What is Systems Biology? Where does it come from?

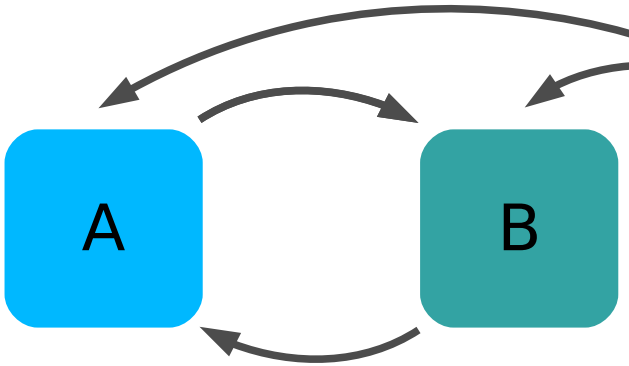
Nicolas Le Novère, The Babraham Institute

n.lenovere@gmail.com

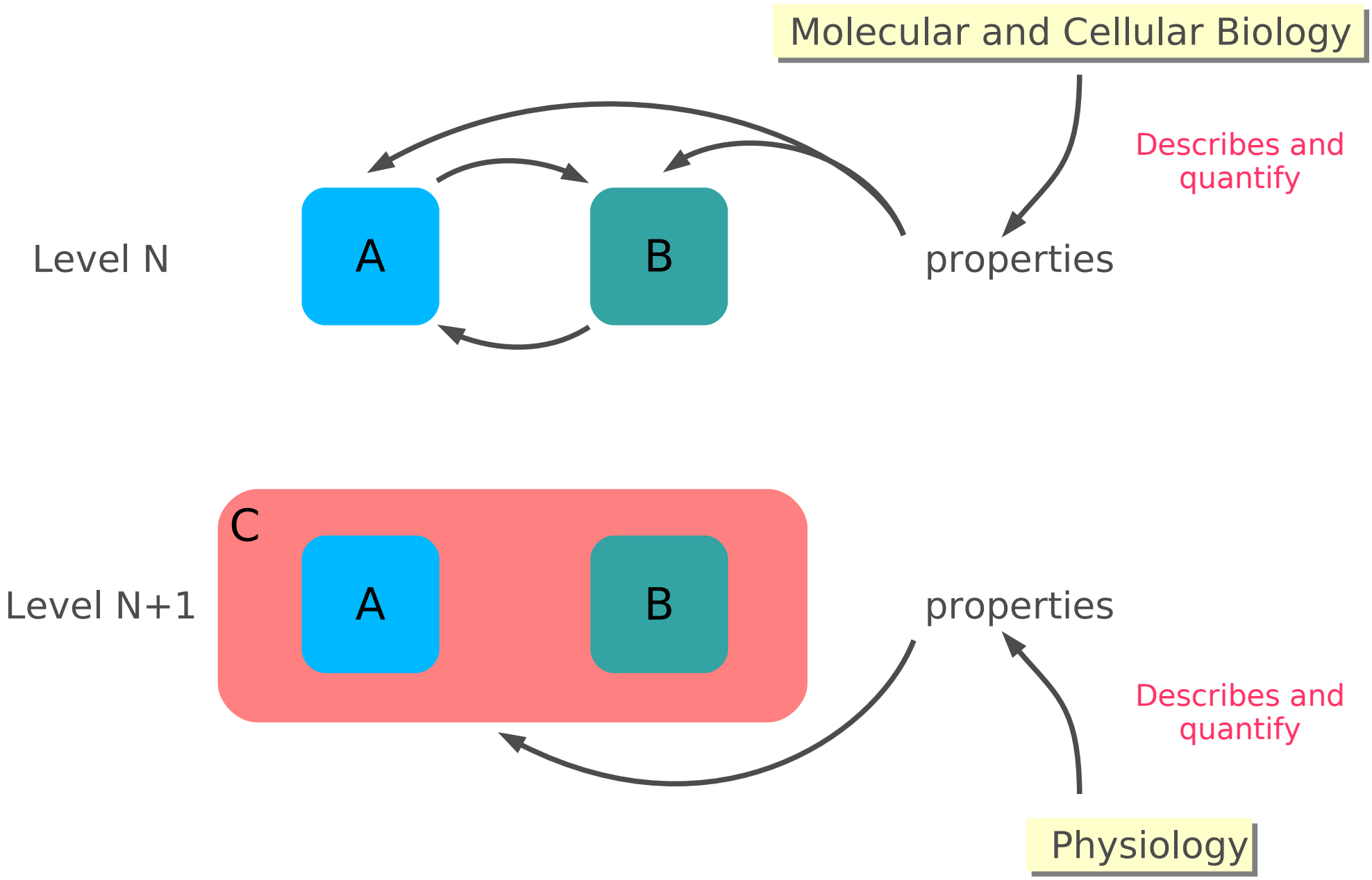
Molecular and Cellular Biology

Describes and quantify

Level N



properties


Molecular and Cellular Biology
Describes and quantify
Level N
A
B
properties
C
Level N+1
A
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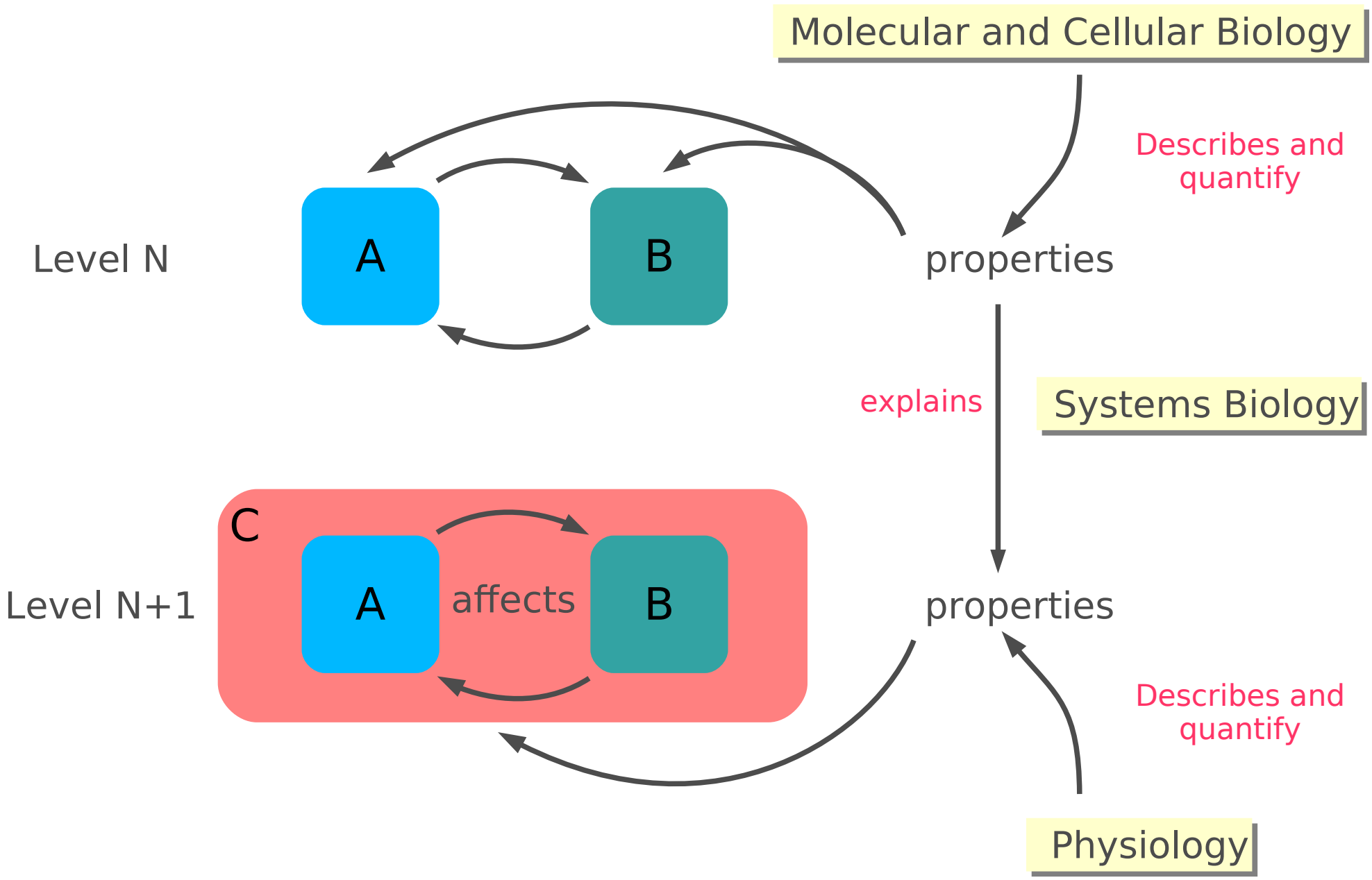
properties
Describes and quantify
Physiology


