HPC/Exascale Centre of Excellence in Personalised Medicine

Practical session with PhysiCell

José Carbonell Caballero
Thalia Diniaco

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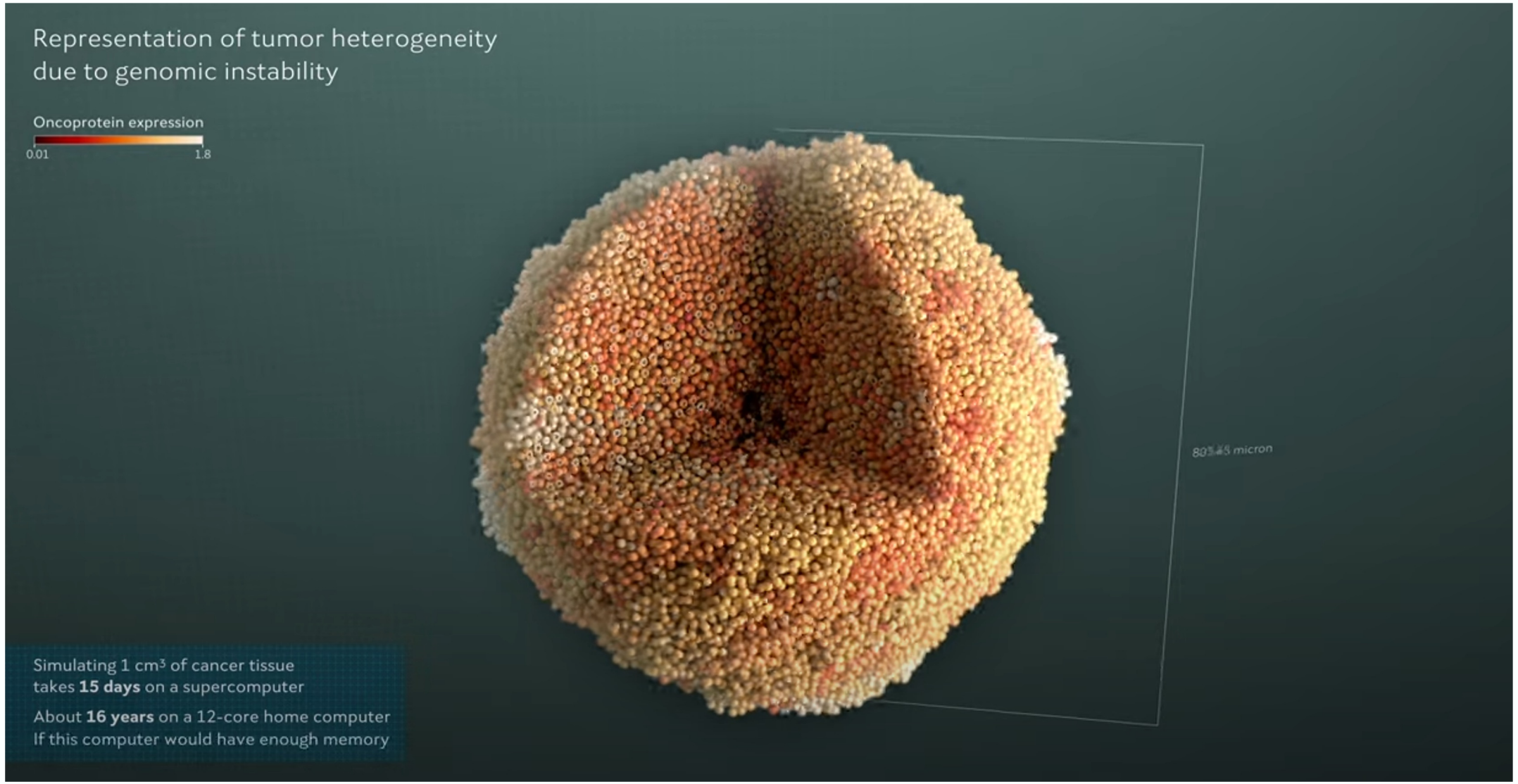
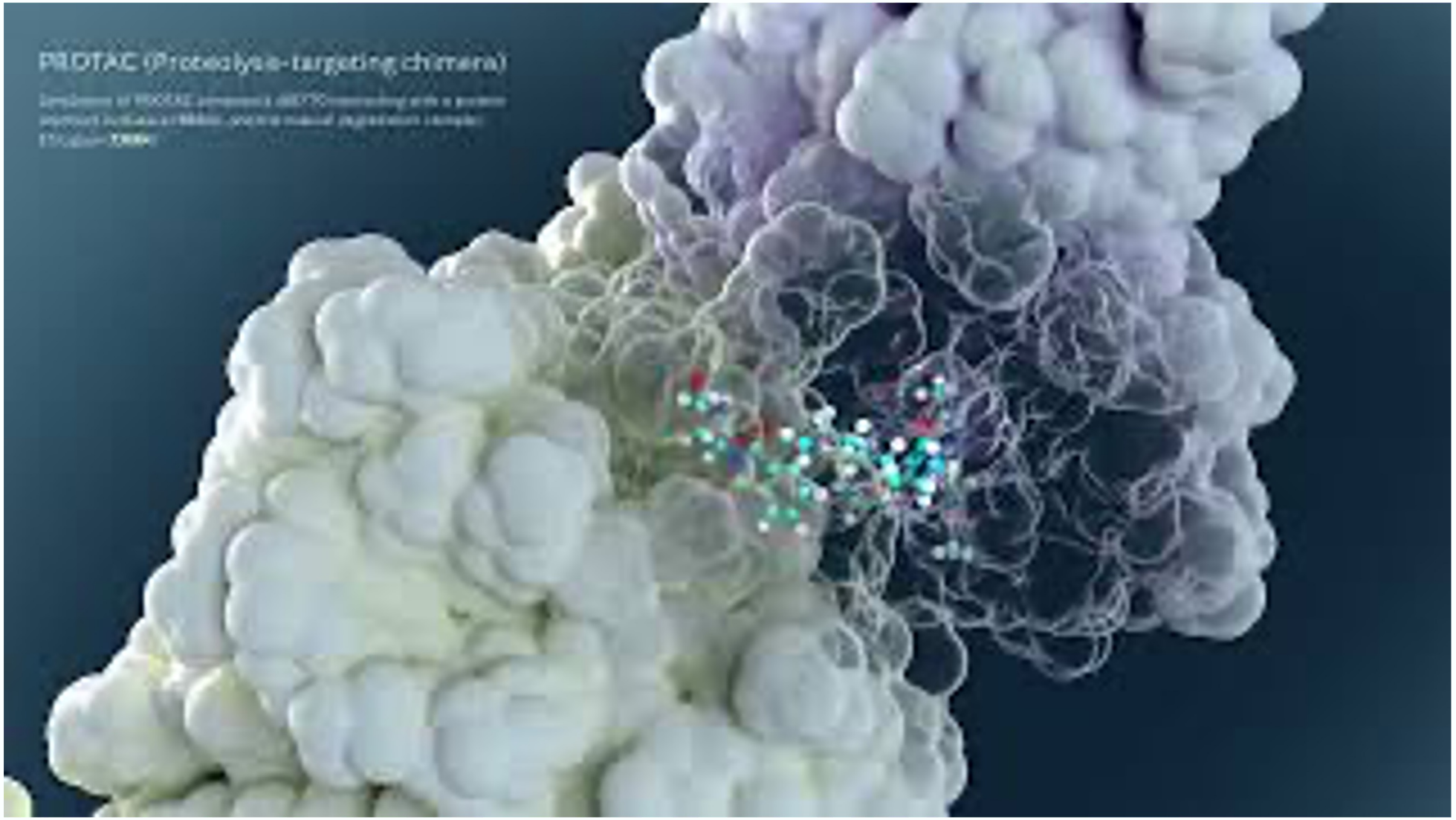
Simulating a cellular microenvironment

