zurich med tech

In Silico We Trust

sim4life

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In Silico ...

The digital revolution is extending the frontiers of medicine and medical technology. Computer modeling and simulation (CM&S), or *in silico* technologies, merge computational tools with biology to intuitively, precisely,and reliably perform complex analyses of life sciences applications. With this emerging paradigm, experimental manipulations that are infeasible or prohibitively complex to conduct in real-life experiments can be created while maintaining superior experimental control: the perfect complement to *in vivo* and *in vitro* studies.

ZMT provides *in silico* solutions to the medical device and life sciences industries. Our comprehensive simulation platform, *Sim4Life*, provides a powerful 3D validated biological and anatomical modeling environment for optimizing the effectiveness and performance of medical devices, improving patient safety, and discovering potential new treatments. Built from the ground up, *Sim4Life* provides smooth and fully automated or customizable workflows for applications ranging from exploratory research and medical device development to regulatory documentation for clinical trials and device certification.

... we trust

Our software tools are thoroughly and continually verified to ensure their reliability and performance as they evolve. We place high emphasis on the validation of our computable, functionalized models and medical device and life sciences applications. ZMT also provides test systems for experimental validation procedures that support complex requirements with software tools optimized for test and measurement systems.

At ZMT, we leverage the combined strength of our expertise, experience, cost-effective solutions, and commitment to long and fruitful client relationships to guide you through the long and complex regulatory submission process.

Posable Anatomical Models

ViP 3.x
Virtual Population

ViA 1.x
Animal Models

3rd-Party Models

Physics Models

P-EM-FDTD
Electromagnetics Full Wave Solvers

P-EM-QS
Quasi-Static Electromagnetics Solvers

P-THERMAL
Thermodynamics Solvers

P-FLOW
Fluid Dynamics Solvers

P-ACOUSTICS
Acoustics Solvers

Tissue Models

T-NEURO
Neuronal Dynamics Models

T-CEM43
Tissue Damage Model

Intuitive GUI and Workflow

iSEG
Medical Image Segmentation Tool Set

MODELER
Advanced Modeling Tool Set

MESHER
Robust, Effective Meshing

OPTIMIZER
Multi-Parameter Multi-Goal Optimizer

SWEEPER
Fully Configurable Parameter Sweeps

ANALYZER
Versatile Postprocessor and Analyzing Tool Set

PYTHON
Control Via Python Scripting

Licensed Modules

MRI
- IMANALYTICS
- M-MUSAIK
- M-TxCOIL
- M-BCAGE
- M-SYSSIM
- M-GRAD
- M-IMSAFE

MODELER
- M-POSER
- M-REMESH

CALCULATORS
- M-PPCALC
- M-DISPFIT

PROCESSING
- M-MATCH
- M-TALATLAS
- M-MBSAR

IMPORT
- M-HUYGENS
- M-IMG
- M-VOX

High Performance Computing Auto-Scheduler & Control

ARES

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The Core:
Computable Human Phantoms

At the core of *Sim4Life* is a comprehensive set of computable human phantoms empowered by the most powerful physics solvers and the most advanced tissue models that provide a realistic biological and anatomical environment for conducting fundamental mechanistic studies, testing the effectiveness and safety of medical devices and treatments, and supplementing clinical trials. Based on the Virtual Population ViP 3.x models of the IT'IS Foundation at ETHZ (www.itis.ethz.ch/vip), the computable human phantoms are functionalized for prediction of real-world biological and physiological phenomena for any defined patient population. All tissues are linked to a continually updated properties database.

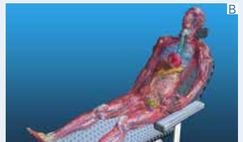
The powerful *Sim4Life* meshers allow high-fidelity discretization of the complex computable human phantoms combined with any implant or external device.

A complementary interactive morpher allows the demographic coverage of the parameterized anatomical models to be extended, e.g., to explore underrepresented or pathological anatomies in clinical trials. A flexible physics-based poser is also included with the models.

Physicians and biologists rigorously validate the models and the associated material database. Comprehensive documentation for all natively supported computable human phantoms is available.

All Virtual Population (ViP) models are natively supported with full resolution and do not require simplification.

A The Poser allows for easy and realistic postural manipulation, e.g., holding a phone in an anatomically correct position.
B Posed in a sitting position.
C Pig model and other anatomical models can be imported without reducing complexity.



Electromagnetics Full Wave Solvers

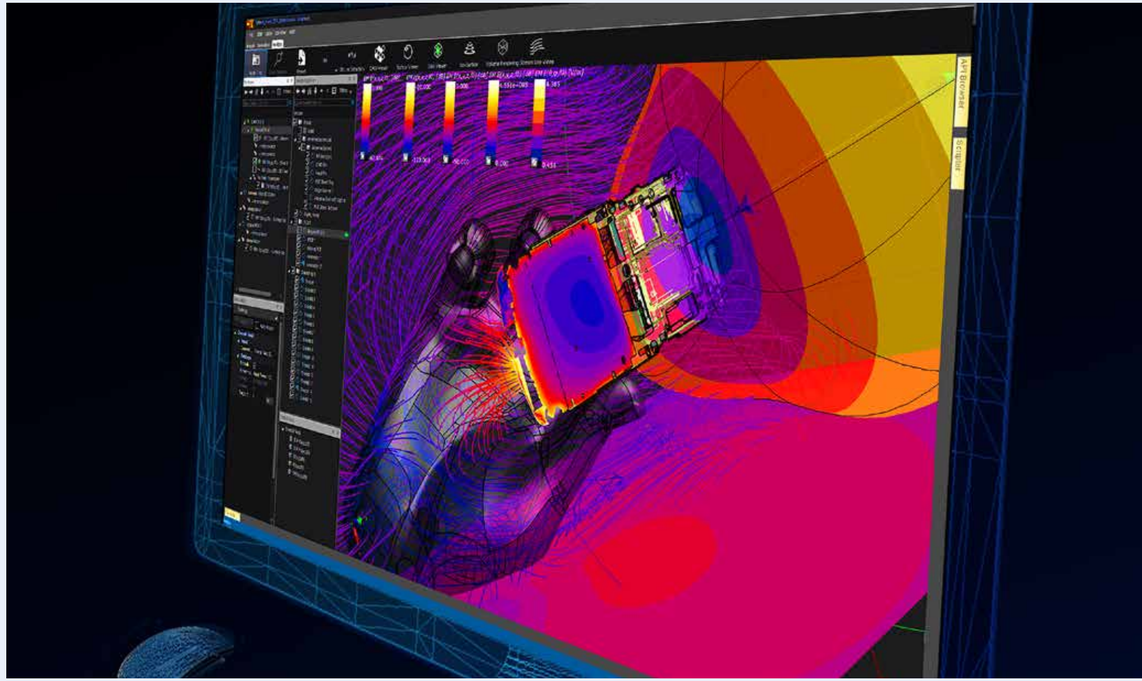
The Electromagnetics Full Wave Solvers (P-EM-FDTD) enable accelerated full-wave, large-scale EM modeling (>billion voxels) with Yee discretization on geometrically adaptive, inhomogeneous, rectilinear meshes with conformal sub-cell correction and thin-layer models, with support for dispersive materials. The solver includes a unique adaptive subgridding algorithm (from Acceleware) that facilitates the highest possible effectiveness in local mesh refinement.

Optimal simulation speed is achieved with native GPU and MPI accelerations, which were developed by our team who first introduced EM accelerated solvers together with Acceleware in 2006.

