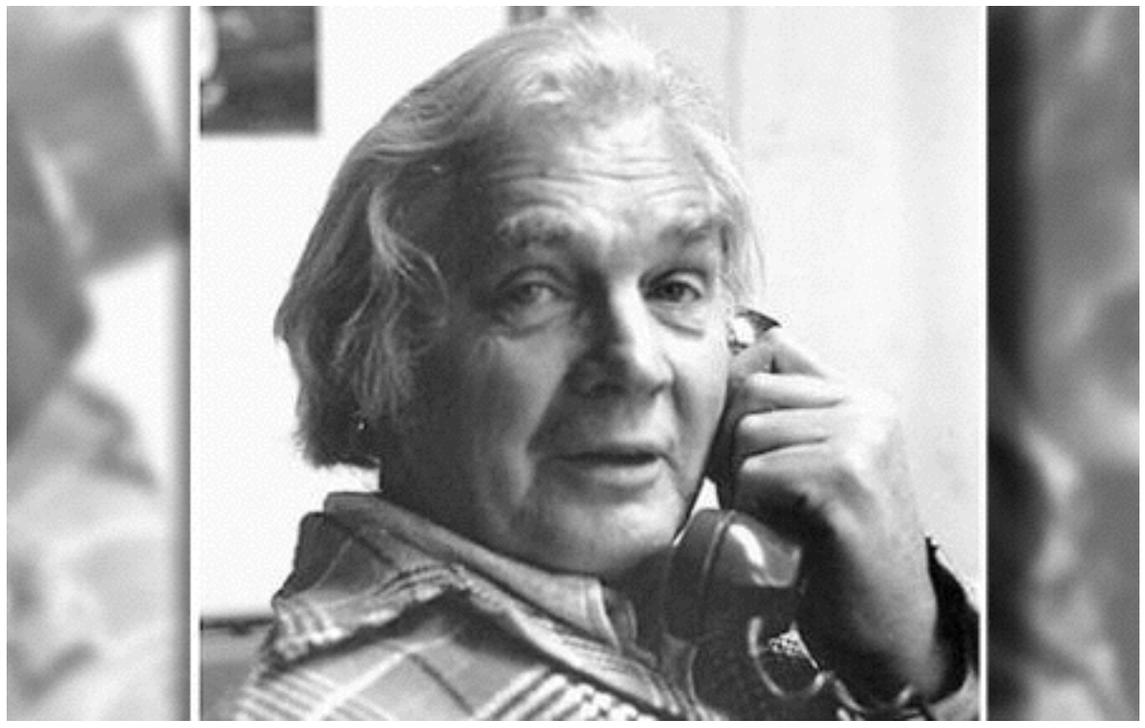
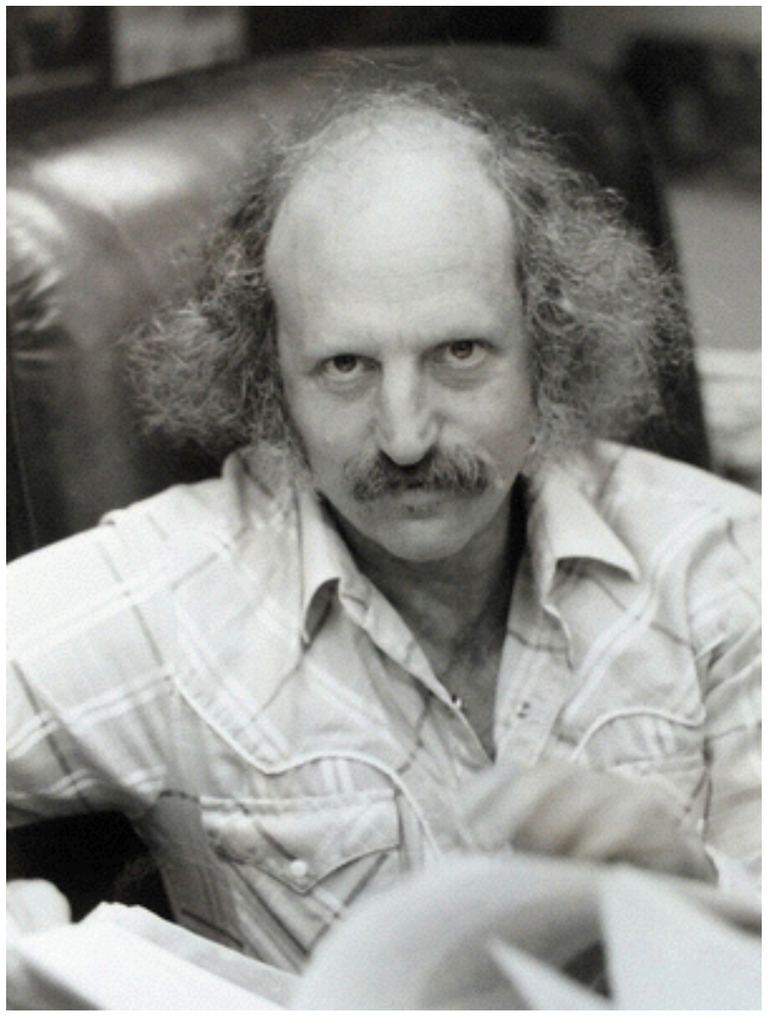
circuitos genéticos

CdC Mérida 2016



Roy Britten



Eric Davidson

Gene Regulation for Higher Cells: A Theory

New facts regarding the organization of the genome provide clues to the nature of gene regulation.

