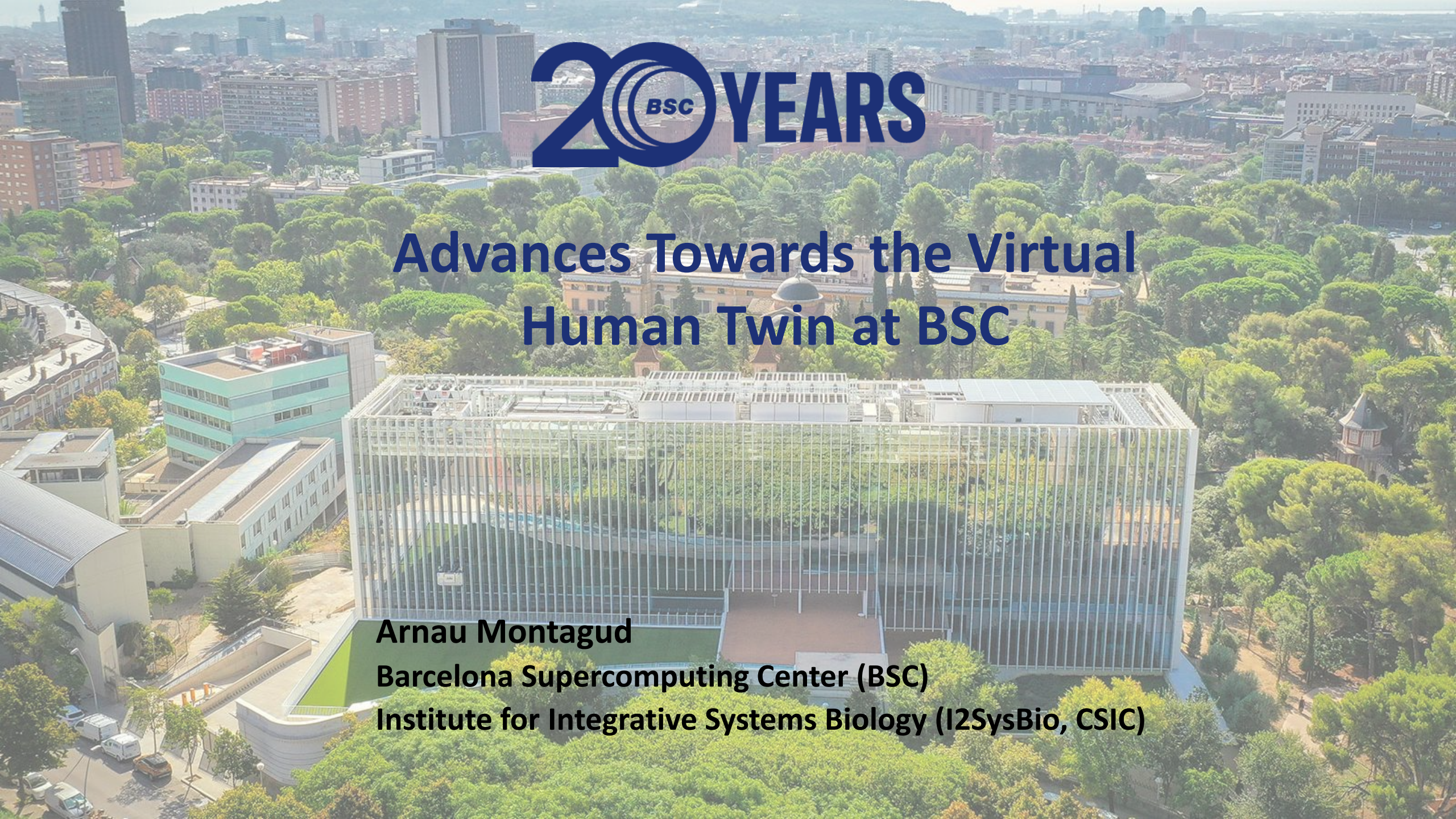


Advances Towards the Virtual Human Twin at BSC

Arnau Montagud
Barcelona Supercomputing Center (BSC)
Institute for Integrative Systems Biology (I2SysBio, CSIC)

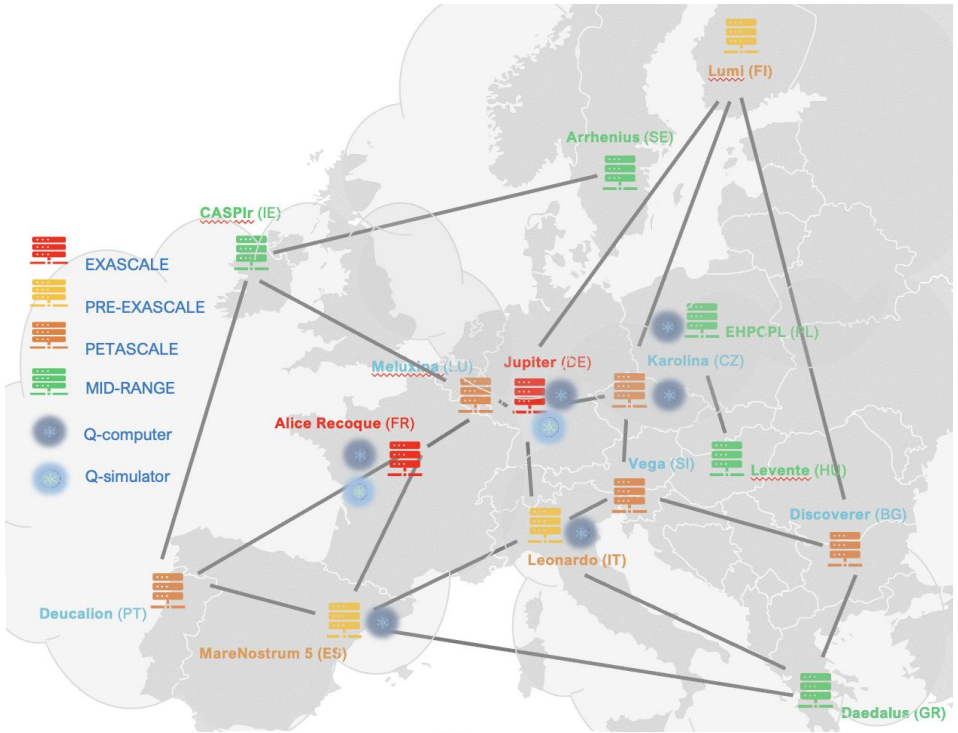
HPC a National and European Infrastructure

#EuroHPC Joint Undertaking

The European High Performance Computing Joint Undertaking (EuroHPC JU) will pool European resources to develop top-of-the range exascale supercomputers for processing big data, based on competitive European technology.

Member countries are Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Türkiye and United Kingdom.

