

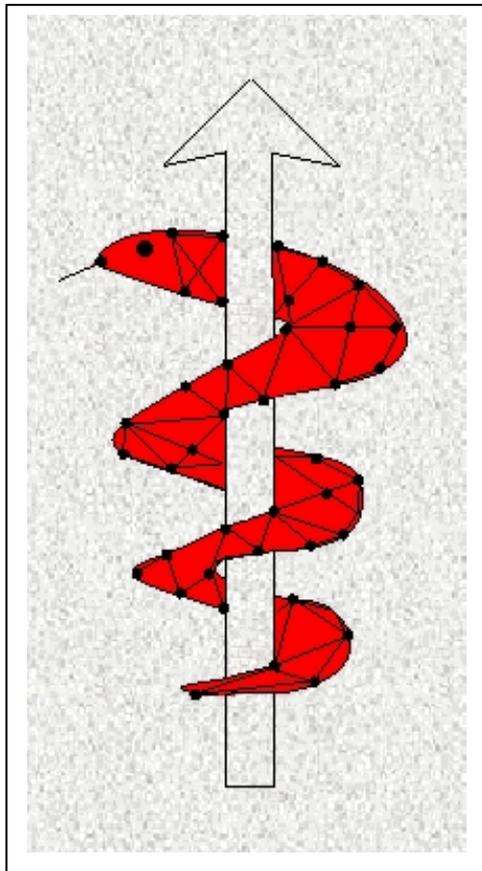


The IST Programme Project No. 10378

SimBio

SimBio - A Generic Environment for Bio-numerical Simulation

<http://www.simbio.de>



Deliverable PP3 Final Report

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1 Foreword

This final report covers the full project duration and gives an overview of the technical progress made, results and conclusions of all project workpackages in addition to providing a summary of these and of the project objectives. The report includes material contained in the two previously released public progress reports (deliverables PP1, PP2 – available on the project web-page: <http://www.simbio.de>). Activities reported are in line with the project workplan as defined by Contract Amendment **No. 2**, following the successful SimBio-NAS proposal to provide an extended evaluation and validation subtask, Subtask 7.4. It should be noted that the two additional partners from Maribor, Slovenia (the University of Maribor and the Teaching Hospital of Maribor, referred to by acronyms UNI-MB and SBM, respectively) commenced activities in the project at the end of Project Month 27.

2 Summary

The central objective of the SimBio project was to produce a generic simulation environment for advanced clinical practice and health care; a key feature being the input of individual medical scan data to the modelling and simulation process. The necessary components of such an environment are:

- Discrete Representation of the Physical Problem (Medical scan data is transformed into a finite element mesh, data for tissue modelling within the finite elements is provided);
- Numerical Solution System (including SimBio-internal parallel finite element solvers and numerical library routines, together with interfaces to allow for the use of external numerical software);
- Inverse Problem & Optimisation Component (providing a framework for inverse problem and design optimisation solver development - based on the use of the numerical solution system – and also including sensitivity and reliability analysis);
- Visualisation (Advanced, and standard, visualisation tools will be included via SimBio-internal tools and interfaces to external software).

The SimBio environment was designed for execution on parallel and distributed computing systems, the component interaction exploiting CORBA as a portable object-oriented interoperability architecture. Remote use of HPC platforms allows the computational demands of the simulation (or other compute-intensive components) to be met. While the techniques developed have a wide range of possible application, the potential impact is demonstrated for specific areas through the SimBio evaluation & validation applications: electromagnetic source localisation in the brain, analysis of time-series data of the brain, maxillo-facial mechanics, knee-mechanics and prosthesis design/analysis.

The following paragraph provides a summary of the project deliverables as foreseen by the contract workplan (Technical Annex).

At project month 6, design reports for the software component developments and requirements specifications were to be produced (all public reports). By the mid-point milestone, all intermediate versions of the software components were to be in place (and public release notes on the software available) together with preliminary evaluation reports on these by the applications. Final versions of the software components were scheduled for completion at project month 30, with public release notes, and the final applications evaluation reports available (public docs) at project completion.

All deliverables were achieved in line with the project's Technical Annex, with no revisions to the workplan being necessary. The project demonstrated the possibility to create software chains in a distributed environment, including remote-site HPC systems, in order to carry out patient-specific numerical simulations based on medical scan data. The medical/clinical advantages of using such numerical modelling approaches were demonstrated and documented in various publications. All software components necessary for the above demonstrations were developed or extended within the project and their interaction within the environment enabled through the use of standard data formats or the construction of appropriate software interfaces.

Scientific publications on the use of numerical modelling for medical applications and on the global SimBio approach - patient-specific numerical simulation - have raised awareness of the possibilities for the medical community. Software components developed (or extended) within the project will be available for use outside the Consortium: either as open source software for research or via commercial licenses. In addition, public access to the materials database, providing input to the numerical modelling process, will be provided. Future Grid services (or Grid service showcases) will build on some of the SimBio project developments.

2.1 The SimBio Consortium

For further information and links to individual partners web-sites, see: <http://www.simbio.de>

Participant Role	Participant number	Participant name	Participant short name	Country	Status	Date enter project	Date exit project
S	1	NEC	NEC	UK	C	1	36
S	2	MPI of Cognitive Neuroscience	MPI	FRG	P	1	36
S	3	A.N.T. Software	ANT	NL	A	1	36
U	4	Biomagnetisches Zentrum Jena	BMZ	FRG	A	1	36
S	6	Centre National de la Recherche Scientifique	CNRS-DR18	F	A	1	36
S	7	ESI Group	ESI	F	P	1	36
S	8	Sheffield University	USFD	UK	P	1	36
U	9	Smith & Nephew	S&N	UK	A	1	36
U	10	U. Maribor	UNI-MB	SI	P	27	36
U	11	Teaching Hospital Maribor	SBM	SI	P	27	36

Subcontractor

Subcontractor number	Subcontractor name	Subcontractor short name	Country	Date enter project	Date exit project
1	Sheffield Teaching Hospitals NHS Trust	STHT	UK	12	30

Note: the initial contract and workplan included the Laboratory for Medical Image Computing, Department of Electrical Engineering, K.U. Leuven, but this Partner was unable to contribute and withdrew from the project following the first external project review (For further info see Section 4.9)

An additional collaboration with the research group for Surgical Simulation and Navigation at **caesar** (Center of Advanced European Studies and Research, Bonn, Germany) was concluded for additional activities related to Workpackage 8 in Years 2 & 3. (For further info see Section 4.8.2)

3 Project Objectives

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 which has been performed, in some restricted applications, in the past.

The SimBio generic environment will allow future users to develop application specific tools to improve practices in many areas. Demonstrable impact for specific areas will be achieved through the SimBio evaluation & validation applications which 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, with state-of-the-art protocols and tools, 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 this project.
- **Numerical Solution System.** SimBio-internal parallel finite element 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.

The Subtask 7.4 introduced in the Final project Year has the objective to perform a site-independent evaluation and validation of the SimBio environment, focusing on latter of the 3 applications areas above. The evaluation and validation of the application related to the optimisation of prostheses design consists in comparisons of the simulated performance of the operated knee with recommended target values and with the performance of a healthy knee (kinematics and mechanical results).

4 Final Status reports per Workpackage

4.1 *Workpackage 1: Geometric Model Generation*

4.1.1 Subtask 1.1: Image Processing

The objective of Subtask 1.1 is to provide tools that will accept raw medical scan data and process them into a form suitable for mesh generation. Modules for format conversions, adaptation of standard co-ordinate systems, intensity adjustments, registration of time-series images, and for segmentation while correcting intensity inhomogeneities were developed. There were a number of changes to the schedules and to the strategies adopted in subtask 1.1, partly associated with the withdrawal of partner KU Leuven due to staff recruitment problems. Nevertheless all tools were delivered in timely fashion, and the changes did not interfere with the successful completion of other workpackages.

- Deliverable 1.1a consisted of a detailed description of the preliminary ST1.1 tools, their future development and the image file format that would be supported; it was delivered on time.
- The VISTA format was adopted as the standard data exchange format for the SimBio programme.
- MPI produced intensity-based segmentation and image manipulation tools for Linux. These tools were also exercised in Sheffield. Two modules for segmenting the skull from MR images were developed, enabling the standardisation of a head dataset by intensity and orientation and its segmentation into white matter, grey matter, cerebro-spinal fluid, skull and extra-cranial tissue. MPI has completed image processing tools for head segmentation of CT and MRI datasets. In order to setup biomechanical and electromagnetical forward models, a finite element mesh must be provided that describes the individual object under study precisely and covers all material compartments as relevant for the given problem. In addition to the intracranial compartments white matter, grey matter and cerebrospinal fluid (CSF), the meninges have to be taken into account for biomechanical simulations. The meninges consist of a thin layer of tough skin which encapsulates the brain and separates it into mechanically partially decoupled compartments, the hemispheres and the cerebellum. This sheath is at most 1 mm thick, but relevant for a precise modelling of mass shifts in the intracranial compartment. The skull has a rather low electric conductivity and a rather high stiffness in relation to other tissues of the head. The thickness of the skull varies between 2 and 8 mm depending on the region, which is expected to influence simulation results strongly. The skull is imaged best by cranial computer tomography (CCT). However, the relatively high radiation dose is prohibitive for research purposes, but may be acceptable for clinical questions. Thus for EM simulations in SimBio, we segment the skull from PD-weighted MR images. As we are primarily interested in intracranial processes, the extracranial tissues (e.g., skin, muscles, facial bones, fat, connective tissue, nerves) are collectively given a single label. The complete segmentation procedure as encapsulated in *vcompseg* needs approximately 3 minutes computation time on a typical Linux workstation. CCT datasets of the head are much easier to segment, as we are interested in discriminating soft tissue from bone only for biomechanical simulations as specified in ST7.2, group A. However, the gantry and head holders should be removed for modelling, so some pre-processing is required. The module *vctseg* implements this functionality. The components of the toolbox from MPI have been well-tested during their development and should prove robust.
- A number of approaches to constructing the knee models were explored. There are two fundamental problems in the implementation of the original SimBio intensity-based segmentation algorithms in this context: the first is that there is not good separation between the intensities of different tissue elements, and the second is that there is not a clear interface on the medical images between touching components such as the articular cartilage of the femur and of the tibia. A third problem is that the geometry and meshes representing articulating surfaces need to be very smooth, placing significant constraints on the

performance of mesh generation algorithms. A completely new approach, not envisaged in the original proposal, was implemented. The chosen methodology utilised the nonlinear registration algorithms to morph a template mesh into the patient mesh. A mapping function was defined based on the registration of the reference image, on which the template mesh had been constructed, to the patient image. This effectively embeds knowledge of the structure of the knee into the mesh generation process.