Molecular and Cellular Biology
Describes and quantify
Level N
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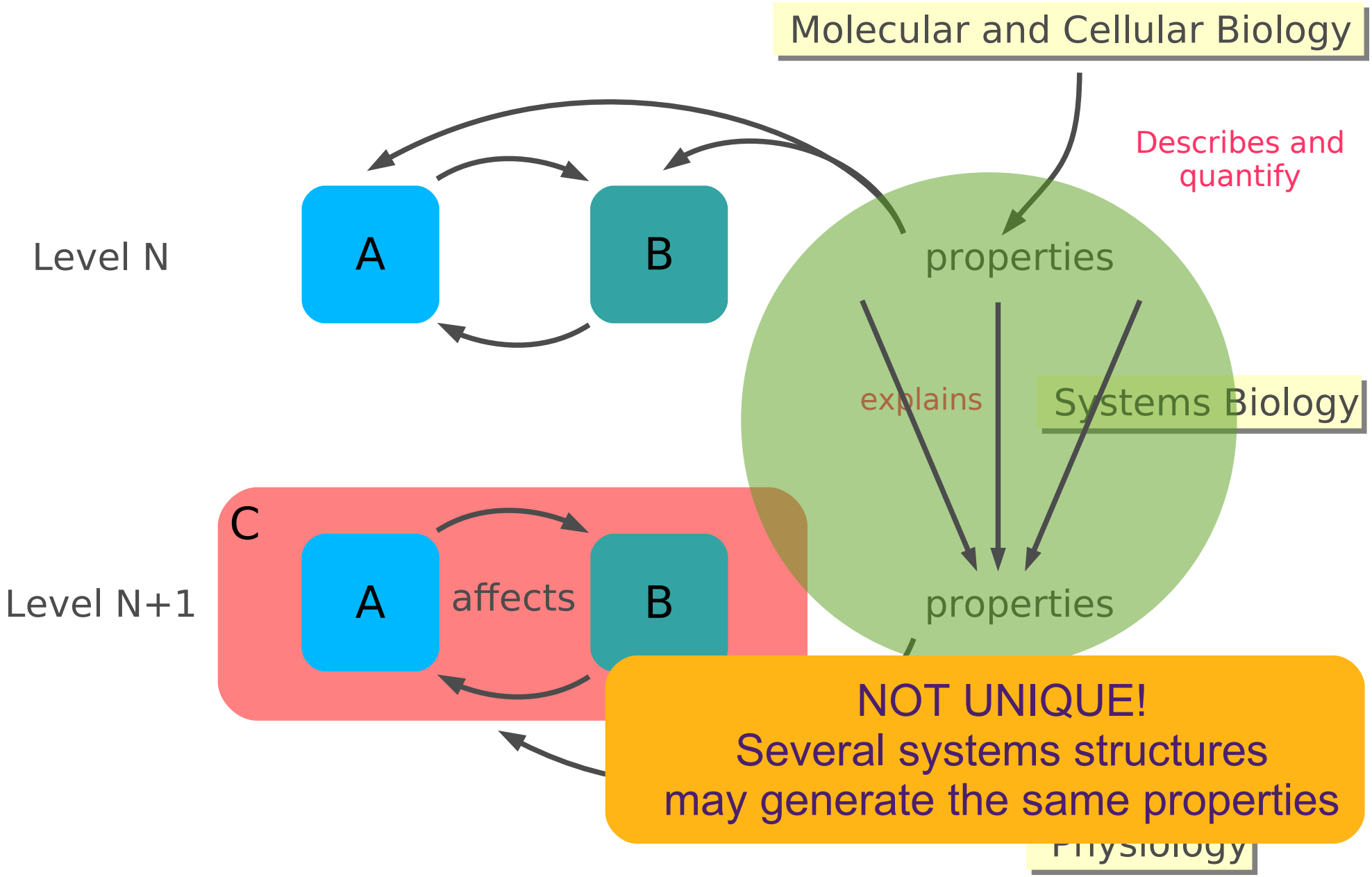
properties
explains
Systems Biology
C
Level N+1
A
affects
B
properties
Describes and quantify
Physiology


Molecular and Cellular Biology
Describes and quantify
Level N
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Systems Biology
C
Level N+1
A
affects
B
properties
NOT UNIQUE!
Several systems structures
may generate the same properties
Physiology

What Systems Biology is not!

Purely theoretical

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Purely theoretical: Most systems biologists are actually experimental biologists

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Based on large datasets

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Focused on biomolecular systems

What Systems Biology is not!

Purely theoretical: Most systems biologists are actually experimental biologists

Based on large datasets: in a system of two enzymes, the behaviour of both reactions is different than the ones observed in isolation

Focused on biomolecular systems: systems biology is scale-free, and a biological system can be made up of molecules, cells, organs or individuals

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

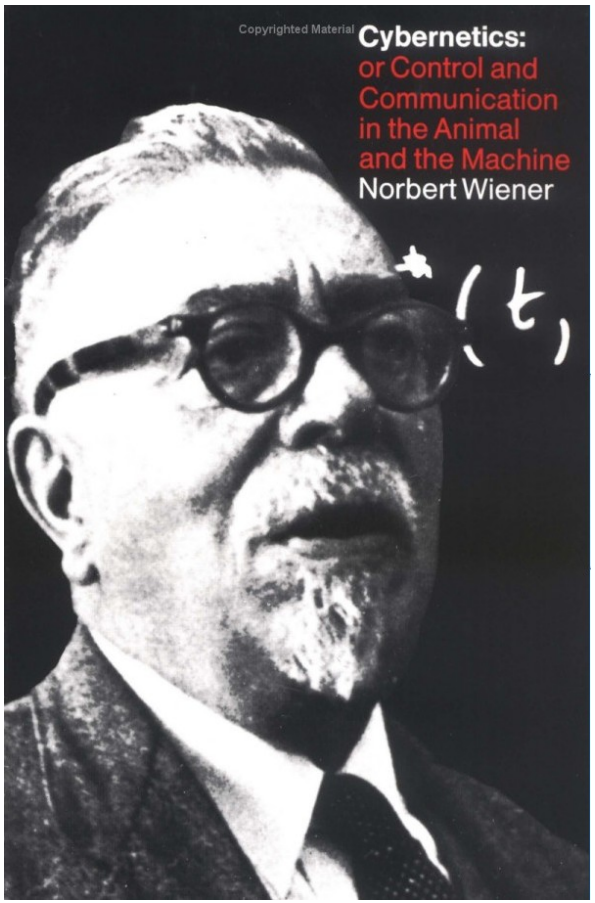
Description of the components of the world

