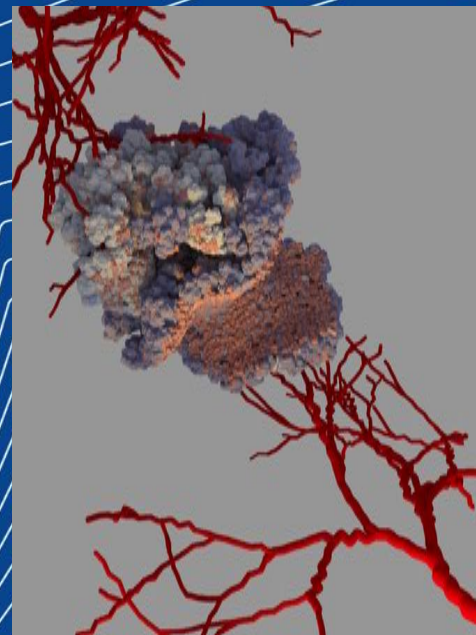


MULTISCALE MODELING: TUMOR DEVELOPMENT

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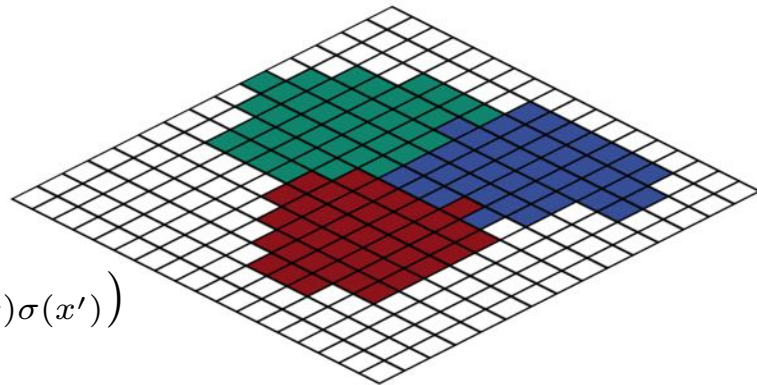


MULTI LEVEL – MULTI SCALE

Cellular Potts Model (microscale)

- Grid based cell dynamics simulation
- Graner, François; Glazier, James (1992)
- Metropolis Monte Carlo acceptance of new states based on H_{CPM}
- Mostly applied in 2D

$$\begin{aligned} H_{\text{CPM}} = & \sum_{\sigma \in \text{cells}} \lambda_V (V(\sigma) - V_0(\sigma))^2 \\ & + \sum_{\sigma \in \text{cells}} \lambda_S (S(\sigma) - S_0(\sigma))^2 \\ & + \sum_{x \in \text{voxels}} \sum_{x' \in \text{neighbors}} J_{\tau(\sigma(x))\tau(\sigma(x'))} (1 - \delta_{\sigma(x)\sigma(x')}) \\ & + \dots \end{aligned}$$



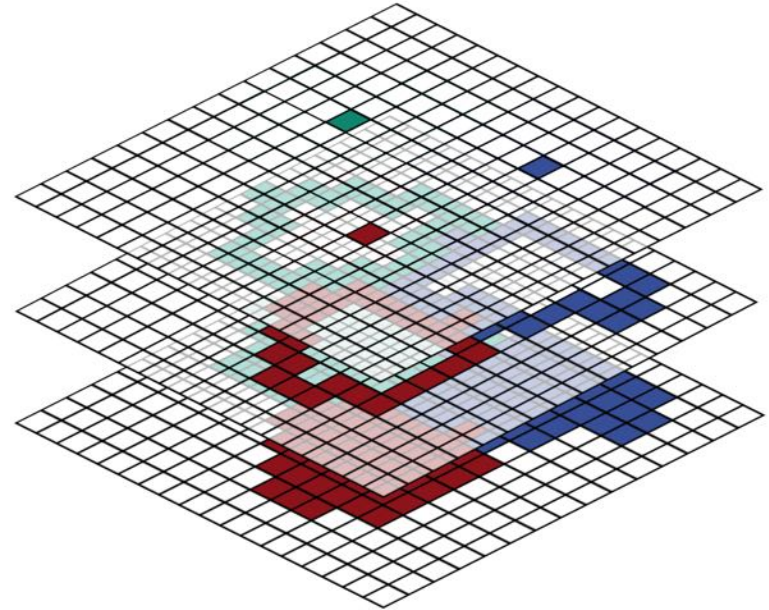
MULTI LEVEL – MULTI SCALE

Agent based (macroscale)

