Journée RIC – CRIStAL — 2020-10-01

BioComputing

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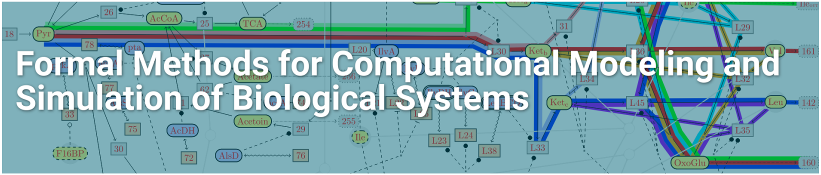
Centre de Recherche en Informatique, Signal et Automatique de Lille

Université de Lille
cnrs
centralelille

BioComputing

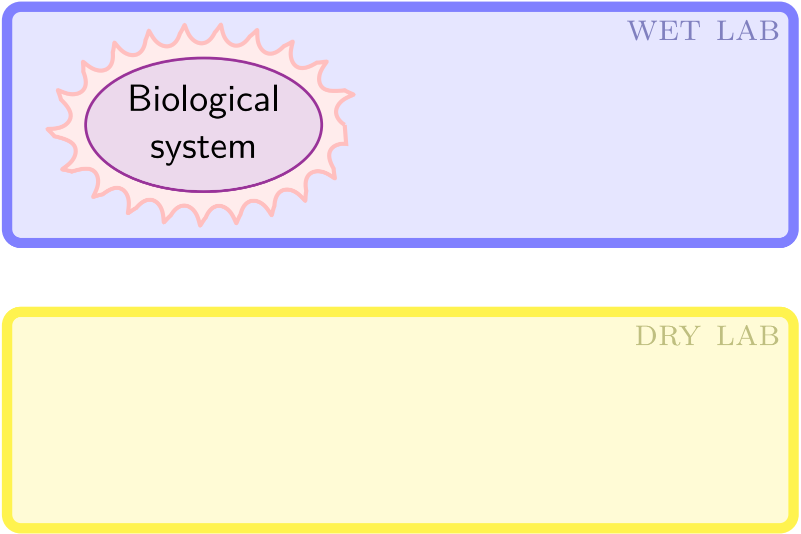
BioComputing   Members   Publications   Job & Project Offers   Software   Funding



Because of ever increasing experimental data and knowledge, life scientists are now faced to highly complex biological systems with huge size. They involve many interactions that are more and more measurable both in time and space with possibly observable stochastic effects. Modeling and simulation are thus essential for the rational understanding of the dynamic behavior of living organisms. Besides of understanding, models are particularly valuable for their predictive power that allows for *in-silico* experiments. These aim at deciphering between costly and long wet lab experiments to be carried out.

The BioComputing group develops and studies *formal methods and languages* for modeling and simulation of biological systems. Our approach is mainly based on methods used for the static analysis of programs (within the fields of semantics of programming languages, logic and concurrency theory). A model is designed as a set of abstract *interaction rules* between biological entities possibly equiped with *kinetic laws* that specifies how long and how likely an interaction can occur. Such

In Silico Model and Experiments



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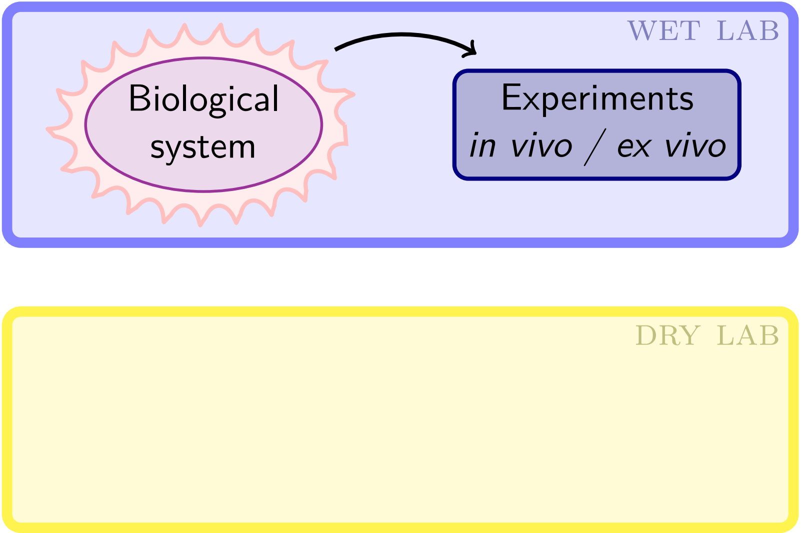

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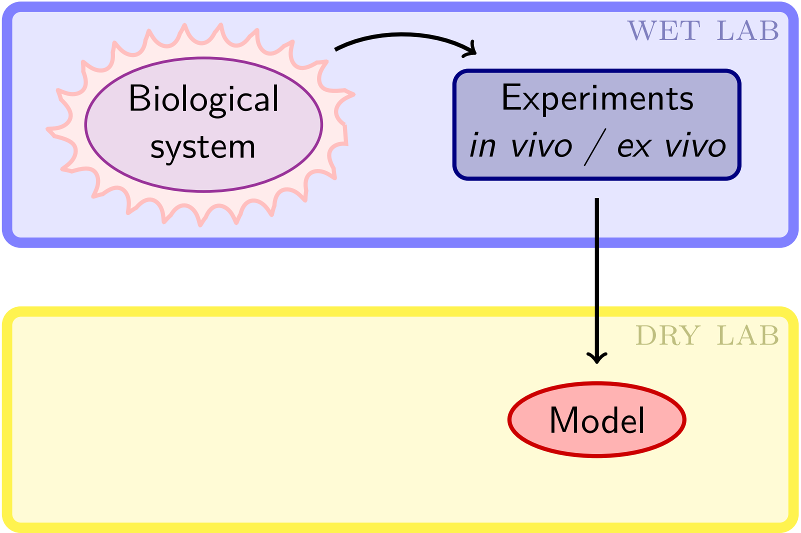

