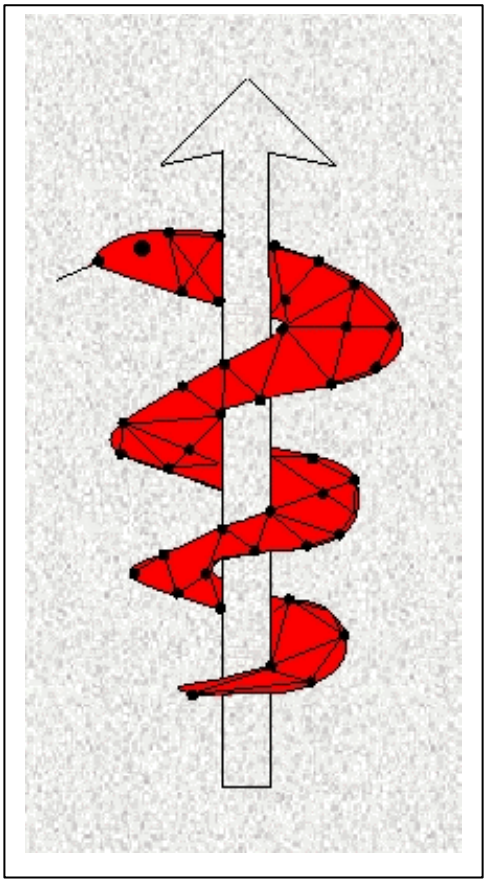
The IST Programme
Project No. 10378

SimBio

SimBio - A Generic Environment for Bio-numerical Simulation

http://www.simbio.de



Deliverable PP1
Annual Progress Report

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The SimBio Consortium :

NEC Europe Ltd. – UK
A.N.T. Software – The Netherlands
CNRS-DR18 – France
Sheffield University – UK
MPI of Cognitive Neuroscience – Germany
Biomagnetisches Zentrum Jena – Germany
ESI Group – France
Smith & Nephew - UK

1 Annual Project Progress Report - Project Months 1-12

Foreword

This report covers project months 1 to 12 (April 1st, 2000 - March 31st, 2001) of the SimBio project and provides a status report on project progress.

1 Project Overview

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

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

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

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

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

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

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

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

1.1 The SimBio Consortium

The Consortium comprises[1] four industrial partners and four public research organisations stemming from four European countries and represents a well-balanced mixture of private and public partners whose activities range from basic research to industrial production. The core activities of the partners cover the following fields: health care product manufacturing, clinical practice, medical and clinical research, clinical imaging and data processing software, numerical simulation software, HPC systems and software solutions. The heterogeneous character of the Consortium has been designed to best address the scientific requirements imposed by the problems to be solved.

C&C Research Laboratories, NEC Europe Ltd. (NEC) targets its activities on HPC technology and numerical algorithms and will build on its collaborations with other partners in the area of Finite Element (FE) technology. NEC is also the project co-ordinator.
The signal and image processing (SIP) group of the Max-Planck-Institute (MPI) of Cognitive Neuroscience is specialised in medical image analysis and synthesis. The SIP group combines this expertise with knowledge on parallel processing. The research of the MEG group of the MPI is focussed on developing software and hardware to maximise the information output from EEG/MEG measurements. The groups from MPI will contribute to all areas of SimBio component development and will evaluate the impact of the approach using bio-electromagnetic and bio-mechanical applications. Direct collaborators with MPI in the algorithmic and simulation areas is the software company A.N.T. Software B.V., which focuses on software for source localisation methods based on EEG and MEG measurements. Biomagnetic and biomechanical tissue properties are the main research areas, and corresponding project roles, of the University of Technology of Compiègne (UTC), and Biomagnetic Center, Department of Neurology, Friedrich-Schiller-University Jena (BMZ). BMZ operates the only animal Micro-SQUID MEG system in Europe.
ESI will exploit its leading industrial code PAM-SAFE™, creating an interface to the simulation environment, and develop new modelling and solution options in the code. ESI will support the development of the SimBio environment (with expertise in modelling, FE technology and software systems) and the performance of Knee model simulations, building on its previous collaboration with the University of Sheffield.
The University of Sheffield (UFDS) has a large experience in biomedical applications of the finite element method. Together with ESI a biomechanical ESPRIT project, KneesUp, has successfully been accomplished having an anatomically detailed knee model as a result. UFDS will contribute to the development of the mesh generation component and will lead the knee-prostheses validation and evaluation work. Smith and Nephew, a leading healthcare product supplier, will evaluate the use of bio-numerical simulation for industrial design optimisation of prostheses.

