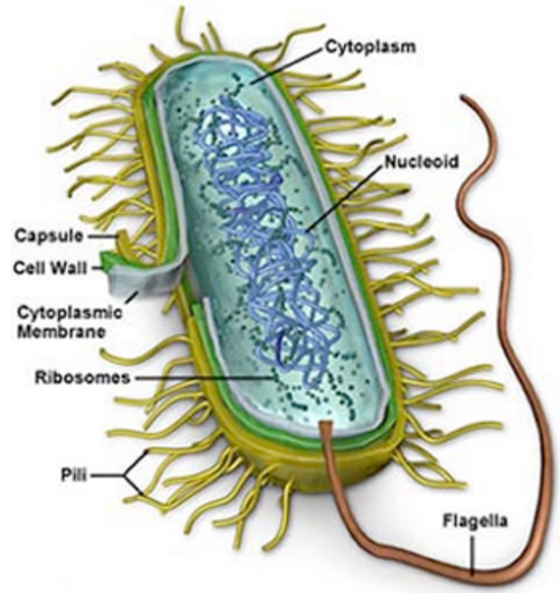

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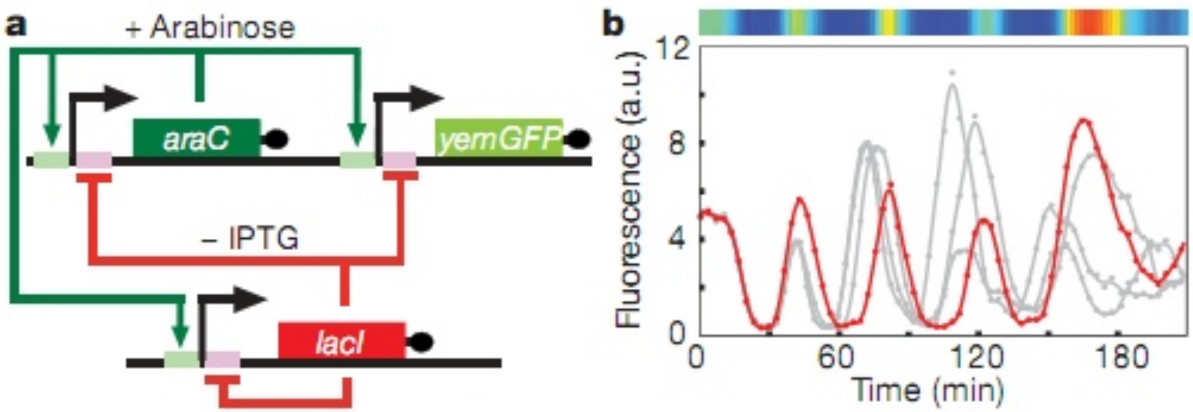

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Prokaryotes

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Ron Weiss et al.
Programmed population control by cell-cell communication

2005
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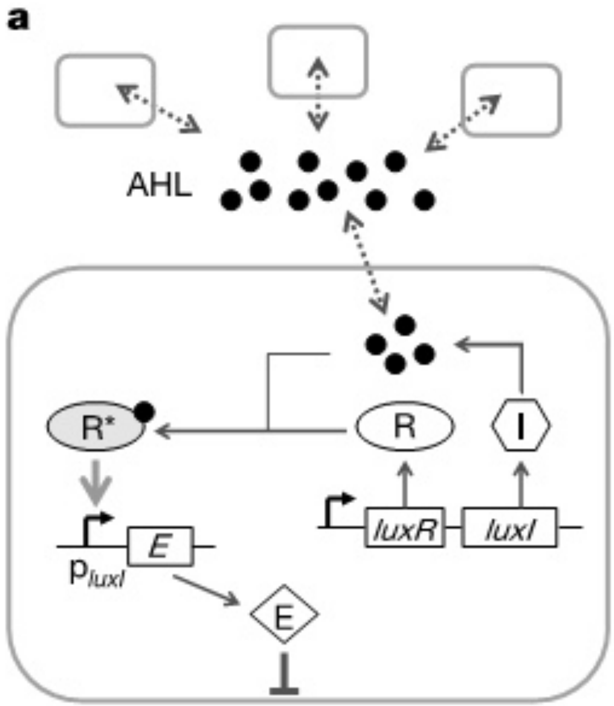
A synthetic multicellular system for programmed pattern formation

Control of population (communication)

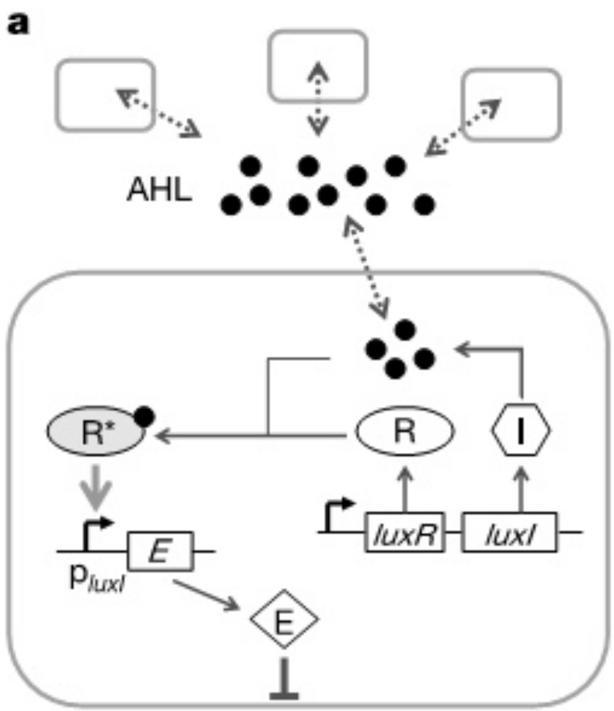
Verhulst equation:



You L. et al. (2004) Programmed population control by cell-cell communication. *Nature* **428**, 868-871

Control of population (communication)

Verhulst equation: $$\frac{dx}{dt} = mx\left(1 - \frac{x}{k}\right) - ex$$



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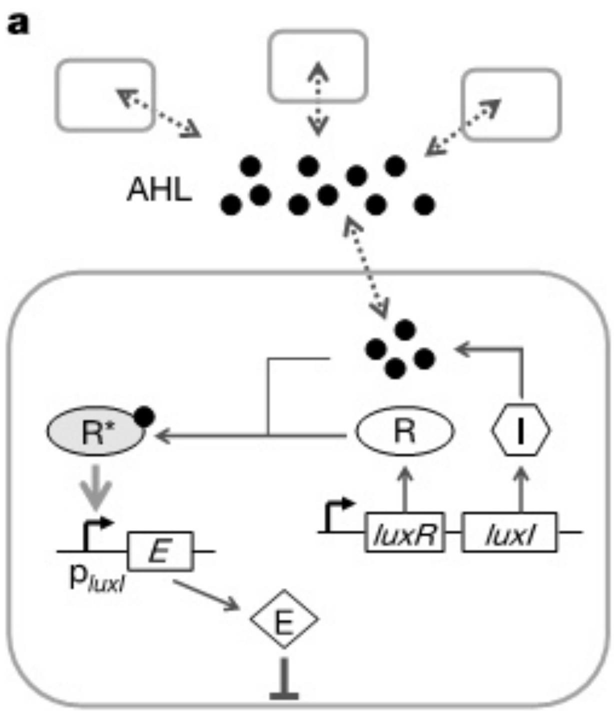

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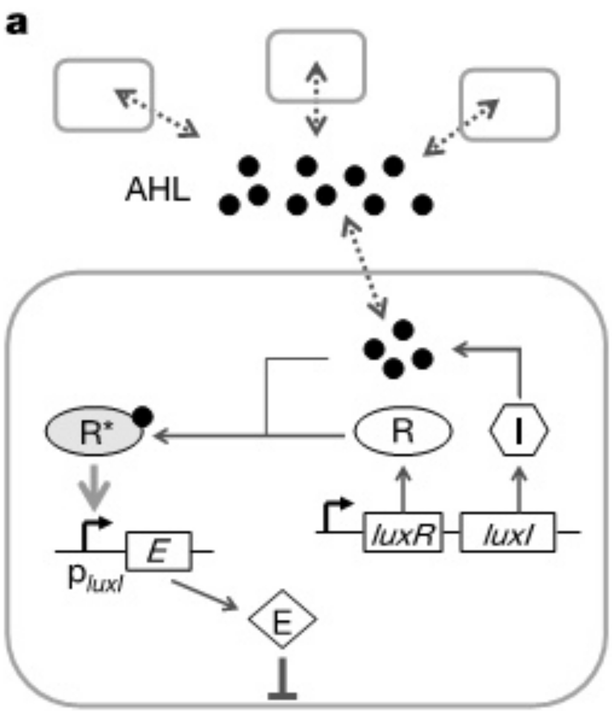

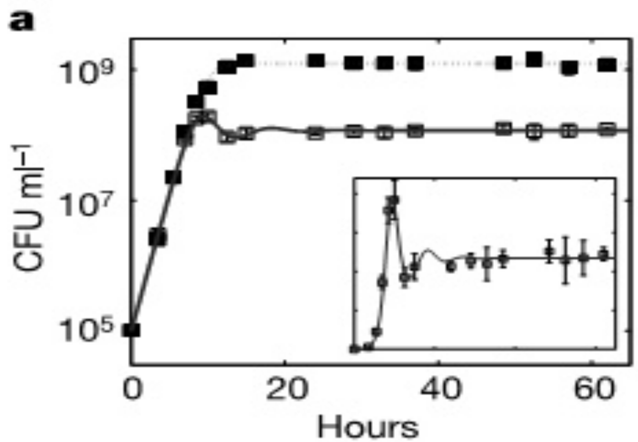

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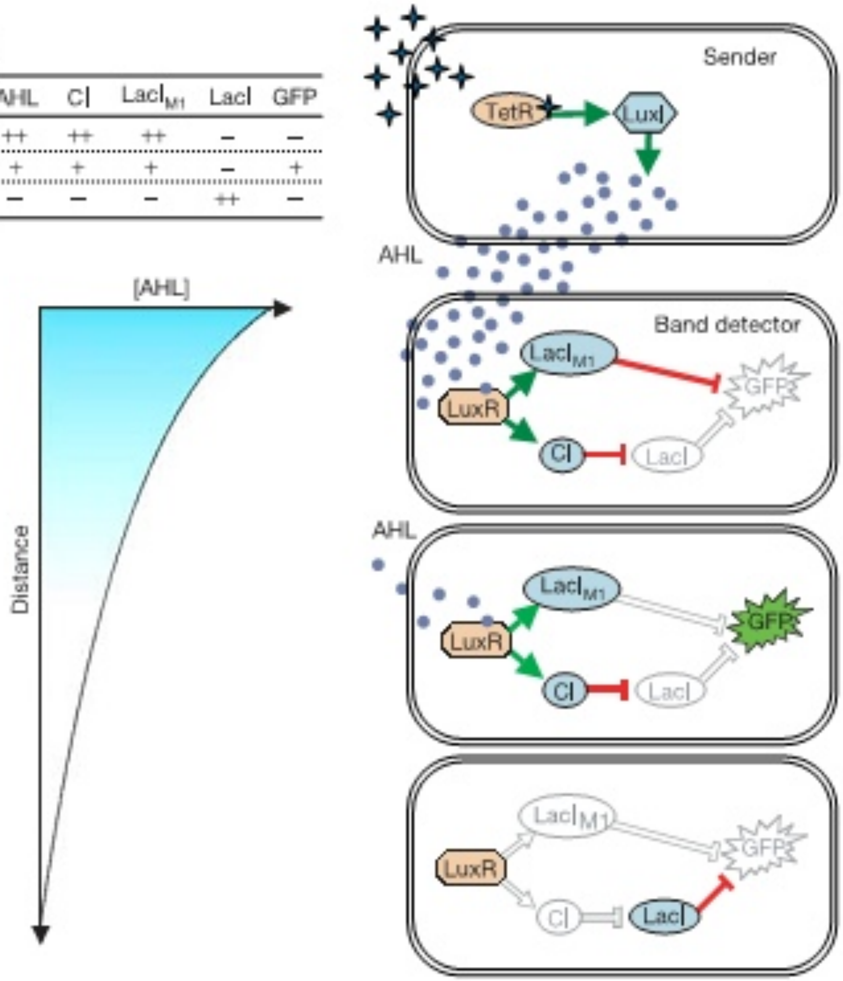
Pattern formation (communication)

a

AHL	CI	$LacI_{M1}$	LacI	GFP
++	++	++	–	–
+	+	+	–	+
–	–	–	++	–



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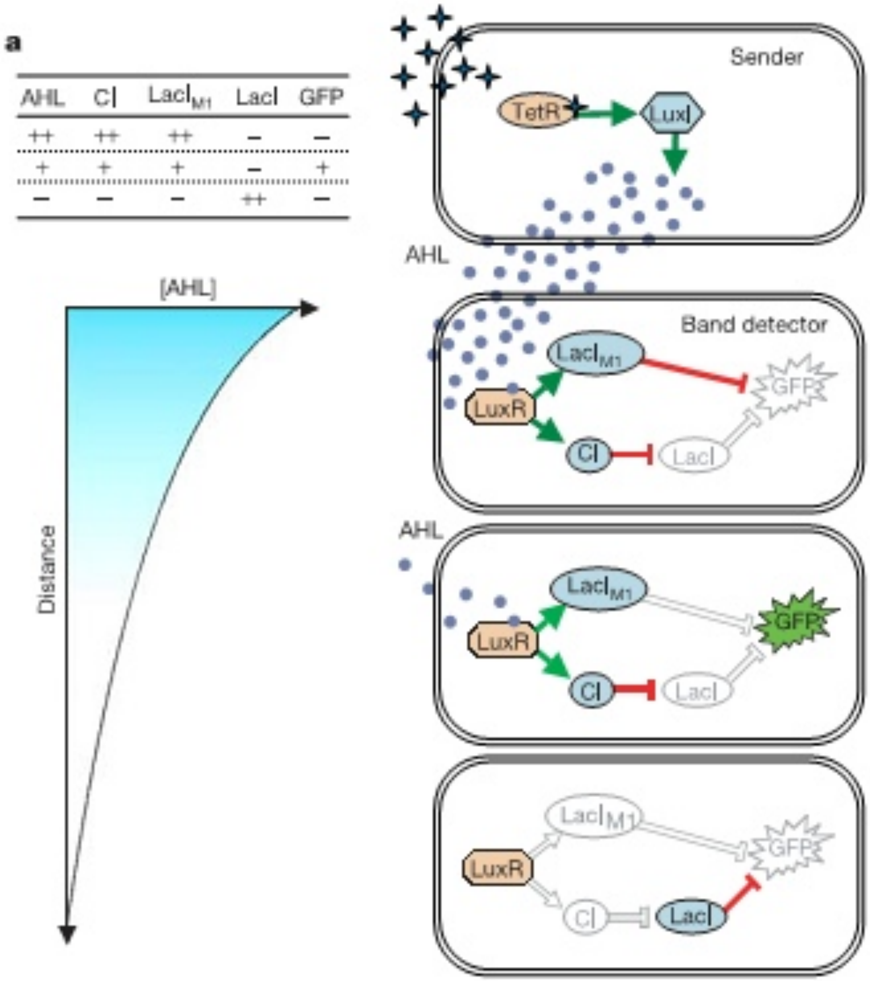
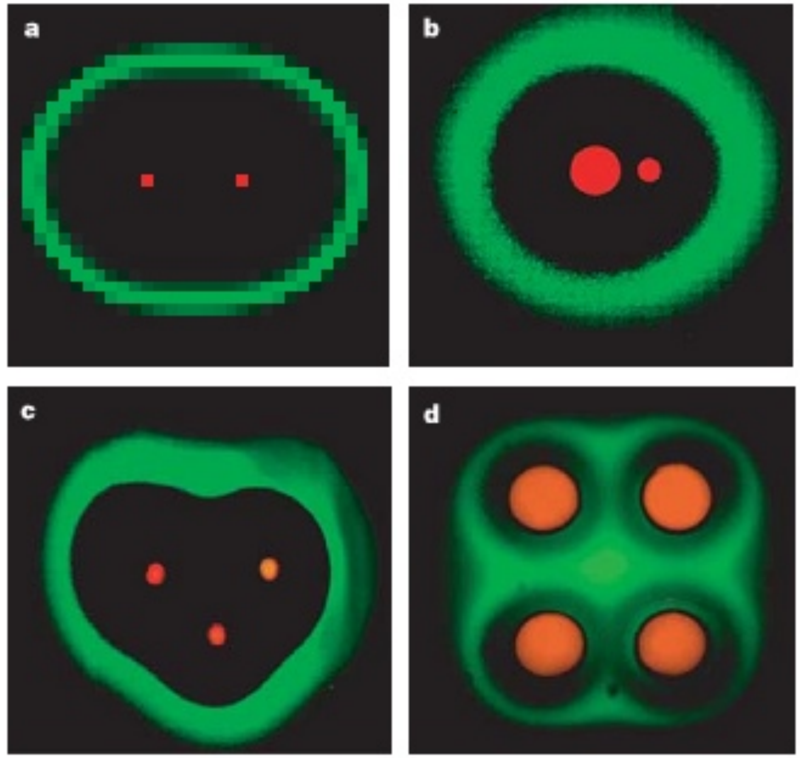
Pattern formation (communication)