- The inclusion of Maribor (ST7.4) in the consortium from July 2002 provides additional external validation of the SimBio tools.

The final release of the ST1.1 tools was made in PM30. No major modifications have been required. Since the release, all the WP1 tools have been ported to the Windows Environment via the Cygwin freeware dynamic link library in addition to the Linux release. Since Uni-MB's involvement in the Project, to overcome some registration issues resulting from using a different acquisition protocol, a small modification to the constraints in the registration algorithm has been made. These changes have been supplied Uni-MB, but have yet to be implemented in the official Simbio release; STHT commit to making these minor changes before the end of the project.

Following Uni-MB and SBM's involvement via the Simbio-NAS project, STHT has developed a methodology for mapping template images between different MR sequences. This methodology involves segmenting the new MRI data set manually, and then registering the segments of the new data set to the existing template. The new MR images are mapped spatially via manual segments to the USFD template images and mesh, thereby generating a new MR sequence template that is spatially identical to the USFD template. This process is not ideal, because it requires a manual segmentation for every new MR sequence used. However, because the registration only involves binary images it is likely to be very robust. The process is performed only once for each new imaging; thereafter the standard morphing process is applied.

4.1.2 Subtask 1.2: Mesh Generation

Within the SimBio project two novel approaches for mesh generation based on medical scan data have been realised and one tool has been evaluated:

- VGrid, a voxel-based volumetric mesh generator
- the Mesh Template approach based on mapping
- the ZMD image processing tool has been evaluated together with PamGen3D™ for surface based mesh generation

The VGrid Mesher

VGrid is a volumetric mesh generator based directly on the 3D medical image data.

The final version offers the options to generate

- uniform hexahedral meshes (taking care of fine structures like e.g. the skull)
- non-uniform tetrahedral meshes (taking care of fine structures as above)
- smooth tetrahedral meshes (using a novel algorithm described below)

Non-uniform mesh generation

Vgrid produces a hierarchical representation (octree) of an image to enable material dependent non-uniform resolution.

The originally pursued strategy of applying a delaunay tessalation to the boundary nodes of an octree cell (to arrive at a tetrahedral mesh) was skipped because a valid triangulation could not be guaranteed with this approach (results included non-matching cells across octree faces, and degenerate elements, so-called slivers).

Therefore, a different algorithm has been designed, which follows a recursive idea: If we have a (simplicial) subdivision of the boundary facets of an octree cell, we get a subdivision of the octree cell itself by connecting its midpoint with the boundary simplices. For the boundary facets themselves, we

can apply the same idea recursively. This tessellation is evidently consistent across facets, because the subdivision of a facet depends only on the data of the facet, namely, its boundary nodes.

This algorithm has the following useful properties:

- It runs completely locally, that is, considers only the nodes of the current octree cell
- It guarantees consistency across octree boundaries
- It guarantees a minimum quality of the resulting tetrahedra
- It is insensitive to vertex coordinates, and therefore very stable
- It is very efficient (linear in the number of nodes)
- It provides meshes of high surface smoothness.

Generalised volumetric marching tetrahedra

This non-uniform tessellation algorithm still produces axis-aligned meshes. In order to achieve smooth boundaries, further action has to be taken. For this reason, the marching tetrahedra algorithm, typically used to generate surface meshes from Cartesian grids, was generalized to generate volume meshes with smooth boundaries from arbitrary tetrahedral meshes with a scalar separating function. Depending on the signs of vertex values of this function, 4 essentially different cases can be distinguished, which lead to different subdivision patterns. The novel aspect of this algorithm is the consideration of cases where the zero-level of the separating function passes exactly through a vertex. These cases are of particular importance for the SimBio context, where the separating function is not given analytically, but must be defined by interpolation from the voxel data, resulting in a discrete set of possible values.

Quality of the resulting meshes

The algorithm described before does guarantee a minimum quality of the resulting tetrahedra. This is evident from the following observation: First, the non-uniform meshing algorithm does generate only a finite number of different tetrahedra, the worst-case quality depending essentially on the balancing level of the octree. Second the marching tetrahedra algorithm does generate only a finite number of configurations, due to the limited set of values of the separating function. While an analytical investigation of the occurring cases has not been performed, numerical studies show that the quality of resulting element is acceptable (using the mesh quality tool described in D12c).

The algorithms developed within SimBio have proven quite powerful and open for extensions. They will form the basis of future mesh generation developments.

The Mesh Template Tool

To ensure a successful project outcome (with respect to the smoothness of mesh surfaces), the mesh template mesh generation method was developed in parallel. The approach relies on utilising the registration tools developed under Subtask 1.1 and described in D1.1c to morph a pre-existing mesh. Although considerable effort is expended in creating the template mesh initially, much of the effort in ensuring smooth surfaces and good element quality is rewarded by the subsequent automatic generation of patient-specific meshes that have inherently smooth surfaces.

In addition to the mesh template approach for the generation of patient specific finite element meshes, several tools have been developed to aid in the generation of the template mesh. The tools centre on producing smooth surfaces that do not contain ‘terracing artefacts’, which result from pixelation of the data in the medical images.

The ZMD Tool and PAMGen3D™

The ZMD tool is an intensity based image processing software. Its main application is the automatic segmentation of arteries. For the knee, though the whole process is not automatic, it was possible to extract in a few steps the outer surface of the main structures such as bone, ligament and cartilage (T1 sequence) with a good quality. Regarding other structures such as cruciate ligaments, separation between cartilages or menisci, the images provided do not contain enough information to allow as accurate a segmentation.

Second, an automatic sequence of operations was designed for meshing segmented images of the knee into 3D tetrahedral elements, using PAMGen3D™. This sequence was used to generate meshes of 3 structures, while proved inefficient for 7 others. The level of manual work and try-fail attempts necessary with these remaining structures defeat the aim of automatic mesh generation. The generated meshes are also not suitable for explicit finite element calculations. This is due to the fact that the mesh generator tool being designed for flow applications does not strive for reducing the number of elements but on following the surface geometry. Making these surfaces smoother while reducing the number of elements requires a lot of manual work.

Comparison of the different meshing approaches

The volumetric approach followed by Vgrid shows the best promises for an automatic yet high-quality mesh generation process. While in the end-project status, there are still some deficiencies (surfaces could be smoother, number of elements could be further reduced), these can be corrected by future algorithmic enhancements.

The mesh template approach can lead to very good meshes, but requires a good deal of prior manual work for preparing a mesh template. The success of the method depends crucially on the availability of a smooth mapping between template and patient geometry, that is, both have to be sufficiently close to each other.

Finally, a standard surface based approach does not lead to satisfying results without further manual intervention.

4.2 Workpackage 2: Compilation of Material Database

Soft tissue investigation

In the beginning of the project we have developed a conventional experimental environment including set up and protocol procedures, which allow performing reliable experiments comparable to the approach developed and applied by other groups. Therefore a traction machine had been set up, which allows carrying out experiments on small samples of soft tissue in compression mode. Numerous inventions and modifications had to be realized to meet our goal to be able to perform experiments on the small fragile samples of brain tissue. Therefore we had e.g. to integrate in the traction machine a temperature and humidity controlled chamber. This enabled us to deal with the extremely sensitive brain tissue under reproducible conditions and to increase significantly the precision of measurements. To meet better the needs of realistic modelling we had to expand our experimental equipment further to enable us to investigate all types of brain tissues. Since initially we took into account the brain matter only we had in the following to extend our investigations to membrane structures also. This means that we had to enlarge our experimental environment for traction experiments. So we performed in the final project phase experiments on Bovine cranial *pia mater* tested quasi statically in traction. The curves obtained could be divided into 1) an initial physiological part, 2) an elastic part, and 3) rupture, which was defined by the maximum force that could attain a sample. The important stiffness determined for the *pia mater* in these preliminary experiments shows that it is very important to include membranous structures into a realistic model as well. Therefore we will continue this work.

One of the most intriguing problem one faces in small sample biomechanical experimentations is the reliable and reproducible sample harvesting and cutting. This rests a permanent problem and we took much efforts to ameliorate the generally known experimental setups.

Our work concerning the MRSI-technique turned out to be extremely difficult since we faced enormous problems in detection and evaluation of force induced geometry changes in a reliable manner and with a sufficient resolution. Actually we put much efforts in an amelioration of the MRI-sequences and the possibility to get higher effective contrast by fusing images of different protocols. The work on these problems continues. To start with a relatively simple situation we acquired MRI and US images from the aorta in 3D with a sufficient time resolution of the cardiac cycle, which

means different intra-vascular pressures. These pressures are directly measurable or can at least be estimated. They induce time dependent deformations of the vessel, which provide together with the forces acting on the vessel wall a basis to determine vessel mechanical properties in vivo. This work will be continued.

For to investigate further other soft tissue directly of interest for the consortium – as the meniscus of the knee - we extended the so far performed compression experiments by applying increasing deformation rates in the three different directions. We found evidence for a complex strain depending but in any case thixotropic like behaviour. This means that material properties entering realistic simulations of knee movements have to be controlled and adapted dynamically. We will continue this work also beyond the end of the Simbio project to determine more detailed reliable quantitative data.

Electrical Conductivity Measurements (DT-MRI)

In EEG/MEG source localization the human head is modeled as a volume conductor. The skull and the white matter are known to have anisotropic conductivity with a ratio of up to 1:10. Recently, formalisms have been described for relating the effective electrical conductivity tensor of white matter tissue to the effective water diffusion tensor as measured by diffusion tensor magnetic resonance imaging (DT-MRI). First studies show that skull and white matter conductivity anisotropy have an influence on the forward solutions for EEG and MEG.