EuroHPC Joint Undertaking



MareNostrum5

ACC – Accelerated
Intel Sapphire Rapids
NVIDIA Hopper
Peak perform: 260 Pflops
Sustained HPL: 163 Pflops

GPP - General Purpose
Intel Sapphire Rapids
Peak perform: 45,4 Pflops
Sustained HPL: 35,4 Pflops

NGT ACC - Next Generation
Peak perform: 6 Pflops
Sustained HPL: 4,24 Pflops

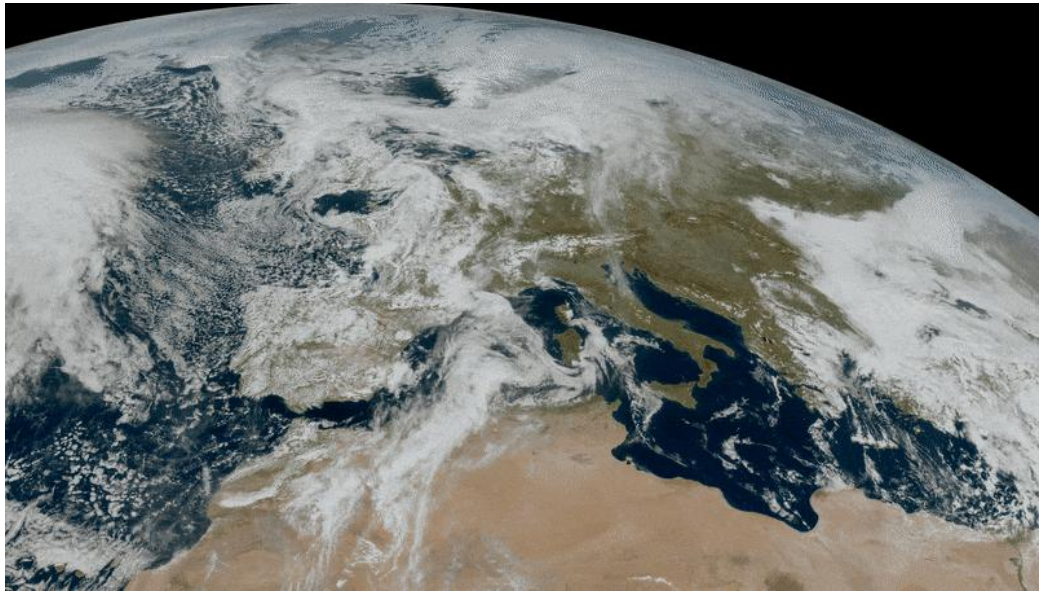
Consortium

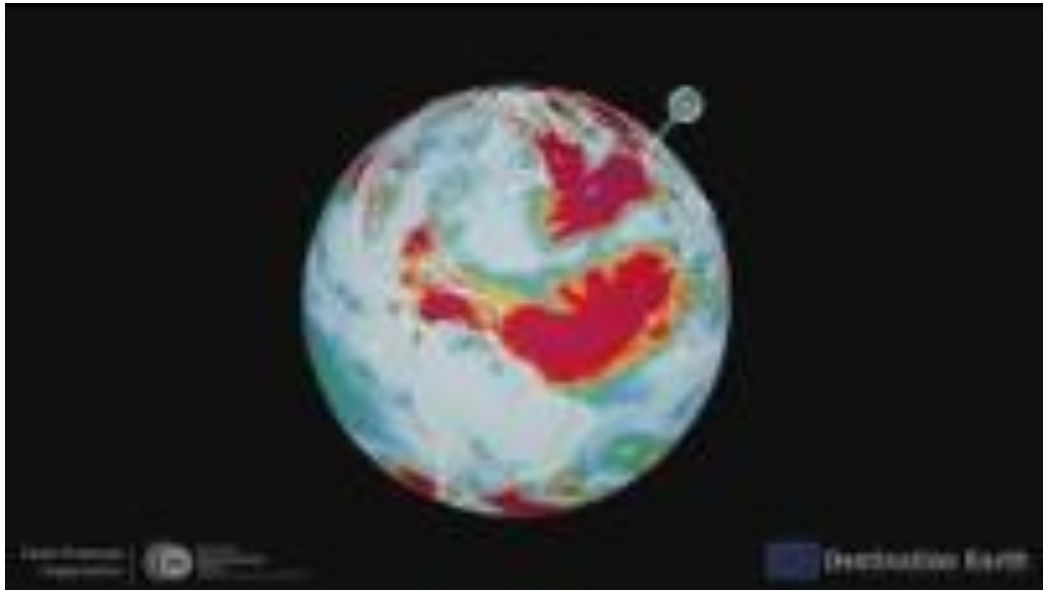
RES
RED ESPAÑOLA DE SUPERCOMPUTACIÓN

BSC Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Destination Earth: towards a DT for climate change adaptation

- The Digital Twin for Climate Change Adaptation, in which BSC plays a crucial role, is implemented by a partnership procured by ECMWF and involves 12 EU institutions.
- The high-resolution simulations using pre-exascale supercomputers in Europe, such as MareNostrum 5 or LUMI.
- This Climate Digital Twin is a pioneering effort to
  - the production of global climate projections for the upcoming decades and
  - provide globally consistent Earth system and impact sector information from global to local scales.
  - https://platform.destine.eu/



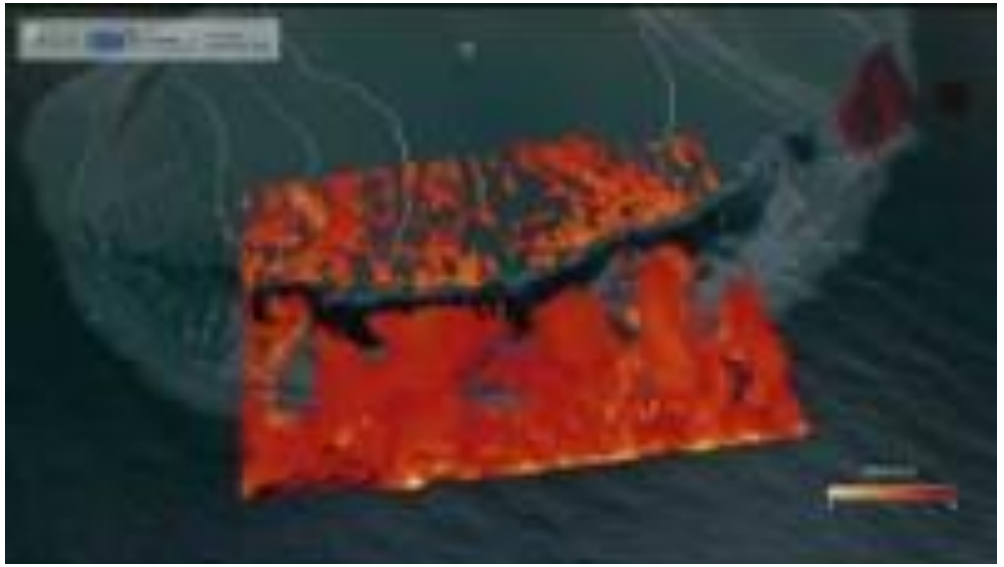


https://www.youtube.com/watch?v=R2aYVeuR6tE&list=PLbABsNMD2jhy5zsINz9VIuOzVsrM0_vwu

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Alya is a DT-enabling tool to simulate complex physics

- The Alya System is a Computational Mechanics code with two main features:
  - Specially designed for running efficiently in HPC
  - Capable of solving different physics, each one with its own model characteristics, in a coupled way.
  - All complex coupled problems solved by Alya retain the efficiency.
- Among the problems it solves are In/Compressible Flows, Non-linear Solid Mechanics, Thermal Flows, N-body collisions, etc.



ELEM
THE VIRTUAL HUMANS FACTORY

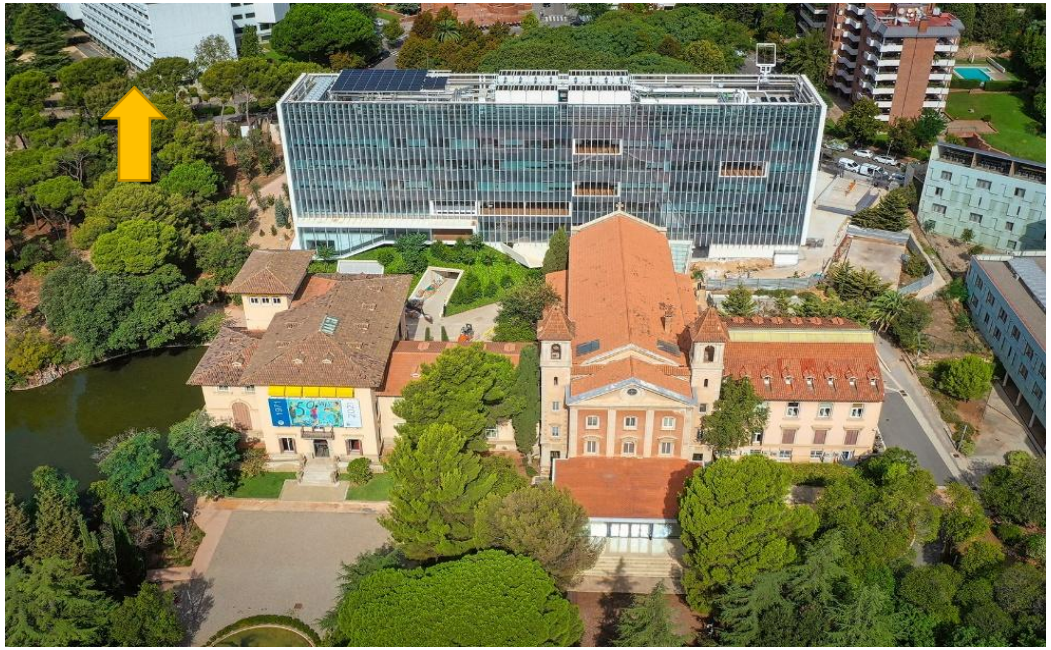
Barcelona Supercomputing Center
Centro Nacional de Supercomputación