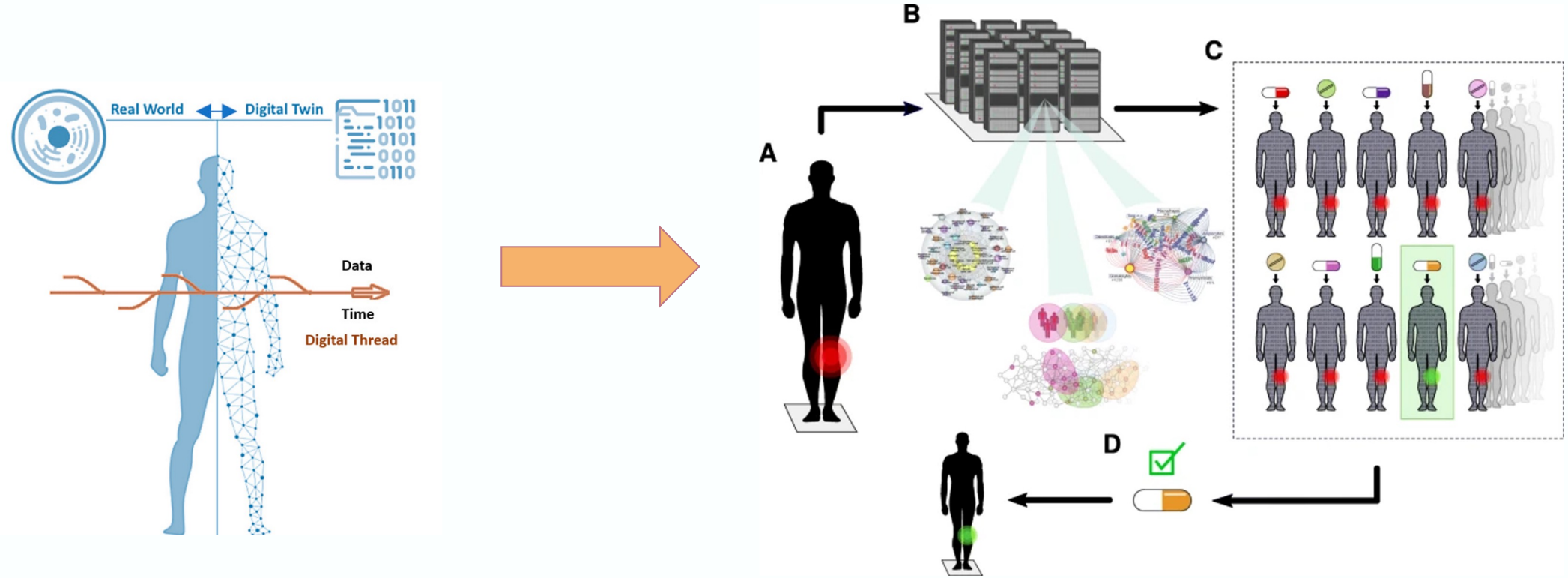


Simulating a cellular microenvironment



Personalised Medicine and Digital Twins

Towards patient-specific treatments

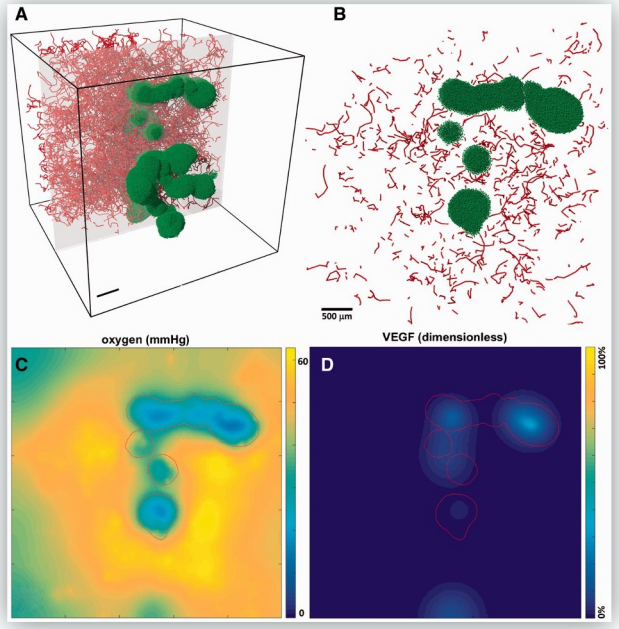


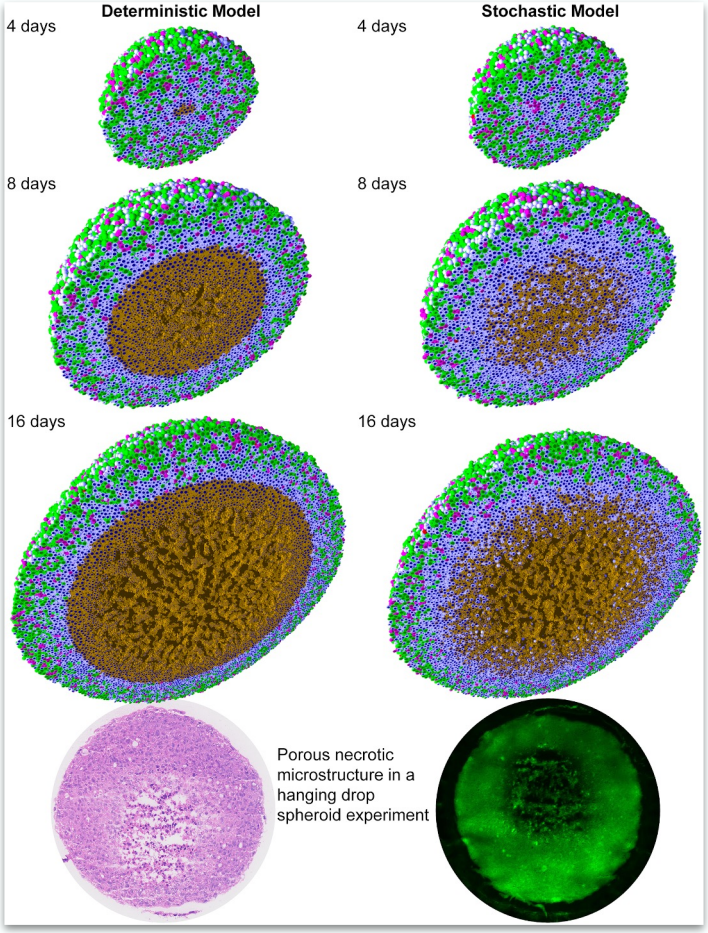
Björnsson, B., Borrebaeck, C., Elander, N. et al. Digital twins to personalize medicine. Genome Med 12, 4 (2020).

Core tools

PhysiCell

- Physics-based virtual microscope
- Implements Agent-Based programming
- Cell phenotype and cell-cell interactions
- Diffusion transport solver