The diffusion tensors of the whole head of a subject was measured in 8 DT-MRI sessions. Each session produced 4 axially oriented, 5 mm thick slices with in-plane resolution of $2 \times 2 \text{ mm}^2$. Co-registered T1-MR images allowed the registration of the DT-MR data on the 3D T1-MR data set. The highest fractional anisotropy value was found in the splenium of the corpus callosum (0.74)

The measured conductivity tensors were used to set up an anisotropic finite element model. The eigenvectors of the water diffusion tensors were used to compute the conductivity tensors for each white matter finite element of the brain with an anisotropy ratio of 1:10 (transversal : longitudinal to the white matter fibre direction).

Finite element simulations of the potential distribution in the brain showed the influence of the conductivity anisotropy on source localization.

Material-Database

An extensive collection of data of living tissues mechanical and electrical properties has been executed. The database delivered as D2a has permanently been extended based on periodically evaluations of literature. Thus a broad collection of most actual and interesting data of living tissues properties is now available in standard literal form.

Even so this meets already the interest of a big number of users there rests the problem that most material properties depend highly on numerous parameters, which might change during a real world experiment as well as during a simulation. Here one value given in a table is not sufficient to perform a realistic simulation, see the above mentioned thixotropi of the meniscus. This parameter dependency of material properties is investigated by numerous authors, which publish their results in form of graphs. These cannot be entered directly in tables and are there for not usable for the purpose of modelling and simulation.

To overcome these problems we extend the information accessible in our database by digitizing graphs and creating from this tables, which provide parameter depending numbers, which can be entered directly in simulations. For to present this information together with the complete bibliography in an easy accessible manner, we developed and installed an according database structure using the standard database 'MS-ACCESS'. This database is accessible via WWW. Furthermore a MySQL-version has been developed, which will be connected as the VivMat-Website to the WWW in the nearest future.

4.3 Workpackage 3: Numerical Solution System

The Numerical Solution System (NSS) for the SimBio environment consists of full problem solvers (simulation codes) and linear solver libraries and a partitioning tool. The NSS was developed during the first two years of the project, 1.4.2000 – 31.3.2002. The final version of the numerical solution system (NSS) comprises the following components:

I. Linear Solver Libraries and Partitioning Tool:

- **DRAMAtool**, a software component for partitioning finite element meshes for efficient parallel execution.
- **An interface for PEBBLES**, a public domain library for parallel equation solving (AMG-preconditioned CG).
- **PILUTS**, a highly efficient NEC linear equations solver library (**P**arallel **I**ncomplete **L**U with **T**hreshold preconditioned **S**olvers).

II. Full Problem Solvers:

- **NeuroFEM**, a full Finite Element (FE) code for parallel execution with coupling for parallel solvers (SimBio: static electromagnetics in the brain).
- An interface for **PAM-SAFE**, a fully non-linear explicit FE code for biomechanical applications (SimBio: knee-mechanics).
- **HeadFEM**, a non-linear fully parallel FE code for special biomechanical applications (SimBio: head-mechanics).

Much of the initial technical development work focussed on integration of software components within the Numerical Solution System and improved component interaction by a definition of a common, platform-independent, binary, VISTA-file format - with mesh partitioning and parallel library routines being interfaced to the NeuroFEM and HeadFEM code. For enhanced parallel application efficiency a tool (DRAMAtool) that provides mesh or matrix partitioning and basic data-migration has been implemented on top of the DRAMA load-balancing library. The DRAMAtool can be coupled via the common VISTA file format. The underlying DRAMA library has been extended to give special support to the SimBio applications for the partitioning of sparse symmetric matrices. The PILUTS linear equations solver library includes state of the art parallel, single level sparse solvers for real symmetric positive definite, general real symmetric (CG, symQMR) and real non-symmetric matrices (BiCGStab) together with a selection of preconditioning methods (scaling methods, symmetric or non-symmetric incomplete block factorisations with threshold and distributed Schur complement algorithms) for convergence acceleration. The PILUTS solvers have been enabled to use the DRAMA-partitions (giving improved convergence of parallel runs) and have been “weakly” coupled to the application codes NeuroFEM and HeadFEM.

The kernel of the NeuroFEM-simulator is the FE-solver system, since thousands of large equation systems have to be solved within the inverse source localisation procedure. Preconditioned conjugate gradient methods with state of the art pre-conditioners tuned to the special Maxwell-equation operator were added to the old serial CAUCHY-solvers. The serial version of the algebraic multi-grid preconditioned CG method (PEBBLES) has been "strongly" integrated into NeuroFEM by means of an element-wise coupling. A file-based interface to the factorisation pre-conditioners of the PILUTS library has been developed to enable initial tests of the parallel PILUTS version based on node-partitioned data. The integration of the parallel AMG pre-conditioner parPEBBLES based on element-partitioned data and an element-wise coupling is in an advanced state. Building on this development a strong coupling between NeuroFEM and the PILUTS library has been implemented. Finally, the integration of the parallel AMG pre-conditioner parPEBBLES based on element-partitioned data and an element-wise coupling has been completed.

Starting from an initial version of the HeadFEM simulation code that was developed with a linear solver based on the AZTEC library a new modular, object oriented version was implemented in C++ for the direct integration of the PILUTS library. The new version was designed to allow an easy integration of new solver libraries and to facilitate the development and integration of improved non-linear FE-modelling routines necessary for the head-mechanical simulations in SimBio.

First tests have been performed with PAM-SAFE to evaluate the current tetrahedral formulation response with respect to the hexahedral formulation. The second step of the development focussed on interfacing the SimBio formats (VISTA etc.) to the PAM-GENERIS format, on investigating the best way of introducing the fibres within a bio-mechanical component of arbitrary shape, which is

modelled by 3D tetrahedral or hexahedral elements and on an investigation of the parallel performance of PAM-CRASH on LINUX clusters.

Further information on the above, together with background information on all software components can be found in the design report, D3a, the preliminary software release report, D3b, and the final release report, D3c. Those reports also detail and motivate the further development plans (D3a, D3b) and the final status, installation and use of the software (D3c). The following sections summarise the status of the final implementation per software package:

DRAMAtool: The DRAMAtool calculates suitable domain decompositions for improved parallel efficiency. It exploits the features of the DRAMA library, which give special support to the SimBio applications for the partitioning of sparse symmetric matrices. The repartitioner tool uses file interfaces based on the latest common VISTA format definition. It can be linked with VGrid, NeuroFEM, HeadFEM and the PILUTS solver (standalone-) tool in a linear chain. The software is fully functional including a test-suite for verification. It has been released via the SimBio web-page at the end of March 2002.

NEC Solver Library PILUTS: Integration has been concluded. All PILUTS methods, CG, symQMR, and BiCGstab can be called with a common interface now. The specific iterative solver is selected by a parameter. For advanced preconditioning BiCGstab, simple diagonal scaling, simple row and column scaling, block Incomplete *LU* factorisation with Threshold (ILUT), block ILUT with preceding diagonal scaling, block ILUT with preceding row and column scaling, distributed Schur complement (DSC) preconditioning using ILUT for local diagonal matrix blocks, DSC preconditioning with preceding row and column scaling using ILUT for local diagonal matrix blocks, and DSC using complete *LU* decompositions of the local diagonal matrix blocks are available. The PILUTS library was successfully integrated and tested in the simulation codes HeadFEM and NeuroFEM. The PILUTS software was also released at the end of March 2002.

NeuroFEM: Realistic solution times for inverse source reconstructions in isotropic high resolution tetrahedra and cube head models were achieved by using parallel computers with a moderate number of processors. The Algebraic MultiGrid (AMG) methods are used as efficient preconditioner for the CG algorithm in the finite element solution software NeuroFEM. On an SGI ORIGIN computer the speedup was 75 on 12 processors for the parAMG solver compared to the Jacobi-CG method (7.5 through AMG-CG compared to the Jacobi-CG and 10 through parallelisation). The computation time for one forward simulation was reduced to 1.5 sec using 12 processors of a PC-Cluster and the parallel algebraic multigrid preconditioned CG solver. Furthermore, it was shown that the AMG-approach is stable towards realistic head tissue anisotropy in the brain. The NeuroFEM software was tested and released together with the inverse toolbox of ST4.1. It is available to the project partners for evaluation via the SimBio web page.

PAM-SAFE: The PAM-SAFE code is a commercial product marketed by ESI. The PAM-SAFE™ package, the solver and its pre-processor, GENERIS™, have been enhanced to facilitate the modelling of biological materials, especially the menisci. Two types of tetrahedral elements have been developed for the project: 4-nodes and 10-nodes tetrahedral elements. It is important to take into account the microstructure of the biological material, in particular for the knee model, the microstructure of the menisci and of the ligaments. A major advance was the development of an improved definition of the orientation of fibres. In order to enable the remote computing evaluation within Subtask 7.4 in the final project period, work has been invested into a port to the Linux-SCore environment of the NEC PC-cluster (GRISU). This included adaptations for the Intel compiler and the SCORE system in addition to the incorporation of the FLEXLM licence system for Linux.

HeadFEM: HeadFEM is designed for the pre-operative planning of maxillo-facial surgery. It is a fully parallel code for the solution of non-linear, finite deformation, large strain finite element problems employing neo-Hookean hyperelastic compressible and incompressible (for soft tissue modelling) constitutive equations. The solution to the non-linear equations is achieved using the non-linear Newton-Raphson iterative method. The HeadFEM implementation uses the Finite Element

Interface (FEI) definition from Sandia National Laboratories, which serves as an abstraction layer between finite element routines managing matrix-assembly and linear-solver modules. Via FEI, HeadFEM is linked to the NEC PILUTS linear solver library, which comprises a variety of state of the art parallel iterative solution (CG, BiCGstab, symQMR) and preconditioning procedures ranging from simple diagonal scaling to incomplete Cholesky, threshold and distributed Schur complement (DSC) methods. For improved parallel efficiency, the partitioning tool based on the DRAMA load-balancing library is used. The HeadFEM solutions have been verified against reference results obtained with the commercial FE code ADINA™ for several engineering problems with simple CAD geometry. The final release includes a test-suite for verification purposes. The tests are based on a comparison of reference output with output from a current run. The software has been released to the project via the SimBio web page at the end of March 2002.

