Bio-numerical simulations with SimBio: project aims and objectives

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Abstract
The SimBio project will produce a generic simulation environment for advanced clinical practice and health care. A key feature is the input of individual patient data to the modelling and simulation process. While future SimBio users will be able to develop application specific tools to improve practices in many areas, the project evaluation & validation will demonstrate improvements in: non-invasive diagnosis and pre-operative planning, design of prostheses and of the operative procedures for their implantation. The SimBio environment components are: discrete representation of the physical problem; numerical solution system; inverse problem and optimisation; visualisation. The SimBio environment will be designed for execution on parallel and distributed computing systems, particular attention being paid to component interoperability. The compute-intensive environment components will be implemented on HPC platforms.

1 Introduction

The SimBio project ("SimBio – a generic environment for bio-numerical simulation", project number IST-1999-10378) is a three year research and technological development (RTD) project financed by the European Commission's Information Societies Technology (IST) programme. The project commenced on April 1st, 2000.

The central objective of the SimBio project activities is the improvement of clinical and medical practices by the use of numerical simulation for bio-medical problems – "Bio-numerical simulation". Building on existing experience with particular applications, a generic simulation environment will be produced which will provide an innovative enabling technology for advanced clinical practice and health care. A key feature in the SimBio project is the possibility to use individual patient data as input to the modelling and simulation process - in contrast to simulation based on "generic" computational models.

The SimBio generic environment will allow future users to develop application specific tools to improve practices in many areas. The impact for specific areas will be achieved through the SimBio evaluation & validation applications that will:

- improve non-invasive diagnosis and pre-operative planning,
- improve both the design of prostheses and the operative procedures for their implantation.

In order to meet the computational demands of the SimBio environment simulations, the compute-intensive environment components will be implemented on High Performance Computing (HPC) platforms. The interoperability of the environment components will be realised using a portable object-oriented interoperability architecture, such as CORBA, since the environment components may be executing on distributed, heterogeneous systems. The SimBio environment will be comprised of the following components:

- **Discrete Representation** of the Physical Problem. This includes in the first instance the generation of the 3D voxel database derived from medical scan data including the individual material properties. For the detailed modelling follows the generation of a finite element mesh and the provision of data for tissue modelling within the finite elements. One of the ultimate goals of this project is to establish the use of individual elasticity/conductivity profiles for each patient in clinical routine and to obtain improved patient outcome based on the generic tools and algorithms developed in the project.
- **Numerical Solution System**. SimBio-internal parallel finite element (FE) solvers and numerical library routines will be provided, together with an interface to allow for external (e.g. commercial) codes to interact with the SimBio environment. The solution system is based primarily on the meshes provided by the first component.
- **Inverse Problem**. The technology for inverse problem solution developed in the project will be encompassed in this component which will provide a framework for inverse problem solver development, based on the use of the numerical solution system. Furthermore, the box should include tools for the fast and comprehensive assessment of the effects of modelling errors and simplifications.
- **Visualisation**. The simulation of bio-medical data often requires advanced - particularly accurate or of high resolution - visualisation tools and these will be included in the visualisation component via both SimBio-internal tools and interfaces to external software. Standard visualisation requirements are also possible via the interface.

The generic environment will be validated and evaluated by three specific applications, which are then able to provide a demonstration of the impact of SimBio employment within the clinical and health care area. The SimBio applications are:

- electromagnetic source localisation within the human brain based on electroencephalography (EEG) and magnetoencephalography (MEG) measurements at the surface of the head;
- bio-mechanical simulations of the human head, including modelling of neurodegenerative diseases;
- the design of novel replacement parts for the menisci of the human knee joint and methods for their surgical implantation.

2 The SimBio Consortium

The Consortium comprises four industrial partners and five public research organisations stemming from five European countries and represents a well-balanced mixture of private and public partners whose activities range from basic research to industrial production. The core activities of the partners cover the following fields: health care product manufacturing, clinical practice, medical and clinical research, clinical imaging and data processing software, numerical simulation software, HPC systems and software solutions. The heterogeneous character of the Consortium has been designed to best address the scientific requirements imposed by the problems to be solved.

C&C Research Laboratories, NEC Europe Ltd. (NEC) targets its activities on HPC technology and numerical algorithms and will build on its collaborations with other partners in the area of Finite Element (FE) technology. NEC is also the project co-ordinator.

