

What is Systems Biology? Where does it come from?

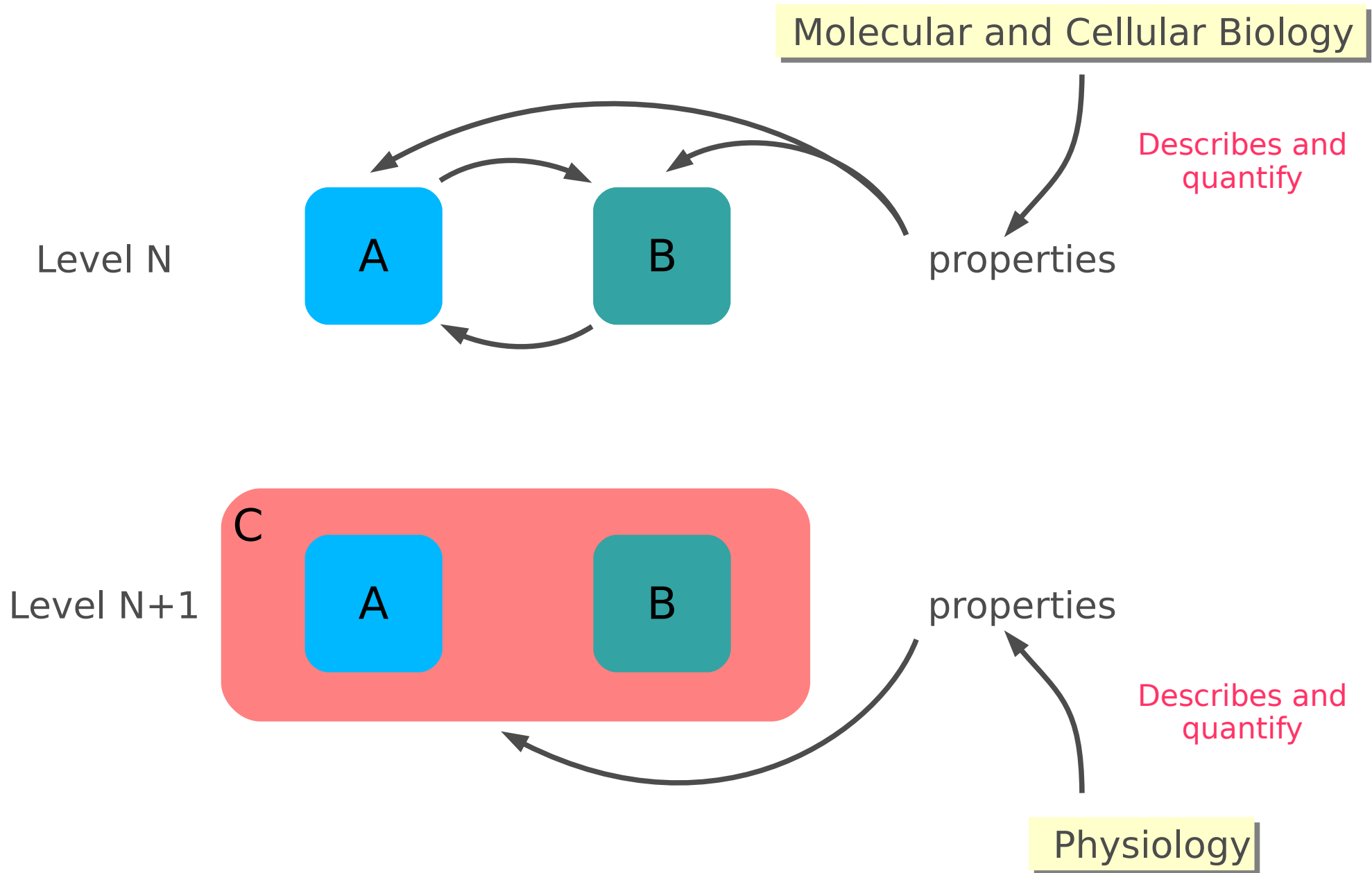
Nicolas Le Novère, The Babraham Institute