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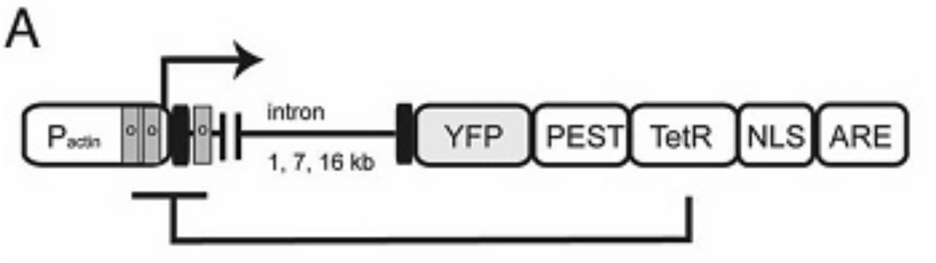
Eukaryotes

2008

Swinburne et al.
Intron length increases oscillatory periods of gene expression in animal cells

Oscillators in mammalian cells



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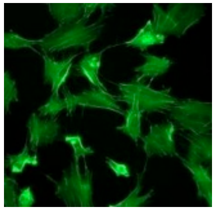

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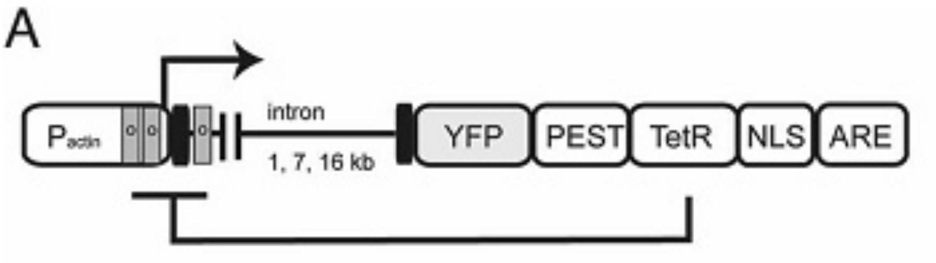

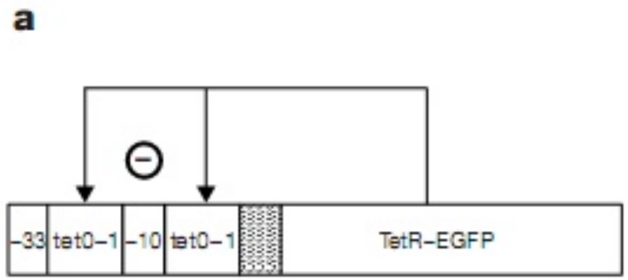

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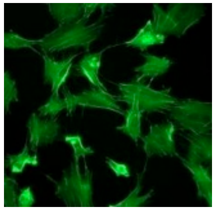

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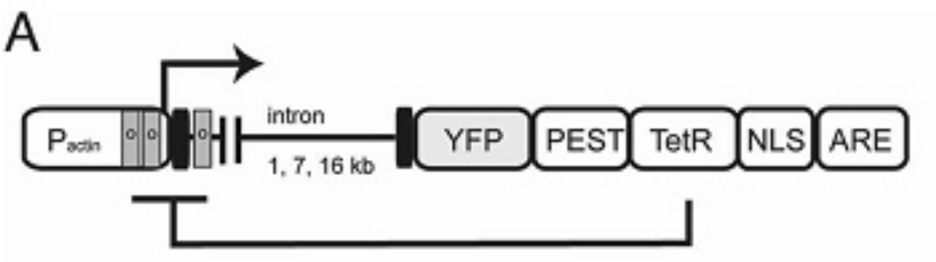

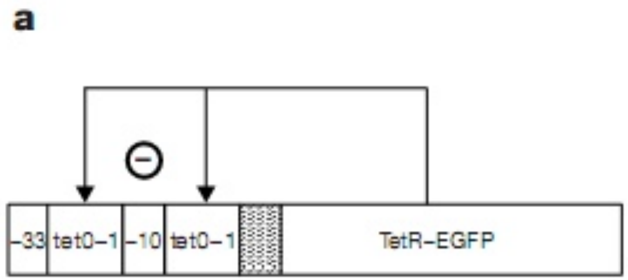

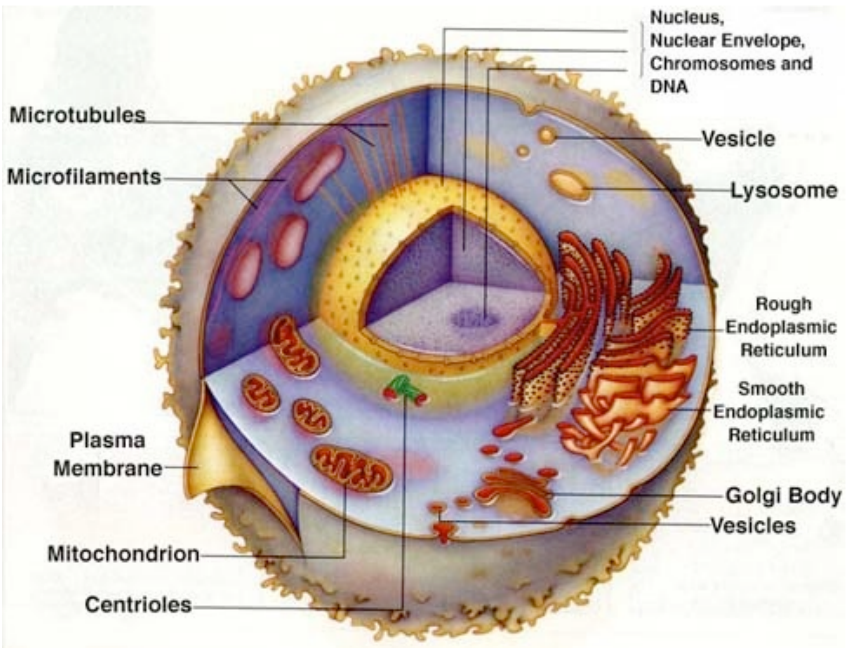

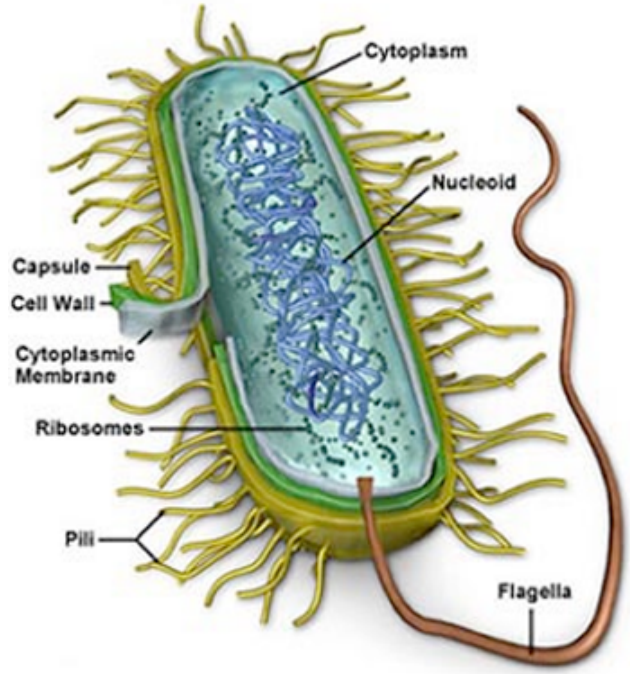

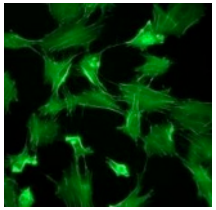

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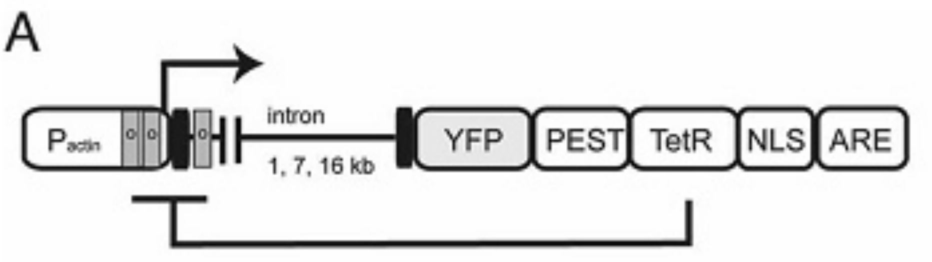

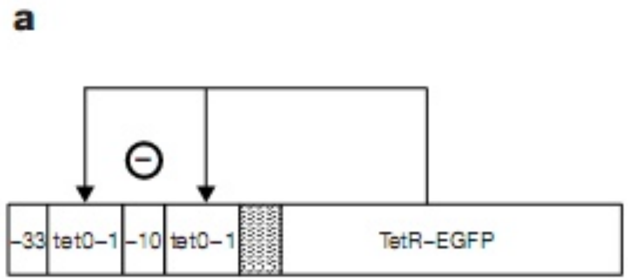

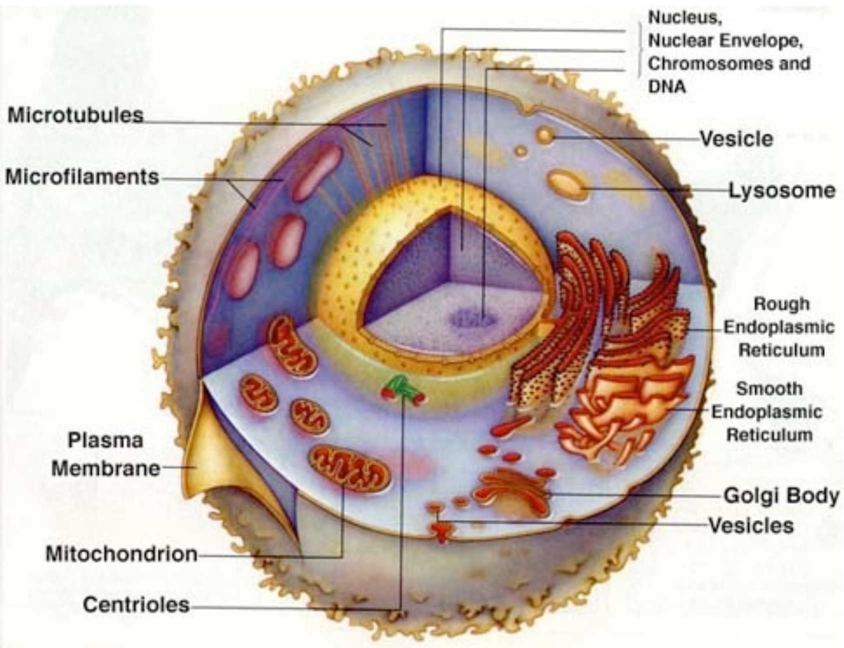

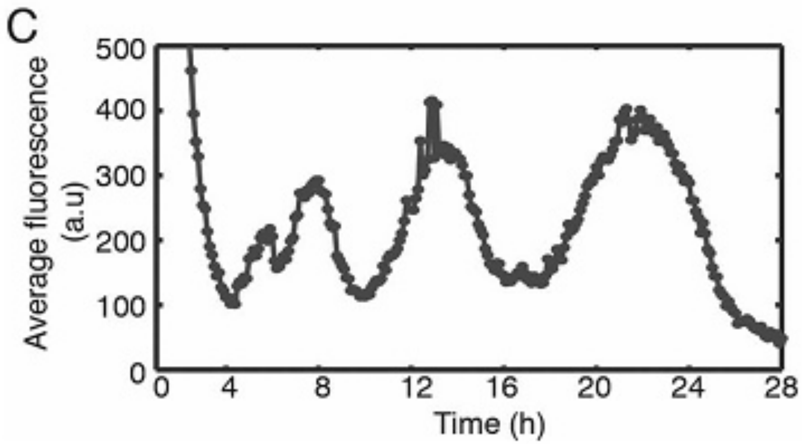

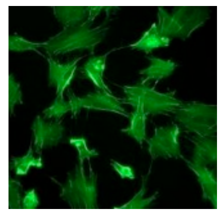

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Part II: Cellular Computation

Cellular Computation

COMPUTATION

↓

Computation is a general term for any type of information processing

↓

Decision making process

Which type of computation?

digital vs. *analog*

Why are cellular switches Boolean? General conditions for multistable genetic circuits

Javier Macía [a,1], Stefanie Widder [a,*,1], Ricard Solé [a,b]

[a] *Complex System Lab (ICREA-UPF), Barcelona Biomedical Research Park (PRBB-GRIB), Dr. Aiguader 88, 08003 Barcelona, Spain*
[b] *Santa Fe Institute, 1399 Hyde Park Road, Santa Fe, NM 87501, USA*

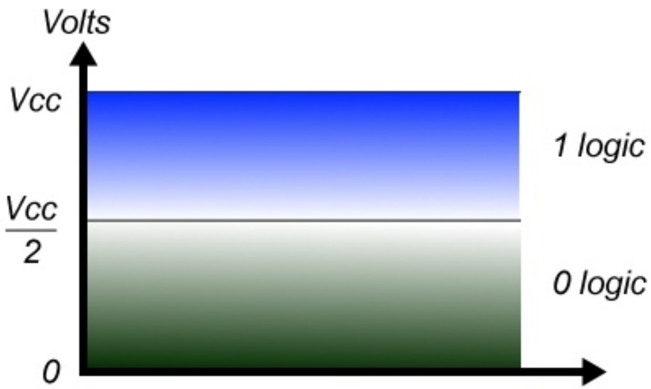
Digital computation

How it works in electronics?

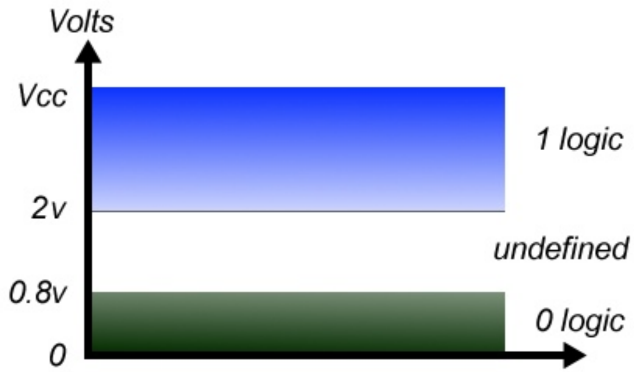
Examples of binary logic levels:

Technology	L voltage	H voltage	Notes
CMOS	0V to $V_{CC}/2$	$V_{CC}/2$ to V_{CC}	V_{CC} = supply voltage
TTL	0V to 0.8V	2V to V_{CC}	V_{CC} = 5V ±10%

0 logic 1 logic



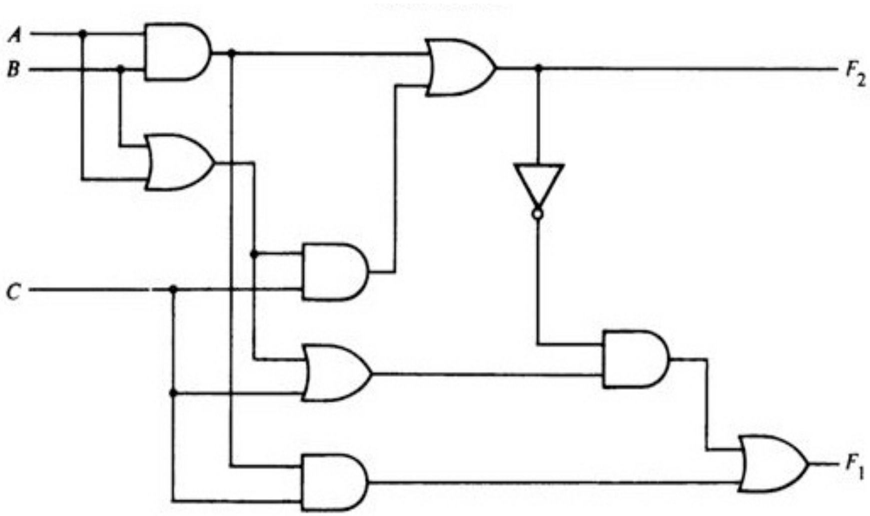
CMOS



TTL

Can we mimic electronics?