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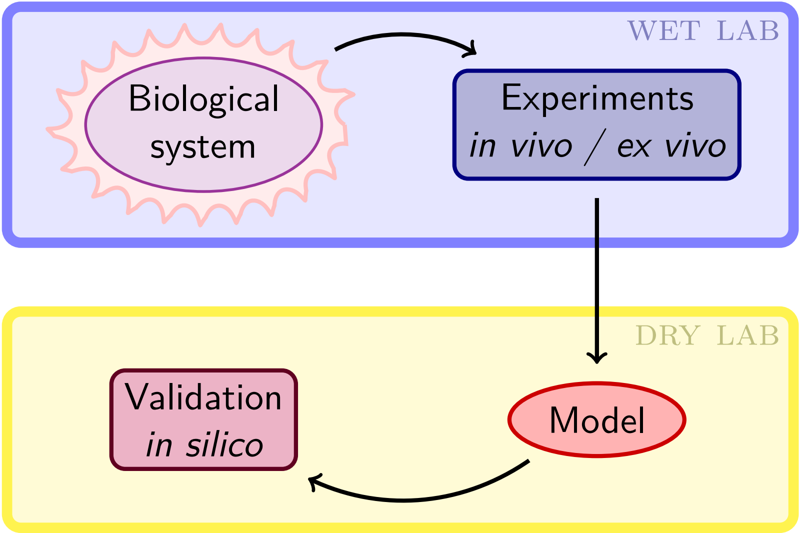

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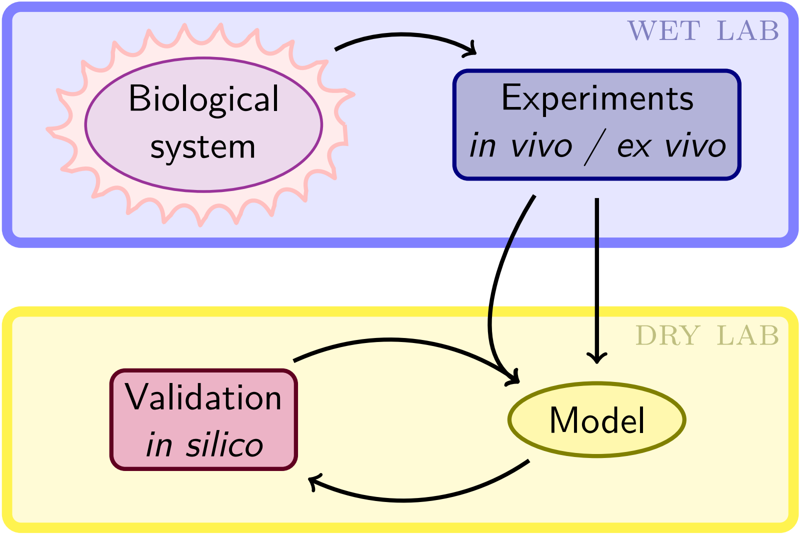

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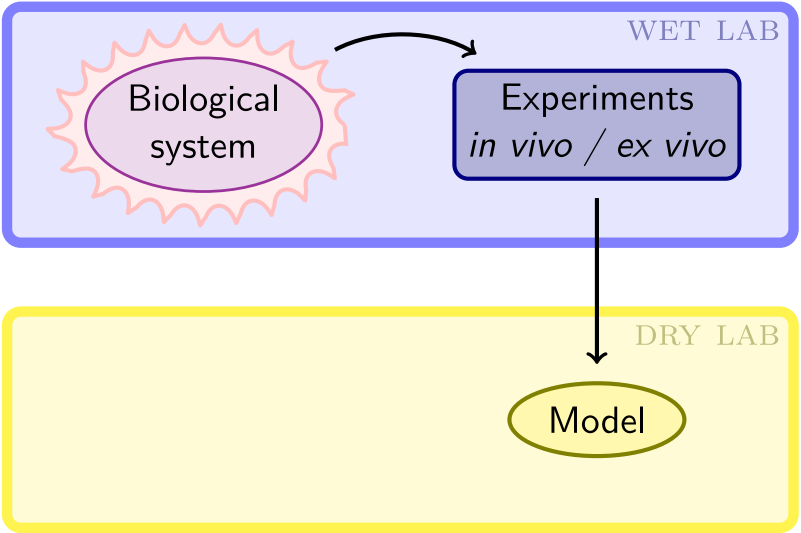

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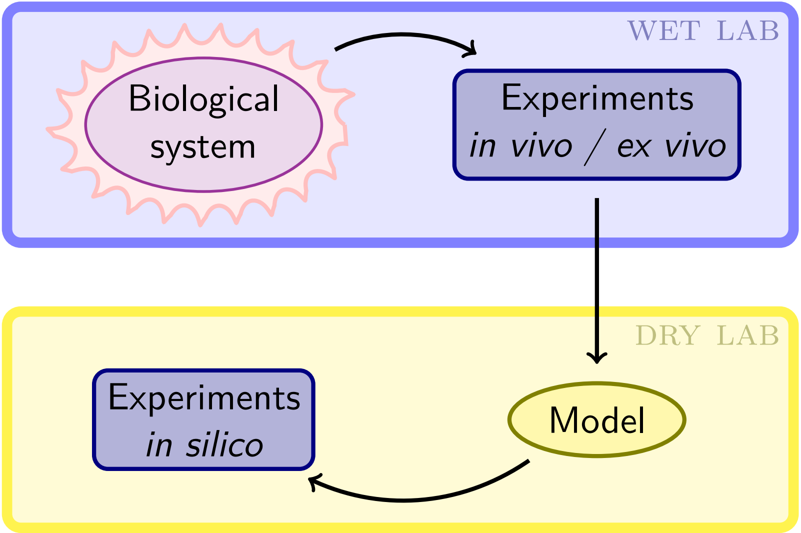