- Properties on cell level
- Signaling (drugs, nutrient)
- Processing of signals
- Cell division

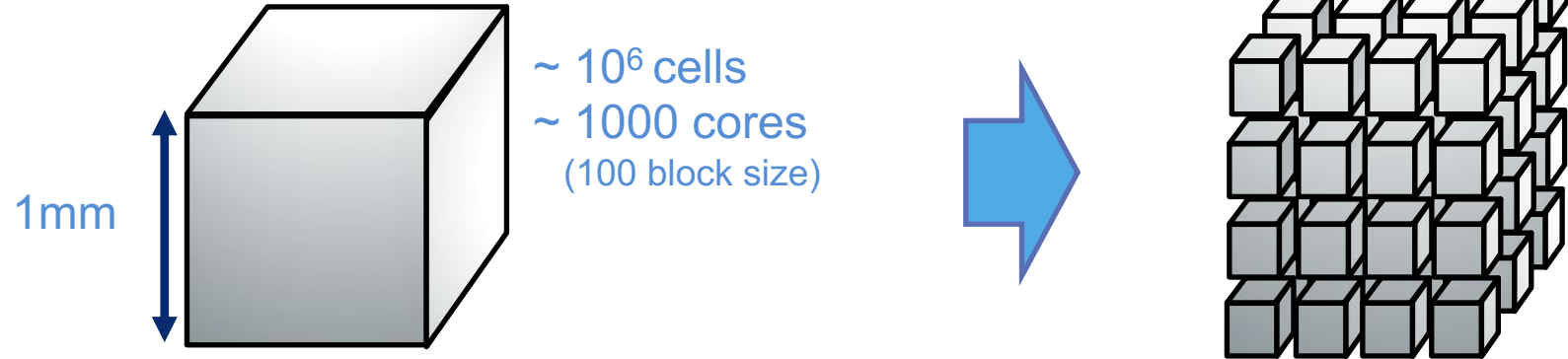
In between (mesoscale)

- Diffusion of signals
- According to the surface of cells

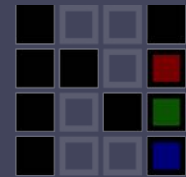
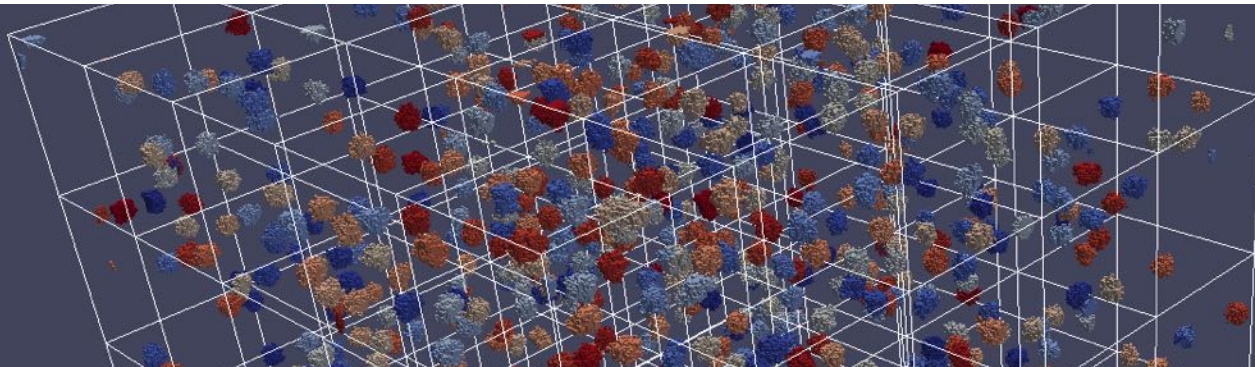


PARALLELIZATION

MPI parallelization in newly developed simulation framework



[Berghoff et al. "Massively parallel stencil code solver with autonomous adaptive block distribution." *IEEE Transactions on Parallel and Distributed Systems* 29(10) 2018.]