The signal and image processing (SIP) group of the Max-Planck-Institute (MPI) of Cognitive Neuroscience is specialised in medical image analysis and synthesis. The SIP group combines this expertise with knowledge on parallel processing. The research of the MEG group of the MPI is focussed on developing software and hardware to maximise the information output from EEG/MEG measurements. The groups from MPI will contribute to all areas of SimBio component development and will evaluate the impact of the approach using bio-electromagnetic and bio-mechanical applications. Direct collaborators with MPI in the algorithmic and simulation areas are the University of Leuven (K.U.Leuven), addressing aspects of the registration and segmentation problem, and the software company A.N.T. Software B.V., which focuses on software for source localisation methods based on EEG and MEG measurements. Biomagnetic and biomechanical tissue properties are the main research areas, and corresponding project roles, of the University of Technology of Compiègne (UTC), and Biomagnetic Center, Department of Neurology, Friedrich-Schiller-University Jena (BMZ). BMZ operates the only animal Micro-SQUID MEG system in Europe.

ESI will exploit its leading industrial code PAM-SAFE™, creating an interface to the simulation environment, and develop new modelling and solution options in the code. ESI will support the development of the SimBio environment (with expertise in modelling, FE technology and software systems) and the performance of Knee model simulations, building on its previous collaboration with the University of Sheffield.

The University of Sheffield (UFDS) has a large experience in biomedical applications of the finite element method. Together with ESI a biomechanical ESPRIT project, KneesUp, has successfully been accomplished having an anatomically detailed knee model as a result. UFDS will contribute to the development of the mesh generation component and will lead the knee-prostheses validation and evaluation work. Smith and Nephew, a leading healthcare product supplier, will evaluate the use of bio-numerical simulation for industrial design optimisation of prostheses.

3 Technical innovations in SimBio

3.1 Development of a material database for human tissue properties

The material database containing electrical and mechanical properties of human tissue of individuals is mainly achieved by the application of magnetic resonance strain imaging (MRSI) and diffusion tensor imaging (DTI). Both methods basically rely on magnetic resonance imaging (MRI) and have been developed very recently.

3.1.1 Development of an individual conductivity tensor map using DTI

Multimodal MR-imaging strategies in combination with high level registration and segmentation algorithms and the application of the mathematical homogenisation theory to the voxel-wise measured, anisotropic water diffusion leads to an *individual conductivity tensor map* of the considered BOI. This map accounts for an exact representation of various tissue types with regard to their specific anisotropic resistance, a prerequisite for modelling in e.g. EEG and MEG. Pathological conditions such as e.g. skull holes and brain lesions like tumours or cerebral ischemia, strongly changing the resistance of the involved head tissues, can now be modelled individually and appropriately. This material modelling is highly innovative compared with today's realistically shaped volume conductor models (boundary element methods), where e.g. the head layers brain, skull and scalp can only be assigned constant and isotropic resistance values. This will improve the diagnostic performance of EEG and MEG and will have a large impact not only on basic and clinical research but also on patient outcome in a variety of diseases.

3.1.2 Development of an individual mechanical tissue behaviour map using MRSI

Until now strain imaging techniques have been applied for some isolated ‘in vitro’ organs (kidneys) only. So we will set-up this technique for the “in-vivo brain“, which will provide detailed knowledge of material properties of ‘in place’ substructures in the brain in general. Furthermore the projected ‘advanced in vivo strain imaging’ of patients brain will provide most important insights in individual mechanical brain properties and processes for diagnostics and therapy. Development and installation of this method will be a demanding part of the project and at the moment it is unforeseeable which state of realisation will be reachable during the runtime of the project.

3.2 Improved mesh generation for medical applications

Innovations are also to be expected in the generation of finite element meshes based on medical image data. Due to the preceding segmentation and material modelling of the considered body parts, the generated meshes are not only optimised from a numerical point of view, but they can especially be refined to satisfy the needs of the individually achieved segmentation results and the individually measured material properties. The merging of existing solutions (proposed by NEC&MPI and ESI&USFD) will lead to a fast and stable mesh generation process.

3.3 Inverse Problem Innovations

Solutions of the general inverse problem have undergone a rapid development in the past decade. Currently, most source localisation schemes have been developed assuming simple physical behaviour for the materials surrounding the source. Likewise, only a plain and unconstrained model of the sources has been used. The SimBio approach enables us to incorporate advanced material knowledge by exploiting the flexibility of the finite element method. This has also a strong influence on the inverse problem techniques and thus necessitates the further development of inverse solution methods. As a result of this project, we will present a tool-set of optimisation and reconstruction algorithms for inverse problems tuned for the joint use with the improved material modelling.

