

HPC/Exascale Centre of Excellence in Personalised Medicine

HPC boosts mathematical models' promises of personalized medicine

Vincent Noël[1]

[1]Computational Systems Biology of Cancer,
Institut Curie, INSERM U900, Mines ParisTech, PSL Research University, Paris

Fifth ISC Workshop on HPC Applications in Precision Medicine



The PerMedCoE project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement N°951773

- PerMedCoE
- Drug synergies for cancer treatment
- COVID-19 Disease progression
- Future work

PerMedCoE

› HPC/Exascale Centre of Excellence for Personalised Medicine in Europe

MOTIVATION

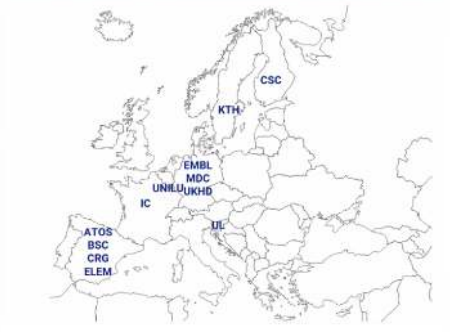
Simulation of cellular mechanistic models is essential for the translation of omic data to medical relevant actions, and should be accessible to the end-users.

VISION

› Develop a roadmap to scale-up essential software for cell-level simulation

› Provide an efficient and sustainable entry point to the HPC/exascale-upgraded methodology

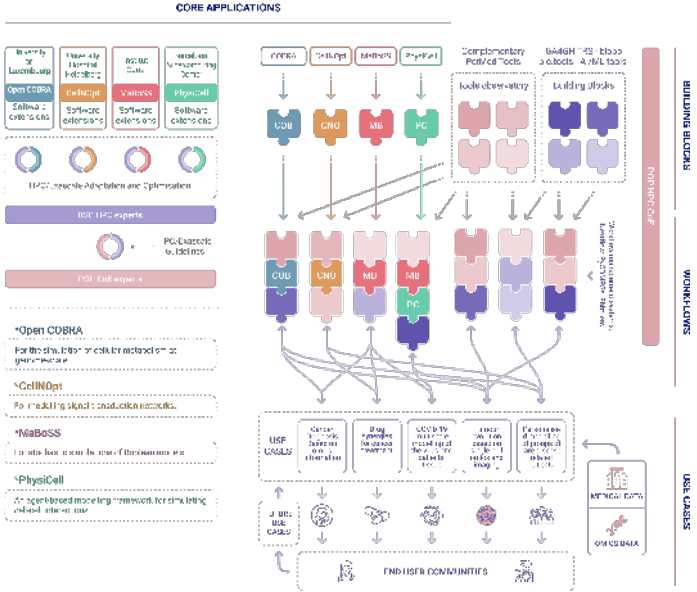
Consortium of 12 partners from 7 EU Member States



PerMedCoE

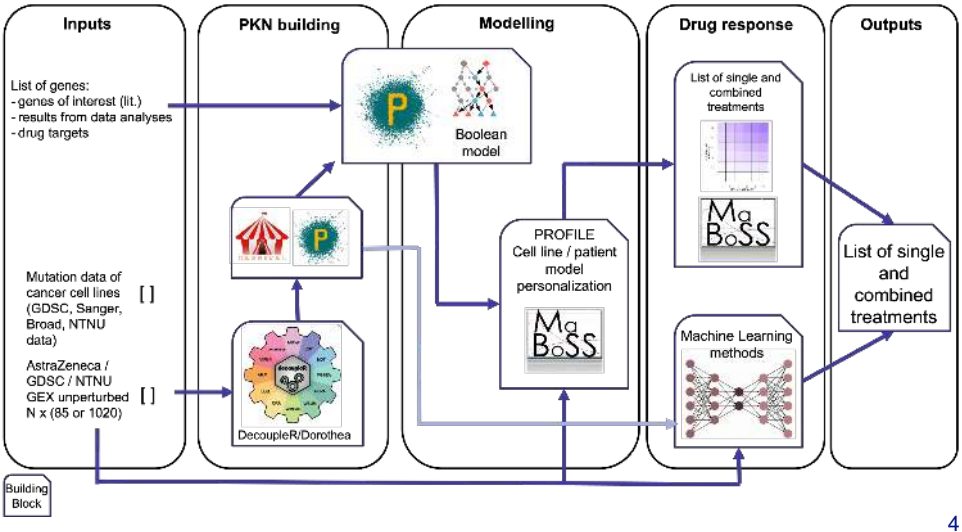
› Objectives

- › Optimize cell-level simulation software
- › Build pipelines to answer use cases
- › Train biomedical professionals
- › Integrate PerMed communities into the European HPC ecosystem