https://www.youtube.com/watch?v=6qjG6tnjlXw&list=PLbABsNMD2jhzVukMI2D2JssuJDc9Gf1sJ

https://www.youtube.com/watch?v=IAMnrdy-u4E

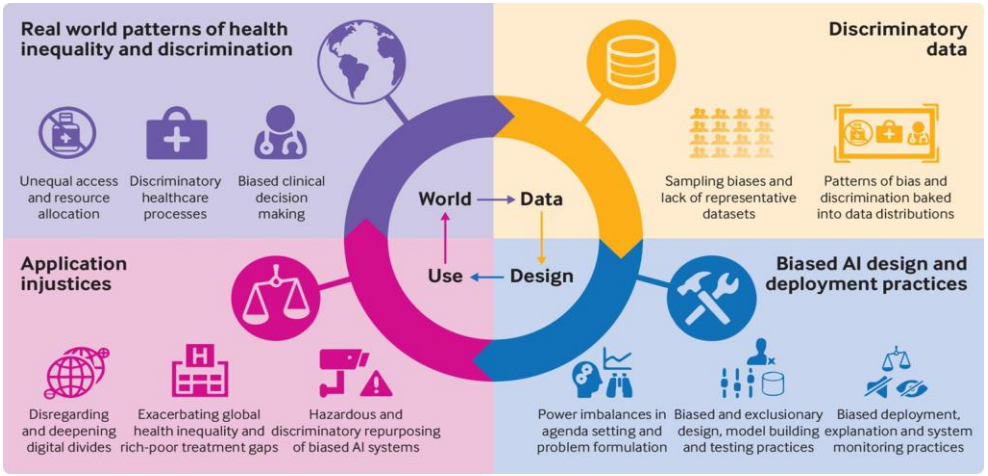
AI Factories will be used to complement digital twins

- Call for Expression of Interest to improve EuroHPC supercomputers with AI capabilities
  - AI-optimised supercomputer
  - Associated “AI Factories” activities and services
- AI Factories will provide the computing power, data, support and talent, to offer a wide and exhaustive range of services to AI startups and researchers needed fort the development of European generative AI models and applications.
- Global budget: 130 – 150 M€
  - I+D services: 30 – 50 M€
  - AI Compute: 90 – 100 M€
- Partnerships: local and global



European Commission

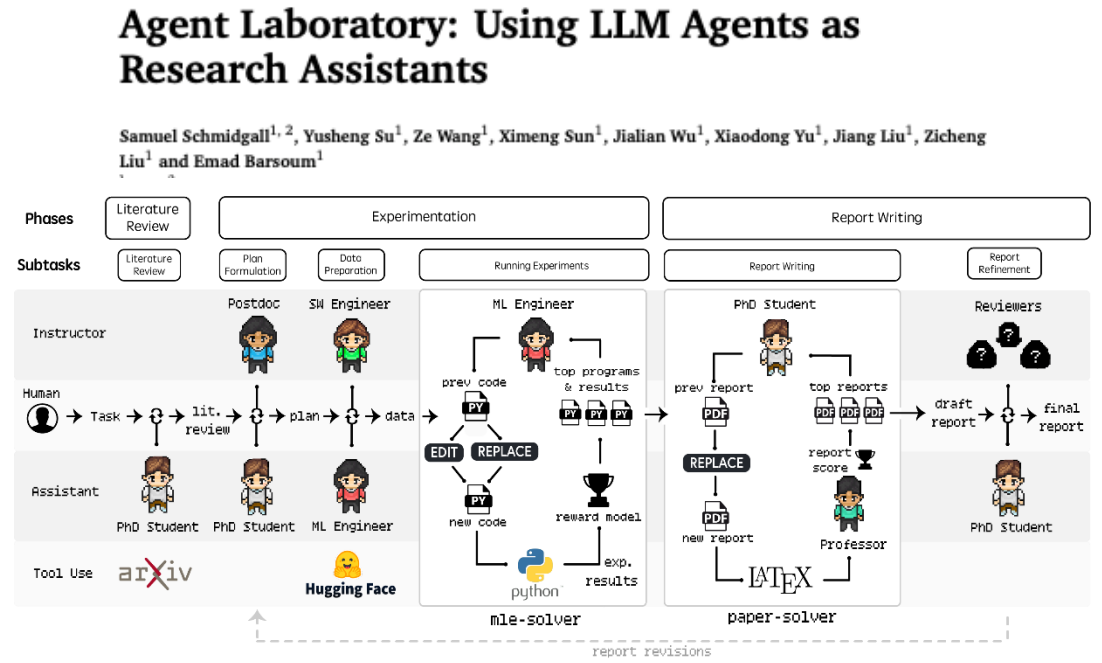
EU AHEAD – coordination evaluation of ML/AI models

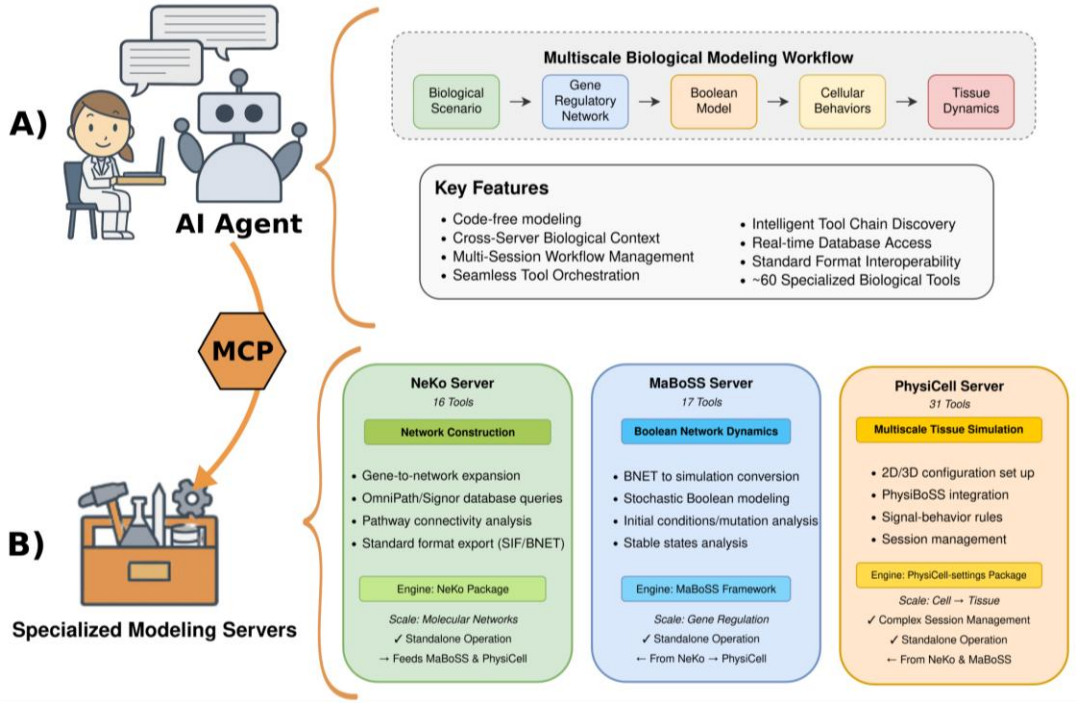


Barcelona Supercomputing Center
Centro Nacional de Supercomputación

AI agents are poised to revolutionise DTs

- AI agents are autonomous software systems that use AI to achieve specific goals and perform tasks on behalf of users, often with minimal human intervention.
  - They can perceive their environment,
  - make decisions, and
  - take actions to achieve their objectives.
- These agents leverage technologies like large language models (LLMs) and can be integrated into complex workflows to automate processes and improve efficiency





