MaBoSS Ecosystem

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Basel, BC2, 9 Sept. 2019

Outline

1. What is MaBoSS

2. MaBoSS with WebMaBoSS

3. MaBoSS environment with unix

4. MaBoSS with Jupyter notebook

   - UPMaBoSS for population modeling

   - Ensemble models

5. PhysiBoSS for agent-based spatial population modeling

What is MaBoSS? Markovian Boolean Stochastic Simulator

A(nother) tool for pathway modeling

Boolean:

Boolean node state: 0 or 1 for node *i*.

Boolean network state: vector   of Boolean node state for a given network. For each node *i*, $\vec{S}$.

Stochastic:

Probability space over network state space (not on Boolean state): give a probability for each network state.

Stochastic process: time dependant probabilities.

$$P(\vec{S},t) \in [0,1], \sum_{\vec{S} \in \Sigma} P(\vec{S},t) = 1$$

What is MaBoSS? Markovian Boolean Stochastic Simulator

Markov:

Markov process: stochastic process defined by
1) Transition rates: In MaBoSS, define rate value (time^{-1}) and condition for activation and inhibition of nodes
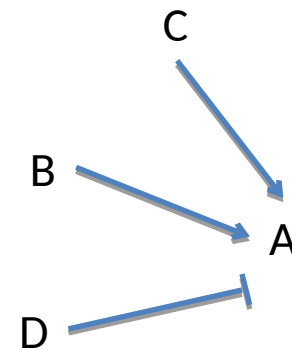
```
Node A {
    rate_up = (C AND B OR NOT D) ? 1.0 : 0.0;
    rate_down = (C AND B OR NOT D) ? 0.0 : 4.5;}
```

2) Initial condition:
p[(A,B,C,D)=(0,0,0,0)]=0.7
p[(A,B,C,D)=(1,0,0,0)]=0.2
p[(A,B,C,D)=(1,1,1,1)]=0.1

# What is MaBoSS? Markovian Boolean Stochastic Simulator

Simulator:

Simulation algorithm (Gillespie algorithm) for estimating probabilities from transition rates and initial condition.

Simulation parameters: time length, number of trajectories.

C++ software:

- Inputs: *bnd* (Boolean Network Descriptor) file and *cfg* (Configuration) file

- Outputs: csv files for probabilities and asymptotic states.
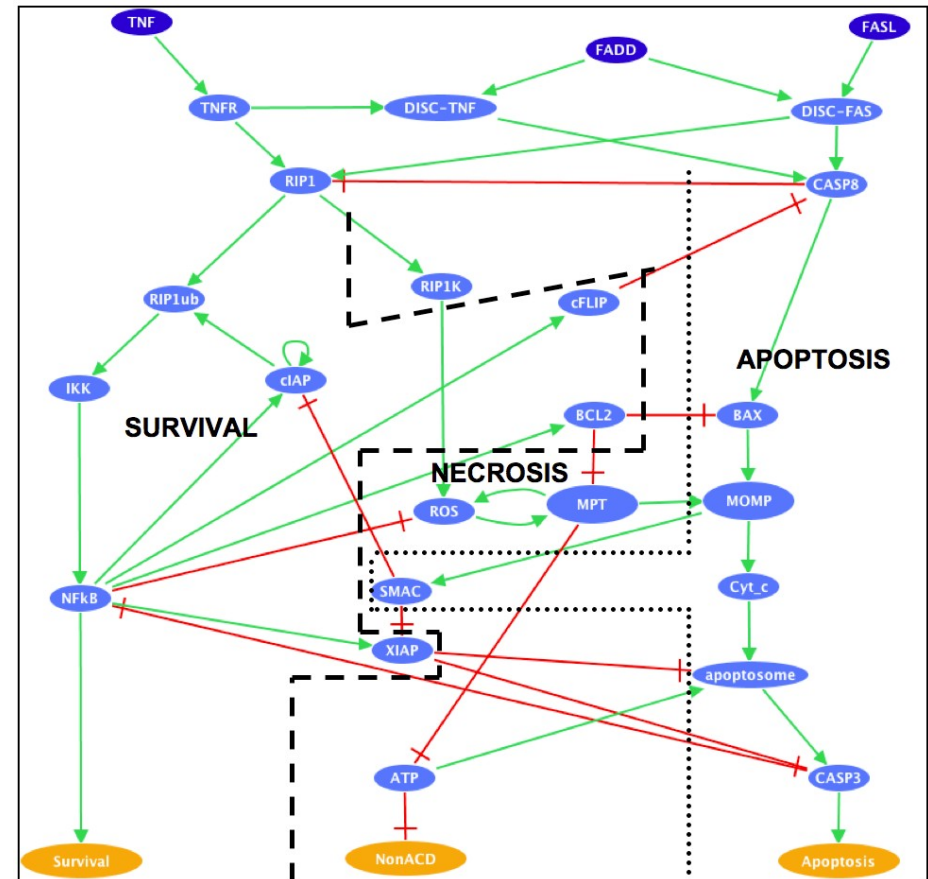
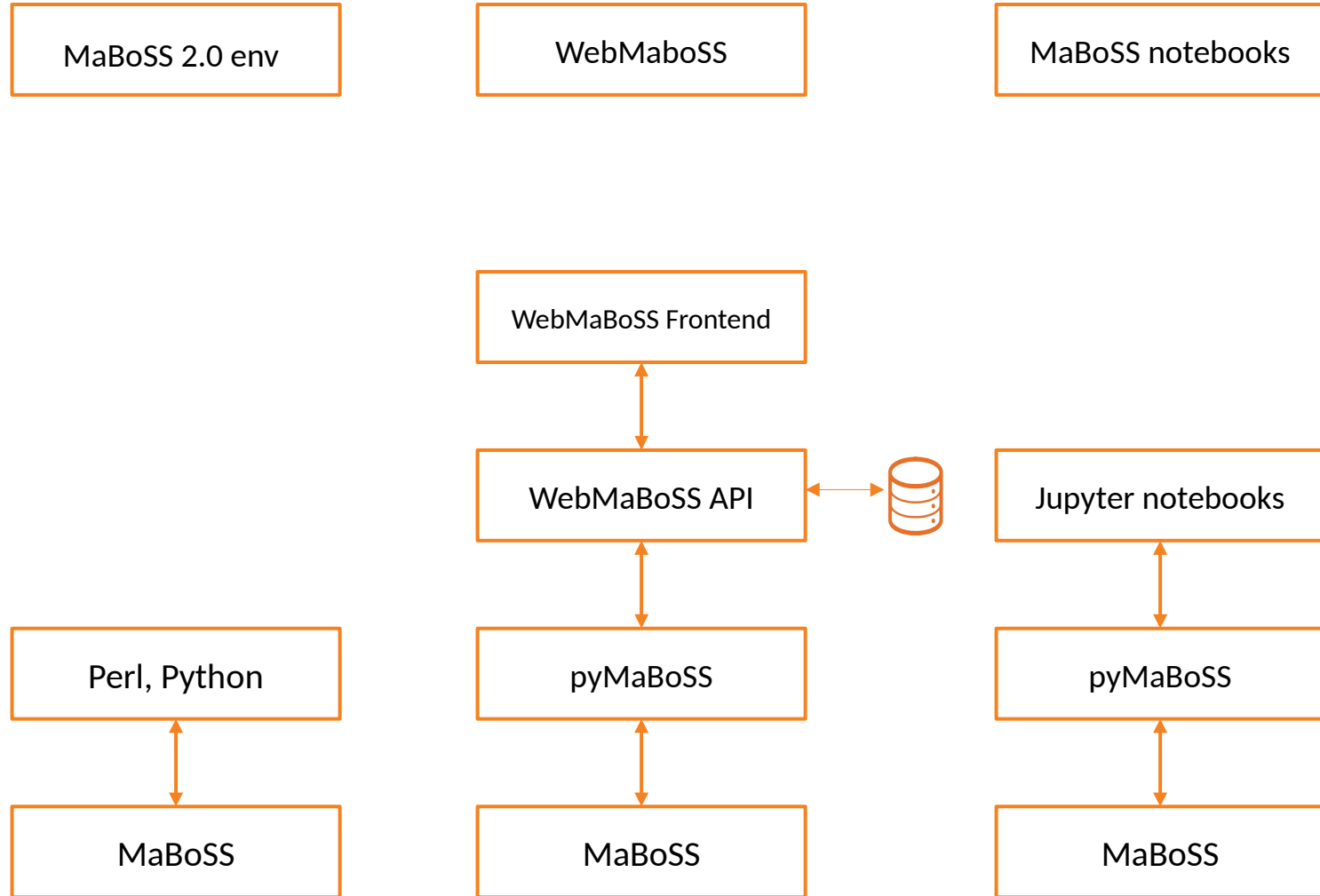# What is MaBoSS? Markovian Boolean Stochastic Simulator
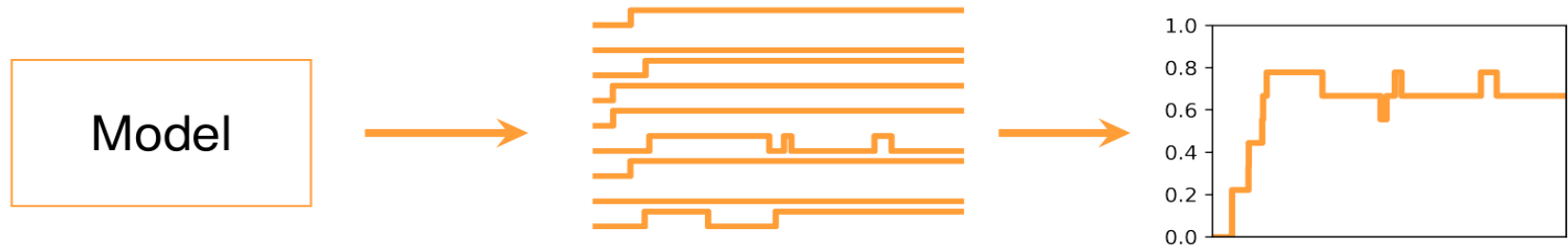
- Uses logical model skeleton to simulate dynamical models