Roy J. Britten and Eric H. Davidson

Cell differentiation is based almost certainly on the regulation of gene activity, so that for each state of differentiation a certain set of genes is active in transcription and other genes are inactive. The establishment of this concept (*1*) has depended on evidence indicating that the cells of an organism generally contain identical genomes (*2*). Direct support for the idea that regulation of gene activity underlies cell differentiation comes from evidence that much of the genome in higher cell types is inactive (*3*) and that different ribonucleic acids (RNA) are synthesized in different cell types (*4*).

Little is known, however, of the molecular mechanisms by which gene expression is controlled in differentiated cells. As far as we are aware no theoretical concepts have been advanced which provide an interpretation of certain of the salient features of genomic structure and function in higher organisms. We consider here experimental evidence relating to these features. (i) Change in state of differentiation in higher cell types is often mediated by simple external signals, as, for example, in the action of hormones or embryonic inductive agents. (ii) A given state of differentiation tends to require the integrated activation of a very large number of noncontiguous genes. (iii) There exists a significant class of genomic sequences which are transcribed in the nuclei of higher cell types but appear to be absent from cytoplasmic RNA's. (iv) The genome present in higher cell types is extremely large, compared to that in bacteria. (v) This genome differs strikingly from the bacterial genome due to the presence of large fractions of repetitive nucleotide sequences which are scattered throughout the genome. (vi) Furthermore, these repetitive sequences are transcribed in differentiated cells according to cell type-specific patterns.

In this article we propose a new set of regulatory mechanisms for the cells of higher organisms such that multiple changes in gene activity can result from a single initiatory event. These proposals are presented in the form of a specific, relatively detailed model at the level of complexity which appears to us to be required for the genomic regulatory machinery of higher cells. We make no attempt to arrive at definitive statements regarding these proposed mechanisms; obviously evidence is not now available to support any model in detail. Our purpose in presenting an explicit theory is to describe the regulatory system proposed in terms of elements and processes which are capable of facing direct experimental test. It is hoped that our relatively detailed commitment will induce discussion and experiment, and it is expected that major modifications in concept will result.

Undoubtedly important regulatory processes occur at all levels of biological organization. We emphasize that this theory is restricted to processes of cell regulation at the level of genomic transcription.

We begin by describing our usage of certain terms and their role in the model, and then present the model itself. We then consider relevant experimental observations and certain testable implications of the model. Finally, some general implications of the model for evolutionary theory are mentioned.

Elements of the Model

The following definitions are intended only to clarify the usage of certain terms in our discussion of this model.

Gene: A region of the genome with a narrowly definable or elementary

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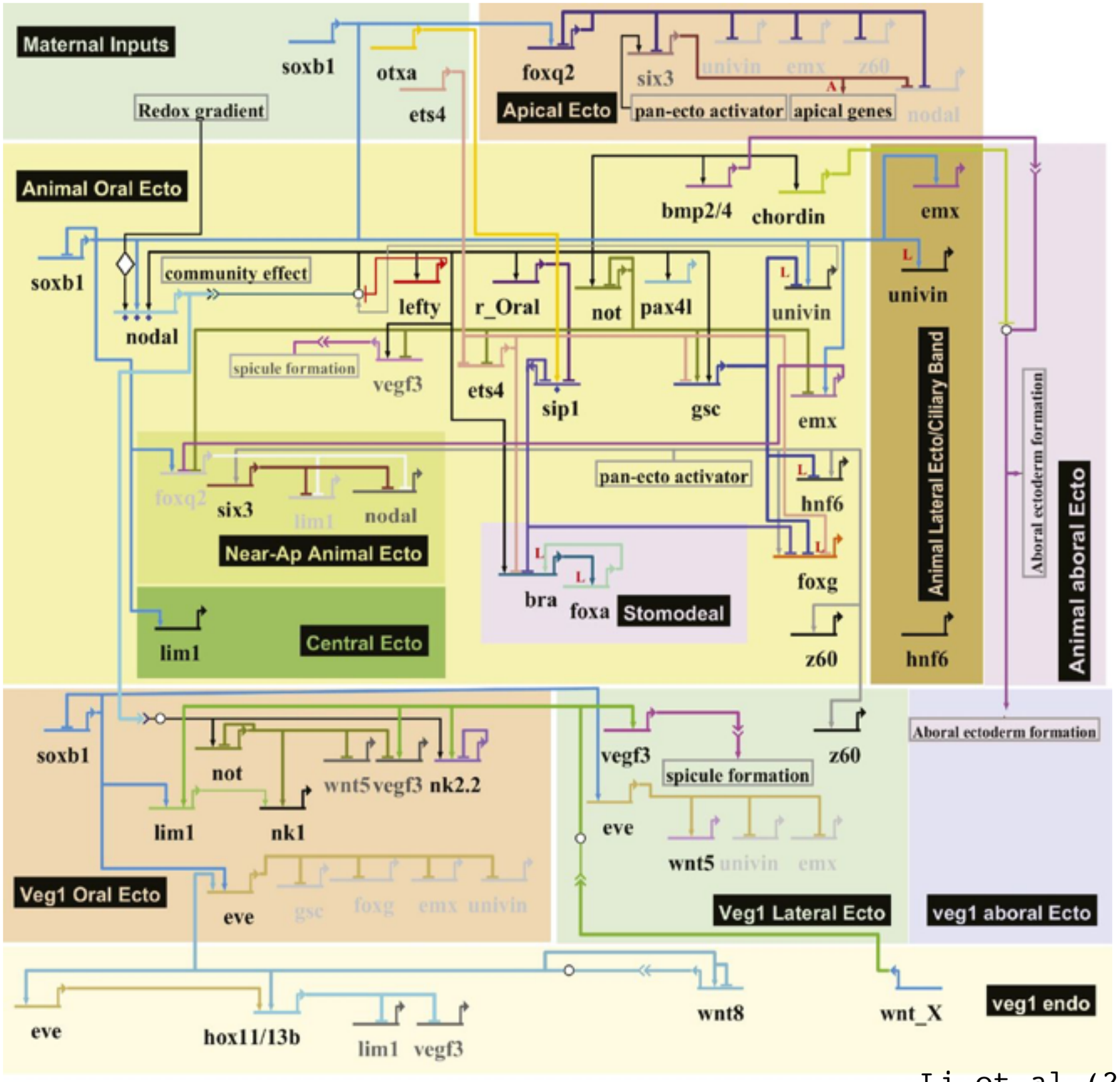
circuitos genéticos



