PhysiBoSS-Models

A database for multiscale models

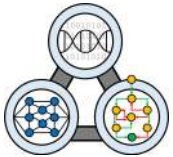
Vincent Noël

Institut Curie, INSERM U1331, Mines ParisTech

PSL University

September 30th

17th Brazilian Symposium on Bioinformatics



institut Curie

Inserm

La science pour la santé
From science to health

MINES ParisTech

PSL RESEARCH UNIVERSITY PARIS

About me



› 2004 - Bachelor degree in Computer Science
› 2008 - Master degree in Computational Biology
› 2012 - PhD in Applied Mathematics



› 2014 - Postdoc at Instituto Butantan in São Paulo

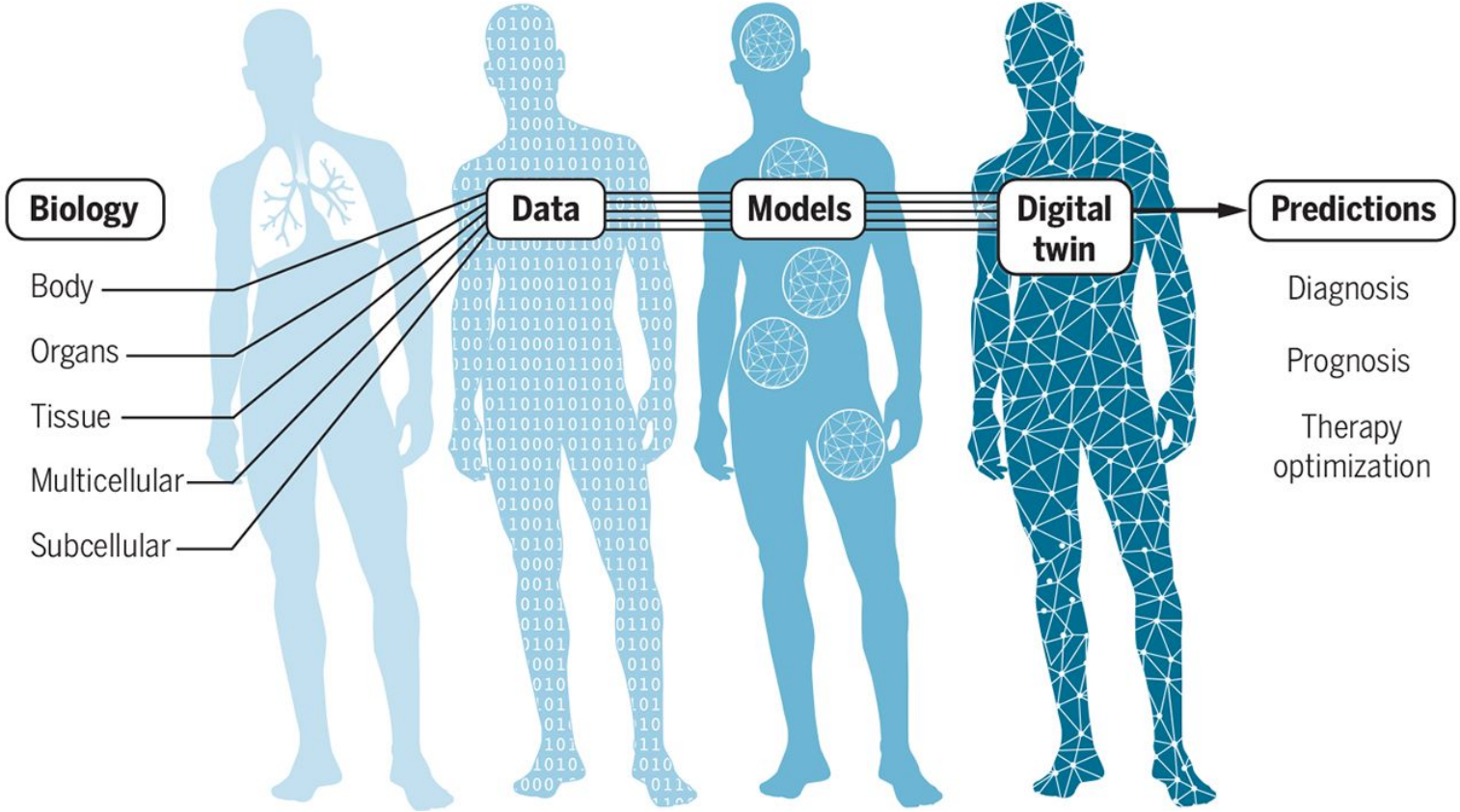


› 2018 - Postdoc at Institut Curie in Paris
› 2021 - Researcher at Institut Curie in Paris