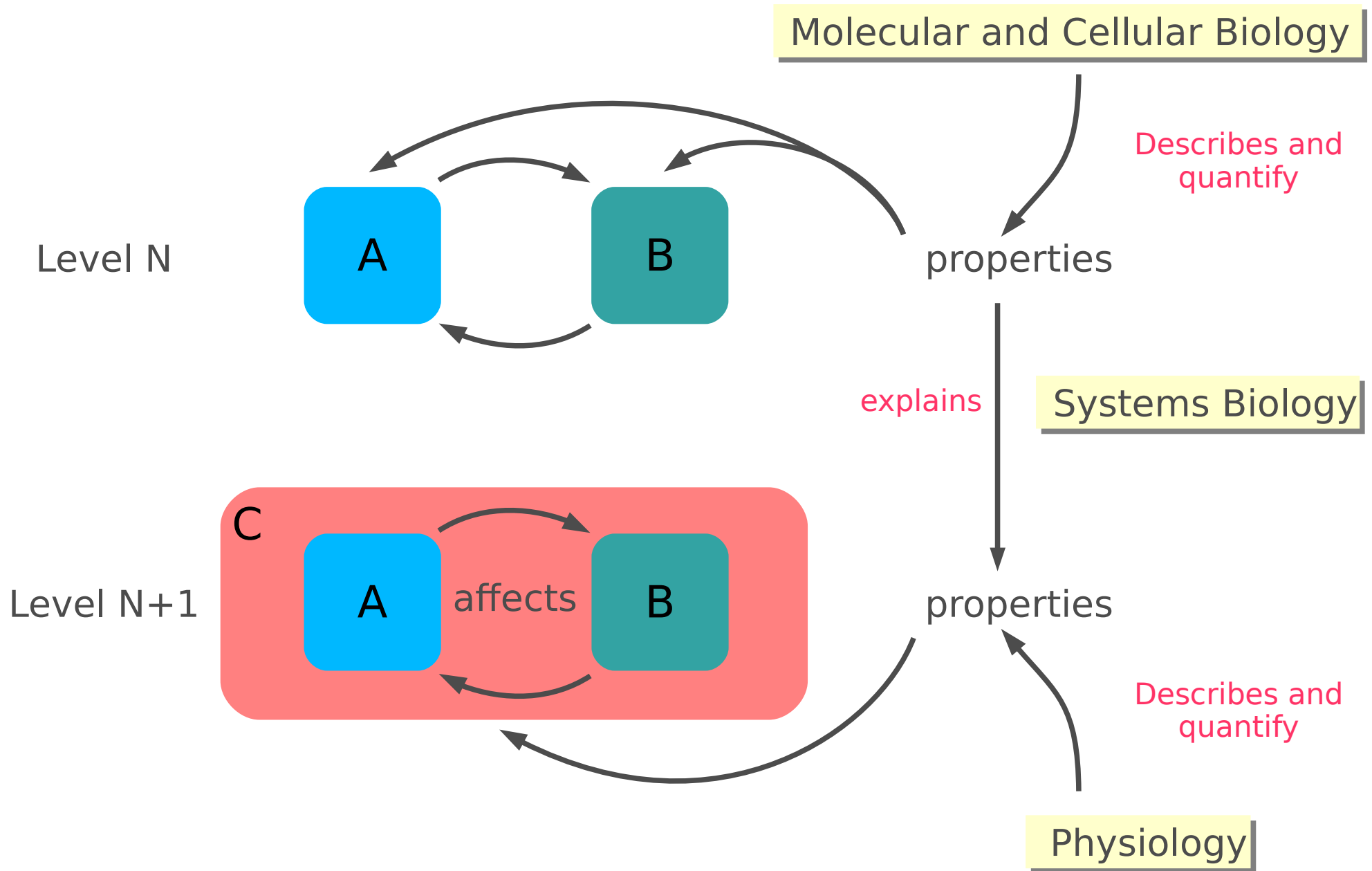
n.lenovere@gmail.com

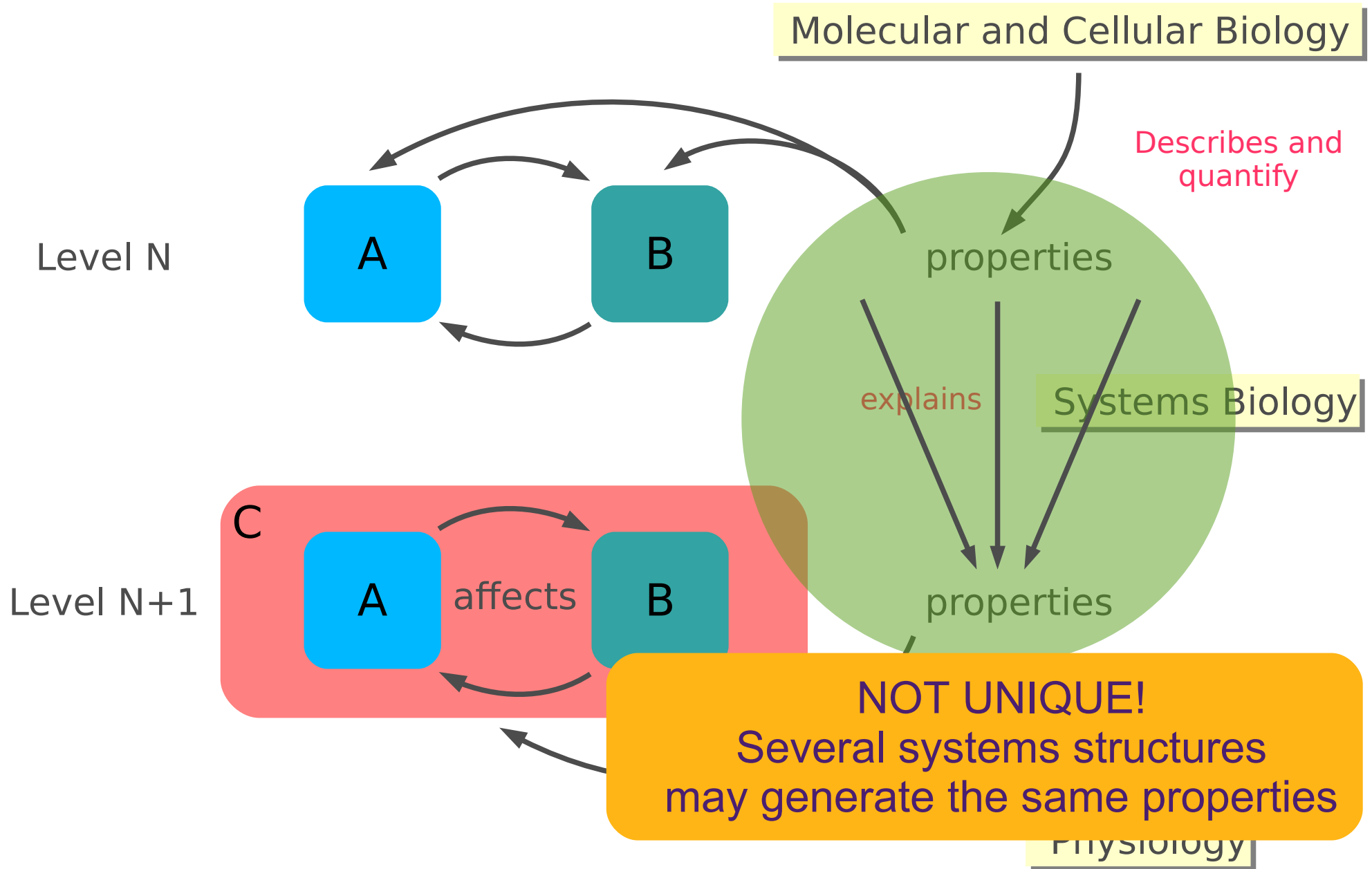
Molecular and Cellular Biology

Level N









What Systems Biology is not!

Purely theoretical: Most systems biologists are actually experimental biologists

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Systems Biology is the study of the *emerging* properties of a biological system, taking into account all the *necessary* constituents, their *relationships* and their *dynamics*

Emergence of the notion of system

XXI

XX

XIX

XVIII

XVII

XVI

Global Description
of the world

astronomy
classical mechanics,
anatomy, physiology

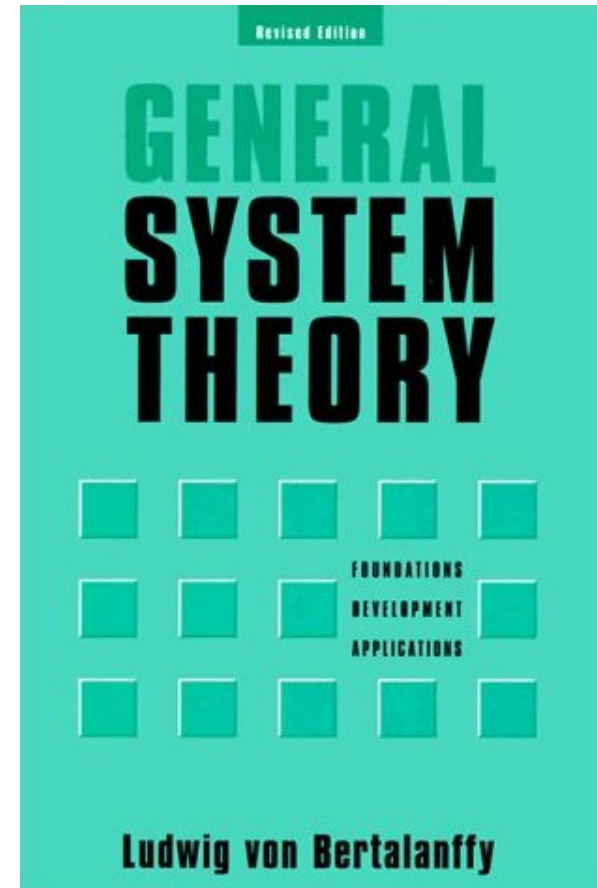
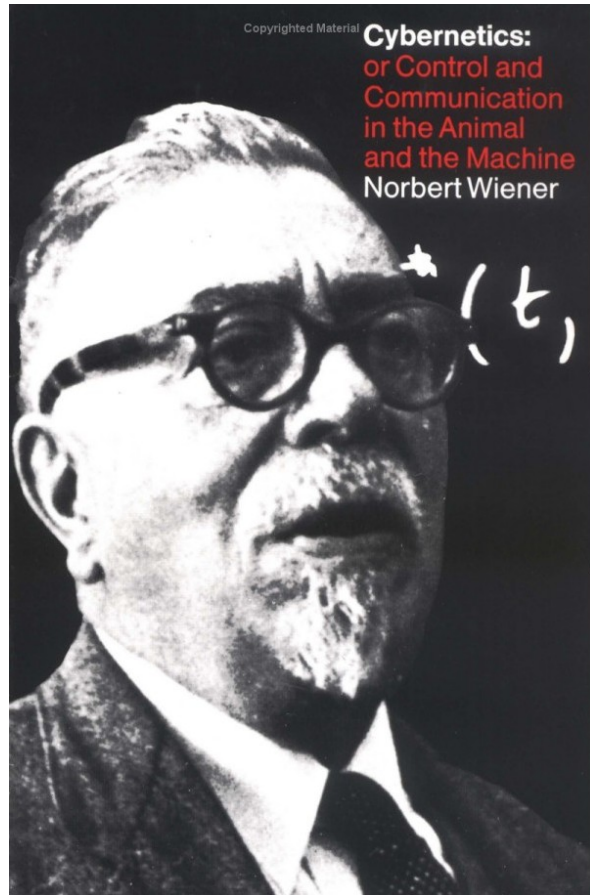
Description of the
components of
the world

particle physics,
quantum mechanic,
biochemistry,
structural biology,
molecular biology