Intelligent Tool Orchestration for Rapid Mechanistic Model Prototyping: MCP Servers as AI-Biology Interfaces

Marco Ruscone, Miguel Vazquez, Alfonso Valencia

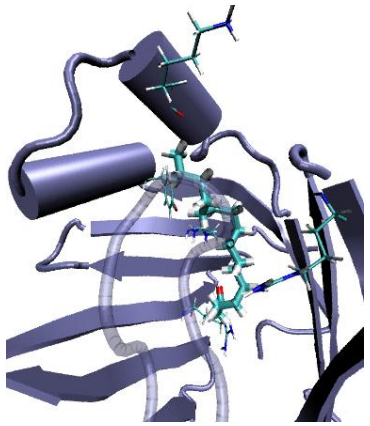
doi: https://doi.org/10.1101/2025.09.10.675105

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

BSC pioneers DT in Life Sciences

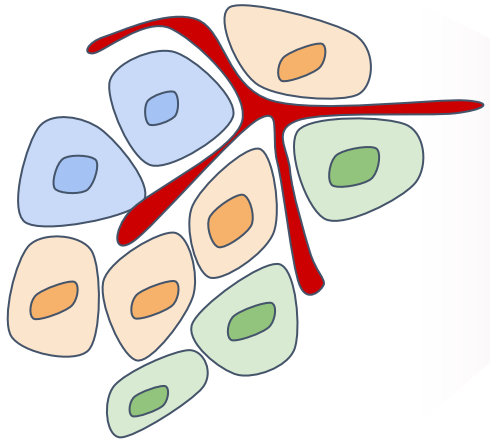
From cells to tissues and organs

PELE tool



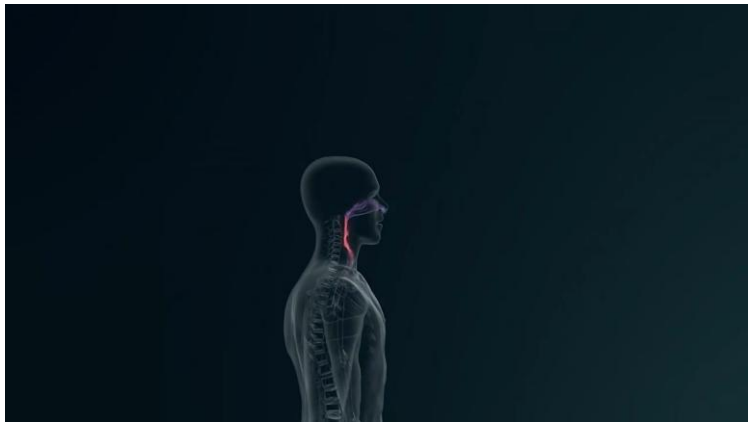
Borrelly et al. (2005) J. Chem. Theo. Comput

PhysiBoSS tool



ALYA tool

https://www.bsc.es/news/bsc-news/alya-red-computational-heart



https://www.youtube.com/watch?v=yyBLPaU057A

Per Med CoE

HPC/Exascale Centre of Excellence in Personalised Medicine

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

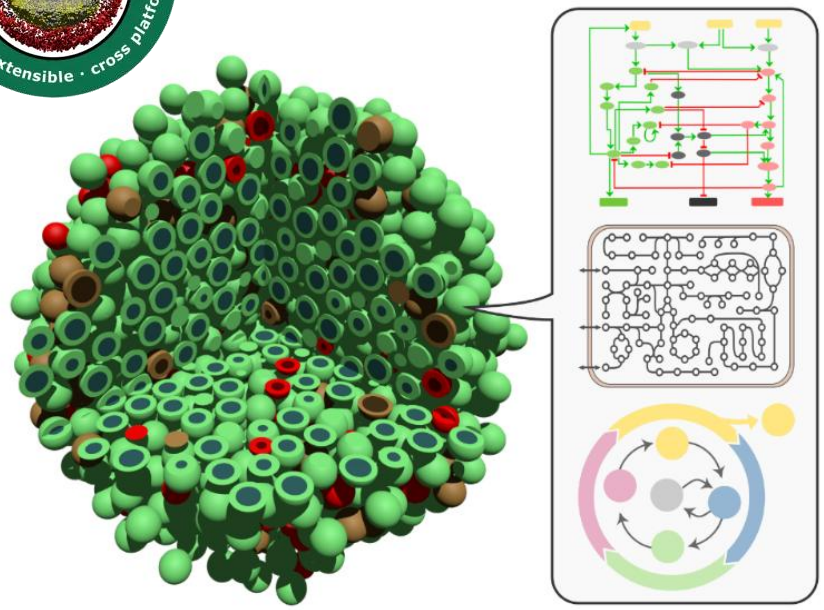
Virtual Human Twins initiative for health and care

European Virtual Human Twins

- EU Initiative Goals:
  - Foster collaboration among academia, industry, and innovators;
  - integrate advanced supercomputing and AI;
  - break silos via a unified platform;
  - promote interoperability and scaling.
- Major Milestones:
  - Launch of the VHT Initiative alongside MareNostrum5.
  - Signature of the Virtual Human Twins Manifesto by 75+ stakeholders.
  - 80 M€ Horizon Europe funding for integrated, multi-scale patient models.
  - 24 M€ platform for model integration and validation started in June 2025.
- Benefits of the Advanced Platform:
  - Secure,
  - open-source,
  - AI-optimised infrastructure

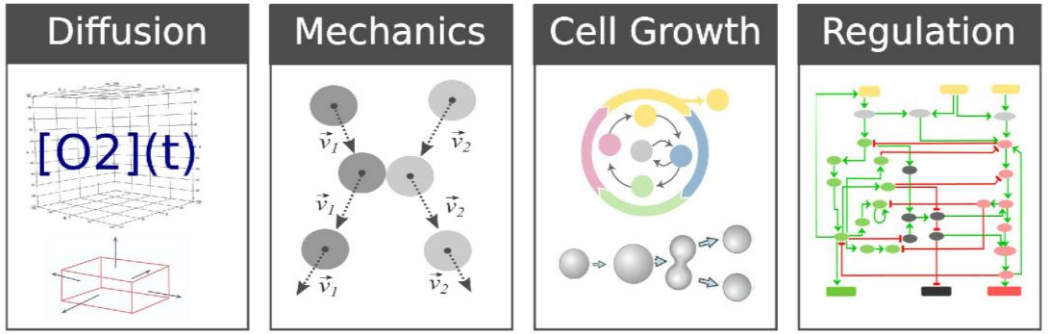
Barcelona Supercomputing Center
Centro Nacional de Supercomputación