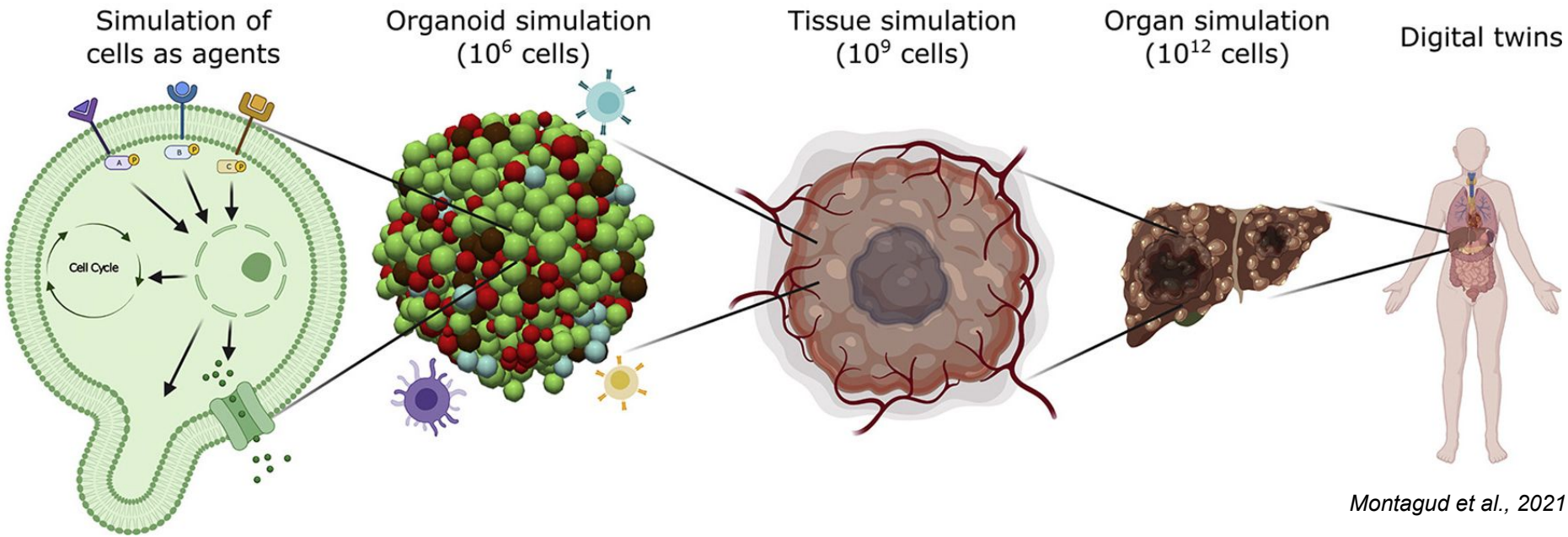
› 2025 - Visiting Researcher at FMUSP in São Paulo

Toward a digital twin



Lauberbacher et al., 2021

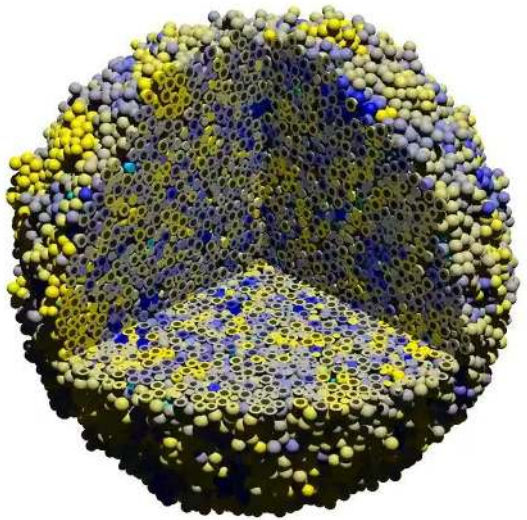
A multiscale problem



Montagud et al., 2021

Modeling organoids/tissues

- **Multi-cellular** systems
- **Spatial** information
- Multiple cell **types**
- Extra-cellular **environment**
- Interactions