Li et al (2014) PNAS

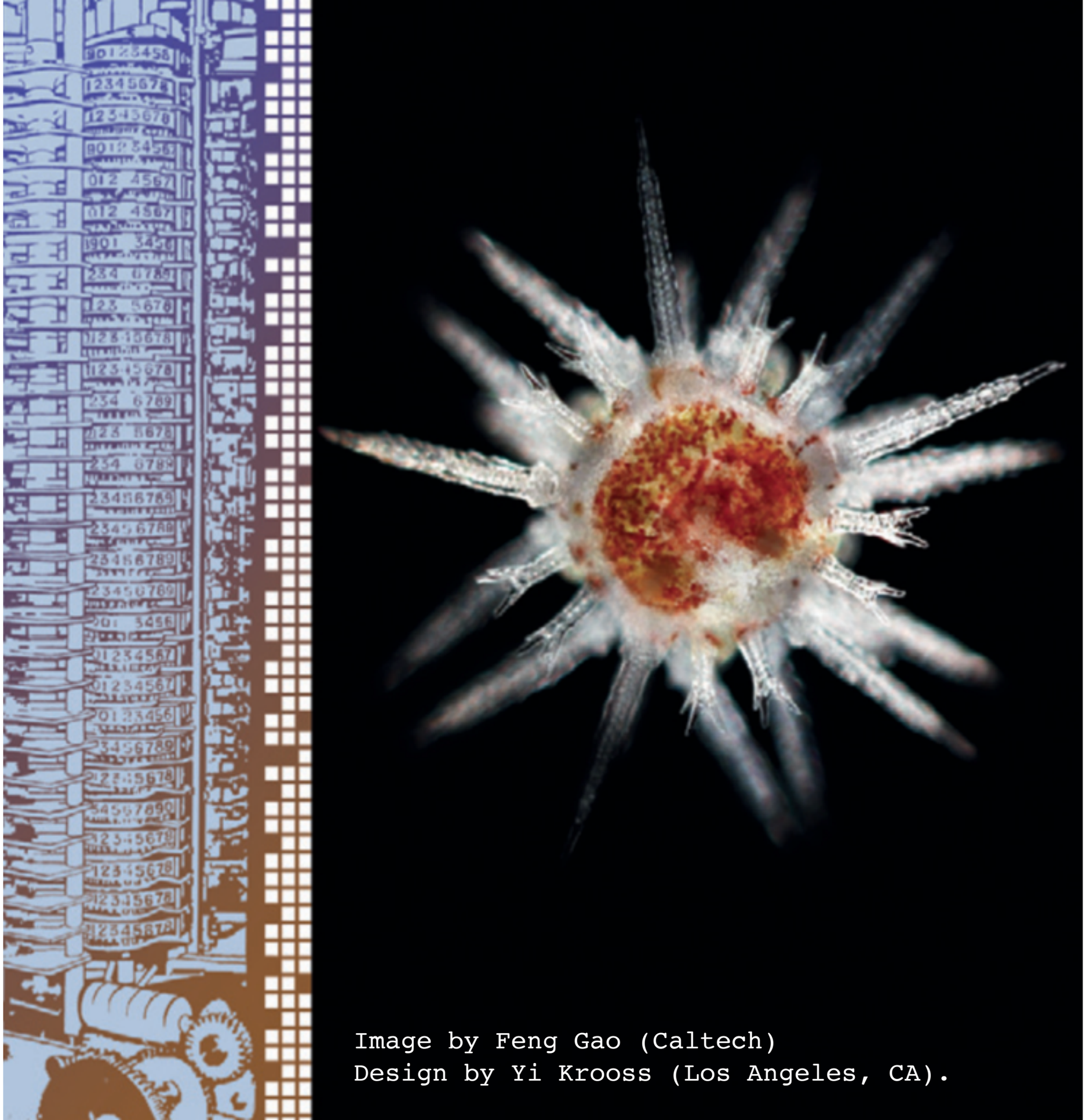