[1] See also Section 2.9 concerning the withdrawal of one of the original partners

2 Progress per Worktask

2.1 Workpackage 1: Geometric Model Generation

2.1.1 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.

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.
However, due to the withdrawal of KUL from the Project the Commission approved a delay of six months for the delivery of Deliverable 1.1b (the first official software release). Rearrangement of Subtask 1.1 has resulted in USFD taking over as Sub Task leader with CSUH acting as its sub-contractor while MPI remains a partner. The extra member of staff required by CSUH has been recruited already so no further delays are expected.

MPI has released working versions of their intensity-based segmentation and image manipulation tools for Linux, which are also running at USFD. Two modules for segmenting the skull from MR images were developed. In summary, it now possible to standardise a head dataset by intensity and orientation and to segment a it into is materials white matter, grey matter, cerebro-spinal fluid, skull and extra-cranial tissue. Currently, the third project-internal release of these tools is available.

Initial testing of the tools by USFD demonstrated a shortcoming of the *dcmtov* converter. This was caused by the use of Picker dicom images at USFD. MPI has provided a modification and the converter is now working for USFD dicom images. Further testing of the utility of the segmentation tools for the knee will be conducted by USFD.

The shift of effort in ST1.1 has resulted in the development of combined image segmentation/ mesh generation approach, the so-called *mesh template* approach, which will be carried out by USFD. This approach will use pre-defined priors to permit an atlas-based image mapping to be applied to "morph" a parameterised template mesh into a subject-specific mesh. Initial progress has been promising with good results using a non-linear registration of exemplar images of the femur and menisci to subject image of the femur and menisci. This approach is being developed as a solution to the anticipated problem of applying an intensity-based segmentation approach to the knee, whereby significant overlap in intensity values between tissues occurs.

To be compatible with existing Workpackage 1 tools, USFD will release its ST1.1 tools for Linux and in addition, intends to provide the existing ST1.1 tools for the SGI platform running under the Irix 6.5 OS. The USFD tools will support the Vista file format agreed by the Consortium.

No further delays are anticipated and D1.1b is expected on time at Project Month 18.

2.1.2 Subtask 1.2: Mesh Generation

The VGrid meshing tool has been extended by two techniques that enable the smoothing of the surfaces of hexahedral and tetrahedral finite element meshes. The first option exploits the possibility that nodes of a hexahedral FE mesh can be shifted to a certain extent with a positive effect on the accuracy of the simulation results. This method has proven to be robust for digital meshes and a first evaluation has underlined its positive effects for our applications.

The implementation of another approach that is designed to smooth tetrahedral meshes has recently been finished. So far, the tetrahedral output meshes have been evaluated by visual inspection only. Though the method creates additional mesh nodes and likewise increases the computational demands the first results are regarded as promising. Furthermore, an operator has been realised that generates triangular surface representations of anatomical objects based on these tetrahedral meshes.
A specialised cache access scheme has been implemented in order to accelerate the transgressing of graph data structures.
In contrast to earlier versions the new release supports the single output file approach. This means that all necessary information for the simulation is stored in a single file. This statement is true for sequential as well as for parallel execution of the simulation code. The VGrid output files are now completely stored in VISTA binary format.

As an alternative approach USFD is exploring a method of mesh generation that combines the process of mesh generation with image segmentation. It has been termed the Mesh Template (MT) approach. The development and implementation of this meshing technique has been started with the beginning of the project.
Initial parameterised exemplar meshes of the menisci were created in Matlab™. The exemplar meshes are now being built using the pre-processor of ANSYS™ 5.6. Progress on the creation of the mesh templates is well underway and the template bones of the knee i.e. femur, tibia, fibula and patella have been created and scaled to represent a typical size of knee joint. The first results obtained with this novel method are very encouraging. The representations of the complex anatomical objects are very precise and provide a high quality of the finite elements.