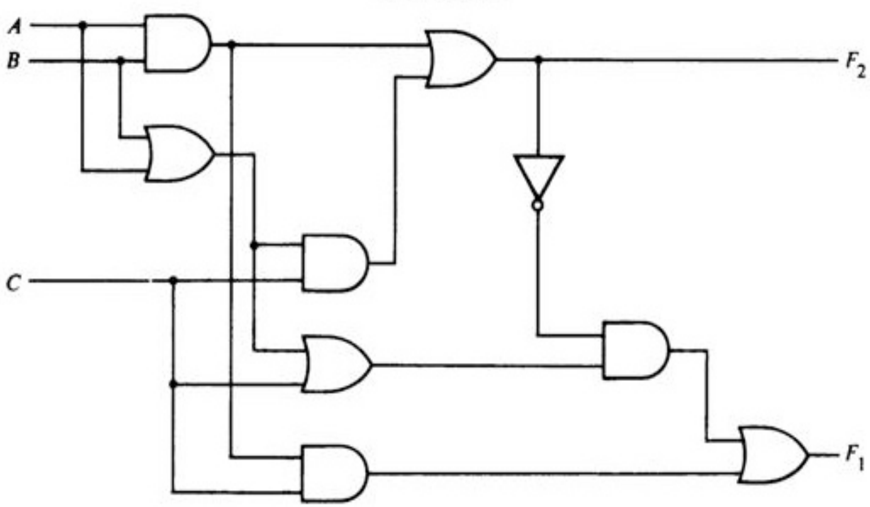
- Circuits can be built connecting small number of different logic gates



Can we mimic electronics?

- Circuits can be built connecting small number of different logic gates

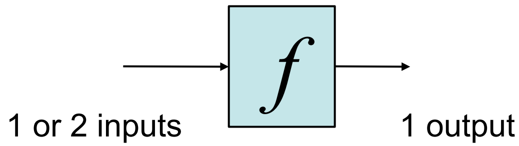
What is a logic gate?



Can we mimic electronics?

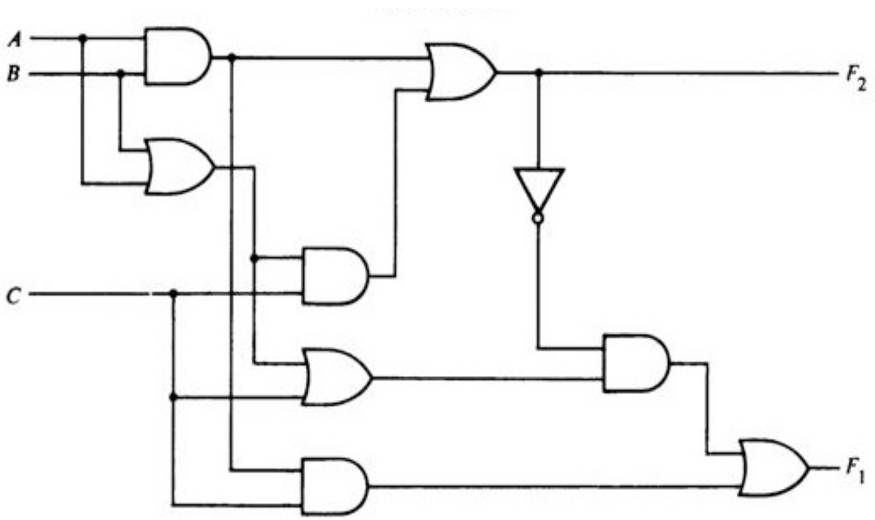
- Circuits can be built connecting small number of different logic gates

What is a logic gate?

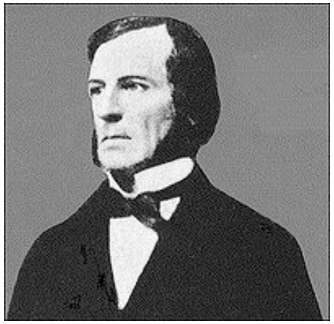


f = Truth Table

a	b	c
0	0	0
0	1	0
1	0	0
1	1	1



Can we mimic electronics?



George Boole

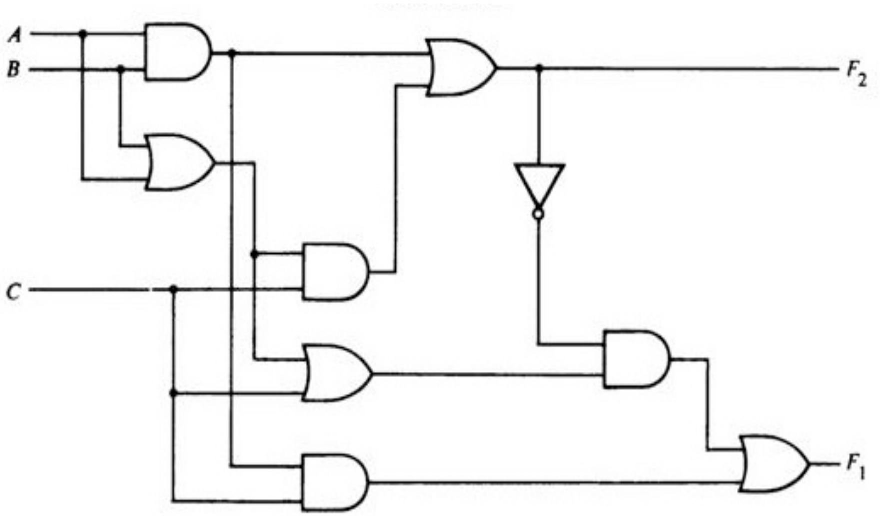
Boolean logic is a complete system for logical operations.

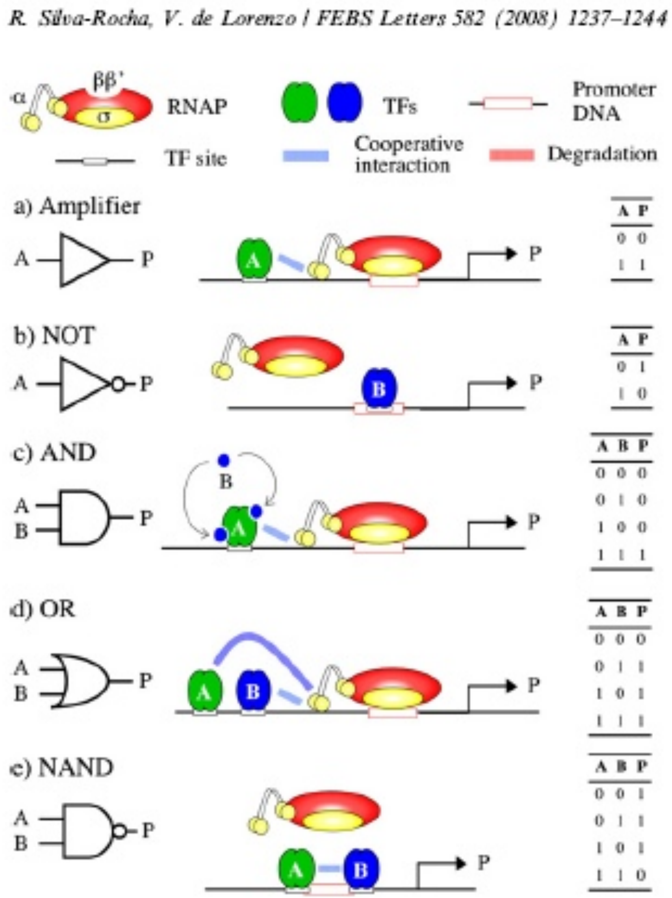
$$f: \{0,1\}^N \rightarrow \{0,1\}^M$$

Possible functionally complete sets: Ω={AND, OR, NOT}
Ω={NAND}
Ω={NOR}

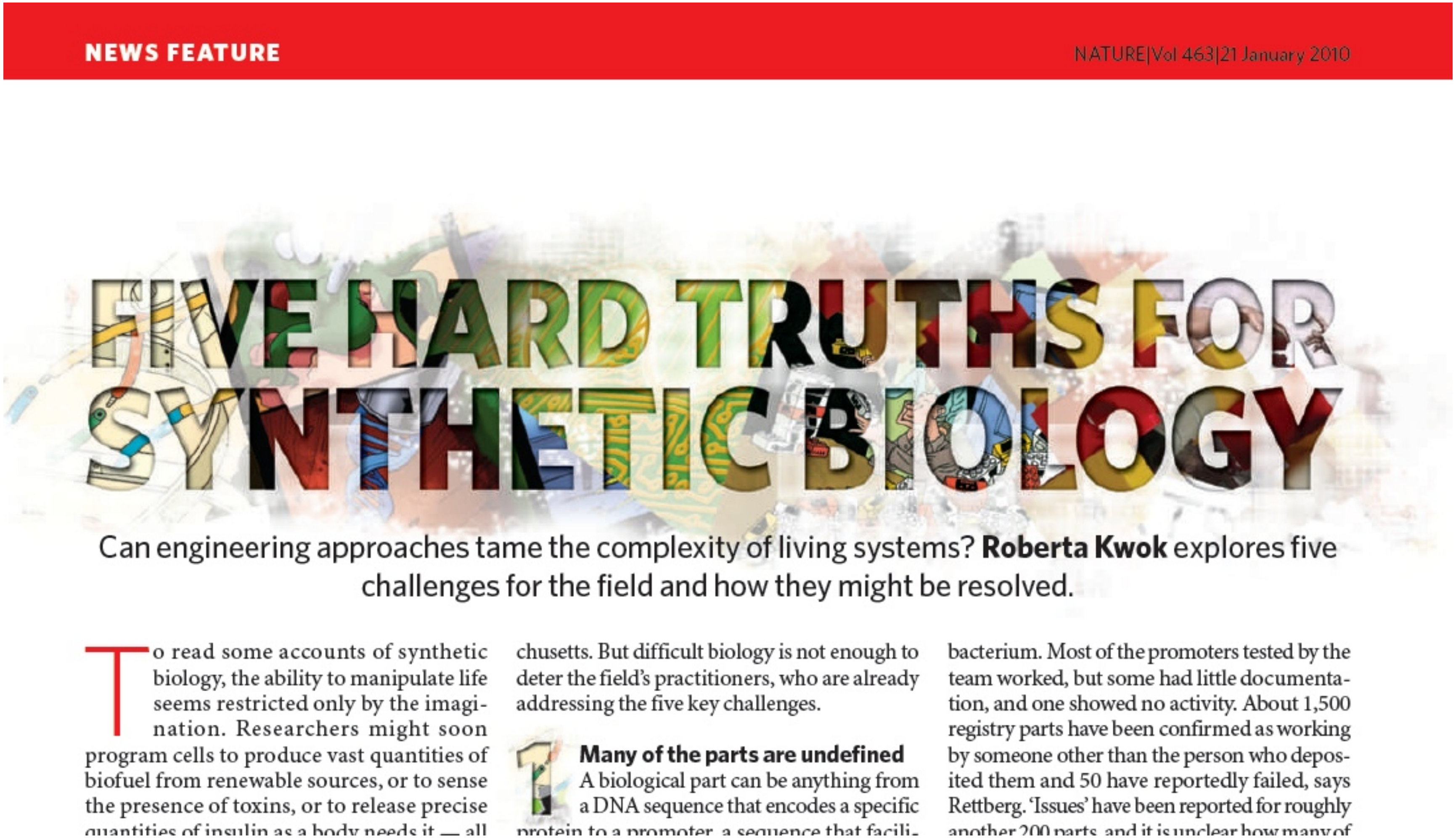
Can we mimic electronics?

- Circuits can be built connecting small number of different logic gates





Can we mimic electronics?



NEWS FEATURE NATURE|Vol 463|21 January 2010

FIVE HARD TRUTHS FOR SYNTHETIC BIOLOGY

Can engineering approaches tame the complexity of living systems? **Roberta Kwok** explores five challenges for the field and how they might be resolved.

To read some accounts of synthetic biology, the ability to manipulate life seems restricted only by the imagination. Researchers might soon program cells to produce vast quantities of biofuel from renewable sources, or to sense the presence of toxins, or to release precise quantities of insulin as a body needs it — all

chusetts. But difficult biology is not enough to deter the field's practitioners, who are already addressing the five key challenges.

1 Many of the parts are undefined

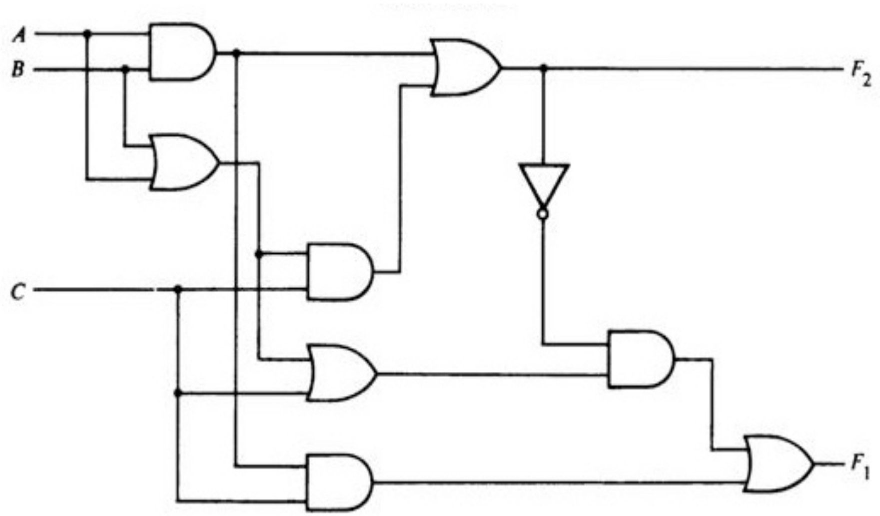
A biological part can be anything from a DNA sequence that encodes a specific protein to a promoter, a sequence that facili-

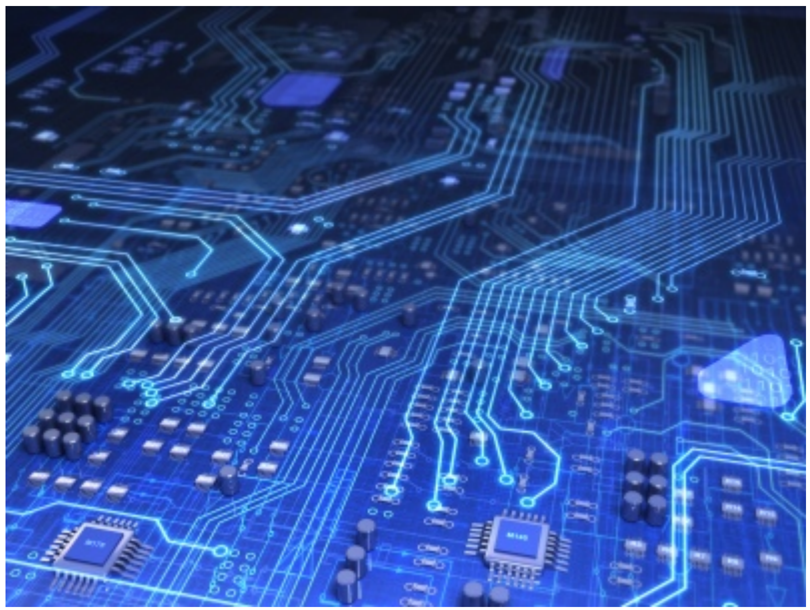
bacterium. Most of the promoters tested by the team worked, but some had little documentation, and one showed no activity. About 1,500 registry parts have been confirmed as working by someone other than the person who deposited them and 50 have reportedly failed, says Rettberg. 'Issues' have been reported for roughly another 200 parts, and it is unclear how many of

Can we mimic electronics?

Limiting problems:

- Wiring
- Increase of the biochemical diversity

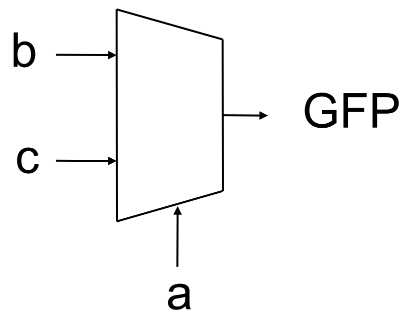




Can we mimic electronics?