Ghaffarizadeh et al., 2018

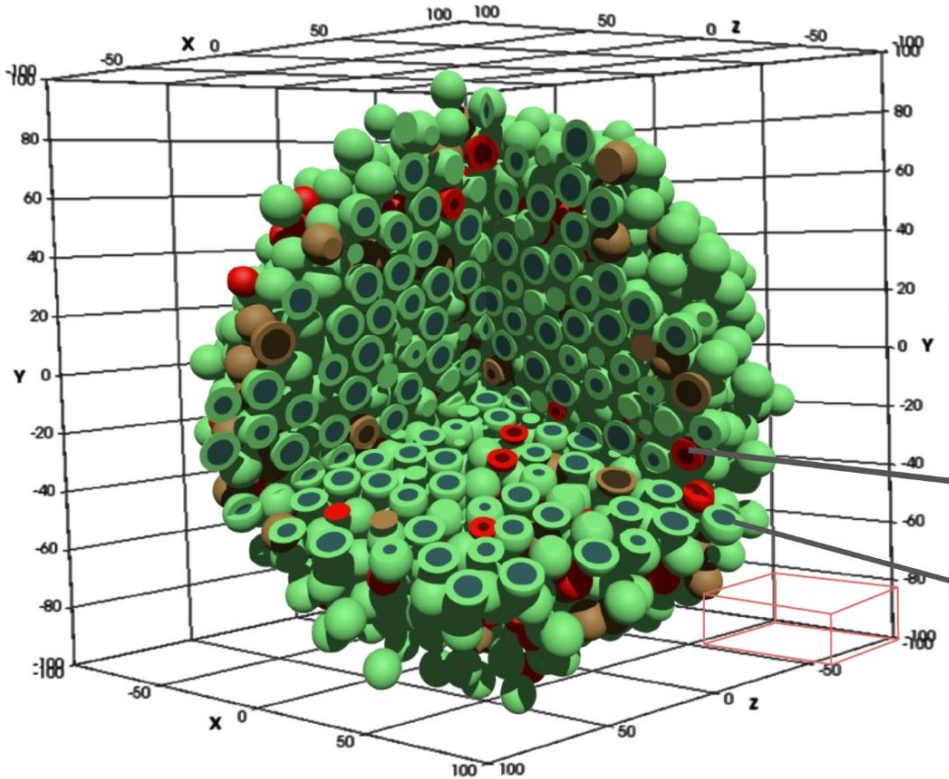
PhysiBoSS = PhysiCell + MaBoSS

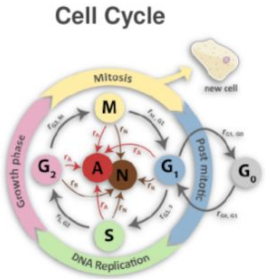


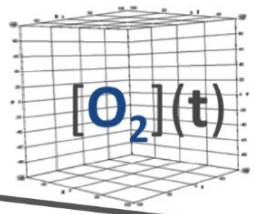
Paul Macklin

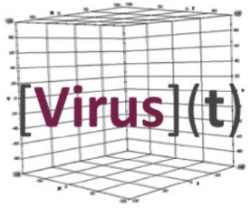


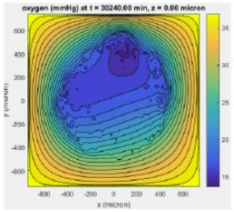
Randy Heiland

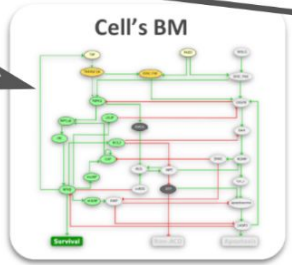


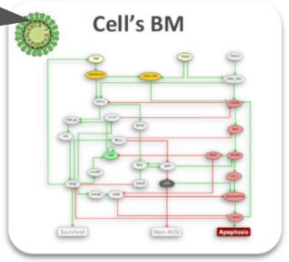












institut Curie

Simplifying usage of PhysiBoSS

› PhysiBoSS started from a **fork** of PhysiCell 1.1.0 (May 2017)

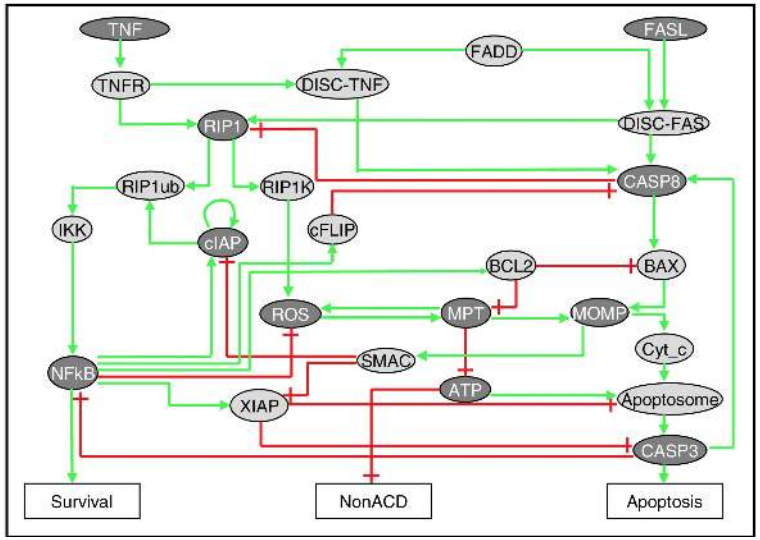
› PhysiBoSS 2.0.0 was merged into PhysiCell 1.9.0 (July 2021) as an **add-on**.

› PhysiCell model building simplified a lot during the years : from pure C++ code, to XML definitions, and now using a **graphical user interface**.

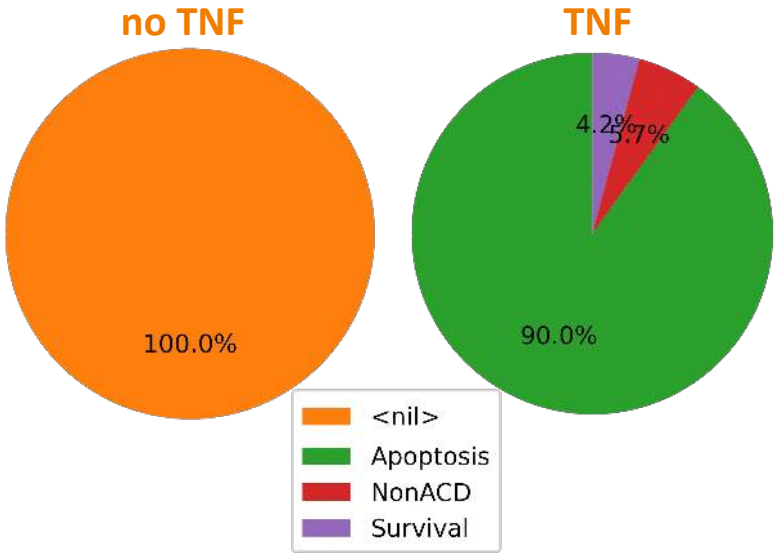
› PhysiBoSS followed along, with now an **automated mapping** between the agent-based model and the intracellular Boolean models.