2.2 Workpackage 2: Compilation of Material Database

Soft tissue samples investigation
In this first project phase we put our main efforts in the development of a conventional experimental set up and protocol procedures, which allow to perform reliable experiments comparable to the approach developed and applied by other groups. A traction machine has been set up which allows to carry out experiments on small samples of soft tissue in compression mode. By this, on the one hand all property data evaluated by us can be compared directly with literature. On the other hand results acquired by the global MRSI-method are directly comparable to in parallel performed traditional sample experiments. This facilitates as well the installation and test phase of the new approach as the interpretation of the acquired material properties.
We have adopted our traction machine to the needs of small sample experiments including an integrated optical deformation control by digital camera.

To be able to perform experiments on small samples of brain tissue we have furthermore integrated in the traction machine in addition a temperature and humidity controlled chamber. This enables us to deal with the extremely sensitive brain tissue under reproducible conditions and increase the precision of measurements. To be able to perform extended dynamic experiments we are on our way to equip our test set up with a second load cell.
Reliable and reproducible sample harvesting and cutting rests one of the key problems in the whole experimental procedure. Basically we use classical biopsy methods which we have adapted to the special properties of the brain tissue and the needs of compression experiments. Anyway further optimisation has to be done to reduce variation in experimental results.

Even though less fragile than brain tissue the small size and geometry together with tissue anisotropy makes meaningful sample acquisition for the knee a delicate task. Anisotropy of the meniscus has already been stated and can easily be related to histological structure. So it is most important to perform sample cutting with respect to this microstructure to get meaningful results. We actually set up a histology based technique of sample cutting for to investigate local anisotropy in different meniscus parts.

MRSI-technique
In first coating experiments we faced problems arising from air-bubbles, which are formed by gas released by the silicon during polymerisation. These gas bubbles enclosed in the originally incompressible material induce pronounced changes of mechanical properties. To overcome this drawback we introduced a multi-step high vacuum procedure. This approach is now an important step in all coating experiments. Further steps taken to realise the MRSI-technique include:

For the brain, a search and evaluation of different materials appropriate to coat living tissue has been perfomed. It turned out that it is mandator to use for different types of soft tissue different types of coating material. For the extremely soft brain tissue the Silicone tested in the beginning turned out to be much to stiff even the softest type. So we looked for and tested a variety of other embedding materials. Finally our choice is a gelatine kindly offered by a big food company together with the know how for reproducible preparations. Obviously by this approach we have overcome the main problems due to polymerisation as exposure time and heat development, material compatibility and appropriate material properties. To ensure the last point we carried out series of compression tests for different types of gelatine with our recently established traction machine in comparison with different brain tissue types.

For the other soft tissue type to be investigated – the menisci of the knee – we'll stick to silicon of the softest type already investigated. It seems to be at the moment the most appropriate choice for embedding of this tissue under all the above-mentioned aspects. Anyway some additional testing will have to be carried out in addition.

Software
A preliminary MRI image acquisition protocol has been set-up to optimise data acquisition of small coated objects.
Routines to perform object reconstruction using our 'VolView' software have been adapted and implemented. Algorithms to fuse volumes and to further evaluate data acquired by deformation experiments are under development and integrated. It is foreseen to test and implement for this purpose the software developed in WP 4.2 if available in time, since it provides a most promising general voxel based approach.

Material-Database

Collection of data of living tissues mechanical and electrical properties is a permanent work, which will continue to the end of the project. A periodical search of literature is performed to keep the database as up-to-date as possible.
We have evaluated literature to set up a broad collection of most actual and interesting data of living tissues properties. This collection of data has been published as our deliverable D2a in standard literal form. We are now developing in expansion of our tasks in the project an extended version on base of the standard database 'ACCESS'. A working group has been formed to develop and install an adequate database structure.

2.3 Workpackage 3: Numerical Solution System

The Numerical Solution System (NSS) for the SimBio environment currently consists of the simulation codes HeadFEM, NeuroFEM and PAM-SAFE, the parallel linear solver library PILUTS (NEC), interfaces to external libraries PEBBLES (U. Linz, Austria) and AZTEC (Sandia National Lab.) and a partitioner tool that is based on the DRAMA library for mesh and matrix partitioning.