- Produces stochastic trajectories

- Allows population interpretation

- SBML package being developed (annotations !)

Example with TNF -> cell fate

Use published cell fate model (GINsim/MaBoSS), available on MaBoSS web page, https://maboss.curie.fr

Different MaBoSS environments

MaBoSS 2.0 env	WebMaboSS	MaBoSS notebooks

	WebMaBoSS Frontend	
	↕	
	WebMaBoSS API	↔ 🛢	Jupyter notebooks
	↕		↕
Perl, Python	pyMaBoSS	pyMaBoSS
↕	↕	↕
MaBoSS	MaBoSS	MaBoSS

WebMaBoSS

User friendly, no need to fully understand MaBoSS inputs-ouputs,
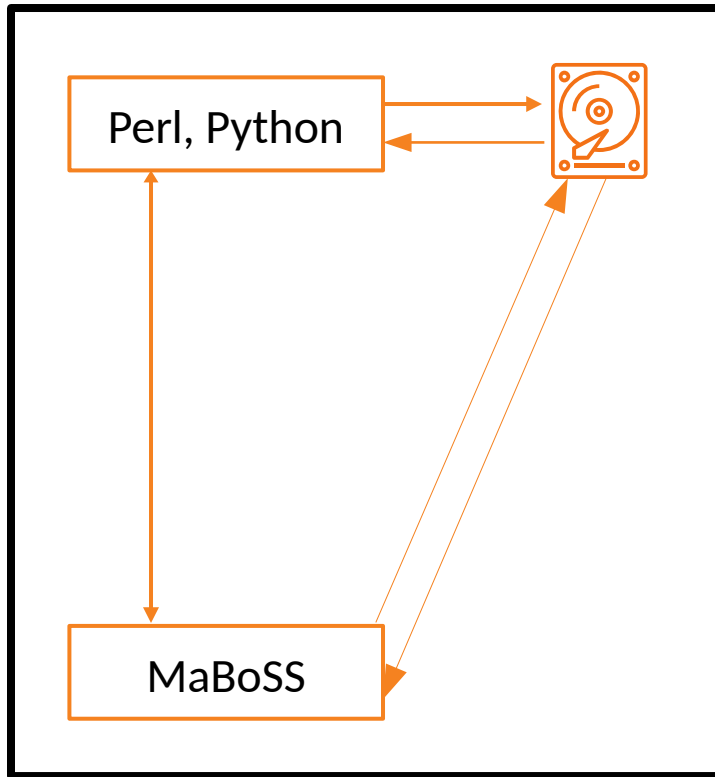interactive figures
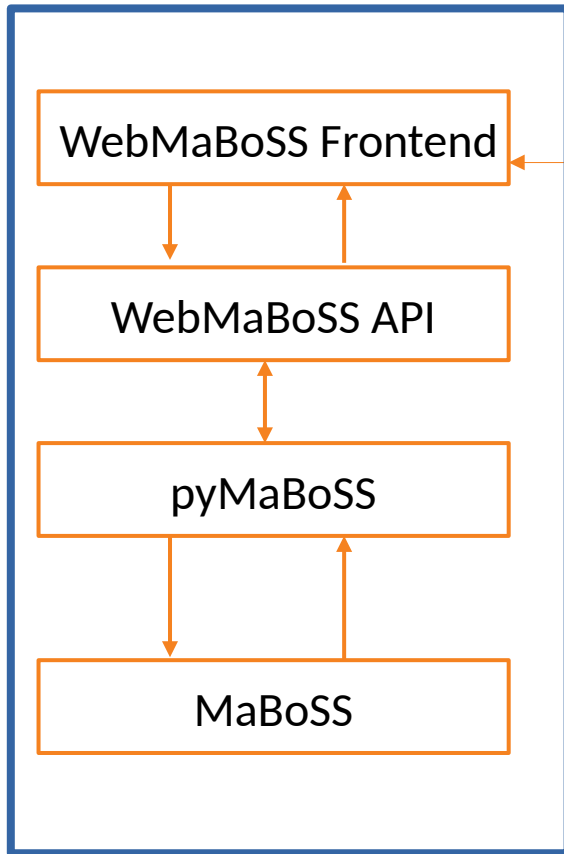
- Web interface (remote computation)