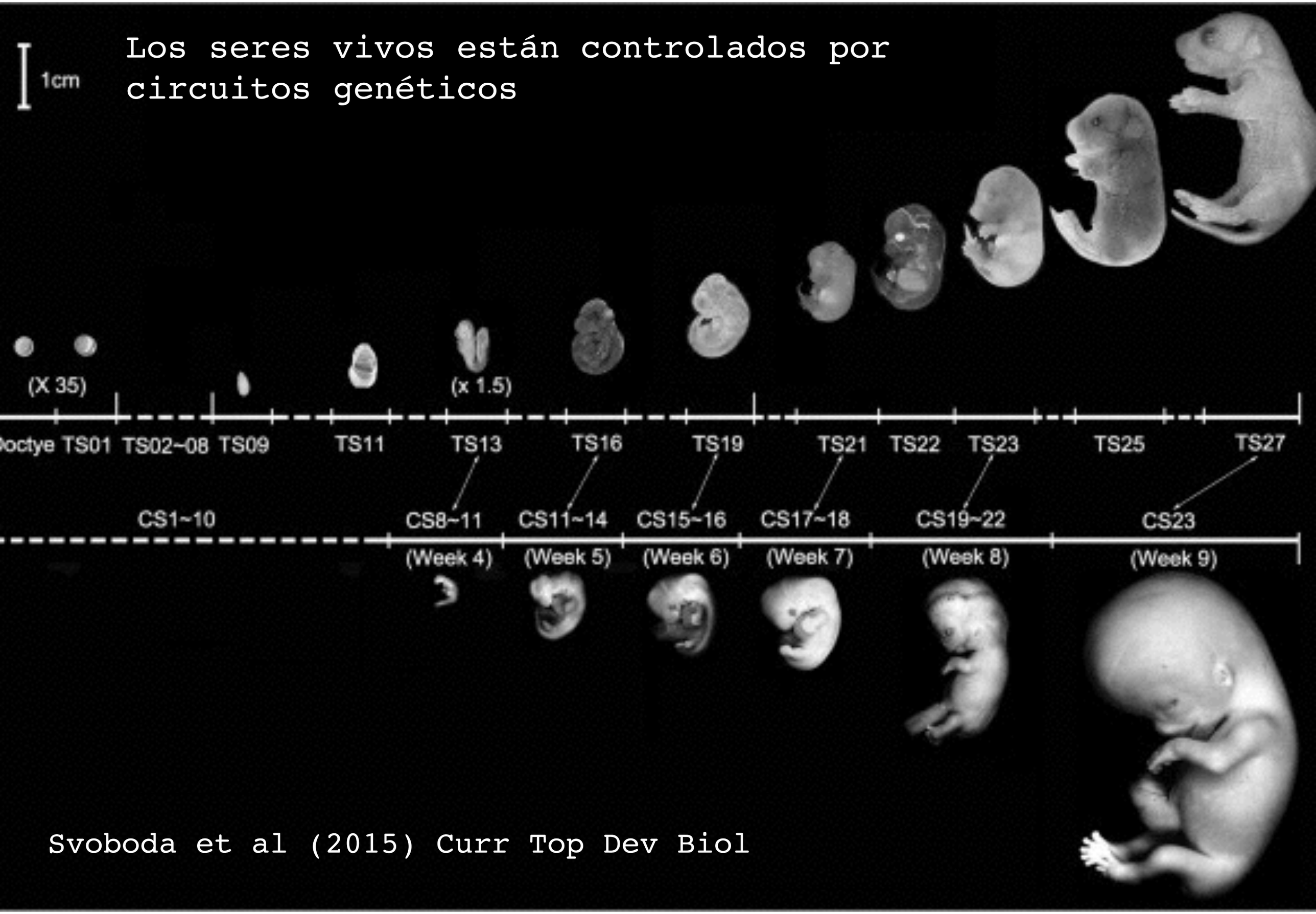
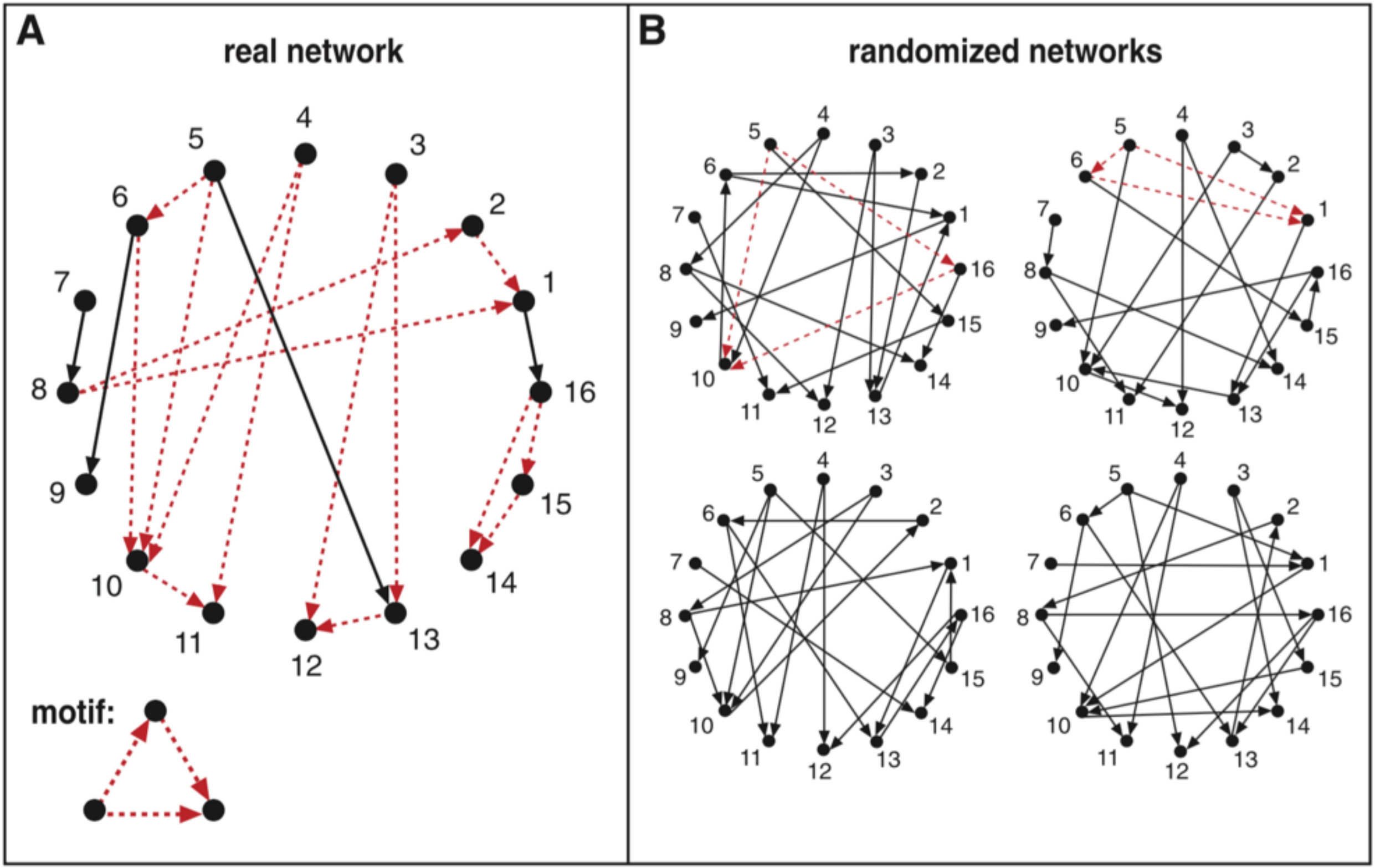