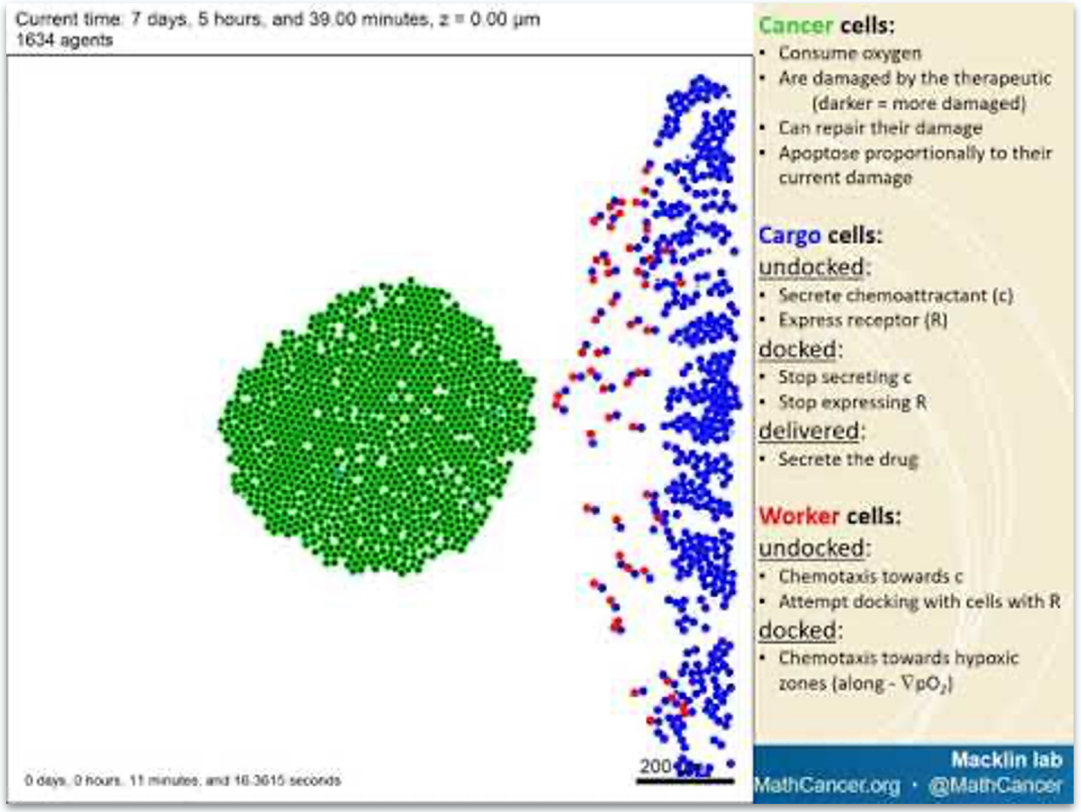




Ghaffarizadeh, A. et al (2018). https://doi.org/10.1371/journal.pcbi.1005991

PhysiCell

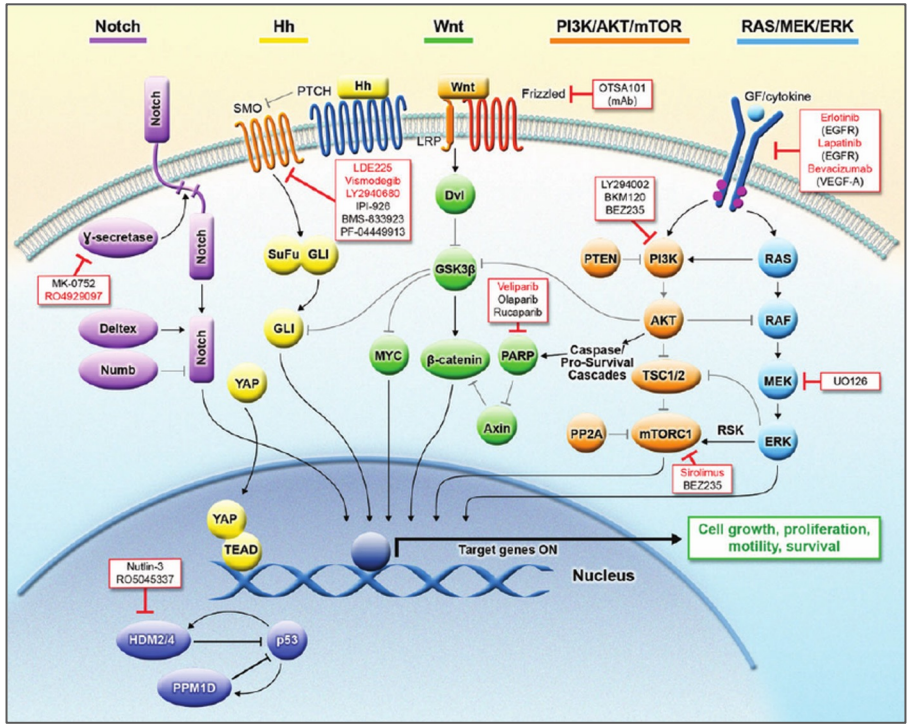
The framework recapitulates main cellular features



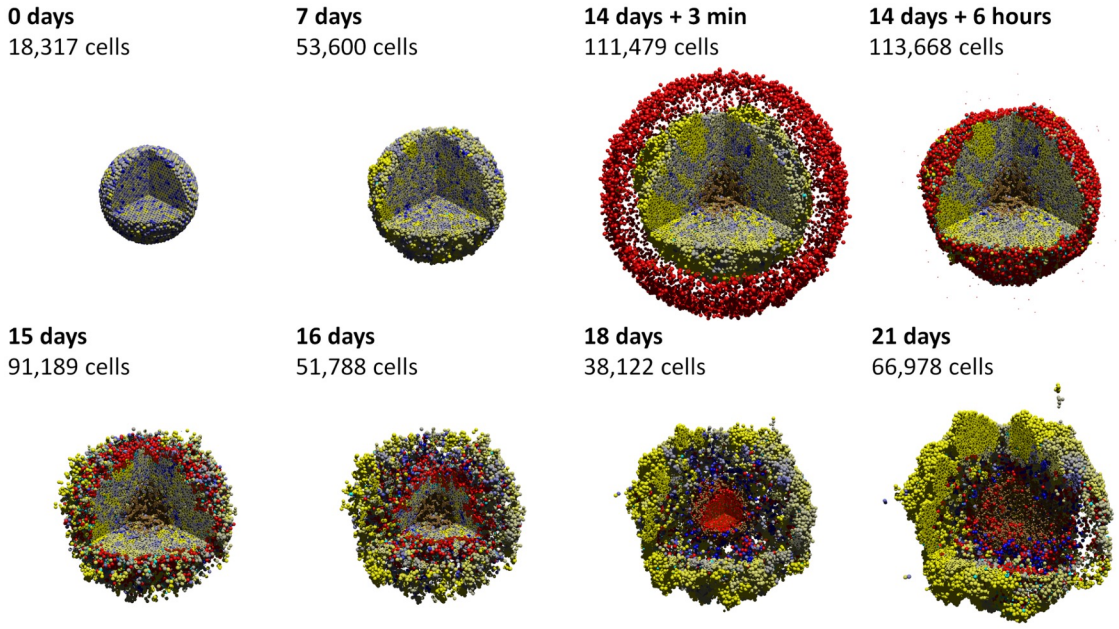
- Cell motility (and chemotaxis)
- Cell cycle phases (GO/G1, S, G2, M)
- Cell death (apoptosis and necrosis)
- Cell volume (nucleus and cytoplasm)
- Cell growth
- Substrate production/consumption
- Physical interaction between cells
- Phagocytosis