- Database to store models/results

- Multiple pipelines implemented (eg mutations)

Demo version available at :

https://webmaboss.vincent-noel.fr

MaBoSS 2.0 environment

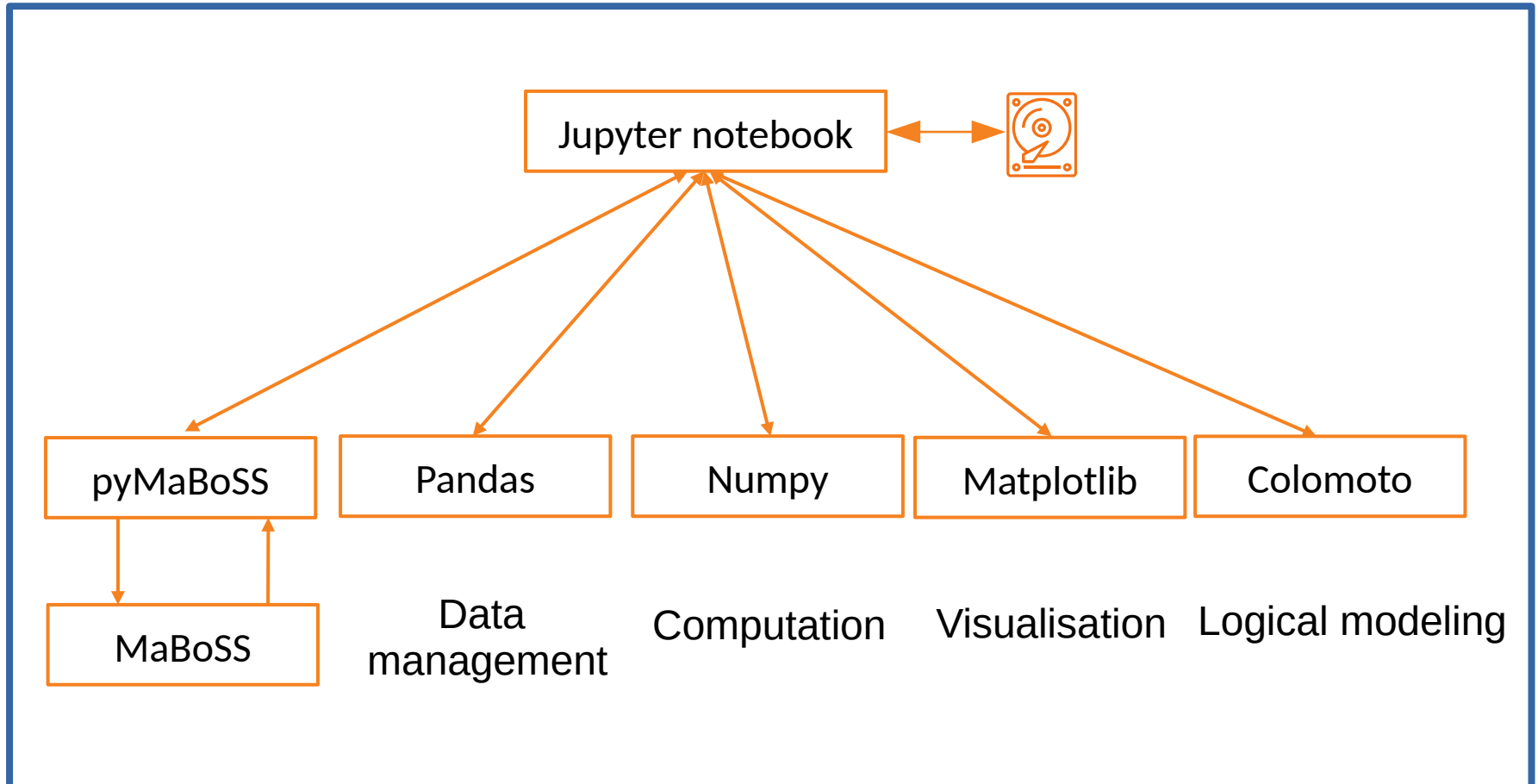Light to install, multiple batch processing, computation on server

