Hessisches Kompetenzzentrum
für Hochleistungsrechnen

Image Analysis and Calibration of High Dimensional Deformable Cell Models in Complex Geometries Using Advanced Interaction Schemes

Project Manager
Sascha Hauck

Principal Investigator
Prof. Dr. Ulrike A. Nuber

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Clusters
Lichtenberg II Cluster Darmstadt

Software
Python

Additional Software
C++, Cuda

Institute
Stem Cell and Developmental Biology, Self-Organizing Systems

University
Technische Universität Darmstadt

Introduction

Organ-like three-dimensional cell aggregates developed in the laboratory represent versatile cellular models for drug development and toxicology assessment and hold great promise for regenerative medicine. They have the potential to serve as an alternative to donated human tissue and to reduce animal testing. Already the smallest functional units in tissues of the human body, such as hepatic lobules, are of diameters larger than one millimeter. Thus, the need of Organ-like three-dimensional structures of sizes in the centimeter regime arises. One of the greatest challenges in this regard is the vascularization of the emerging structure for the cells to survive. This project relies heavily on parameter and morphology studies. These are not only too expensive but also too cumbersome to conduct in the laboratories of the participating groups.

Methods

To tackle this problem we build a digital-twin of the cell-cluster. Therefore, we develop a non-trivial extension to the known deformable-cell model (DCM) that incorporates not only newly modeled versions of known interaction forces but also deformation, growth, cell division and lysis. We further included regions of low interest that use the reduced representation

known as the center-based model (CBM). These regions are predefined and resemble low-resolution regimes, thus speeding-up the process without compromising the morphology of the regions of interest. Since we are working with two different models, the “Handshake” between these two need to be modeled and calibrated carefully to resemble the structures and exhibit essential features of its biological counterpart.
The DCM is built through a triangulation of a cells surface. The finer the resolution, i.e. the more nodes per surface area, the more computational resources are needed. Since most of the forces rely on node-to-node interactions, they can be calculated efficiently using parallel programming. To calibrate the system, we extract crucial parameters from 4D image data. Thus, a sophisticated pipeline was built that incorporates image pre-processing to improve image quality. Subsequently the images are used for cell-tracking. All steps rely heavily on Deep-Neural Networks, mostly the three-dimensional version of the U-Net architecture as well as Siamese-Networks.

Results

The non-trivial force-extensions to the deformable cell model as well as incorporating cell-division and additional external structures resembling blood vessels was successfully reached. First parameter-studies were conducted. Furthermore, the access to the HPC allowed us to develop and test the first versions of our needed image-analysis pipeline.

Discussion

This result is an intermediate step to our final goal of building a digital-twin of the one cubic centimeter cell cluster that is currently developed by the other parties within the FLOW FOR LIFE project. Even though the fundaments of all the different building blocks of the programming project are working on their own, they need to be deeply intertwined. This is a key aspect of the work on this part of the project over the coming months.

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