Sim4Life: A Medical Image Data Based Multiphysics Simulation Platform for Computational Life Sciences

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Introduction: Computational life sciences (CLS) have special requirements that are not well covered by existing commercial simulation platforms. This includes the ability to perform simulations based on medical image data (to define the model geometry, boundary conditions and material parameter distributions), to handle large, complex, realistic and often noisy anatomical models (e.g., generation of high quality meshes based on segmentation label fields), to jointly visualize and post-process simulation results and measurement data (e.g., imaging data), and more. Solvers have to be optimized for the physics of living tissue (e.g., perfusion and thermoregulation models in tissue heating simulation, acoustic propagation and focused ultrasound), and special solvers for biological processes are needed (e.g., EM-neuron interactions and tumor growth models). A dedicated multiphysics simulation platform for CLS has been developed: Sim4Life.

Methods: The platform covers all components from medical image segmentation, over the provision of detailed anatomical models, to geometrical modeling, simulation setup, problem discretization, solving, post-processing, visualization, scripting, and application development.
Fundamental to the concept is the rigorous modularity, the cross-platform compatibility of core components, and the strong integration of Python scripting [1] and vtk [2]. All functionalities are interfaced such that in addition to GUI-based interactions they can be accessed at a high-level through Python scripts. Major components are encapsulated as vtk filters and data can be passed in vtk formats (as well as other open formats such as XDMF [3]), post-processed, and visualized using the full vtk functionality enhanced by a self-developed OpenGL visualization engine. A python interfaced GUI SDK allows the flexible extension of the provided GUI with user-defined plug-ins or the implementation of own applications using the building blocks provided by Sim4Life. Modeling can thus be performed either within the GUI, or through user-generated Python scripts, or in a dedicated user-defined application created using the building blocks from Sim4Life.
For simulations involving anatomical models, either the existing Virtual Population [4] models can be used or new models can be segmented based on medical image data (e.g., MRI, CT). For this a dedicated software was developed that allows coupling highly automated (e.g., improved k-means-based clustering, competitive fuzzy connectedness) with highly interactive (e.g., live wire, interactive watershed transformation, brush) segmentation methods, and that offers filters for noise reduction, hole and island removal, interpolation, etc. The resulting label fields can be either transformed into triangulated surfaces (including volume preserving smoothing and feature preserving simplification) or directly used to generate optimized, unstructured tetrahedral meshes with topologically conforming tissue interfaces (using an octree-based mesher). Posing and morphing functionalities for the anatomical models are available. For simulations involving devices (e.g., pacemaker), either the CAD files can be imported or geometrical modeling can be used together with the anatomical models.
Multiple voxelers and meshers can be used to generate rectilinear meshes and optimized, conformal, high quality unstructured tetrahedral meshes from CAD or segmentation data.
A multitude of solvers for electromagnetism (harmonic and transient FDTD as well as various quasi-static solvers), flow (FEM and pressure-correction FVM), acoustics (full wave FDTD), temperature (FDTD and steady-state), convection-reaction-diffusion (FEM), mechanics (FEM, currently only small-strain), pipeline networks (for vasculature mostly) and neuron dynamics (incl. interface to NEURON [5]) are available. Solvers for structured and unstructured meshes also exist. All solvers are optimized for simulations including complex, inhomogeneous tissue distributions and they contain special physics/biology models of particular relevance to simulations in the human body (e.g., various perfusion models). Currently, only weak (iterative) coupling of solvers is supported. Most solvers support high performance computing (HPC) on various platforms. This includes hardware acceleration

(single and multi-GPU) as well as parallelization (MPI, OpenMP). The parallelization is enabled by using PETSc [6], which provides support for a large range of hardware architectures. Beside the multiple preconditioners offered by PETSc, additional preconditioners (e.g., Schur complement, algebraic multigrid) are available. A generalized framework has been developed that can be used to rapidly implement new HPC enhanced FEM solvers by simply overloading the coefficient calculation routines.

The platform is complemented by post-processing tools for visualization and analysis, as well as an optimization and sensitivity analysis framework.