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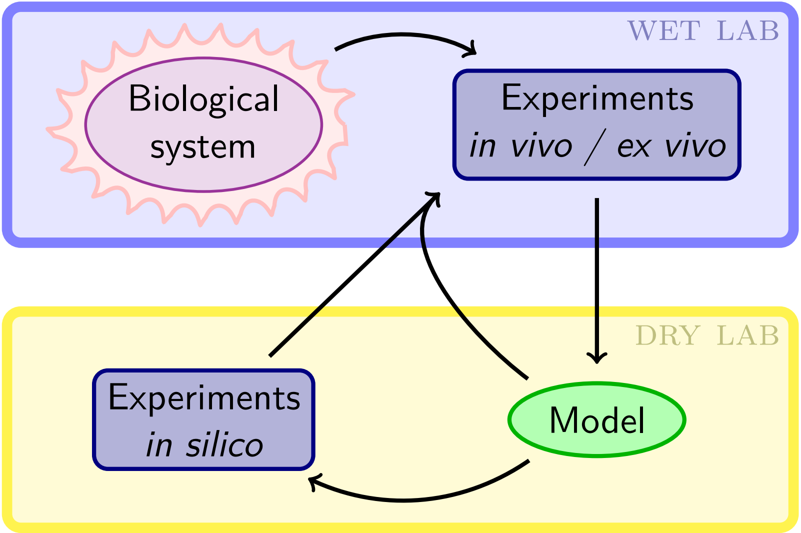

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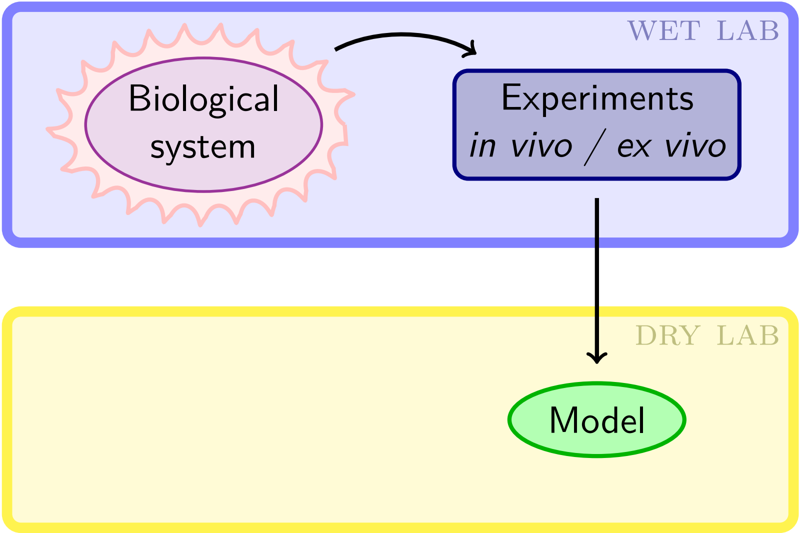

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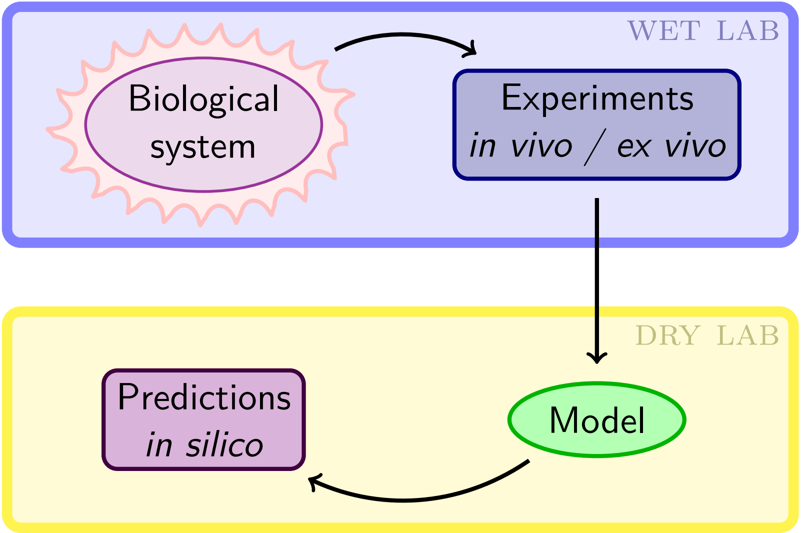