Much of the initial technical development work was focussed on the detailed interaction of software within the Numerical Solution System - with mesh partitioning and parallel library routines being interfaced to the NeuroFEM and HeadFEM codes. A repartitioner tool that provides load-balancing, matrix partitioning and basic data-migration capabilities has been implemented based on the DRAMA library. The DRAMA library has been extended to give special support to the SimBio applications for

the partitioning of sparse symmetric matrices. The PILUTS 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 modified to make use of the DRAMA-partitions (giving improved convergence) and have been "weakly" coupled to the application code NeuroFEM. The next step of the NSS development was to improve the component interaction by a definition of a common platform-independent, binary, VISTA-file format.

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 PILUTS has been developed and first tests of the parallel PILUTS version based on node-partitioned data are now possible. The integration of the parallel AMG-pre-conditioner parPEBBLES based on element-partitioned data and an element-wise coupling is in an advanced state. A strong coupling between NeuroFEM and the PILUTS library is in developing state.

An initial version of the HeadFEM simulation code was developed with a linear solver based on the AZTEC library. It has been used for performance studies and in the evaluation work of Subtask 7.2. 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 FE-modelling routines.

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, and the preliminary software release report, D3b. Those reports also detail and motivate the further development plans.

2.4 Workpackage 4: Inverse Problem Component

2.4.1 Subtask 4.1: Inverse methodology

The release notes for a preliminary release of the generic inverse toolbox are completed. The preliminary release of the generic toolbox contains abstract class structures for the two main subsets of inverse procedures. Methods providing a complete inverse procedure are implemented for both subsets. Thus, inverse source reconstructions using linear estimation and dipole fit methods can be performed. Both methods are representative examples for source reconstruction methods, either for a discrete parameter space or for a continuous parameter space. An accurate FEM model of the head can be used for forward calculations. This head model is part of the NeuroFEM software.

As a basis for the development of the NeuroFEM-software, which is part of the developments within ST4.1. (Integration of finite element based forward simulations for source localisation in the human brain, later applied in SIMBIO-application ST7.1.), the software package CAUCHY'97, described under

`http://www.rwth-aachen.de/neurologie/Ww/Neurologie/cauchy/CauchyFunctionality.htm`, was taken and strongly redesigned. A C++ class-structured software replaces old FORTRAN77 CAUCHY kernel routines and enables the development of the SIMBIO-software on parallel platforms. The NeuroFEM-simulator has been derived from an abstract simulator class defined in the design report of ST4.1.. This allows future comparisons with boundary-element-based forward simulations and analytical series expension formulas for spherical shell geometries, which both are also derived from the abstract simulator-class. The goal is an influence-study of tissue anisotropy on the various inverse algorithms of the ST4.1. toolbox. A dynamical memory management has been introduced throughout NeuroFEM, which replaces the former static allocations and enables a user-friendly application on distributed memory platforms. A first test was carried out where the NeuroFEM-simulator was used as forward simulator within an inverse dipole fit method, described in the ST4.1 design report.

To provide users with possibilities to have access to complete inverse procedures and to have an interface to the SimBio environment, a three shell user interface is implemented for dipole fit and linear estimation source reconstruction methods. The outer shell provides a command line interface to start inverse procedures with possibilities to set procedure options and input and output filenames. For file input and output the “vista” file format, which was chosen as the general SimBio file format, is used.

Thus, two important objectives could be accomplished. The general design of the class structure of the inverse toolbox could be proven and a basis for the integration of the inverse toolbox into the complete SimBio environment could be established.

2.4.2 Subtask 4.2: Inverse field reconstruction

Finite Element (FE) techniques are now commonly employed for simulating bio-mechanical properties of the head, e.g. in surgery simulation or impact simulation. To compute such forward simulations, the magnitude and directions of forces acting on the head need to be specified. If this prior information is not available, time series examinations may be employed and registered by a non-linear transformation. The resulting deformation field is used to derive a force field, based on incorporated realistic material parameters. Force fields need to be analysed for their singularities (force “sources” and “sinks”) in order to provide a comprehensive 3D visualisation. In analogy to the inverse problem of localising sources of electromagnetic brain activity from potential measurements on the scalp, we denote this approach as “inverse” bio-mechanical models. We focused on the problem of setting up a suitable modelling context.
A source volume image is mapped to a target by applying vector-field transformations to the underlying co-ordinate system. In order to produce bio-mechanically plausible results, transformations are constrained to be consistent with the physical properties of deformable elastic solids. Furthermore, transformations need to preserve topology in order to yield an anatomically valid result. A fundamental problem with a large class of image registrations techniques is that the estimated trans-formation g from a template image T to a target S does not equal the inverse of the estimated transformation h from S to T. Thus, a third constraint needs to be enforced that these transformations are consistent, i.e., inverse to one another. An approach which implements these constraints in a rather flexible algorithm was recently proposed by Christensen and is embedded in the mathematical framework of the Grenander model of anatomy.
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 and to optimise computation speed. Along with this development, templated classes for matrices and vector field operations were implemented which use the file i/o as discussed in ST1.1.