For the electromagnetic test application, a pre-surgical source diagnosis under inclusion of the individual conductivity properties can be calculated in an acceptable time (around one day). Though current, less accurate simulations can already be performed within such time-scales, it is obvious that the expected increase in the accuracy of the pre-surgical source localisation through the modelling achieved with the SimBio innovations is of high medical relevance.

3.4 Optimisation of Prosthesis Design and Manufacturing

The modern design cycle now includes “virtual prototyping” before the manufacture of new products, and the simulation of whole humans and their body parts is rapidly developing to inhabit this virtual world. One of the major results of this SimBio test case is the development of a protocol for the design and assessment of prosthetic components based on accurate numerical simulation.

The development and availability of a prosthetic meniscus would represent a major advance in the armoury of the orthopaedic surgeon. One of the primary challenges to be addressed in this context is the development of an adequate understanding of the structural role of the meniscus in the array of loading environments encountered in daily routine, and particularly in gait. This platform will support the specification of the geometrical and structural characteristics of a prosthetic meniscus. The development of this specification, based on an accurate numerical simulation, is a focus of this test application.

4 *Examples of results and developments from the SimBio Consortium*

4.1 Soft tissue modelling at CNRS

The biomedical engineering group at CNRS is contributing to the project MAXILLO-FACIAL SURGERY ENVIRONMENT, which was initiated in 1998. The target is to combine soft tissue material property characterisation using both ultrasound and MRI with visualisation and voxel-based and FE simulation of the entire human head, using the classified tissue properties [gre00]. Figure 1 gives a simplified model of the approach developed so far. A sphere is built up from concentric layers of bone (white) and soft-tissue (orange) (see Fig. 4.1: upper right). After cutting and moving part of the bony outer layer (upper left) soft tissue reaction to this manipulation is simulated. Changes in voxel-positions are visualised by colours (lower left): voxels moved at least once are coloured green, voxels that are no longer occupied are red. The resulting shape is shown in Fig. 4.1: lower right.