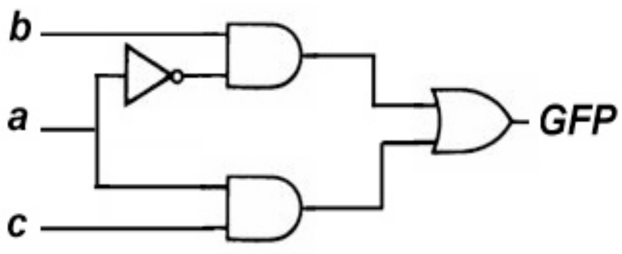
Example:

Multiplexer 2-to-1

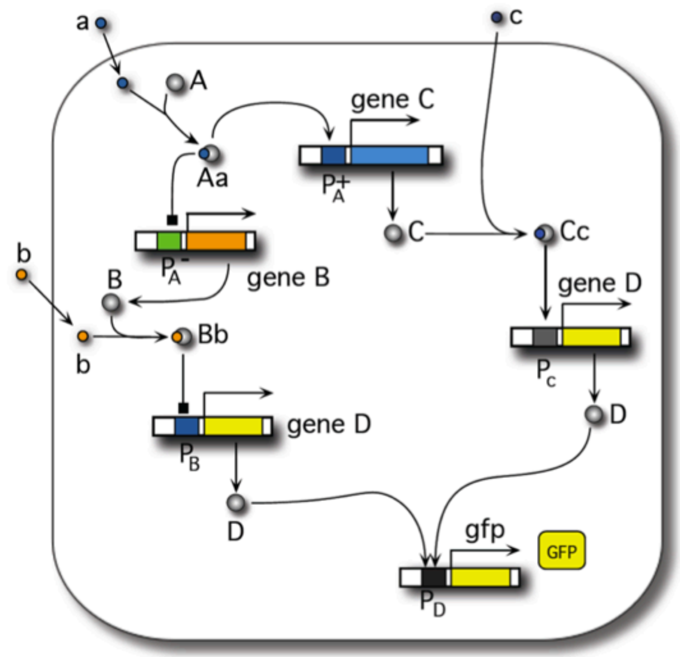


a	b	c	GFP
0	0	0	0
0	0	1	0
0	1	0	1
0	1	1	1
1	0	0	0
1	0	1	1
1	1	0	0
1	1	1	1

Truth table



Logic circuit



Cellular implementation

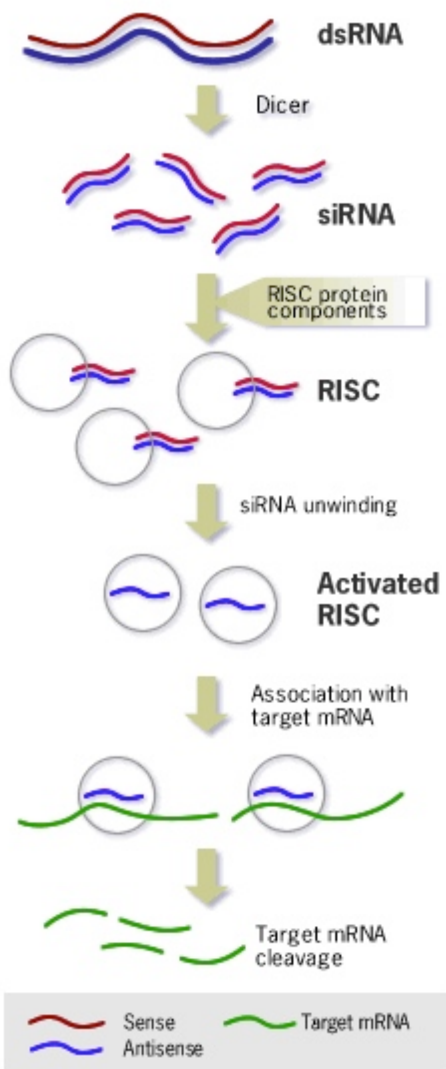
COMPLEXITY

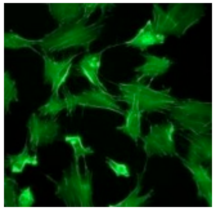
Boolean circuits in single cells

2007

Ron Weiss et al.
A universal RNAi-based logic evaluator that operates in mammalian cells

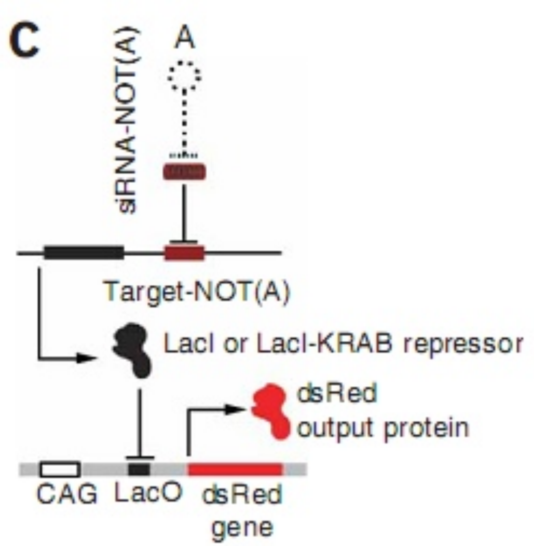
Logic gates (siRNA)





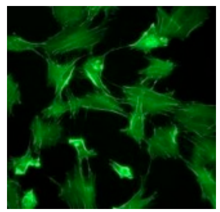
Rinaudo K. et al. (2007) A universal RNAi-based logic evaluator that operates in mammalian cells. *Nature Biotechnology* **25**, 795 - 801

Logic gates (siRNA)

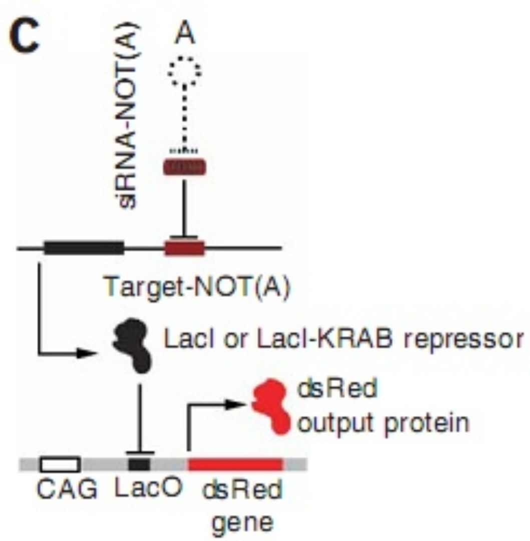


A↑	Output	NOT(A↑)
False	+	True
True	–	False

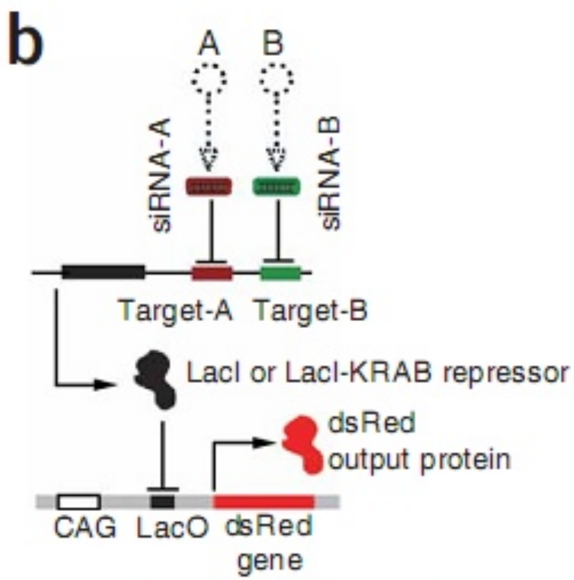
Rinaudo K. et al. (2007) A universal RNAi-based logic evaluator that operates in mammalian cells. *Nature Biotechnology* **25**, 795 - 801



Logic gates (siRNA)

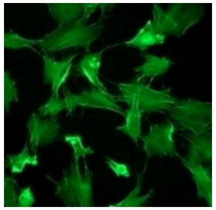


A↑	Output	NOT(A↑)
False	+	True
True	–	False

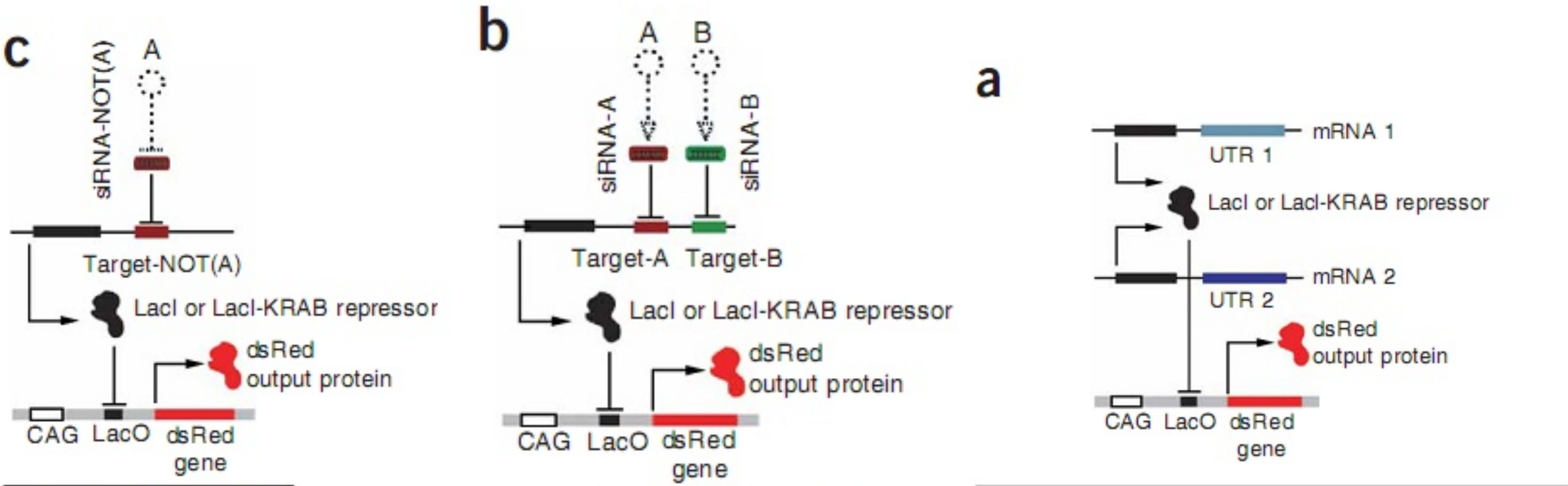


A↑	B↑	Output	A↑ OR B↑
False	False	–	False
True	False	+	True
False	True	+	True
True	True	+	True

Rinaudo K. et al. (2007) A universal RNAi-based logic evaluator that operates in mammalian cells. *Nature Biotechnology* **25**, 795 - 801



Logic gates (siRNA)

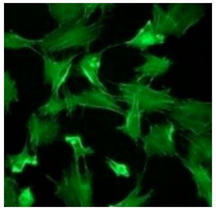


A↑	Output	NOT(A↑)
False	+	True
True	–	False

A↑	B↑	Output	A↑ OR B↑
False	False	–	False
True	False	+	True
False	True	+	True
True	True	+	True

mRNA 1↓	mRNA 2↓	Output	mRNA 1↓ AND mRNA 2↓
False	False	–	False
True	False	–	False
False	True	–	False
True	True	+	True

Rinaudo K. et al. (2007) A universal RNAi-based logic evaluator that operates in mammalian cells. *Nature Biotechnology* **25**, 795 - 801



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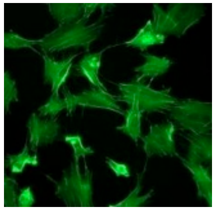
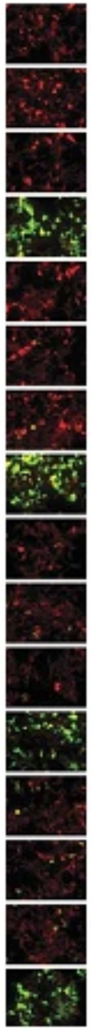
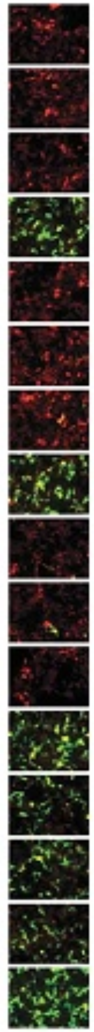


a

D1: (A AND B AND C) OR (D AND E)

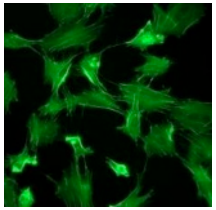


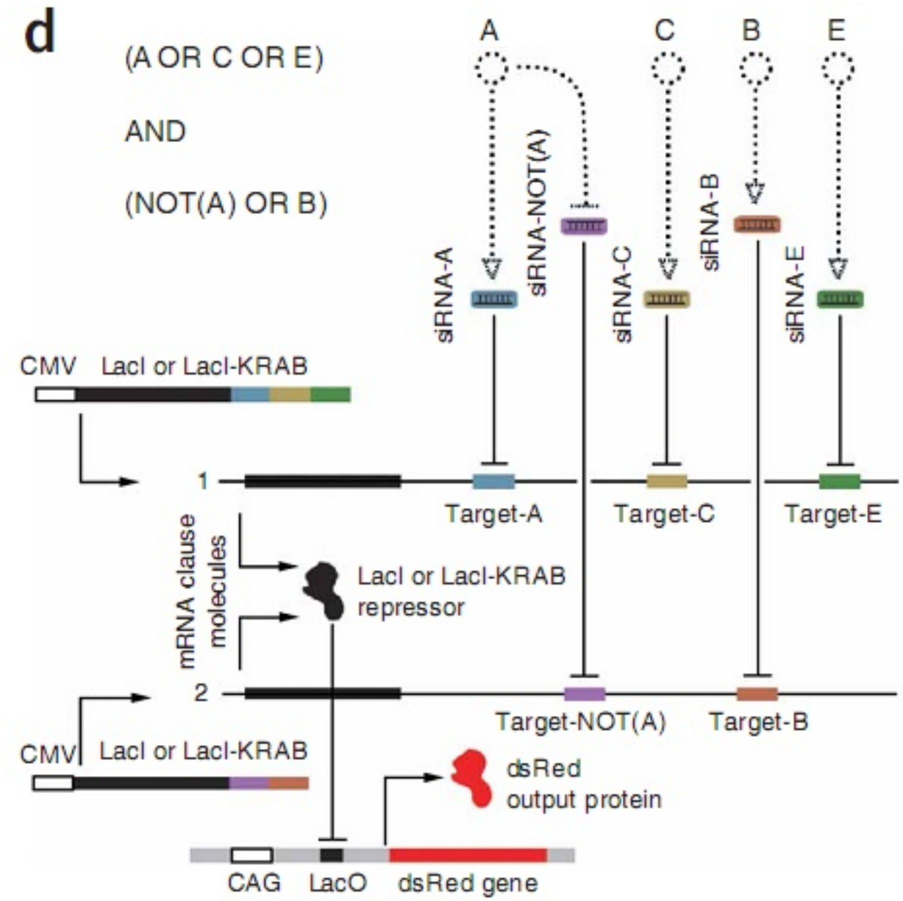
A	B	C	D	E	siRNA A B C D E	D1	Int. a.u.
F	F	F	F	F	+ + + + +	F	0.03
F	F	F	F	T	+ + + + –	F	0.02
F	F	F	T	F	+ + + – +	F	0.03
F	F	F	T	T	+ + + – –	T	1.23
F	F	T	F	F	+ + – + +	F	0.03
F	F	T	F	T	+ + – + –	F	0.03
F	F	T	T	F	+ + – – +	F	0.03
F	F	T	T	T	+ + – – –	T	1.19
F	T	F	F	F	+ – + + +	F	0.04
F	T	F	F	T	+ – + + –	F	0.05
F	T	F	T	F	+ – + – +	F	0.03
F	T	F	T	T	+ – + – –	T	1.01
F	T	T	F	F	+ – – + +	F	0.14
F	T	T	F	T	+ – – + –	F	0.18
F	T	T	T	F	+ – – – +	F	0.09
F	T	T	T	T	+ – – – –	T	1.10

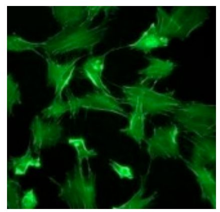


A	B	C	D	E	siRNA A B C D E	D1	Int. a.u.
T	F	F	F	F	– + + + +	F	0.02
T	F	F	F	T	– + + + –	F	0.03
T	F	F	T	F	– + + – +	F	0.03
T	F	F	T	T	– + + – –	T	1.23
T	F	T	F	F	– + – + +	F	0.02
T	F	T	F	T	– + – + –	F	0.04
T	F	T	T	F	– + – – +	F	0.03
T	F	T	T	T	– + – – –	T	1.25
T	T	F	F	F	– – + + +	F	0.07
T	T	F	F	T	– – + + –	F	0.09
T	T	F	T	F	– – + – +	F	0.05
T	T	F	T	T	– – + – –	T	1.24
T	T	T	F	F	– – – + +	T	1.00
T	T	T	F	T	– – – + –	T	1.02
T	T	T	T	F	– – – – +	T	1.02
T	T	T	T	T	– – – – –	T	2.98

Rinaudo K. et al. (2007) A universal RNAi-based logic evaluator that operates in mammalian cells. *Nature Biotechnology* **25**, 795 - 801







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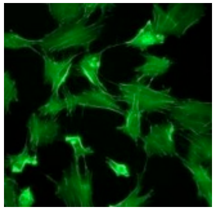


Mimic electronics is not the optimal solution.
New approaches are required!.