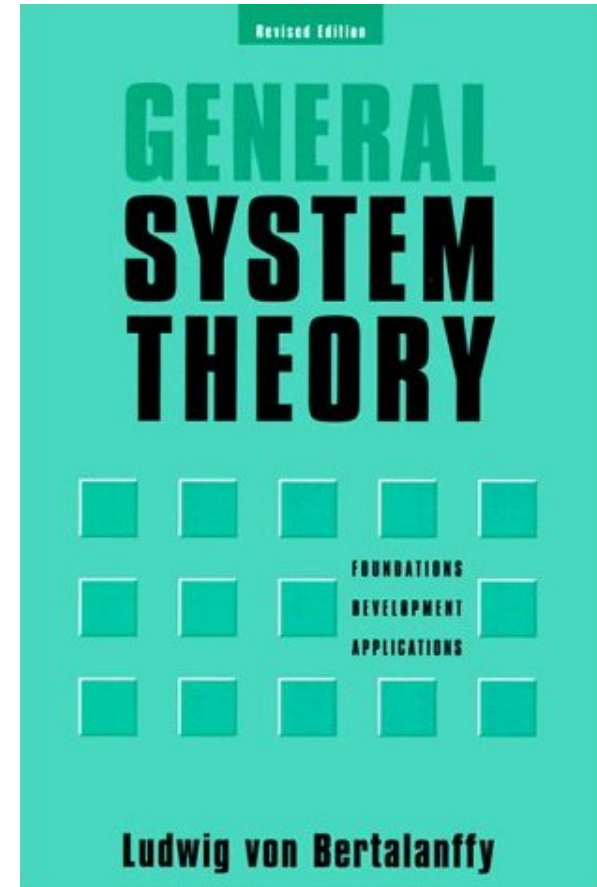
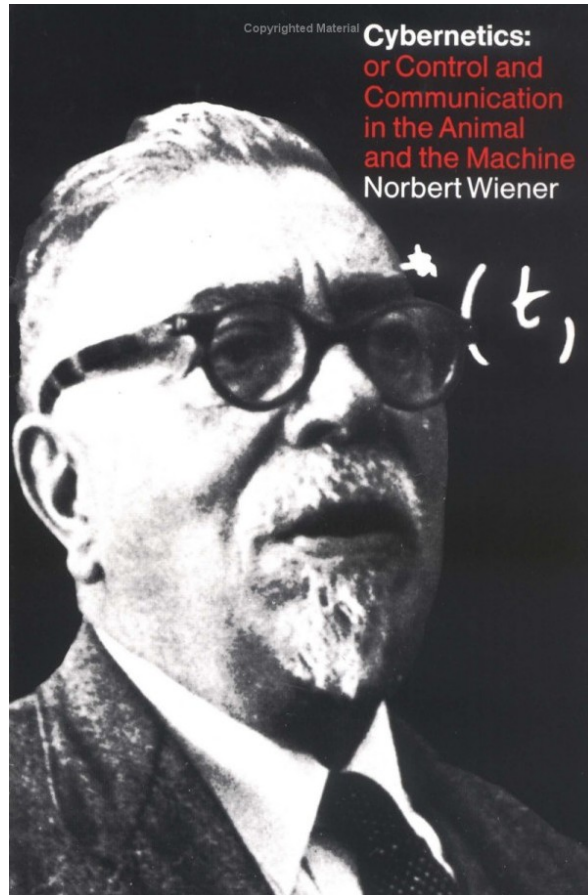
Description of
interacting
components

Cybernetics,
Information theory,
telecommunications,
automata,
multi-agents,
Systems Biology