- Multiples post-processing scripts (plotting, analysis, ...)

- Multiples batching scripts (sensitivity analysis, mutations, ...)

MaBoSS notebook

Reproducible data analysis, multiple simulation within python coding,
with access to a variety of libraries
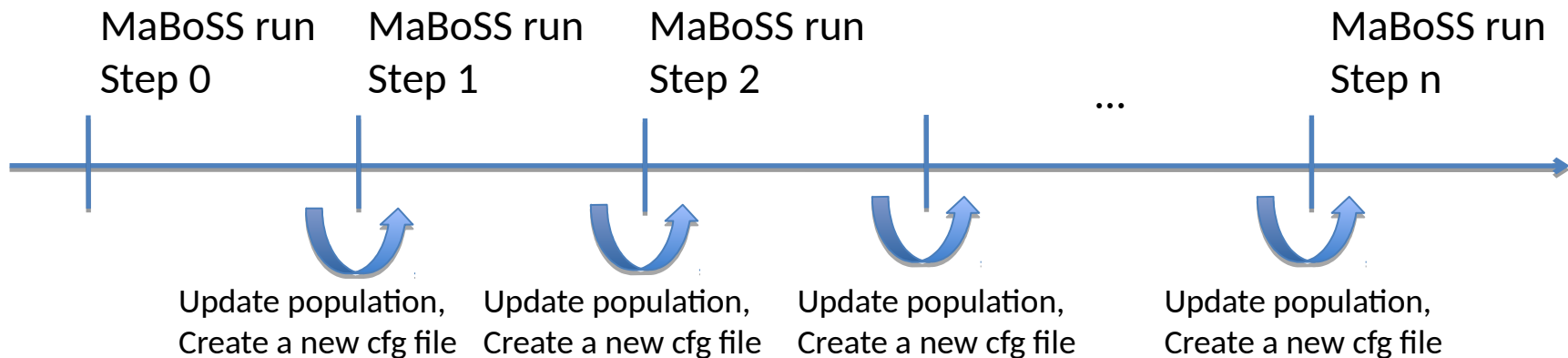
UPMaBoSS

Use a signalling pathway(s) inside each cell -> MaBoSS model.

Specify, in the new *upp* file

1. Node for cell death,

2. Node for cell division,

3. Inter-cell communication (ligand -> receptor for instance), by defining update of external variable(s) according to probabilities and population size

Outputs:

-   size of cell population over time,

-   probabilities of "network states" over time

MaBoSS run
Step 0

MaBoSS run
Step 1

MaBoSS run
Step 2

...