Extending PhysiCell

Introducing molecular pathways into multiscale agents



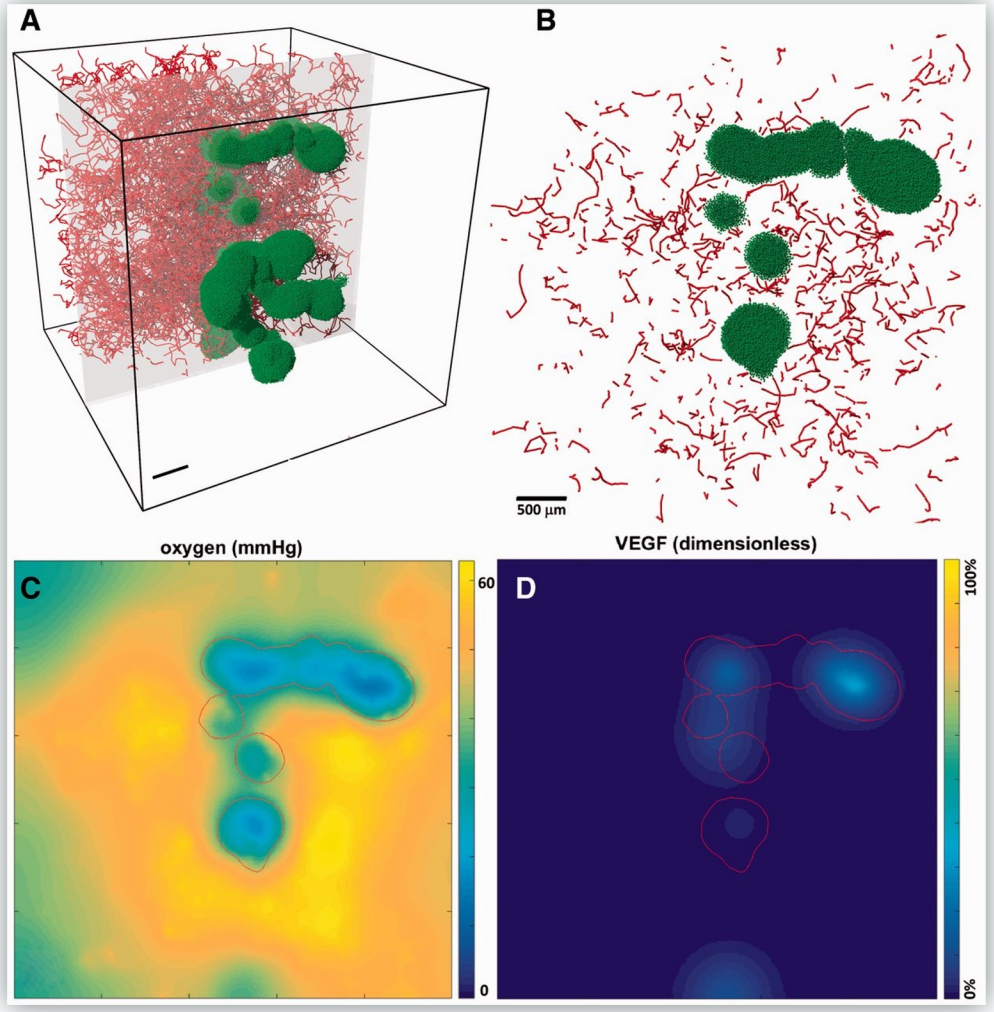
Tobey J et al..Neuro-Oncology, Volume 16, Issue 1, (2013)



Ghaffarizadeh A et al. PLoS Comput Biol. 2018

PhysiCell

BioFVM (diffusive transport solver)



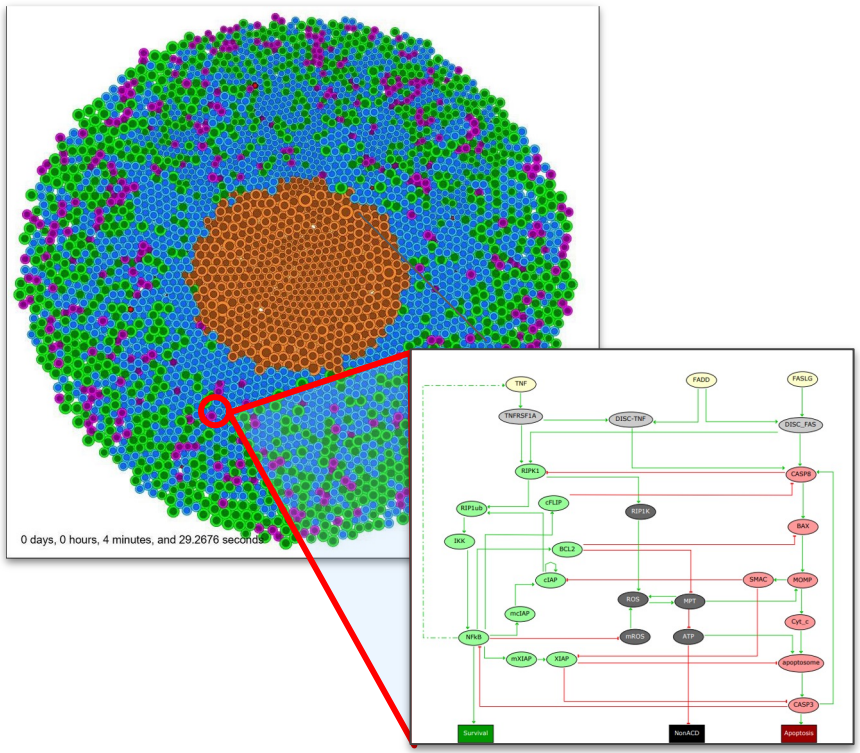
$$\frac{\partial \vec{\rho}}{\partial t} = \overbrace{\vec{D}\nabla^2\vec{\rho}}^{\text{diffusion}} - \overbrace{\vec{\lambda}\vec{\rho}}^{\text{decay}} + \overbrace{\vec{S}(\vec{\rho}^* - \vec{\rho})}^{\text{bulk source}} - \overbrace{\vec{U}\vec{\rho}}^{\text{bulk uptake}}$$

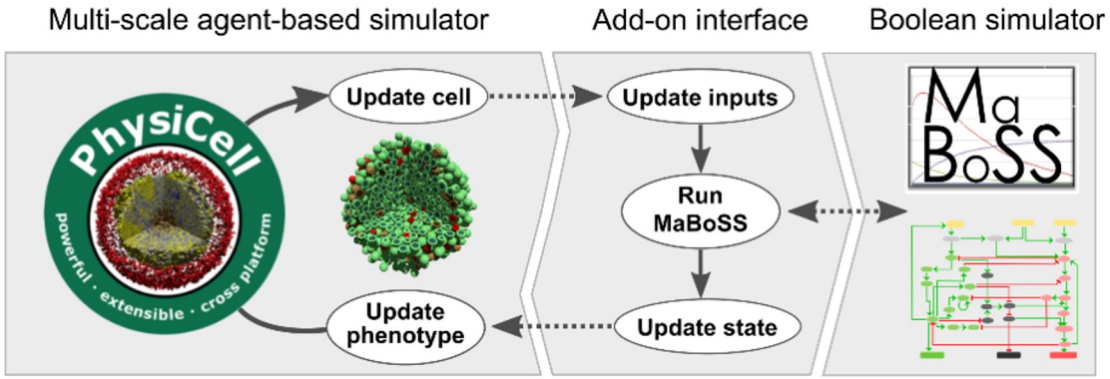
$$+ \overbrace{\sum_{\text{cells}k} 1_k(\vec{x}) \left[\vec{S}_k(\vec{\rho}_k^* - \vec{\rho}) - \vec{U}_k\vec{\rho}\right]}^{\text{sources and uptake by cells}} \text{ in } \Omega$$

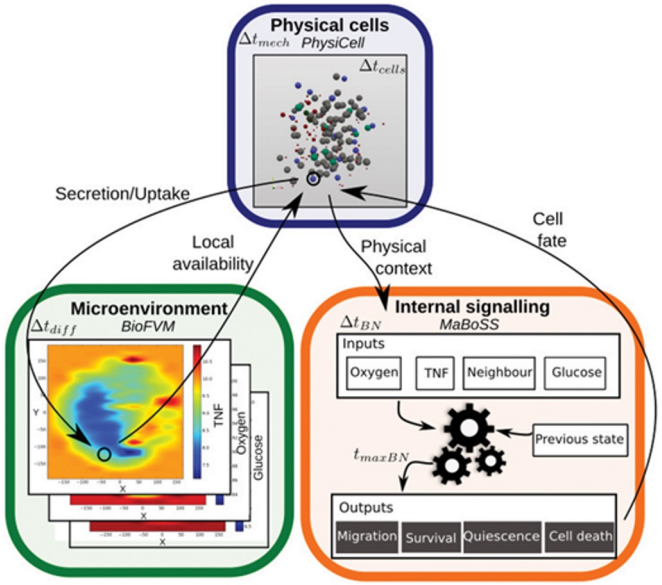
Extending PhysiCell

PhysiBoss (PhysiCell + MaBoSS)