› We have published a PhysiBoSS **tutorial**, showcasing the recent efforts by presenting 4 use cases.

Simulating the effect of TNF treatment on a tumor



Calzone et al., 2010



› Upon TNF treatment, 95% of the cells die but 5% **survive**.

Simulating the effect of TNF treatment on a tumor

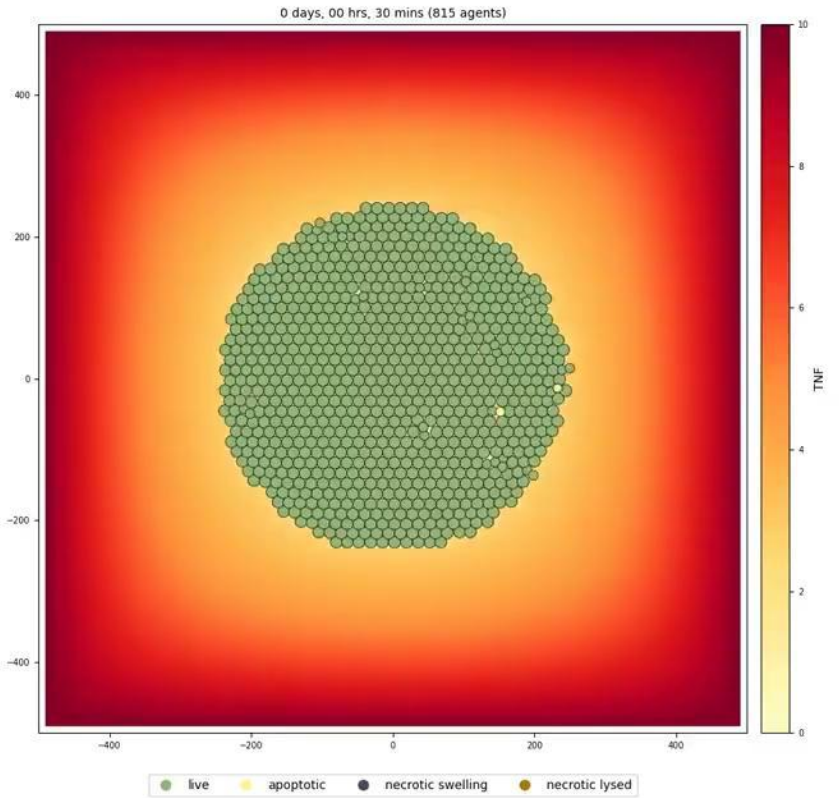
› TNF signal **linked** to TNF node

› Apoptosis node **linked** to Apoptosis rate

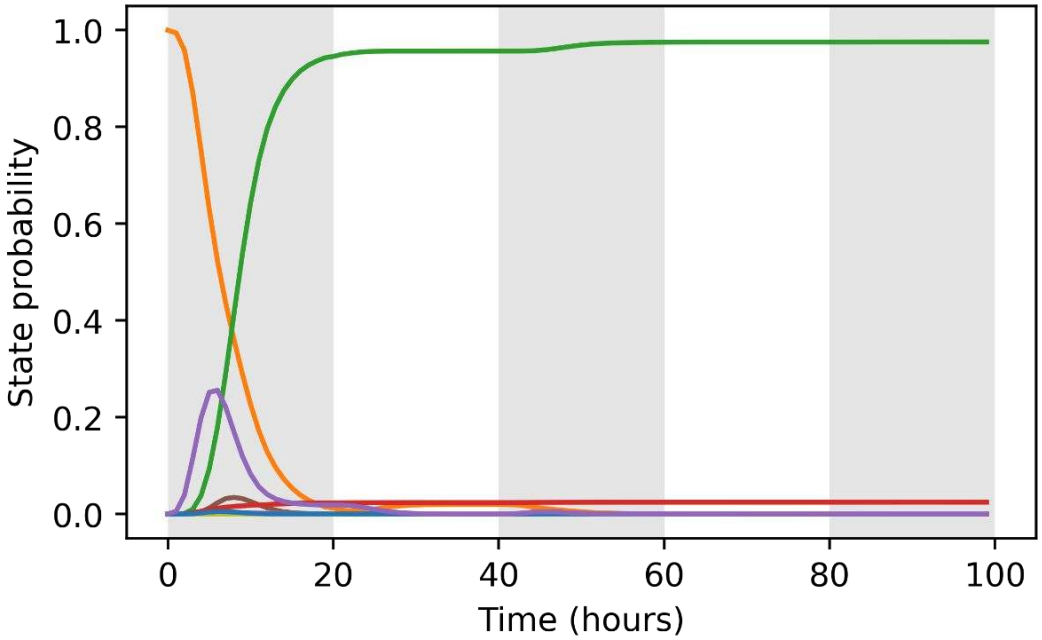
› Necrosis node **linked** to Necrosis rate

