CBGP
CENTRO DE BIOTECNOLOGÍA Y GENÓMICA DE PLANTAS
UPM-INIA

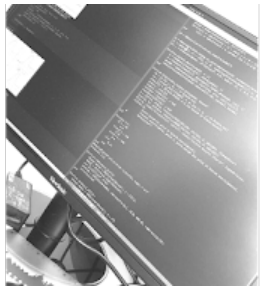
POLITÉCNICA

UNIVERSIDAD POLITÉCNICA DE MADRID

Biocomputing with synthetic biological systems

Ángel Goñi-Moreno

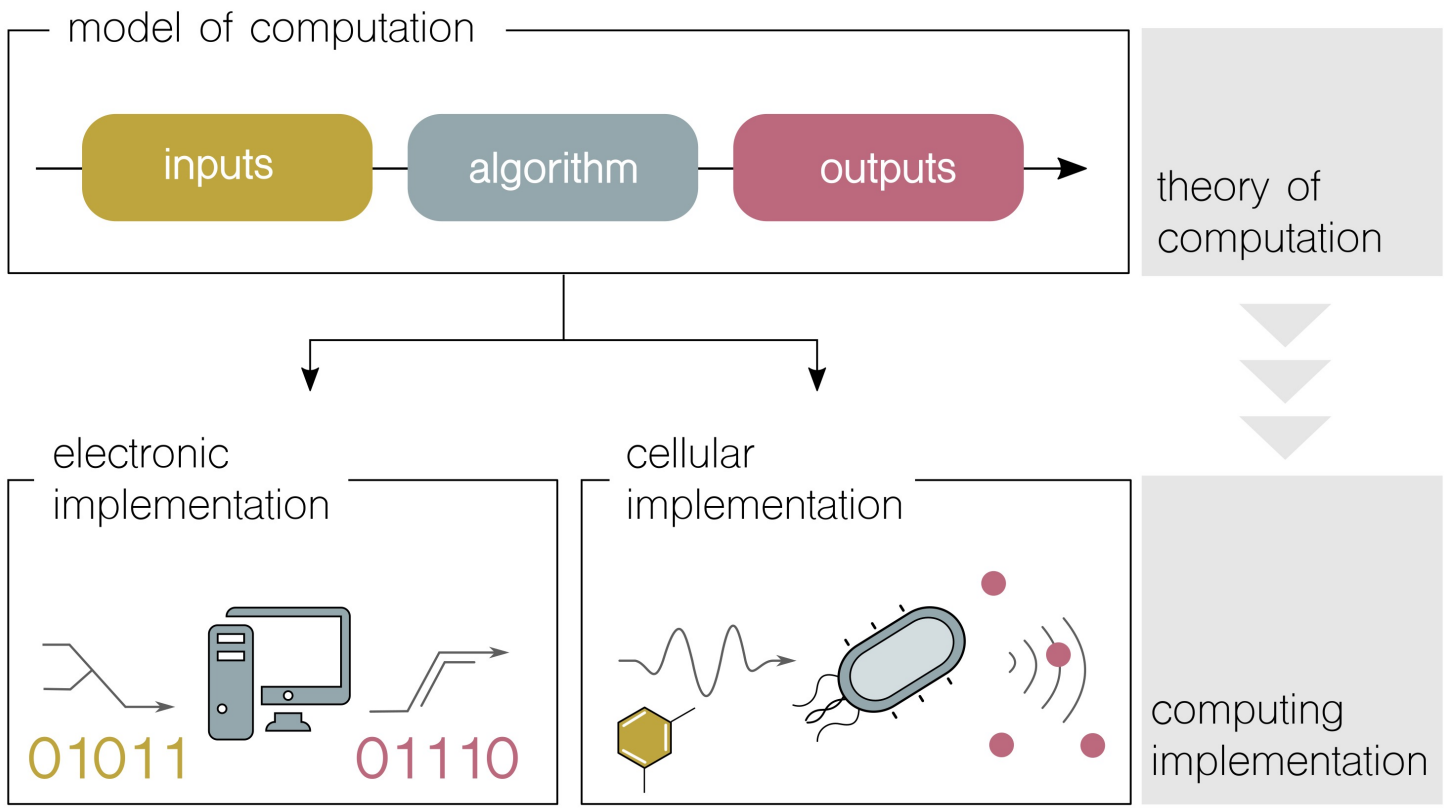
@AngelGMoreno

What do I mean by *computing*?

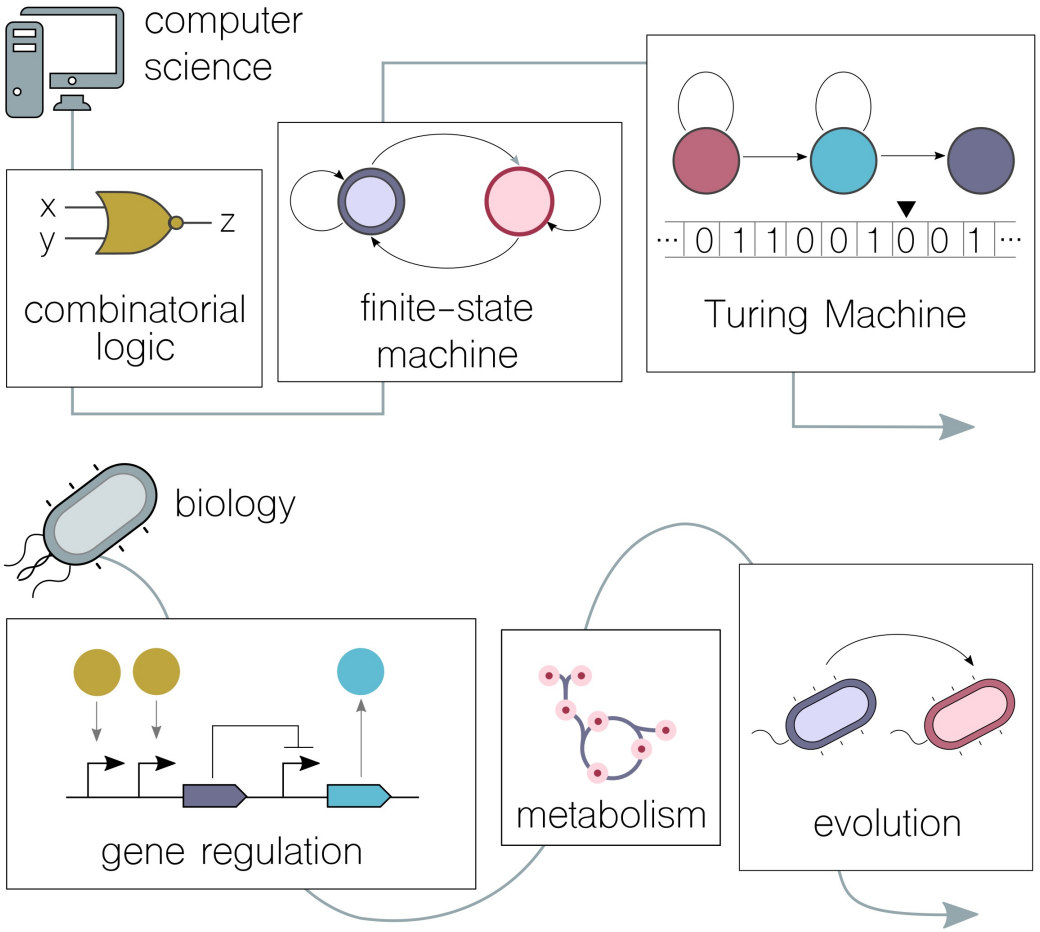
- I don't mean bioinformatics.
- I don't mean computational biology.
- I don't use the term as a metaphor.
- I do mean the ability of a system to solve information-related problems.