Cell state and decisions depend on embedded boolean models





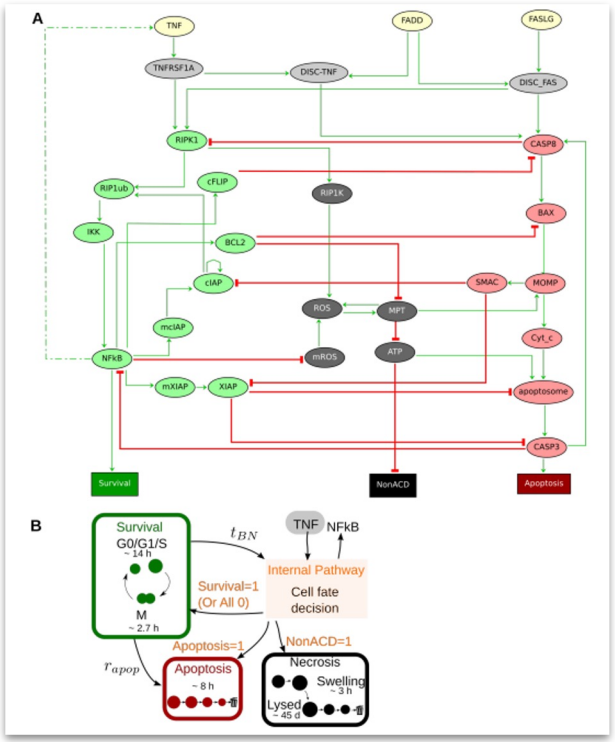


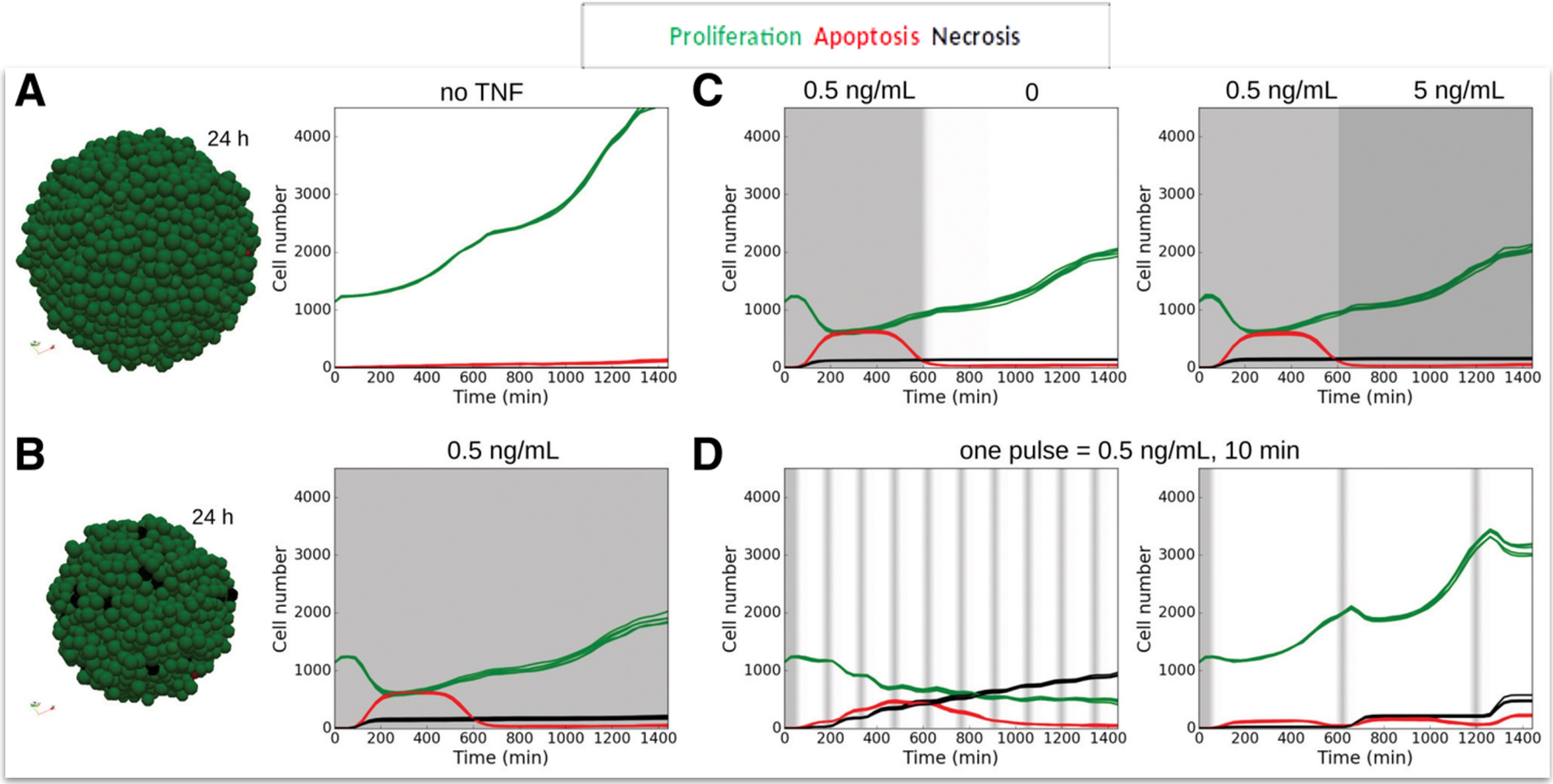
Letort, G., Montagud, A. et al (2019). Bioinformatics, 35(7), 1188–1196. https://doi.org/10.1093/bioinformatics/bty766

Extending PhysiCell

Agent-based + probabilistic logical models (PhysiCell + MaBoSS)