2.5 Workpackage 5: Visualisation

The simulation of bio-medical data often requires advanced visualisation tools, capable of particularly accurate or high resolution visualisation. The SimBio environment needs a visualisation module (VM) which 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. The SimBio VM is designed to meet such requirement. It is able to visualise simulation results with fast change of viewing parameters. It allows the visualisation of conductivity and diffusion tensors as well as vector fields and iso-lines interpolated in force and electro-magnetic potential fields. Changes of time-dependent variables are visualised with high update rates. The render engine takes advantage of the underlying hardware architecture.
The VM is 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) that provides elements such as windows, menus, dialog boxes, etc. OpenGL is a graphics library designed for efficient rendering of 3D geometrical objects, which is also capable of displaying pixel images. The OpenGL library offers all the low-level graphics functionality required to create the advanced visualisation routines for the SimBio project. A specific extension for the Qt library makes the integration of the functionality provided by OpenGL into a GUI built using Qt straightforward. The signal-slot mechanism provided by the Qt library is a well suited infrastructure for linking properties, such as 3D position and zoom, between different views.
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 are implemented, to make data available to the cosmopolitan medical, clinical and engineering communities for presentation, publication and further investigation with external software tools.
A VM prototype is scheduled for a first release within the next few weeks.

2.6 Workpackage 6: Component Interaction

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

After a first phase of evaluation (CORBA + WEB based solutions) and presentation to 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.

Furthermore, the SimBio environment should enable distributed software execution at two sites:
1) At the “local” site, the complete pre-computing will be performed. To be more precise: independent of the employed tools and their interactions, the output of this pre-compute phase is the corresponding mesh. Subsequent to simulation results having been produced, or for checking of the results of the pre-compute phase, visualisation is also performed locally.
2) The other site, a remote compute server, is responsible for performing the designated simulations. A locally situated compute server could be handled by the user without resource to the data transfer software/mechanisms required for remote execution.

To generate the SimBio request that will describe the user’s simulation, we will provide to the end-user an editor; This editor will be used to define the user needs (application and parameters) and then will generate a SimBio Request (or Simulation request) File. This editor will be called ‘SimBio Scenario Editor’ and developed by SI using C++, QT and xerces. It will be available for public domain release.

The contents of the Request will be analysed by a special application. This program launches the programs sequentially according to their appearance in the request. It is also in charge of initiating the job submission on the compute server. This application is called 'SimBio pilot' and was developed at NEC using C++, CORBA and xerces. The implementation of the environment execution layer has also been taken over by NEC.

During the last six months, the implementation of the two described task has begun and a simple prototype is now available. Of course, improvements will be made during the next project periods, depending on the partner's evaluation. The number of components into the SimBio WP6 will also increase in the future depending on the developments made by other partners in other workpackages.

2.7 Workpackage 7: Validation & Evaluation

2.7.1 Subtask 7.1: Source Localisation

A miniaturised dipole has been developed and successfully tested during the last year. Phantom investigations have been performed. The patent application for the miniaturised dipole is in preparation. The physical and physiological source model has been established. Experimental procedures and modalities and data recording have been adapted and standardised. First measurements for both source models have been performed successfully.

High resolution MRI brain scans have been acquired. Based on this data first diffusion weighted scan has been realised.