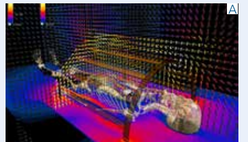
The unique bidirectional Huygens box approach overcomes the difficulties associated with models that extend across multiple scales and require widely varying resolutions.

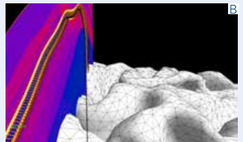
These solvers, the most frequently applied of their kind in near-field dosimetry, have been extensively verified and documented according to the IEEE/IEC 62704-1 standard as well as validated by comparisons with measured data (>200 publications). Comprehensive documentation is available for *Sim4Life*.

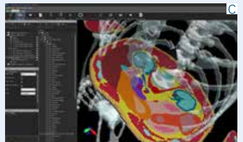
Near-field and over-the-air optimization of complex transmitters for handheld or body-mounted devices.



A MRI birdcage design: analysis of load dependence.
B Evaluation of an MRI-safe DBS implant.
C Fast and accurate rectilinear discretization of an anatomical human model.







Quasi-Static EM Solvers

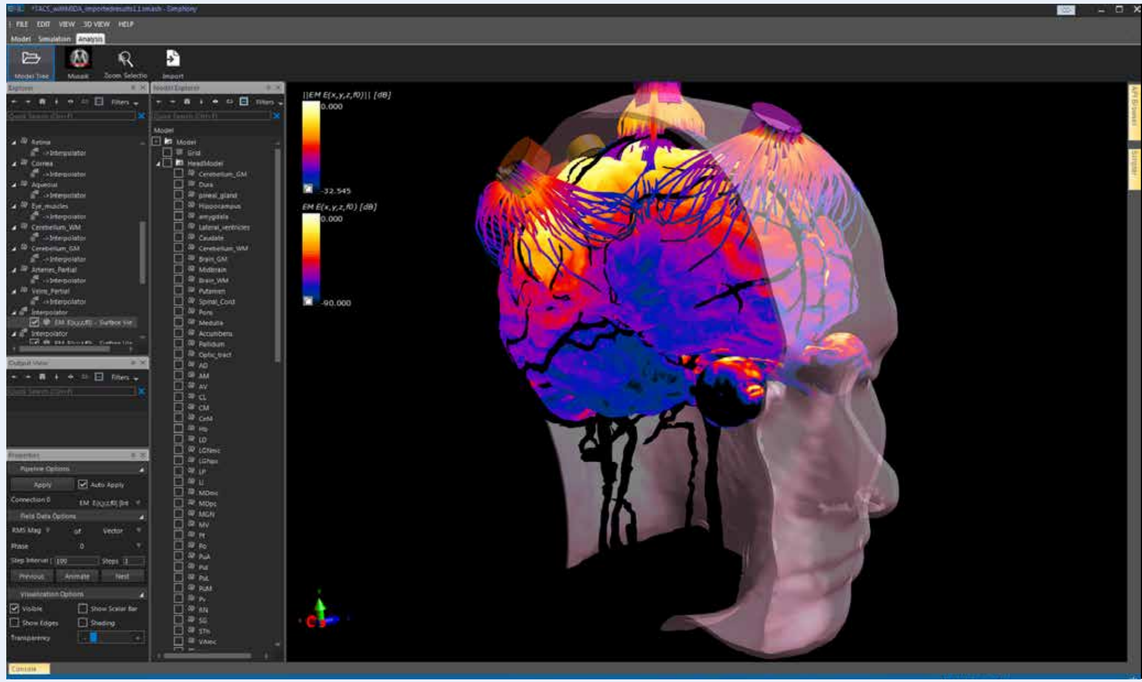
The Quasi-Static Electromagnetic Solvers (P-EM-QS) enable the efficient modeling of static and quasi-static EM regimes by applying the finite element method on graded voxel meshes. The solvers address the most challenging low frequency problems at the cutting edge of medical and EM compliance applications, e.g., simulations of EEG, MRI gradient coil fields, transcranial magnetic or current stimulation, and deep brain and spinal cord stimulator implants.

Each solver is optimized for a different approximation of Maxwell's equations, offering improved speed, convergence, and accuracy for a wide range of scenarios.

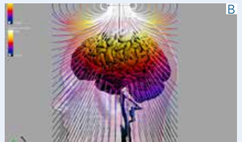
Measured data and user-defined field or current distributions can be used as sources.

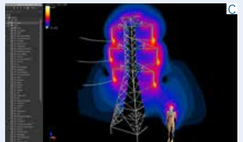
The P-EM-QS solvers are verified and validated, and the uncertainties have been quantified with analytical and full-wave solutions and by comparison with measurement data. Comprehensive documentation is available for *Sim4Life*.

Analysis of phosphene generation by transcranial alternating current stimulation.



A Gradient coil design and optimization.
B Assessment of nerve excitation during transcranial magnetic stimulation.
C Exposure evaluation of high power systems during maintenance.





Thermodynamics Solvers

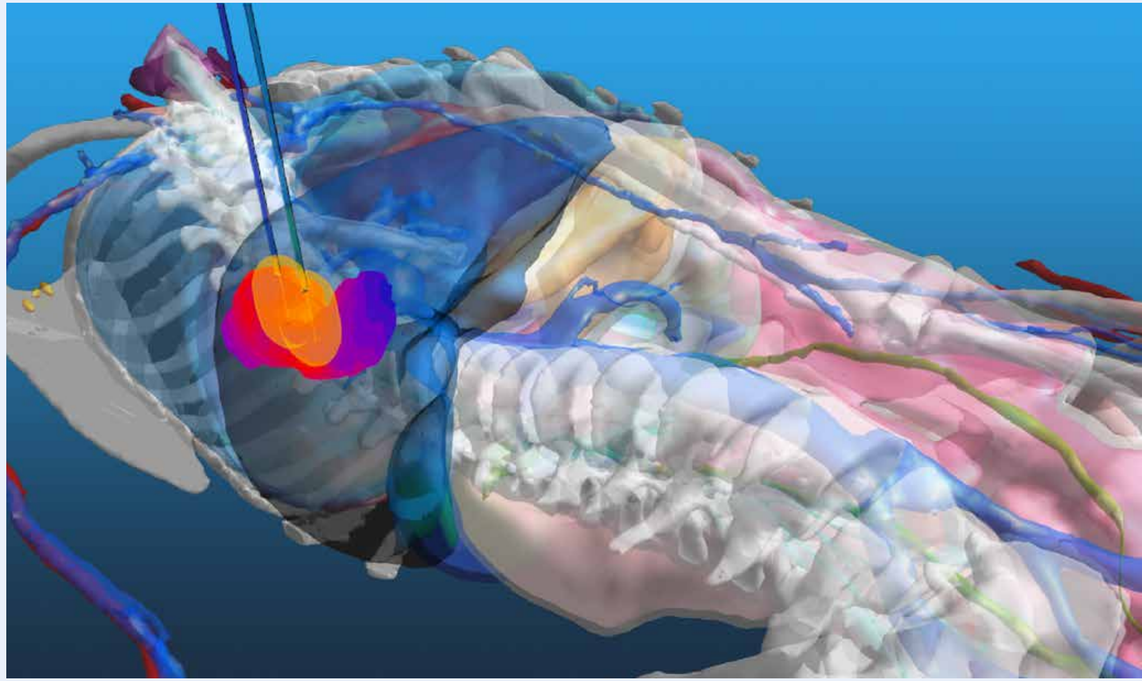
The Thermodynamics Solvers (P-THERMAL) enable the modeling of heat transfer in living tissue with advanced perfusion and thermo-regulation models. The two solvers adapted from SEMCAD X are based on 1) the finite-difference time-domain solver with conformal surface correction and 2) a steady-state finite volume solver to support adaptive rectilinear meshes and arbitrary active domain shapes.