Image by Feng Gao (Caltech)
Design by Yi Krooss (Los Angeles, CA).

Los seres vivos están controlados por circuitos genéticos



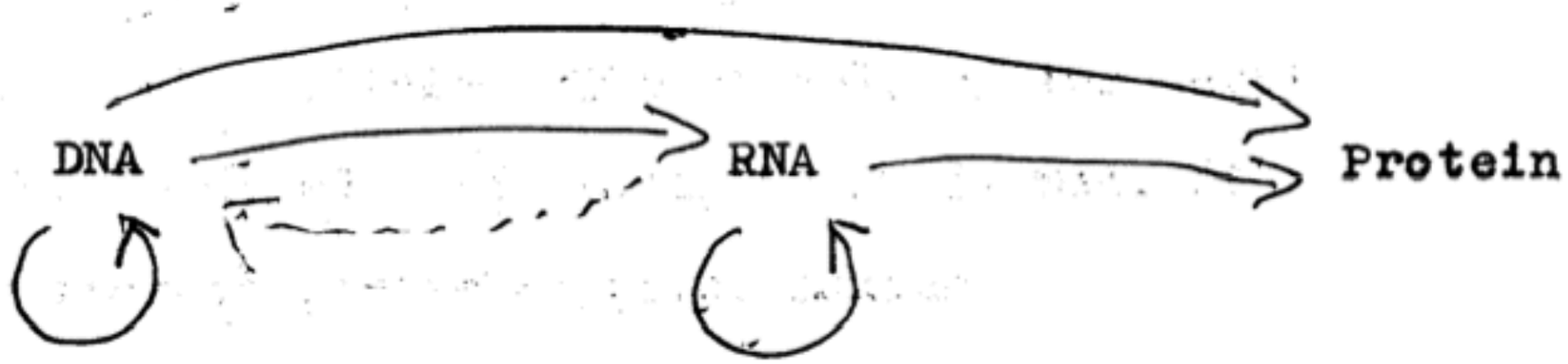
Svoboda et al (2015) Curr Top Dev Biol



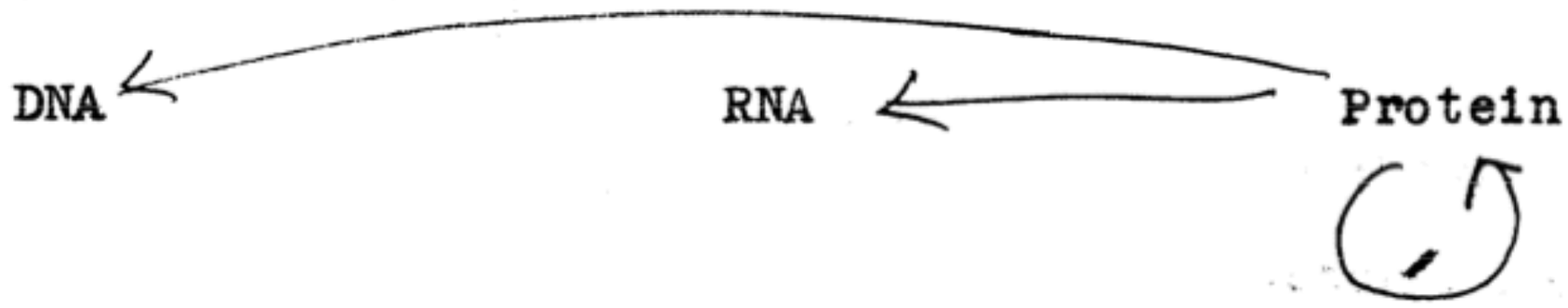
Milo et al (2002) Science

dogma central

