A HIGH PERFORMANCE COMPUTING-BASED APPROACH FOR THE REALISTIC MODELING AND SIMULATION OF EEG ACTIVITY

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ABSTRACT
An original simulation framework specifically conceived and designed to achieve high performance three-dimensional (3D) realistic modeling and simulation of electro-encephalographic (EEG) brain activity, named TEBAM (True Electrical Brain Activity Mapping), is presented. We describe the integrated ICT framework that has been proposed and developed for TEBAM, specifying the design characteristics, implementation and tools interconnections. TEBAM relays on patient's specific realistic head modeling, based on identification of the various head structures necessary for an accurate model building by means of suitable clinical imaging protocols presented in this paper. TEBAM is implemented and optimized with a very flexible approach to solve in short time, by means of High Performance Computing resources, the large scale computations needed. 3D simulation results can be visualized in TEBAM framework in different multimodal ways, combining the anatomical information with the computed results to give an optimal insight of computation output, relying also on stereographic visualization.

Keywords: High Performance Computing, EEG simulation, realistic head modeling, multimodal neuroimaging

1. INTRODUCTION

Mathematical models of generation of electro-encephalographic (EEG) brain potentials are a powerful and helpful tool to better analyze and understand the mechanisms involved in the development of brain activity in normal or pathological conditions. By means of modeling and simulation in computers, the neural sources of the scalp recorded EEG potentials can be non-invasively estimated and imaged, and the origin and evolution of brain activity can be first studied *in silico*, where hypotheses can be formulated and studied prior to their validation in vivo, thus reducing the requirements of many complex intrusive techniques.

A key point towards the simulation and visualization of neural sources of EEG brain activity within the specific patient's head with both high spatial and temporal resolution is the multimodal integration of EEG and clinical imaging data, as the former allow measurement of EEG activity with an optimal temporal resolution while the latter are characterized by a very high spatial resolution (Baillet, Mosher, and Leahy 2001). The EEG inverse problem is the process of estimating the characteristics of the neural sources responsible for a given EEG distribution measured at the scalp electrodes. This can be achieved by means of iterative computational methods with a large number (several hundreds) of iterative EEG forward simulations to find the optimal source parameters corresponding with the measured EEG potentials (Baillet, Mosher, and Leahy 2001). To accomplish this non trivial task, a suitable simulation framework should be available. First of all, a precise and realistic representation of the electrical properties of the specific subject's head, in terms of shape and electric conductivities, is necessary to achieve an accurate EEG forward simulation (Baillet, Mosher, and Leahy 2001). Moreover, the adopted head model should also be able to incorporate various sets of tissues with different conductivities (Vatta, Bruno, and Inchingolo 2005). This is extremely important in clinical applications in which also pathological formations as brain lesions (which are characterized by a large variability in shape and conductivity) have to be included in the head model (Vatta, Bruno, and Inchingolo 2002). Once built, realistic head models require the use of demanding numerical computer methods for EEG forward problem solution and hence for electrical brain activity mapping (Baillet, Mosher, and Leahy 2001). A suitable, flexible and performing simulation framework should therefore account for all these constraints.

In this paper, an original simulation framework named TEBAM (True Electrical Brain Activity Mapping) is presented. TEBAM was specifically designed and implemented to account for all the above mentioned constraints. In the following sub-sections are presented the design specification, the imaging protocols requirement for accurate head modeling, the structure and implementation of TEBAM followed by the validation and testing of the framework.

2. SIMULATION OF THE EEG POTENTIALS GENERATION

The EEG forward problem, which has to be iteratively solved in TEBAM's framework for electrical brain activity mapping, is governed by Poisson's differential equation (Bronzino 1985)

$$\nabla \cdot (\sigma \nabla \Phi) = \nabla \cdot \vec{J}_i = \rho \quad (1)$$

where $\vec{J}$ i is the applied current density of the neural brain source (A/m^2), σ is tissue electrical conductivity (Ωm)$^{-1}$, and Φ is the electric potential in the problem domain. Realistic head models impose numerical computational methods for the solution of eq. 1, as the Finite Difference Method (FDM), which has been implemented in TEBAM framework thanks to its characteristics of flexibility which also allow an easy implementation of anisotropic electrical conductive domains. This typically involves the solution of a large and sparse linear algebraic equations system (Ax=b). Hence, the main characteristics of the bioelectrical problems computations in TEBAM framework are: 1) Large-scale, i.e., large memory and CPU time requirements; 2) Iterative, as electrical brain activity mapping requires EEG forward problem solution to be performed iteratively; 3) Multistep, as simulations are typically composed of a fairly complex steps sequence that are arranged in pipeline and classified as modeling, simulation computing and visualization.