The solvers allow for the coupled simulation of local vascular effects with discrete networks (1D trees) and, in the near future, computational fluid dynamics (CFD) results.

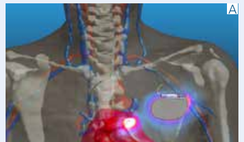
Exclusive thermal damage and effect quantification models, e.g., T-CEM43, are included.

The P-THERMAL solvers have been extensively verified and validated by comparison with analytically solvable cases, experimental measurements under controlled conditions, and *in vivo* measurements. Comprehensive documentation is available for *Sim4Life*.

Treatment planning for liver RF ablation (SAR, CEM43 thermal tissue damage assessment).



A *In vivo* temperature evaluation of RF-safe pacemakers.
B Optimization of liver tumor FUS ablation with breathing motions considered.
C Optimized positioning and steering of hyperthermia applicator arrays.



Fluid Dynamics Solvers

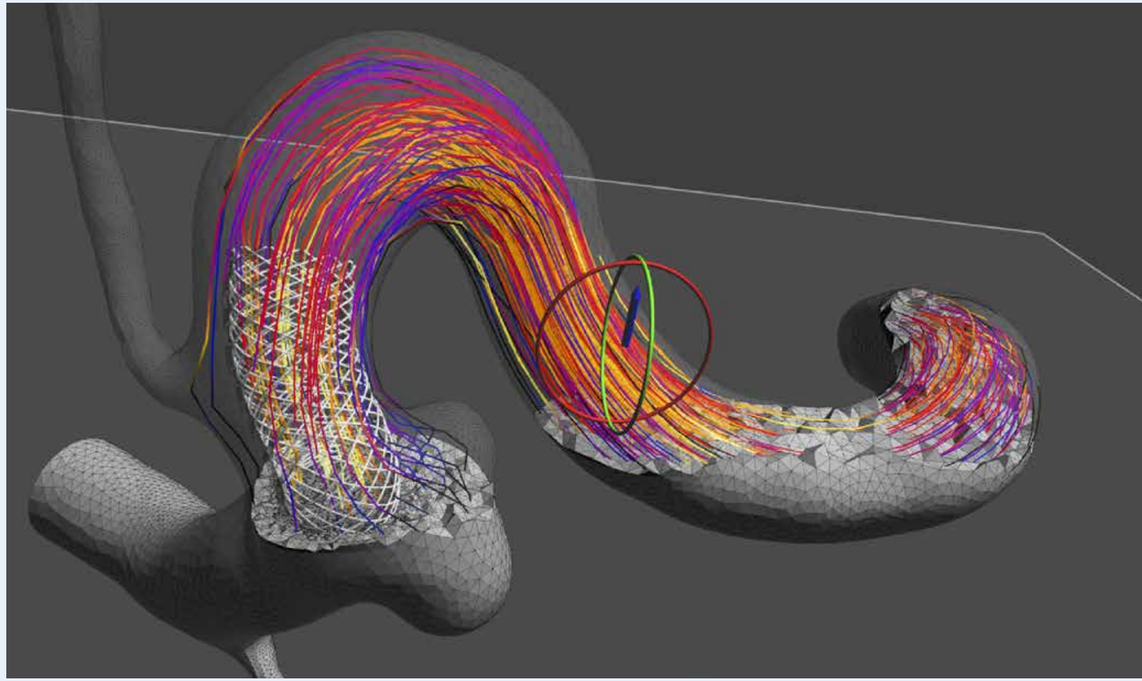
The high performance Fluid Dynamics Solvers (P-FLOW) facilitate the modeling of realistic physiological and pathological biofluidic scenarios in the presence or absence of vascular implants. Stationary and transient Navier-Stokes and Stokes equations are efficiently solved with either a finite element method with Schur complement preconditioning, adaptive time-stepping, and tunable stabilization or a finite volume method based on a smoothed pressure correction algorithm. Both solver types rely on platform-independent fast parallel processing, runtime solver monitoring, and advanced convergence criteria.

P-FLOW includes built-in general-purpose mesh generation tools for complex domain discretization.

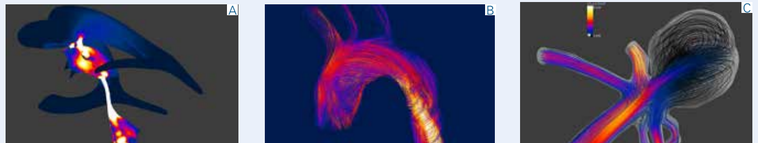
A set of standard boundary conditions and specialized boundary conditions for realistic blood flow modeling (e.g., developed flow, Windkessel model) can be applied and arbitrarily transiently modulated. Initial conditions based on experimentally measured data can be imposed. Easy extraction of key parameters like wall shear stress and powerful visualization tools complement the intuitive and efficient workflow.

The solvers are comprehensively and continually verified by comparison with analytical solutions for selected problems and benchmark cases. Detailed documentation is available for *Sim4Life*.

Blood flow and wall shear stress (WSS) as a function of flow diverter stent placement.



A WSS distribution within the choroid plexus of the cerebral ventricular system.
B Simulation of aortic flow for the investigation of the magneto-hemodynamic effect.
C Analysis of an aneurysm.



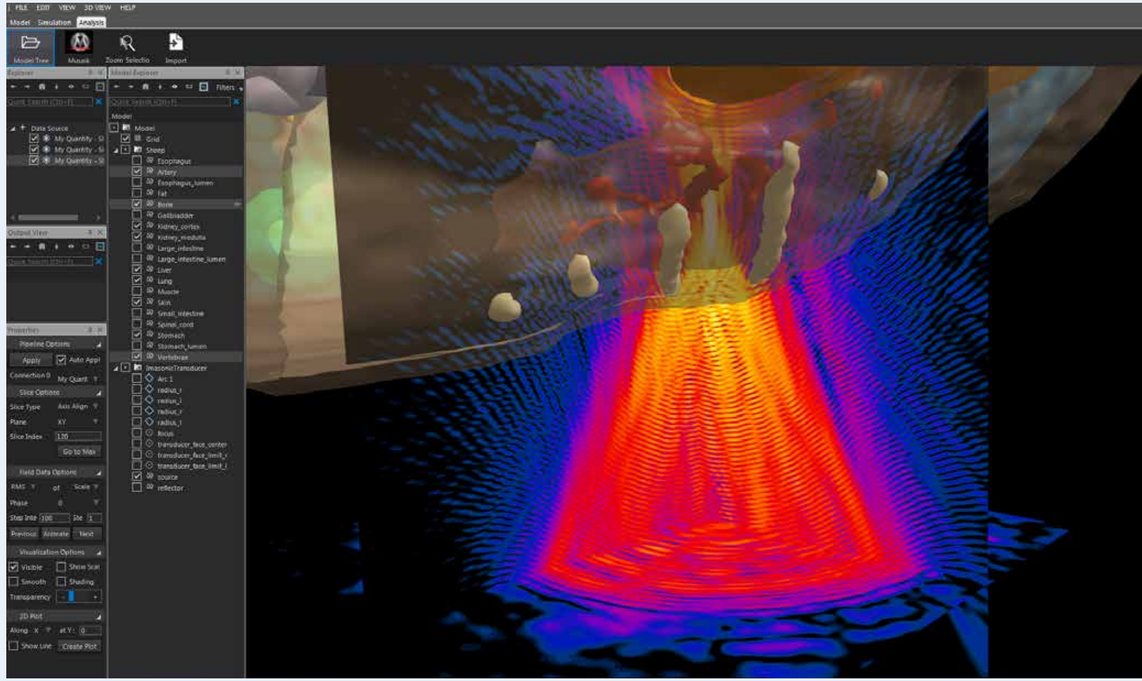
Acoustics Solvers

***Sim4Life* offers a novel full-wave Acoustics Solver (P-ACOUSTICS) based on the linear pressure wave equation (LAPWE), extended and optimized for heterogeneous, lossy materials for the modeling of the propagation of pressure waves through highly inhomogeneous media like tissue and bone. All relevant phenomena like scattering, reflection, refraction, diffraction, interference, and absorption are captured by this method. The dissipated acoustics energy can be translated into a heat source for *Sim4Life*'s thermal solver (P-THERMAL) to capture the coupling of acoustic and thermal phenomena.**