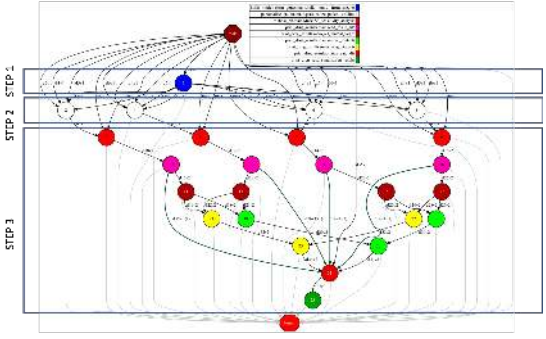
Drug synergies for cancer treatment

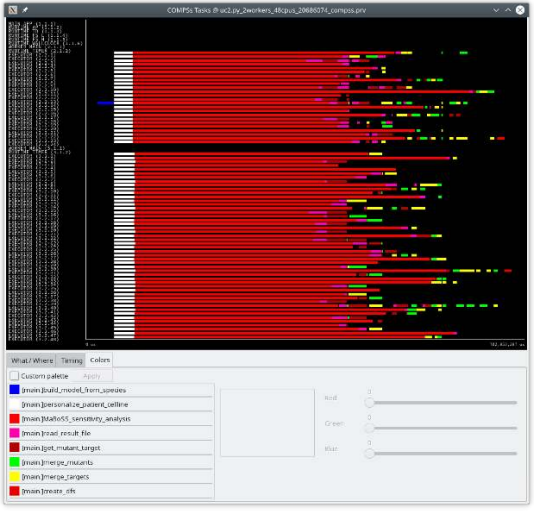
› Pipeline



Drug synergies for cancer treatment

› Execution on MareNostrum4





› Running on multiple cell lines in parallel

› Combinations of simulations on drug candidates could be parallelized further

Drug synergies for cancer treatment

Objectives

Short term

- Refine parts of the workflow
- Test the workflow on existing clinical trials and compare the results of the model with medical doctors' decisions

Long term

- Provide a generic model including the main alterations in cancer (TP53, KRAS, BRAF, PIK3CA, . . .)
- Run the pipeline with omics data of each patient
- Extract combinations of treatment per (group of) patient(s)
- Submit them to medical board

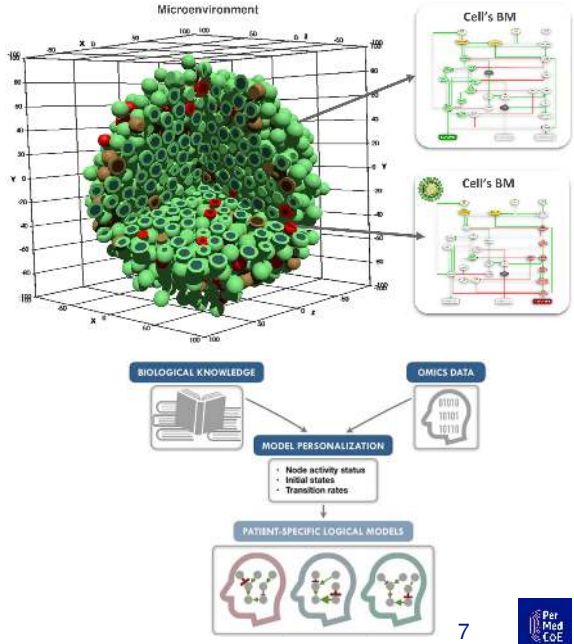
COVID-19 Disease progression

What do we want:

- Model the cell types and the intracellular pathways which have been identified as playing a role in COVID-19
- Identify biomarkers and therapeutic targets
- Explain severity in patients

How are we doing it:

- Using PhysiBoSS (PhysiCell + MaBoSS) applied to SARS-CoV-2 infection
- Personalize using single-cell RNAseq data from patients using PROFILE

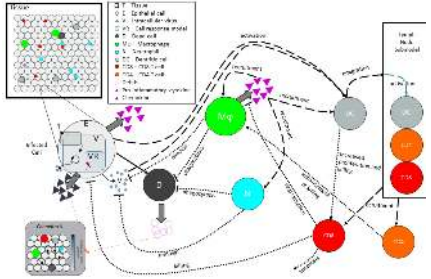


M. Ponce-de-Leon, et al. (2022) PhysiBoSS 2.0: a sustainable integration of stochastic Boolean and agent-based modelling frameworks. bioRxiv
J. Béal et al. (2019) Personalization of logical models with multi-omics data allows clinical stratification of patients. Frontiers in physiology

COVID-19 Disease progression

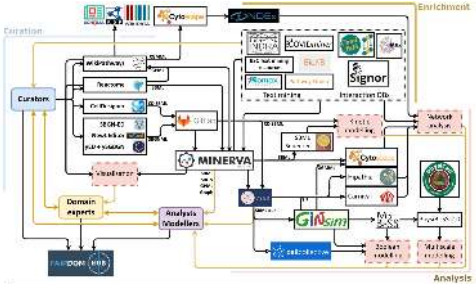
SARS-CoV-2 tissue simulator

- PhysiCell model representing SARS-CoV-2 infection
- Represents Virus, Epithelial cells, CD4, CD8, Macrophages, Dendritic cells, Neutrophils
- Good phenomenological model
- Lacks mechanistic details