The TEBAM pipeline is composed by 5 steps: 1) Construction of a model of the physical problem domain, in terms of shape and physical properties, given by the patient-specific volume of the head (Baillet, Mosher, and Leahy 2001); 2) Application of boundary conditions and/or initial conditions, as source modeling and specification of initial data for the iterative computations are required; 3) Computing, as EEG forward and inverse solutions can be computed by solving a linear system of algebraic equations, derived from the numerical solution of eq. 1; 4) Validation and test of the results, as during the development phase results correctness has to be checked upon simple physical test domains for which independent solutions methods are available; 5) Visualization, as simulation results have to be visualized by means of suitable Scientific Visualization tools (Schroeder, Martin, and Lorensen 1996). Fig. 1 shows an example of result of the computational process.

TEBAM was designed as an integrated framework in which visualization is linked with computation and geometric design to interactively explore (steer) a simulation in time and/or space. In synthesis, the TEBAM problem solving framework has been designed to address the following issues: 1) Integration in data collection of multimodal anatomo-functional data; 2) Integration in data analysis, as modeling, simulation and visualization aspects of the problem have to be used in chorus; 3) Interactivity, to understand cause-effect relationships; 4) Extensibility, to get not a monolithic solution for one problem but possibility of reuse for solving also new problems; 5) Scalability, as although a full EEG inverse problem solution in short time requires the use of High Performance resources, tools can be run even on high-end PCs.

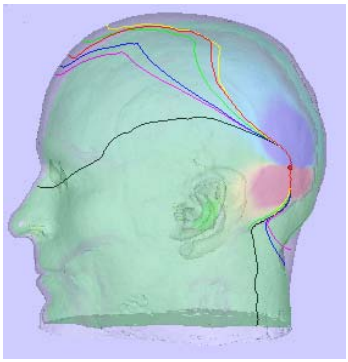


Figure 1: Visualization of current lines originated by a neural EEG dipolar source located approximately in visual cortex.

3. ARCHITECTURE OF THE SYSTEM

TEBAM provides an optimized dataflow programming framework, based on modules which implement components for computational, modeling and visualization tasks to build an interactive framework in which the researcher is free to change various parameters as mesh discretization, iterative solution method, neural source placements and visualization tools displayed.

The main bricks of TEBAM are: 1) building of the patient-specific realistic head model; 2) numerical EEG forward and inverse problem solution, with multiple iterative forward solutions; 3) visualization of the computed results.

As first step, a 3D voxel matrix is created, modeling the volume conductor of the head of the specific patient under analysis. This is done with segmentation of a suitable set of clinical images of the subject's head by means of 3D Slicer (3D Slicer UG 2006) and then assigning a scalar or a tensorial conductivity value to each identified pixel, according to the isotropic or anisotropic conductivity of the specific head model compartment (Bruno et al. 2006). The needed requirements in terms of clinical imaging protocol for accurate head modeling are discussed in Section 4.

The second step implies the building and solution of the large and sparse linear algebraic equations system (Ax=b) derived from the numerical FDM discretization of eq. 1. TEBAM framework has been designed to build and solve efficiently the equations system of step 2, giving high flexibility in the choice of solution methods and being able to run with small modifying either on mono-processor PC or, in parallel, upon large High Performance Computing (HPC) Systems. HPC resources are an adequate instrument for a consistent reduction in solution time for solving of large scale problems, as the computational load is subdivided using more CPUs and inter-CPUs communication is managed by MPI (Message Passing Interface). The need for code