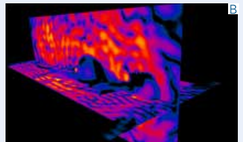
An adaptive rectilinear grid is used to discretize the computational domain with feature-specific granularity and inhomogeneous perfectly matched layers (PML) boundary conditions are used to close the problem. The numerical solver, which is based on a non-uniform finite difference time domain (FDTD) method, is substantially accelerated by either GPU or OpenMP processing.

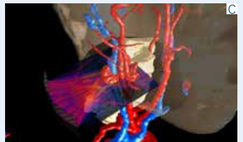
The P-ACOUSTICS solvers have been extensively validated, and the associated uncertainties have been quantified with analytical solutions, benchmarks, and robotic 3D-scan hydrophone measurements in complex setups. Comprehensive documentation is available for *Sim4Life*.

Precise ablation of liver tumor located behind the ribs, with respiratory motions.



A Optimized transcranial phase aberration correction for a large-array focused ultrasound (FUS) neurosurgery system.
B Evaluation of fetal exposure to acoustic stimuli.
C HIFU treatment planning for neck cancers.





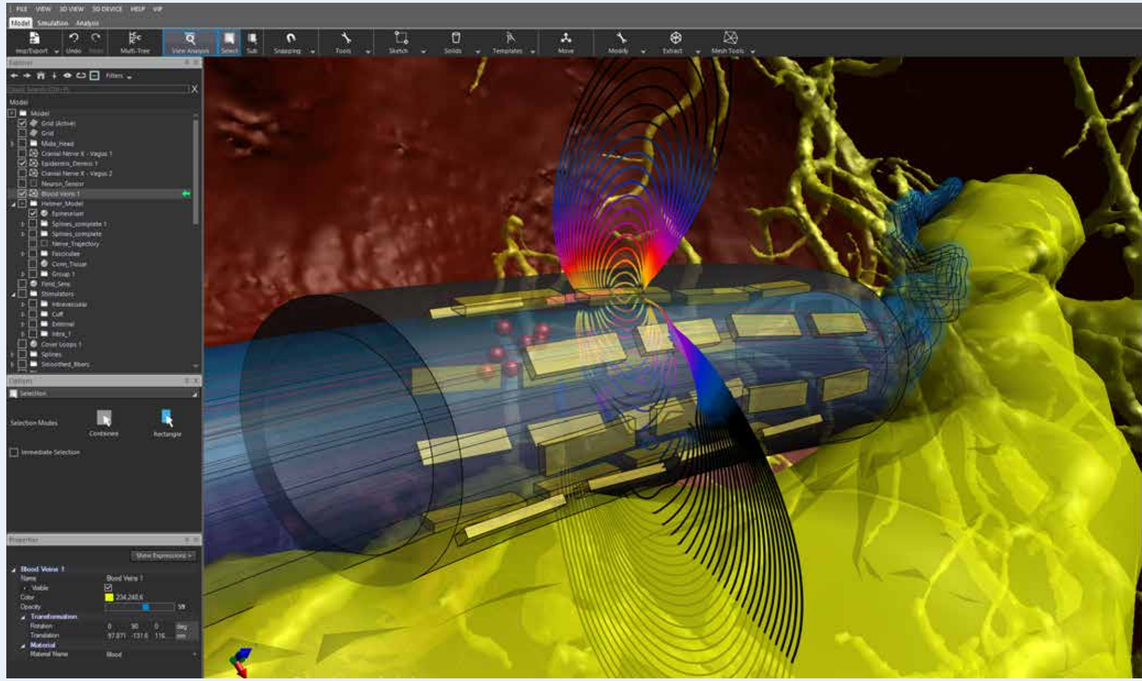
Neuronal Dynamics Models

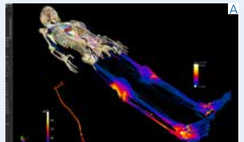
The Neuronal Dynamics Solver (NEURON) enables the modelling of EM-induced neuronal activation, inhibition, and synchronization with either complex multi-compartmental representations of neurons with varying channel dynamics or generic built-in models. The solver is ideal for studying interaction mechanisms, evaluating and optimizing neuro-stimulating devices, and assessing safety issues.

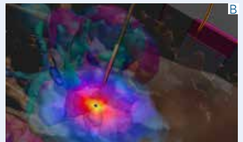
The SENN model (safety standards) and more complex models can be placed inside whole-body models to take advantage of the heterogeneous tissue phantoms and resulting fields. The GUI facilitates the integration of other neuronal models from commonly used databases or independently derived models.

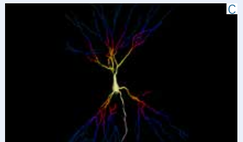
NEURON has been validated against published data and *ex vivo* and *in vivo* measurements, and is continually advanced and verified.

Stimulation of the vagus nerve with a multi-element cuff electrode array.









A Neuronal response modeling in MRI gradient switching fields with RF-induced local temperature increases considered.
B Improved deep-brain stimulation (DBS) treatment analysis with incorporation of the Morel stereotactic atlas of the thalamus.
C Propagation of the transmembrane voltage in a rat hippocampus neuron with a detailed dendritic tree.

Medical Image Segmentation Tool Set

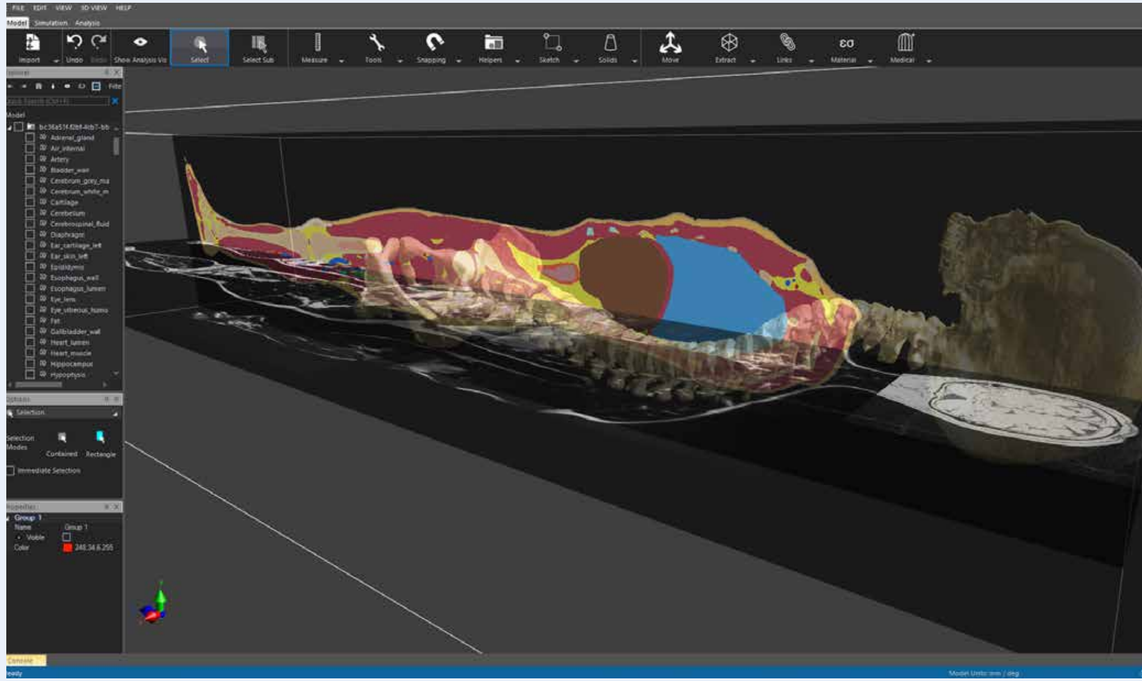
The Medical Image Segmentation Tool Set (iSEG) is a fully integrated segmentation toolbox for the efficient, fast, and flexible generation (including pre- and post-processing) of anatomical models from various types of imaging data. A wide selection of segmentation methods, including competitive region growing approaches, fuzzy connectedness analysis, level-set methods, topologically flexible interpolation, and dedicated vasculature segmentation, ensures the efficient and flexible generation of surface models.