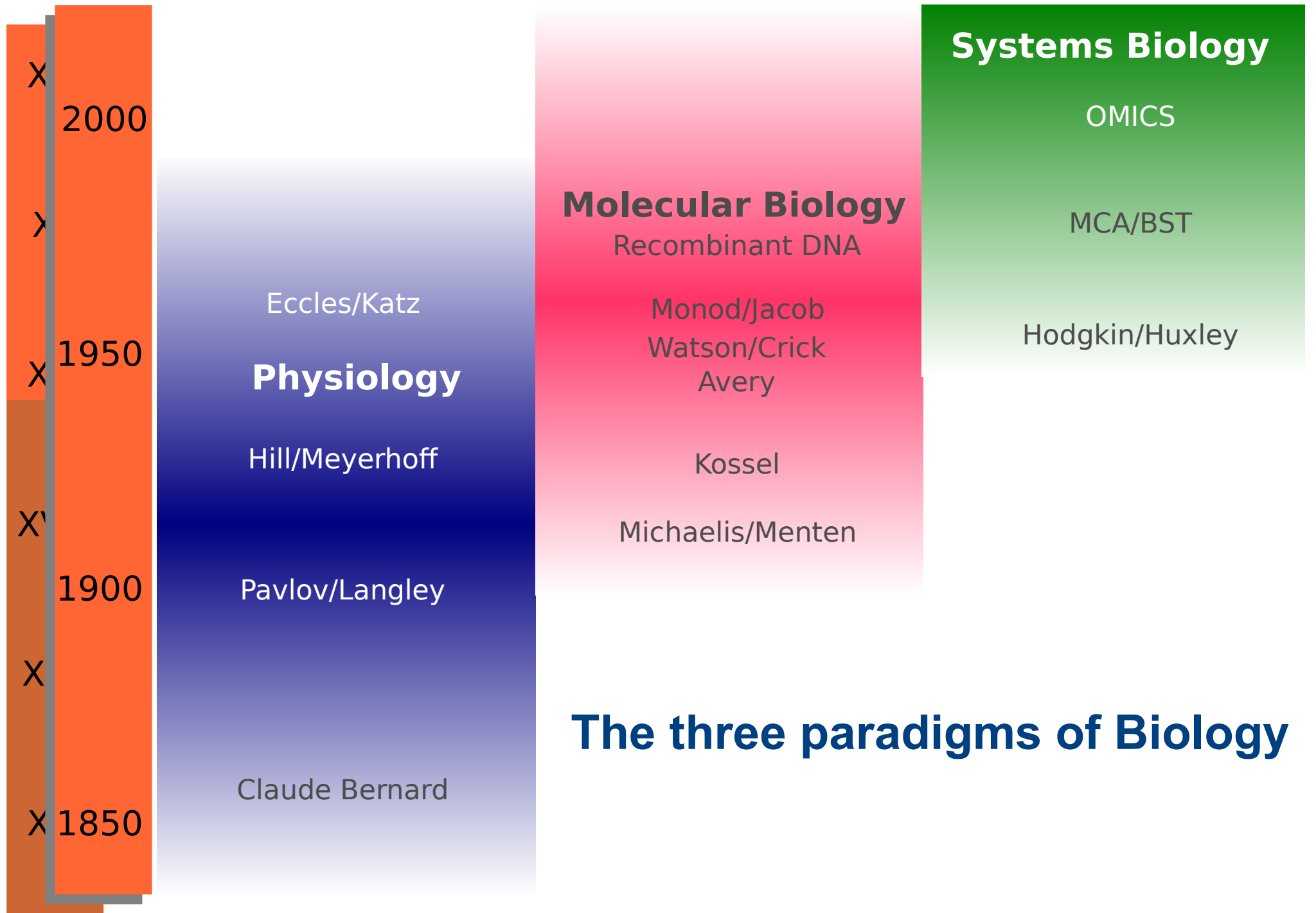
Systems are conceptualised mid-XXth



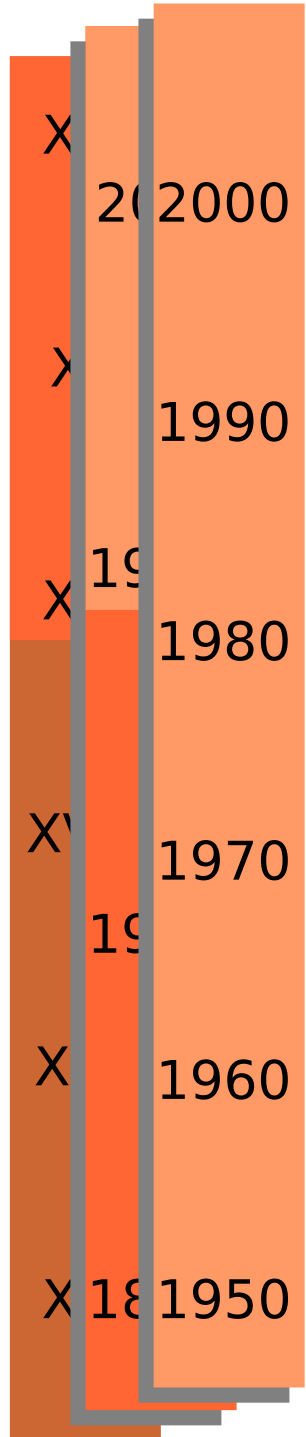
Systems are conceptualised mid-XXth



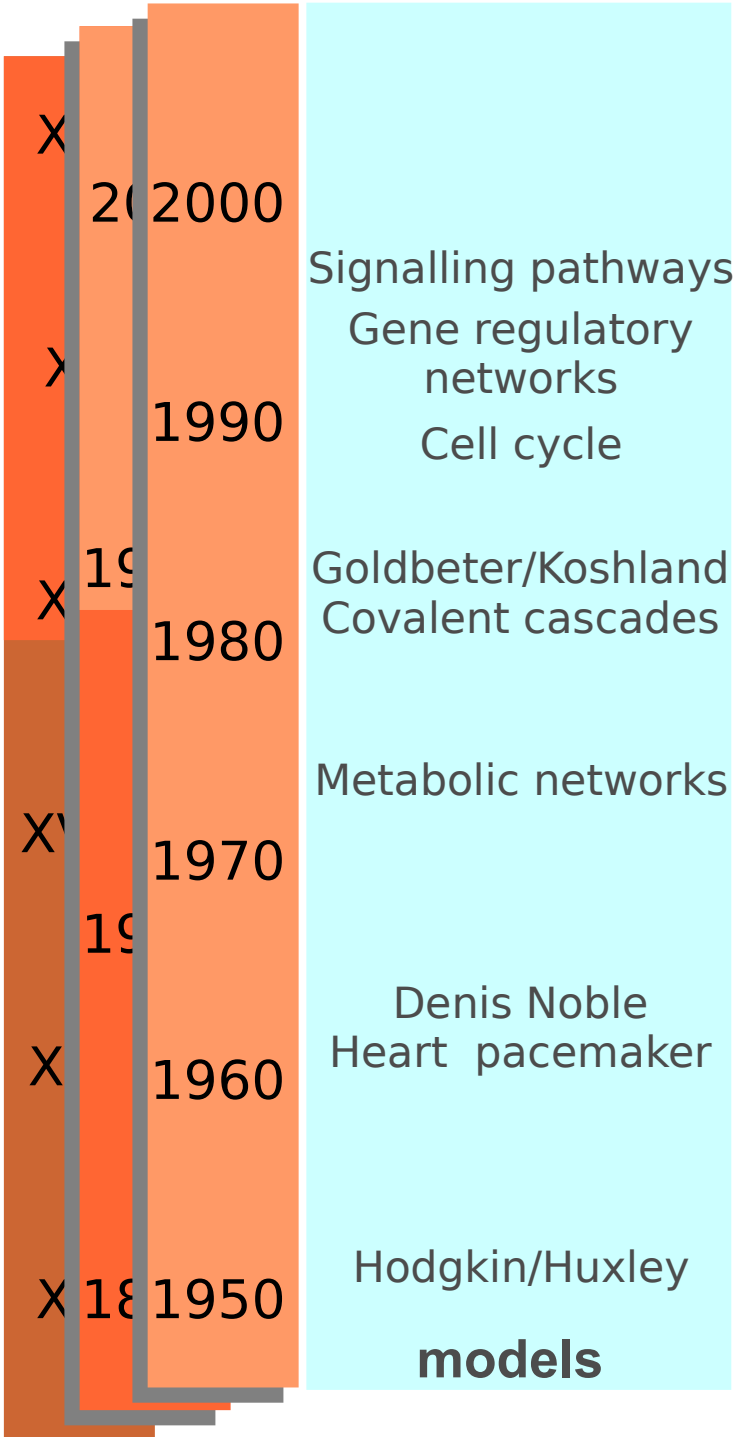
"[A system consists of] a dynamic order of parts and processes standing in mutual interaction. [...] The fundamental task of biology [is] the discovery of the laws of biological systems"
Ludwig von Bertalanffy, Kritische Theorie der Formbildung, 1928