4.4 Workpackage 4: Inverse Problem Component

4.4.1 Subtask 4.1: Inverse methodology

The application of electromagnetic source reconstruction methods in medical and scientific applications requires a variety of inverse algorithms, which have to be tailored and adjusted to a specific problem with respect to patient needs or to an experimental setup in neuroscience.

Therefore a generic inverse toolbox was created, which includes a huge variety of state of the art inverse procedures. The core of the toolbox is realized as a class library. It consists of two major parts: 1. A flexible and modular framework, which provides in the final release an almost complete set of state of the art inverse methods. Inverse procedures can be coupled to forward solvers for spherical, BEM and FEM head models (both EEG, MEG). 2. A software framework to assess the sensitivity of inverse results to inaccuracies, errors and simplifications of the forward model.

The class library contains besides the already implemented algorithms definitions how new algorithms can be easily adapted to the inverse toolbox. This assures that the inverse toolbox is generic and can be adapted to a variety of application fields.

To obtain an easy access to the inverse toolbox a three shell user interface was created. This interface ensures the co-operation with the other software packages of the SimBio environment (e.g. mesh generation, visualization).

The coupling of the inverse procedures with the time consuming FEM forward computations on a parallel computer system could be achieved on two levels. The first level uses a file coupling of results computed on a parallel system. The second level combines both the serial algorithms of the inverse toolbox, which have to be called recursively for a selection of the inverse methods, with the parallel forward computations using a close coupling between inverse procedure and forward computation. High speed-ups were achieved on parallel computers and on LINUX Clusters. In addition to the originally planned FEM forward solver for EEG, a parallel forward solver for MEG was implemented according to the evaluation and validation plan of ST 7.1.

The content of the inverse generic toolbox is documented in the release notes of the final release of the subtask 4.1. Besides a description how to use the toolbox on the level of the three shell user interface guidelines are provided how implemented algorithms can be combined in a new way and how new algorithms can be added. This ensures that the idea of a “toolbox” is proceeded to users of the inverse toolbox and to developers of software for inverse source reconstruction procedures.

First applications of the sensitivity analysis framework were presented at the BioMag 2002 conference in Jena. The sensitivity of the inverse source localization towards conductivity anisotropy in high resolution FEM head models was shown with the inverse dipole fit algorithm on a parallel computer. Our results demonstrate that skull and white matter anisotropy has a big influence on moving single

dipole source localization results. The forward calculation and inverse localization errors indicate the necessity of the chosen complex realistic head model.

A new version of the ASA source localization software of A.N.T. Software uses the generic inverse toolbox as the mathematical core for inverse and signal processing algorithms. The new ASA software is in use as well at clinical as at scientific sites. The MEG group of the MPI of Cognitive Neuroscience in Leipzig integrated the inverse toolbox in their signal analysis environment and uses the toolbox for the analysis of experiments using MEG registrations.

4.4.2 Subtask 4.2: Inverse field reconstruction

Structural changes of body parts may be revealed by time-series images. To detect and analyse these changes, a non-linear registration may be employed, resulting in a high-dimensional field of displacement vectors. This field is used to derive a force field, based on incorporated realistic material parameters. Force fields need to be analysed for their singularities (“sources” and “sinks”) in order to provide a comprehensive 3D visualisation.

In order to produce bio-mechanically plausible results, transformations are constrained to be consistent with physical tissue properties. Furthermore, transformations need to preserve topology in order to yield an anatomically valid result. Two approaches have been pursued within this subtask, consistent linear-elastic and fluid dynamic image registration. Both approaches differ with respect to their applicability. The consistent linear elastic scheme allows for smooth transformation fields, but is restricted to small deformations. The fluid dynamic approach explicitly considers large deformations. Both elasticity operators are driven by realistic material parameters, as provided in database WP2.

An implementation of this framework was developed and underwent extensive testing. Different sets of simulated images were developed for testing the correctness of the implementation. Both registration approaches are computationally expensive, so additional effort was spent on performance optimisation. Both, software and report D4.2c, were made available as the final results of ST4.2 in October 2002.

4.5 *Workpackage 5: Visualisation*

The simulation of bio-medical data often requires advanced visualisation tools, capable of particularly accurate or high resolution visualisation. A visualisation module (VM) was developed for the SimBio environment that is capable of displaying all types of data encountered in the project: 3D image volumes, surface and volumetric meshes, dense and sparse vector fields, dipoles, electrodes, and distributions of computed physical parameters (such as forces, potentials) over these domains. Means for interacting with geometrical data, overlaying of geometrical objects on geometrical objects and image data on image data and the use of clip planes for geometrical objects were implemented in addition.

The VM was built using the Qt™ [[Qt](#)], OpenGL® [[OpenGL](#)] and Vista [[Vista](#)] libraries under X-windows™ and Linux®. Qt is a library for building graphical user interfaces (GUIs), OpenGL is a graphics library designed for efficient rendering of 3D geometrical objects, which is also capable of displaying pixel images. The Vista library offers efficient data structures and associated algorithms for creating and working with the data objects discussed in Deliverable 1.1a. Export filters to standard animation and graphic formats were implemented, to make data available to the cosmopolitan medical, clinical and engineering communities for presentation, publication and further investigation with external software tools.

An accompanying document specifies the implemented functionality. Both, software and report, were made available as the final results of WP5 in August 2002.

4.6 **Workpackage 6: Component Interaction**

The Workpackage 6 activities were carried out by ESI and NEC with discussions on requirements and deployment possibilities involving all SimBio partners.

After a first phase in which CORBA and WEB based solutions were evaluated and presented to the other partners (see Deliverable 6a), the decision was made to adopt a simple design concept for the Component Interaction. The basic idea was to have something with a complexity similar to shell scripts but easier for the novice to use. The main goal is for the SimBio environment to enable distributed software execution involving at least two sites:

- At the *local* site, the complete pre and post-processing is performed. This includes software for mesh generation and for visualising the results produced during all phases of the simulation.
- At the *remote* site, the designated HPC simulation is performed.

Each sequence of steps the user wants to perform in his or her simulation is described by a simple XML based workflow description language designed by NEC. Once created, these workflows are then executed by NEC's simple workflow enactor, the so-called "*SimBio Pilot*". To enable end-users to conveniently generate the SimBio requests that describe the user's simulation, ESI created a simple workflow editor called the "*SimBio Scenario Editor*" using QT for the graphical components. This editor, in accordance with the QT public license, has been released as open-source software.

CORBA was employed for the purposes of connecting the local site with the remote site. For this end, NEC developed application specific proxies which the users could integrate into their workflow. These proxies were statically linked so that the end user does not need to establish a complete CORBA environment just to run SimBio applications.

The final prototypes of the *Pilot* and *Editor* were delivered by to the remaining project partners in October of 2002, although upgrades, taking into account of new hardware at NEC, were made in the first half of 2003.

The following table shows the applications which have been completely integrated in the SimBio environment:

Table 1 List of SimBio applications that have been integrated into the SimBio Editor.

Application	Owner
Inverse Toolbox	ANT
PamGeneris, PamSafe and PamView	ESI
NeuroFEM, VSegment3D, VFluid3D, VReg3D and VLet3D	MPI
Vgrid and HeadFEM	NEC & MPI (Joint ownership)
VReglocal3d, VTransform3d and VCompSeg	Sheffield

Furthermore, a simple GUI allows users to add new applications when necessary, thus making the environment easily extensible.

4.7 Workpackage 7: Validation & Evaluation

4.7.1 Subtask 7.1: Source Localisation

The focal physical source model

A miniaturised dipole has been developed and successfully tested within the project. The major design criterion was that the dipole is small enough for simulating the pyramidal cells in the brain. First, tests of qualified materials were conducted. Twisted insulated copper wires with a diameter of 0.22 mm were used as feeding wire for the dipoles. The ends of the feeding wire were manufactured by cutting one of both wires and continue it by soldering a not insulated copper wire with a diameter of 0.06 mm. The 0.06 mm wire was wrapped around the 0.22 mm wire. The length of this winding was 10 mm. The winding was soldered and insulated by varnish. Only 0.5 mm of the ending of the dipole was left blank, whereas a thin layer of epoxy resin insulated the rest of the dipole. Phantom investigations have been performed as additional validation. A patent for the miniaturised dipole is pending (DE 101 43 705 A1). The physical source model has been established. Experimental procedures and modalities and data recording have been adapted and standardised. Measurements with the focal physical source models have been performed successfully. The results were used in the validation of the electromagnetic source localization software.

The physiological stimulus modality

The physiological source model was established. The median and the tibial nerve were stimulated while the magnetoencephalogram and the electrocorticogram were recorded simultaneously. The spatial distance between the centres of the cortical areas is in a range of about 2 to 3 mm. We focused our investigations to the first peak, which is known as the first answer in the somatosensory cortex S1 and is not affected by any cortical activities. This peak appeared in both signals at the same time. Stimulation yielded a clear dipolar field pattern for the magnetic and a monopolar potential pattern for the electric signal. The results of the source localization are dipoles in the expected cortical area for median and tibial nerve. The localized sources were within an accuracy of 1 mm in the expected cortical areas. The spatial distance between both nerves was in a range of 2.0 +/- 0.5 mm comparable with the anatomical difference.

The conductivity tensors

The conductivity tensor describes the direction dependency of the conductivity, which is also known as anisotropy. The used approach essentially derives the cross-property relationship between the conductivity and diffusion tensors through an effective medium representation of the tissue geometry. In the limit of small intracellular diffusion, the cross-property relation predicts a linear relationship between the conductivity and diffusion tensors. We measured diffusion tensors in the brain, transformed them into conductivity tensors and set up a model including this conductivity tensor information. This model, for the first time, includes individual tissue anisotropy and FEM was used to solve the inverse problem.