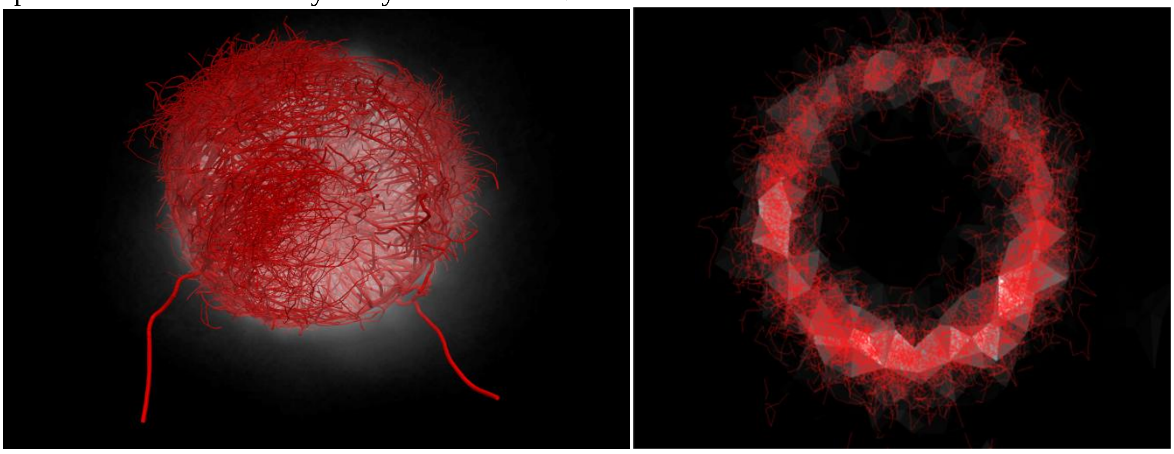

Figure 1: Simulation tumor growth (see text): (left) vasculature tree and signaling molecule concentration, (right) cross-section showing the necrotic core.

Results: The main focus areas are design and optimization of medical devices, basic research (investigation of mechanisms/interactions), safety assessment, and (patient-specific) treatment planning. The platform has been applied to a large number of relevant problems. Four illustrative examples will be presented here:

Hyperthermia cancer treatment planning: A comprehensive hyperthermia treatment planning platform has been implemented. RF deep hyperthermia treatment focuses EM energy from an antenna array into the tumor to heat it, which results in preferential killing of the tumor cell. Patient image data are segmented, a script-based wizard then helps positioning the patient model in a (phased antenna array) applicator model and takes care of material assignment, discretization, simulation, optimization and report generation. EM simulations are performed for each antenna using the FDTD solver, the steering parameters are optimized, e.g., with a genetic algorithm *(Figure 3)*, and the resulting transient heating (considering thermoregulation) is calculated and translated into a tissue damage (Arrhenius model) or thermal dose prediction (CEM43). Real time re-optimization based on patient feedback has been achieved. The platform has also been employed to develop a novel head and neck applicator *(Figure 3)* and to assess the impact of metallic implants. It was validated using dosimetric measurements and clinical information.

Tumor growth modeling: The growth of a tumor has been simulated considering the interplay between cell proliferation, apoptosis, growth factors, signaling molecules, oxygen, vasculature growth and mechanical stress. This involved a coupled system of convection-reaction-diffusion equations and mechanical simulations performed using the FEM solvers and a pipeline solver. The model correctly reproduces tumor features such as necrotic core, brush shaped vasculature capsule *(Figure 1)* or the incident angle of exophytic tumors. It has been used to study the impact of various treatment approaches such as the administration of vasculature disruptive agents or hyperthermia.

Magneto-hemodynamic effect as a biomarker: Blood flow inside a strong magnetic field (e.g., MRI magnet) leads to surface potential changes that can be measured as changes in an electrocardiogram. To investigate whether such changes can be used as biomarkers for blood flow features (e.g., to measure cardiac output or recirculation), simulations based on medical image data from a volunteer have been performed and compared to experimental measurements. Both the geometry and the inflow boundary conditions have been extracted from MRI measurements and used to perform flow simulations (FEM with dedicated Schur-complement preconditioner for incompressible flow) of the aorta and vena cava *(Figure 2)*. The induced surface potential change could then be determined using the low frequency EM solver *(Figure 2)* and correlated with flow features.