That is, we <u>may</u> be able to have

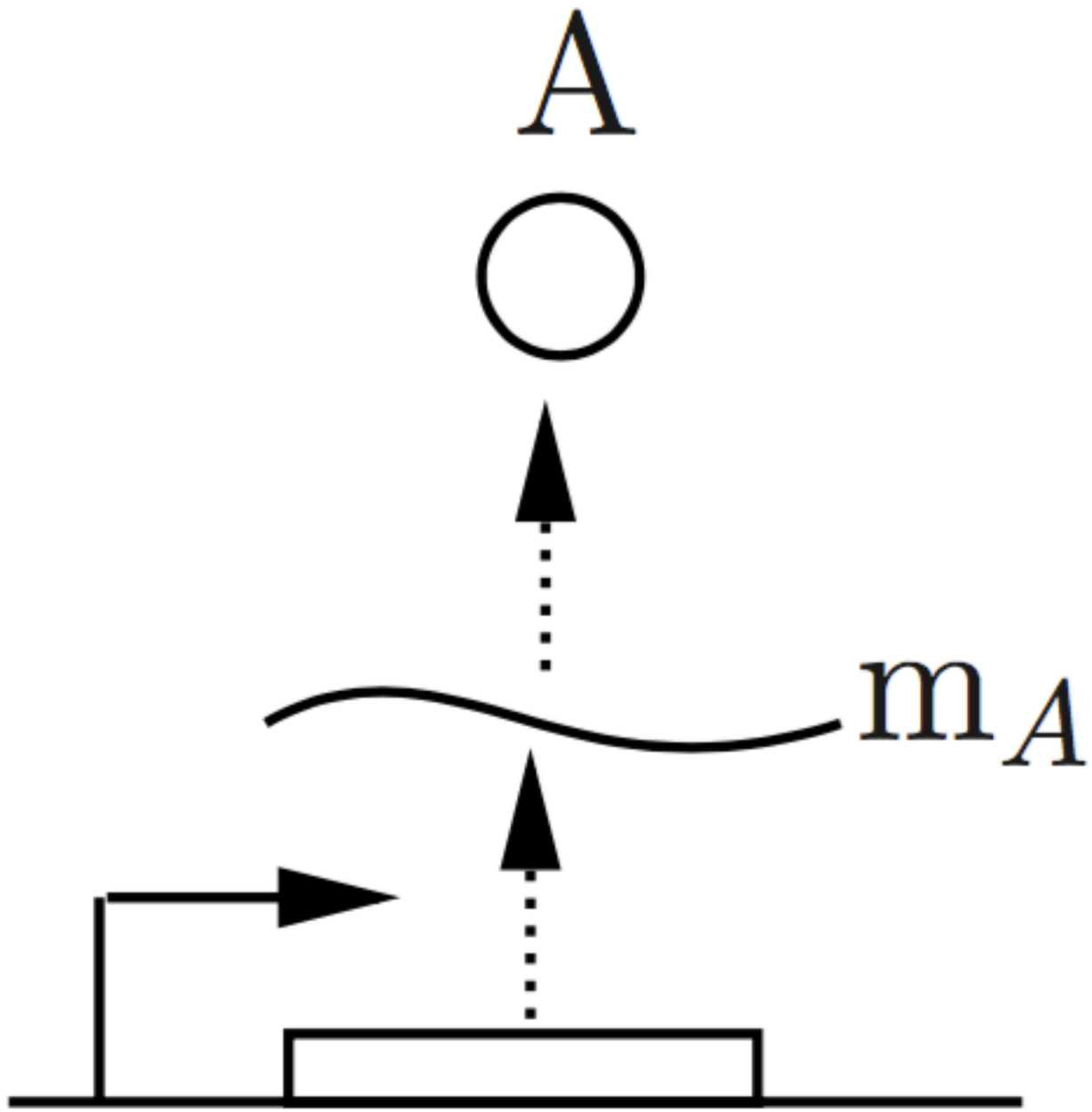


but <u>never</u>

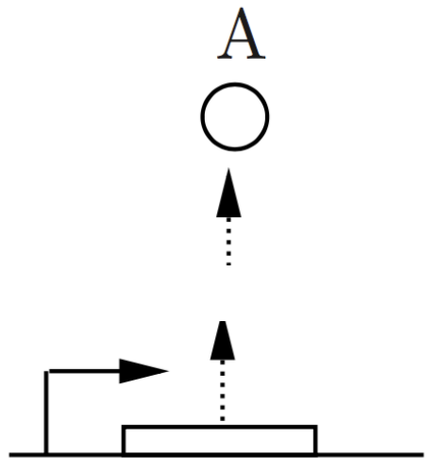


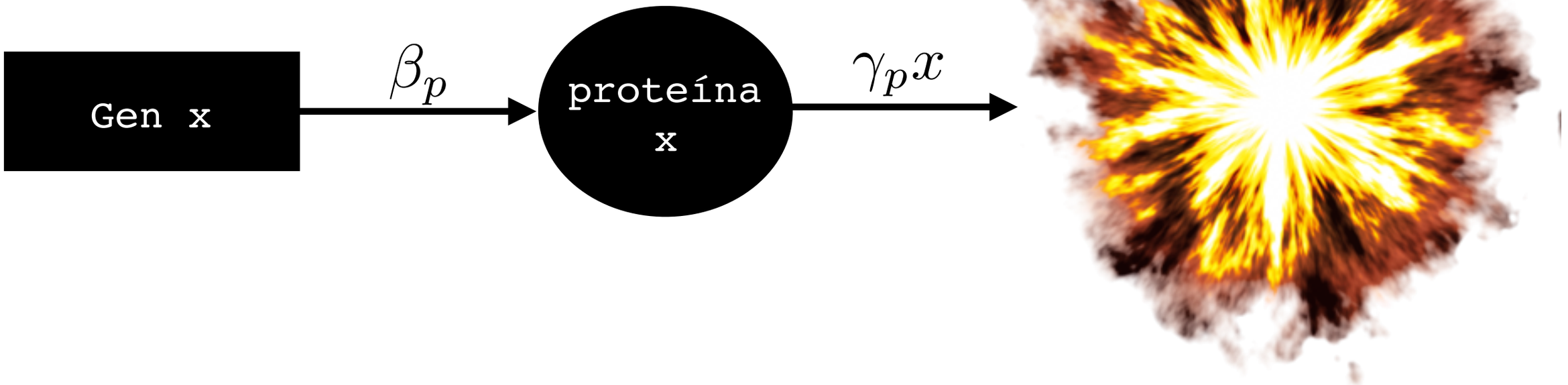
where the arrows show <u>the transfer of information</u>.

Francis Crick (1956) Ideas on Protein Syn

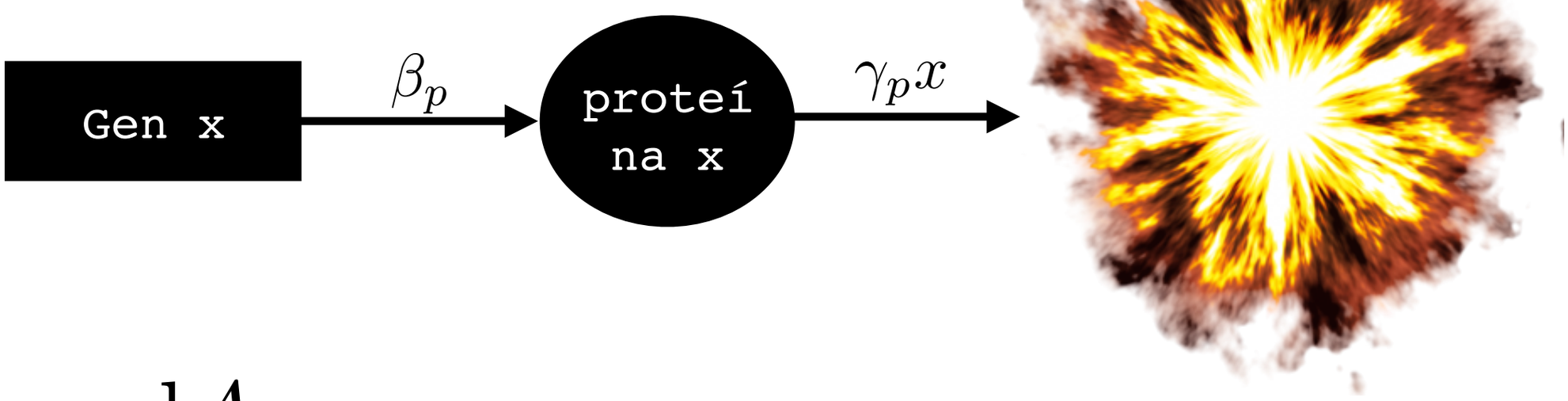

