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 3.0
  - Virtual Population
- ViA 1.0
  - Animal Models
- Third-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 (coming soon)

### Intuitive GUI and Workflow
- iSEG
  - Medical Image Segmentation Tool Set
- MODELER
  - Advanced Modeling Tool Set
- MESHER
  - Robust & Effective Meshing
- ANALYZER
  - Versatile Postprocessor and Analyzing Tool Set
- PYTHON
  - Control Via Python Scripting

### Licensed Modules
- MRI
  - 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
- ARES

### Auto-Scheduler & Control
- ARES
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, providing 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 3.0 models of the IT’IS Foundation at ETHZ (www.itis.ethz.ch/vip), the computable human phantoms are functionalized to predict 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 extends the demographic coverage of the parameterized anatomical models, e.g., to explore underrepresented or pathological anatomies in clinical trials. A flexible 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.
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.
The Electromagnetics Full Wave Solvers (P-EM-FDTD) enable accelerated full-wave, large-scale EM modeling (> billion voxels) using Yee discretization on geometrically adaptive, inhomogeneous, rectilinear meshes with conformal sub-cell correction and thin layer models, offering support for dispersive materials. The solvers also include unique features for EM safety assessments (see M-IMSAFE).

Optimal simulation speed is achieved with native GPU and MPI accelerations, which were developed by our team that 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 strongly varying resolutions.

As the most frequently applied solvers in near-field dosimetry, they 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.
A  MRI birdcage design: Analysis of load dependence.
B  Evaluation of an MR-safe DBS implant.
C  Fast and accurate rectilinear discretization of an anatomical human model.
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 using analytical and full-wave solutions and by comparison with measurement data. Comprehensive documentation is available for Sim4Life.
Gradient coil design and optimization.

Assessment of nerve excitation during transcranial magnetic stimulation.

Exposure evaluation of high power systems during maintenance.
The Thermodynamics Solvers (P-THERMAL) enable the modeling of heat transfer in living tissue using 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 using discrete networks (1D trees) and, in the near future, 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.
A  In vivo temperature evaluation of RF-safe pacemakers.
B  Optimization of liver tumor FUS ablation considering breathing motions.
C  Optimized positioning and steering of hyperthermia applicator arrays.
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 using 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.

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.
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.
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 employing a non-uniform finite difference time domain (FDTD) method is substantially accelerated by using either GPU or OpenMP processing.

The P-ACOUSTICS solvers have been extensively validated and the associated uncertainties have been quantified using analytical solutions, benchmarks, and robotic 3D-scan hydrophone measurements in complex setups.

Comprehensive documentation is available for Sim4Life.
A  Optimized transcranial phase aberration correction for a large array FUS neurosurgery system.
B  Evaluation of fetal exposure to acoustic stimuli.
C  HIFU treatment planning for neck cancers.
The Neuronal Dynamics Solver (NEURON) enables the modelling of EM-induced neuronal activation, inhibition, and synchronization using 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 continuously advanced and verified.
Neuronal response modeling in MRI gradient switching fields considering RF induced local temperature increases.

Improved DBS treatment analysis facilitated by the head model incorporating the Morel stereotactic atlas of the thalamus.

Propagation of the transmembrane voltage in a rat hippocampus neuron with a detailed dendritic tree.
The Medical Image Segmentation Tool Set (iSEG) is a fully integrated segmentation (including pre- and postprocessing) toolbox for the efficient, fast, and flexible generation 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 (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.

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.
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 MR imaging data and segmented bones and organs of an anatomical model.
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.

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.

Uniquely capable of converting triangular surface meshes into parameterized CAD models, e.g., NURBS-based.

Offers integrated functionality to extract, smooth, and simplify tissue and organ surfaces from segmented medical image data.
Interactive Poser tool applied to a standard hand model in Sim4Life.

Easy placement of CAD-based human model inside MRI birdcage (Python supported).

User-friendly positioning of an anatomical model in a CAD structure of a 24-channel hyperthermia applicator.
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. (coming soon)

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 creating surface models from medical image data for any Sim4Life solver.
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.
A novel pipeline architecture allows for the setup 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 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.

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  Wall shear stress visualization.
C  Visualization of current distribution on an internal device structure (MTE).
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 US solvers (P-EM-FDTD & P-ACOUSTICS) supporting the latest hardware, e.g., NVIDIA MAXWELL architectures (K80, Titan, etc.).