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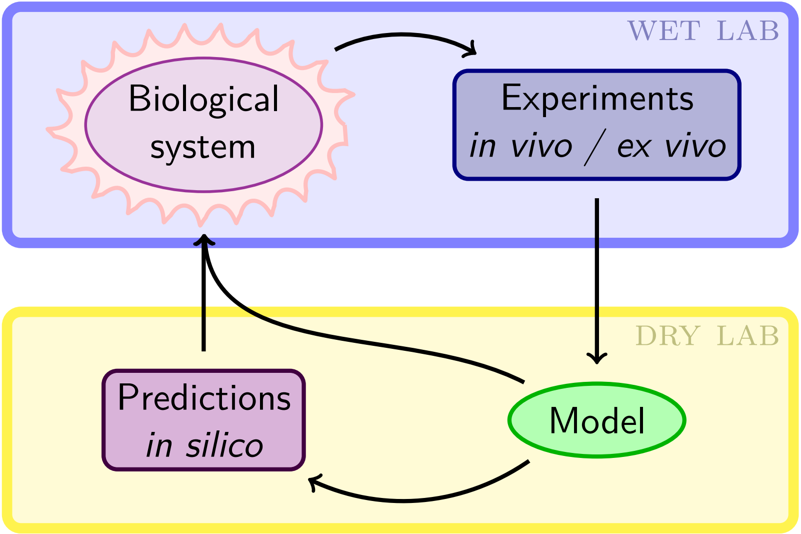
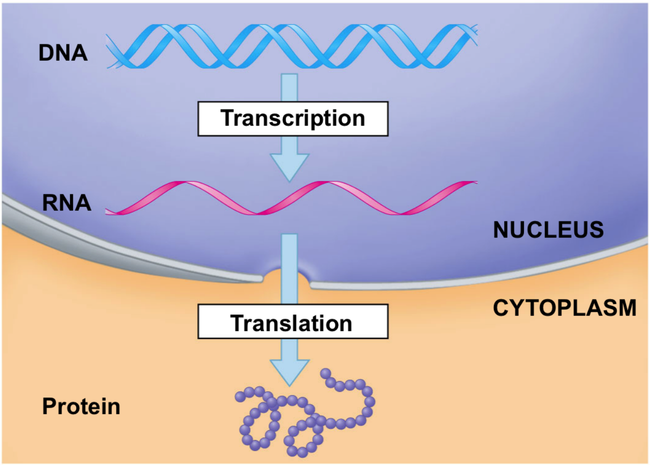


Preliminary Abstraction



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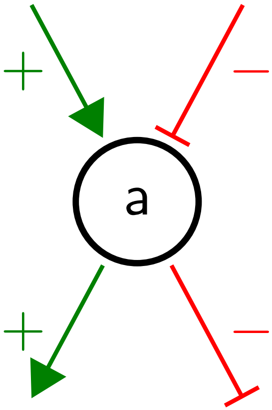

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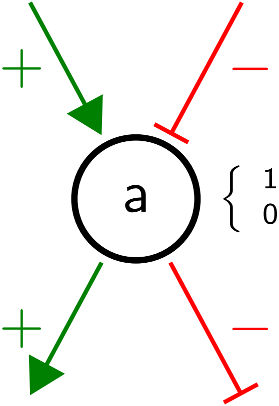


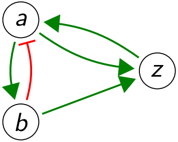
$$\left\{ \begin{array}{l} 1 = \text{active} \\ 0 = \text{inactive} \end{array} \right\}$$

Analysis and Control of Large Models

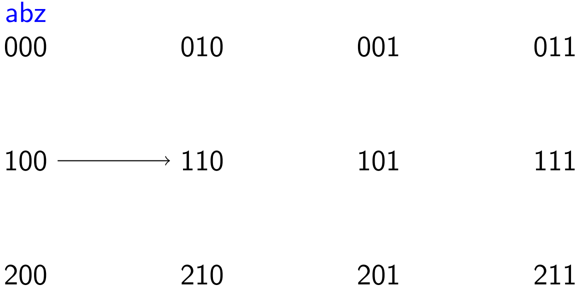
State-graph

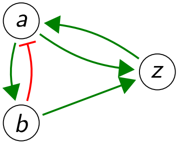
abz

000	010	001	011
100	110	101	111
200	210	201	211

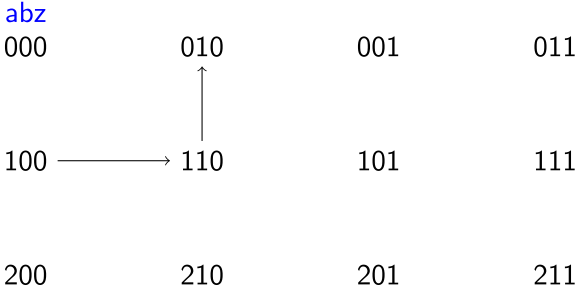


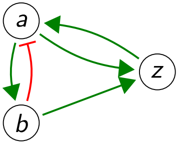
State-graph





State-graph





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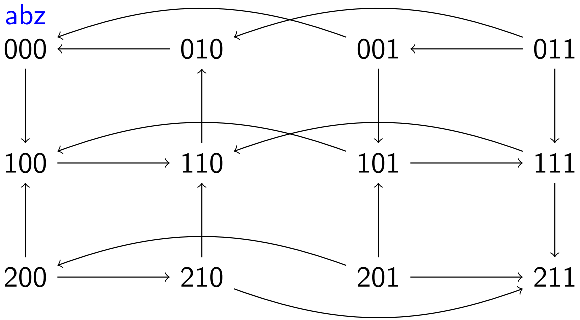
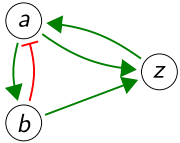
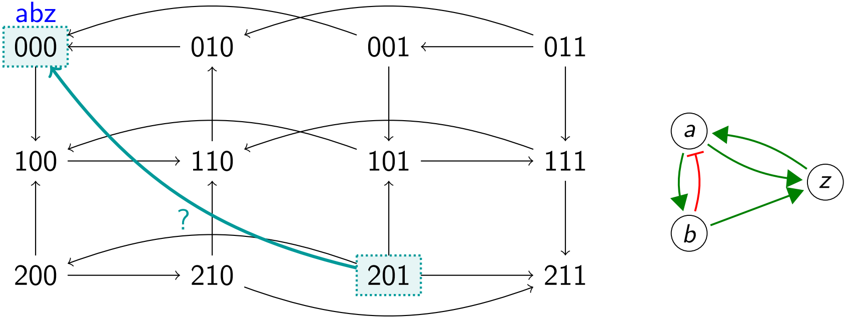