parallelization and for the use of HPC in TEBAM was due to the magnitude of the problems addressed. In fact, a conductive head model derived from segmentation of a series of MRI images with adequate spatial resolution leads to a linear equation system with millions of unknowns for the solution of a single EEG forward problem. As the EEG inverse problem solution requires several iterative EEG forward problems solutions, HPC becomes then mandatory to reduce computation times especially for clinical applications purposes. In TEBAM a typical parallelization strategy, named "divide and conquer", has been adopted. Each CPU solves the problem in its sub-domain and MPI is used to exchange values necessary to each CPU for contour values (see Fig. 2). A specifically designed application was written in C++, compiled in Visual C 6.0 and in gcc 3.0 frameworks to build up a multi platform application, capable of running on either windows or linux machines. Libraries rely upon wxWidgets (Smart, Hock, and Csomor 2005), freeware and open source multiplatform library to help in creation of graphic user interfaces (GUI) and in several other tasks, VTK (Schroeder, Martin, and Lorensen 1996) for head model data reading and for all the interactive 3D visualization pipeline and Petsc (Balay et al. 2002) for linear system solution and parallelization issues. The solution application uses the PETSc libraries for twofold reasons: to create an open-source tool entirely based upon open-source libraries and because these libraries allow a high level of abstraction to leave "transparent" the low level calls and message exchanges between CPUs, hence allowing focusing on optimization and search for stable and accurate solution methods. The third step, visualization, is described in Section 6.

4. IMAGING PROTOCOL FOR ACCURATE HEAD MODELING

Accuracy achievable in EEG source imaging is influenced by errors committed in head modeling (Vatta, Bruno, and Inchingolo 2002). Clinical images, typically MRI and CT, are used for head model building. Head modeling accuracy mainly relies on correct identification, by image segmentation, of head structures characterized by different electrical conductivities to be modeled as separate compartments,

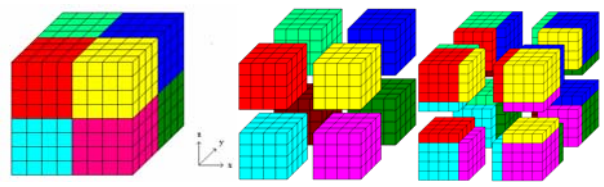


Figure 2: Parallelization: the problem domain is divided in a suitable number of sub-domains (left). Each CPU is assigned a sub-domain to be solved locally (center). A number of "ghost points" must be created in each sub-domain, where values computed by other CPU will be stored (exchanged by MPI) to give correct border values to each sub-domain (right).

assigning each an appropriate conductivity value (Vatta, Bruno, and Inchingolo 2002). Brain lesions show large variability and an intrinsic difficulty for segmentation (Vatta, Bruno, and Inchingolo 2001); hence, acquisition of finely tuned images (e.g., MRI with contrast medium injection) is often required, but this kind of images is not the best also for identification of standard head structures as scalp, skull, etc. The possibility of deriving information about tissue anisotropy from clinical images is also desirable (Vatta, Bruno, Di Salle et al. 2008). Notably, the MR-based diffusion tensor imaging (DT-MRI) has recently been suggested to map the conductivity tensor of the brain given the high correlation between electrical conductivity tensor and water self-diffusion tensor, with the potential to further refine the head modeling by taking the anisotropy of white matter into account. In general, one imaging procedure giving best results in some conditions, e.g., for identification by its image contrast of a specific head structure, may not be the optimum in other situations.

The available clinical imaging protocols used for the purpose of clinical morphological analysis have been analyzed from a segmentation point of view, to define the procedures most suitable for accurate identification, also in the presence of pathology, of the head structures necessary for head modeling, also accounting for the above described modeling issues. The following sets of clinical images have been analyzed: Proton Density, FLAIR T2, Inversion Recovery, Spin Echo with contrast medium injection, Spin Echo DP/T2, Spin Echo T1, T2 dry, Turbo SE T2 and CT. The following head model compartments have been identified by means of image segmentation: skin, fat tissue, skull, cerebrospinal fluid (CSF), ventricles, gray matter (GM), white matter (WM), medulla and cerebellum, eyes, muscle, internal air and brain lesions. Results of segmentation applied to the adopted image sets to identify the above listed head structures for head modeling purposes demonstrate that an appropriate multi-modal image set has to be acquired for accurate model compartments identification. Tab. 1 summarizes, for each image set, tissues identifiable by segmentation with a qualitative evaluation referenced to an anatomical brain atlas. A protocol has then been identified and proposed for acquisition of multi-modal patient's specific imaging data, to be integrated for head model building for EEG brain activity mapping (Vatta, Bruno, Di Salle et al. 2008). The best imaging sequences, among the ones adopted in clinical environment, for the identification of the different head tissues which have to be included in the head model, are summarized in Tab. 2.