Multicellular computation

1. Distribute the computation into different types of engineered cells.

2. The final output of the circuit can be produced in different cell types.

3. Restricted communication among cells: each cell can only transmit the signal to another specific cell and that there should be no reversibility on the signal.

4. The same engineered cells can be used in different circuits

Multicellular computation based on standard (NOR) approach

LETTER

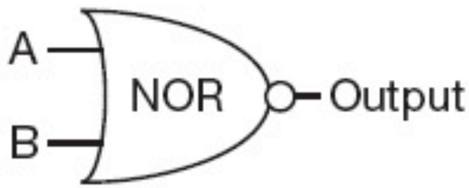
doi:10.1038/nature09565

Robust multicellular computing using genetically encoded NOR gates and chemical 'wires'

Alvin Tamsir[1], Jeffrey J. Tabor[2] & Christopher A. Voigt[2]

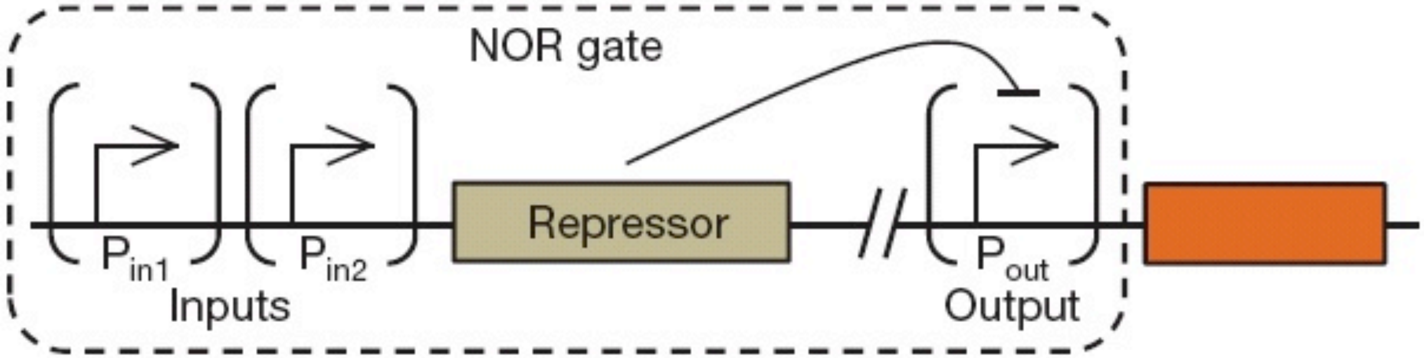
Multicellular computation based on standard (NOR) approach

a

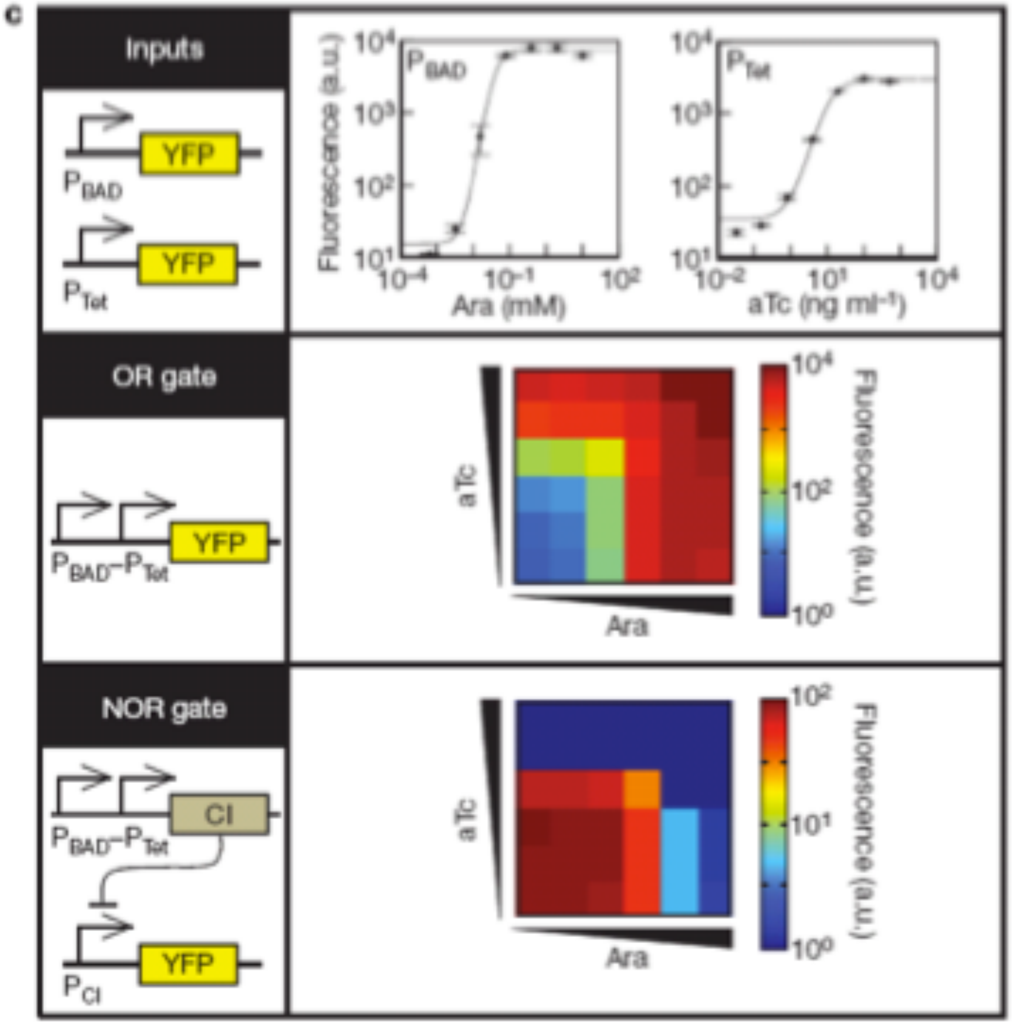


Inputs		
in1	in2	Output
0	0	1
0	1	0
1	0	0
1	1	0

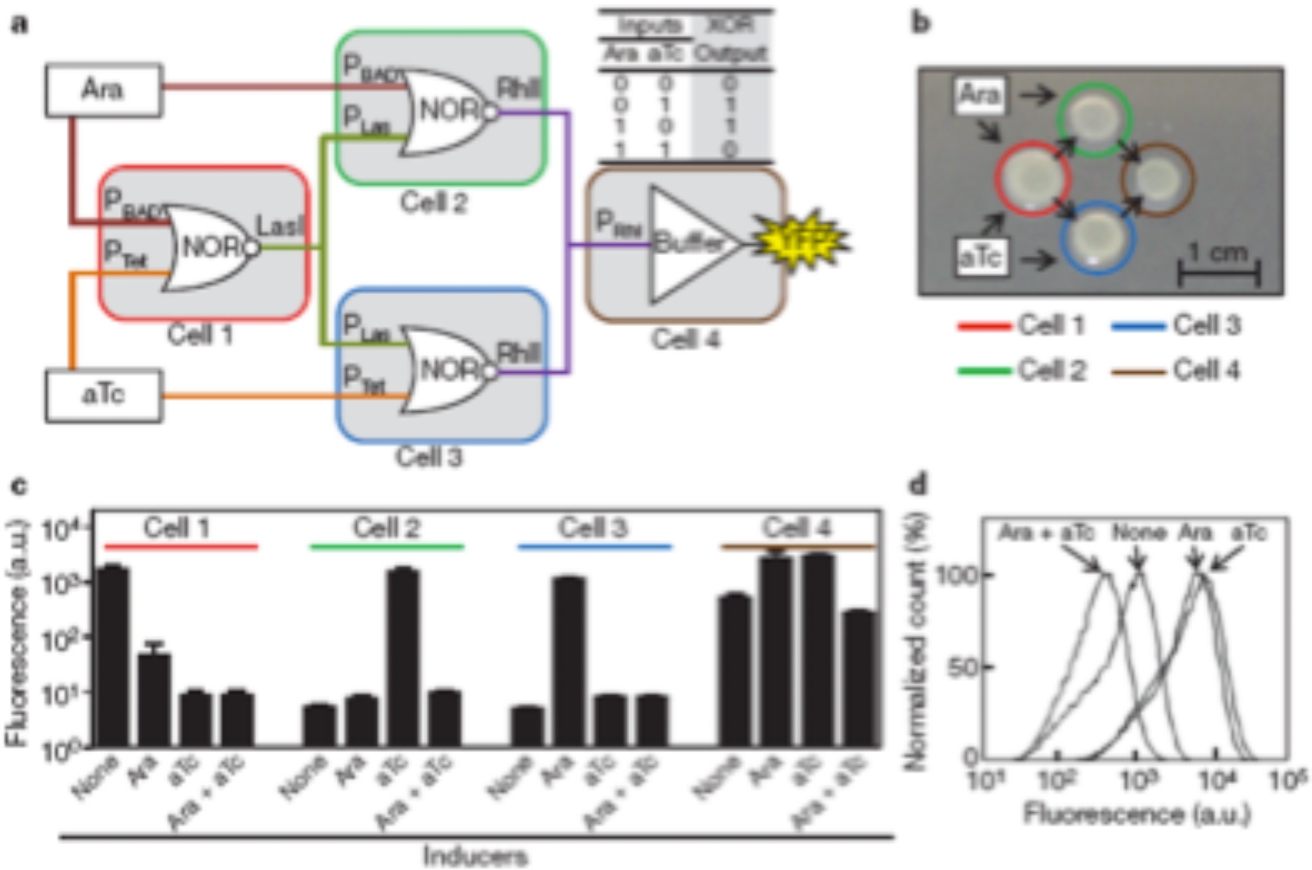
b

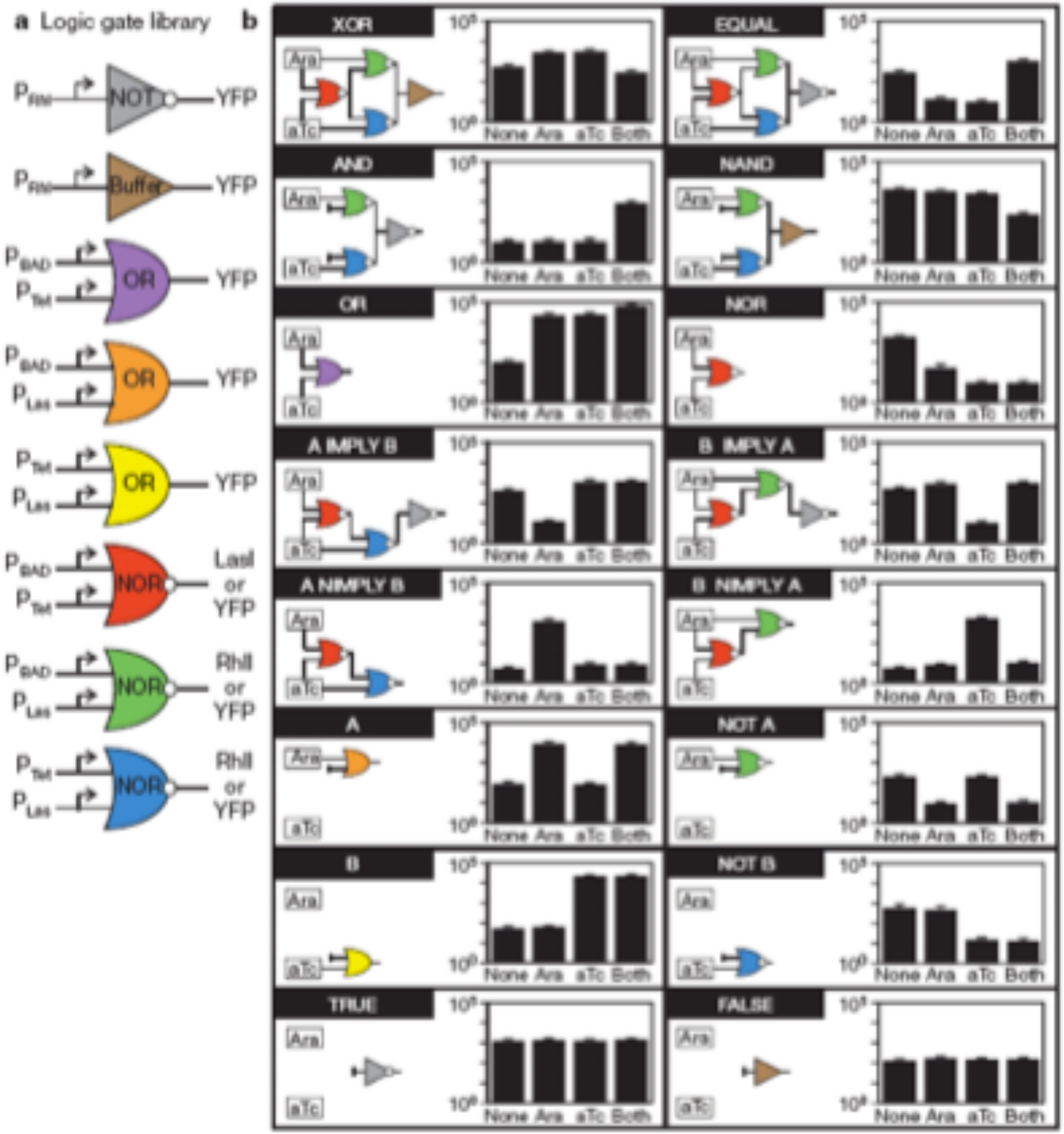


Multicellular computation based on standard (NOR) approach



Multicellular computation based on standard (NOR) approach





jueves 21 de julio de 2011

Multicellular computation based on non-standard approach: Distributed Output Production

LETTER

doi:10.1038/nature09679

Distributed biological computation with multicellular engineered networks

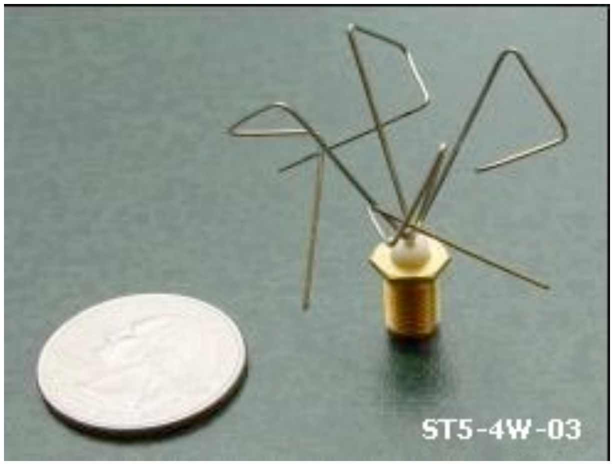
Sergi Regot[1]*, Javier Macia[2]*, Núria Conde[1,2], Kentaro Furukawa[3], Jimmy Kjellén[3], Tom Peeters[1], Stefan Hohmann[3], Eulàlia de Nadal[1], Francesc Posas[1] & Ricard Solé[2,4,5]

Can evolution help us?

Evolutionary algorithms can find the optimal solution.

Can evolution help us?

Evolutionary algorithms can find the optimal solution.



Can evolution help us?

Evolutionary algorithms can look for the optimal solution.

- Population of multicellular "organisms"
- Each cell implements a simple logic gate
- Cell can be "connected" by secreting/sensing signals e.g. diffusible molecules ("wires")
- The final output of the circuit can be produced in different cells
- "Organisms" can mutate at different levels

Can evolution help us?