PhysiBoSS

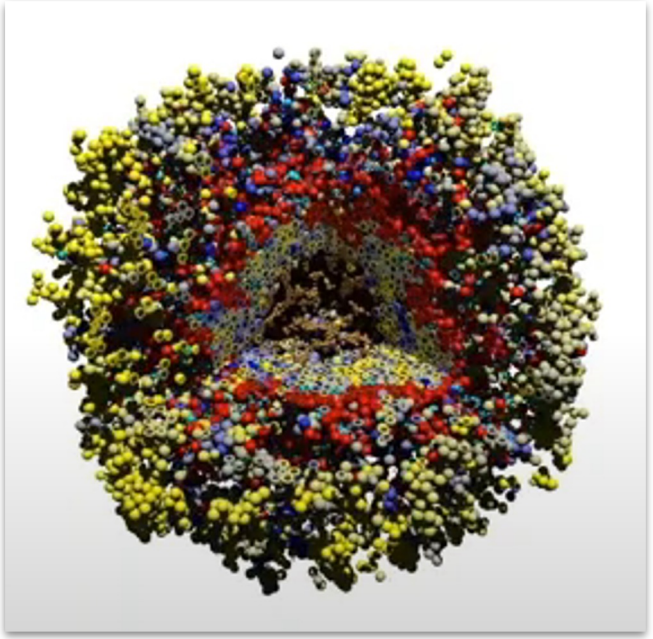




Per Med CoE

Letort, G., Montagud, A., et al. (2019). Bioinformatics, 35(7), 1188–1196

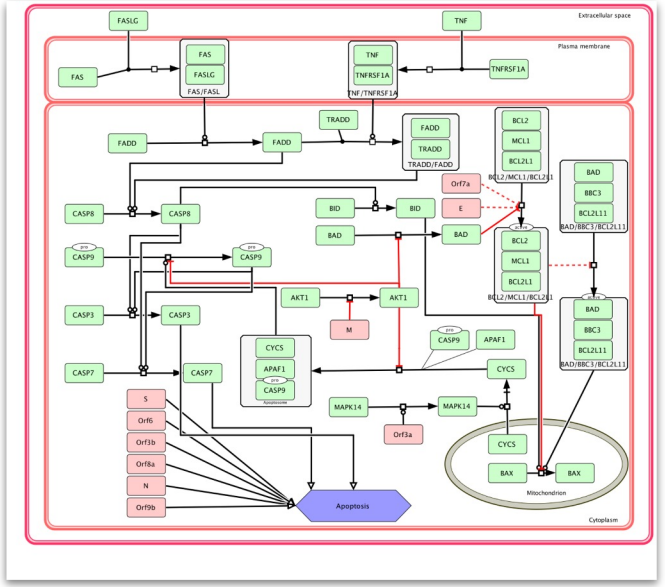
Cell level simulations



Per Med CoE

HPC

Molecular Pathways

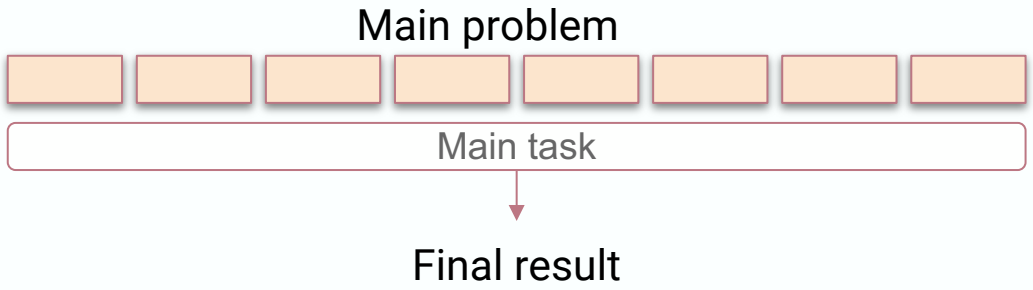


Parallel computing

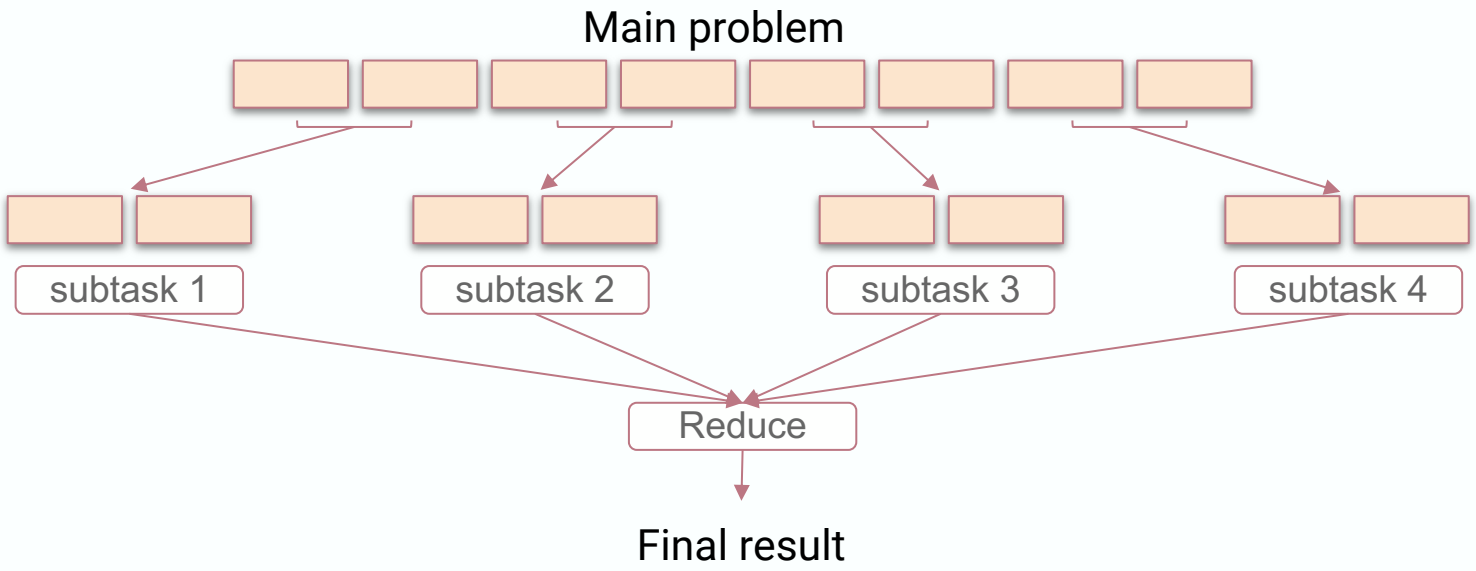
Traditional approaches

- Native support
- Based on logical threads
- POSIX threads (IEEE)

Serial computing

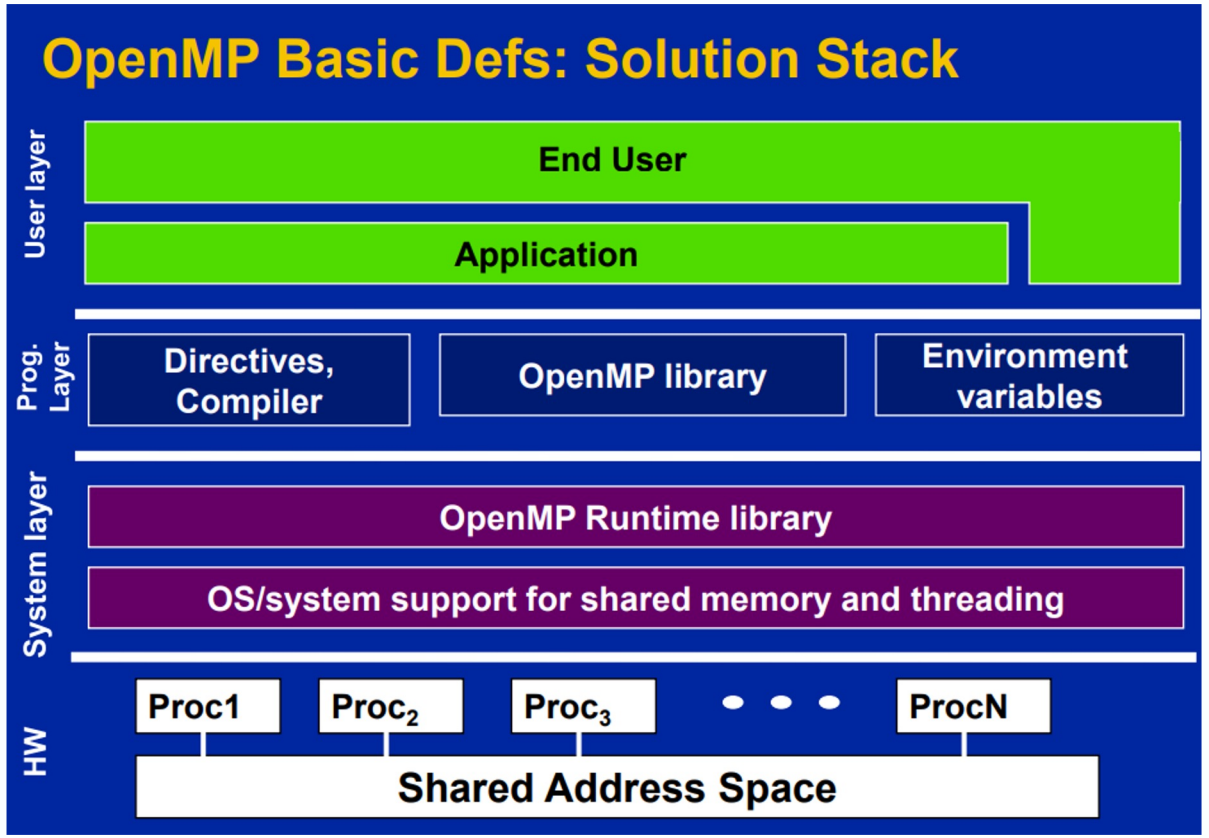


Parallel computing



OpenMP

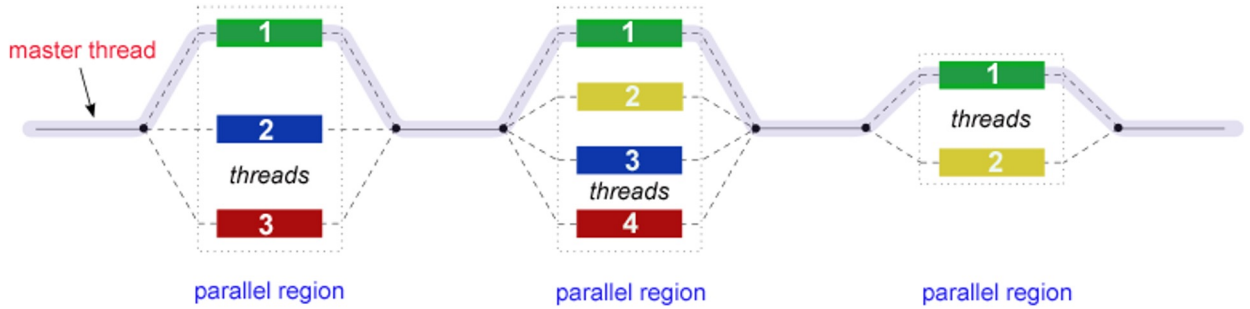
- Directive-based
- Simple and flexible interface for developing parallel application
- API for direct multi-threaded, shared memory parallelism
- Comprised of three primary API components:
  - Compiler Directives
  - Runtime Library Routines
  - Environment Variables