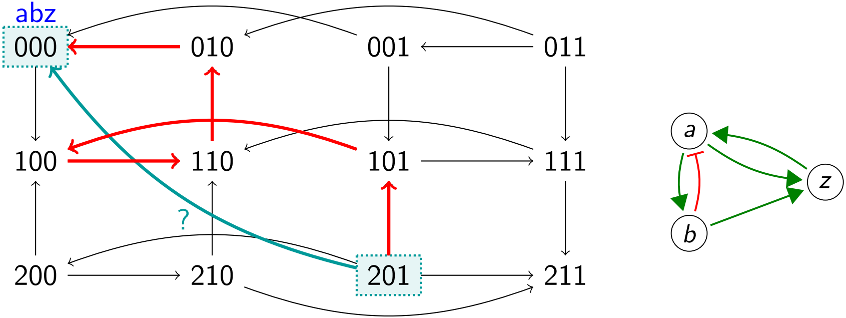


State-graph



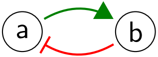
Reachability = from **201**, can I reach **000**?

State-graph

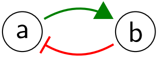
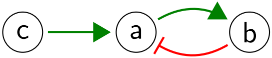


Reachability = from **201**, can I reach **000**?

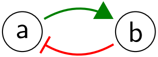
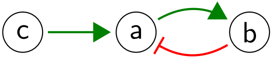
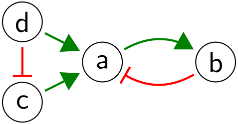
Combinatorial explosion

Model	**Possible states**
	4

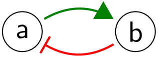
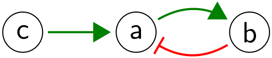
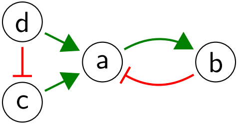
Combinatorial explosion

Model	**Possible states**
	4
	8

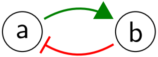
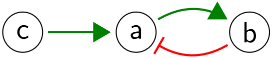
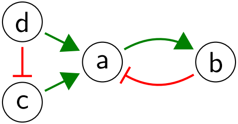
Combinatorial explosion

Model	**Possible states**
	4
	8
	16

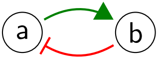
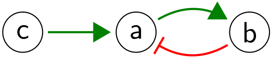
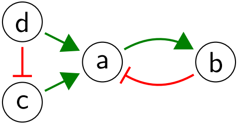
Combinatorial explosion

Model	Possible states
	4
	8
	16
⋮	⋮
(10)	1024

Combinatorial explosion

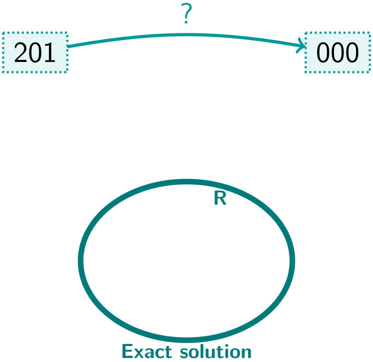
Model	Possible states
	4
	8
	16
⋮	⋮
(10)	1024
(20)	1048576

Combinatorial explosion

Model	**Possible states**
	4
	8
	16
⋮	⋮
(10)	1024
(20)	1048576
(100)	1267650600000000000000000000000

Approximation of the Dynamics

[Paulevé *et al.*, *Mathematical Structures in Computer Science*, 2012]
[Folschette *et al.*, *Theoretical Computer Science*, 2015a]



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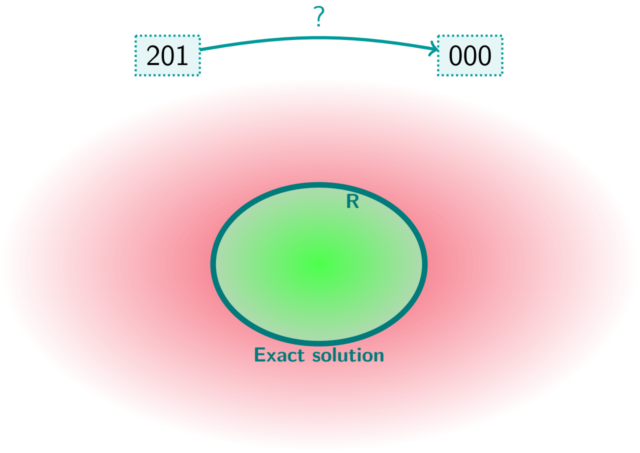

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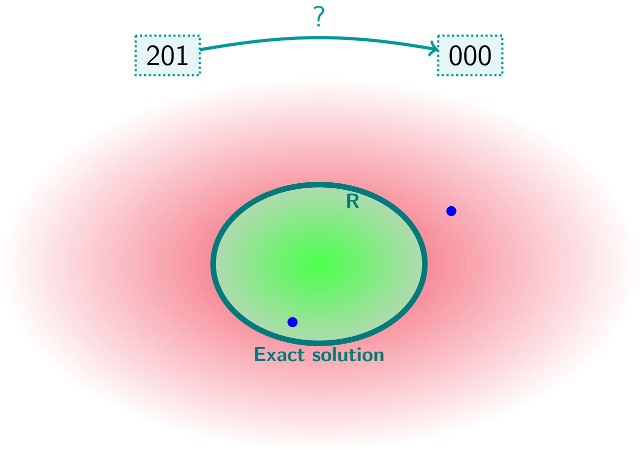