Conclusion

We performed a validation and evaluation of all parts of the SimBio generic software environment related to electromagnetic source localization. We found a very good agreement of the between the various modalities and thus the software was successfully validated. The most outstanding scientific success of this work was the inclusion of individual conductivity tensor information into this modeling chain. The aim to use patient specific data within a generic environment was accomplished. The results demonstrate that the SimBio generic software environment will improve clinical and medical practices.

4.7.2 Subtask 7.2: Bio-mechanical Head Model

The clinical usefulness of bio-mechanical head modelling using the SimBio environment was demonstrated by three different example problems. Two different simulation strategies were pursued:

- Forward models: The real locations and strengths of forces (or corresponding hypotheses) are known a priori. The consequences of these forces acting on the whole system are computed, visualised and evaluated. Computed deformation fields may be compared with scan data in order to check the validity of simulation results.
The Clinic for Maxillofacial Surgery, University Clinic Leipzig, is treating patients with in-born deformations of the skull. A stereotactic frame (a so-called *halo*) is mounted to the head by three fixation screws on each side of the head. The force exerted on the head by mounting the halo frame was measured with pressure sensors. Realistic material parameters were entered into a simulation of the mounting process. 22 cases were studied.
- Inverse models: No prior information about forces is available. In this case, time series examinations are employed and analysed by a non-linear transformation. The resulting deformation field is used to derive a force field, based on incorporated realistic material parameters. Force fields are analysed for their singularities (“force sources” and “sinks”) in order to provide a comprehensible 3D visualisation. Two different data collections were used:
 1. Patients with mild cognitive disturbances were examined behaviourally, clinically and by various neurophysiological and neuropsychological scales at the Department of Psychiatry, University Clinic Leipzig, during the course of the LEILA study. The study currently comprises of 150 patients, in which the first examination time point (TP1) was completed, and follow-up examinations (TP2) were conducted during the last 12 months. 33 suitable cases with well-defined lesions were selected.
 2. Patients with focal brain damage (after cerebral infarction, hemorrhage or severe head trauma) are treated at the Day Care Clinic of Neuropsychology, University Clinic Leipzig. Patients are scanned routinely by MRI at the time of admission and discharge (approx. 3 resp. 12 months after onset). 29 suitable cases with well-defined lesions were selected for analysis.

This validation and evaluation study was completed in March 2003. Results are compiled as Deliverable D7.2c.

4.7.3 Subtask 7.3: Knee Prosthesis

Workpackage 7.3 focussed on the application of SimBio tools to the study of the human knee. Three subtasks were identified, covering simulation, validation and evaluation. The primary achievements have been:

- the selection of appropriate high-resolution static and fast-acquisition psuedo-dynamic mri scan sequences for segmentation of bone, articular cartilage and meniscus and for kinematics evaluation respectively. Details are presented in the public deliverables.
- the development of an mri-compliant exercise rig for kinematic evaluation under relatively controlled conditions.
- the establishment of a dataset of three-dimensional medical images of the knees of a series of normal subjects and of patients pre- and post-operation, containing both high resolution static scans and psuedo-dynamic scans. Eleven patients were recruited. All were MR scanned pre-operatively, while four were not recalled for post-operative scanning due to additional pathologies or the necessity to implant metalwork into the knee during the operation. Five patients had data that were suitable for simulation trials. The pathologies included three medial meniscal injuries, one lateral meniscal injury and a postero-lateral corner injury.
- the development of a new tool, exploiting the registration algorithms developed in workpackage one, for quantification of knee kinematics from the dynamic scan data. We believe that these tools offer an accuracy in the assessment of knee kinematics that was hitherto unachievable.
- the investigation of the application of a range of segmentation and mesh generation algorithms to the construction of patient-specific knee meshes. We believe that we have demonstrated

that the best approach for knee applications is the morphing of a template mesh. Mesh smoothness is an important issue for the evaluation of joint kinematics.

- contribution to the development of the novel SimBio template-based patient-specific mesh generation algorithm (see workpage one), and its testing on the SimBio dataset.
- construction of a template finite element knee model of the reference dataset. The final template mesh consisted of 3,464 8-node solid elements, 13,120 shell elements, the majority of which were defined within rigid bodies representing the bone components of the knee and the remainder used in the contact interface definition), and 232 bar/beam elements.
- the simulation of the kinematics of the knees of the study group (normal and patient applications), and comparison with the results of the supporting experimental programme.

There has been some change of emphasis as the programme has progressed:

- The construction of patient-specific meshes for the knee proved more difficult than was originally anticipated, primarily because the intensity-based segmentation algorithms did not produce good results in the context of the knee. This increased the amount of effort that went into the patient-specific mesh generation within workpackage 7.3.
- The development of a specification for a meniscal prosthesis was not undertaken, partly because Smith and Nephew, the commercial partner for the knee tasks, had reduced interest and partly because effort was directed elsewhere.
- Significant effort was expended in the support of the new workpackage, 7.4. This was regarded as a very positive aspect of the programme, because a number of issues relating to the dissemination of the SimBio tools to potential customer sites (which otherwise would not have been addressed within the work programme) were resolved.

A protocol adopted for patient studies might follow that adopted within this workpackage.

- The patients were scanned in Sheffield, (the data being anonymised at acquisition); the DICOM data for each patient was transferred through the Hospital firewall to a secure University SGI machine where it was converted to the VISTA file format using the WP1 image processing tools. The patient VISTA image volume was then transferred to the Linux SCORE Cluster at NEC in Bonn where it was registered to the pre-segmented template volume using the *vreglocal3d* algorithm. The registration process takes approximately 40 minutes per patient using a single processor (there is no parallel version available at present). Ideally the image processing should take place locally but for demonstration purposes this has been done using the remote NEC computing facilities. In comparison, using a local 2.4GHz Linux P4 (Intel compiler), the registration process takes approximately 20 minutes, hence the reason for not parallelising the registration algorithm. Once the registration is complete, the mapping produced is applied to the template mesh, using the *vttransform* algorithm to morph the template mesh into a patient-specific mesh, which takes less than a minute.
- Once the mesh had been morphed it was transferred back to Sheffield, where patient-specific information, (e.g. femur lengths, limb masses, applied forces) were applied to the PAM “include” file, (a specification file of all boundary conditions) to prepare the simulation run. The new VISTA mesh was imported into PAM GENERIS, associated with its include file and saved as a PAM-specific .pc file. This .pc file was transferred back to the NEC SCORE Cluster and run on the PAM-SAFE parallel solver. A simulation run takes approximately 7.86 hours to reach approximately 45° of knee flexion (300ms) using 4 processors. In contrast, using three processors on the Origin 2000 SGI (four 250MHz R10K processors, 2560Mb RAM) at USFD the same run takes 25.8 hours.

Based on the experience and expertise developed within SimBio, we would suggest that:

- the mesh morphing method has been demonstrated to work well for generating patient-specific finite element knee meshes. Despite the amount of time spent developing the template mesh, we believe that the template mesh approach is the most appropriate one for the knee, because of the problems demonstrated in segmenting clinical knee images by an intensity-based approach and the difficulties in obtaining a mesh that is sufficiently smooth for kinematic simulations.

- further development will be required to take into account major pathologies, such as significant meniscal tears, by generating template pathologies from which a clinician could select the most appropriate prior to morphing the template mesh. At present, the algorithm will attempt to “crush” elements in the template to best match the losses of tissue indicated from the patient image. There are several ways in which this issue could be addressed, but an examination of the vector fields produced by the registration process and the implementation of a decision tree based on their properties has great potential.
- the kinematic results from the simulations do not demonstrate the clinically important “screw-home” of the femur on the tibia from full extension to partial flexion, which is clearly seen in the validation trials. It is likely that additional work will be required to model the complex nature of the cruciate and collateral ligaments. At the start of the programme we felt that available 3-D material models and finite elements were not developed sufficiently to address this. Current advances may permit solid modelling of the ligaments to be investigated as a post-project development. The development of a more advanced template featuring these elements is recommended.
- further work is required on the measurement of muscle forces and of the pretension in ligaments in order to improve the applicability of the simulations to the *in vivo* condition.

4.7.4 Subtask 7.4: Site-independent evaluation and validation

Objective of the Subtask 7.4 was to perform site independent SimBio generic environment installation and evaluation/validation of results generated in order to solve the problem of Design of novel replacement parts for the menisci of the human knee joint and methods for their surgical implantation. Subtask 7.4 addresses the same application as Subtask 7.3, thus, all steps involved in Subtask 7.3 should be reproduced in the Subtask 7.4 (from data acquisition to simulation and result interpretation).

4.7.4.1 Subtask 7.4.1: SimBio Environment Installation

The first assignment under Subtask 7.4 was to install the SimBio environment at the potential end-user site and, thus, enabling bio-numerical simulations on specific patient data.

Hardware and software installation

The installation of the SimBio environment in Maribor, i.e. tools like vreglocal3D, vtransform, PAM-Suite tools, the SimBio Editor and Pilot, performed without any difficulties.

Patient data acquisition (MR imaging protocols)

Two types of patient data in form of MR images need to be acquired as an input into the SimBio environment or for the validation purposes: 1) high resolution MR images of patients' knees close to full extension and blocked in position using a solid block to minimise motion artefacts (i.e. static MR images), and 2) low resolution MR knee images while undergoing light exercise by using MR exercise rig (i.e. pseudo-dynamic MR images). Both partners from Maribor, i.e. partners UNI-MB and SBM, have access to Toshiba Visart 1.5T MR scanner, while the partner USFD uses Philips Eclipse 1.5T MR scanner. The final parameters of Toshiba's MR scanner for acquiring both types of MR knee images were decided by clinicians after consultation with the partner USFD.