Tim Mattson

Parallel computing

```
#include <stdio.h>
#include <omp.h>

int main(int argc, char** argv){
    int partial_Sum, total_Sum;

    #pragma omp parallel private(partial_Sum) shared(total_Sum)
    {
        partial_Sum = 0;
        total_Sum = 0;

        #pragma omp for
        {
            for(int i = 1; i <= 1000; i++){
                partial_Sum += i;
            }
        }

        //Create thread safe region.
        #pragma omp critical
        {
                //add each threads partial sum to the total sum
                total_Sum += partial_Sum;
        }
    }
    printf("Total Sum: %d\n", total_Sum);
    return 0;
}
```



Example ploop.1.c

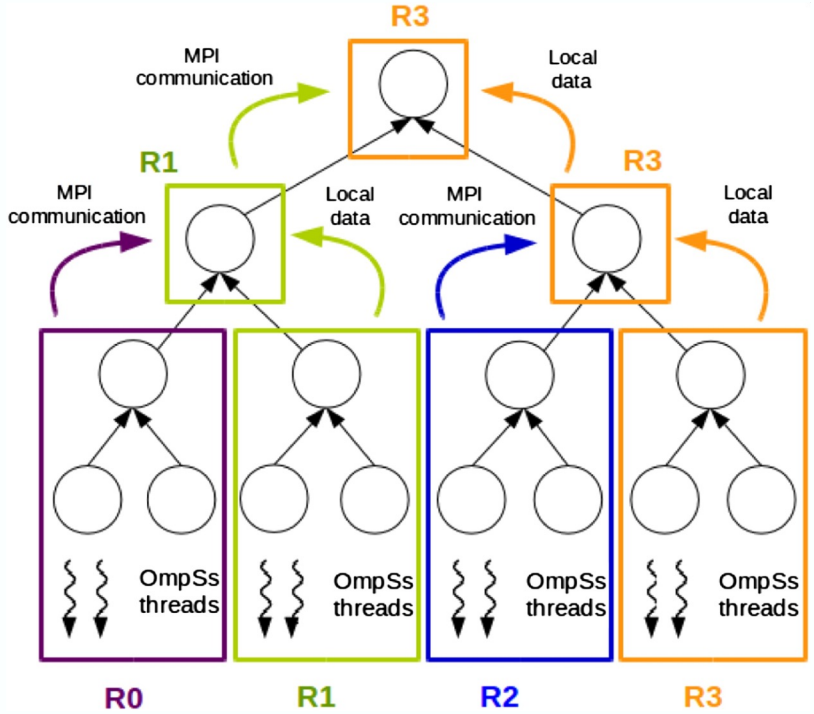
```
S-1    void simple(int n, float *a, float *b)
S-2    {
S-3        int i;
S-4
S-5    #pragma omp parallel for
S-6        for (i=1; i<n; i++) /* i is private by default */
S-7            b[i] = (a[i] + a[i-1]) / 2.0;
S-8    }
```

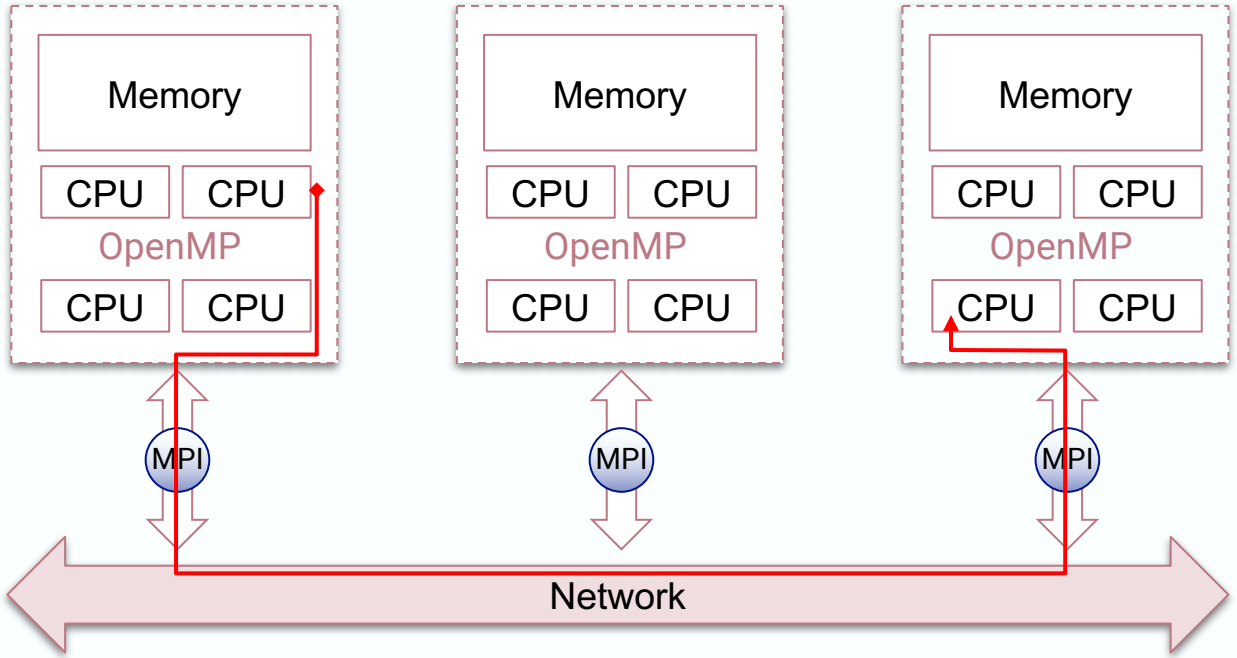
credit by HPC at Lawrence Livermore National Lab

Distributed computing

Message Passing Interface (MPI)

- API for coordinating different nodes to jointly perform a given task
- Communication via the local network (latency is an issue)
- Several nodes work as a single machine
- Different implementations (OpenMPI, Intel MPI)