The cell as a physical computer



The same theoretical model of computation can be physically implemented in different ways; the nature of the computations remains the same.

More than logic circuits

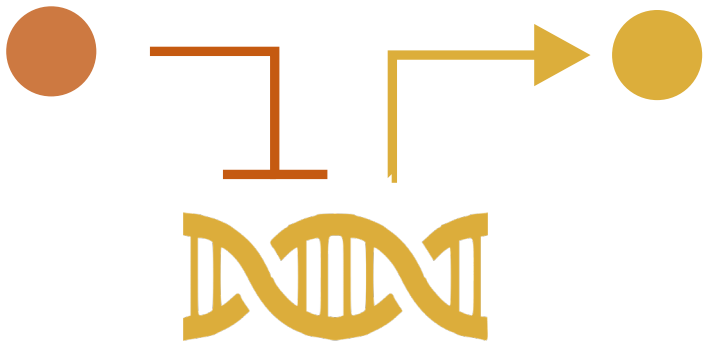


Grozinger et al. Pathways to the cellular supremacy in biocomputing. Nature Communications (2019)

- The logic circuit paradigm is an extremely conservative approach for engineering cellular computations.
- Computer science has developed models of computation that are far more powerful than combinatorial logic, such as finite-state machines or the Turing Machine.
- Similarly, living systems have evolved a variety of computational processes to allow cells to process information. New solutions!