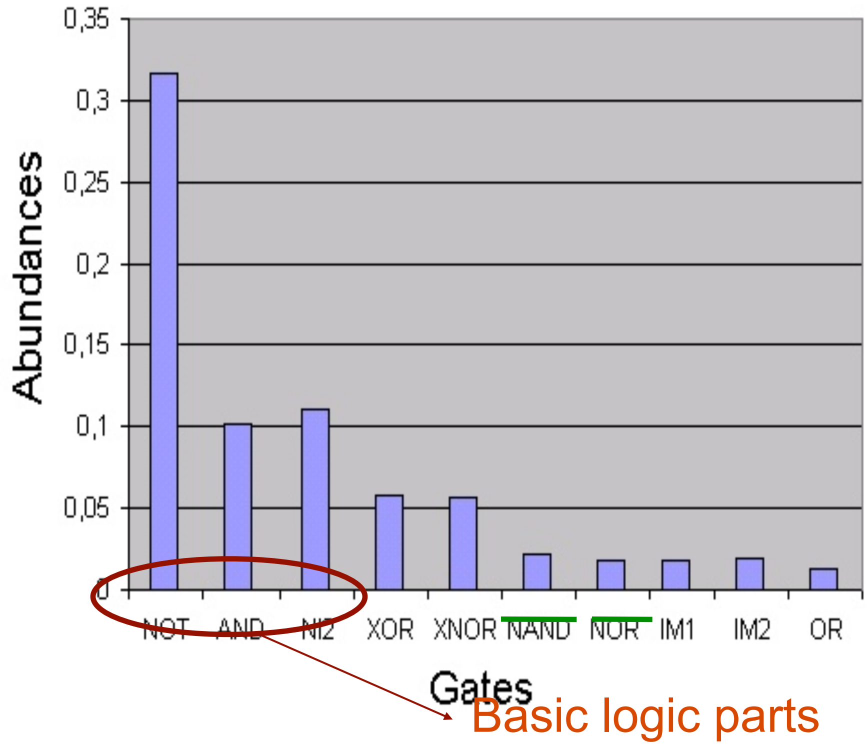
Fitness

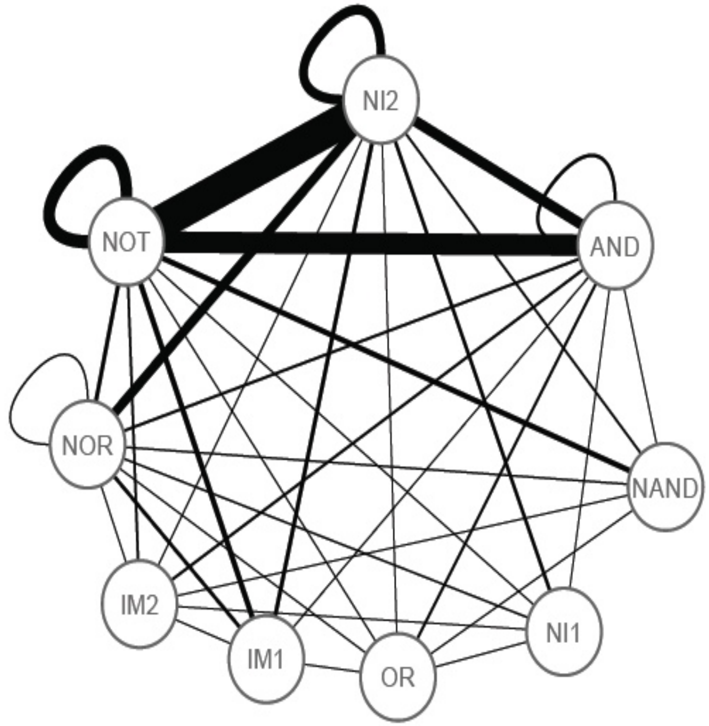
→ "Organisms" must implement a predefined Boolean function

→ Minimal cost, i. e minimal number of "wires" and minimal number of cells.

→ Minimal diversity of cellular types

Results of evolutionary algorithms



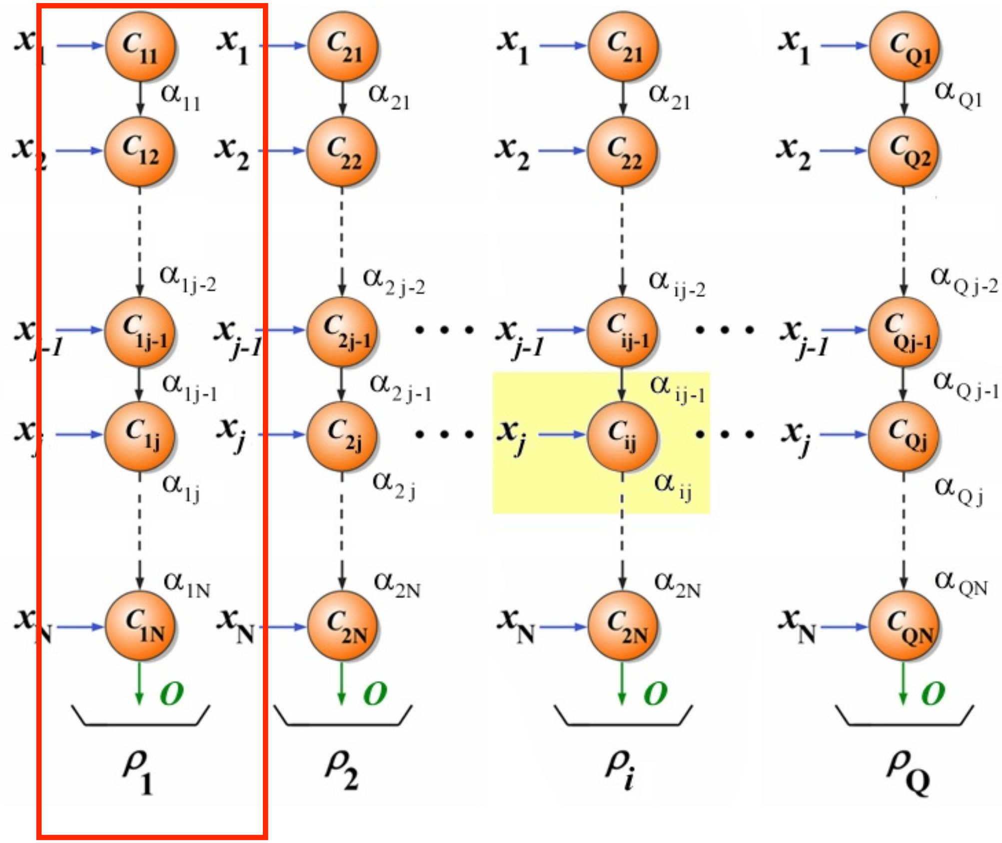


Multiplexer 2 to 1

General implementation

$$f = [\theta^{s_{11}}{}_{11}(x_1)\ \ AND\ \ \theta^{s_{12}}{}_{12}(x_2) \times\times\times\ AND\ \ \theta^{s_{1N}}{}_{1N}(x_N)]\ \ OR\ \ [\theta^{s_{21}}{}_{21}(x_1)\ \ AND\ \ \theta^{s_{22}}{}_{22}(x_2) \times\times\times$$

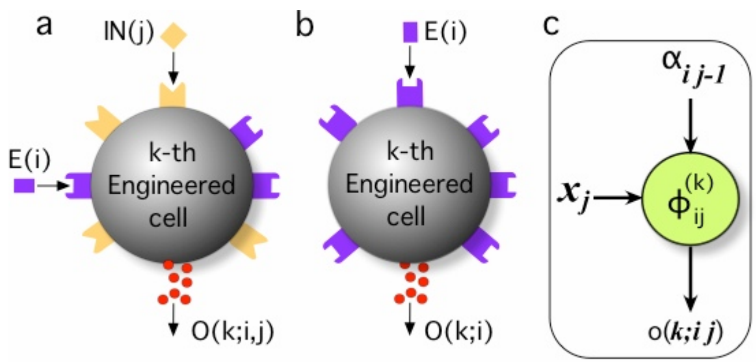
$$AND\ \ \theta^{s_{2N}}{}_{2N}(x_N)]\ \times\times\times OR\ \ [\theta^{s_{\mu 1}}{}_{\mu 1}(x_1)\ \ AND\ \ \theta^{s_{\mu 2}}{}_{\mu 2}(x_2) \times\times\times\ AND\ \ \theta^{s_{\mu N}}{}_{\mu N}(x_N)]$$



General implementation

$$f = [\theta^{s_{11}}{}_{11}(x_1) \;\; AND \;\; \theta^{s_{12}}{}_{12}(x_2) \times\times\times \; AND \;\; \theta^{s_{1N}}{}_{1N}(x_N)] \;\; OR \;\; [\theta^{s_{21}}{}_{21}(x_1) \;\; AND \;\; \theta^{s_{22}}{}_{22}(x_2) \times\times\times$$

$$AND \;\; \theta^{s_{2N}}{}_{2N}(x_N)] \;\; \times\times\times OR \;\; [\theta^{s_{\mu 1}}{}_{\mu 1}(x_1) \;\; AND \;\; \theta^{s_{\mu 2}}{}_{\mu 2}(x_2) \times\times\times \; AND \;\; \theta^{s_{\mu N}}{}_{\mu N}(x_N)]$$



d

x_j	α_{ij-1}	$\phi^{(1)}_{ij}$
0	0	0
0	1	0
1	0	0
1	1	1

AND

x_j	α_{ij-1}	$\phi^{(2)}_{ij}$
0	0	0
0	1	1
1	0	0
1	1	0

N-IMPLIES

e

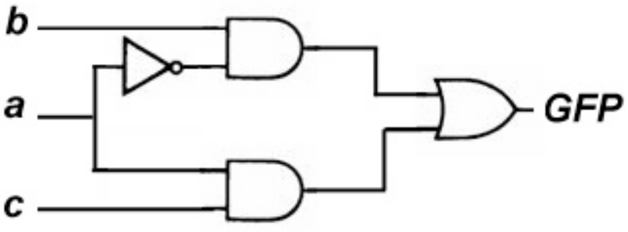
x_j	$\phi^{(3)}_{ij}$
0	0
1	1

IDENTITY

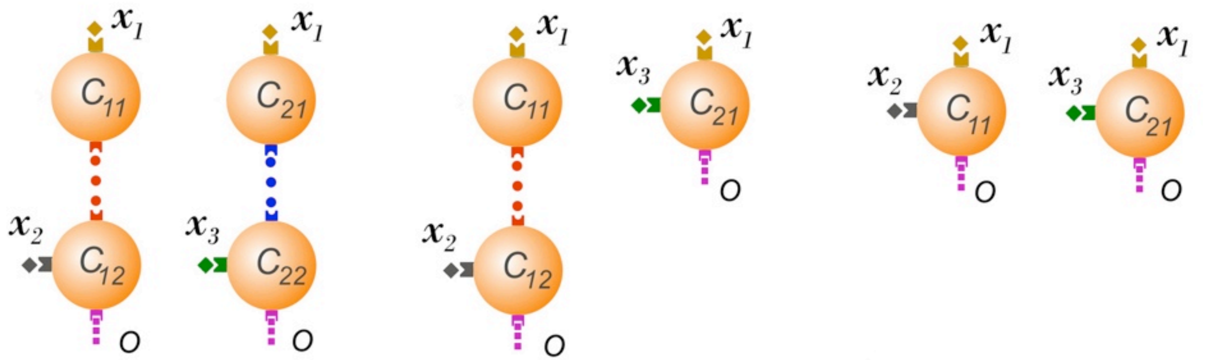
x_j	$\phi^{(4)}_{ij}$
0	1
1	0

NOT

Cellular implementation



$$f = \underbrace{\left[\theta^{NOT}{}_{11}(x_1)\ \ AND\ \ \theta^{Id}{}_{12}(x_2)\right]}_{\rho_1}\ OR\ \underbrace{\left[\theta^{Id}{}_{11}(x_1)\ \ AND\ \ \theta^{Id}{}_{13}(x_3)\right]}_{\rho_2}$$



ρ_1		ρ_2	
C_{11}	NOT	C_{21}	Id.
C_{12}	AND	C_{22}	AND

ρ_1		ρ_2	
C_{11}	NOT	C_{21}	AND
C_{12}	AND		

ρ_1		ρ_2	
C_{11}	N-IMPLIES	C_{21}	AND

x_j	α_{ij-1}	$\phi_{ij}^{(1)}$
0	0	0
0	1	0
1	0	0
1	1	1

AND

x_j	α_{ij-1}	$\phi_{ij}^{(2)}$
0	0	0
0	1	1
1	0	0
1	1	0

N-IMPLIES

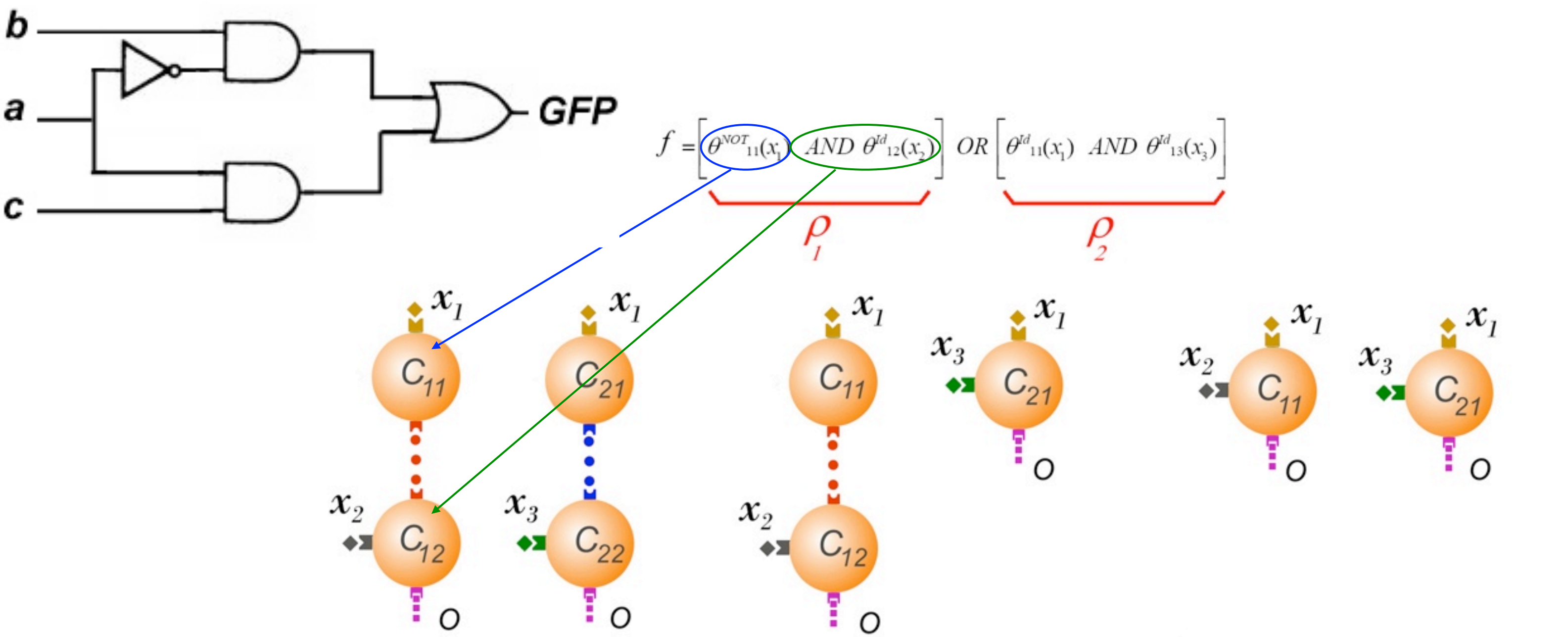
x_j	$\phi_{ij}^{(3)}$
0	0
1	1

IDENTITY

x_j	$\phi_{ij}^{(4)}$
0	1
1	0

NOT

Cellular implementation



ρ1		ρ2	
C_{11}	NOT	C_{21}	Id.
C_{12}	AND	C_{22}	AND

ρ1		ρ2	
C_{11}	NOT	C_{21}	AND
C_{12}	AND		

ρ1		ρ2	
C_{11}	N-IMPLIES	C_{21}	AND

x_j	α_{ij-1}	$\phi_{ij}^{(1)}$
0	0	0
0	1	0
1	0	0
1	1	1

AND

x_j	α_{ij-1}	$\phi_{ij}^{(2)}$
0	0	0
0	1	1
1	0	0
1	1	0

N-IMPLIES

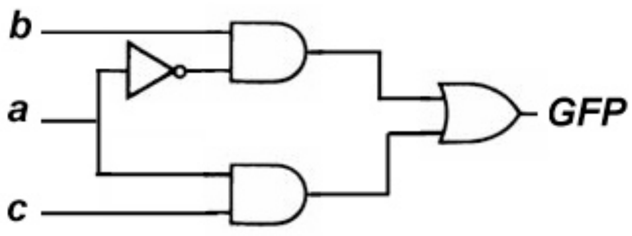
x_j	$\phi_{ij}^{(3)}$
0	0
1	1

IDENTITY

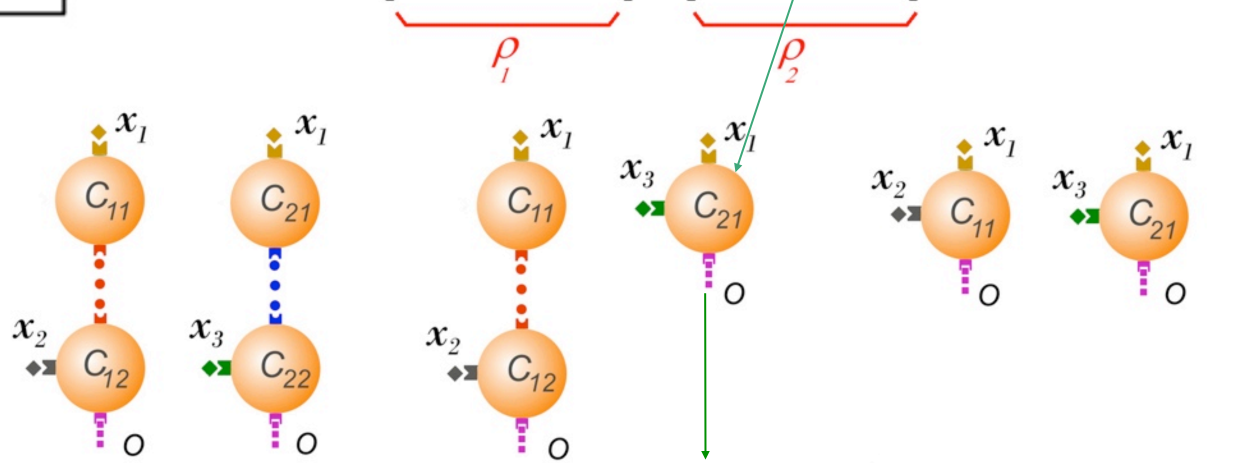
x_j	$\phi_{ij}^{(4)}$
0	1
1	0

NOT

Cellular implementation



$$f=\left[\theta^{NOT}_{11}(x_1)\ \ AND\ \ \theta^{Id}_{12}(x_2)\right]\ OR\left[\theta^{Id}_{11}(x_1)\ \ AND\ \ \theta^{Id}_{13}(x_3)\right]$$