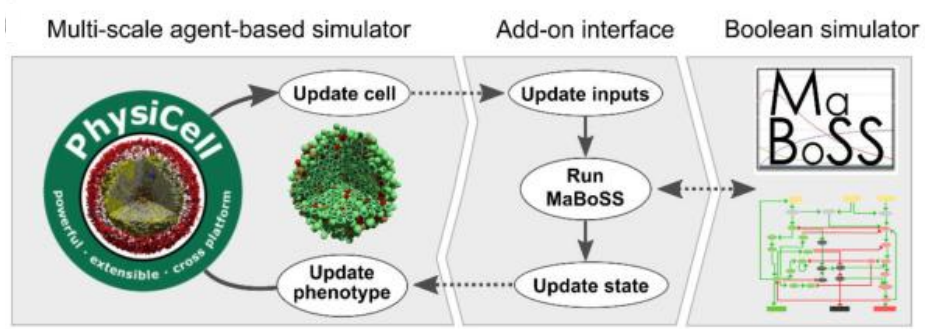
Agent-based for multiscale modelling

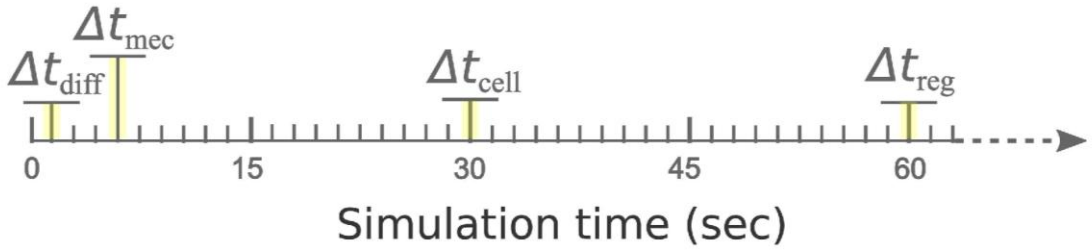


Time scales

- Δt_{diff}: (diffusion/transport): 0.01 min
- Δt_{mec}: (cell movement): 0.1 min
- Δt_{cell}: (cell processes): 6 min
- Δt_{reg}: (Boolean simulation): 10 min







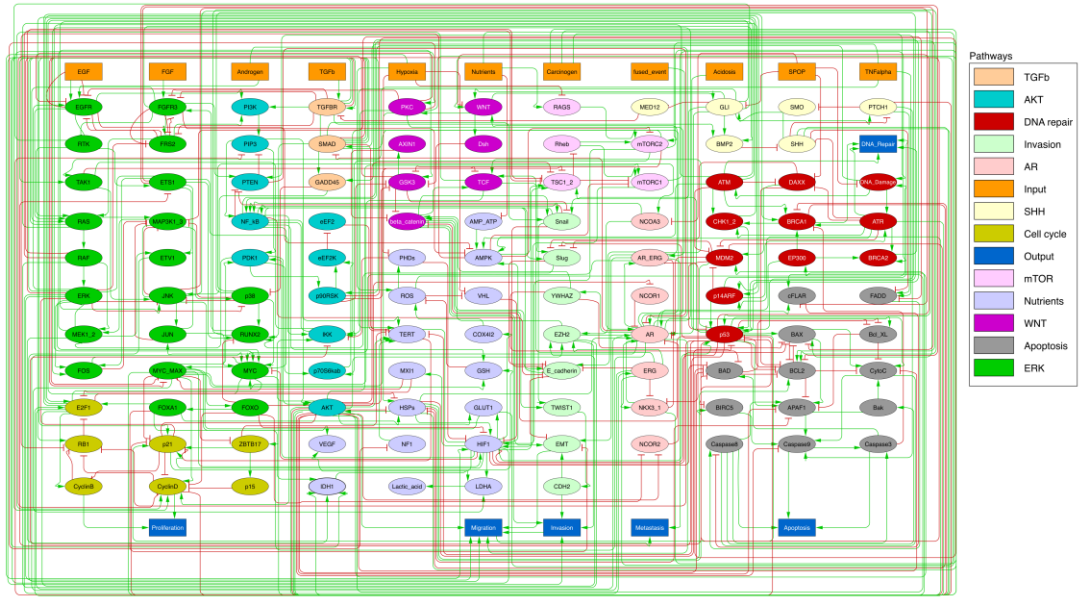
Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Letort et al. (2019). *Bioinformatics,* bty766

Montagud, et al. (2021) *Curr Op in Syst Bio*, **28**, 100385

Ponce-de-León et al. (2023). *npj Syst Biol App*, **9**:54

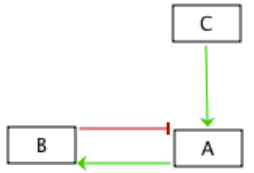
Boolean modelling for signalling pathways



Montagud, et al. (2022). *eLife*, 11:e72626

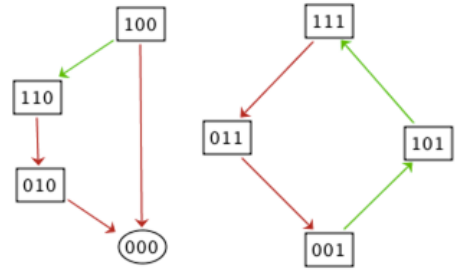
- Set of discrete variables as abstractions of activity level linked by logical rules as signed interactions

Regulatory graph & logical rules



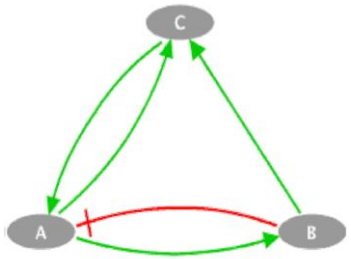
A = !B & C
B = A
C = input

Solutions

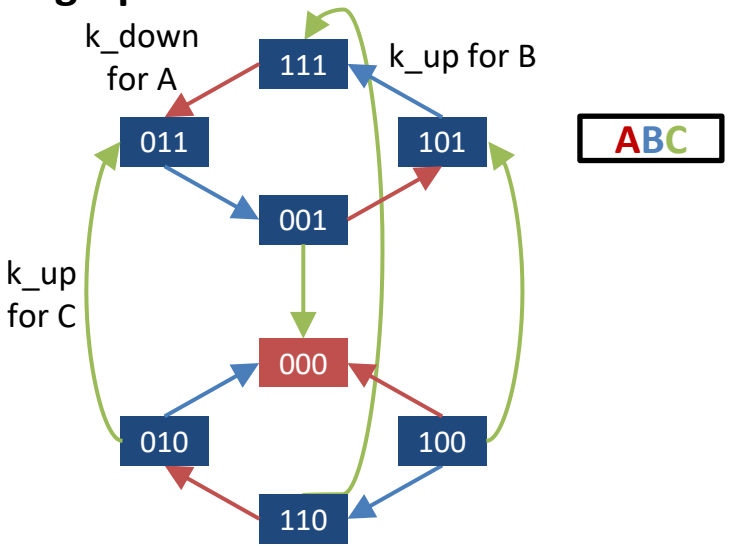


- Continuous time Markov process on the Boolean transition state space
  - Each Boolean state has an associated probability
  - Rate of change associated to each transition
    - rate up and rate down
  - Stochasticity, time, probabilities, …