DNA-based logic

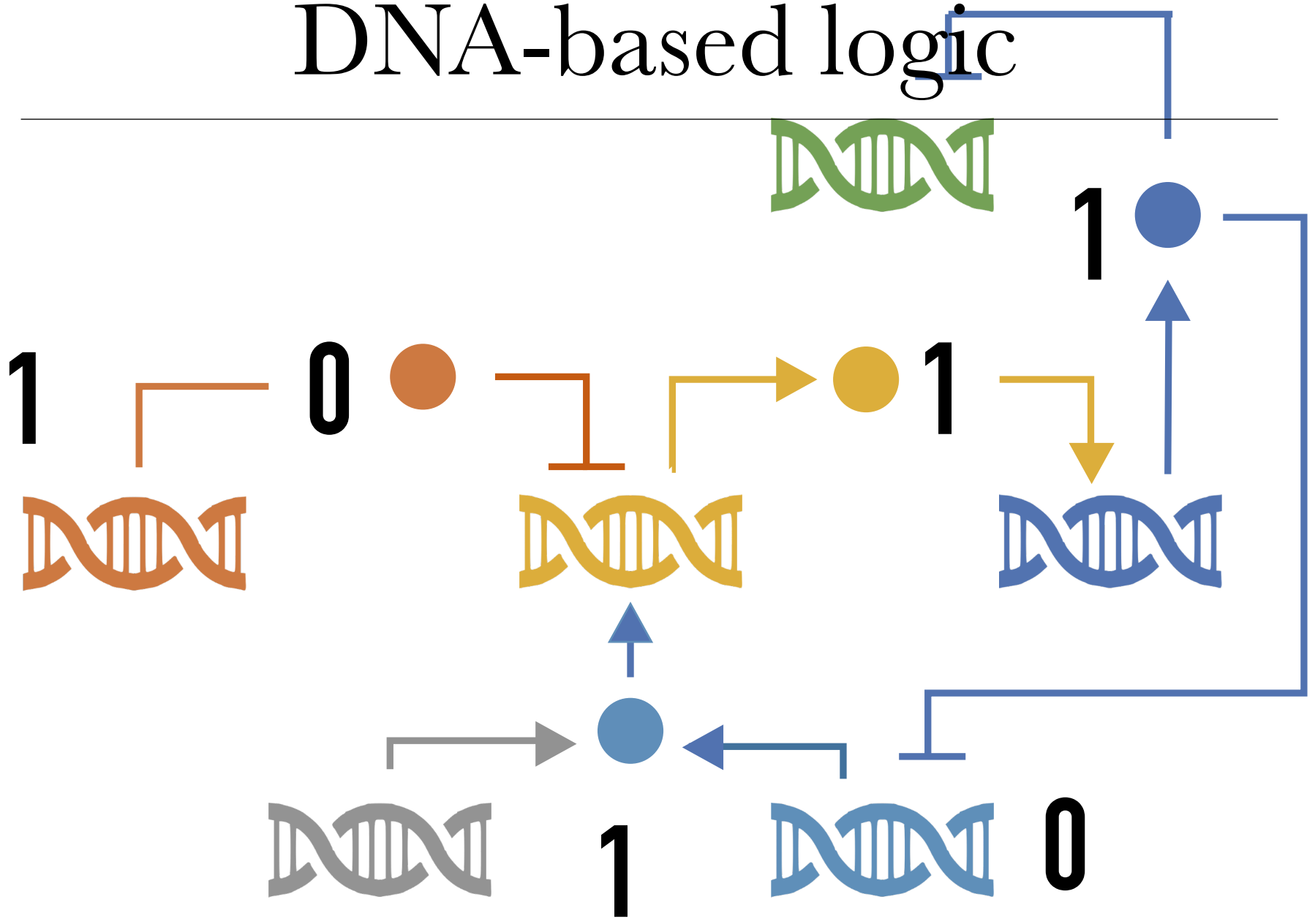
DNA-based logic



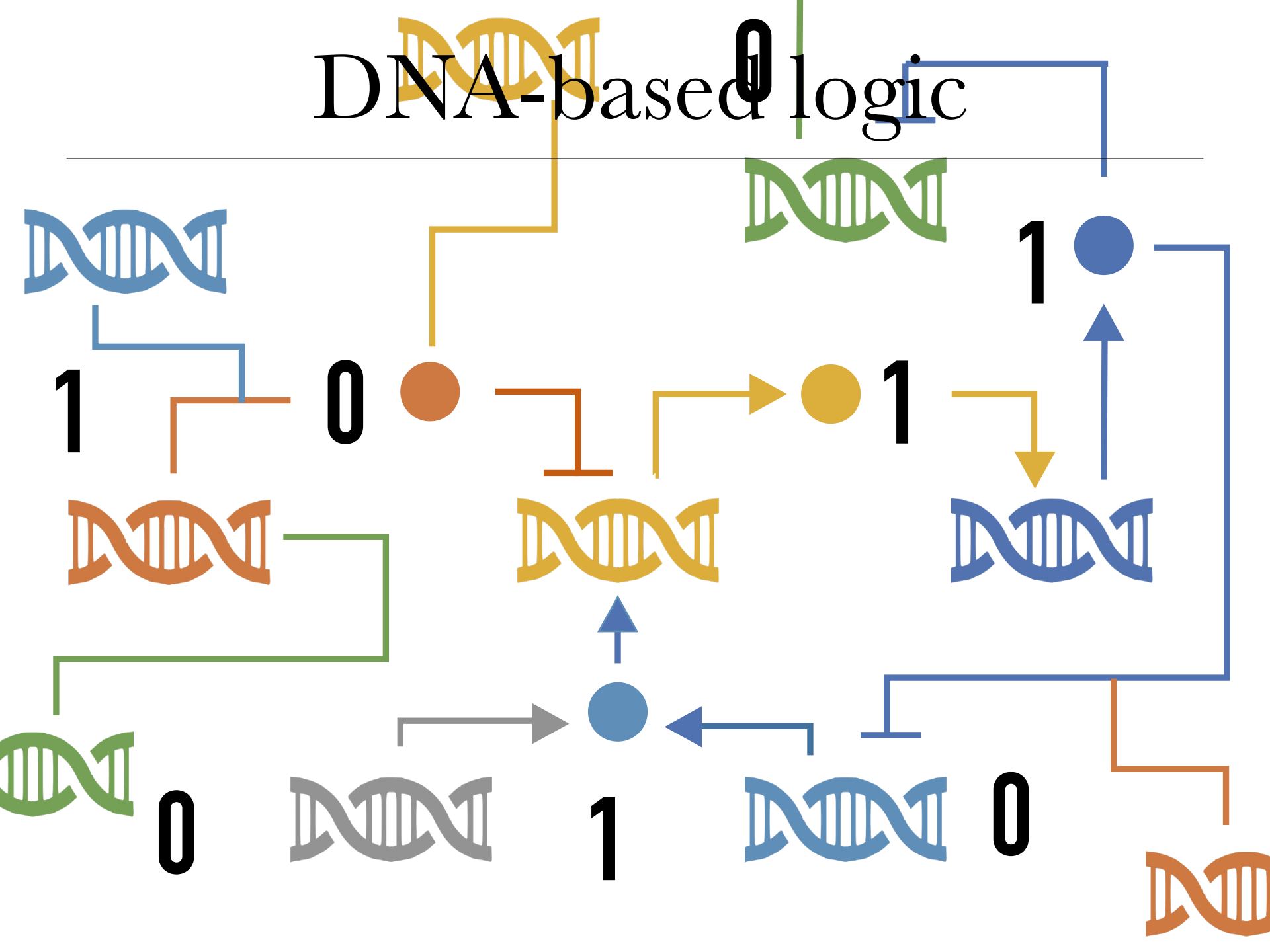
DNA-based logic

DNA-based logic

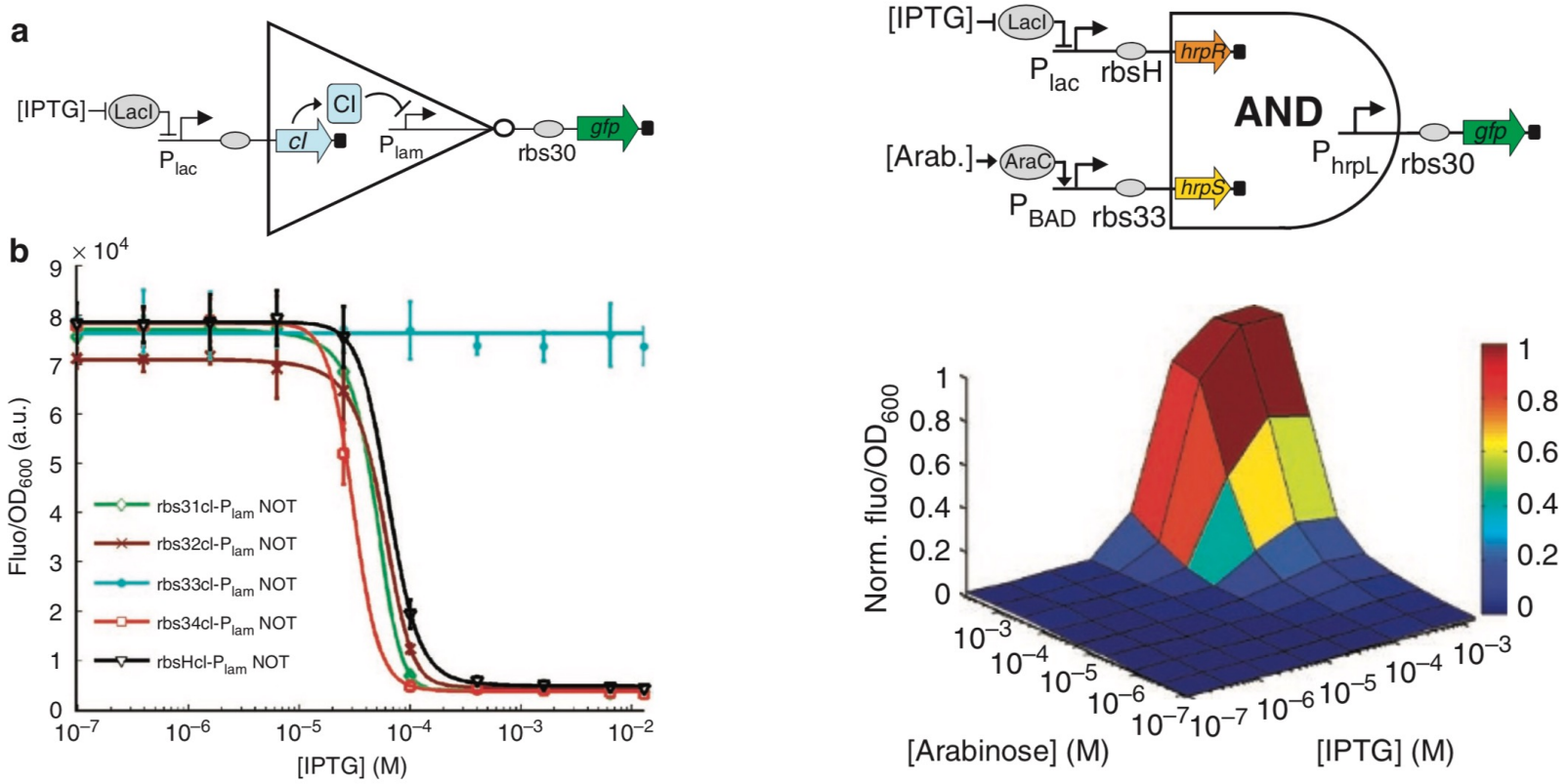
DNA-based logic



DNA-based logic

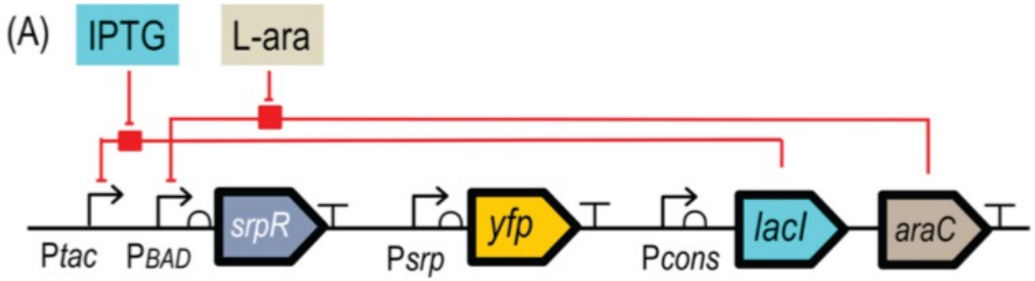


Genetic Logic Gates



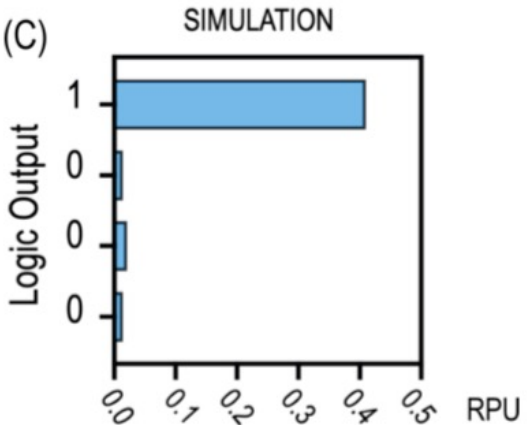
Wang, B. Engineering modular and orthogonal genetic logic gates for robust digital-like synthetic biology. Nature Communications (2011) DOI: 10.1038/ncomms1516

Genetic Logic Gates



(B)