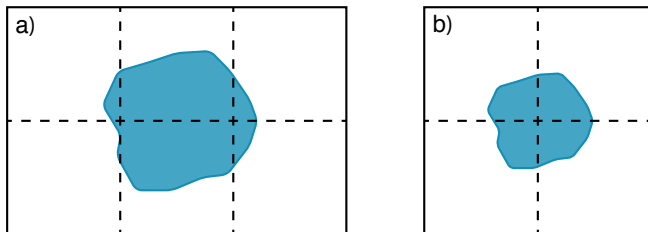


NASTJA

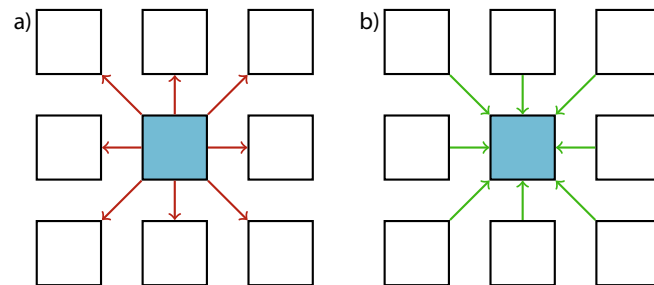
COMMUNICATION

Avoid global communication

- Halo transfer
 - six direct neighbors
 - up to 27 neighbors
- Cell properties
 - a) Global, if we can not locate a cell
 - b) Local, if we know a cell is only in the neighborhood



Only local communication

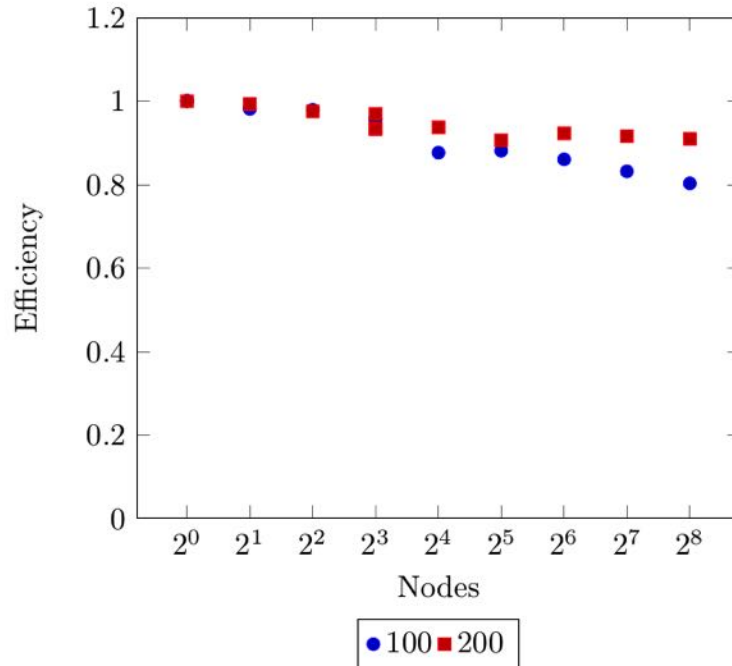


- Sending to and receiving from neighbors
 - Halo transfer
 - Cell properties

EXCELLENT SCALING

Summary of Cell Simulation in the NAsTJA-Framework

- Cell simulations
- Parallel up to 1 million cells – 1 billion DoF
- CPM with modular in energy contributions
- Modular actions
- Cell division
- Cell death
- General signaling