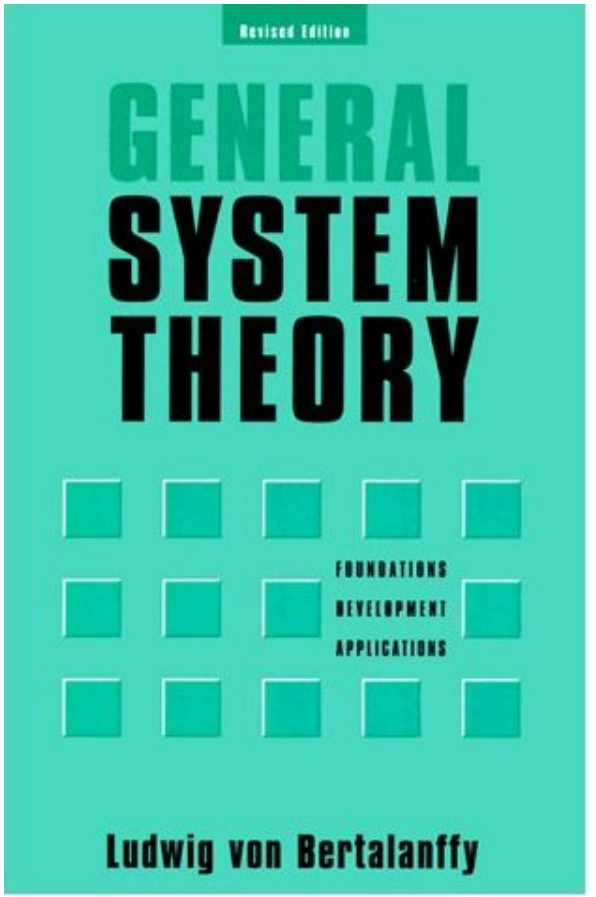
particle physics,
quantum mechanic,
biochemistry,
structural biology,
molecular biology

Description of interacting components

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

Systems are conceptualised mid-XXth





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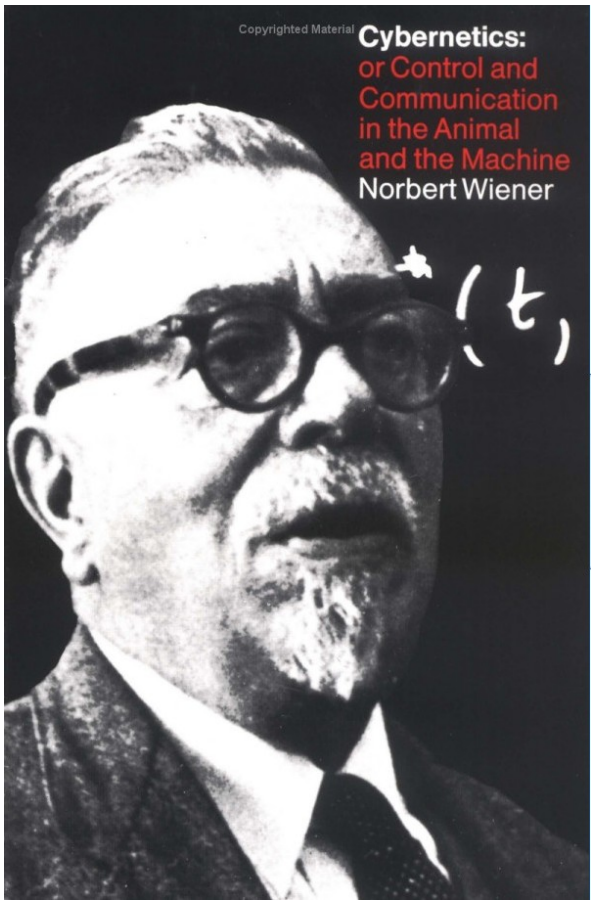
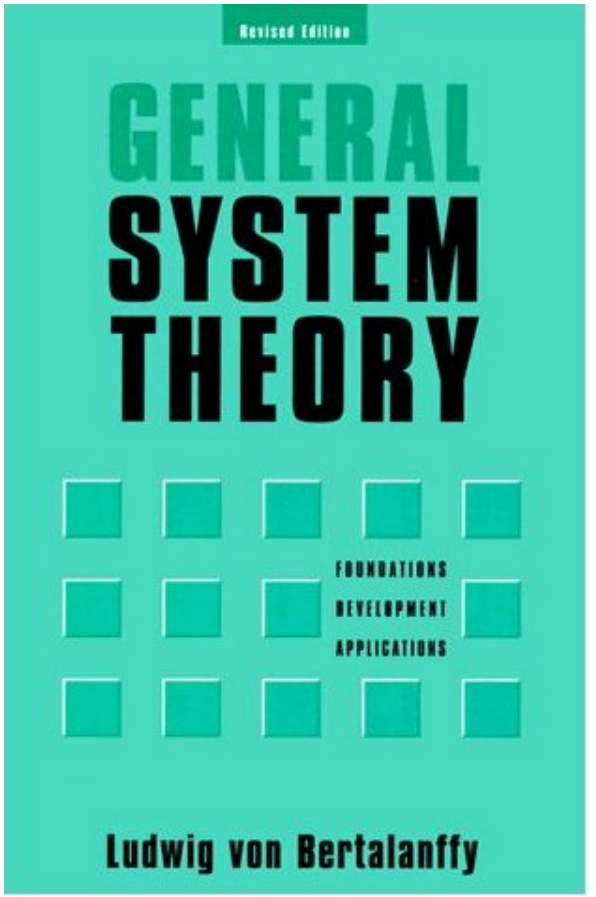
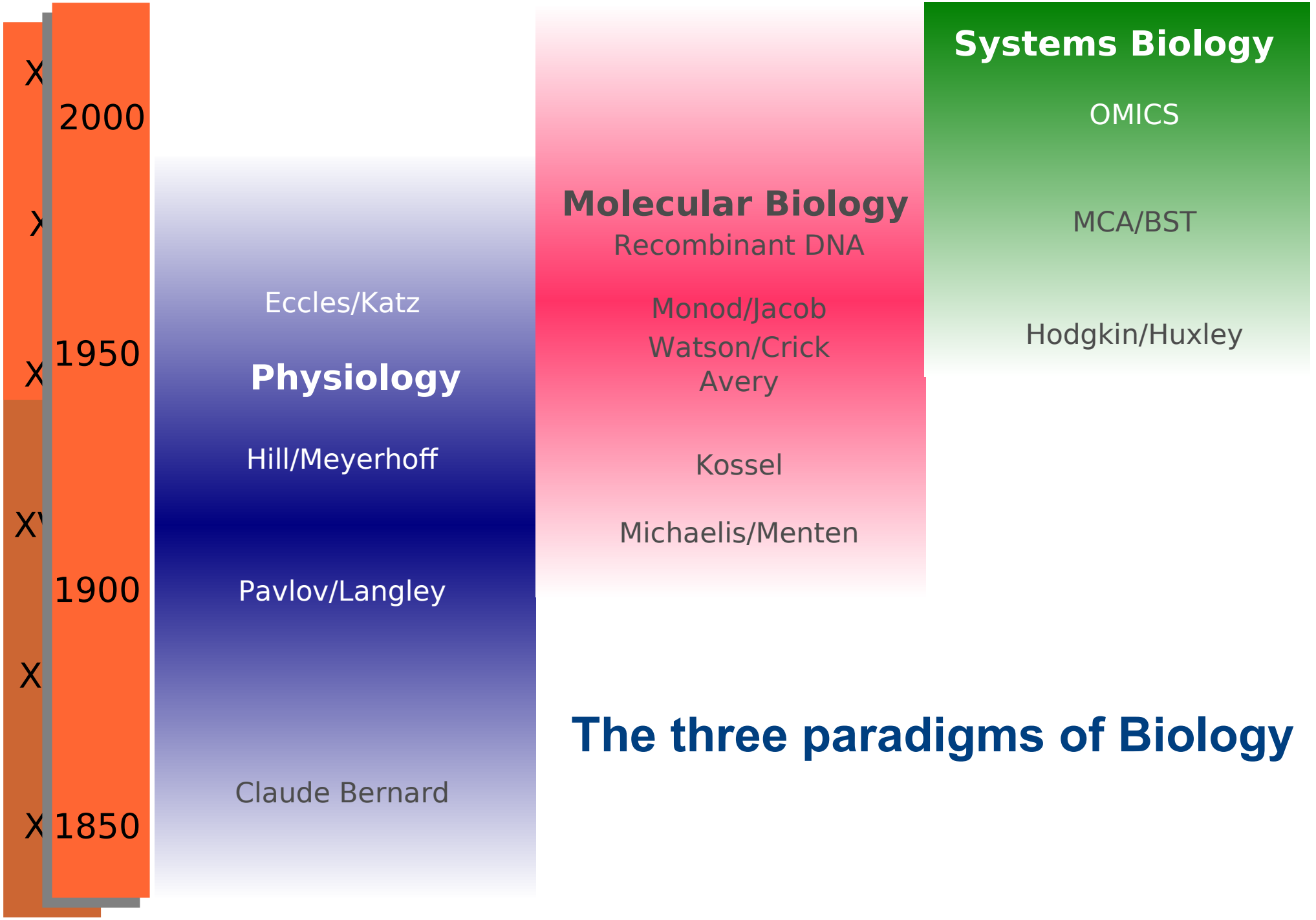
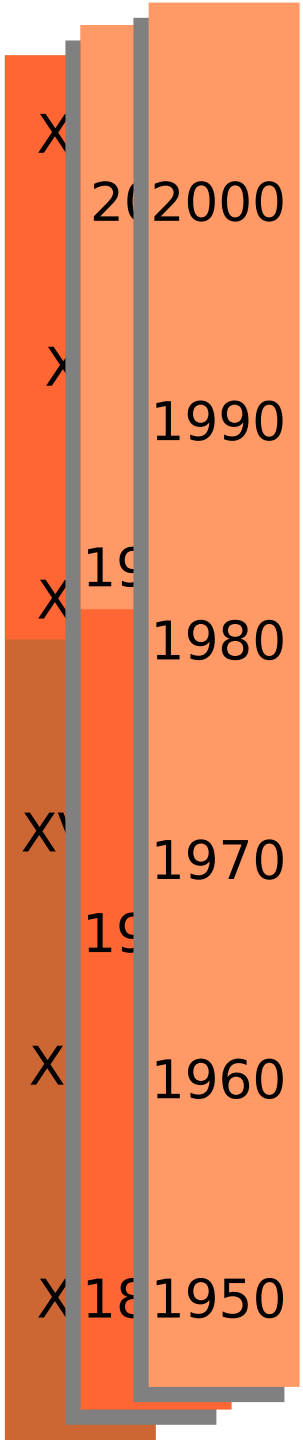