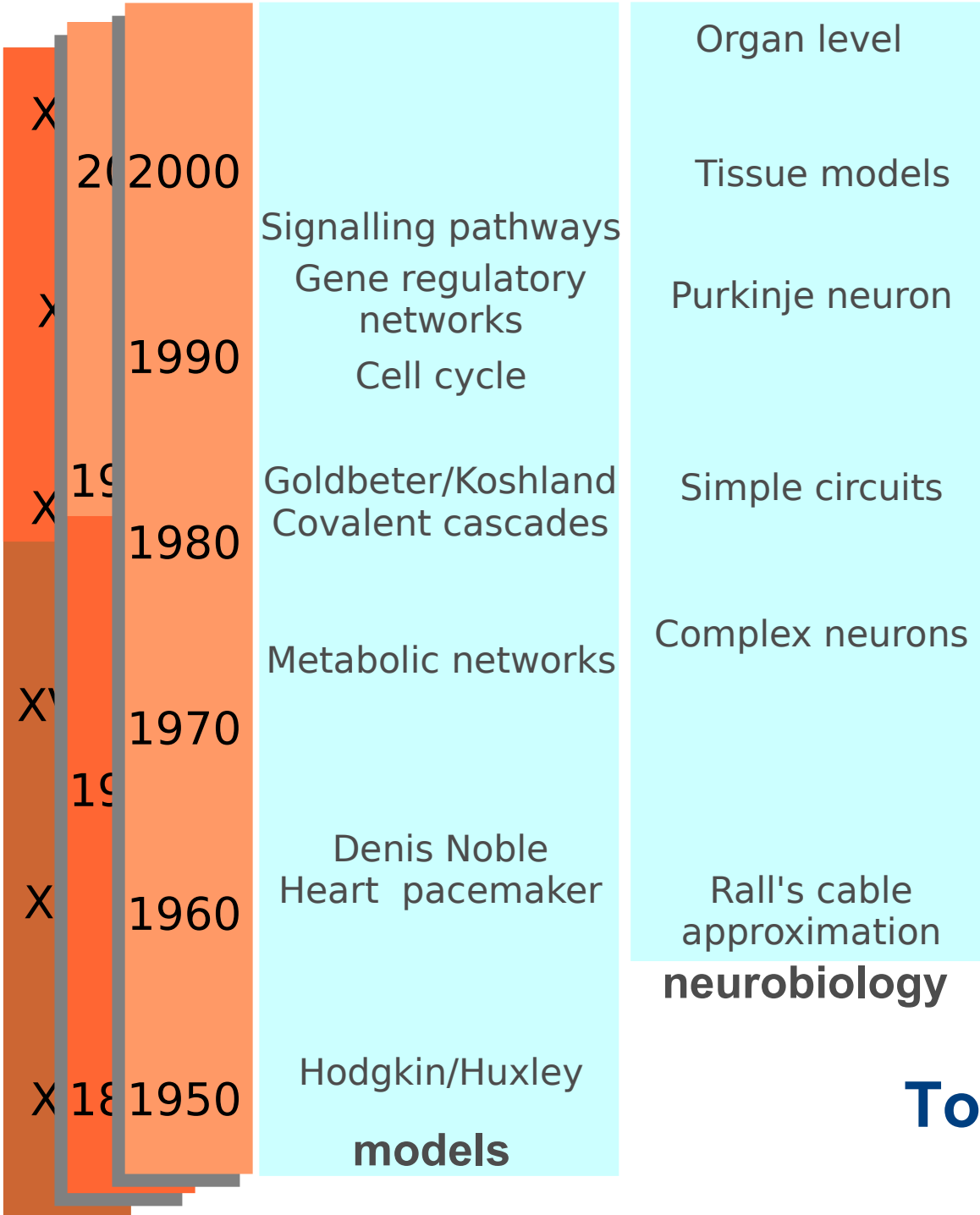
The three paradigms of Biology



Towards Systems Biology



Towards Systems Biology



Towards Systems Biology

1960s and 1970s

- Mihajlo Mesarovic: 1966 Symposium
“general systems theory and biology

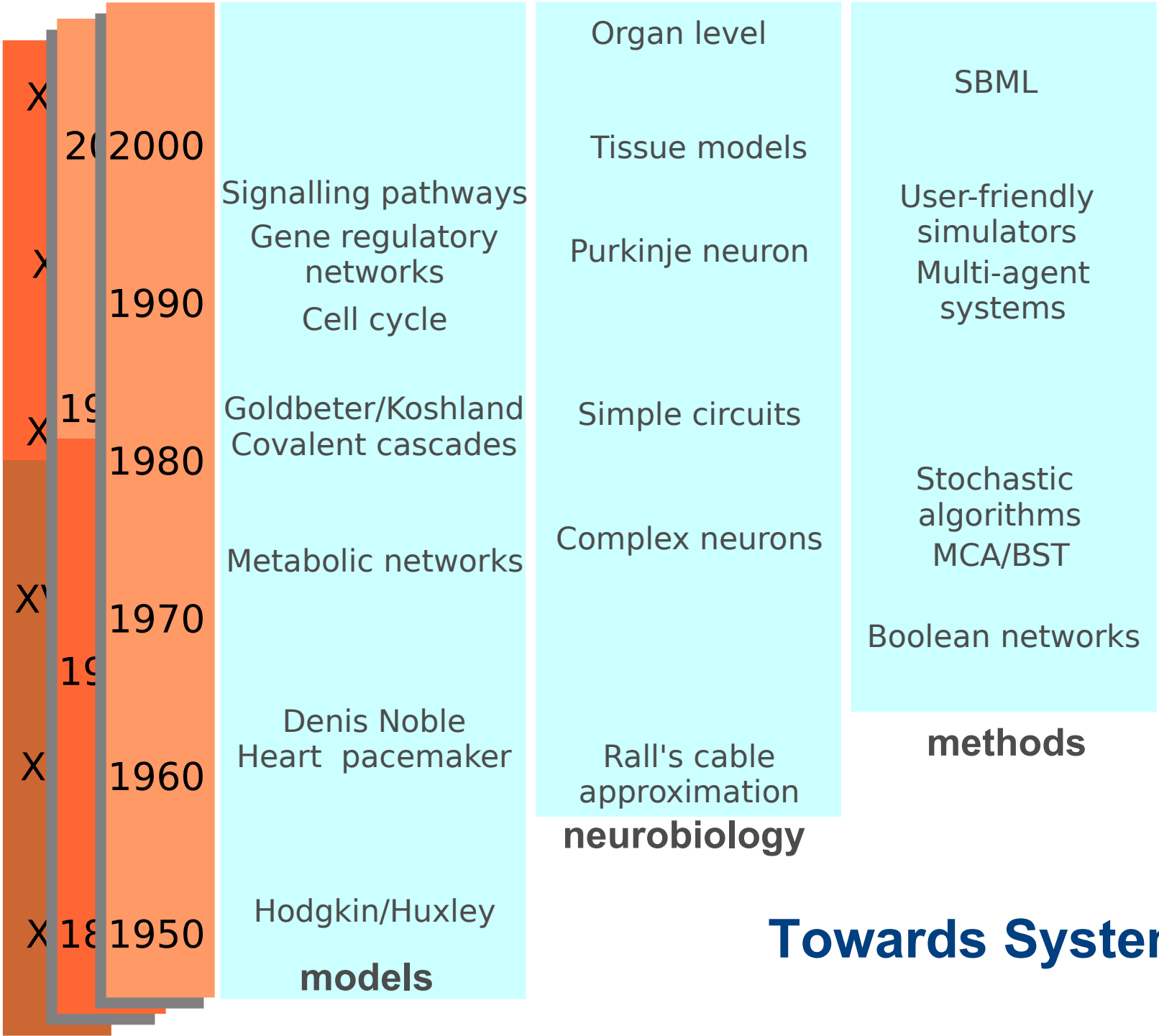


- Stuart Kaufmann,
Rene Thomas: 1969-73
boolean networks for
gene regulation



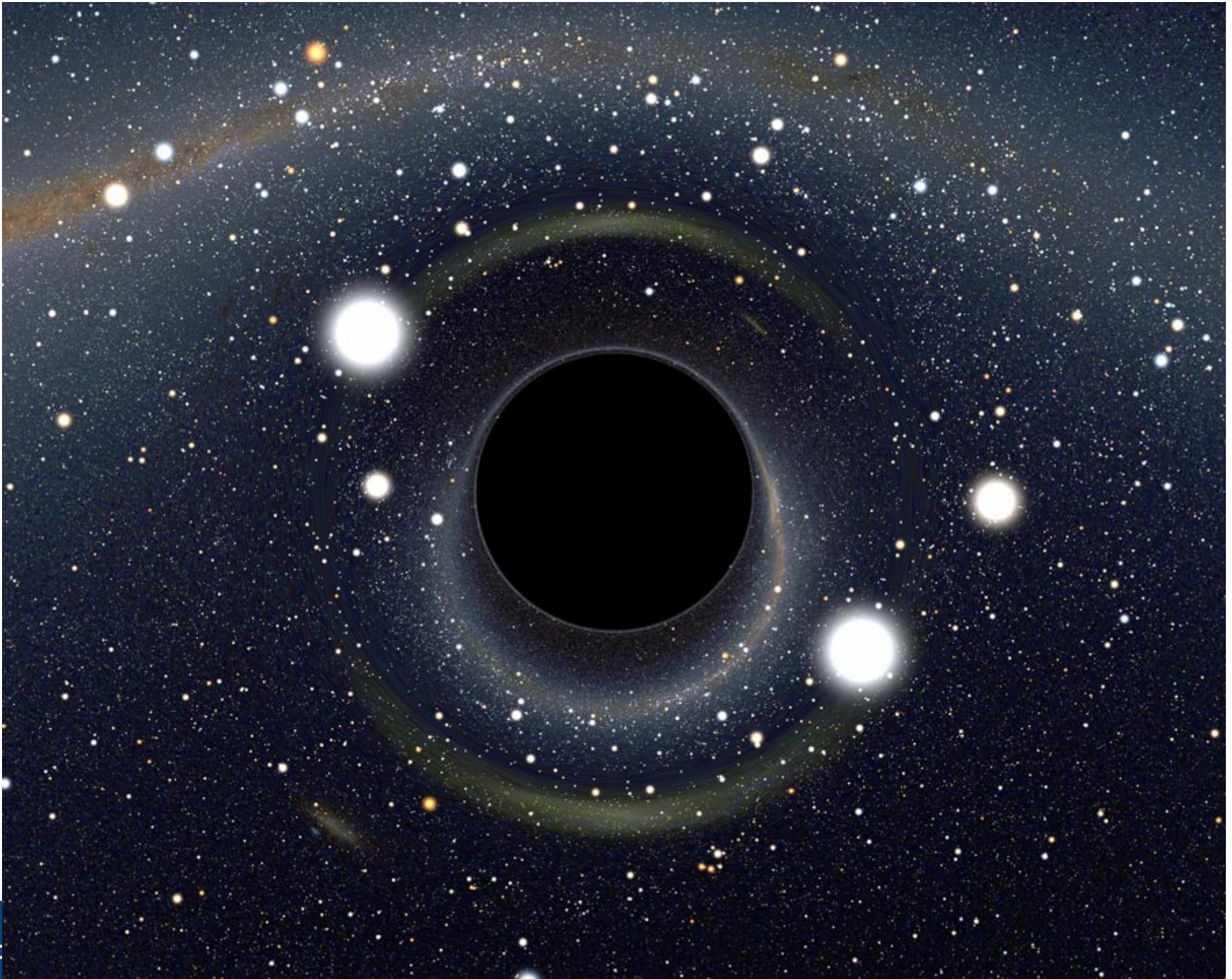
- Henrik Kacser:
Metabolic control analysis,
Michael Savageau:
Biochemical Systems Theory