A
m_A

Modelado de circuitos genéticos





Modelado de circuitos genéticos



$$\frac{\mathrm{d}A}{\mathrm{d}t} = \text{producción} - \text{degradación}$$

$$\frac{\mathrm{d}A}{\mathrm{d}t} = \beta_A - \gamma_A A$$

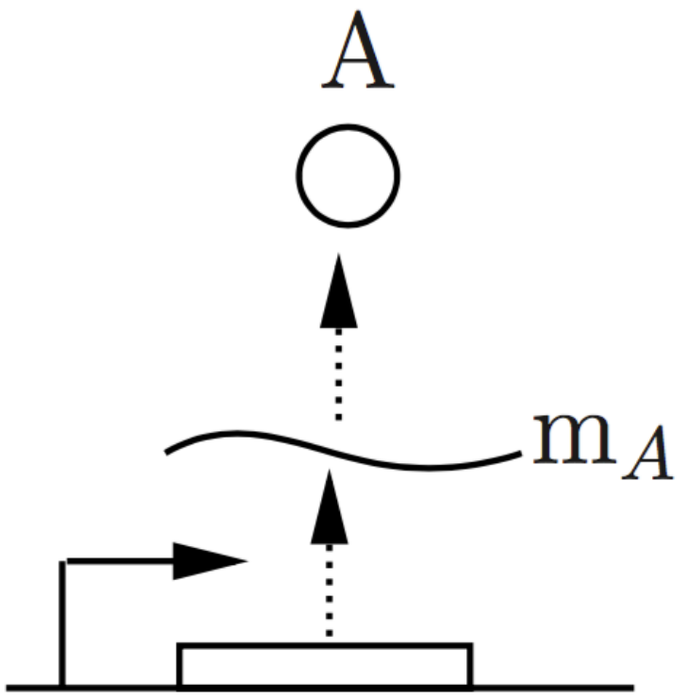
$$\gamma = \gamma_{dilucion} + \gamma_{degradacion}$$