Ptac	PBAD	Output
0	0	ON
0	1	OFF
1	0	OFF
1	1	OFF
IPTG	Ara	

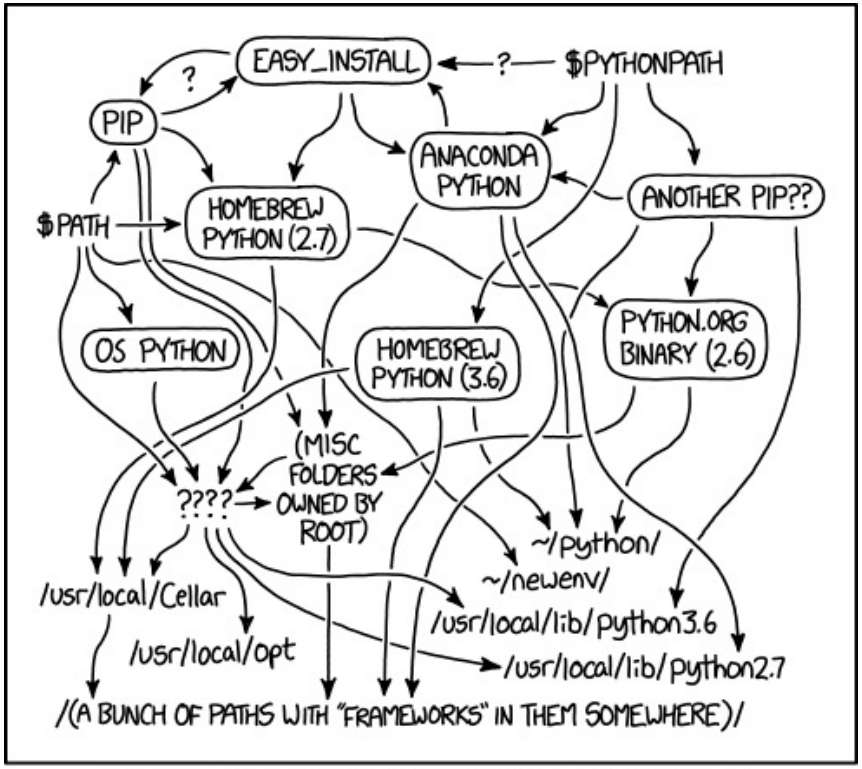


Automated Design and Implementation of a NOR Gate in *Pseudomonas Putida*

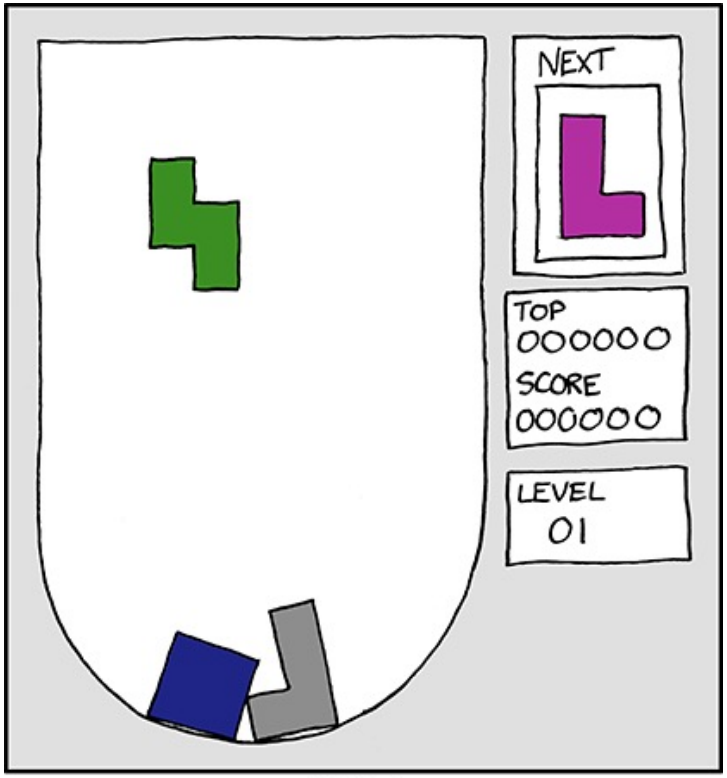
Huseyin Tas, Lewis Grozinger, Angel Goñi-Moreno, Victor de Lorenzo

Synthetic Biology, ysab024, https://doi.org/10.1093/synbio/ysab024
Published: 12 August 2021 **Article history** ▾

Dependency Hell



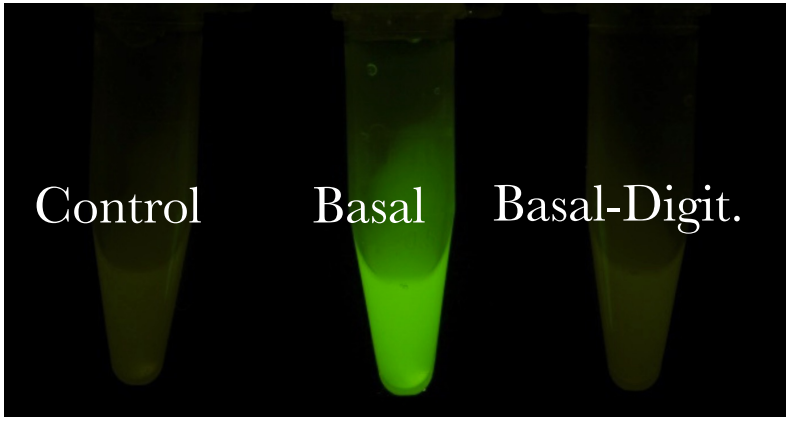
MY PYTHON ENVIRONMENT HAS BECOME SO DEGRADED THAT MY LAPTOP HAS BEEN DECLARED A SUPERFUND SITE.

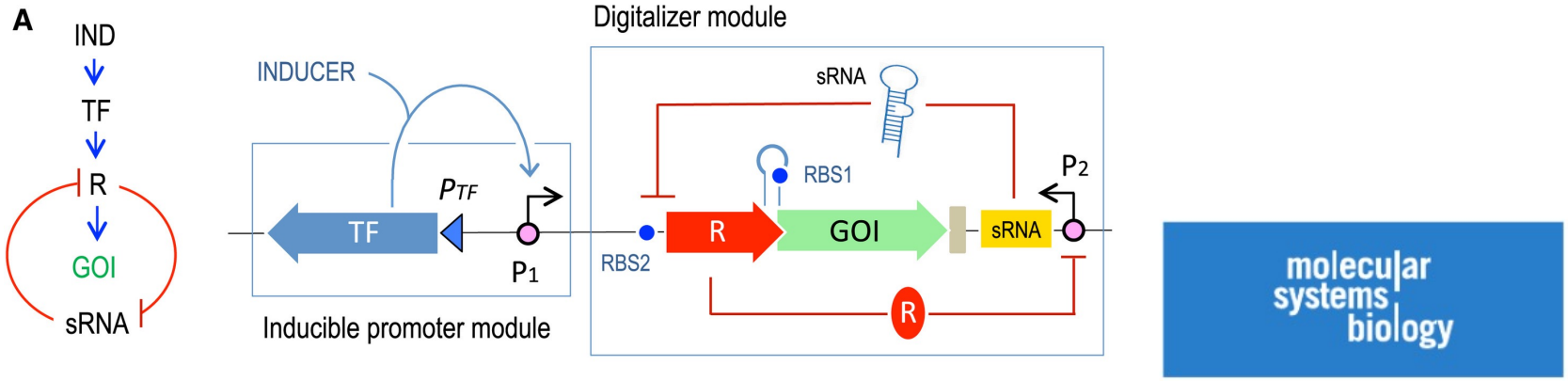


HELL

Stochastic computing

- Digitalizing gene expression: getting rid of the noise to build combinatorial (on/off) circuits.