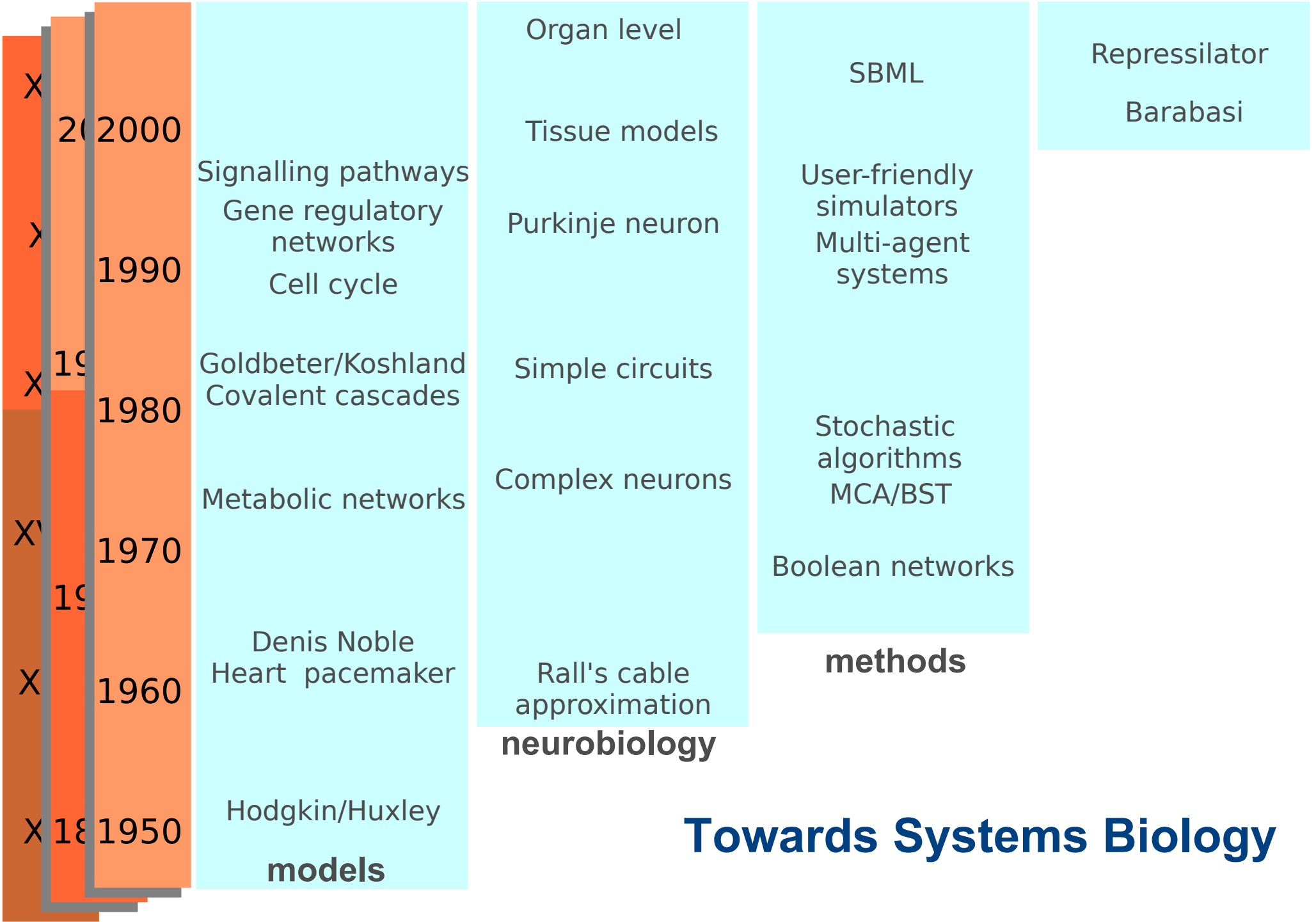
Towards Systems Biology

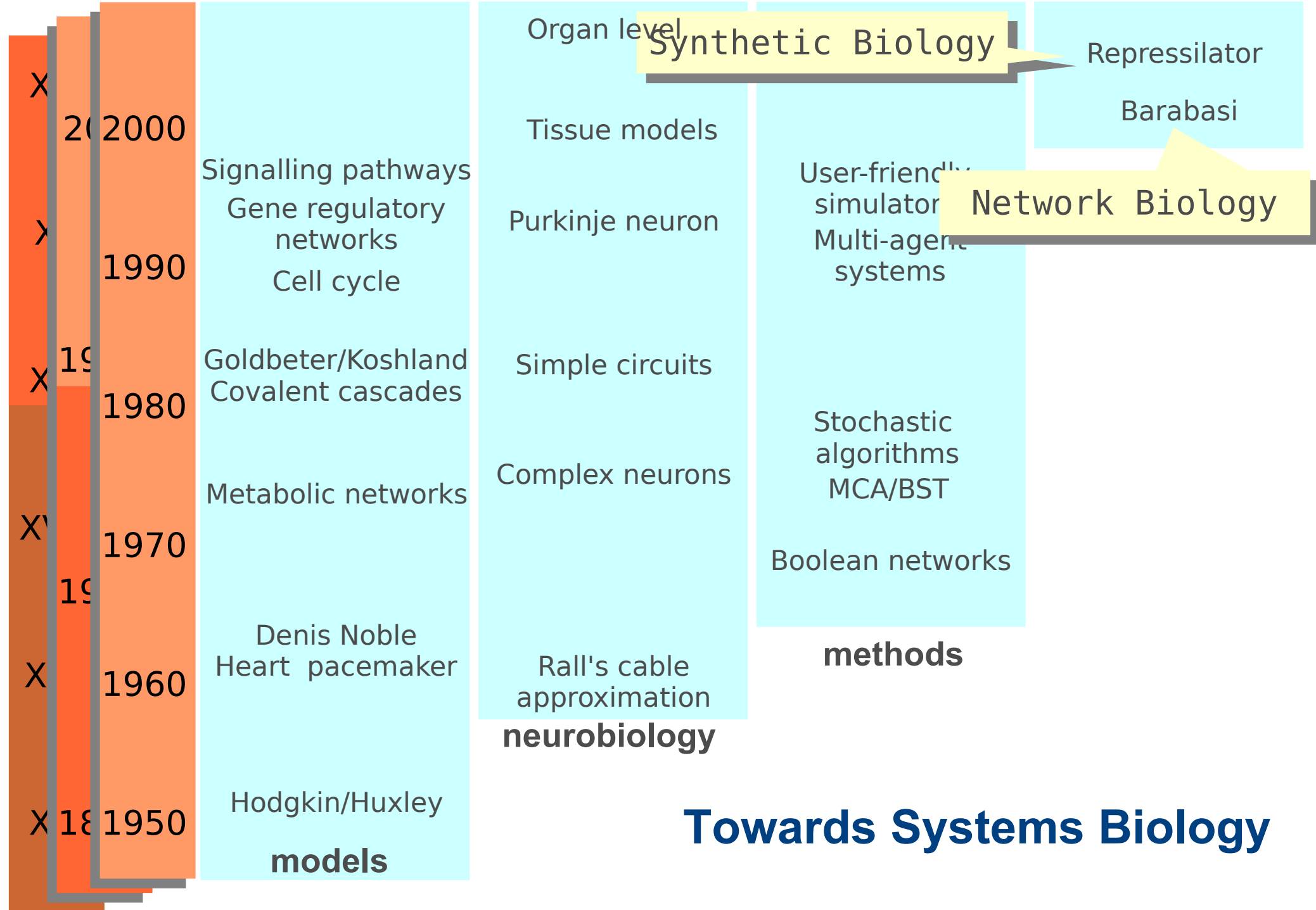
80s: The reign of Molecular Biology



1990s: the community matures

- Publication of modelling work in high visibility journals, e.g.:
 - Tyson. modeling the cell-division cycle - cdc2 and cyclin interactions. *PNAS* 1991; McAdams and Shapiro. Circuit simulation of genetic networks. *Science* 1995; Barkai and Leibler. Robustness in simple biochemical networks. *Nature* 1997; Neuman et al. Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy. *Science* 1998; Yue et al. Genomic cis-regulatory logic: Experimental and computational analysis of a sea urchin gene . *Science* 1998; Bray et al. Receptor clustering as a cellular mechanism to control sensitivity. *Nature* 1998; Bhalla and Iyengar. Emergent properties of signaling pathways. *Science* 1998
- Structuring of the community that models metabolism
- Large-scale modelling and simulation projects
 - E-Cell project 1996; The Virtual Cell 1998
- Availability of high-throughput data on parts and interactions
 - Two-hybrids (1989); microarrays (1995) etc.
- Large-scale funding for wet+dry studies of biological systems
 - Alliance For Cellular Signalling (<http://www.afcs.org/>). First of the NIH “glue grants” 1998