MaBoSS run
Step n

Update population,
Create a new cfg file

Update population,
Create a new cfg file

Update population,
Create a new cfg file

Update population,
Create a new cfg file

Example with TNF -> cell fate

Use published cell fate model (GINsim/MaBoSS), available on MaBoSS web page, https://maboss.curie.fr

Production of TNF induced by NFkB
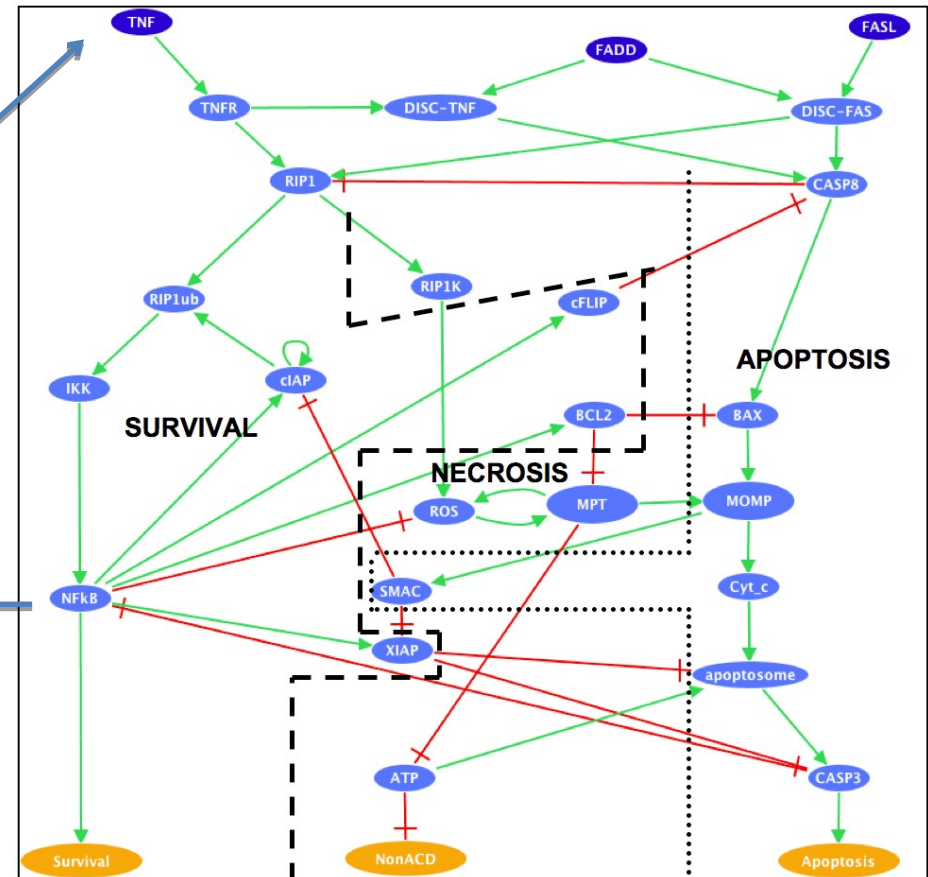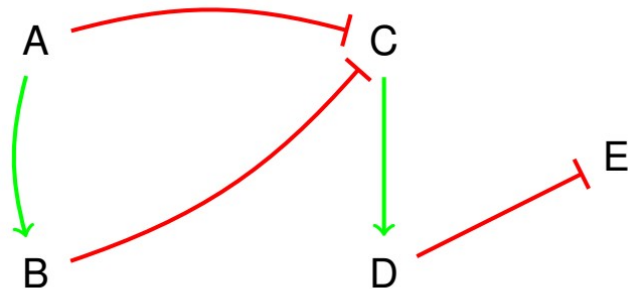