In scope of patient data acquisition partners from Maribor added two significant improvements to the existing protocol developed by partner USFD for pseudo-dynamic MR imaging: 1) improvement of the MR exercise rig, and 2) optical force measuring system for measuring the force on the foot plate pedal of the MR exercise rig. Under this subtask another two important activities should be reported. Partner SBM took care for a recruitment of 8 patient volunteers for the SimBio study. The second activity concerned usage of imaging material from Toshiba's MR scanner in the SimBio software chain. To enable this, appropriate interfaces were developed by partner UNI-MB.

4.7.4.2 Subtask 7.4.2: Validation of Image Segmentation

Among the main goals of Subtask 7.4 is also a validation of the SimBio environment image segmentation results. For this purpose two tools were developed by partner UNI-MB: an IST (i.e. An Image Segmentation Tool) and an IPVT (i.e. An Image Processing Verification Tool) tool.

An Image Segmentation Tool (IST)

The IST tool has been designed as a MR image manipulation and analysis software. The tool is in the first place meant as a helping tool for a manual segmentation of the MR images, where the physician, with ease and quality, annotates the regions of interest (ROI) inside the two-dimensional slice of the MR sequence. The interesting regions (e.g. meniscus, patella) are shown by their own colour and marked with a descriptive text. The annotations of regions can be stored in a XML document. The IST application has an advanced and user-friendly graphical interface (GUI). It supports many useful routines, such as copying the annotations from previous slices, importing the annotations, zoom, etc.

An Image Processing Verification Tool (IPVT)

This tool statistically evaluates the segmentation ability of the SimBio environment registration routines based on a comparison with references provided by the clinicians. A graphical users interface and a simple 2D image processing verification process was finished around the project months 30, while advanced statistical measures, especially for the 3D verification process, and report generation, were finished around project month 35. The primary goal of the IPVT tool is validation of image segmentation results, but it is also applicable as a training system. The application is interactive and has an advanced, efficient and user-friendly GUI. The main power of the IPVT tool is its ability to statistically assess an efficiency of arbitrary segmentation algorithm. This is achieved by comparing segmentation results of algorithm with references.

Validation

A validation of the SimBio environment image segmentation results was performed in the following manner: first, several slices from the MR image sequence through the knee was manually annotated by clinicians using the IST tool (i.e. references). Afterwards, these knee image sequences were processed by the SimBio image registration routine (i.e. VRegLocal3D) and mapping function (i.e. VTransform). A template knee model constructed by partner USFD was used in this registration procedure. The result of this phase was a patient specific 3D knee mesh, which was obtained by mapping template knee mesh with function VTransform using mapping matrix calculated by VRegLocal3D routine.

The obtained segmentation results were afterwards compared with the references by using the IPVT tool. Two types of verification were performed: 2D and 3D verification. By 2D verification the patient 3D knee mesh was first sliced according to appropriate voxel dimensions and, afterwards, so obtained segments were compared to manual annotations provided by orthopaedic surgeons. However, by 3D verification the obtained patient 3D knee mesh from the SimBio environment was compared to a 3D knee reference model constructed from sparse manual annotations provided by orthopaedic surgeons. A 2D and 3D verification of the image registration results pointed out a satisfying match between the SimBio environment results and expected results in form of expert's manual annotations. These findings were confirmed also by orthopaedic surgeons.

4.7.4.3 Subtask 7.4.3: SimBio Evaluation and Validation

The last activity under Subtask 7.4 was to thoroughly evaluate/ validate SimBio environment from its overall applicability point of view and, especially, the results were validated from possible end-users. This activity was split in two parts: a) the SimBio environment final results evaluation; and b) the GUI assessment from possible end-user with some recommendations.

SimBio environment final result evaluation

Final result of the SimBio environment process chain is a simulation of knee kinematics in the PAM Suite tools (PAM Generis, Safe, and View). The goal was to imitate the real patient knee kinematics by simulating a fine element (FE) knee model as realistic as possible.

Inputs into PAM-Suite modelling procedure are patient specific FE knee mesh stored in Vista format file, a footpad and materials data files. The next step in the SimBio environment processing chain is a modelling of such patients' knee models by using Pam-Suite tools. By this modelling the procedure set by partner USFD was followed. Partner UNI-MB and SBM also experimented with this procedure and altered some modification into patient models with intention to see how the knee simulation will respond (material properties of cartilages, altering of friction parameter, removing of ACL bars). The response of the SimBio environment was satisfying.

Inspection of PAM Safe simulation results in the PAM View pointed out that simulated knee kinematics almost completely match expectations of clinicians (are almost realistic). The simulation results from 10° and till 40° or 60° of flexion are correct, if the knee is flexed till 90°, a disturbance of patella motion is seen. These results were achieved by applying a larger force. However, this protocol does not expect such high flexion as far as 90°.

Final results besides visual inspection could be just partially validated. Pseudo-dynamic MR knee images were acquired for purpose of validating the kinematics behaviour of the FE knee models. In the validation procedure just kinematics behaviour of the bone tibia and femur were followed. The Euler rotation angles for the tibia with respect to the femur were observed. First, these rotation angles were calculated using the dynamic patient data obtained by pseudo-dynamic MR imaging. Afterwards, the same angles were calculated from the simulation results obtained by PAM Safe simulation.

When comparing Euler rotation angles calculated from the PAM Safe simulation results and compared to the gait cycle rotation angles taken from the literature, a big similarity was noticed. However, when we try to calculate the same Euler rotation angles from the pseudo-dynamic patient data, no meaningful results were obtained. After inspection, it was noticed that the dynamic registration of dynamic binary volume to the static binary volume for particular bone, was not performed well. There can be several reasons for this (e.g. resolution mismatch of static and pseudo-dynamic patient data, inappropriate distortion correction applied on MR scanner). Therefore, we were not able to validate the final SimBio environment results with quantitative measures.

SimBio Editor and remote computing facility

Many different autonomous software programs form the SimBio environment. Outputs from one program actually present inputs for the next program in the SimBio chain. Running SimBio environment in such way is very inconvenient for an operator and could lead to some potential errors. Therefore, the SimBio Editor was developed under WP 6. It enables definition of arbitrary scenarios composed from calls to the SimBio environment tools. For our test application the scenario was divided in two parts: local and remote part. The local part encompasses steps from MR patient imaging to a patient specific 3D knee mesh and initial modelling step in the PAM Generis. The remote part of scenario is liable for performing the PAM Safe simulation on a modelled patient knee mesh and for a visualisation of simulation results by using the PAM View. Running the SimBio environment process chain from the Editor is straightforward.

As a potential end-user we also tested the ability of the SimBio environment to perform the PAM Safe simulation remotely on the HPC NEC cluster. Remote computing facility is already supposed in the SimBio Editor, therefore, no additional program block need to be defined. The PAM Safe simulation executed on NEC cluster by using 16 nodes significantly speeds up simulation.

Graphical user interface and recommendations

The SimBio environment has actually three major GUI's: a) the SimBio Editor, b) the PAM Generis pre-processor, and c) the PAM View. PAM Generis and View are commercial software tools. The front-end of the SimBio environment is actually the SimBio Editor. This program has standard GUI with menu structure, toolbars, and mouse interaction. The usage of this program is straightforward. The main potential difficulty is to define a scenario. However, once the scenario is defined, the only modification needed is just changing of patient name.

It should be also noted that the input into the SimBio environment chain is the patient MR knee image sequence. This process is not automated now. Currently, the end-user must ensure by himself the transfer of MR imaging material from scanner to appropriate format for the SimBio environment (i.e. Vista format). This is not acceptable for the potential end-user. The execution of the SimBio chain is broken in the middle, when the manual PAM modelling of the patient specific 3D knee mesh is required. This modelling usually requires one hour of trained technician time. The

potential end-user should therefore employ/train such personnel, which might be disapproved by some end-users. The SimBio environment returns final results in form of simulations, which can be visualized in the PAM View. The trained personnel only can interpret such results to clinicians. This is not the most advantageous solutions. Much better will be, if the SimBio environment will interpret by itself the simulation results from the medical point of view. Therefore, the post-processing routine is suggested for such interpretation.

Overall grade

The SimBio environment returns very promising results regarding knee kinematics. However, there is still need for fine tuning of all tools involved in the SimBio environment. The main focus should be put to the MR imaging variability with respect to different scanners and possibilities of its reduction. Before putting the SimBio environment in the clinical practice, more extensive validation study on bigger patient data set should be carried out. The new project, extension of the SimBio project, oriented more toward clinical practise is thus suggested.

4.8 Workpackage 8: Info Dissemination

4.8.1 Project web-page

The project web-page (www.simbio.de) was brought on-line on schedule (deliverable D8a) and provides both a medium for information dissemination as well as a vehicle for the project-internal exchange of documents (a separate CVS-repository, installed on the same "SimBio server" is used for software exchange) through password-protected pages.

All public deliverables can be downloaded from the web-page in addition to certain presentations and publications. Future open-source releases of SimBio tools and components will either be downloadable from the project web-page or from sites linked from the SimBio page.

4.8.2 Collaboration with caesar

The software framework Julius has been extended and the core program interfaces were finalised. Currently there exist two versions: one stand-alone sample application built on a subset of the available modules and specifically adapted to provide a typical workflow for the radiologist. This workflow consist of data import/export, visualization of multiple datasets simultaneously in 3D and slice views with arbitrary orientation, simple segmentation techniques, manual editing, surface extraction from volumetric data and measurement of distances and volumes. The second version is split into the core program and individual plugins, which can be freely combined to create a user specific environment or application. The framework can be extended by adding plugins from the caesar homepage or created by third party developers. Within the SimBio context specific plugins have been developed at caesar and made available to the project members. The Vista importer now supports volumes, surfaces, meshes, tensor and vector data. The stereo plugin augments visual impact of any type of 3D model and allows for visual validation of complex 3D topologies like meshes or disconnected structures. The flythrough generator produces animations on the fly from movement paths defined by user selected waypoints. It has been augmented to generate movie-streams in addition to picture sequences. A further plugin implements a generic hardware interface for all kinds of 2D and 3D navigation, tracking and feedback hardware. Based on this interface several input devices were connected. Among them are computer mouse, Flashpoint active optical tracking system, Polaris optical tracking system (in active and passive modes) as well as two types of the Phantom haptic interface. Any number of these devices can be used to simultaneously navigate and interact with all or selected subgroups of the loaded datasets. Overlay methods can be used to visualize two or more datasets at the same time in the slice view diagram. Currently several polymesh or volumetric datasets can be shown simultaneously in the 3D view and combinations of any types in the slice view. Cut planes allow for the superposition of volume and slice view information. Further information is included in the (additional) deliverable D8Xd.