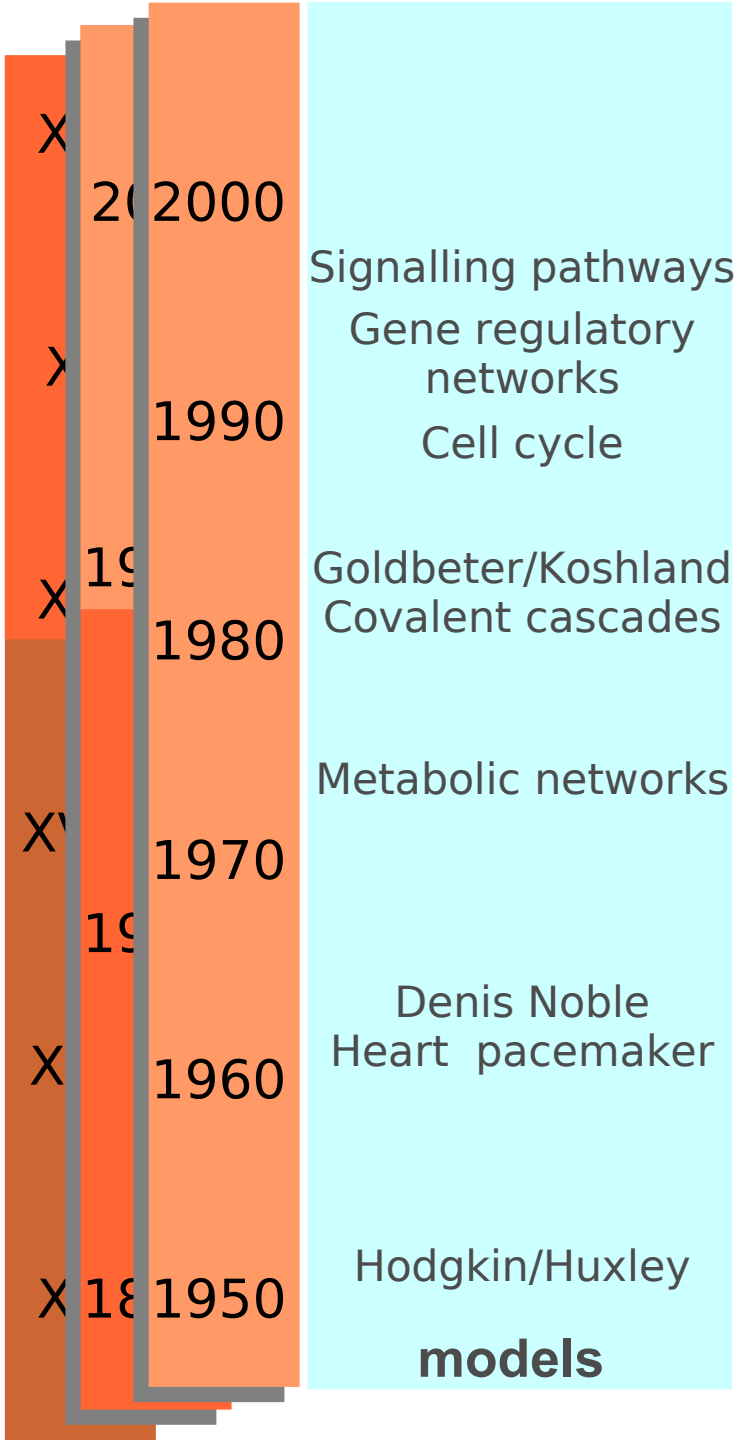
"[A system consists of] a dynamic order of parts and processes standing in mutual interaction. [...] The fundamental task of biology [is] the discovery of the laws of biological systems"
Ludwig von Bertalanfy, Kritische Theorie der Formbildung, 1928