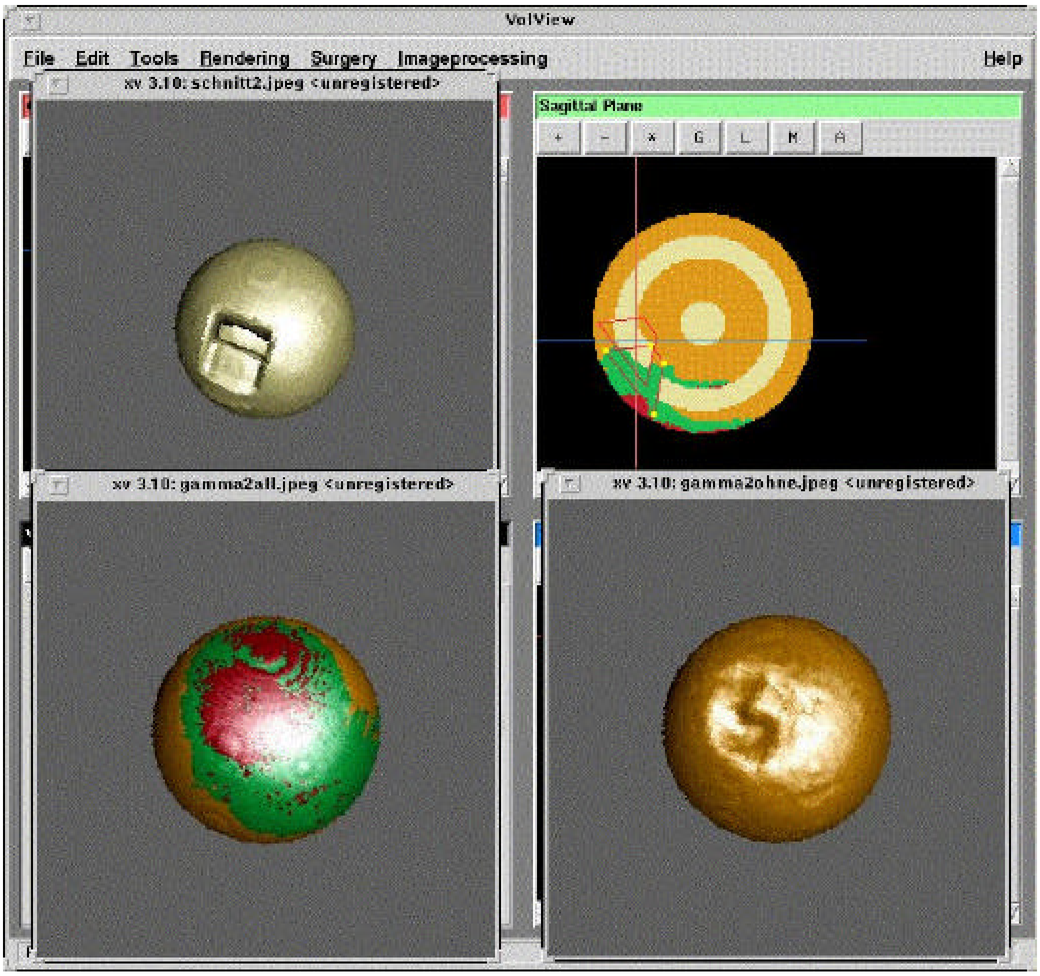


Figure 4.1.: Simulation of soft tissue (orange) adaptation to change in bony structure (white).

4.2 Improved and accelerated FE-volume conductor modelling in EEG/MEG-source localisation

Localising the current distribution in the human brain from extra-cranial EEG/MEG-measurements is an inverse problem whose solution requires the repeated simulation ("forward solution") of the electric/magnetic propagation for a given dipolar source in the brain using a volume-conduction head model. Two of the related issues arising are exemplified here: improved physical modelling and efficient numerical solvers for the forward solutions.

Recent studies at MPI and BMZ[1] have used the Diffusion Tensor Imaging Effective Medium Approach, DTI-EMA [tu98], to determine the influence of white matter anisotropic conductivity on the various EEG/MEG-source localisation algorithms and source localisations. Figure 4.2 shows a DTI-MRI fibre orientation map based on a U-FLARE sequence. Eigenvector orientations corresponding to the largest eigenvalue are projected onto the imaging plane, and overlaid on a T_1 weighted image (MDEFT sequence). Visualisation in regions of low diffusion anisotropy was suppressed. Further information about the exact parameters of the measurements can be found in [wo9]. Preliminary results on the influence of white matter anisotropic conductivity on localisation accuracy [hau99] support the use of anisotropic modelling, as featured in the SimBio project, to provide improved diagnostic performance of EEG and MEG.

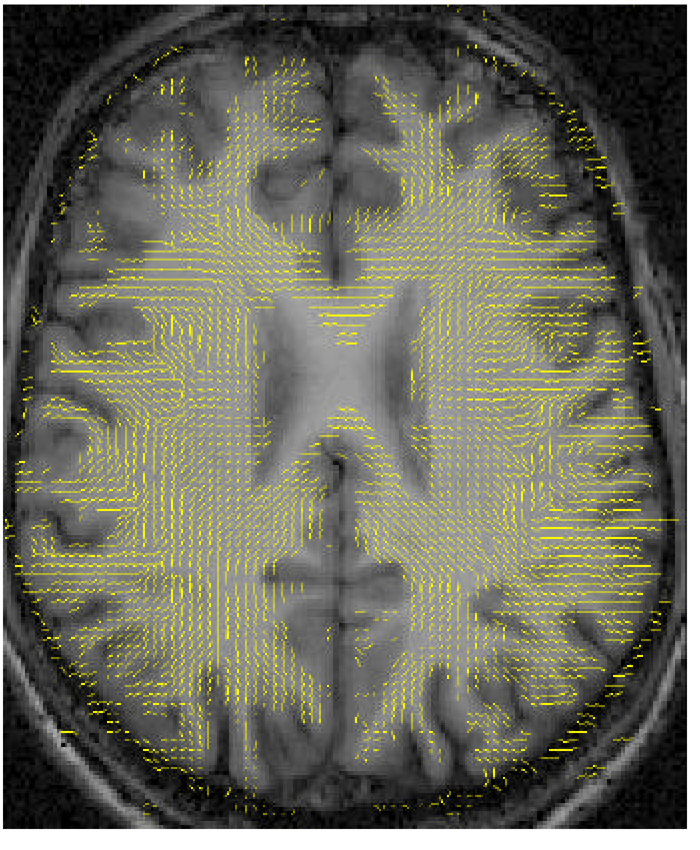


Figure 4.2: DTI-MRI image of the human brain showing eigenvector orientations.