Boolean state transition graph



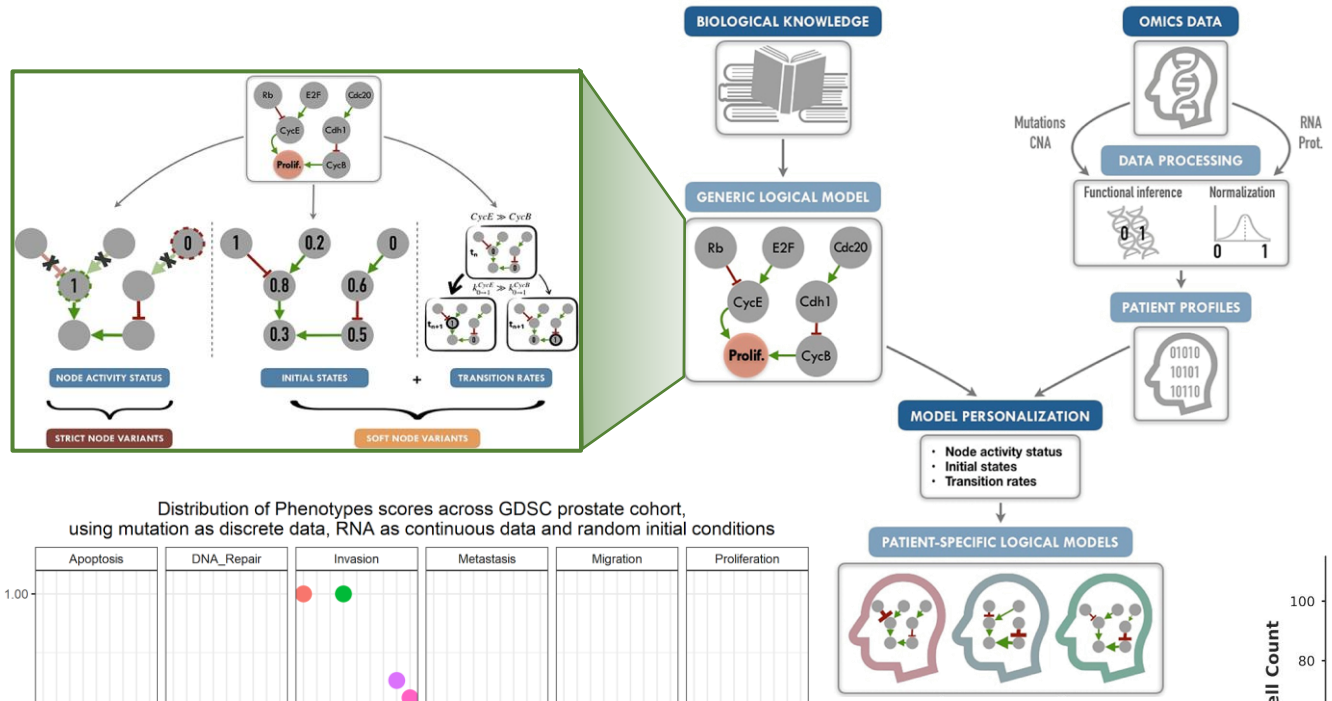
Stoll et al. (2012)
BMC Syst Biol, 6:116