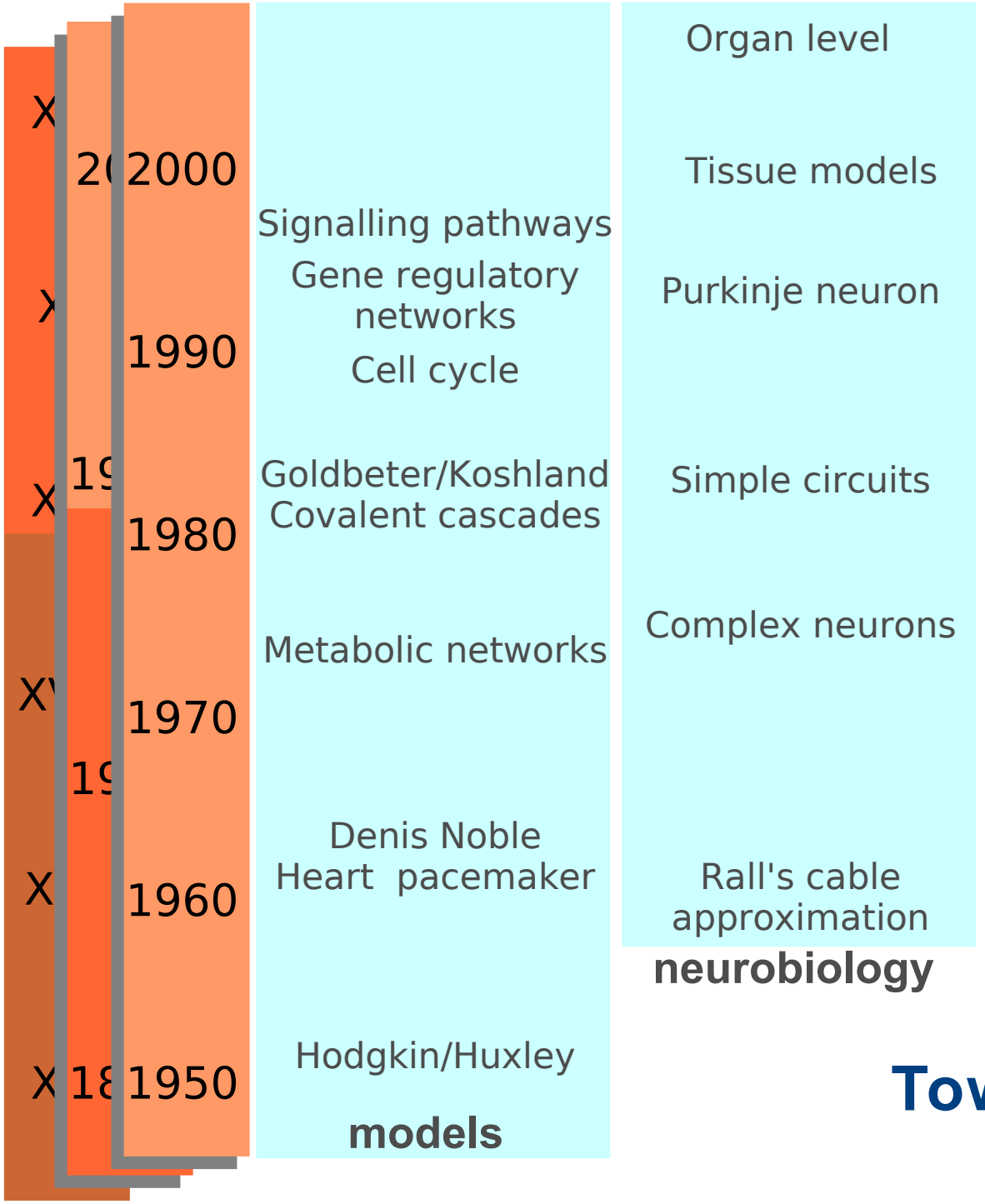
The three paradigms of Biology



Towards Systems Biology



Towards Systems Biology



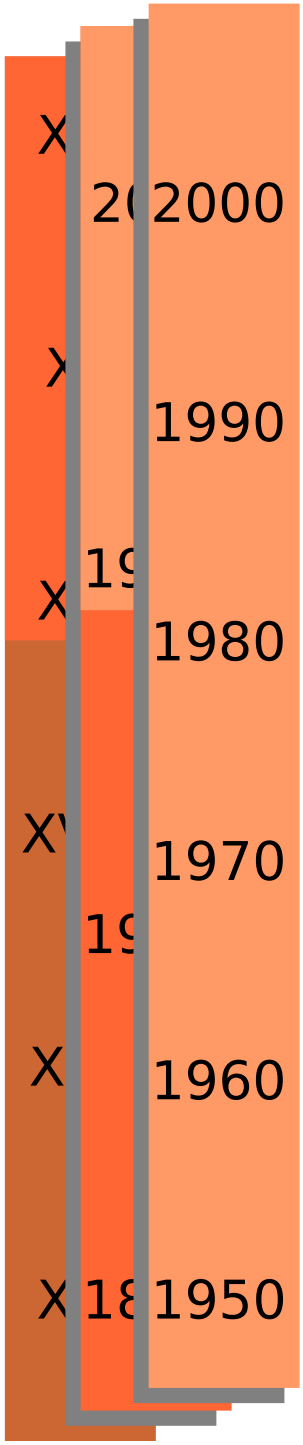
Towards Systems Biology

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



2000

1990

1980

1970

1960

1950

Signalling pathways

Gene regulatory networks

Cell cycle

Goldbeter/Koshland Covalent cascades

Metabolic networks

Denis Noble Heart pacemaker

Hodgkin/Huxley

models

Organ level

Tissue models

Purkinje neuron

Simple circuits

Complex neurons