iSEG features a unique set of flexibly combinable automatic, semi-automatic, and interactive segmentation algorithms. Novel algorithms based on competitive segmentation methods, for example, optimize the generation of models with many different tissues. Anatomical reference atlases are also available.

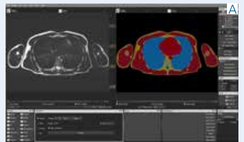
iSEG is capable of handling a variety of image data (e.g., compatible with all standard CT and MRI image formats) and large-scale models.

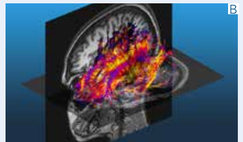
iSEG offers unique possibilities for medical diagnosis/treatment and basic research applications, e.g., for personalized modeling and treatment planning, or to investigate physical and physiological processes in realistic anatomical environments.

Co-visualization of image data and segmented regions.



A Slice view during MRI data segmentation.
B Visualization of image data and DTI-based fiber tracking to facilitate the realistic placement of neuron models.
C Overlay of MRI imaging data and segmented bones and organs of an anatomical model.





Modeler

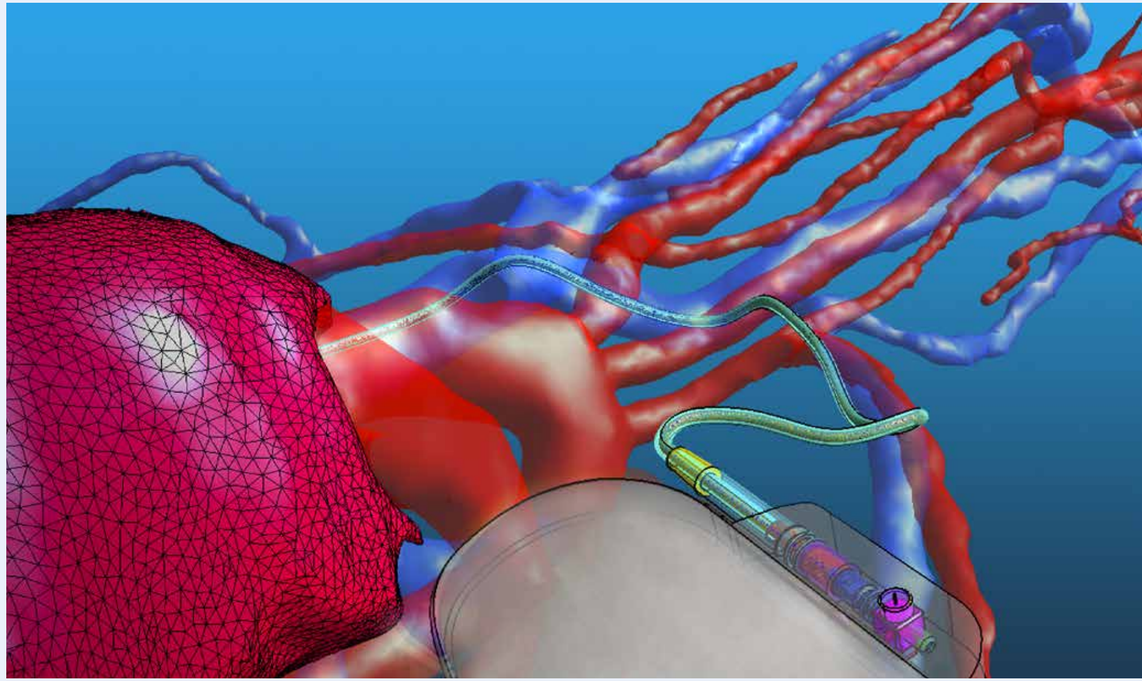
***Sim4Life* integrates a powerful parametric 3D modeling environment based on the ACIS toolkit for generating advanced interactive CAD models and high-quality surface models from, e.g., segmented image data. The fast OGL- and VTK-based rendering engine allows interactive visualization of large and complex volumetric data sets and CAD models. Specialized tools will be continually provided upon user request to handle specific tasks, such as vasculature modeling and processing.**

Sim4Life provides integrated, advanced, and interactive CAD modeling without the need for a preprocessor or live-link; and handles complex anatomical models, e.g., ViP models, and massive CAD models.

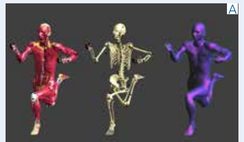
The platform is uniquely capable of converting triangular surface meshes into parameterized CAD models, e.g., NURBS-based.

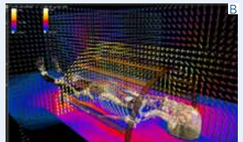
Sim4Life offers integrated functionality to extract, smooth, and simplify tissue and organ surfaces from segmented medical image data.

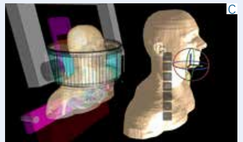
Sim4Life facilitates the placement of detailed CAD pacemakers in complex anatomical models.



A Interactive physics-based Poser tool applied to a human model in *Sim4Life*.
B Easy placement of CAD-based human model inside MRI birdcage (Python supported).
C User-friendly positioning of an anatomical model in a CAD structure of a 24-channel hyperthermia applicator.