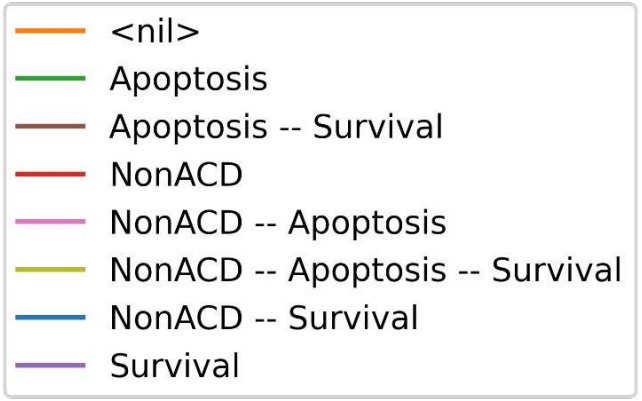
› Simulating the Boolean model **until steady state** (≈ 24h)

› Resistant cells **dominate** quickly



Simulating the effect of TNF treatment on a tumor





› When stopping the treatment, these surviving cells **go back** to their naive state and can be targeted by a **new wave** of treatment.

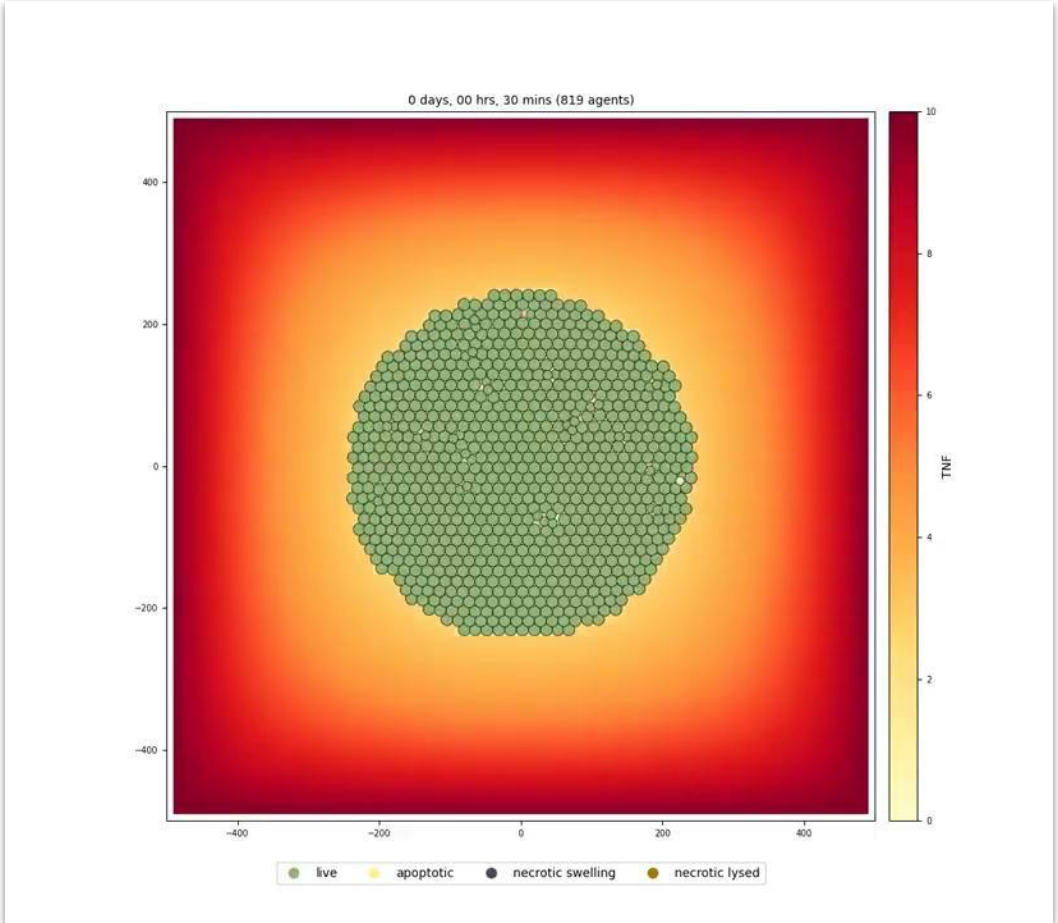
Simulating the effect of TNF treatment on a tumor

› Resistance to TNF treatment can be **"forgotten"**

› Removing and reintroducing TNF **periodically**

› We are able to **control** the size of the resistant population

› With the right **timings**, we can get rid of the tumor



Lessons from writing the tutorial

› Compiling (C++) model from source is the **limiting step** for many.

› We need easily available, compatible, **binary distributions** of PhysiCell.

› PhysiBoSS (because of external libraries), or any model including custom C++ code needs their **own binaries**.

› PhysiBoSS is already providing binary distributions for **linux**, **mac** and **windows**, automatically produced by GitHub actions.

› PhysiBoSS models are spread on multiple GitHub repositories. Some are in the PhysiBoSS official repository, but need actualization for every new version.