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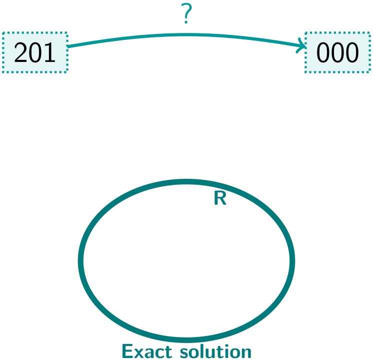

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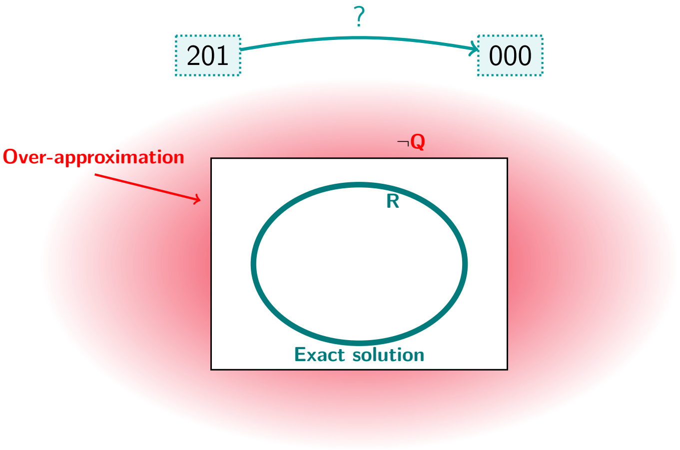

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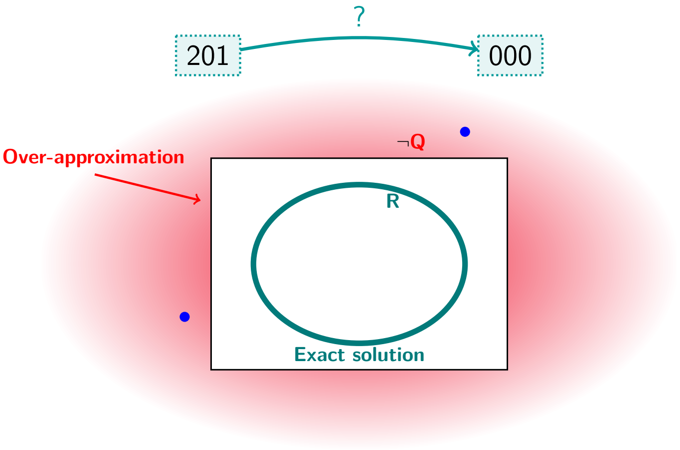

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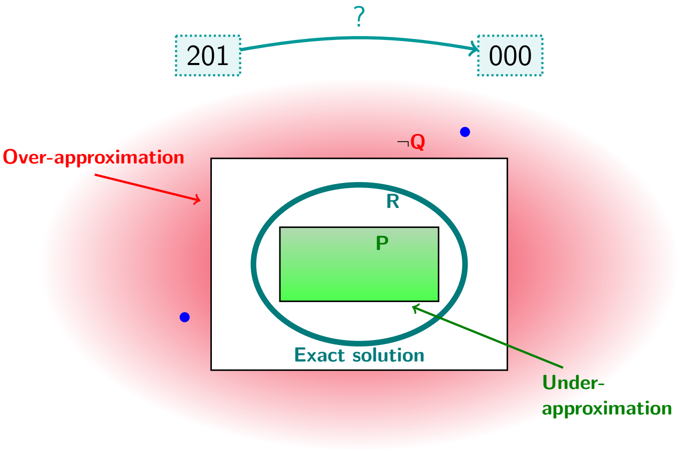

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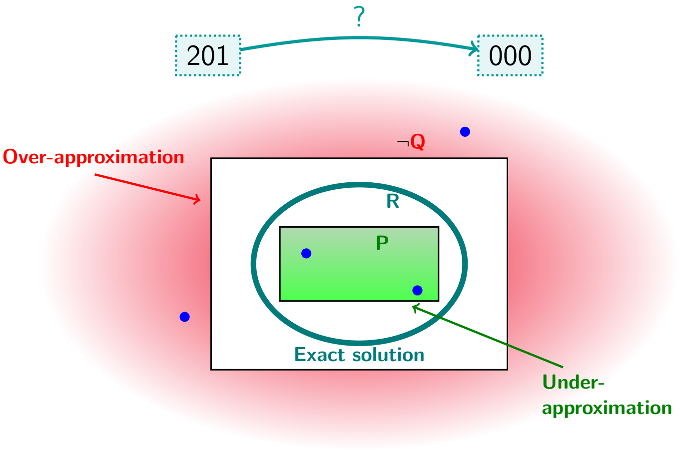

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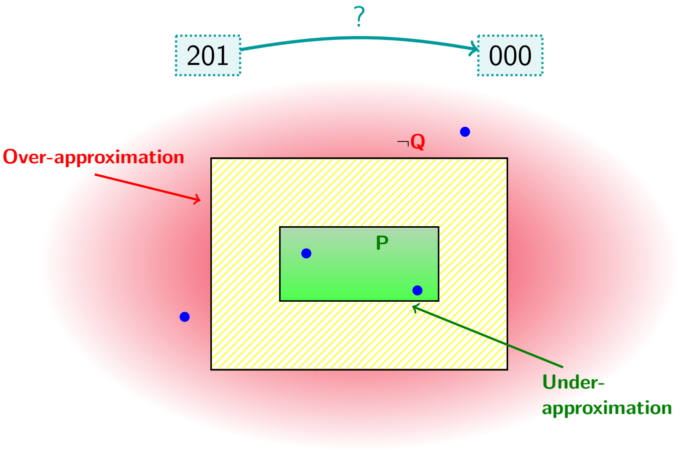