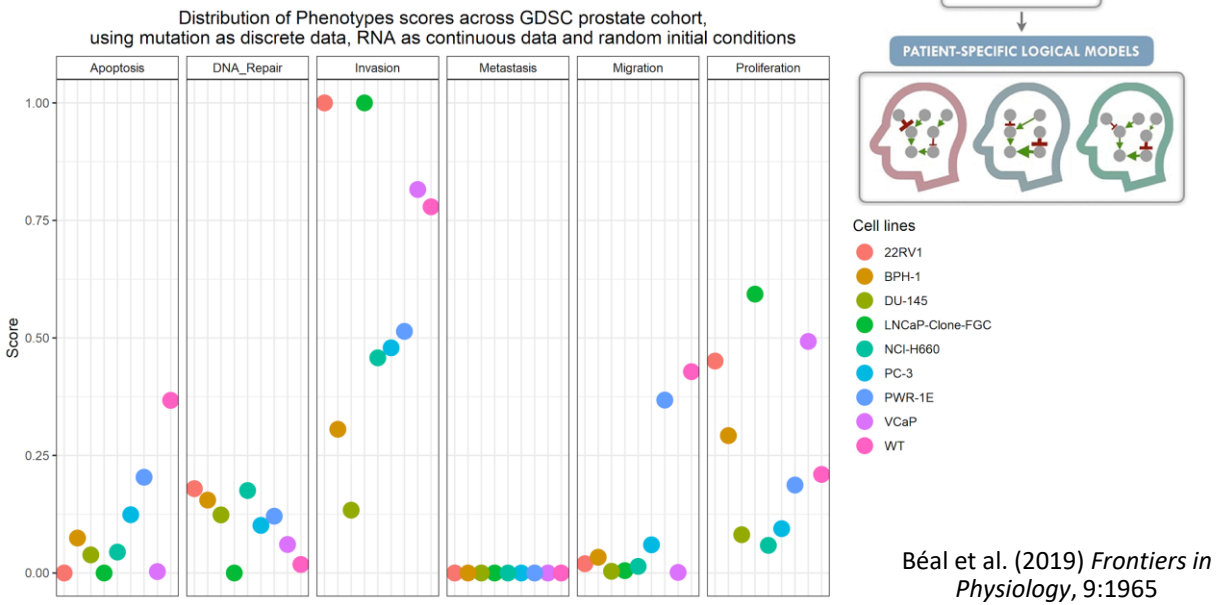


Barcelona Supercomputing Center
Centro Nacional de Supercomputación

Simulating patient-specific models

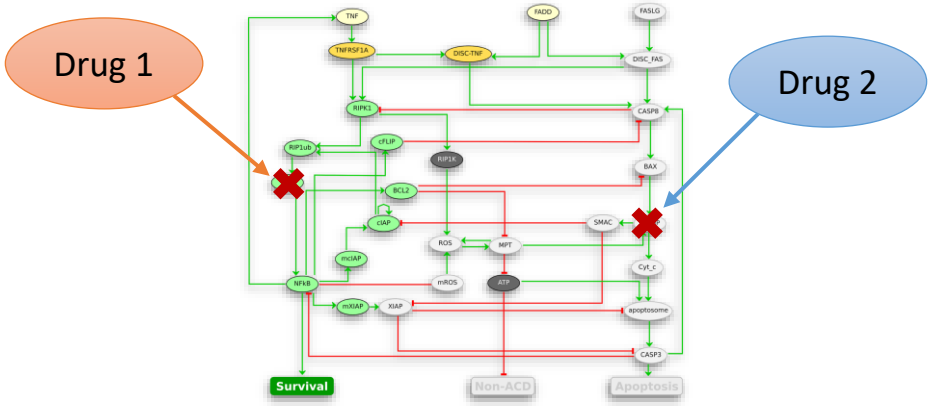
Personalisation of intracellular models

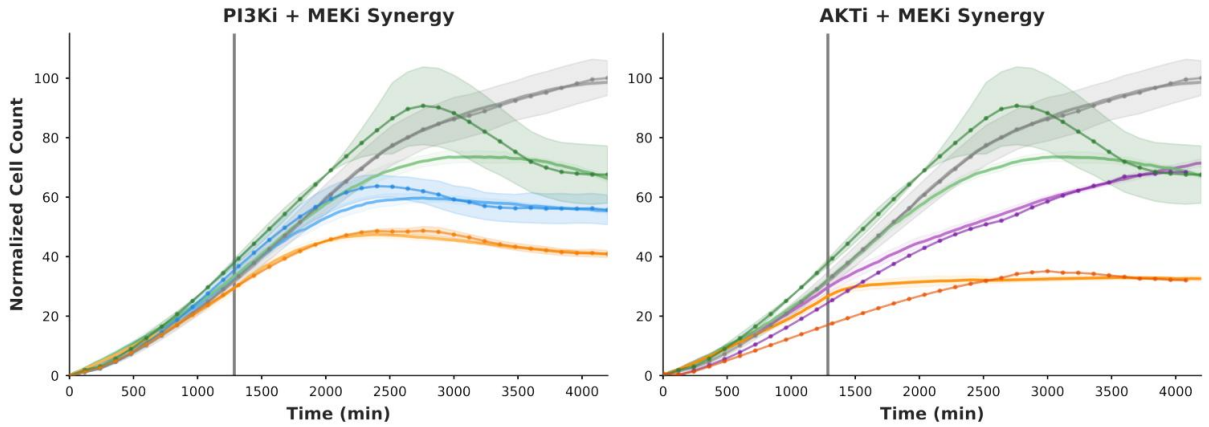




Béal et al. (2019) *Frontiers in Physiology*, 9:1965

Different combinations of drugs

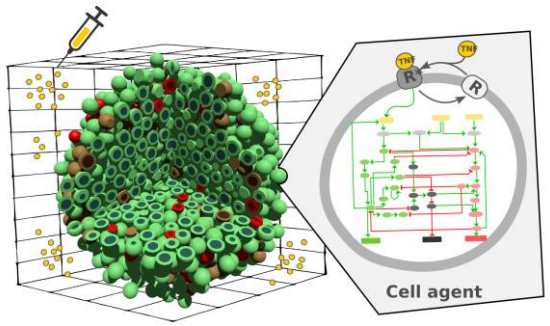


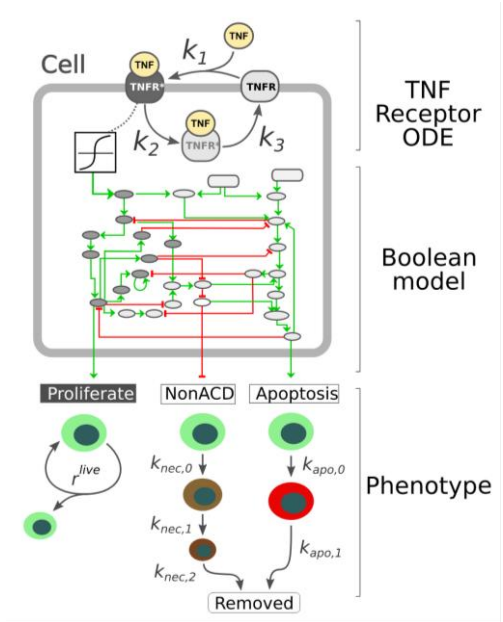


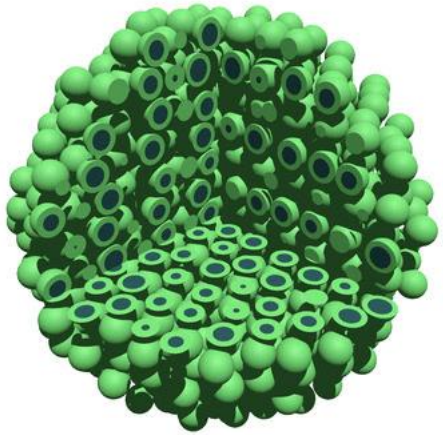
Emergent prediction of drug synergy from a model calibrated on single-agent responses.

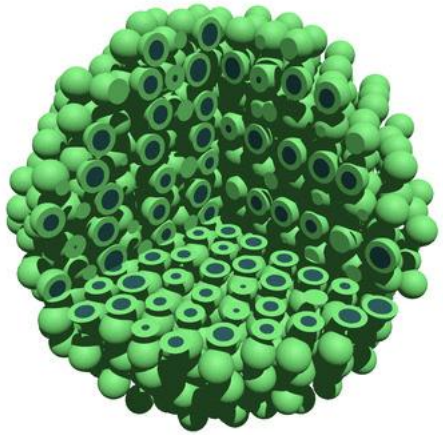
Hayoun-Mya et al. *under preparation*

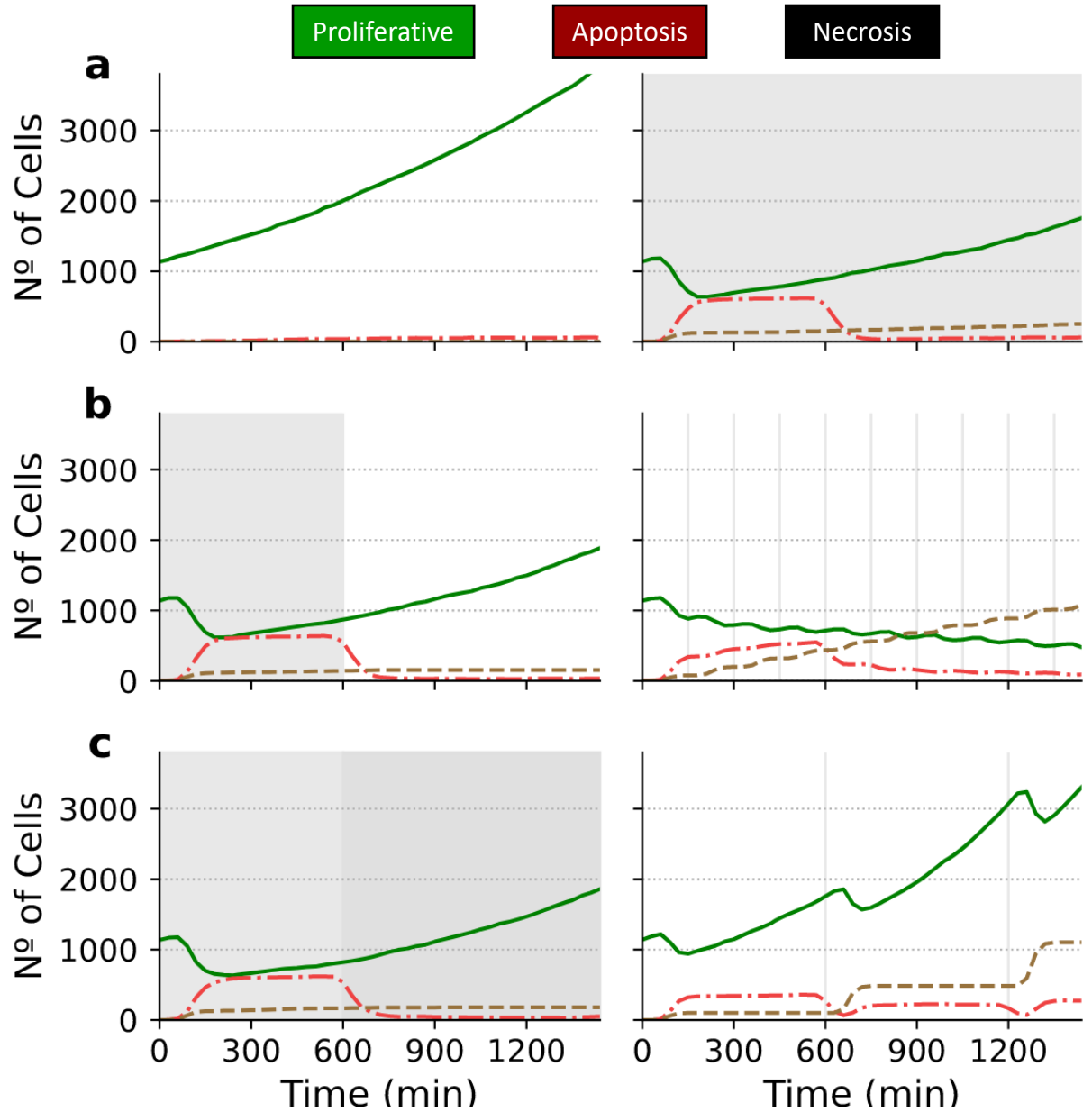
PhysiBoSS allows for finding optimal drug regimes