4.8.3 Publications & Presentations

4.8.3.1 Publications

P. Aïmedieu, R. Grebe, I. Idy-Peretti: Study of Brain White Matter Anisotropy. Proceedings 23rd Ann.Int.Conf. IEEE Engineering in Medicine and Biology Society, (1254) p100, 2001.

P. Aïmedieu, "Comparative study of the influence of the sacrificing procedure on the mechanical properties of the white matter of cow brains", Archives of Physiology and Biochemistry, Volume 110 supp September 2002, p119.

A. Anwander, A. Basermann, G. Berti, J. Fingberg, U. Hartmann, A. McCarthy, C. Wolters, S. Woods, F. Zimmermann, "Bio-numerical simulations with SimBio", in: T. M. Buzug, U. Hartmann, A. H^ulster, M. Kohl-Bareis, T. Wilhein (eds), Physikalische Methoden der Laser- und Medizintechnik, pp 114-120, VDI Verlag, 2003.

A. Anwander, M. Kuhn, S. Reitzinger, C. Wolters, "A Parallel Algebraic Multigrid Solver for Finite Element Method based Source Localisation in the Human Brain".. Preprint-series (No.35/2001) of the MPI for Mathematics in the Sciences Leipzig (available via internet <http://www.mis.mpg.de/cgi-bin/preprints.pl>), to "Computing and Visualization in Science", Springer 2001

A. Anwander, M. Kuhn, S. Reitzinger, C. Wolters, "Fast High Resolution Finite Element Method based Source Localization in the Human Brain", in the book series "Forschung und wissenschaftliches Rechnen" (Research and scientific computing), Heinz-Billing-Vereinigung e.V., 2001

D.C. Barber. "Automatic generation of Regions Of Interest for Radionuclide Renograms." Proceedings of Medical Image Understanding and Analysis 2003 (In Press)

G. Berti, "Generic programming for mesh algorithms: Towards universally usable geometric components", Proceedings of the Fifth World Congress on Computational Mechanics (WCCM V), July 7-12, 2002

Fingberg J., Berti G., Hartmann U., Basermann A., Wolters C., Anwander A., McCarthy A., Woods S.: "Bio-numerical simulations with SimBio", NEC R&D journal, HPC Special Issue, 44(1), 2003

Fingberg J., Berti G., Hartmann U., Basermann A., "Head-mechanical simulations with SimBio", NEC R&D journal, Bio-Informatics Special Issue, 43(4), 2002

L. Flemming, J. Haueisen, U. Tenner, F. Gießler, M. Eiselt, "Source Localisation accuracy in an animal model", Proceedings 3rd Int. Symposium an Non-invasive Functional Source Imaging (NFSI 2001), Innsbruck, Austria, Biomedizinische Technik 46(2): 138 - 140, 2001.

D. Güllmar, T. Jaap, M.E. Bellemann, J. Haueisen, J.R. Reichenbach, "DTI Measurements of Isotropic and Anisotropic Media", Biomedizinische Technik Band 47 Ergänzungsband 1, 2002, 420 – 422

U. Hartmann, F. Kruggel, T. Hierl, G. Lonsdale, R. Klöppel, "Skull mechanics simulations with the prototype SimBio environment", Proceedings of the 1st M.I.T. Conference on Computational Fluid and Solid Mechanics, (K.J. Bathe, editor), Elsevier (Oxford), Vol. 1, pp. 243-246, 2001

U. Hartmann, G. Lonsdale, G. Berti, J. Fingberg, A. Basermann, R. Grebe, P. Aïmedieu, D. R. Hose, A. McCarthy, F. Kruggel, M. Tittgemeyer, C. Wolters, T. Hierl, "Bio-numerical simulations with SimBio: Selected Results", Proceedings of Int. Workshop on Deformable Modeling and Soft Tissue Simulation, Bonn, Nov. 14-15 (to appear)

D. Heric, B. Potocnik: "An Image Segmentation Tool (IST)", in Proceedings of the 4th EURASIP Conference focused on Video / Image Processing and Multimedia Communications (EC-VIP-MC 2003), Faculty of Electrical Engineering and Computing, Zagreb, 2-5 July 2003, Croatia.

G. Lonsdale, R. Grebe, U. Hartmann, D. R. Hose, F. Kruggel, J.M.T. Penrose, C. Wolters, "Bio-numerical simulations with SimBio: project aims and objectives", Proceedings of the Symposium on Computational Biomechanics, May 24-25, 2000, RIKEN, Saitama, Japan

A. D. McCarthy, "Development and validation of a virtual environment as a training tool for surgeons in knee arthroscopy", PhD Thesis, U. Sheffield, December 2000

McCarthy A.D., Hose D.R., Barber D.C., Wood S., Darwent G., Chan D., Bickerstaff D.R. and Wilkinson I.D. A registration-based MR method for calculating in-vivo 3-D knee joint motion: Validating finite element simulations. Proceedings of the International Society for Magnetic Resonance in Medicine, May 10-16, 2003

McCarthy, A.D., Wilkinson, I.D., Hose, D.R., Barber, D.C., Wood, S., Darwent, G., Chan, D. and Bickerstaff, D.R. Musculo-Skeletal Simulation: Finite Element Meshes Derived From Magnetic Resonance Volumes. Proceedings of the International Society for Magnetic Resonance in Medicine, May 18-24, 2002

S. Mehta, D.C. Barber, E. van Beek, J.M. Wild, F.C. Hamdy. "Delineation of the prostate capsule in 3D-Trans Rectal Ultrasound images using image registration." Proceedings of Medical Image Understanding and Analysis 2003 (In Press)

M. Tittgemeyer and F. Kruggel, "Visualising deformation fields computed by non-linear image registration", *Comput. Visual. Sci.*, 5, 45-51, 2002.

Tittgemeyer, M., Wollny, G., and Kruggel, F., "Inverse Biomechanical Models of The Brain: Clinical Applications", Workshop on Visual Analysis, Image Based Computing and Applications, Warsaw, May 2002.

M. Tittgemeyer, G. Wollny, and F. Kruggel, "Monitoring structural change in the brain: application to neurodegeneration", in Proceedings of ECCV (International Workshop on Growth and Motion in 3D Medical Images), J.Sporring, W. Niessen, J. Weickert (Eds.), Copenhagen, pp. 9-17, 2002.

G. Wollny and F. Kruggel, "Computational cost of non-rigid registration algorithms based on fluid dynamics", *Trans. Med. Imag.*, 8, 2002.

Wollny G., Tittgemeyer M., and Kruggel F., "Segmentation of vector fields by critical point analysis: application to brain deformation". In: Proc. of 16th Int. Conf. on Pattern Recognition (ICPR'02), Aug 2002, Quebec, Canada, Vol. 1, pp. 524-527, IEEE Comp Society Press. 2002

C. H. Wolters, A. Anwander, M. A. Koch, S. Reitzinger, M. Kuhn and M. Svensen, "Influence of Head Tissue Conductivity Anisotropy on Human EEG and MEG using Fast High Resolution Finite Element Modeling, based on a Parallel Algebraic Multigrid Solver", Series: "Forschung und wissenschaftliches Rechnen", T.Plesser and P.Wittenburg (Eds.), <http://www.mpg.de/billing>, 2001.

C.Wolters, S.Reitzinger, A.Basermann, S.Burkhardt, U.Hartmann, F.Kruggel, A.Anwander, "Improved tissue modelling and fast solver methods for high resolution FE-modelling in EEG/MEG-source localization", Proceedings of the 12th Int. Conf. on Biomagnetism, BIOMAG2000, August 13-17, 2000, Helsinki. (in press)

S. Wood, D.C. Barber, A.D. McCarthy, D. Chan, I.D. Wilkinson, G. Darwent and D.R. Hose, "A novel image registration application for the in vivo quantification of joint kinematics.", Proceedings of MIUA 2002 Conference, 22-23 July, 2002

Biomag 2002 Proceedings: Nowak H., Haueisen, J., Gießler, F., Huonker, R., , Biomag 2002: Proceedings of the Thirteenth International Conference on Biomagnetism, VDE Verlag Berlin, Offenburg, 2002

Anwander A., Wolters C., Dümpelmann M., Knösche T.R., "Influence of realistic skull and white matter anisotropy on the inverse problem in EEG/MEG-source localization".

Dümpelmann M., Knösche T.R., Anwander A., Wolters C., "Sensitivity of inverse source reconstruction results towards forward model inaccuracies: Application of a universal sensitivity analysis software framework on different tissue conductivity ratios".

M. Eiselt, L. Flemming, F. Gießler, J. Haueisen, U. Zwiener, "Somatosensory evoked cortical activity in rabbits depends on functional micro-states of the brain." pp. 448-L. Flemming, F. Gießler, J. Haueisen, J. R. Reichenbach, M. Eiselt, "Source localization accuracy in an animal model".

L. Flemming, M. Eiselt, F. Gießler, J.R. Reichenbach, J. Haueisen, U.Zwiener, "Evidence of somatosensory evoked 600 Hz activity in the rabbit's brain"

D. Güllmar, T. Jaap, M.E. Bellemann, J. Haueisen, J.R. Reichenbach, "Investigation and Validation of Diffusion Tensor Imaging Using Model Substances".

C. H. Wolters, M. Kuhn, A. Anwander and S. Reitzinger, "Fast Anisotropic High Resolution Finite Element Head Modeling in EEG/MEG-source localization"

Publications from caesar related to the developments covered by the collaboration with SimBio

von Rymon-Lipinski B., Jansen T., Hanssen N., Lievin M., Keeve E., "A Software Framework for Medical Visualization," Proceedings of IEEE Visualization '02, Boston, MA, October 27 November 01, 2002.