Rall's cable approximation

neurobiology

SBML

User-friendly simulators

Multi-agent systems

Stochastic algorithms

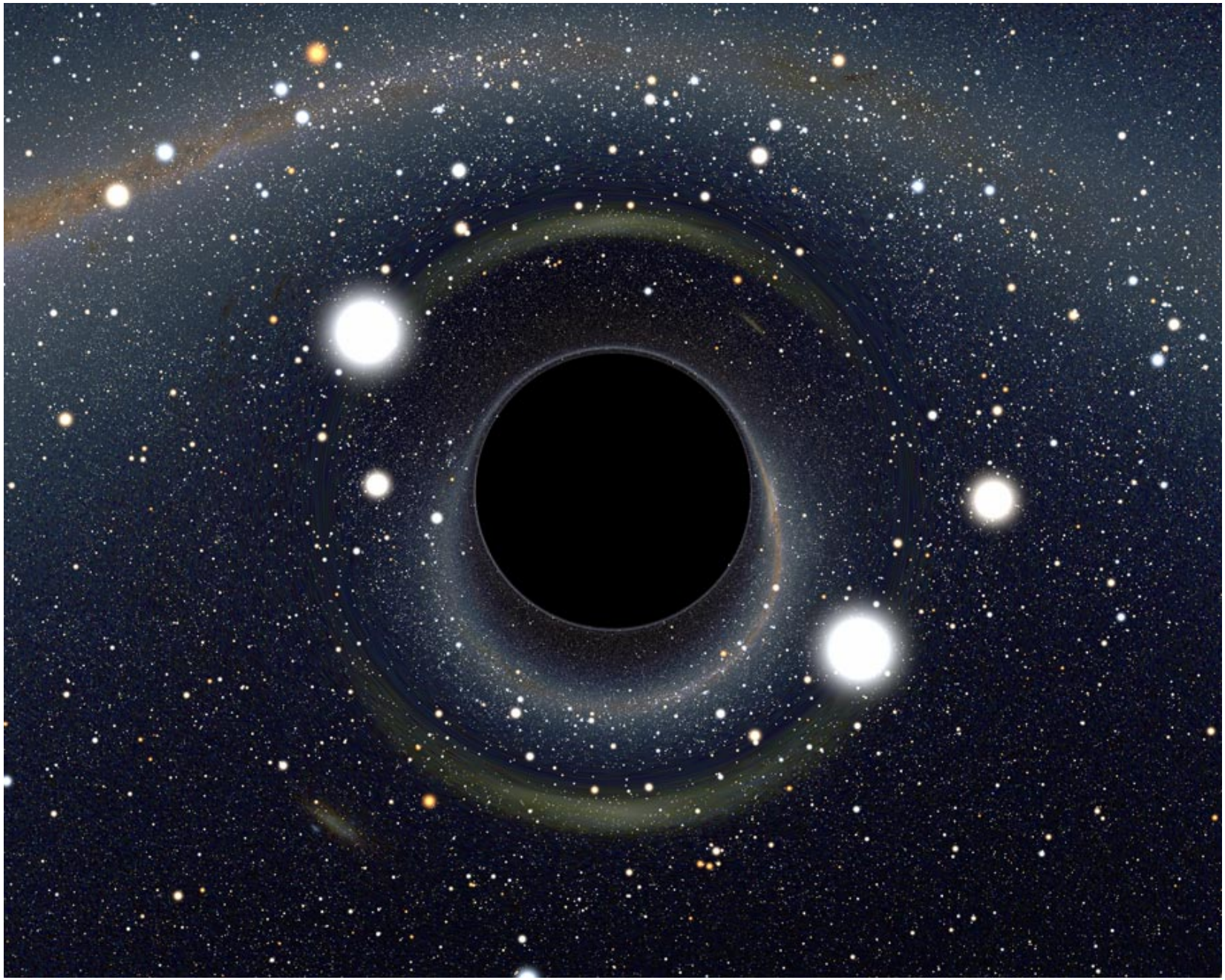
MCA/BST

Boolean networks

methods

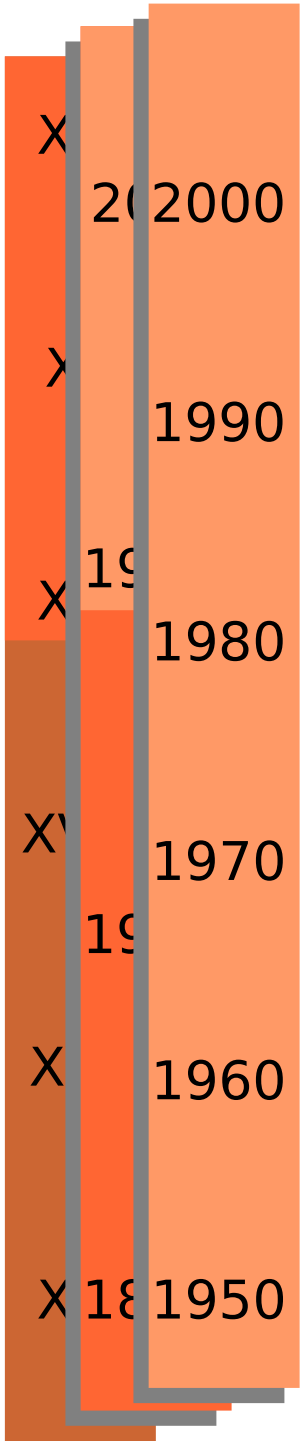
Towards Systems Biology

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 ad 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. First of the NIH “glue grants”. 1998



Signalling pathways

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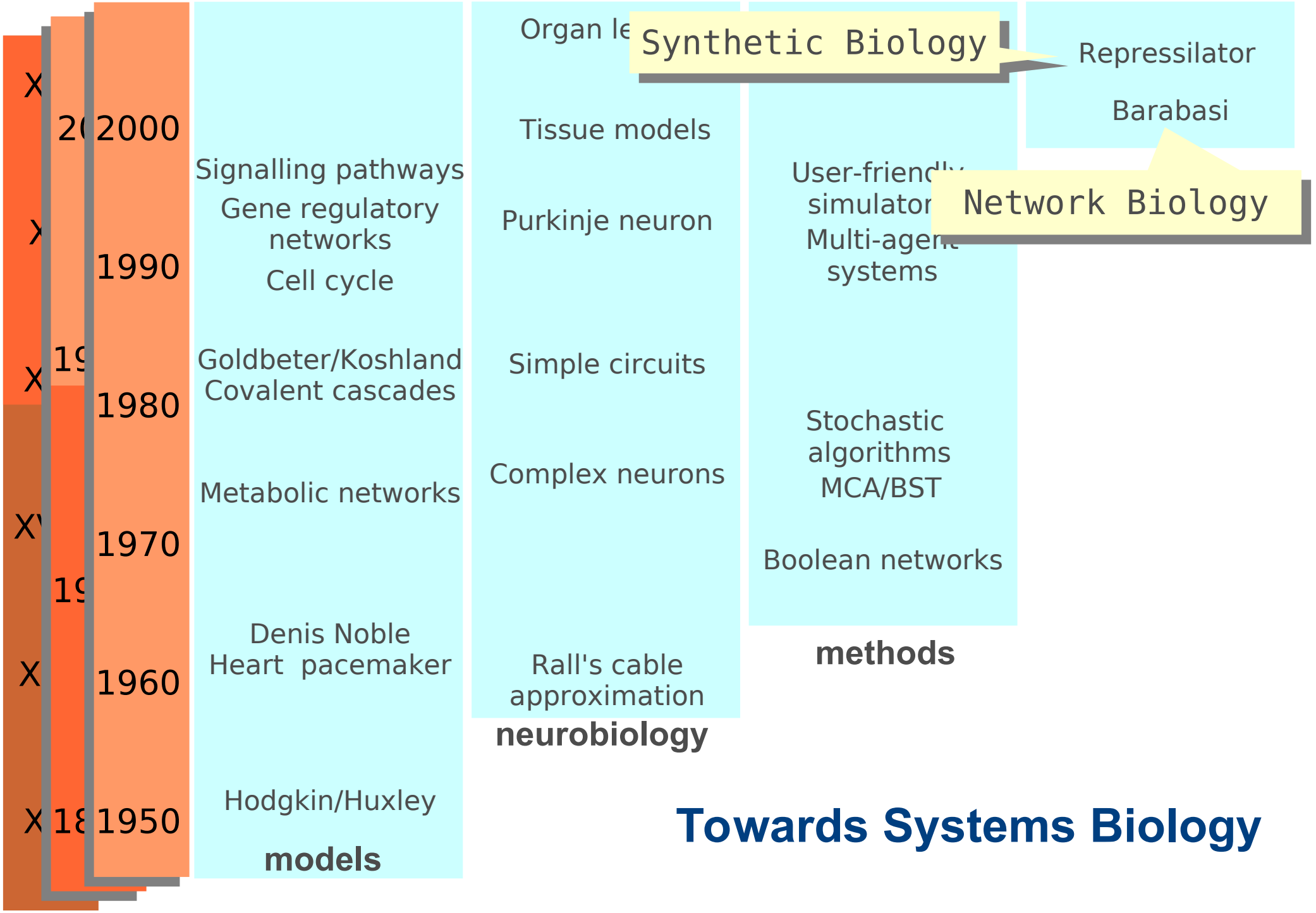
Repressilator