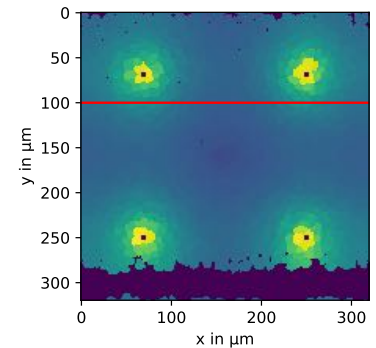
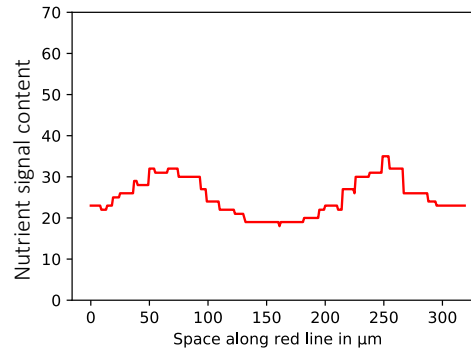
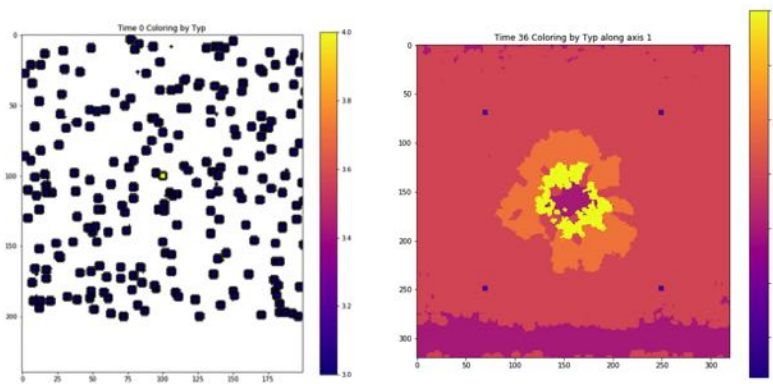
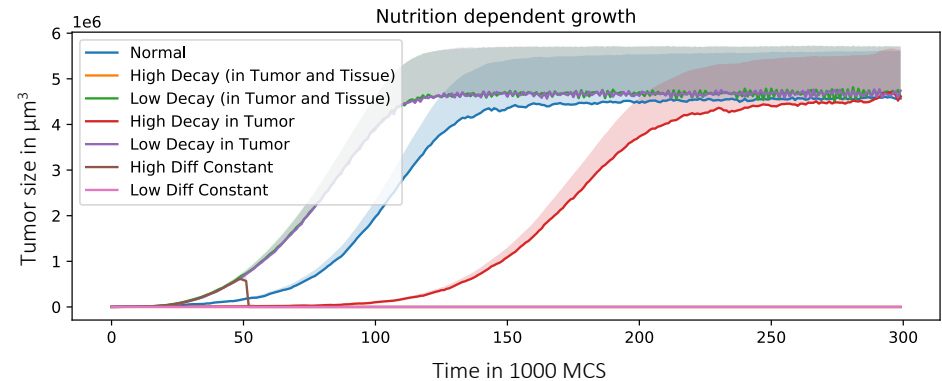