ρ_1		ρ_2	
C_{11}	NOT	C_{21}	Id.
C_{12}	AND	C_{22}	AND

ρ_1		ρ_2	
C_{11}	NOT	C_{21}	AND
C_{12}	AND		

ρ_1		ρ_2	
C_{11}	N-IMPLIES	C_{21}	AND

x_j	α_{ij-1}	$\phi^{(1)}_{ij}$
0	0	0
0	1	0
1	0	0
1	1	1

AND

x_j	α_{ij-1}	$\phi^{(2)}_{ij}$
0	0	0
0	1	1
1	0	0
1	1	0

N-IMPLIES

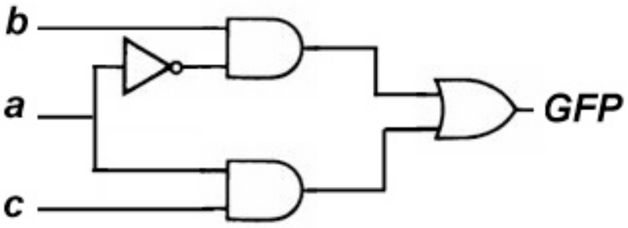
x_j	$\phi^{(3)}_{ij}$
0	0
1	1

IDENTITY

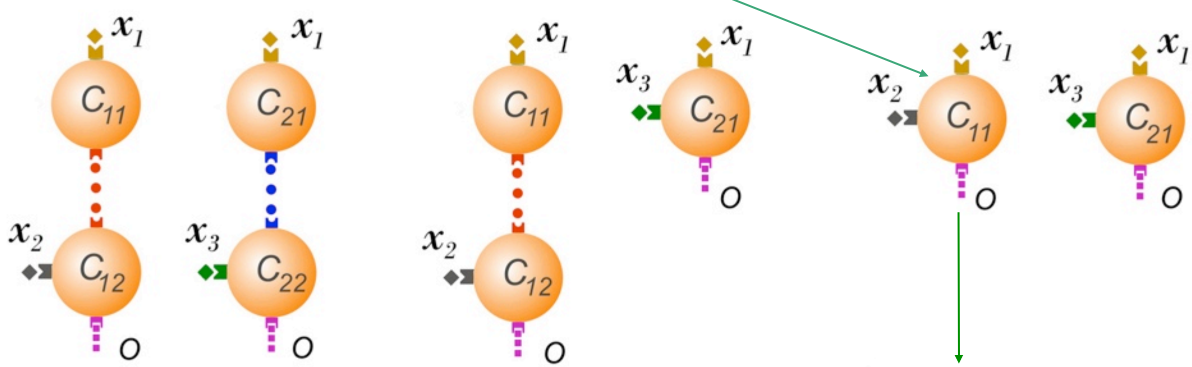
x_j	$\phi^{(4)}_{ij}$
0	1
1	0

NOT

Cellular implementation



$$f = \underbrace{\left[\theta^{NOT}{}_{11}(x_1)\ \ AND\ \ \theta^{Id}{}_{12}(x_2)\right]}_{\rho_1} OR \underbrace{\left[\theta^{Id}{}_{11}(x_1)\ \ AND\ \ \theta^{Id}{}_{13}(x_3)\right]}_{\rho_2}$$



ρ_1		ρ_2	
C_{11}	NOT	C_{21}	Id.
C_{12}	AND	C_{22}	AND

ρ_1		ρ_2	
C_{11}	NOT	C_{21}	AND
C_{12}	AND		

ρ_1		ρ_2	
C_{11}	N-IMPLIES	C_{21}	AND

x_j	α_{ij-1}	$\phi^{(1)}_{ij}$
0	0	0
0	1	0
1	0	0
1	1	1

AND

x_j	α_{ij-1}	$\phi^{(2)}_{ij}$
0	0	0
0	1	1
1	0	0
1	1	0

N-IMPLIES

x_j	$\phi^{(3)}_{ij}$
0	0
1	1

IDENTITY

x_j	$\phi^{(4)}_{ij}$
0	1
1	0

NOT

Cellular implementation

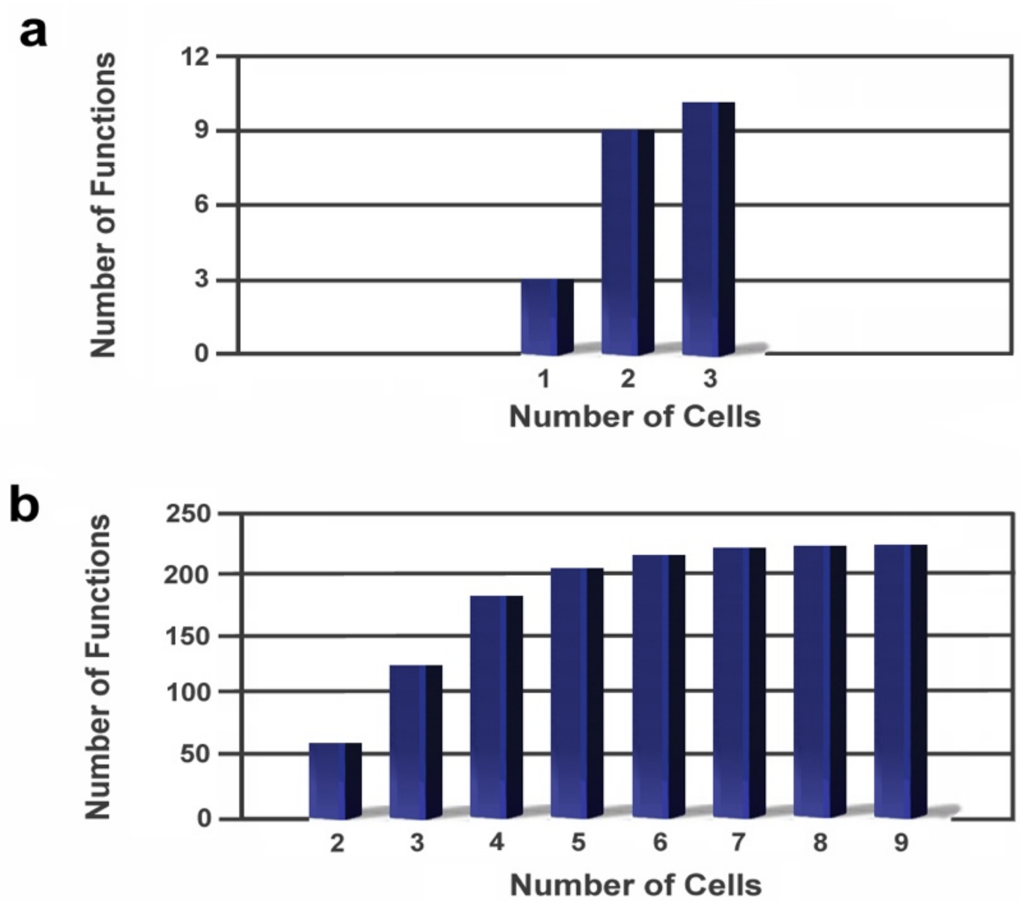


Figure S2. **Number of possible boolean functions versus the number of different cells required for their implementation.** Each graph represent the number of (non-null) functions that can be implemented with a defined number of engineered cells that receive 2-inputs (**a**) and 3-inputs (**b**).

Cellular implementation

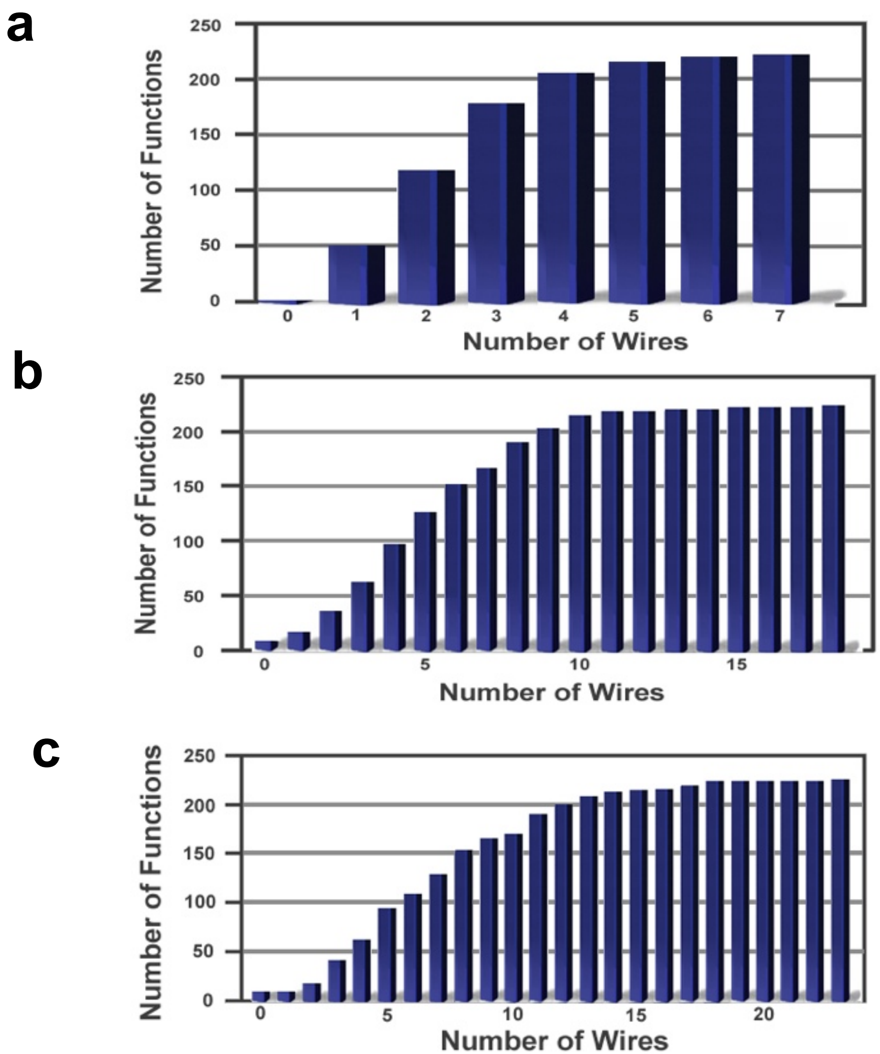
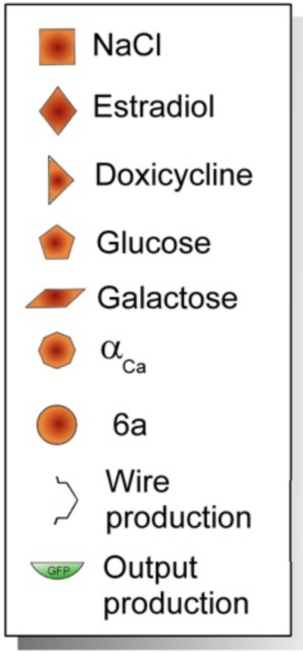
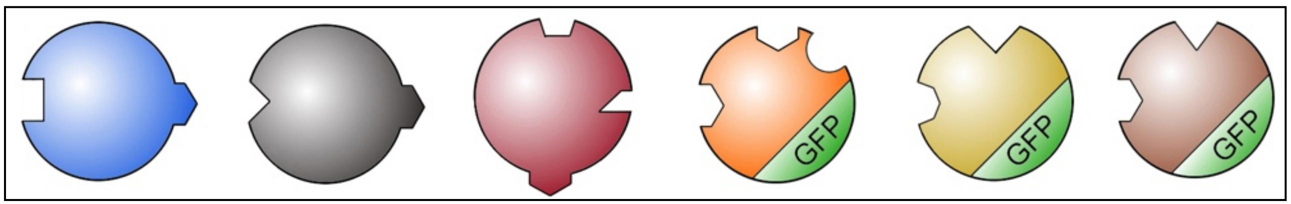


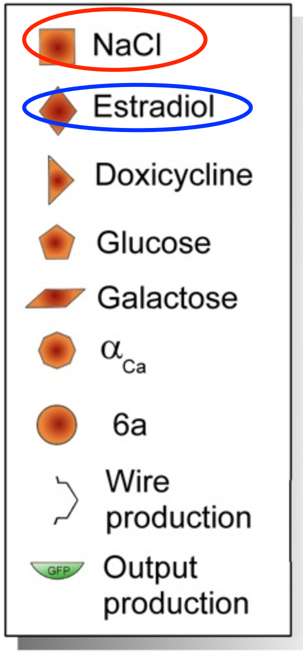
Figure S3. **Number of possible boolean functions versus the number of different wires required for their implementation upon different approaches.** (a) Multicellular approach, (b) standard approach based on NAND logic, (c) standard approach based on NOR logic