Barabasi

Towards Systems Biology



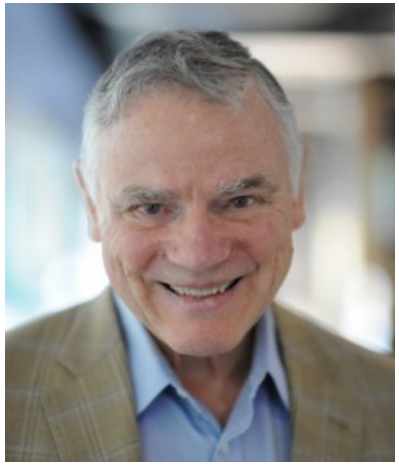
Towards Systems Biology

Formal revival of Systems Biology

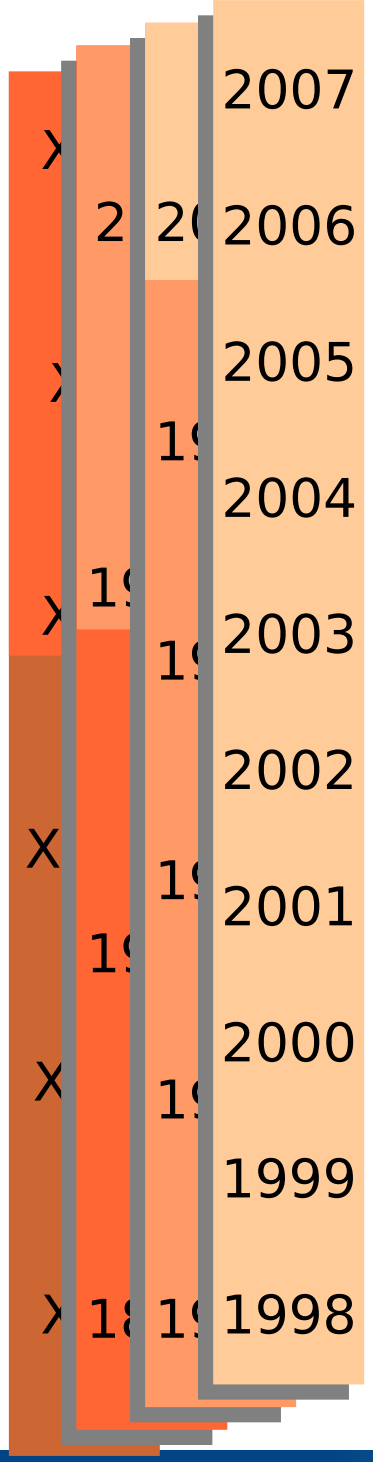
- "Modelling" Systems Biology

  - 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)

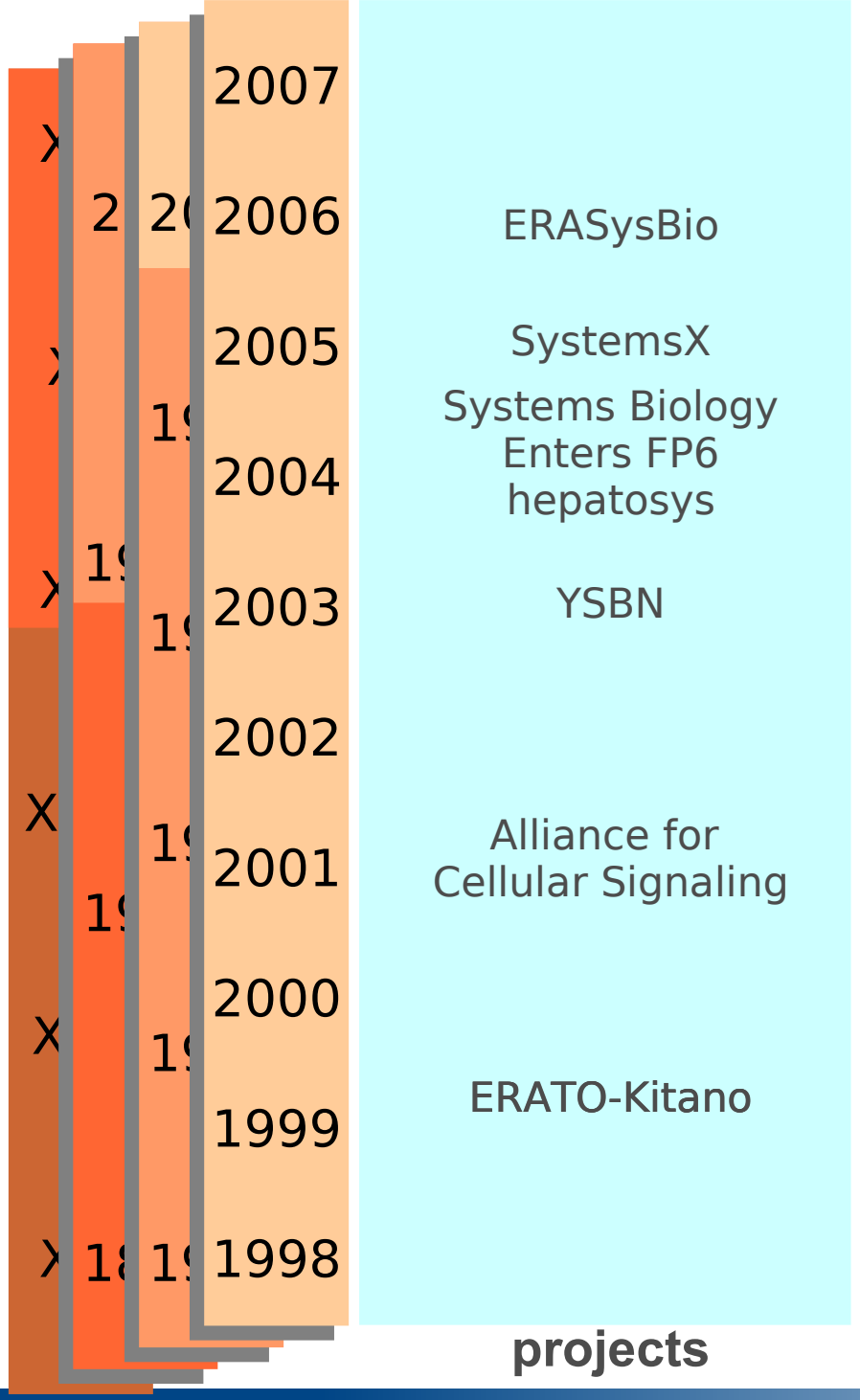
- "Network" Systems Biology



  - 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


2007
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ERASysBio
SystemsX
Systems Biology
Enters FP6
hepatosys
YSBN
Alliance for
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ERATO-Kitano
projects

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Alliance for
Cellular Signaling

ERATO-Kitano

projects

Choi
Boogerd Grierson
Palsson
BMC Sys Bio
Alon Szallasi
Kriete MSB
Klipp Kaneko

IEE Sys Bio

SBML

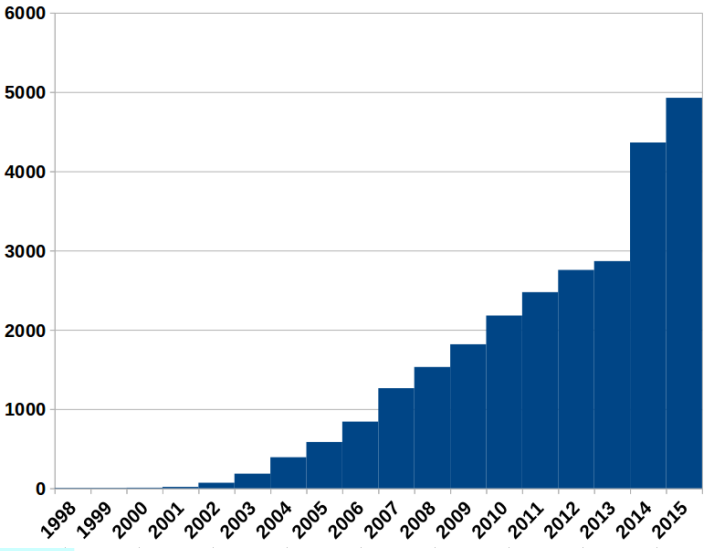
Science special issue

"Foundations of
Systems Biology"
Ideker/Hood

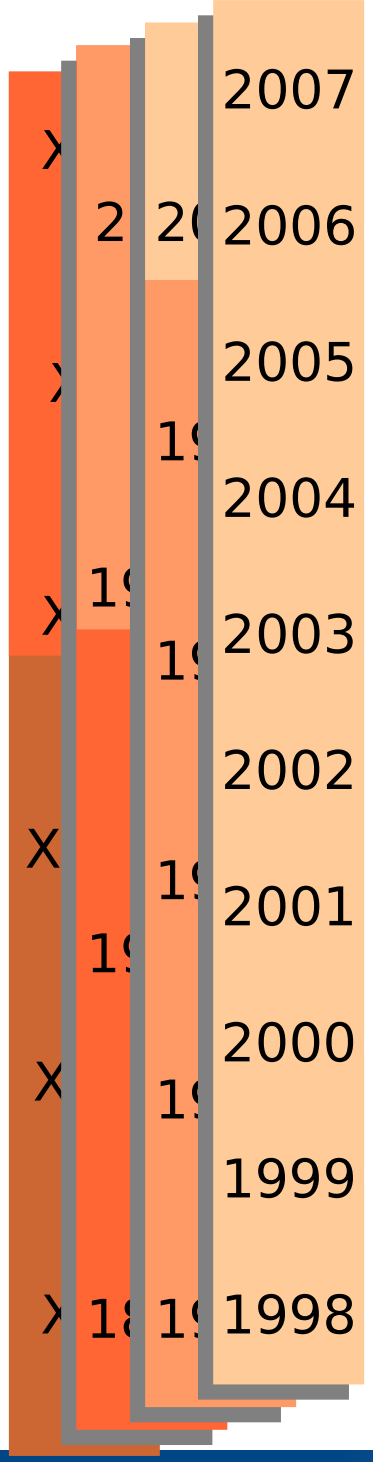
Von Dassow
"Computational
Cell Biology"