The MPI parallelization-based FEM solver framework (P-EM-QS & P-FLOW) optimally uses multi-core processors, clusters, and super-computers to guarantee extreme performance for demanding tasks.

A unified interface supports cloud computing on any of the major providers, e.g., Amazon or Google.
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.

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.

**Segmentation**

**Morphing**

**CAD**

**Human Phantoms**

**Discretization**

**Multiphysics**

**High Performance Solvers**

**Physiology and Tissue Models**

**Analysis Visualization Reports**

OPEN SCRIPTABLE FRAMEWORK WITH A POWERFUL GRAPHICAL USER INTERFACE AND HIGH PERFORMANCE COMPUTING SUPPORT

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 & Analysis/Postprocessing): SAR distribution showing significant exposure of the tumor.
**Sim4Life** features Python, a powerful scientific scripting language offering a vast range of third-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 modules to the **Sim4Life** user community.
Implementation of user-customized GUI elements via Python.

Metamaterial study: edge-shaped structure made of split-ring resonators (SRR) and wires.

Automated modeling/placement of 3D solids for large-scale parameter studies or performance optimization.
ZMT and third-party licensed modules extend created by ZMT or third-parties 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.
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<th>MRI</th>
<th>Modeling</th>
<th>Calculators</th>
<th>Processing</th>
<th>Import</th>
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<td>Framework for MRI receive coil array design, optimization, and performance verification (based on simulation results or experimental data).</td>
<td>The VIP models (3.0 or higher) can be manipulated to a desired position (volume preserving, influence regions).</td>
<td>An integrated Pipeline/Analysis Calculator enables calculations of any simulated values/distributions, normalization, etc.</td>
<td>A versatile matching circuit application for multiport devices, such as RX/TX MR coil or antenna arrays.</td>
<td>Hybridization platform to import EM near-field patterns, calculated with different numerical methods (FDTD, FEM, MoM), into the generalized Huygens Source.</td>
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<td>M-TxCOIL postprocessing engine provides RF shimming, IEEE SAR averaging, and worst-case SAR analysis.</td>
<td>Refinement, simplification, and mesh healing for more accurate or lighter handling/processing (tets, quadrilaterals) using user-defined parameters.</td>
<td>A dispersive material fitting engine, based on Genetic Algorithms, calculates parameters for different dispersive models (user-defined discrete frequency data).</td>
<td>Automatic identification and hierarchical labeling of brain/substructures, e.g., for the characterization of the electromagnetic exposure of the brain (&gt;1000 different sites).</td>
<td>Import various image data (e.g., standard MRI and CT image formats) for segmentation/modeling and simulation settings (boundary conditions, inhomogeneous parameter distributions).</td>
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<td>Parameterized MRI volume coil designer for birdcage coil geometries and associated simulation settings.</td>
<td>MRI scanner simulator predicts scattering EM field effects on MR images for arbitrary pulse sequences.</td>
<td>SAR evaluation tool for transmitters that simultaneously operate at different frequency bands.</td>
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<td>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.</td>
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<td>MRI Gradient coil designer and optimization engine (considers interactions with present scatterers, e.g., patients/implants and RF coils).</td>
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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 cutting-edge applications.

Our customer support team is readily available to guide you step-by-step when instruction manuals and troubleshooting are not enough.
ZMT Zurich MedTech AG was founded in 2006 as a spin-off company of the Swiss Federal Institute of Technology (ETH) and the Foundation for Research on Information Technologies in Society (IT’IS Foundation).

ZMT offers tools and best practices for targeted life sciences applications to simulate, analyze, and predict complex and dynamic biological processes and interactions.

Sim4Life, ZMT’s *in silico* platform, is built on the largest available set of highly detailed computable human phantoms, functionalized for physical and physiological modeling. Sim4Life adds high-performance computing, powerful CAD, post-processing and visualization, leading to extraordinary realism. Models, solvers and assessment are thoroughly verified and validated, and complemented by validation hardware.

Our software and hardware solutions support efforts from research, product development, clinical trials, regulatory compliance to treatment planning.

ZMT collaborates closely with IT’IS, SPEAG, and many leading research groups at universities in Switzerland, Europe, USA, and Asia to develop tools for streamlining and accelerating analyses of complex medical technologies and biological processes and interactions.

ZMT serves an international customer base from its headquarters located in Zurich, Switzerland, and through a global network of distribution partners.