APPLICATIONS

MODELING TUMOR GROWTH

Nutrient transport

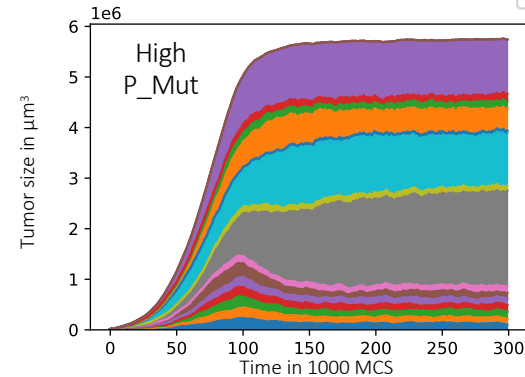
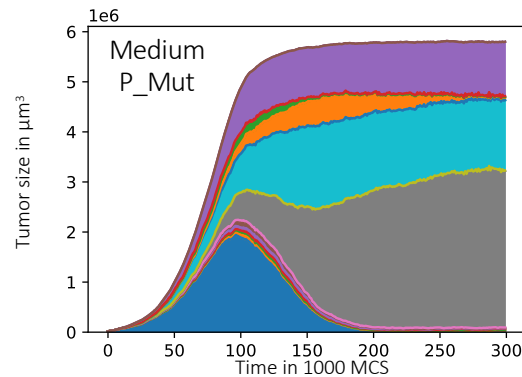
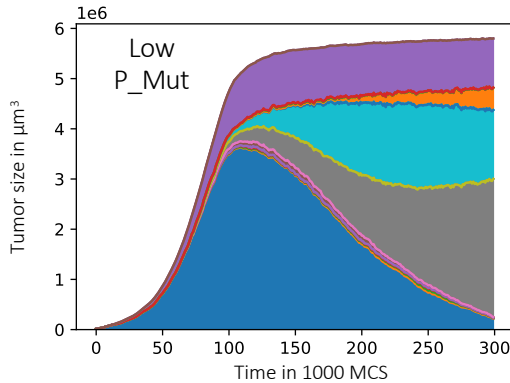
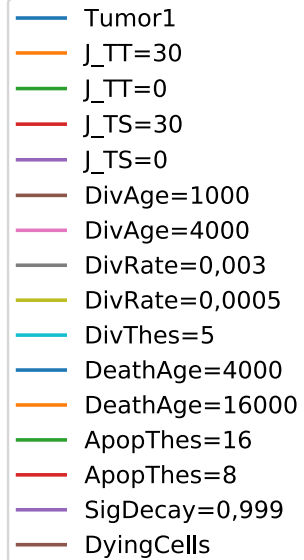
- Nutrient transport from bloodvessels
- Celldivision dependant on nutrition
- Necrosis can be induced



TUMOR HETEROGENEITY

Evolution of tumor cell type composition

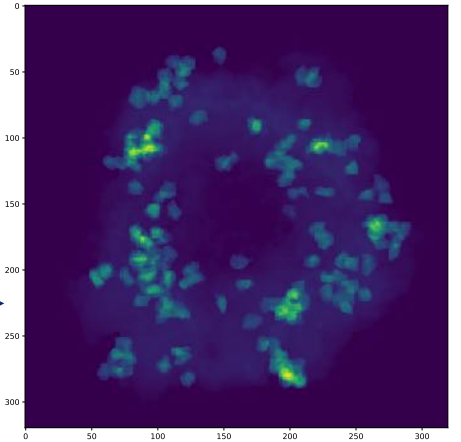
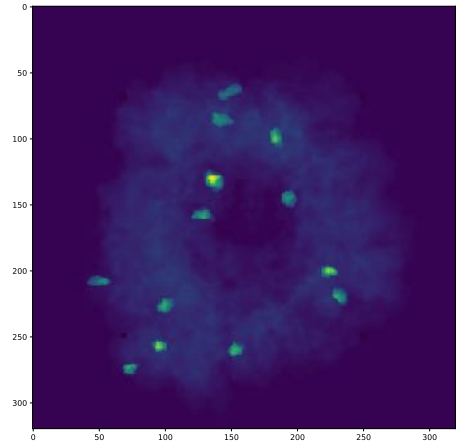
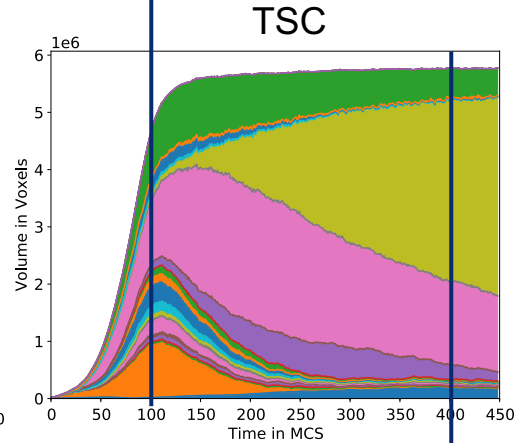
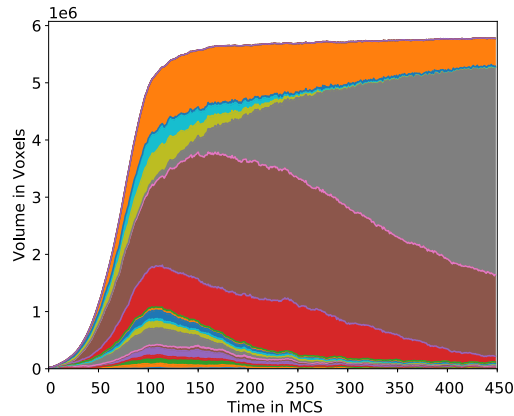
- N different tumor cell types with varying parametrization
- Mutation events occur at cell division
- Constant mutation probability between all cell types