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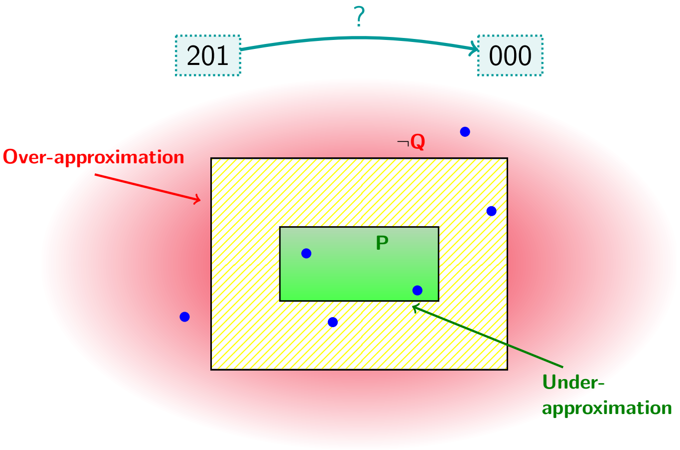
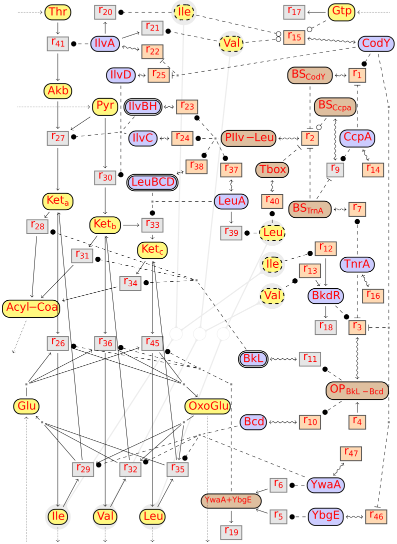


Leucine Reaction Network

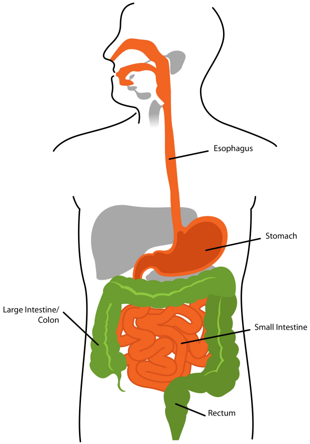
[Allart *et al.*, *Computational Methods in Systems Biology*, 2019]



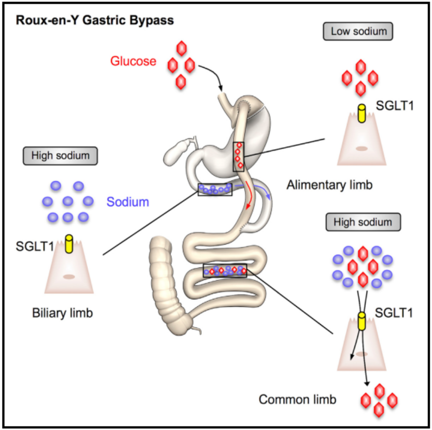
Diabetes Prediction

Gastro-Intestinal Anatomy

[https://foodandhealth.com/digestive-diseases-awareness/]
[Baud *et al.*, *Cell Metabolism*, 2016]



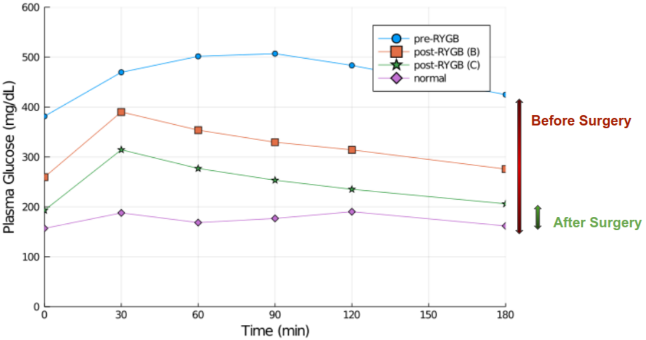
Gastro-intestinal anatomy



Roux-En-Y Gastric Bypass

Effects of Bariatric Surgery

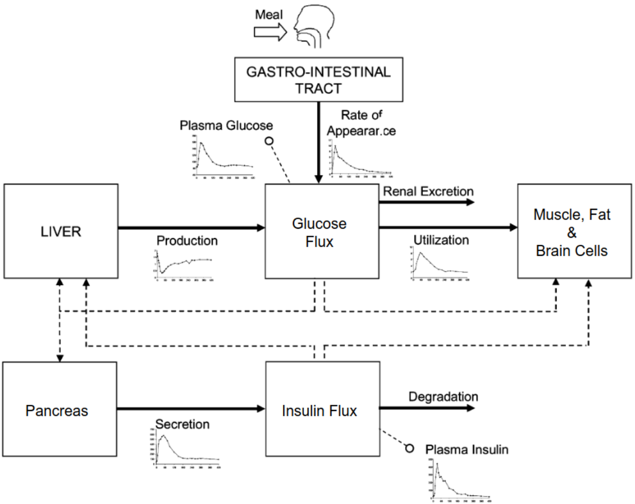
Courtesy of Pattou and coll.