COVID19 Disease Map

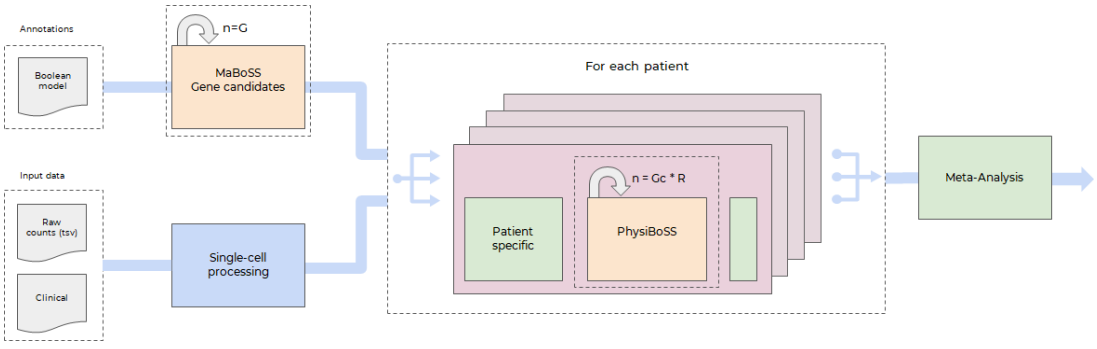
- Massive community collaboration
- Production of mechanistic maps
- Manual curation
- Generation of SBML logical models



M. Getz et al. (2021) Iterative community-driven development of SARS-CoV-2 tissue simulator, bioRxiv
M. Ostaszewski et al. (2021) COVID19 Disease Map, a computational knowledge repository of virus–host interaction mechanisms. Molecular Systems Biology, 17, e10387.

COVID-19 Disease progression

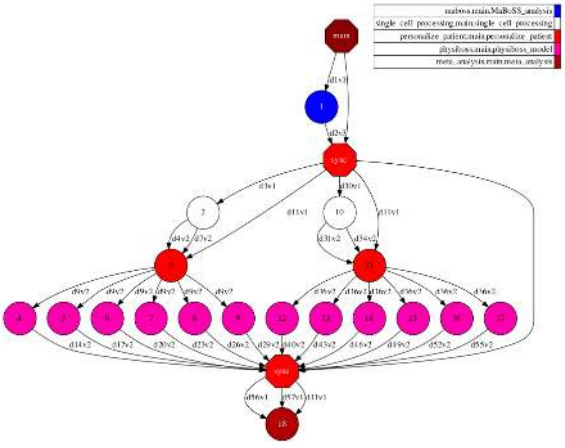
› Pipeline

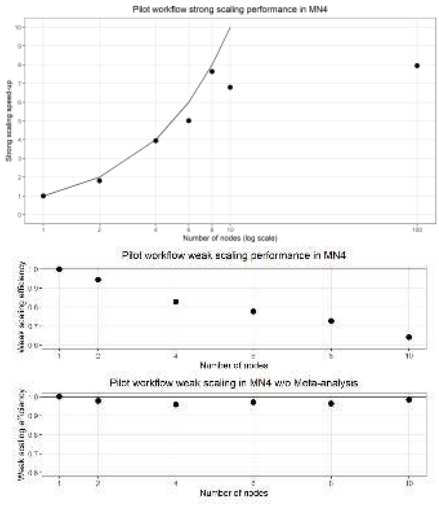


- Find candidates among genes in the boolean models
- Personalize Boolean models with patient data
- Test candidates on personalized PhysiBoSS model

COVID-19 Disease progression

› Execution on MareNostrum4





› Running multiple patients, drug candidates and replicates in parallel

› Unnecessary synchronization in the meta analysis building block

COVID-19 Disease progression

- Objectives

Short term

- Use final version of SARS-CoV-2 tissue simulator
- Include more Boolean models
- Increase PhysiBoSS simulation time
- Improve meta-analysis building block

Long term

- Reproduce mild/severe covid outcome
- Provide the community with tools to predict disease progression

Future work

Community-driven benchmarks

Developing more use-cases

- Cancer diagnosis based on omics information
- Tumor evolution based on single-cell omics and imaging

Training

- Webinars
- Virtual course : Signaling pathways and their integration into multiscale models
- Workshop at ECCB2022 in Barcelona : Simulating cellular behaviours: advancing HPC-enabled Computational Biology

Aknowledgments

Institut Curie

- Laurence Calzone
- Vincent Noël
- Marco Ruscone
- Emmanuel Barillot

Heidelberg University

- Pablo Rodríguez-Mier
- Attila Gabor
- Julio Saez Rodriguez

Barcelona Supercomputing Center

- Arnau Montagud
- Javier Conejero
- José Carbonell
- Miguel Vázquez
- Miguel Ponce de Leon
- Alfonso Valencia

CSC – IT Center for Science

- Sampo Sillanpää
- Henrik Nortamo
- Jesse Harrison

Thanks !

Follow us on social media:

www.linkedin.com/company/permedcoe
@permedcoe



The PerMedCoE project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement Nº951773

Per Med CoE

HPC/Exascale Centre of Excellence in Personalised Medicine

www.permedcoe.eu

institut Curie

Inserm
La science pour la santé
From science to health

MINES ParisTech

PSL
RESEARCH UNIVERSITY PARIS