Mesher

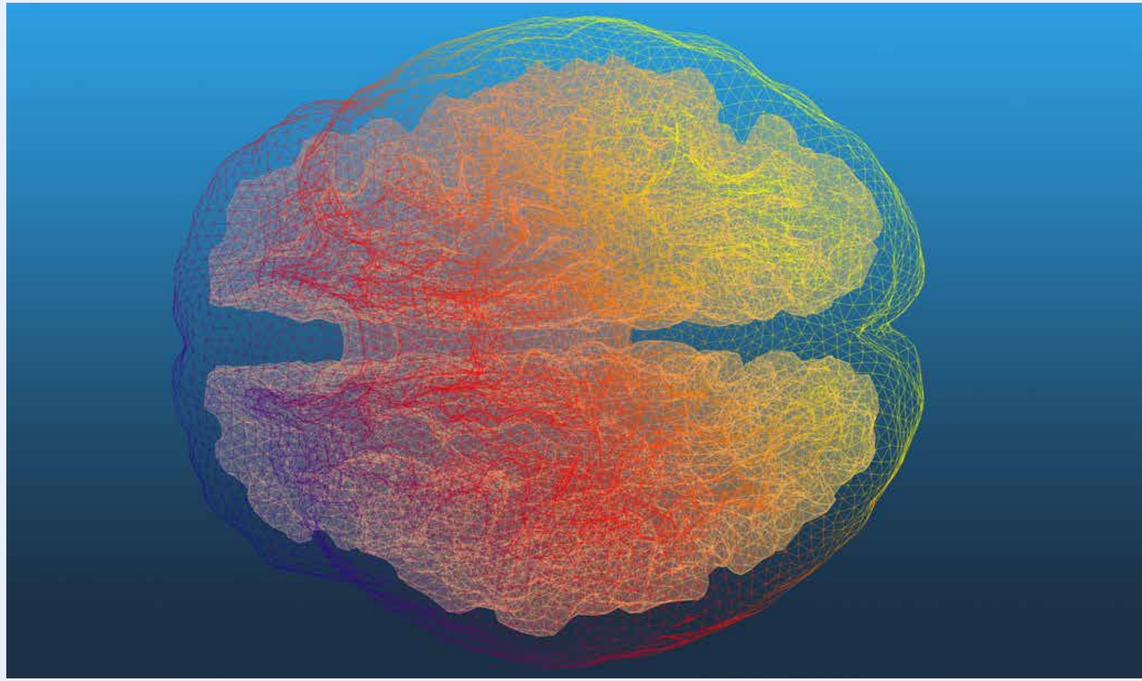
***Sim4Life* offers a unique array of discretization tools, ranging from the interactive generation of geometrically adaptive rectilinear grids by ray-tracing combined with robust intersection testing to Delauney, advancing front, and octree-based methods for unstructured mesh generation in FEM-based solvers. Both irregular anatomical structures and CAD-based models can be handled robustly and flexibly while preserving features.**

Adaptive, rectilinear meshes (e.g., for P-EM-FDTD, P-ACOUSTICS, P-THERMAL) can be generated interactively with excellent heuristics-based automatic grid generation and flexible tuning.

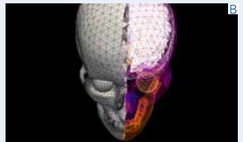
A variety of meshers (e.g., for P-FLOW) capable of generating high-quality element, adaptive, feature preserving, unstructured meshes from CAD data and complex anatomical models are provided.

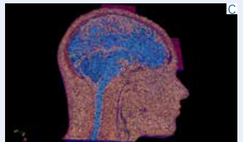
The only surface processing tool capable of producing topologically conforming, high triangle element quality, non-(self) intersecting surface meshes from noisy segmentation data: the ideal basis for unstructured volume mesh generation and creation of surface models from medical image data for any *Sim4Life* solver.

High-quality surface meshes of a human brain structure generated from MRI data with an overlay of the thermal simulation results.



A High-quality multi-domain mesh of selected brain structures (topologically conforming with compatible interfaces).
B Solver-optimized surface meshes of a complex anatomical head model.
C Fully automatic generation of multi-domain volume mesh from segmented data.





Analysis & Visualization
Postprocessor

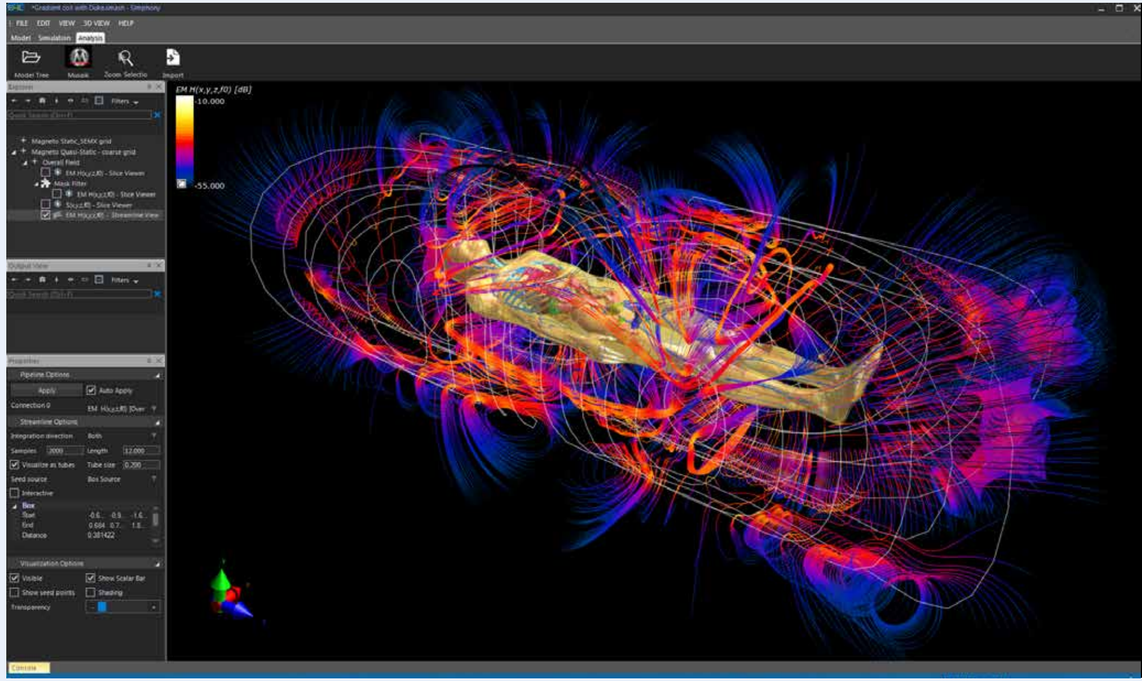
Postprocessing in *Sim4Life* provides complete insight into intricate simulation results and measurement and imaging data through advanced visualization and analysis capabilities. Viewers tailored for medtech simulations (e.g., volume rendering, streamlines, maximum intensity projection, surface fields on arbitrary 3D structures) and calculators for recurring tasks (resampling, filtering, functional evaluation) on unstructured/structured field data are included.

A novel pipeline architecture allows for the set-up of complex analysis sequences and simple reevaluations with modified input data or parameters. Analysis steps can be stored in and reloaded from analysis or visualization “projects”.

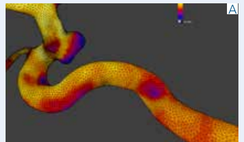
Processing (interpolation, computation of surface integrals/flux, interactive cropping/masking, etc.) and visualization of the simulation results together with the measured/imaging data are performed directly on the models.

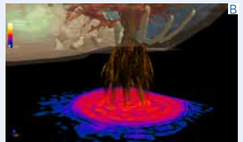
Derived quantities based on any solver results or measurement data can be computed and visualized by maximally exploiting the algorithmic and visualization capabilities of the VTK, including interpolation, integrals, gradient, filtering, DFT, and a generic calculator.

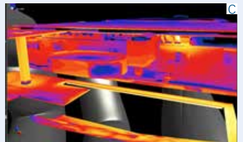
Streamlined view of H-field produced by the loaded MRI gradient coil (1 MHz).



A Wall shear stress visualization.
B Evaluation of pressure distribution during HIFU treatment.
C Visualization of current distribution on an internal device structure (MTE).







