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HPC-enabled multiscale simulation to uncover mechanistic insights in the COVID-19 infection

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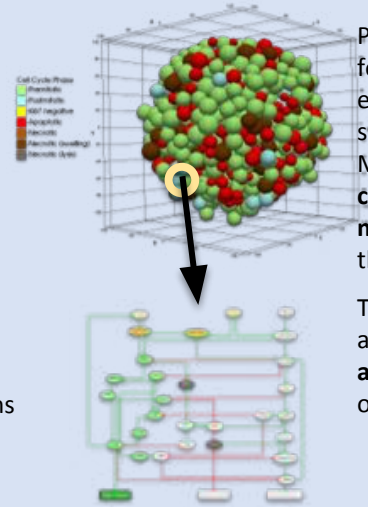
The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has experienced an extremely fast worldwide spreading, producing an unprecedented pandemic situation. We hereby present the use of a framework, termed PhysiBoSS, that integrates MaBoSS, a stochastic Boolean modelling software, into PhysiCell-COVID to allow the leverage of cell- and pathway-specific Boolean models for the study of the COVID infection. Currently, we have incorporated to our prototype a model of apoptosis on human epithelial host cells as a consequence of SARS-CoV-2 infection or T cell induction and hereby present preliminary results.

PhysiBoSS-COVID provides a framework that enables testing of combined genetic and environmental perturbations, and can offer mechanistic insights of SARS-CoV-2 infection, its dissemination among human host cells and its competition against immune cells. In parallel we have developed PhysiCell-MPI, that support distributed parallelism using MPI, allowing for the simulation of large-scale agent-based models of billions of cells and complex heterogeneous environments by efficiently using HPC clusters.

PhysiCell

Multiscale modelling frameworks prove useful in integrating mechanisms that have very different time and space scales, as in the study of viral infection, human host cell demise and immune cells response.

PhysiCell is a multiscale multicellular agent-based tool with the highest potential to be expanded and built upon. It is used for the modelling of the population of cells and can help understand the role of the interactions between cells and their environment.

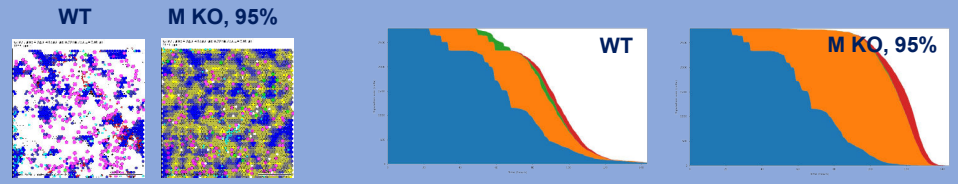


PhysiBoSS

PhysiBoSS merges PhysiCell and MaBoSS and allows for the combined study of genetic and environmental perturbations in many different set-ups. The use of **MaBoSS**, a tool that uses Monte-Carlo kinetic algorithm to perform **continuous time stochastic simulations on logical models**, allows for semi-quantitative evaluation of the model's phenotypes and perturbations.

The solutions can be represented in different forms: a **probability** of network states equivalent to the **asymptotic solutions** of the stochastic simulations, or **time evolution** of the nodes of interest.

PhysiBoSS allows for the mechanistic exploration of COVID-19 infection



With PhysiBoSS we can now inspect mutants that affect epithelial cells' apoptosis and heterogeneous cell populations

Perspectives

- Fully integrate MPI into PhysiBoSS-COVID to scale up the simulations using HPC clusters
- Benchmark it in MareNostrum4: memory allocation problem, we now use *jemalloc*
- Include models of immune cells' differentiation
- Personalise Boolean models with patients' data

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