Keeve, E., Jansen T., Krol Z., Ritter L., von Rymon-Lipinski B., Sader R., Zeilhofer H.-F., Zerfass P., "JULIUS - An Extendable Software Framework for Surgical Planning and Image-Guided Navigation" Fourth International Conference on Medical Image Computing and Computer-Assisted Intervention MICCAI'01, Utrecht, October 14-17, 2001.

von Rymon-Lipinski B., Jansen T., Krol Z., Hanssen N., Ritter L., Keeve E., "An Extendable Application Framework for Medical Visualization and Surgical Planning" Proceedings Computer Assisted Radiology and Surgery CARS'01, Berlin, Germany, June 27-30, 2001.

4.8.3.2 Presentations at International Conferences and Workshops

P. Aïmediu, "Comparative study of the influence of the sacrificing procedure on the mechanical properties of the white matter of cow brains", 27th Annual Congress of the French Biomechanics Society, Valenciennes, 12-13 September, 2002

D. Barber, "A novel image registration application for the in-vivo quantification of joint kinematics", MIUA 2002, 22-23 July 2002, Portsmouth, UK

D. Barber, "Automatic ROI generation using image registration: application to MUGA scans", BNMS Autumn meeting, 12-13 September 2002, Durham UK

D.C. Barber and S. Mehta. "Delineation of the prostate capsule in 3D-Trans Rectal Ultrasound images using image registration." MIUA 2003, 10-11 July, Sheffield, UK

D.C. Barber. "Automatic generation of Regions Of Interest for Radionuclide Renograms." MIUA 2003, 10-11 July, Sheffield, UK

A. Basermann, "Parallel Incomplete Decompositions with Threshold for Preconditioning Sparse Linear Systems and Sparse Eigenproblems", 9th Int. Conf. on Numerical Analysis and Computer Science with Applications, August 13-17, 2000, Plovdiv, Bulgaria (**Invited Lecture**)

D. Bickerstaff and A. McCarthy, "Virtual knee surgery: the way forward?", The Millenium Symposium, 9th Congress of the European Society of Sports Traumatology, Knee Surgery and Arthroscopy (ESSKA 2000) September 16-20, London. (**Invited Presentation**),

L. Flemming,, "Source Localisation accuracy in an animal model", Proceedings 3rd Int. Symposium an Non-invasive Functional Source Imaging (NFSI 2001), Innsbruck, Austria, (**Winner of Vitatron student award for the best poster presentation**).

U. Hartmann,, "Skull mechanics simulations with the prototype SimBio environment", 1st M.I.T. Conference on Computational Fluid and Solid Mechanics, Cambridge MA, USA, June 12th-15th

D. R. Hose, "The role of analysis tools in biomechanics applications", NAFEMS Awareness Seminar, 6th February 2001, Institution of Mechanical Engineers, London (**Invited Presentation**),

F. Kruggel, "Clinical applications of biomechanical simulation", EURESCO Conference: Advanced Environments and Tools for High Performance Computing, June 2003, Albufeira, Portugal.

G. Lonsdale, "Bio-numerical simulations with SimBio: project aims and objectives", Symposium on Computational Biomechanics, May 24-25, 2000, RIKEN, Saitama, Japan (**Special Lecture**)

G. Lonsdale, "SimBio – A generic environment for bio-numerical simulation", Int. Workshop on Deformable Modeling and Soft Tissue Simulation, Bonn, Nov. 14, 2001 (**Invited Talk**)

G. Lonsdale, "Numerical simulations for scan-data defined geometries", SSS2001 Conference, U. Tokyo Hongo Campus, 3-5.12.01, Tokyo, Dec. 4th (**keynote lecture**)

A.D. McCarthy, "Engineering in Medicine: Orthopaedic and Cardiovascular applications" Institution of Mechanical Engineers, Young Members Panel, Derby University, 11th February 2003, (**Invited presentation**)

A.D. McCarthy, "The Simbio Project: FE-based knee kinematics", Trent Movement Analysis Group, Ryegate Centre, Sheffield, 4th December 2002 (**Invited presentation**)

Tittgemeyer, M., Wollny, G., and Kruggel, F., "Inverse Biomechanical Models of The Brain: Clinical Applications", Workshop on Visual Analysis, Image Based Computing and Applications, Warsaw, May 2002.

Wollny G., Tittgemeyer M., and Kruggel F., "Segmentation of vector fields by critical point analysis: application to brain deformation". 16th Int. Conf. on Pattern Recognition (ICPR'02), Aug 2002, Quebec, Canada

C.Wolters, S.Reitzinger, A.Basermann, S.Burkhardt, U.Hartmann, F.Kruggel, A.Anwander, "Improved tissue modelling and fast solver methods for high resolution FE-modelling in EEG/MEG-source localization", Proceedings of the 12th Int. Conf. on Biomagnetism, BIOMAG2000, August 13-17, 2000, Helsinki. (Poster Presentation)

S. Wood, "Simbio – Applications to Knee Biomechanics", Stand with presentation material of knee related work at the BIONET Event "Biomechanics in the Decade of the Bone & Joint", Brussels, 27-29th April 2002, (**Invited presentation**)

GMD-NEC Workshop, October 16-17, 2000, St. Augustin

U. Hartmann, "Finite Element analyses for head biomechanics",

E. Haug, "Biomechanical Simulations at ESI in Transport and Medicine",

D. R. Hose, "Simulation of cardiovascular and orthopaedic systems",

F. Kruggel, "MR image preprocessing for generating individual FE models of the brain"

G. Lonsdale, "Bio-numerical simulations with SimBio"

Biomag 2002 Conference : as for proceedings papers above.

Of particular note:

Anwander A., Wolters C., Dümpelmann M., Knösche T.R., Influence of realistic skull and white matter anisotropy on the inverse problem in EEG/MEG-source localization.

Young Investigator Award

4.8.3.3 Other Notable/External Presentations

G. Berti, U. Hartmann, J. Fingberg, "Grid generation for bio-numerical simulation", 26.9.02, , RheinAhrCampus Remagen, Workshop Remagener PhysikTage

J. Fingberg, G. Berti, U. Hartmann, "Bio-numerical simulation in the SimBio and GEMSS projects", 26.9.02, , RheinAhrCampus Remagen, Workshop Remagener PhysikTage (Poster presentation)

J. Fingberg, "FE-Analysis for Bio-Mechanics: Preliminary results of the SimBio project", Colloquium "Parallelverarbeitung in technisch-wissenschaftlichen Anwendungen", Research Centre Jülich, Germany, May 14th, 2001.

J. Fingberg, "The European project SimBio: developing a bio-numeric environment", BVM2002 Conference (Bildverarbeitung für die Medizin = ImageProcessing for Medicine), Leipzig, 10.-12.3.02

D. R. Hose, Interview on computer modelling and dynamic MRI for the human knee within the TV programme "Technofilextra", broadcast on BSKyB, January 2001

G. Lonsdale, "Bio-numerical simulations with SimBio", Toyota Central Research Laboratory, Nagoya, Japan, May 14th, 2001

G. Lonsdale, "Bio-numerical simulations with SimBio", Honda R&D Co., Ltd., Wako Research Centre, Japan, May 15th, 2001

G. Lonsdale, "The European project SimBio: developing a bio-numeric environment", NEC HPC Users Workshop, Dec. 5th 2001, Tokyo BigSight, Tokyo

G. Lonsdale, "Medical Simulation Services on the Grid", IST2002 Conference, Copenhagen, 6.11.02 (**Invited Talk**)

G. Lonsdale, Presentations at Toyota Central Research Lab. including Update on developments in Bio-Numerics and Grid Medical Services (EU Projects SimBio & GEMSS)], Nagoya, 28.2.03

G. Lonsdale, "Medical Services on the Grid", Global Grid Forum Meeting GGF-7, Applications Update Panel (Plenary Programme), Tokyo, 5-7.03.03 (**Invited Talk**)

4.9 Workpackage 9: Management

The project management has acted as contact point for all correspondence between the project and the Commission. Project-internal communication has been simplified by the provision of SimBio mailing lists for each workpackage or subtask. All correspondence via the SimBio lists is automatically archived. The Consortium Agreement (and a subsequent amendment following the SimBio-NAS extension, see below) was constructed, a modification of the Unified Consortium Agreement, and concluded between all partners.

A total of 10 project meetings were held, with Project Management Board (PMB) meetings being included within the (mostly) two-day meetings. The project meetings were used to define and review workplan implementation details and collaborations and also to address exploitation possibilities. Additional technical meetings were used to address workpackage-specific activity and collaboration issues. The project also participated in 3 "concertation" meetings, organised by the IST action line on "Real Time Simulation and Visualisation Technologies".

KUL Withdrawal

Other than participation at the SimBio Kick-off meeting, K.U. Leuven was not in a position to commit personnel to work on any of its project tasks within the first six-months of the project since they were unable to hire appropriate additional staff for the SimBio contract. Following the first external project review at Project Month 6, K.U. Leuven requested a withdrawal from the project. This withdrawal was accepted, since an alternative workplan was developed which allowed the project objectives to be maintained. A contract amendment, based on this modified workplan, was completed and signed in July, 2001.

caesar Collaboration

An additional collaboration with caesar (Center of Advanced European Studies and Research, Bonn, Germany) was concluded to expand the information dissemination activities within Workpackage 8 in

Years 2 & 3. The caesar research group for Surgical Simulation and Navigation investigated the use of three-dimensional visualisation techniques for the evaluation and validation applications within Workpackage 7.

NAS Extension

In October, 2001, the Project Management Board came to a decision on the proposed extension by 2 partners from Maribor, Slovenia (University & Hospital clinic) – a proposal for activities was sent & the proposal construction assigned to the University of Maribor. The SimBio-NAS extension proposal was completed, submitted and approval to negotiate a contract received in April, 2002. The contract amendment was received and signed in June, allowing the modified project workplan to come into force in July. The project period was extended by 3 months (to the end of June, 2003) to allow the new partners from Maribor to complete a full, 12-month evaluation task.