TUMOR STEM CELLS

Evolution of tumor cell type composition

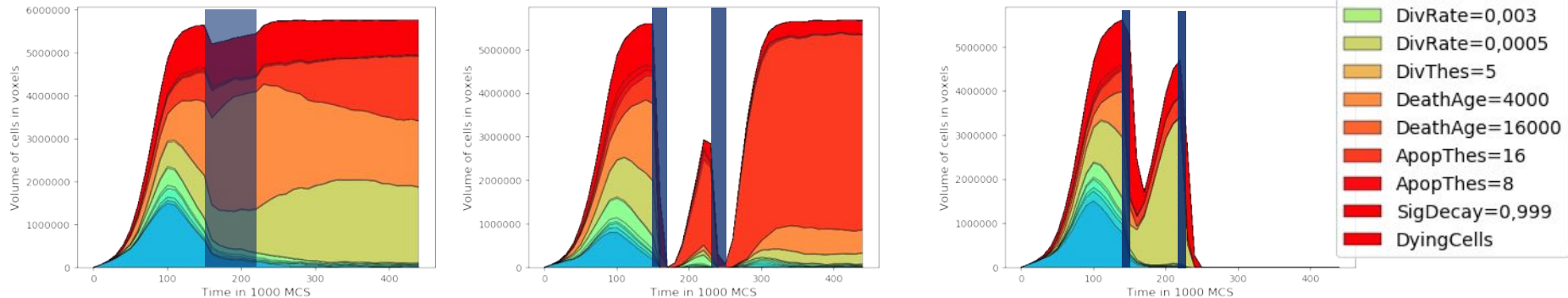
- Slower cell cycle
- Asymmetric division into tumor cell and TSC



TREATMENT MODELS

External suppression of cell division and death chemo- and radiotherapy

- Chemotherapy modeling
- Chemotherapy signal inhibits cell division
- Testing different treatment models and protocols

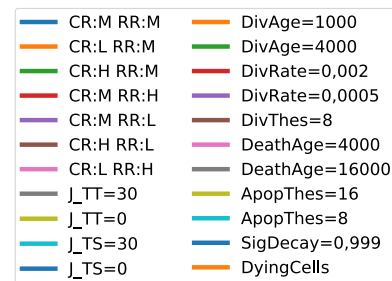
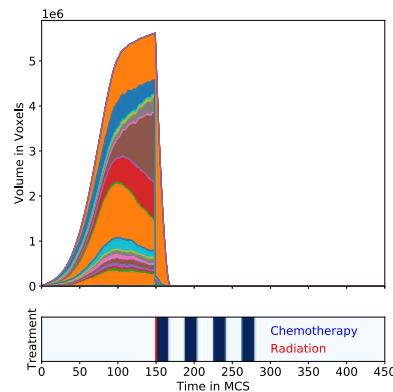
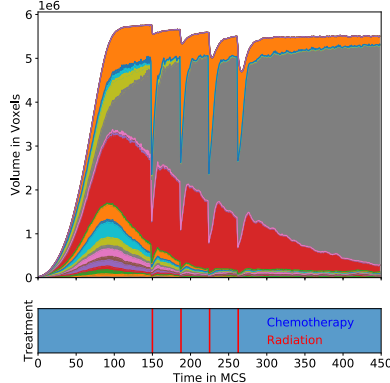
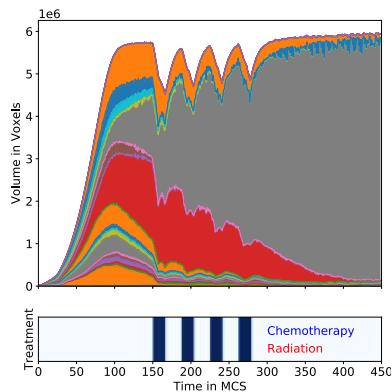


