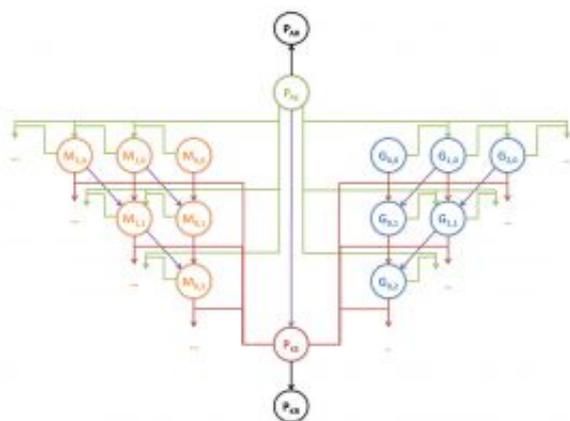
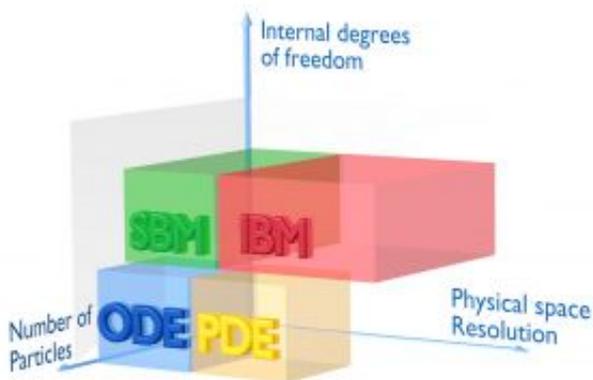


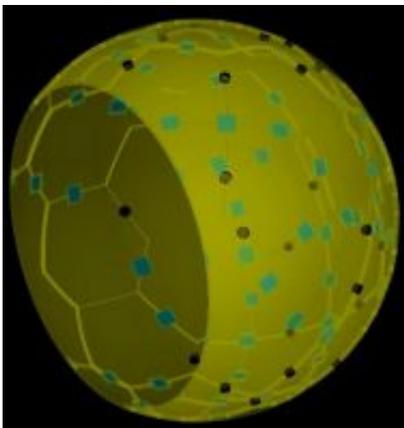
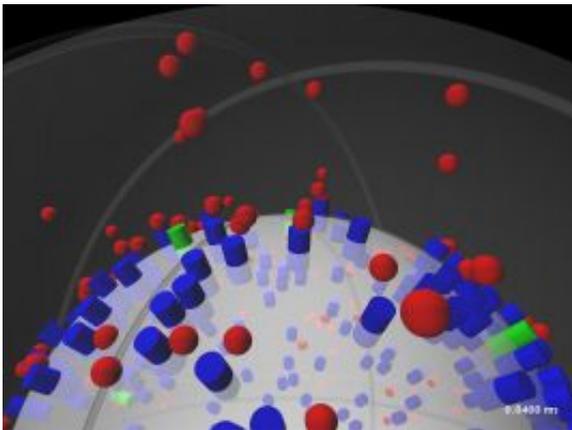
## Mathematical modeling and Computer Simulations of Dynamical Systems

Mathematical modeling is a common approach in various fields of science that aims to abstractly describe real processes in order to make relevant predictions and initiate new conclusive experiments. Since the parameters of mathematical models must be rigorously adjusted in order to make relevant predictions, quantitative characterization of image data is indispensable for constructing consistent virtual infection models. Thus, on the one hand image-based parameter estimation can save a lot of computational resources versus the adjustment of these values during numerous model simulations. On the other hand, for parameters that are not directly accessible in experiment, computer simulations of mathematical models can aid to predict the behavior of the complex biological system under various conditions that may not even be directly accessible in experiment.



Several modeling techniques exist that have the ability for spatio-temporal modeling of biological systems at different levels of complexity. The choice of the approach depends on the purpose of the model as well as on the type and amount of available image data. If the biological process under consideration involves

many constituents that allow modeling the system dynamics in a deterministic fashion, we apply differential equation models that are relatively easy to implement and demand only low computational costs in terms of simulation runtime and computer memory. However, in cases where individual entities and the stochastic nature of their interactions are important, state-based models are used. For instance, we introduced a state-based model for the whole blood infection by *Candida albicans* and quantified innate effector mechanisms by a rigorous parameter estimation using the method of simulated annealing based on the Metropolis Monte Carlo scheme. Going beyond state-based models, we implement agent-based models, for example, to simulate the early immune response of phagocytes against inhaled *Aspergillus fumigatus* conidia in human alveoli. Here, we also develop hybrid techniques to simulate the migration and interaction at the cellular level by agents and the secretion of cytokines by the partial differential equation of diffusion.



In summary, virtual infection models based on image-derived parameters are used to generate predictions that are not directly observable in the image data to initiate new conclusive experiments.