When employing high-resolution models for the FE-modelling of the volume conductor head, each forward solution requires the solution of a large system of equations. For such systems, efficient parallelised sparse matrix solvers become indispensable. A first investigation carried out by MPI and

[1] in collaboration with MGH-NMR Center, Charlestown, USA

NEC [wo99] showed that a diagonally-preconditioned, symmetric QMR method produced excellent parallel scaling on the NEC Cenju-4 and could reduce the time for the solution of a test matrix with approximately 1.4 million non-zero entries to around 1 second.

4.3 Bio-mechanics to support facial-surgery planning

One of the target applications of the SimBio framework is pre-surgical simulation, i.e. modelling of the bio-mechanical forces during and/or induced by surgical interventions. Simulation allows optimising procedures (saving time in the theatre and thus minimising risk for the patient) and planning therapeutical strategies (promising to improve the outcome). At the time being, this is a circular process aiming at improvements of the underlying model: setting up a bio-mechanical model on the basis of individual CT or MRI scans, applying "realistic" material parameters and forces at known locations, finding predicted displacements, verifying simulation results by measuring forces and displacements in the patient. It is expected that models will mature to make safe predictions possible.

In an ongoing collaboration between MPI, NEC and the University of Leipzig (*Centre & Clinic for Dental, Oral & Facial Surgery)* a study is underway to investigate the magnitude of the forces that are present during, for example, the sequence of operations to remedy inborn deformations of the human skull. Figure 4.3 shows the result of a parallel simulation to model the mechanical response of the skull due to forces applied by mounting a surgical frame (a so-called halo) to the head. The steel halo is tightly fixed by screws to the head, thus deforming the skull. A description of the base software used for the studies can be found in [har98].

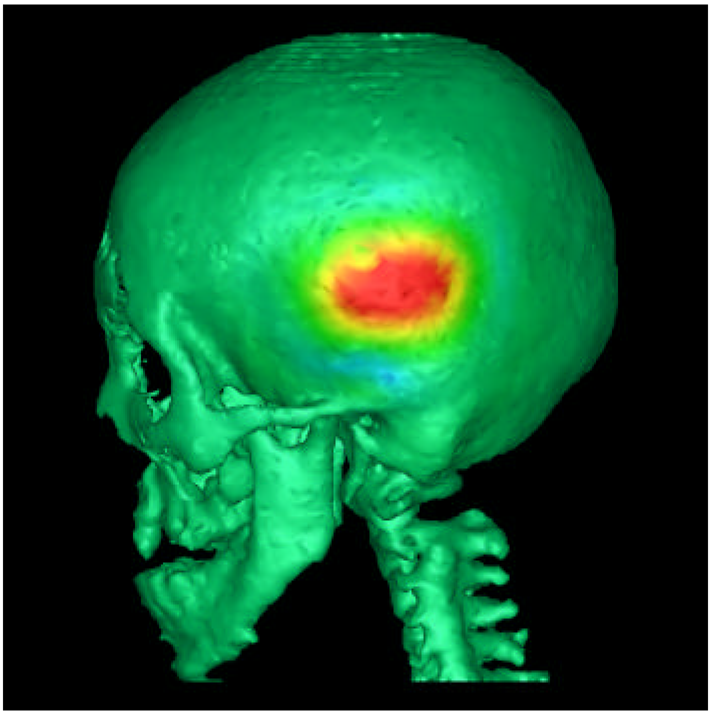
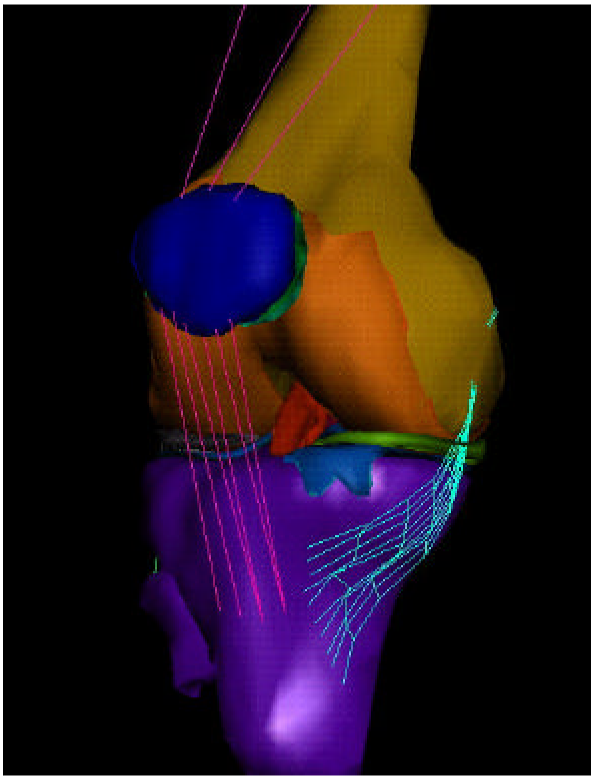


Figure 4.3: Mechanical response of the skull to the applied "halo forces".