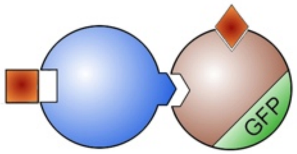
The LEGO® metaphor



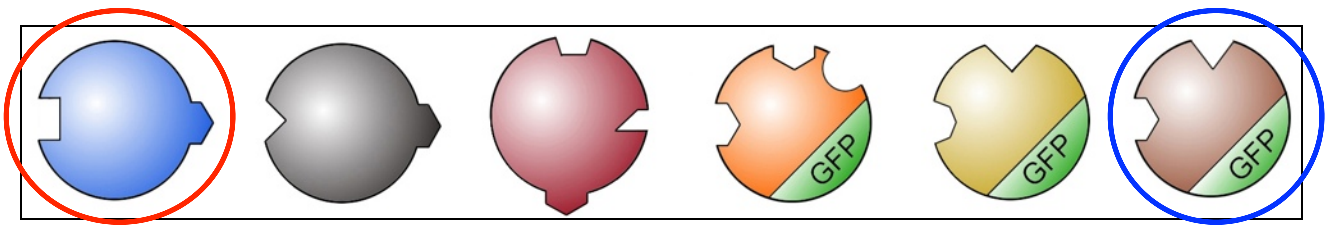


The LEGO® metaphor

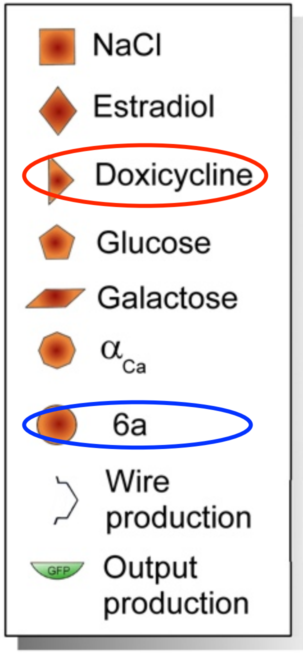


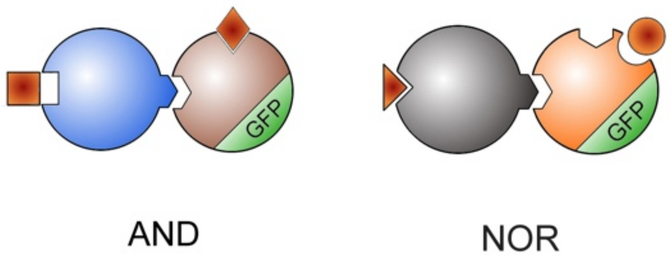


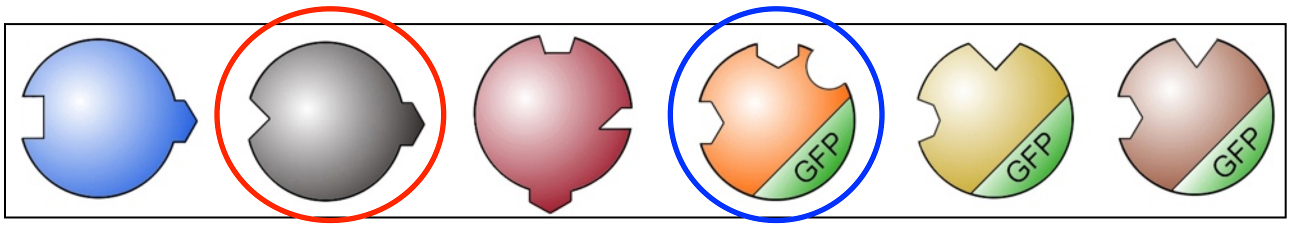
AND



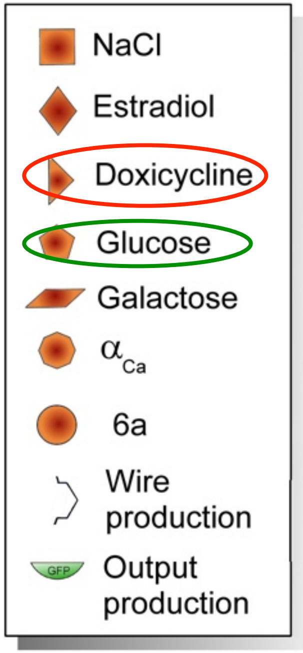
The LEGO® metaphor

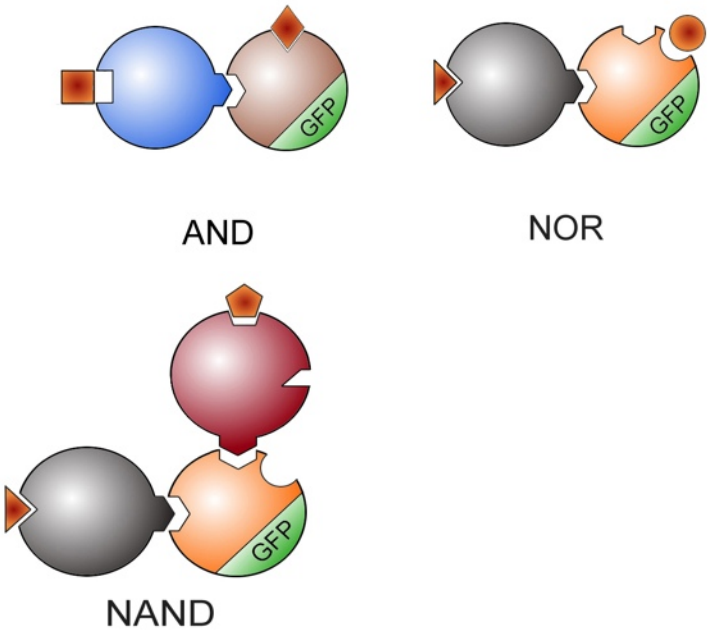


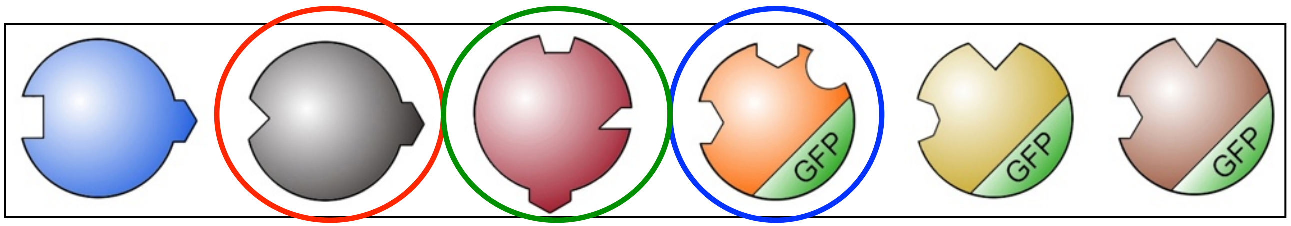




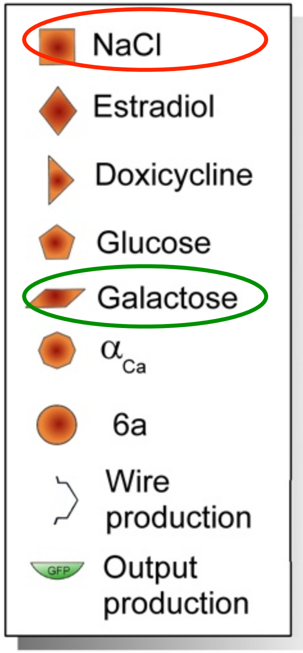
The LEGO® metaphor

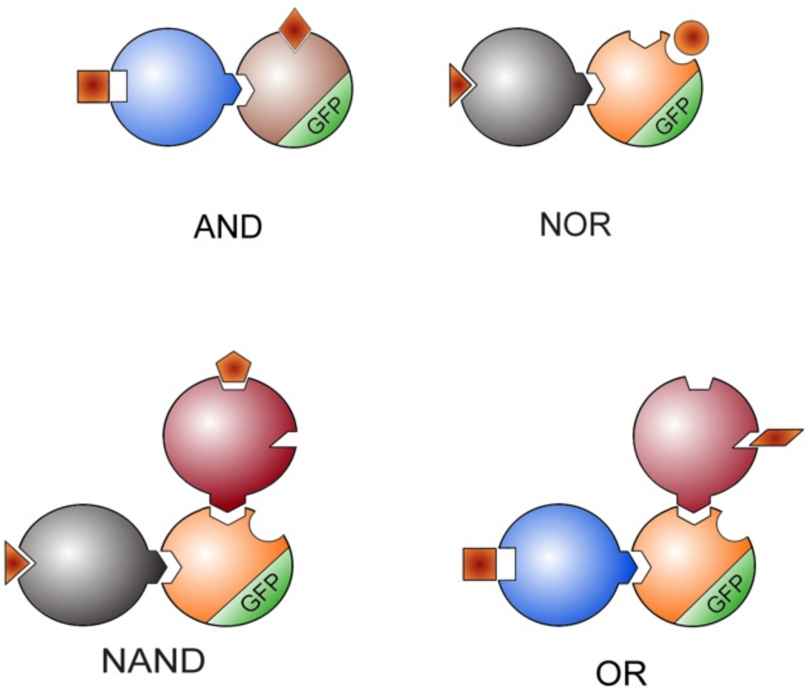


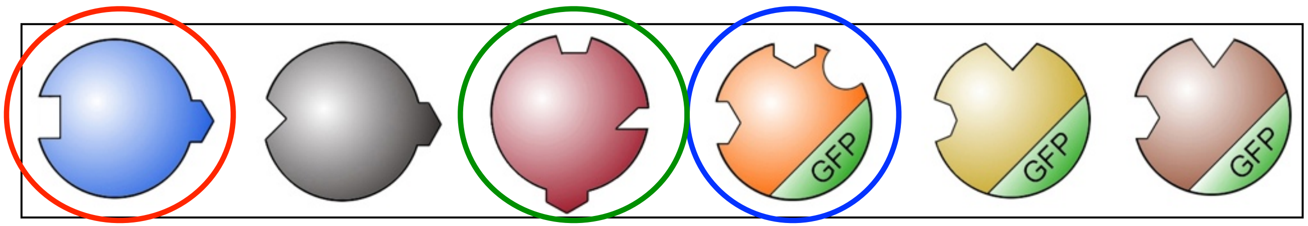




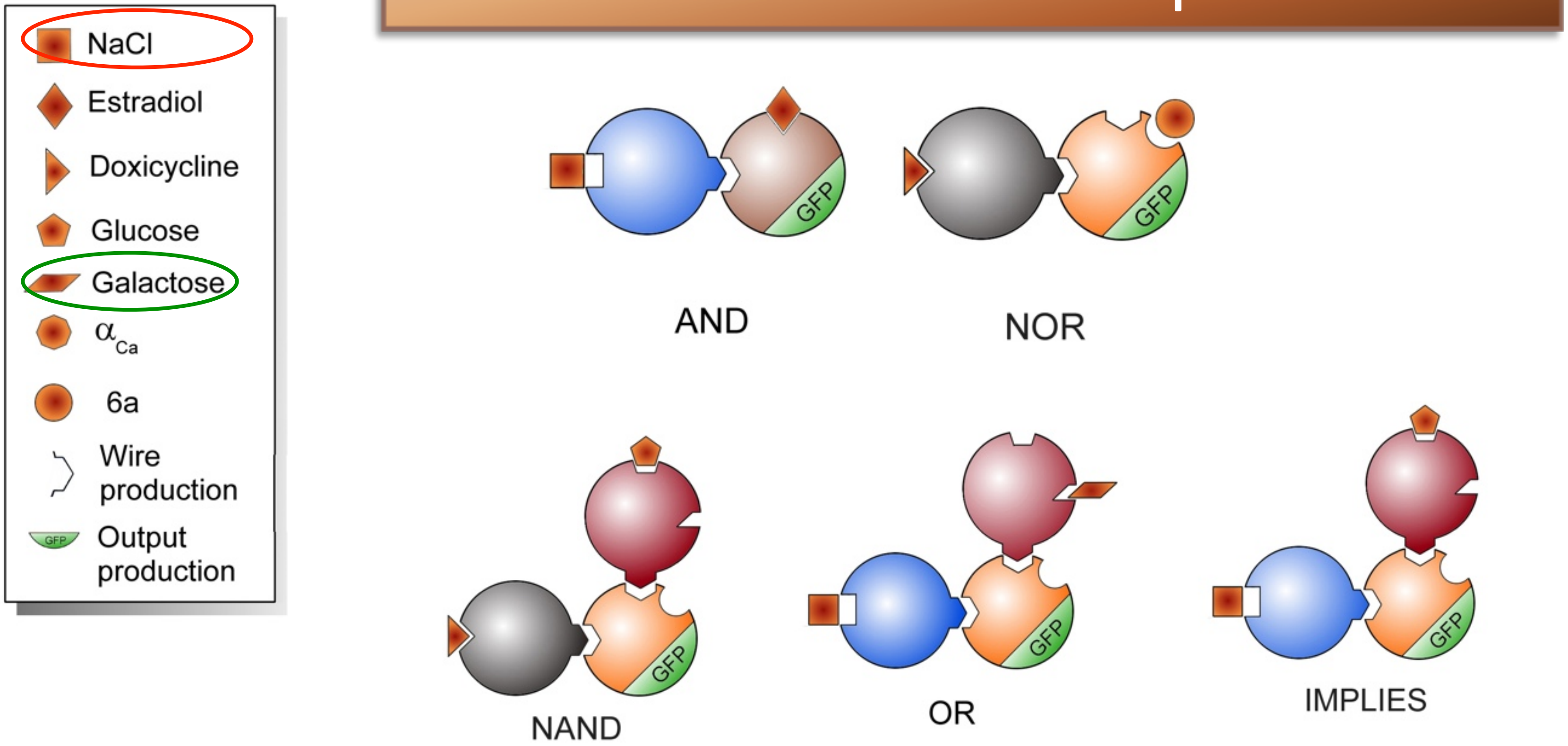
The LEGO® metaphor

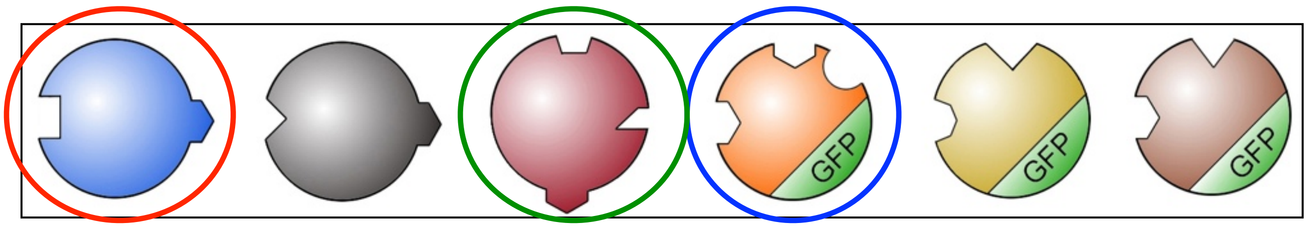




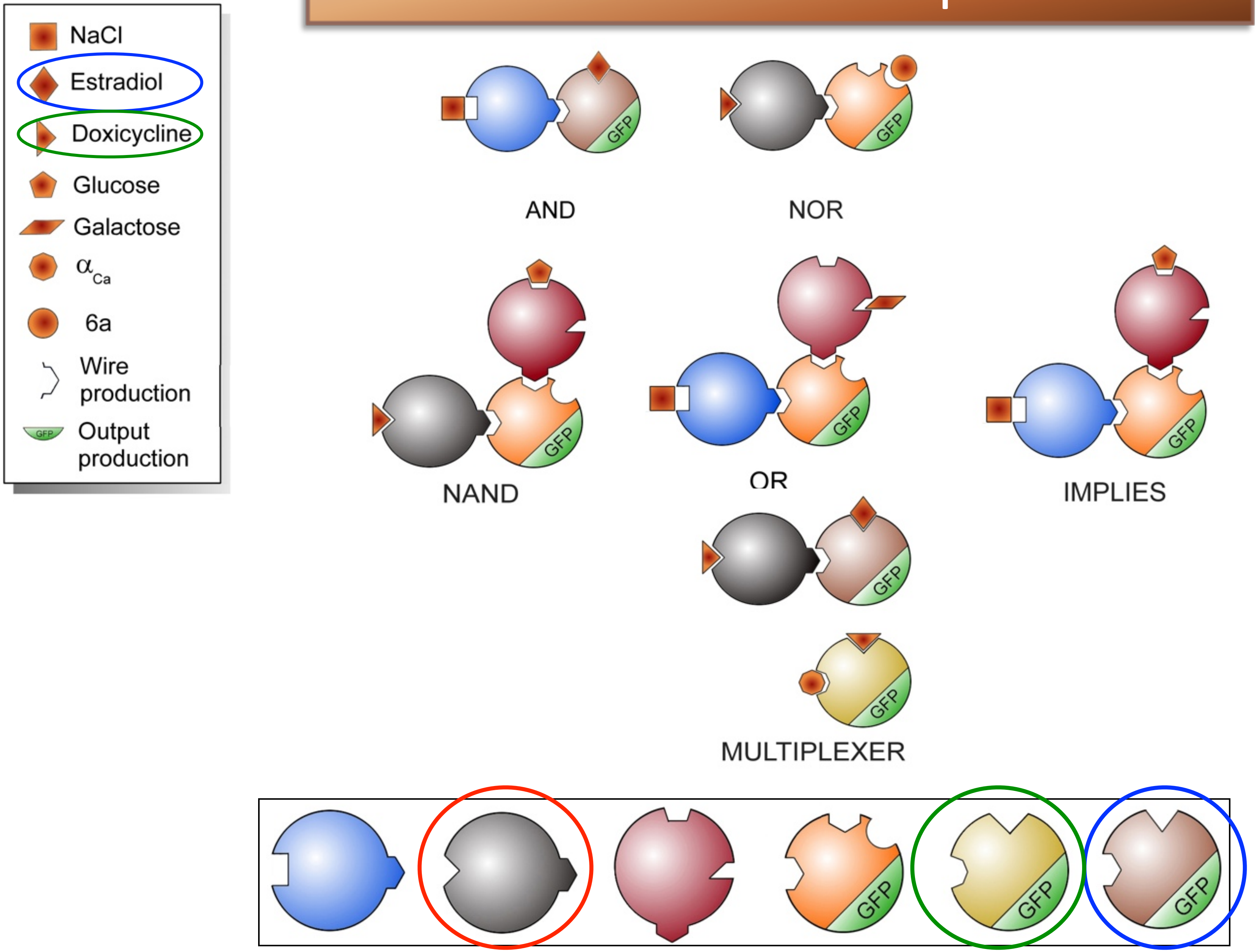


The LEGO® metaphor





The LEGO® metaphor



Conclusions

1. Our approach reduces the wiring requirements and the complexity of the constructs in each cell due to the multi-cellular distribution => We can build more complex circuits.

2. Circuits can be easily reprogrammed or reconfigured just adding or removing few cells.

3. We should solve definitely the wiring problem introducing space as a new computational element

Thank you!!!

UNIVERSITAT POMPEU FABRA

prbb Barcelona Biomedical Research Park