PhysiBoSS-Models Database

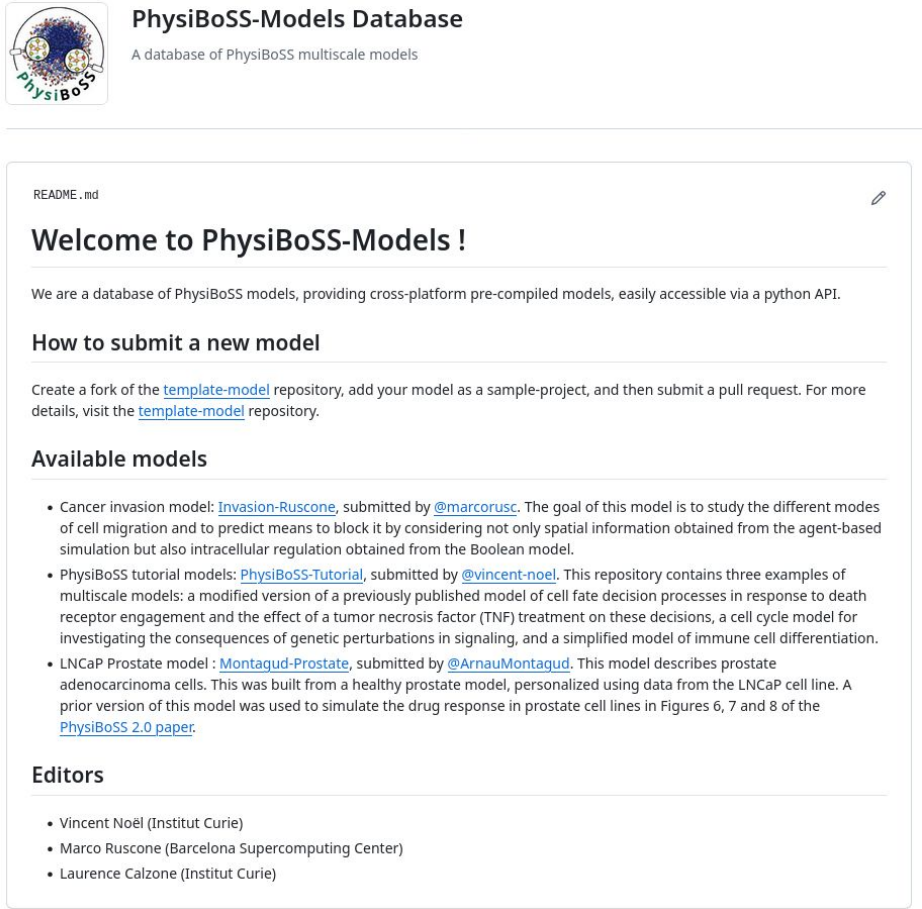
https://github.com/PhysiBoSS-Models

› **Easily** access and simulate published models

› **GitHub**-based

› Following **FAIR, CURE** standards

› Store a collection of **template** models ?



PhysiBoSS-Models Database

A database of PhysiBoSS multiscale models

README.md

Welcome to PhysiBoSS-Models !

We are a database of PhysiBoSS models, providing cross-platform pre-compiled models, easily accessible via a python API.

How to submit a new model

Create a fork of the template-model repository, add your model as a sample-project, and then submit a pull request. For more details, visit the template-model repository.