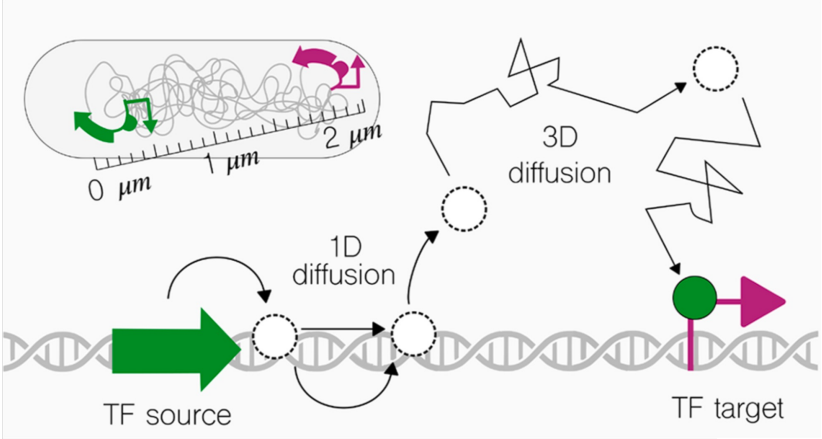


molecular systems biology

Digitalizing heterologous gene expression in Gram-negative bacteria with a portable ON/OFF module

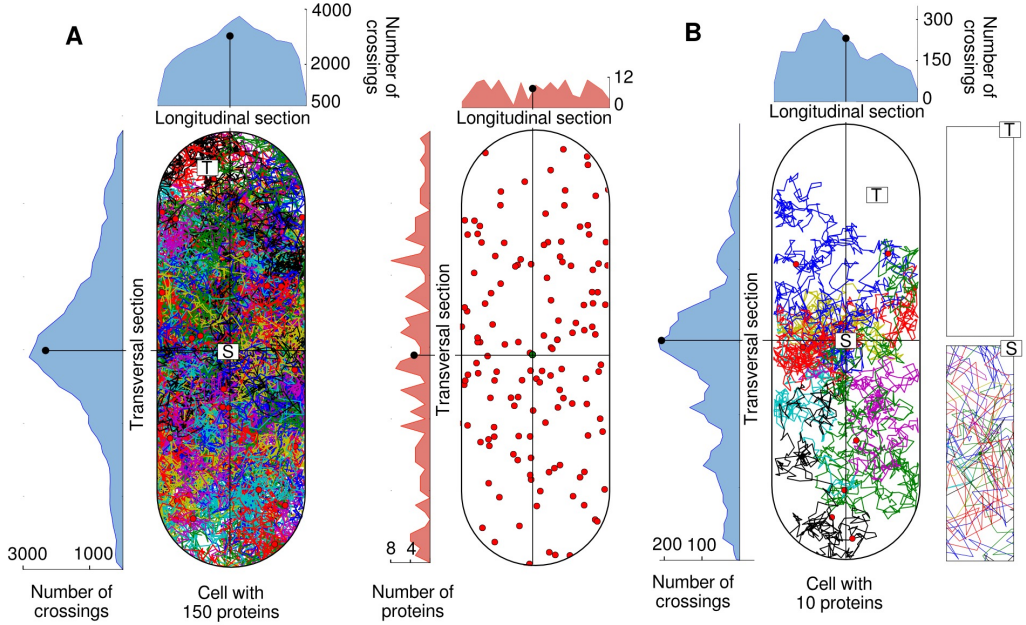
Belén Calles, Ángel Goñi-Moreno† & Víctor de Lorenzo*

Separation between genes

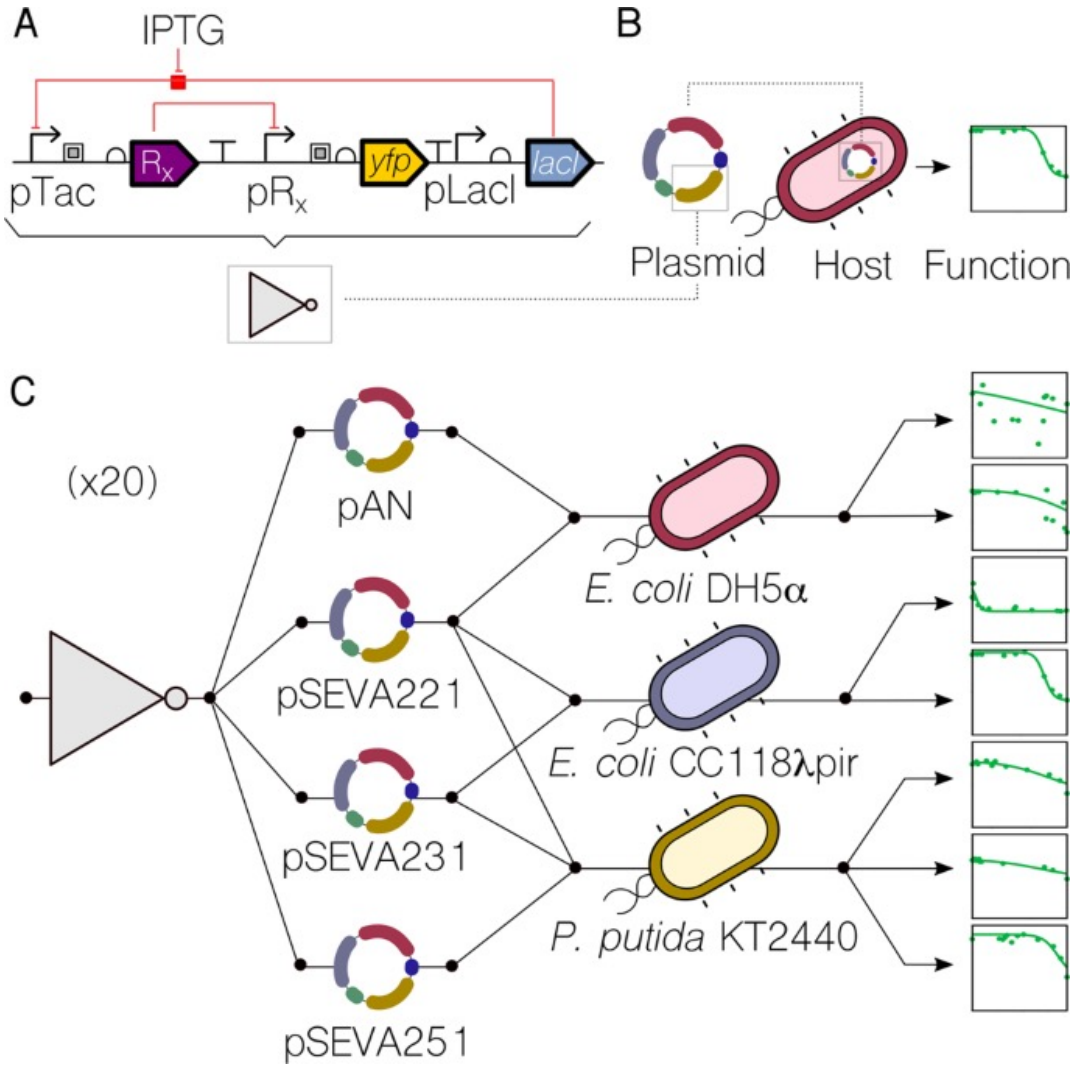


Ruud Stoof et al. A Model for the Spatiotemporal Design of Gene Regulatory Circuits. ACS Synthetic Biology (2019).