The performed studies allowed the identification of a multimodal clinical imaging protocol for the acquisition of patient's data to be integrated for building an accurate volume conductor head model. Contrarily to imaging protocols for sole diagnostic clinical purposes, image acquisition should be performed with a spatial resolution constant in the 3 scan dimensions or at least similar, to attenuate the loss of information due to

Table 1: Quality of segmentation for head tissues in different image sets

Image set	Identifiable tissues	Segmentation quality
Proton Density	GM, WM, ventricles, CSF, eyes	medium
FLAIR T2	CSF, ventricles, skin	excellent
Inversion Recovery	GM, WM, ventricles, CSF, skin	excellent
Spin Echo + contrast medium	ventricles, CSF, eyes, skin	depending on acquisition
Spin Echo PD/T2	CSF, ventricles, eyes	good
Spin Echo T1	GM, WM, ventricles, CSF, eyes, fat	medium
CT	Skull	excellent
T2 Dry	CSF, eyes, glioblastoma	medium
Turbo Spin Echo T2	CSF, eyes, abscess	medium

Table 2: Head tissues and optimal image sets for their identification

Tissue	Image set
GM	Inversion Recovery
WM	Inversion Recovery
CSF	Inversion Recovery
Medulla and cerebellum	Inversion Recovery
Soft bone	CT
Hard bone	CT
Muscle	FLAIR T2
Fat	Spin-Echo T1
Skin	Inversion Recovery, FLAIR
Soft tissue	Proton Density, Spin Echo T1
Internal air	Cannot be separated from bone in MR, cannot be visualized in CT
Eye	T2 dry, Turbo Spin Echo T2

pixels' interpolation between adjacent sections in the 3-D model building-up. CT acquisition should be performed as follows: 1) Acquisition of contiguous slices of reduced thickness (5mm, 3mm better); 2) Acquisition volume, preferably unique and uniform, extending downwards from head vertex to include at least the skull base (first cervix vertebra desirable); 3) Matrixes 512*512. For MRI acquisitions: 1) Contiguous slices of reduced thickness (2 mm or less); 2) Matrixes 512*512. Larger image matrixes and reduced gap between adjacent slices allow higher spatial resolution in models obtained. For accurate head model geometrical definition, the proposed image acquisition protocol provides using the following multimodal scans: CT for skull; MR Inversion Recovery for GM, WM, cerebellum and CSF; FLAIR T2 for muscles and skin; Spin-echo T1 for fat tissue, para-nasal sinuses and brain lesions; Turbo-spin-echo T2 for eyes. Suitable DT-MRI sequences have to be used for information about tissue anisotropy. Distance between adjacent slices should be better limited to 2-3 mm, possibly covering a volume extended from head vertex to the first cervical vertebra. DT-MRI acquisition can be limited to the reduced volume containing the anisotropic tissue under analysis. Resolution requirements are determined by the most demanding modality (DT-MRI), while field of view (model extension) by model completeness.

5. RESULTS

The 3D EEG simulation framework of TEBAM has been validated by means of EEG forward problem solution using a spherical head model for which analytical solutions were available (Vatta, Bruno, and Inchingolo 2005), using the successive over-relaxation (SOR) method. Optimization analysis has been performed to improve code performance regarding both sequential solution and parallelization procedures. PETSc libraries give excellent profiling instruments that allow evaluation of the optimization degree reached by the use of several CPUs in parallel framework. Fig. 3 shows an example of optimization results related to an EEG forward problem solution with a conductive head model matrix of 64x64x115 elements, a low resolution model used for the sake of testing purposes. Simulations were performed with IBM SP5 made kindly available by the Interuniversity Consortium CINECA (Bologna, Italy) to test the performance of the HPC applications presented in this paper.