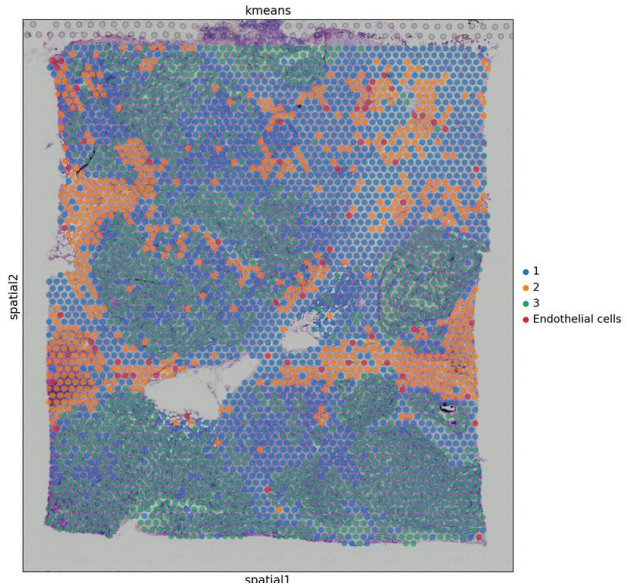


Barcelona Supercomputing Center
Centro Nacional de Supercomputación

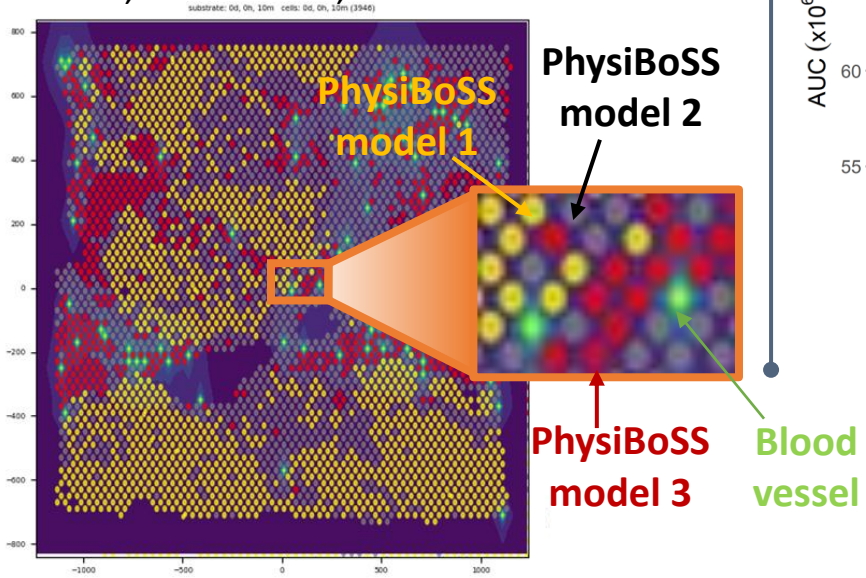
Letort et al. (2019) *Bioinformatics*, bty766
Ponce-de-Leon et al. (2022) *Front Molecular Biosciences, 9*
Ponce-de-Leon et al. (2023) *npj Syst Biol Appl*, **9**:54

Integrating spatial omics in PhysiBoSS

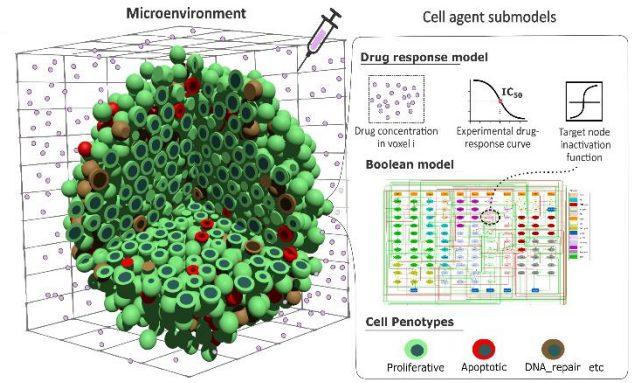
Breast cancer spatial omics

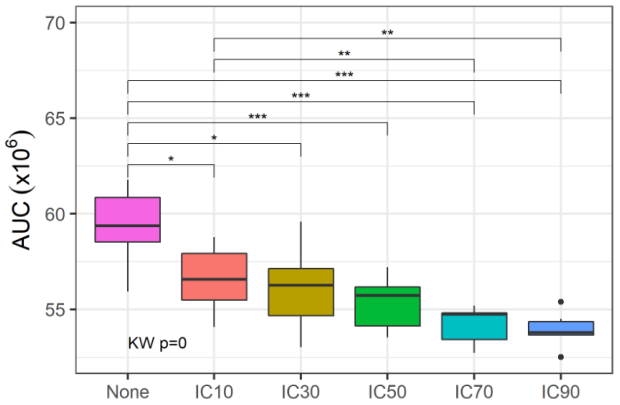


ECM, O2 sources, different cell clusters



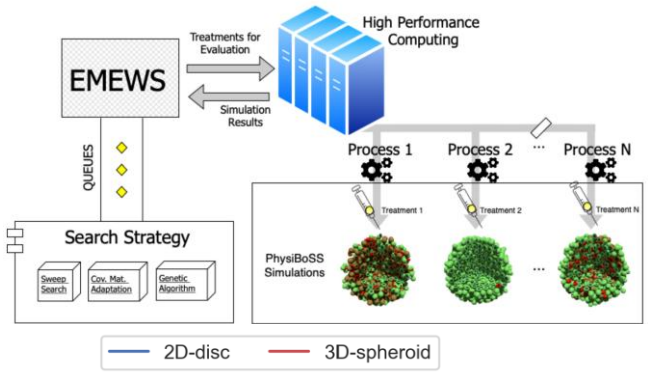
Patient-specific drug response curves

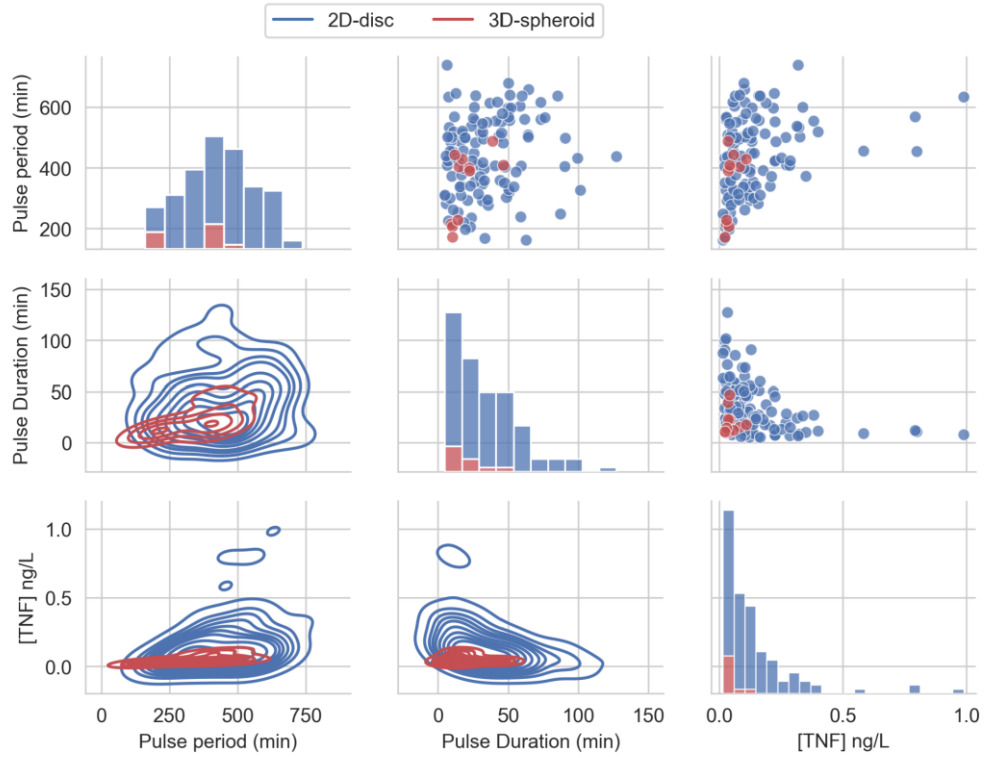




Ponce-de-Leon et al. (2023)
npj Syst Biol Appl, 9:54

High-Throughput Computing to parametrise the simulations





Akasiadis et al. (2022) *Computational Intelligence*, *38*(4), 1–23
Ponce-de-Leon et al. (2022) *Frontiers in Molecular Biosciences*, *9*, 836794

Barcelona Supercomputing Center
Centro Nacional de Supercomputación

20 YEARS

Thank you!

Dept. Life Sciences, BSC
over 250 scientists, engineers and students

arnau.montagud@bsc.es