ECell

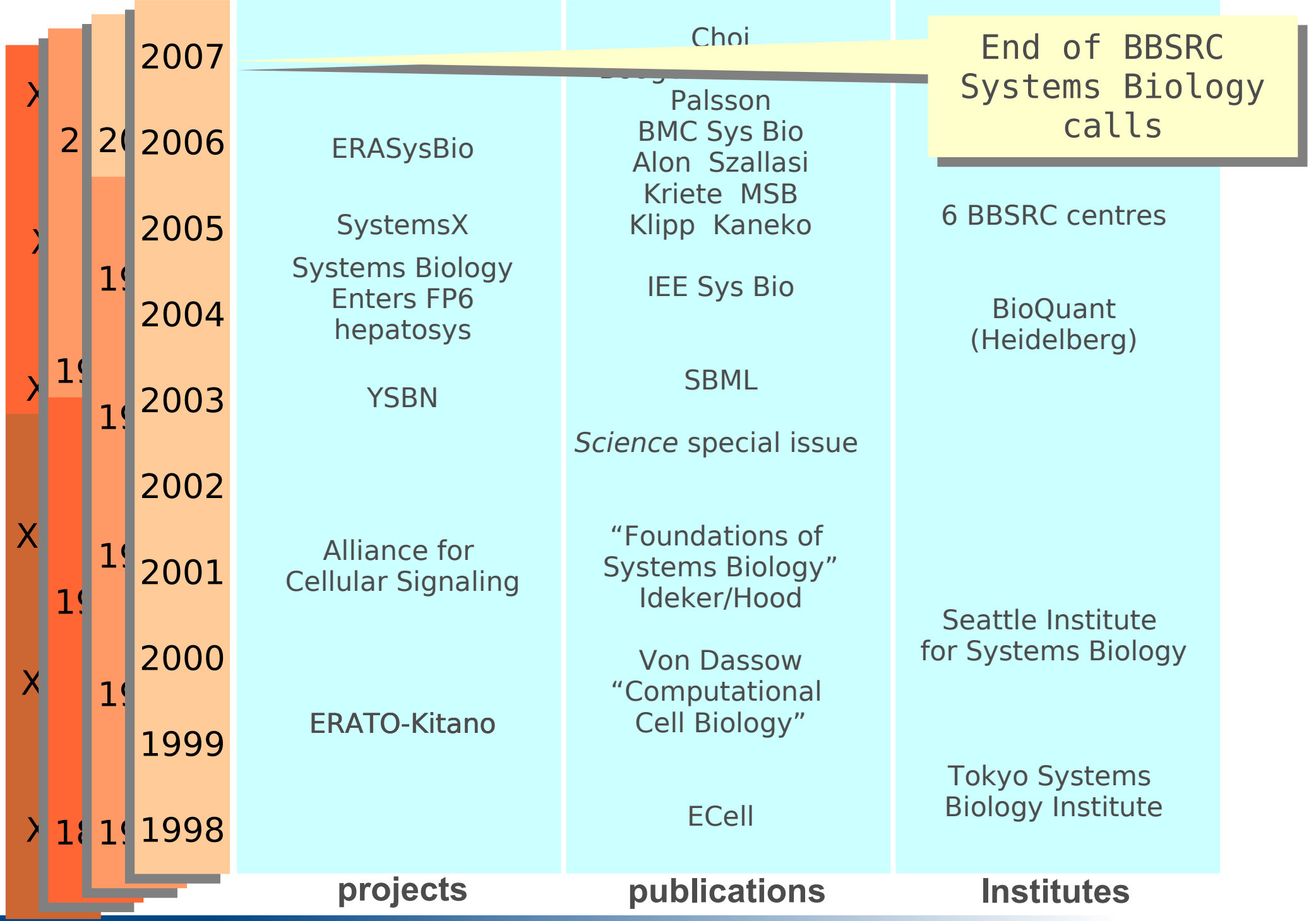
publications



PubMed



	projects	publications	Institutes
2007		Choi Boogerd Grierson Palsson	
2006	ERASysBio	BMC Sys Bio Alon Szallasi Kriete MSB Klipp Kaneko	6 BBSRC centres
2005	SystemsX	IEE Sys Bio	
2004	Systems Biology Enters FP6 hepatosys		BioQuant (Heidelberg)
2003	YSBN	SBML	
2002		*Science* special issue	
2001	Alliance for Cellular Signaling	"Foundations of Systems Biology" Ideker/Hood	
2000		Von Dassow "Computational Cell Biology"	Seattle Institute for Systems Biology
1999	ERATO-Kitano		
1998		ECell	Tokyo Systems Biology Institute


2007
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Choi
Palsson
BMC Sys Bio
Alon Szallasi
Kriete MSB
Klipp Kaneko
IEE Sys Bio
SBML
Science special issue
"Foundations of Systems Biology" Ideker/Hood
Von Dassow "Computational Cell Biology"
ECell
ERASysBio
SystemsX
Systems Biology Enters FP6
hepatosys
YSBN
Alliance for Cellular Signaling
ERATO-Kitano
End of BBSRC Systems Biology calls
6 BBSRC centres
BioQuant (Heidelberg)
Seattle Institute for Systems Biology
Tokyo Systems Biology Institute
projects
publications
Institutes

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: different gene expression networks produce the same cellular phenotype)

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	

The Computational Modeling of Biological Systems (SysMod) Community of Special Interest (COSI) of the International Society for Computational Biology (ISCB) is a forum for discussion about the combined use of systems biology modeling and bioinformatics to understand biology and disease. SysMod encompasses all methods used in bioinformatics and systems biology, as well as all biological systems and all applications areas. The main activities of SysMod include an annual meeting at the Intelligent Systems for Molecular Biology (ISMB) conference organized by the ISCB and an online forum.

Annual meeting

The main activity of SysMod is an annual 1-day meeting at the annual Intelligent Systems in Molecular Biology (ISMB) conference organized by the International Society for Computational Biology (ISCB). The meeting is a forum for discussion about the integration of systems biology and bioinformatics. The meetings include keynote talks, contributed talks, and poster sessions. The third annual SysMod meeting will take place on July 7, 2018 in Chicago. Please see the meeting page for more information.

Google Group

The SysMod Google Group is an forum for discussion among systems biologists and bioinformaticians. Please visit Google Groups to join.

News

The third annual SysMod meeting will be held on July 7, 2018 during the ISMB conference in Chicago.

Twitter feed

SysMod Retweeted

SysMod
@cosi_sysmod

Tomorrow is the deadline to submit abstract for #sysmod #ismb2018. Submit athttps://www.iscb.org /ismb2018-submit/ismb2018-abstracts selecting SysMod in the proposed COSIs. NB: There will be a late poster call, but w/o option of talk.

Apr 4, 2018

SysMod
@cosi_sysmod