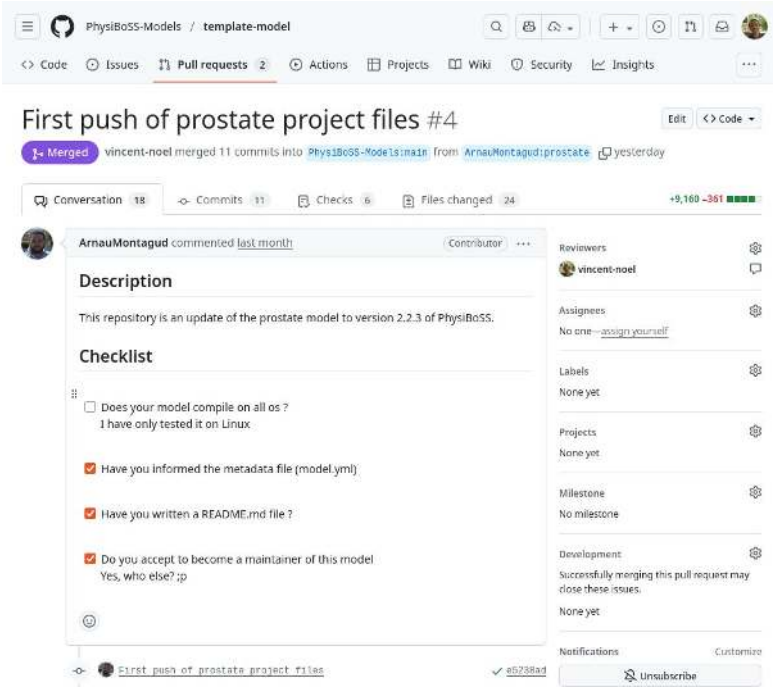
Available models

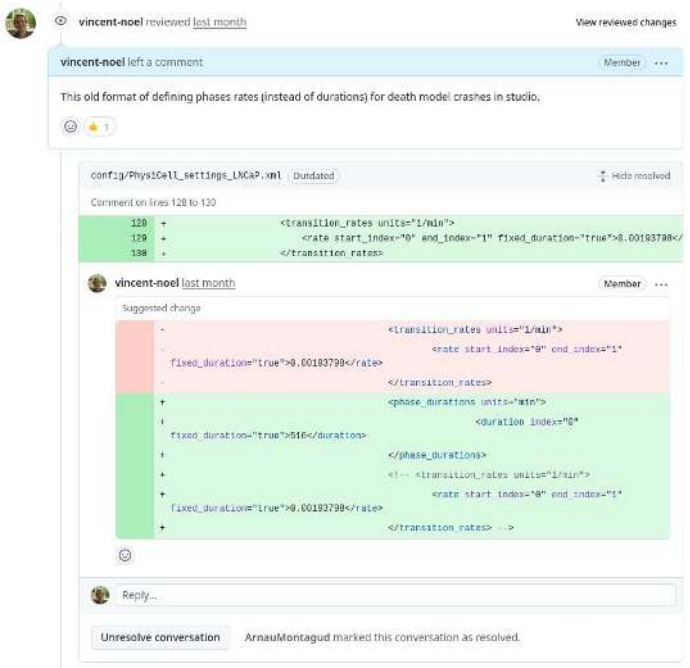
- Cancer invasion model: Invasion-Ruscone, submitted by @marcorusc. The goal of this model is to study the different modes of cell migration and to predict means to block it by considering not only spatial information obtained from the agent-based simulation but also intracellular regulation obtained from the Boolean model.
- PhysiBoSS tutorial models: PhysiBoSS-Tutorial, submitted by @vincent-noel. This repository contains three examples of multiscale models: a modified version of a previously published model of cell fate decision processes in response to death receptor engagement and the effect of a tumor necrosis factor (TNF) treatment on these decisions, a cell cycle model for investigating the consequences of genetic perturbations in signaling, and a simplified model of immune cell differentiation.
- LNCaP Prostate model : Montagud-Prostate, submitted by @ArnauMontagud. This model describes prostate adenocarcinoma cells. This was built from a healthy prostate model, personalized using data from the LNCaP cell line. A prior version of this model was used to simulate the drug response in prostate cell lines in Figures 6, 7 and 8 of the PhysiBoSS 2.0 paper.

Editors

- Vincent Noël (Institut Curie)
- Marco Ruscone (Barcelona Supercomputing Center)
- Laurence Calzone (Institut Curie)