High Performance Computing

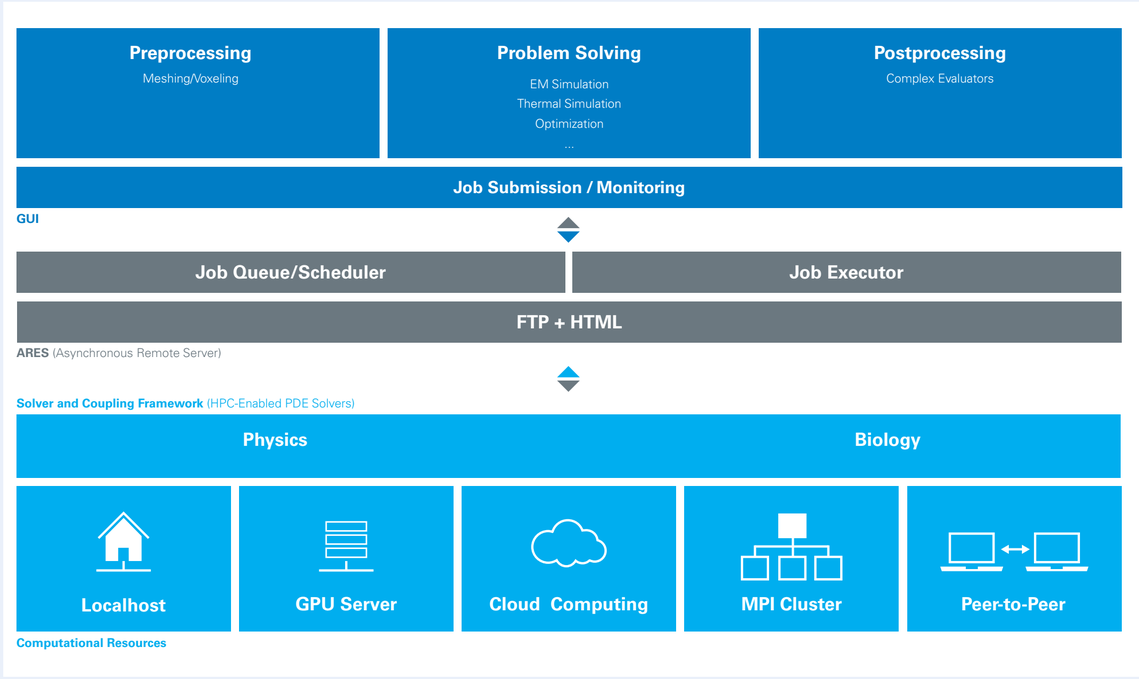
***Sim4Life* offers high performance computing to enable the investigation of complex and realistic models. Multi-threaded execution for modeling, meshing, voxeling, and postprocessing enables parallel processing of heavy tasks without disturbing the workflow. A fully integrated centralized task manager efficiently manages all computationally intensive tasks on the local machine or in the cloud.**

Sim4Life features the fastest GPU-enabled EM-FDTD and ultrasound (US) solvers (P-EM-FDTD and P-ACOUSTICS), supporting the latest hardware, e.g., NVIDIA Maxwell and Pascal architectures (K80, Titan, P100, etc.).

The MPI parallelization-based FEM solvers' (P-EM-QS and P-FLOW) framework makes optimal use of multi-core processors, clusters, and super-computers to guarantee extreme performance for demanding tasks.

A unified interface supports cloud computing on various major providers.

The Asynchronous Remote Server (ARES) automatically distributes any computationally intensive task to local or remote HPC resources (GPU/CPU, cluster, cloud).



Intuitive GUI and Workflow

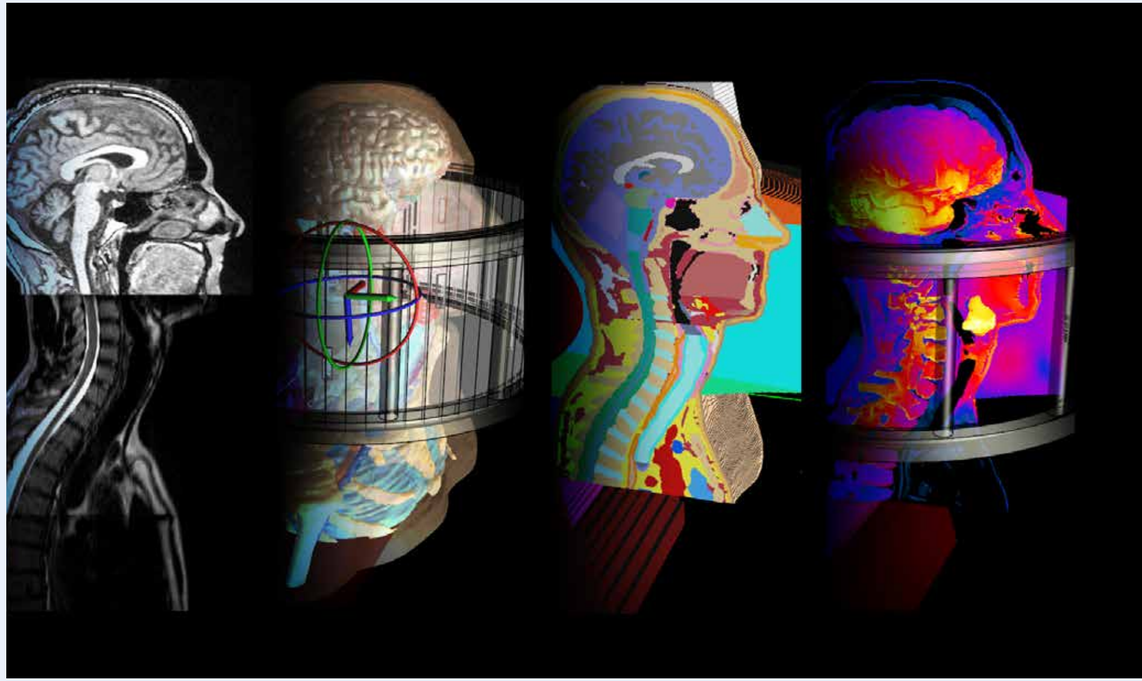
The *Sim4Life* GUI efficiently facilitates all steps in complex multiphysics modeling, from defining the problem, discretizing, simulating, analyzing, to visualizing the results, with clarity and flexibility. The unobtrusive user interface reduces redundant tasks by presenting a clear overview of the model with context adaptive menus and natural user-interaction paradigms. Dedicated tools are available to further reduce user effort for specialized tasks.

The streamlined user interface minimizes the number of required processing steps.

The GUI supports drag-drop-based assignments and features powerful interactive handling, e.g., in geometric modeling, simulation coupling, and material assignment.

Context-dependent menus, options, and functions optimally streamline tasks.

User-friendly and robust workflow in *Sim4Life*: Patient specific hyperthermia treatment of a neck carcinoma.



Workflow A (Segmentation/iSEG): Generation of a surface-based anatomical model from MRI data of a patient with a neck carcinoma.

Workflow B (Modeling): Simulation setup of the anatomical model in a CAD model of a 24-channel hyperthermia applicator.

Workflow C (Discretization): Discretization of the simulation setup with a high-resolution rectilinear grid.

Workflow D (Simulation and Analysis/ Postprocessing): SAR distribution showing significant exposure of the tumor.