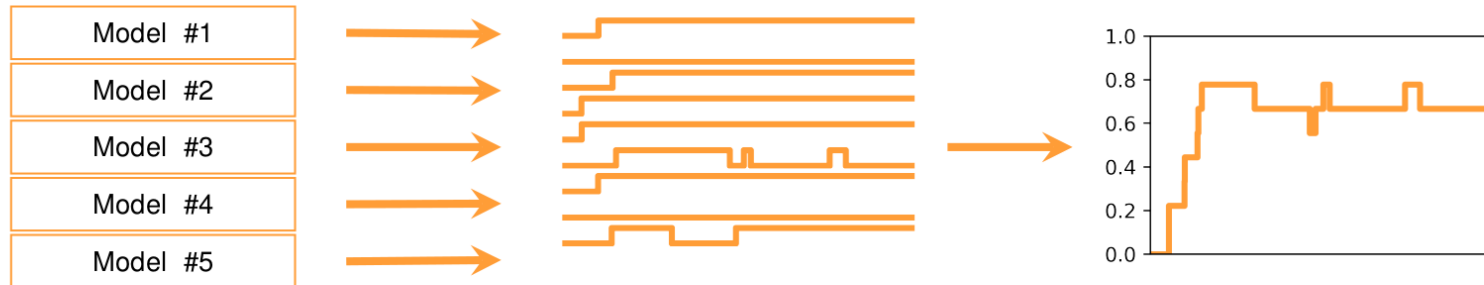Cell Division / Proliferation

Cell Death

Ensemble models

From a set of constraints, produces a set of valid models,
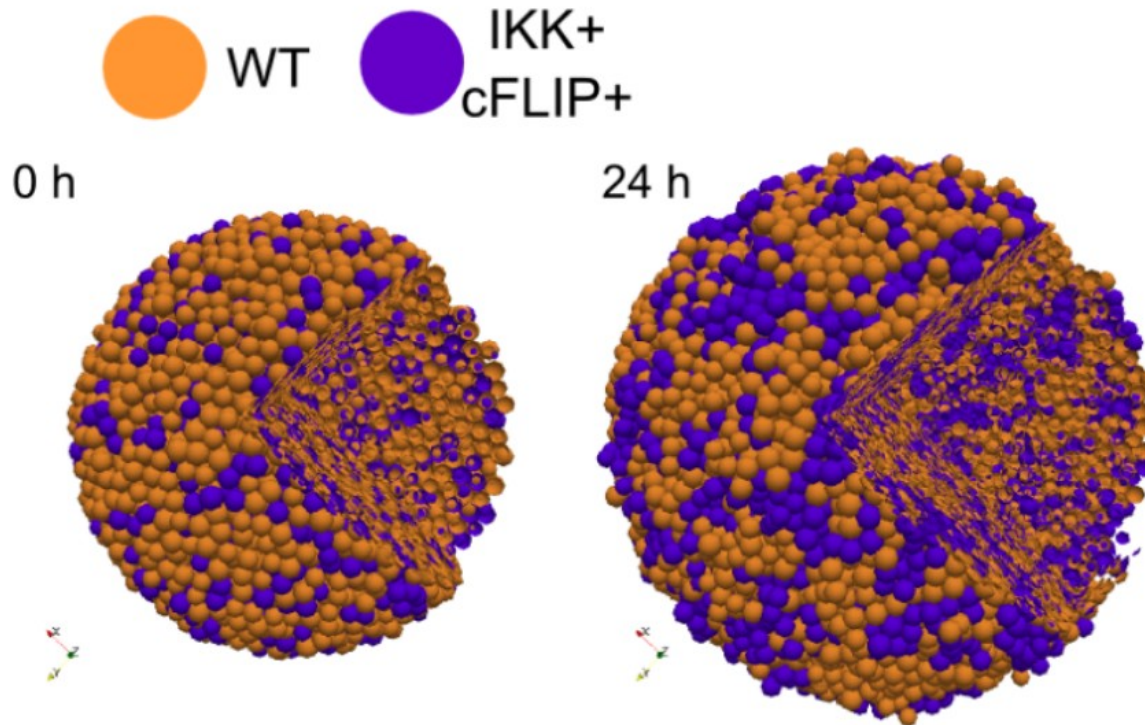and treats them as an ensemble of models.

Constraints :

- Fixpoints
- Reachability
- Biological knowledge

-> Allows diversity of mechanisms within the model, to represent single cell variability, modeling uncertainty.

PhysiBoSS

Flexible and computationally efficient framework
to study heterogeneous cell population growth

=> Agent-based model, with every cell running a MaBoSS model. Allows cell-cell
communication, diffusion.

Acknowledgments

MaBoSS early team

Eric Viara Gautier Stoll Laurence Calzone

MaBoSS ecosystem team

Vincent Noël Aurélien Naldi Denis Thieffry Loïc Paulevé Nicolas Levy

Emmanuel Barillot Gaëlle Letort Stéphanie Chevalier Andrei Zinovyev

https://github.com/vincent-noel/MaBoSS-Ecosystem
https://maboss.curie.fr
https://webmaboss.vincent-noel.fr