Regulators diffusing through the cell would generate heterogeneous occupancy regions.

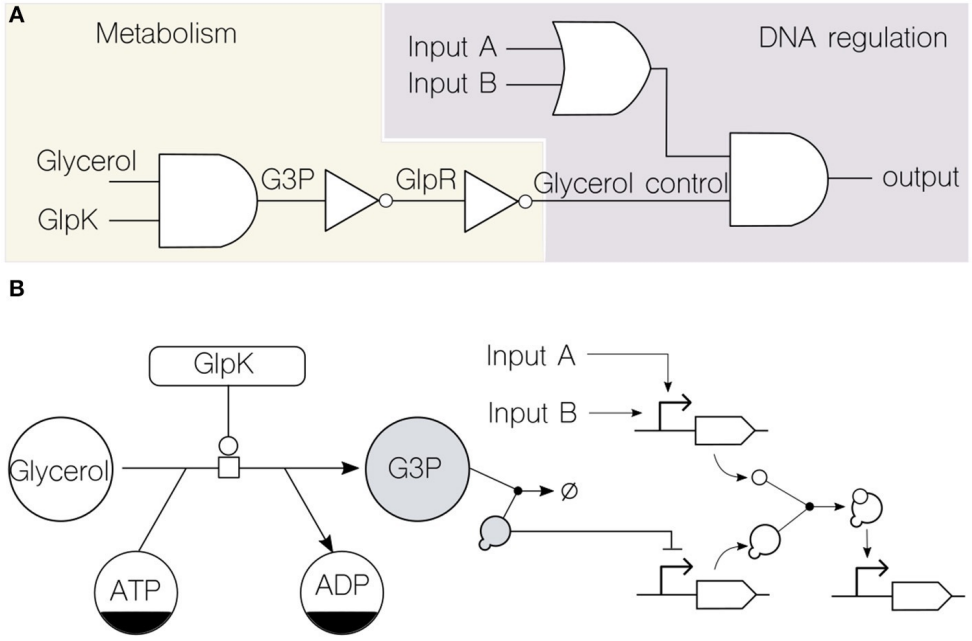


Contextual dependencies

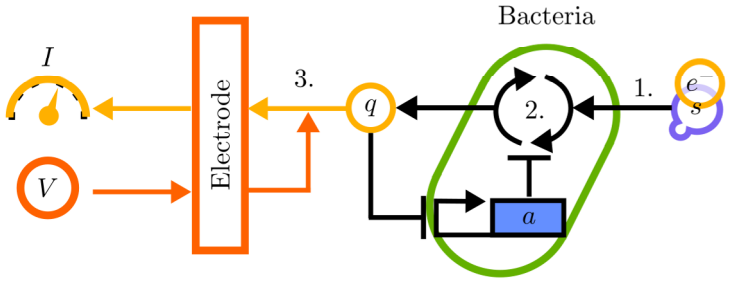


Tas H., et al. Contextual dependencies expand the re-usability of genetic inverters. Nat Commun (2021).

Hybrid circuits

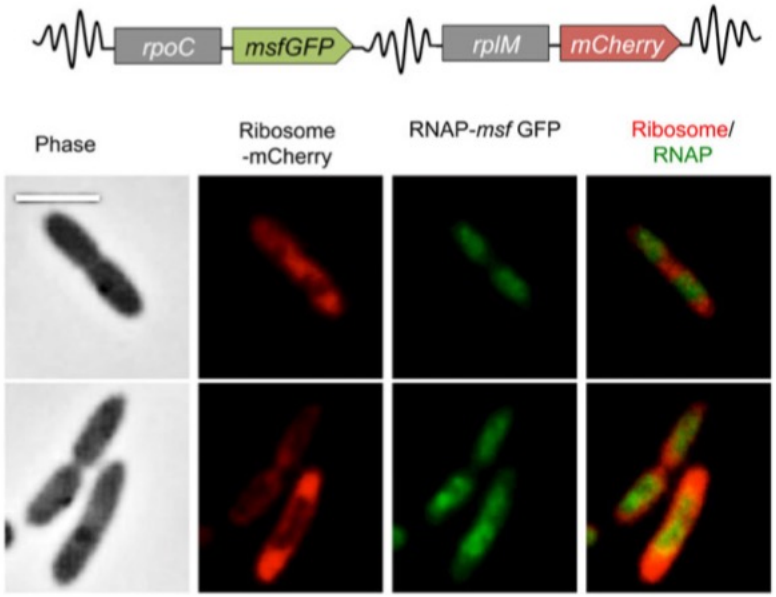


Coñi-Moreno, A., Nikel P. High performance biocomputing in synthetic biology—integrated transcriptional and metabolic circuits. Frontiers in Bioengineering and Biotechnology (2019)

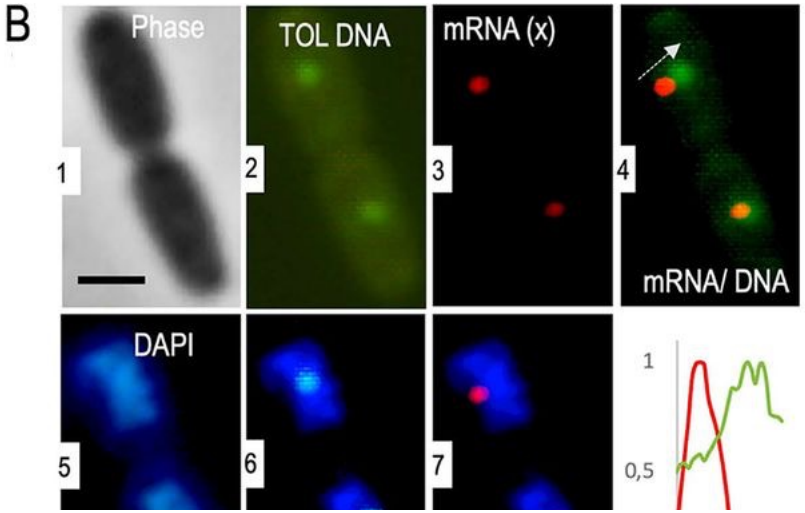


Grozinger et al. An electrogenetic toggle switch design. In prep. (2022)