Distributed computing

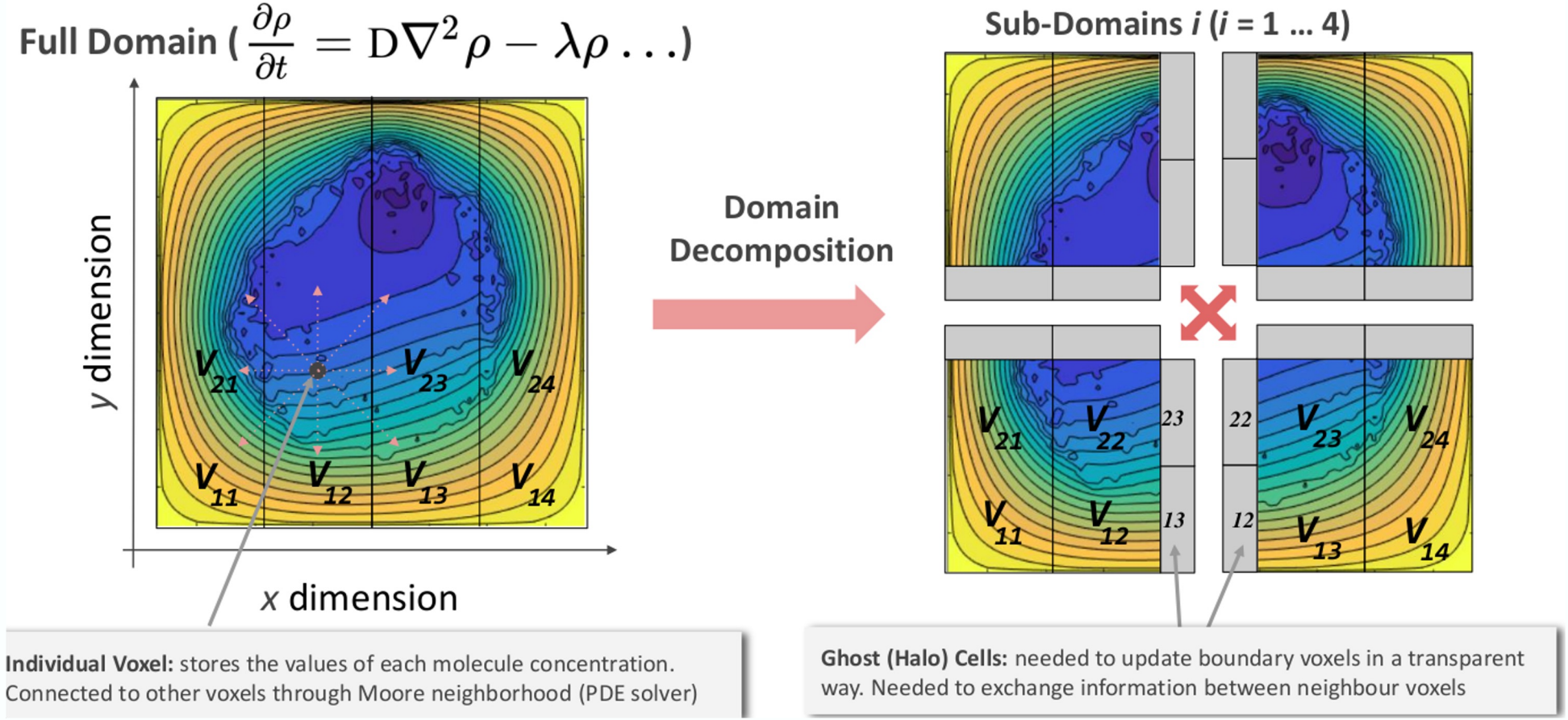
Message Passing Interface (MPI)

```c
#include <stdio.h>
#include <mpi.h>

int main(int argc, char** argv){
    int process_Rank, size_Of_Cluster;

    MPI_Init(&argc, &argv);
    MPI_Comm_size(MPI_COMM_WORLD, &size_Of_Cluster);
    MPI_Comm_rank(MPI_COMM_WORLD, &process_Rank);

    for(int i = 0, i < size_Of_Cluster, i++){
        if(i == process_Rank){
            printf("Hello World from process %d of %d\n", process_Rank, size_Of_Cluster);
        }
        MPI_Barrier(MPI_COMM_WORLD);
    }

    MPI_Finalize();
    return 0;
}
```

https://curc.readthedocs.io/en/latest/index.html

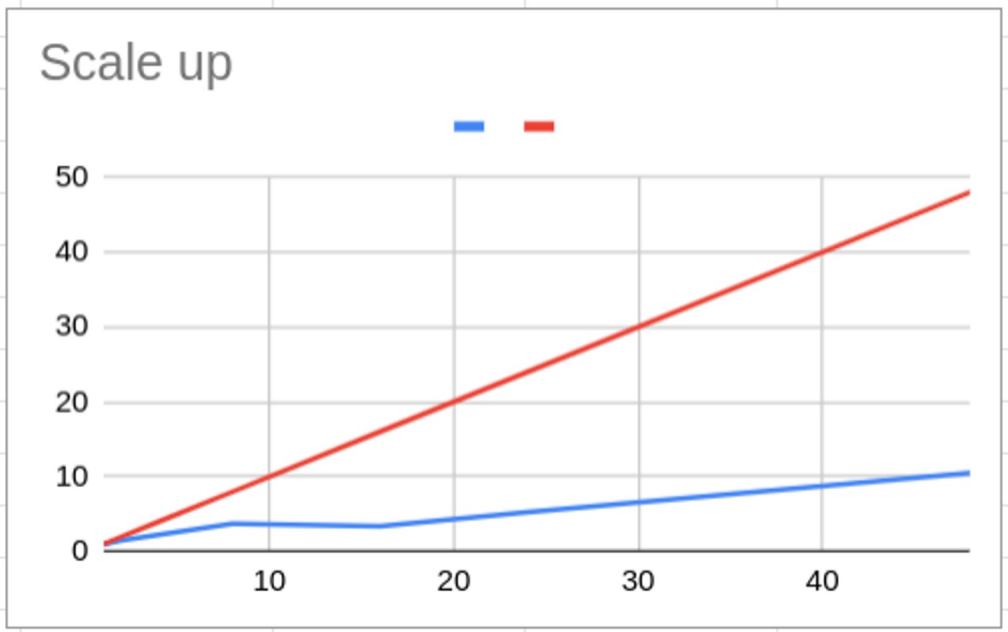
Refactoring strategies in PhysiCell

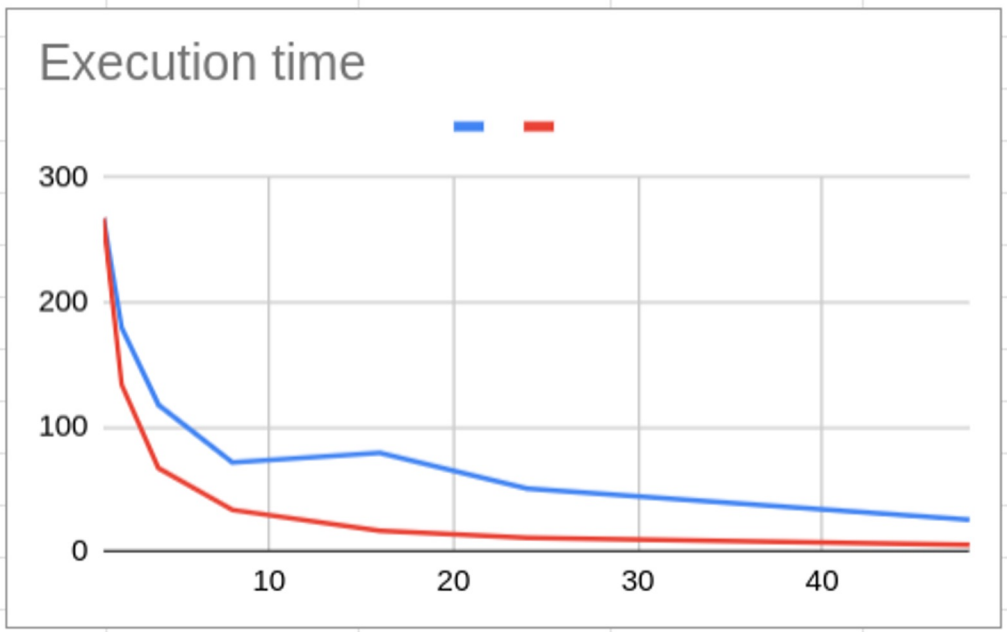
PhysiCell-MPI



Hands-on

		CORES						
		1	2	4	8	16	24	48
NODES	1	266.942	179.2124	117.6434	71.4096	79.2203	50.5011	25.387
	2	123.5726	85.8754	60.0800271	39.0463			
	4	99.2707	77.2388	56.7724				





THANK YOU

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