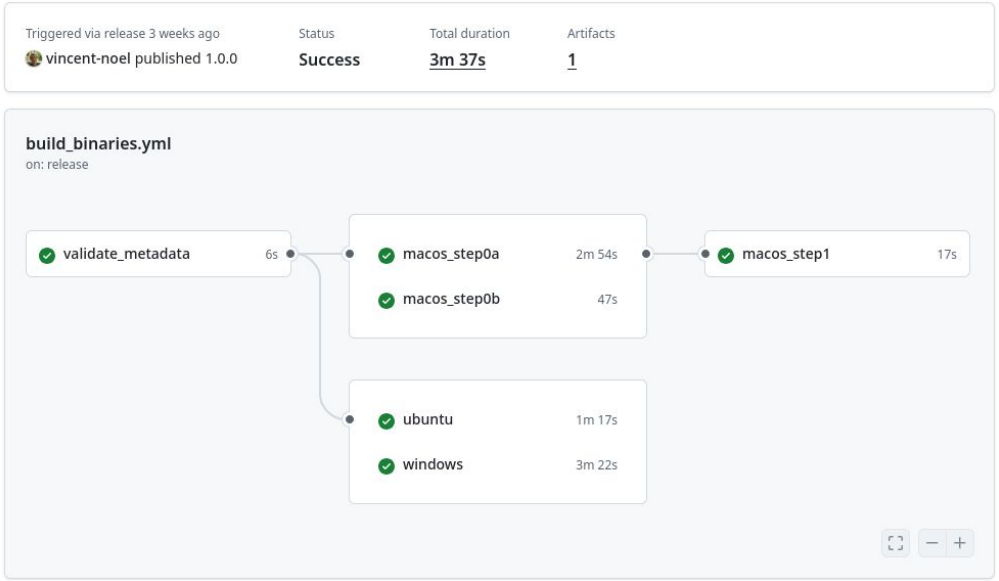
GitHub-powered backend

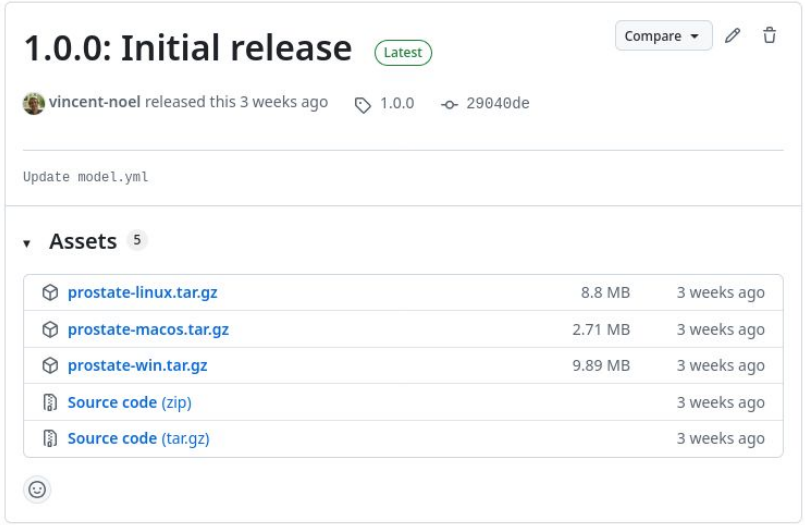




- Model submission as a pull request of the template model
- Using GitHub reviewing features

GitHub-powered backend





› Binaries compiled on GitHub actions, for **linux**, **mac** and **windows**.

› **Zenodo** record generated for each release.

physiboss-models python API

pip install physiboss-models

› Extremely simple

› Initially focused on allowing access to **PhysiCell Studio**

```
[1]: from physiboss_models import Database

[2]: db = Database()

[3]: db.all()

[3]: ['Invasion-Ruscone', 'PhysiBoSS-Tutorial']

[4]: db.download_model('Invasion-Ruscone', path='test')

[5]: db.current_model_info()

[5]: {'short_name': 'invasion-ruscone',
      'version': '2.0.0',
      'binary': 'invasion_model',
      'config': ['config/PhysiCell_settings.xml',
       'config/PhysiCell_settings_2D_cluster_migration.xml',
       'config/PhysiCell_settings_2D_single_cell_migration.xml',
       'config/PhysiCell_settings_2D_trail_migration.xml',
       'config/PhysiCell_settings_2D_p63_ki.xml']}

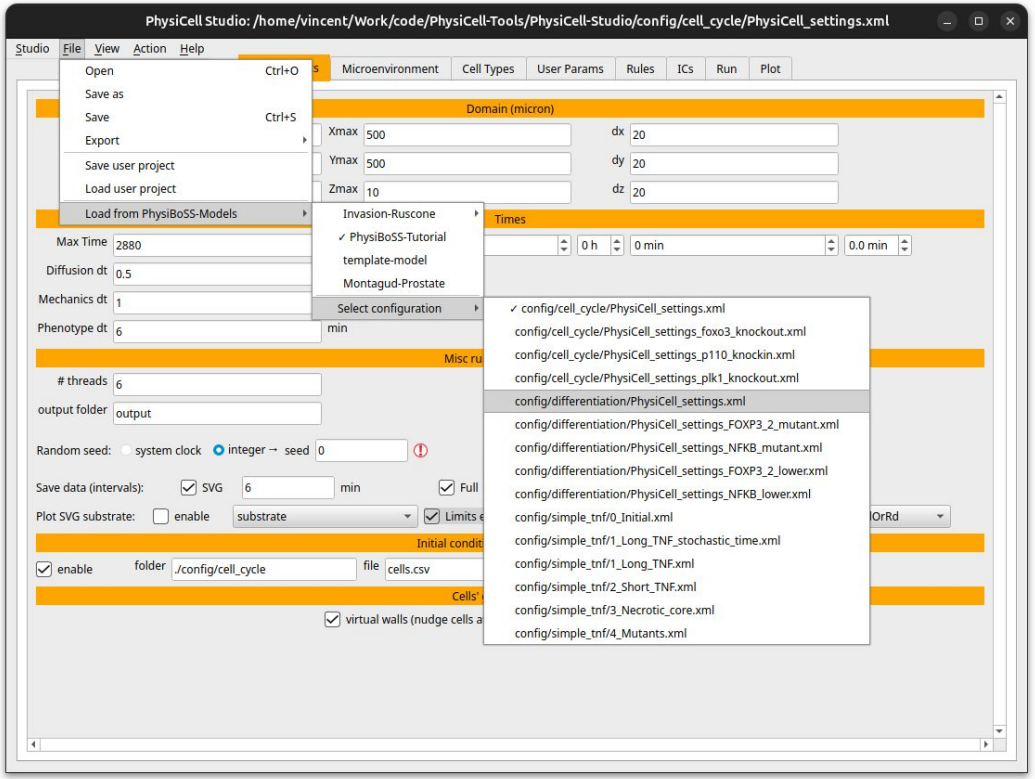
[ ]:
```

PhysiCell-Studio integration

› Models **accessible** with a few clicks.

› Choose among the different **configurations** of the model

› PhysiBoSS **template model** accessible to start a blank project



Perspectives

› PhysiBoSS-Models provides an **easy** way to access published models.

› PhysiCell-Studio **integration** makes reproducing or extending models seamless.

› With future PhysiCell-Studio integration into **Galaxy** platforms, the only thing needed will be a **browser**.

› We need a website, giving access to **videos** and **datasets**.

› We received great interest from the whole **PhysiCell community** and are looking at grant opportunities to ensure **sustainability**.

Acknowledgments

Computational Systems Biology of Cancer

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INDIANA UNIVERSITY

BSC Barcelona Supercomputing Center



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Emmanuel Barillot



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