2.7.2 Subtask 7.2: Bio-mechanical Head Model

In this subtask, the clinical usefulness of bio-mechanical head modelling using the SimBio environment will be demonstrated. The application addresses the delineation of changes of lesions with time and the detection of mechanical forces induced by pathological and surgical processes. Such studies offer a new approach for differential diagnosis and outcome prediction. In addition, simulations will reveal information about the static and dynamic properties of the brain. Two different simulation strategies are pursued:

- Forward models: The real locations and strengths of forces (or corresponding hypotheses) are known a priorily. 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 Facial Surgery at the University Clinic of Leipzig (responsible: Dr. Dr. Th. Hierl) 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. During surgery, sub-parts of the skull are mobilised and attached to the frame by wires. Pulling wires in a certain direction at a certain distance per day will bring skull parts slowly to a desired position, thus correcting the skull deformation. Typically, 1mm shifts per day are achieved, and after 4-5 weeks, are clinically sufficient results is obtained. Because skull parts are now in their "natural" position (and under natural load conditions), a self-contained healing process is induced.
- 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 need to be analysed for their singularities ("force sources" and "sinks") in order to provide a comprehensible 3D visualisation. Since a validation based on physical models is not possible here, force fields will be compared in a group of similar clinical cases for their plausibility and checked against prior neuro-anatomical knowledge. Two different data collections will be studied:

During the course of the Leipziger Langzeit-Studie (LEILA, responsible: Prof. Dr. H.J. Gertz), patients with mild cognitive disturbances are examined behaviourally, clinically and by various neurophysiological and neuropsychological scales. 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. 20 suitable cases with well-defined lesions will be selected.
The Day-Care Clinic of Neuropsychology at the University of Leipzig (responsible: Prof. Dr. D.Y. von Cramon) is treating patients with focal brain damage (after cerebral infarction, hemorrhage or severe head trauma). Patients are scanned routinely by MRI at the time of admission and discharge (approx. 3 resp. 12 months after onset).
Examinations of TP1 and TP2 will be evaluated by inverse bio-mechanical models in order to derive the deforming forces induced by restorative processes after focal brain damage. 20 suitable cases with well-defined lesions will be selected.

In total, 50 patients in three different problem groups will be studied in this validation task. The underlying clinical and modelling questions allow a comprehensive testing of the SimBio tools and the approaches taken for bio-numerical simulation.

2.7.3 Subtask 7.3: Knee Prosthesis

USFD has undertaken further testing of the MR scanning protocols and has subsequently modified the surface coil selection to one that allows a greater range of motion within the bore and which affords an acceptable signal to noise ratio. An additional static sequence has been tested and selected to ensure high quality imaging of the cruciate ligaments. Static imaging of the normal participant knees in the study are scheduled to commence in June 2001. Testing identified additional modifications and improvements to the exercise rig that were necessary, thus causing a slight delay in the expected start of routine dynamic scanning of normal knees. This is not expected to delay D7.3b due at Month 18.

ESI has undertaken an evaluation of the performance of hexahedra, degenerated hexahedra, 4-nodes and 10-nodes tetrahedral, which was performed on a single traction test on a part of the lateral menisci. Two different element formulations were also compared. Also the first validation task, VT1A, was set up on the ESI-improved Knees-Up model. A simulation of knee flexion up to 50 degrees is performed within 50 ms.

2.8 Workpackage 8: Assessment, Exploitation, Info Dissemination

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 (and currently software - though a separate CVS-repository, installed on the same "SimBio server" is expected to replace that function), through password-protected pages.

Publications:

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 (**appeared**)

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**)

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

Presentations at International Conferences and Workshops:

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**),

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

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**)

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

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

Other Notable Presentations:

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

2.9 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 has been constructed, a modification of the Unified Consortium Agreement, and concluded between all partners.

Four project meetings took place in the reporting period. Project Management Board (PMB) meetings were held during the two-day meetings. The project meetings were used to define and review workplan implementation details and collaborations and also to address exploitation possibilities. The first external review of the project took place in October, 2000 and was completed successfully.

An additional collaboration with caesar (Center of Advanced European Studies and Research, Bonn, Germany) has been concluded which will expand the information dissemination activities within Workpackage 8 in Years 2 & 3. The caesar research group for Surgical Simulation and Navigation will investigate the use of three-dimensional visualisation techniques for the evaluation and validation

applications within Workpackage 7 These visualisation techniques will make use of virtual reality environments and tools. In addition to demonstrations of the visualisation possibilities, caesar will produce multi-media or video publicity material for SimBio relating to those demonstrations.

Withdrawal of K.U. Leuven from the Project.

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 is in progress (based on this modified workplan).