Chemotherapy

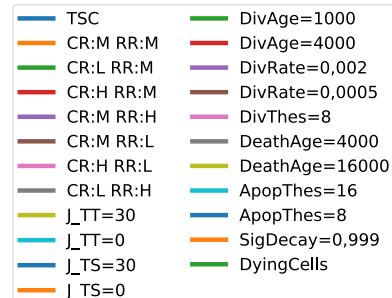
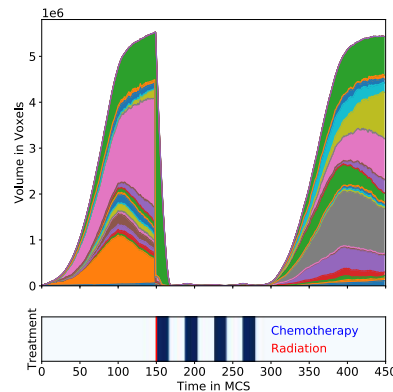
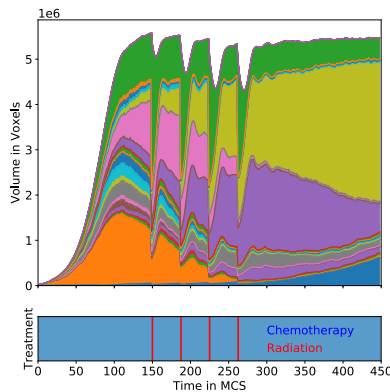
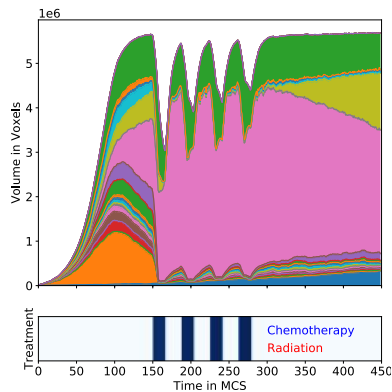
- Radiation induces cell death and alters division rates

TREATMENT RESPONSE

Heterogeneous
Tumor



Heterogeneous
Tumor + TSC

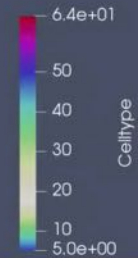
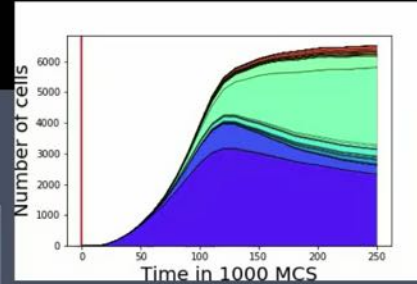
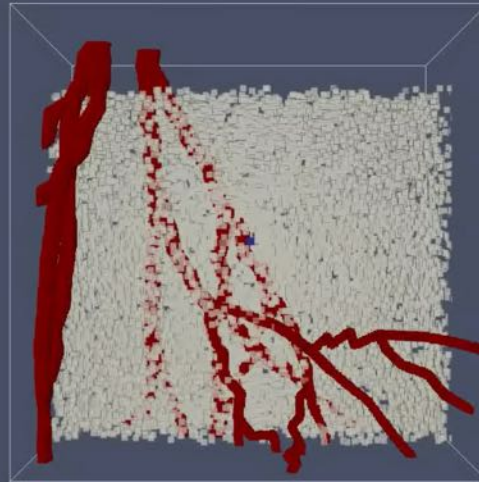