En *E. coli* La dilución domina sobre la degradación (Bionumbers)

$$\gamma_{degradacion} = \frac{1}{1200}\text{min}$$

$$\gamma_{dilucion} = \frac{1}{30}\text{min}$$

Modelado de circuitos genéticos

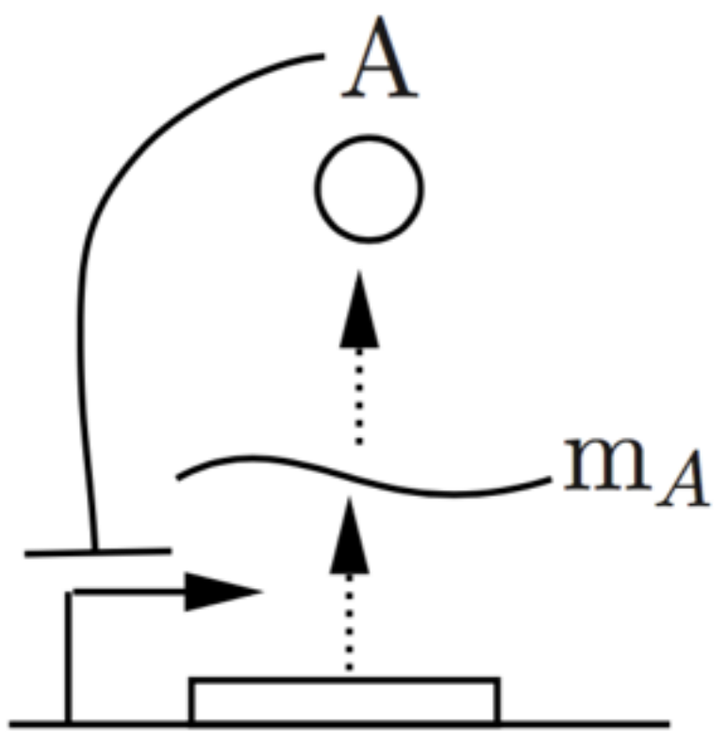


Producción no regulada

$$\frac{\mathrm{d}A}{\mathrm{d}t} = \beta_A - \gamma_A A$$

¿Cómo modelamos circuitos?

$$\frac{\mathrm{d}A}{\mathrm{d}t} = \beta_A F(A) - \gamma_A A$$

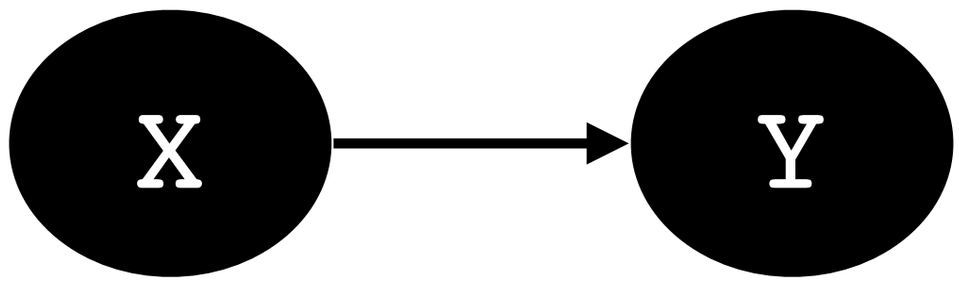


Modelado de circuitos genéticos

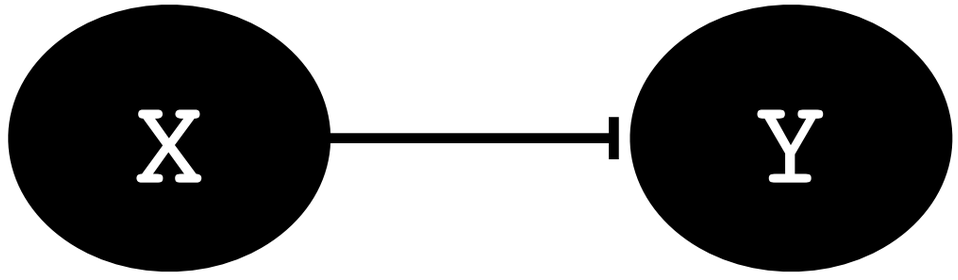
- ecuacion de Hill ipynb

Modelado de circuitos genéticos

alta demanda



baja demanda



Savageau’s Demand Rule (empirical)
Repressor control is correlated with low demand for expression of the regulated structural genes, whereas activator control is correlated with high demand for their expression
M. A. Savageau, “Design of molecular control mechanisms and the demand for gene expression,” PNAS 1977