Formal revival of Systems Biology

■ “Modelling” Systems Biology

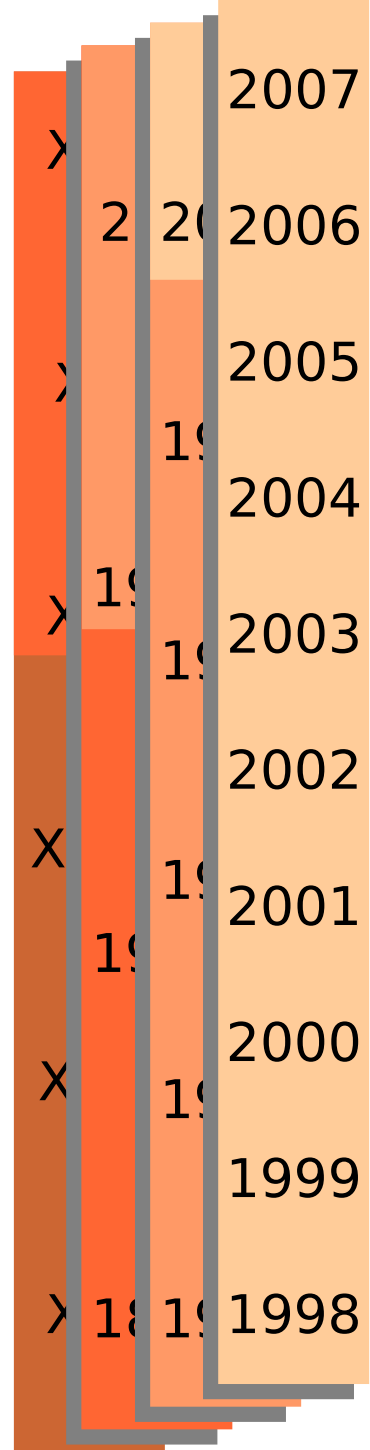


- 1998 - Hiroaki Kitano founds the Systems Biology Institute in Tokyo
- First appearance: Kyoda, Kitano. Virtual Drosophila project: Simulation of drosophila leg formation. *Genome Informatics Series* (1998)
- Kitano, H. Perspectives on systems biology. *New Generation Computing* (2000)