Physics based morphing of anatomical models: The Virtual Population anatomical models have been parameterized with regard to fat content by performing mechanical simulations: the bones were treated as rigid, while the fatty tissue was assigned a growing or shrinking force. The remaining soft tissues deformed passively. This approach required mechanical simulations (linear, small-strain FEM) involving over 100,000,000 elements (meshed with CGAL or a cut-cell octree based mesher) that could be efficiently executed using the HPC enabled solvers (see as well Figure 2 in second abstract). These parameterized models extend the range of the population covered by the Virtual Population models and are valuable, for example, when assessing exposure safety of the general public.

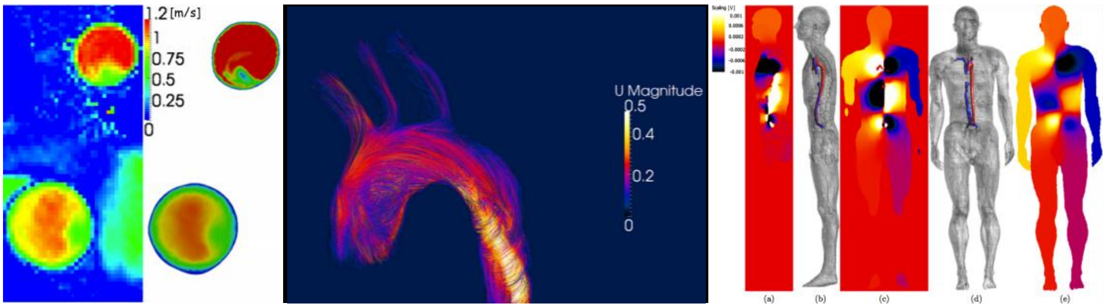

Figure 2: Simulation of magneto-hemodynamic effect (see text): (left) image based inflow boundary conditions, (center) snapshot of flow in aortic arc, (right) resulting surface potential change.

Conclusions: A multiphysics simulation platform optimized for computational life sciences has been developed, with device development and optimization, safety assessment, basic research and treatment planning as primary application areas. It strongly supports medical-image-data-based simulations and simulations involving complex anatomical models. HPC-enabled solvers allow the simulation of large, realistic problems on a wide range of computational architectures. The various solvers (neurons, ultrasound, thermal) have been specially developed for simulations in living tissue. The platform integrates vtk visualization and Python scripting and allows the user to create his own applications or plug-ins. The Sim4Life platform has been employed to tackle a large range of relevant problems.

Acknowledgements: Various components of this work have been supported by different organizations: CTI, SNSF CO-ME, SciEx. Various groups have contributed to the development: ETHZ, Erasmus MC, FDA, MIT, EPFL, CABMM, CSCS Manno, University of Zurich, USZ, SPEAG, ZMT.

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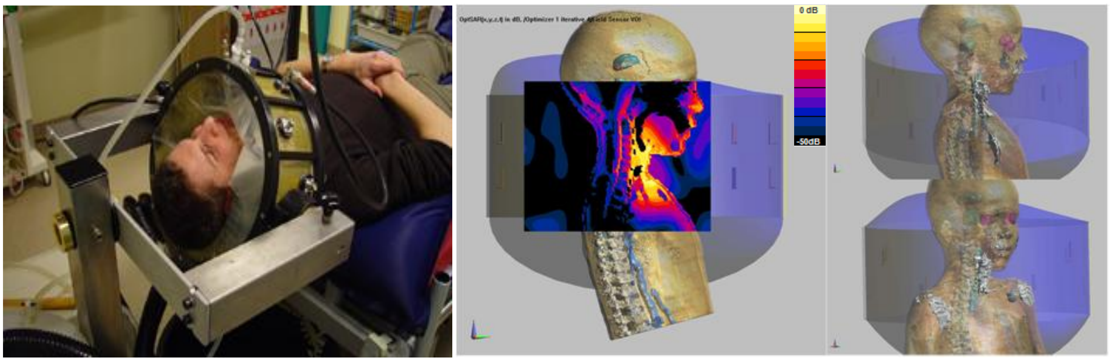

Figure 3: Hyperthermia treatment of cancer (see text): (left) head and neck prototype applicator developed using simulations (photo courtesy of the Hyperthermia Unit, Erasmus MC, Rotterdam), (right) optimized EM energy (SAR) distribution and temperature iso-surfaces.