Python Scripting

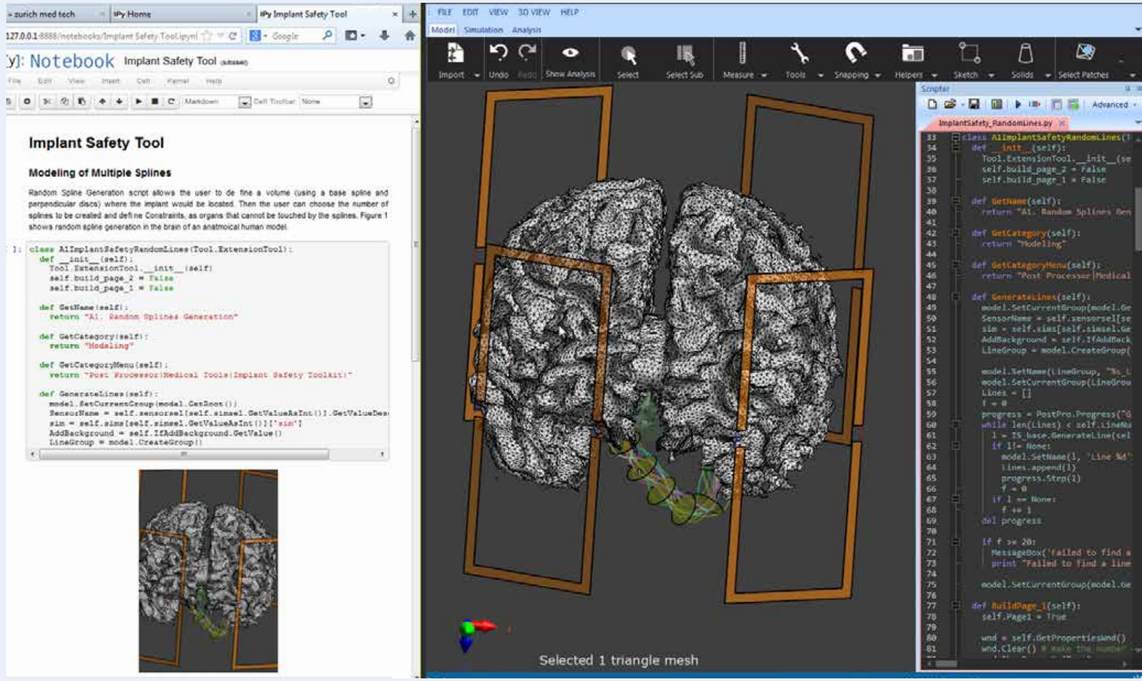
***Sim4Life* features Python, a powerful scientific scripting language offering a vast range of 3rd-party programs.**
The *Sim4Life* Python application programming interface (API) can be used to parameterize and automatize tasks, e.g., geometric modeling, simulation setup, or postprocessing, and to build custom tools and independent applications.

A Python scripting environment and a wide selection of powerful libraries, such as SciPy, NumPy, and pandas, are embedded in *Sim4Life*, and additional packages from online repositories can be installed with the package manager.

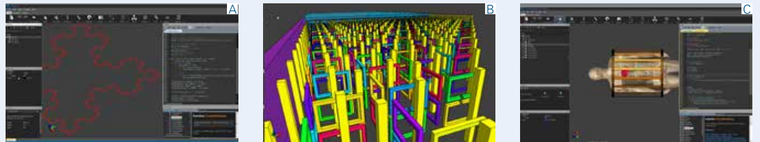
Various easy-to-use Python routines for performing frequent tasks and an extensive API for deep access to the *Sim4Life* framework are provided.

The straightforward Python API is fully customizable: Create and sell individual licensed moduls to the *Sim4Life* user community.

A Python scripting environment provides full interoperability and automation to generate and share customized reports.



A Implementation of user-customized GUI elements via Python.
B Metamaterial study: edge-shaped structure made of split-ring resonators (SRR) and wires.
C Automated modeling/placement of 3D solids for large-scale parameter studies or performance optimization.



ZMT & Third-Party Licensed Modules

ZMT and 3rd-party licensed modules extend *Sim4Life's* functionality and simplify and accelerate complex tasks. The modules can be integrated with all steps, including modeling, simulation setup, discretization, solving, visualization, and analysis.

Sim4Life provides a world-class platform for our global user base to create modules that provide additional expert knowledge on specific fields and applications.

Create and sell individual licensed modules.

Extensions of the *Sim4Life* application can be obtained independent of the *Sim4Life* release cycle.

Selection of modules.

MRI-Safe Implants

IMANALYTICS
Fully automated Tier 3 analysis of RF-induced local power deposition at the electrodes of implantable devices for millions of excitations.

MRI COIL LIBRARIES
RF Birdcage (1.5T and 3.0T) and Gradient coil models to fully cover installed scanners for implant safety assessments.

M-IMSAFE
Intuitive 4-step procedure supports Tier 3 (from the "4 Tier Approach" developed by JWG for AIMD ISO/IEC).

MRI Technology

M-MUSAIK
Framework for MRI receive coil array design, optimization, and performance verification (based on simulation results or experimental data).

M-TxCOIL
M-TxCOIL postprocessing engine provides RF shimming, IEEE SAR averaging, and worst-case SAR analysis.

M-BCAGE
Parameterized MRI volume coil designer for birdcage coil geometries and associated simulation settings.

M-SYSSIM
MRI scanner simulator predicts scattering EM field effects on MRI images for arbitrary pulse sequences.

M-GRAD
MRI Gradient coil designer and optimization engine (considers interactions with scatterers, e.g., patients/implants and RF coils).

Modeling

M-POSER
The ViP models (3.0 or higher) can be manipulated to a desired position (physics-based, with realistic posing).

M-REMESH
User-defined parameters for refinement, simplification, and mesh healing for more accurate or lighter handling/processing of elements (tetrahedrons, quadrilaterals).

Processing

M-MATCH
A versatile matching circuit application for multiport devices, such as RX/TX MRI coils or antenna arrays.

M-TALATLAS
Automatic identification and hierarchical labeling of brain/substructures, e.g., for the characterization of the EM exposure of the brain (>1000 different sites).

M-MBSAR
SAR evaluation tool for transmitters that simultaneously operate at different frequency bands.

M-PPCALC
An integrated Pipeline/Analysis Calculator enables calculations of any simulated values/distributions, normalization, etc.

Import

M-HUYGENS
Hybridization platform to import EM near-field patterns, calculated with different numerical methods (FDTD, FEM, MoM), into the generalized Huygens Source.

M-IMG
Import various types of image data (e.g., standard MRI and CT image formats) for segmentation/modeling and simulation settings (boundary conditions, inhomogeneous parameter distributions).

M -VOX
Import .raw (volume) or .bmp (slices) data and automatically convert data into segmented slices for use and further processing, such as surface extraction, in *Sim4Life*.

Customer Service & Support

ZMT products are designed to increase productivity and generate results.

ZMT Customer Support Services delivers prompt and customized mission-critical support services to help you maintain and maximize the performance of your ZMT products, software, and test systems that are optimally designed to overcome regulatory hurdles.

Our detail-oriented, expert engineers provide timely, proactive, and preventive support to help ensure the intrinsic value of ZMT products for many years. In addition, ZMT collaborates with a large network of leading independent researchers specializing in *in silico* analyses across various research fields to provide support for cuting-edge applications.

Our customer support team is always available to guide you step-by-step when instruction manuals and troubleshooting do not provide the help you seek.

About Us

ZMT Zurich MedTech AG (ZMT) develops and provides innovative software and hardware solutions for targeted life science applications to simulate, analyze, and predict complex and dynamic biological processes and interactions within the anatomical complexity of the human body. ZMT's key product is *Sim4Life,* a unique computational simulation platform for the design and optimization of medical devices and treatments, precision medicine, efficacy and safety evaluations. *Sim4Life* is complemented by experimental instrumentation for validating simulation results.

ZMT serves an international customer base from its headquarters in Zurich, Switzerland, and through a global network of distribution partners. Our solutions are applied in research and product development, as well as in clinical trials, regulatory compliance testing, and treatment planning. ZMT, together with its partner organizations the Foundation for Research on Information Technologies in Society (IT'IS) and Schmid & Partner Engineering AG (SPEAG), forms the Zurich43 alliance.

zurich med tech

ZMT is a member of

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