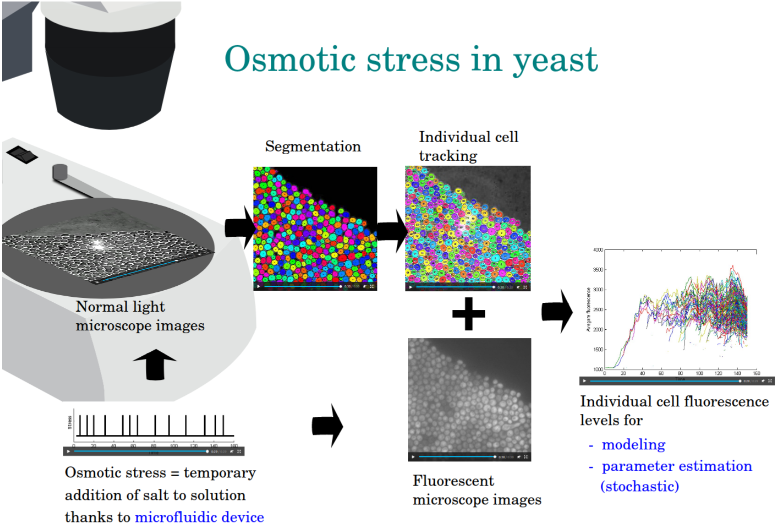
Glucose homeostasis restored by bariatric surgery

Glucose Flux

[Dalla Man *et al.*, *IEEE Transactions on Biomed. Eng.*, 2007]

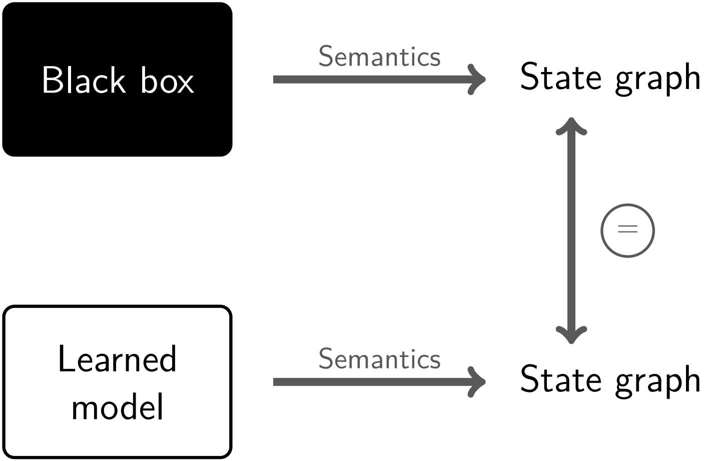


Machine Learning


Osmotic stress in yeast
Segmentation
Individual cell tracking
Normal light microscope images
Osmotic stress = temporary addition of salt to solution thanks to microfluidic device
Fluorescent microscope images
Individual cell fluorescence levels for
- modeling
- parameter estimation (stochastic)

Learning Models from Execution Traces

[Ribeiro *et al.*, *Inductive Logic Programming*, 2018] (ACEDIA)
[Ribeiro *et al.*, *Inductive Logic Programming*, 2017] (GULA)



Learning Models from Execution Traces

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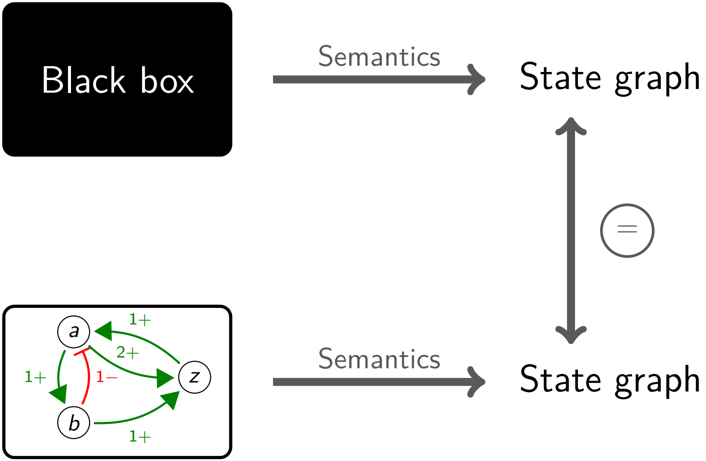

Learning Models from Execution Traces

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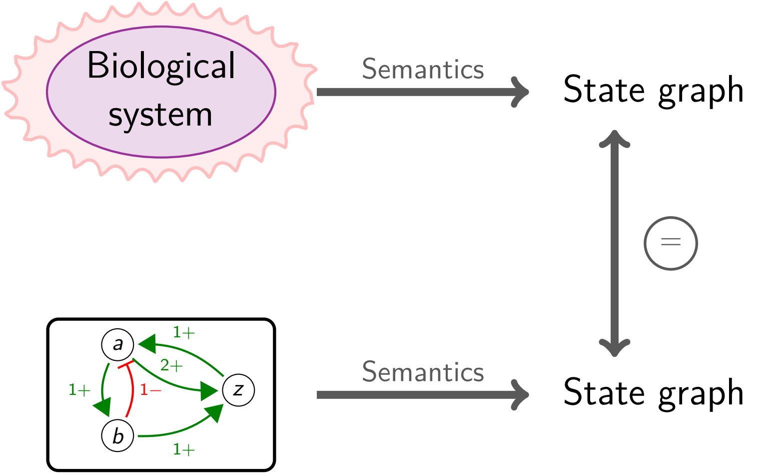

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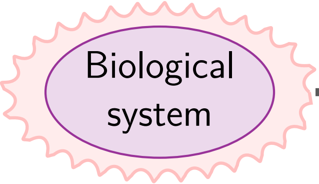
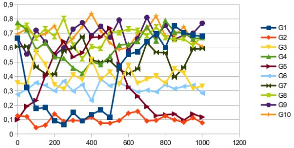
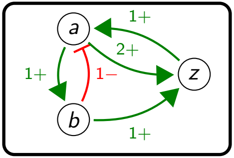


Semantics →



↕ $\simeq$



Semantics →

State graph

BioComputing

http://www.cristal.univ-lille.fr/BioComputing

- Cédric Lhoussaine (head)
- Cristian Versari
- Joachim Niehren
- Mirabelle Nebut
- Maxime Folschette