4.4 The KneesUp project

Within the European Commission-funded project KneesUp (HPCN enabled simulation of the human knee), ESI and the University of Sheffield – including both the Department of Medical Physics & Clinical Engineering and the Department of Orthopaedics – collaborated on the development of a realistic finite element model of the human knee derived from MRI scan slices ([ho98a, ho98b]). This model also included a first prototype of a meniscal implant (see Figure 4.4).

The current model includes bone, articular cartilage, menisci, cruciate, collateral and patella ligaments. Validation against the recorded path of least resistance from 0-90 degrees of flexion is encouraging. Femoral roll back and posterior displacement of the menisci is observed and equates to the published figures. Impact transmission through the extended knee with/without menisci and with a generic total knee replacement shows the same pattern as in published papers.



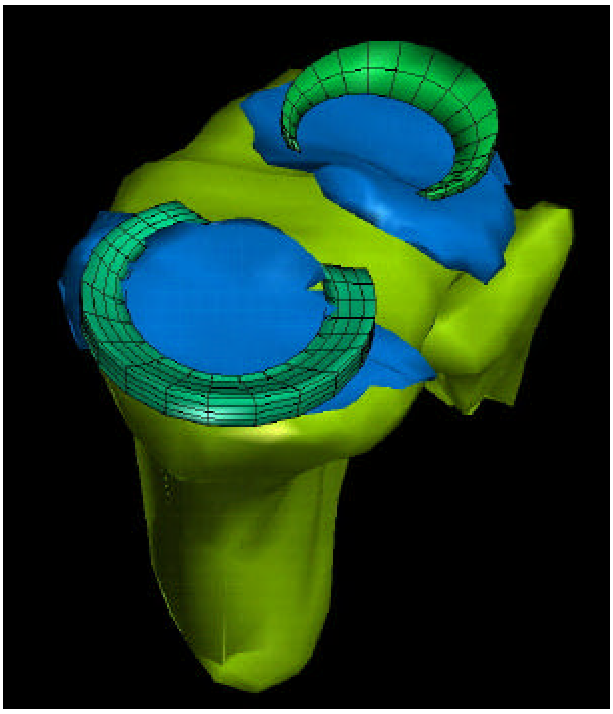


Figure 4.4: The KneesUp human knee model and a detail showing the meniscal replacement.

Simulations performed in the KneesUp project included both medical applications and automotive safety scenarios ([pe98]). For the computation of a gait cycle, simplified hamstring and quadriceps tendons were modelled as cable elements and time variant loading represented the action of the muscles on these tendon elements. A heel strike simulation was performed with and without meniscal replacement. The “automotive” models included lower leg impact through intrusion of the floor panel in a frontal car crash and a pedestrian impact corresponding to a published experimental model.

5 Concluding Remarks

The SimBio environment combines medical imaging and finite element techniques with up-to-date HPC algorithms and technologies. The SimBio project will provide an extensive tool for numerical modelling of human body parts. A major advantage of the SimBio approach is the ability to set up models of body parts of *individual* human beings, both in healthy and pathological condition. This high flexibility is enabled by the use of medical scan data of individuals. It is a new aspect in biomedical simulations to synchronously utilise the medical data sets for the geometry description as well as for the determination of reliable material properties. This concept thus paves the way for the future set-up of virtual dummies of individuals applicable for the investigation of a wide range of medical problems.

The technological development within SimBio has a focus on the construction of a generic simulation environment whose component-based distributed interaction allows for the interworking of technological expertise, from clinical through to engineering and computing systems, in order to provide full solutions to medical, and medical industry, problems. The motivation is to improve the quality of health service that can be delivered to society: a particular strength being the replacement of invasive diagnosis by non-invasive simulation-based techniques.

The evaluator applications featured within the project highlight the improved treatment options possible in the fields of

- ageing (with improved diagnosis and analysis possibilities for treatment of neurological disorders such as Alzheimer's disease),
- disability (with improved design and resulting durability of prostheses) and
- neurosurgery (with increased operation accuracy)

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