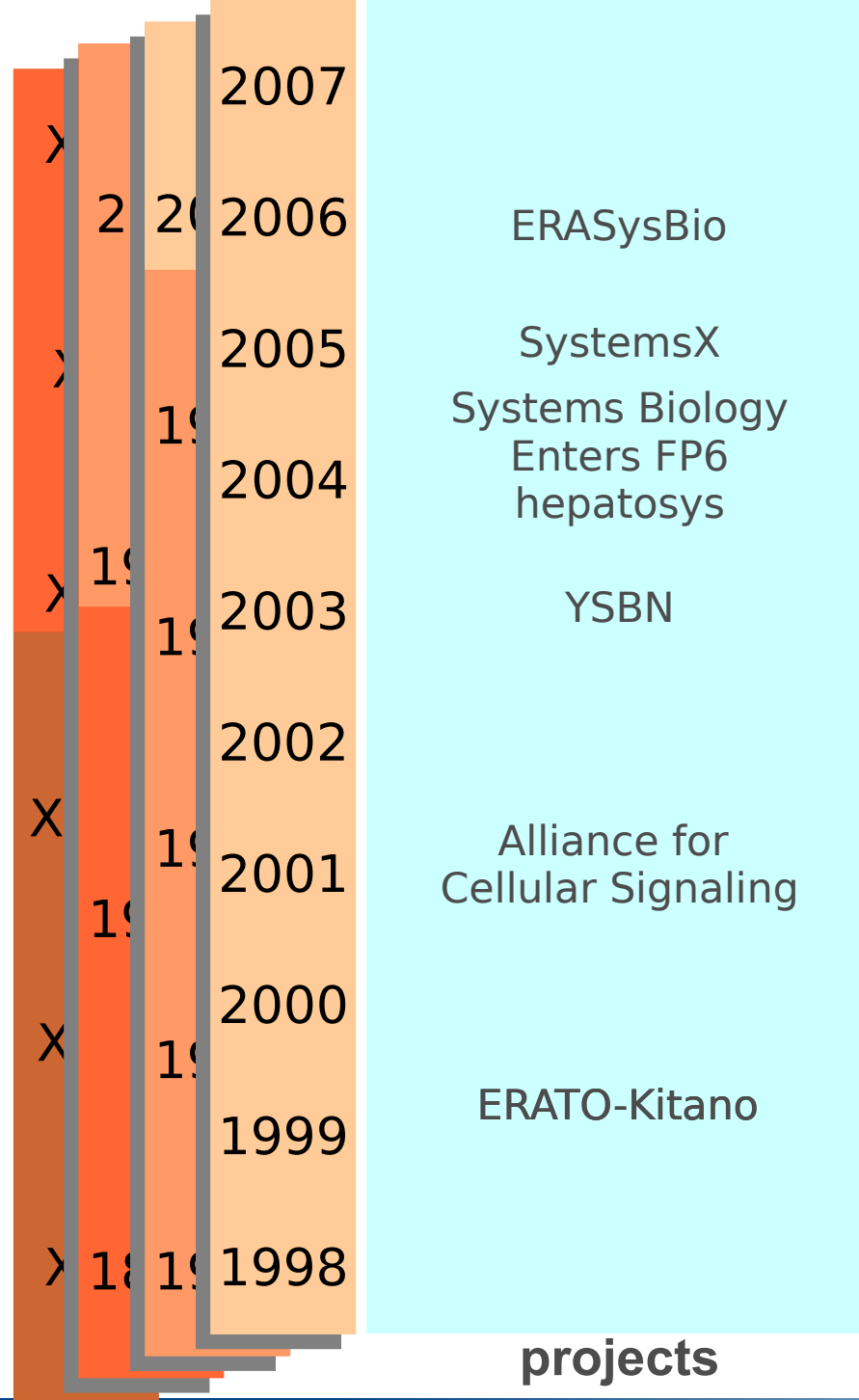
■ “Network” Systems Biology

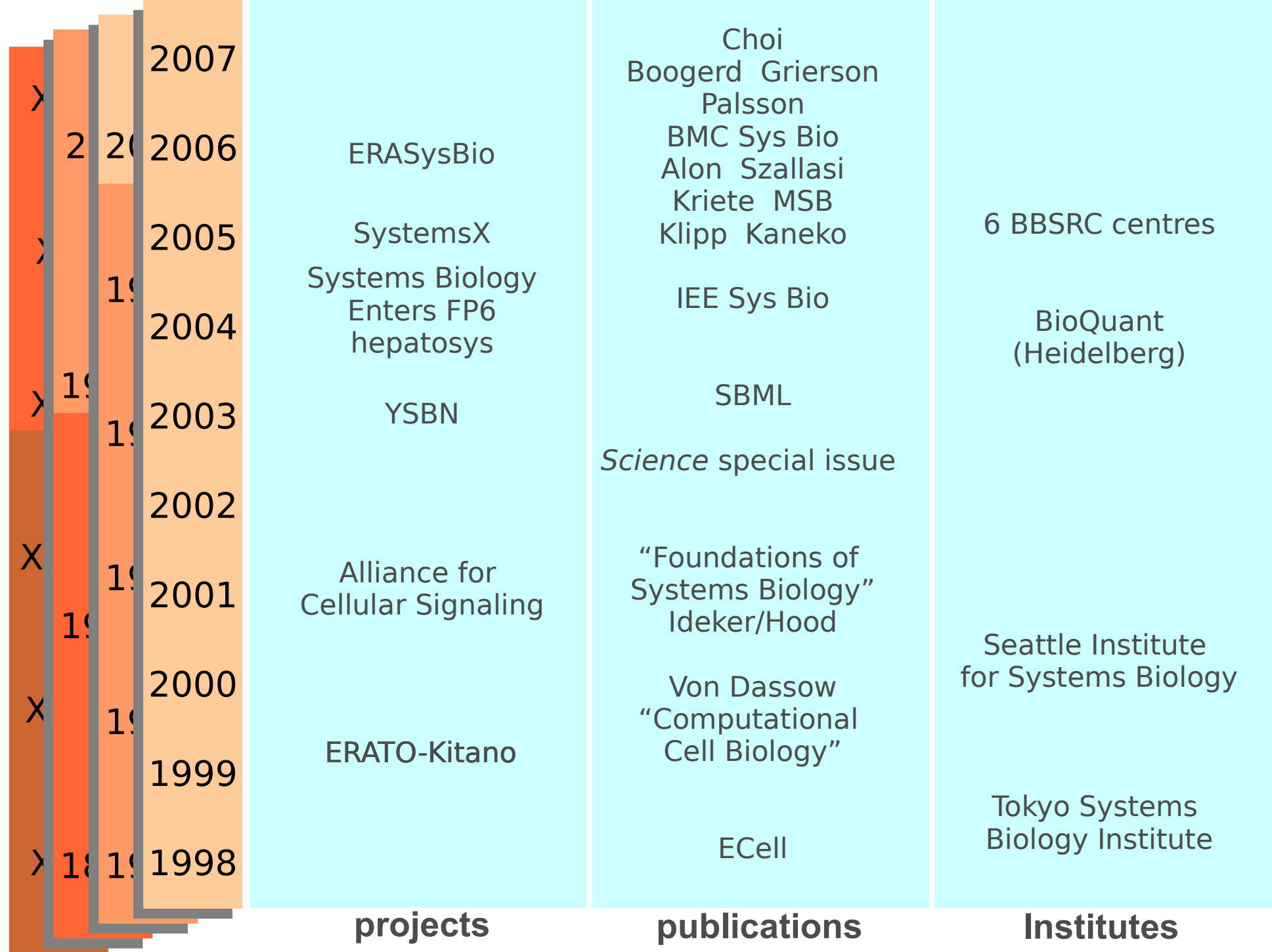


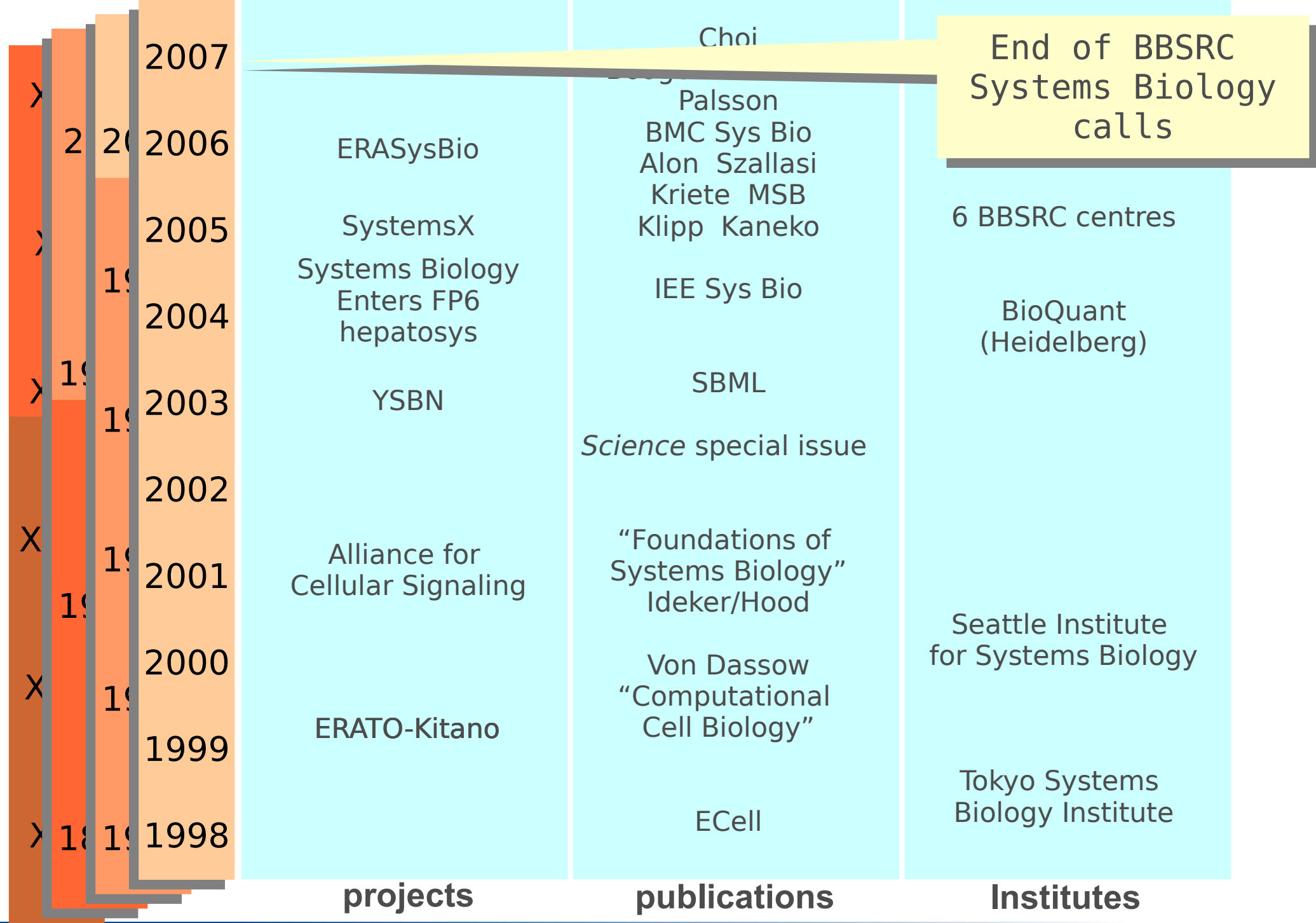
- First appearance: Leroy Hood. Systems biology: new opportunities arising from genomics, proteomics and beyond. *Experimental Hematology* (1998)
- Schwikowski B, Uetz P, Fields S. A network of protein-protein interactions in yeast. *Nat Biotechnol.* (2000)
- 2000 - Leroy Hood founds the Systems Biology Institute in Seattle



Rise of Systems Biology as a paradigm







Two kinds of Systems Biology?

Systems-wide analysis (omics)

- Born: 1990s
- Technologies: high-throughput, statistics
- People's background: molecular biologists, mathematicians
- Key lesson: the selection of a phenotype is done at the level of the system, not of the component (gene expression puzzle)

Application of systems-theory

- Born: 1960s
- Technologies: quantitative measurements, modelling
- People's background: biochemists, engineers
- Key lesson: the properties at a certain level are emerging from the dynamic interaction of components at a lower level

Bottom → up Vs Top → down



Build the system

literature

network inference

Put numbers

biochemistry

“omics”

Parametrise

parameter search

not (always) relevant

Analyse

Simulation

structural analysis,
steady-state analysis

perturb

Inhibition, stimulation,
suppression, overexpression

Bridging Systems Modelling and Systems-wide analysis

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Computational Modeling of Biological Systems (SysMod)

(Redirected from [Main Page](#))

The *Computational Modeling of Biological Systems* (SysMod) Community Of Special Interest aims at bridging the gap between bioinformatics and systems biology modeling. With advances in genomics these fields have recently started to converge. For example, systems modeling has become more reliant on bioinformatic network inference to build models and has begun to use transcriptomics and proteomics data to train models. More communication between systems modelers and bioinformaticians is needed to further integrate these fields. In particular, more communication between systems modellers and bioinformaticians is needed to build models of whole cells, organs and organisms. Furthermore, the promises of precision medicine lie, in part, on the interplay between bioinformatics-based analysis of patient data and model-based predictions of treatments.

SysMod is a [Community of Special Interests \(COSI\)](#) within the [International Society for Computational Biology](#).

News: The next SysMod annual meeting will be held on July 22nd 2017, as part of the [ISMB conference](#).

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08 Jul



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15 Jun



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