TUMOR HETEROGENEITY SIMULATION

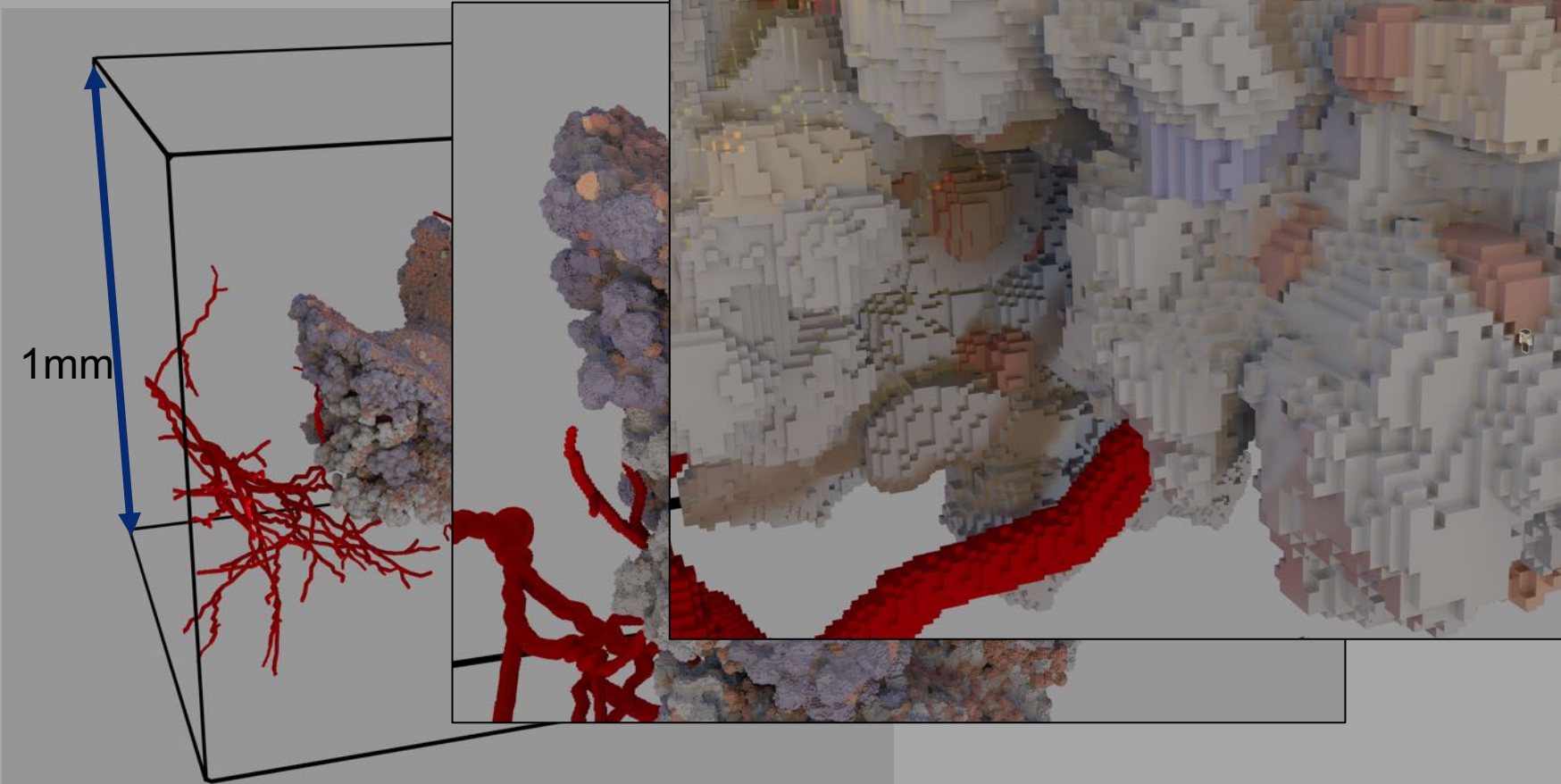
320³ Voxels

4 h runtime on
JURECA

Heterogeneity
enabled



LARGE SIMULATION

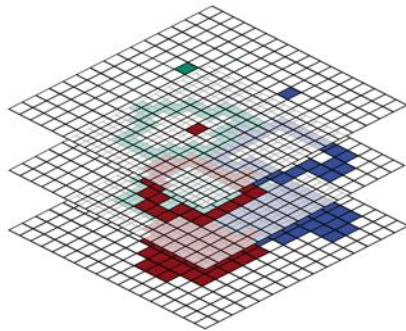


A

SUMMARY

Features

- Modular structure of the model and energy terms
- Excellent scaling -> 10^6 s of cells
- Multiscale: mm scale simulations at μm resolution
- Cell-to-cell signaling
- Agent based layer for cell properties



Applications

- Tumor development
- Heterogeneity
- TSC
- Treatment response