Hardware (vs. software)

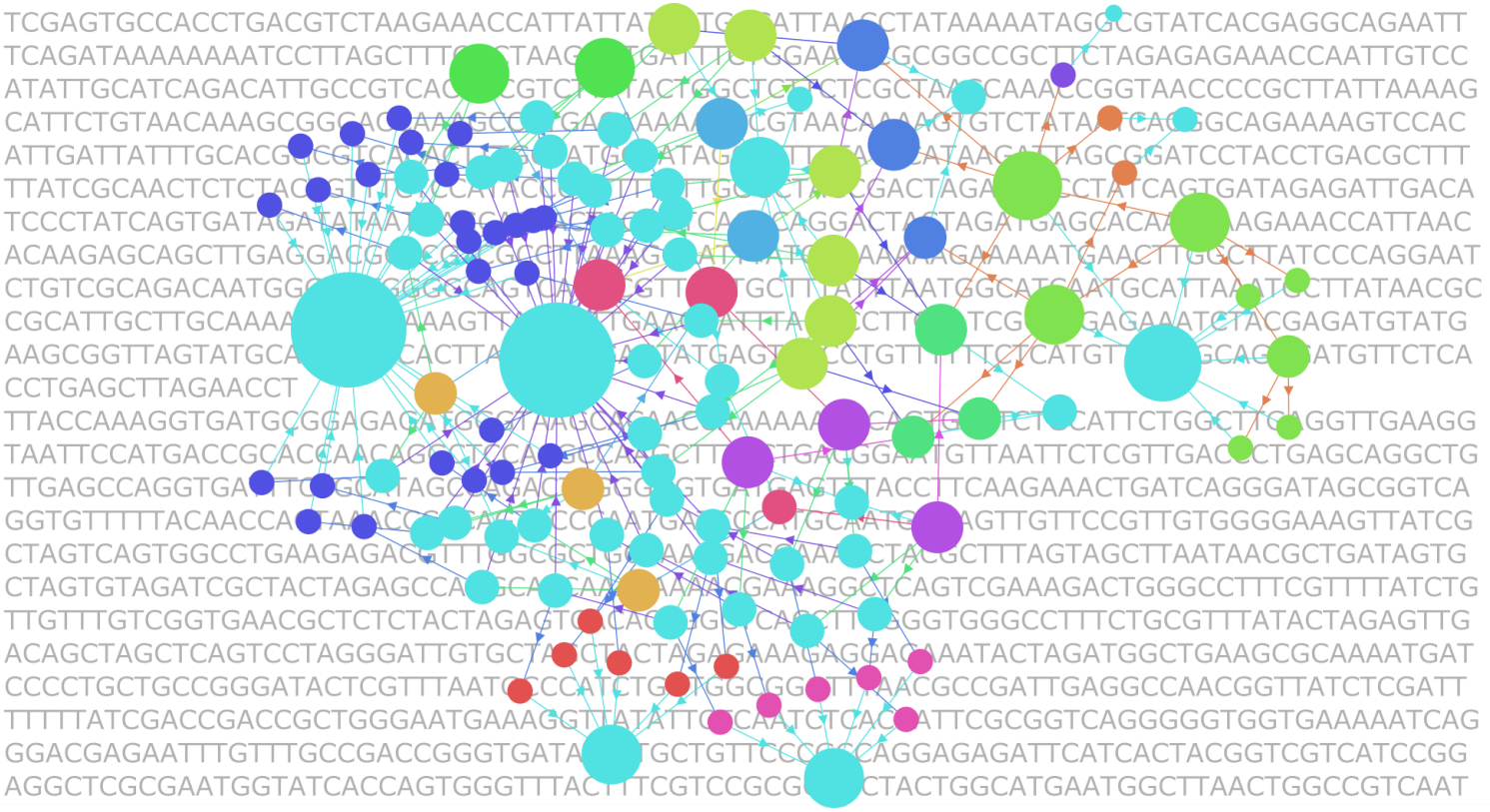


Kim J., et al. Spatial organization of the gene expression hardware in Pseudomonas putida. Environmental Microbiology (2019)



Kim J., et al. Subcellular architecture of the xyl gene expression flow of the TOL catabolic plasmid of Pseudomonas putida mt2. mBio (2021)

Information standards



Crowther M., et al. A network approach to genetic circuit designs. bioRxiv (2022)

Cellular supremacy

nature COMMUNICATIONS

PERSPECTIVE

https://doi.org/10.1038/s41467-019-13232-z OPEN

Pathways to cellular supremacy in biocomputing

Lewis Grozinger[1], Martyn Amos[2], Thomas E. Gorochowski[3,4], Pablo Carbonell[5], Diego A. Oyarzún[6,7], Ruud Stoof[1], Harold Fellermann[1], Paolo Zuliani[1], Huseyin Tas[8] & Angel Goñi-Moreno[1*]

Synthetic biology uses living cells as the substrate for performing human-defined computations. Many current implementations of cellular computing are based on the "genetic circuit" metaphor, an approximation of the operation of silicon-based computers. Although this conceptual mapping has been relatively successful, we argue that it fundamentally limits the types of computation that may be engineered inside the cell, and fails to exploit the rich and diverse functionality available in natural living systems. We propose the notion of "cellular supremacy" to focus attention on domains in which biocomputing might offer superior performance over traditional computers. We consider potential pathways toward cellular supremacy, and suggest application areas in which it may be found.

CBGP
CENTRO DE BIOTECNOLOGÍA Y GENÓMICA DE PLANTAS
UPM-INIA

POLITÉCNICA

UNIVERSIDAD POLITÉCNICA DE MADRID

Biocomputing with synthetic biological systems

Ángel Goñi-Moreno

@AngelGMoreno