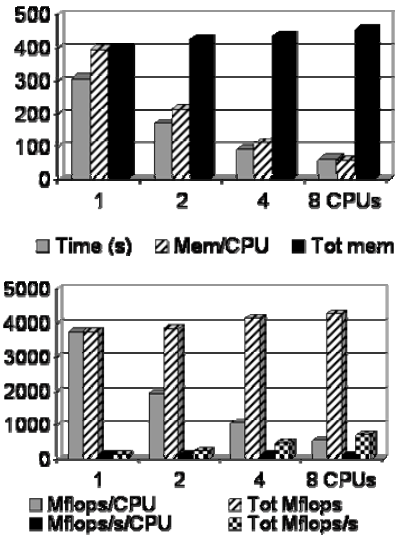
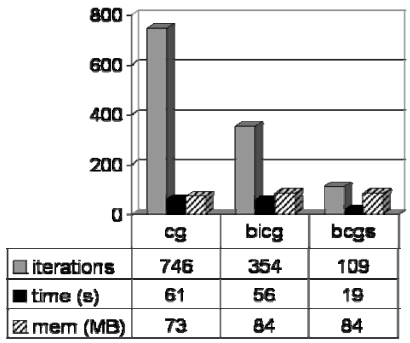
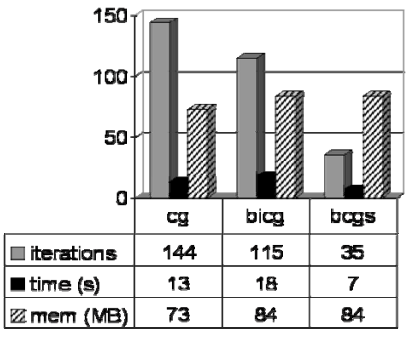


Figure 3: Compared performances with 1, 2, 4 or 8 CPUs on CINECA IBM SP5. (Top) solution times (in seconds) and memory used (in MB); (Bottom) number of floating point operations (in Mflops) by each CPU and for whole problem solution.

PETSc libraries give also a good flexibility and easiness in the choice of suitable iterative solution methods and error tolerances. Next optimization step was then the search for solution methods and tolerances able to guarantee the best performances without sacrificing accuracy in EEG forward problem solution and in 3D EEG source reconstruction. Tests were carried upon a conductive head model constructed out from segmentation of a set of 115 MRI sagittal 256x256 scans. The obtained 3D conductivity matrix (the head model) was sub-sampled to two volumes with lesser resolution to reduce computational load during tests. The following iterative solution methods have been tested and analyzed: Successive Over-relaxation (SOR); Symmetric SOR (SSOR); Conjugated Gradients (CG); Bi-Conjugated Gradients (BiCG); Squared Bi-Conjugated Gradients (BCGS). Different tolerance criteria were examined as parameter for choice of stopping iterative solution, with tolerance values for relative error norm ranging from 10^{-6} to 10^{-12}. Comparisons between three iterative methods are shown in Fig. 4, for an EEG forward problem simulation on a 64x64x115 head model on a mono-processor system (AMD Athlon XP, 2,2 GHz). Tables show performance comparison of the three methods in terms of iterations number needed to reach the required tolerance, solution time and memory needed. In this problem the CG method converges in a larger iterations number but with less memory needs and in shorter time than BiCG. BCGS show the best performances in solution time but



	cg	bicg	bcgs
iterations	746	354	109
time (s)	61	56	19
mem (MB)	73	84	84



	cg	bicg	bcgs
iterations	144	115	35
time (s)	13	18	7
mem (MB)	73	84	84

Figure 4: Performance comparison with different iterative solution methods (cg = conjugate gradients; bicg = bi-conjugate gradients; bcgs = squared bi-conjugate gradients). (Top) results for reaching a tolerance of 10^{-7}; (Bottom) tolerance of 10^{-6}.

with larger memory requirement. The optimization and parallelization procedures lead to a large improvement in the performance, shortening computational time from 45 to less than 1 minute (forward problem solution on a 128x128x115 model).

6. VISUALIZATION

The visualization pipelines developed for TEBAM make full use of several data-fusion techniques (see Fig. 5, in which are shown some examples of EEG forward solutions computed on high resolution head models) and of 3D stereographic rendering and have been

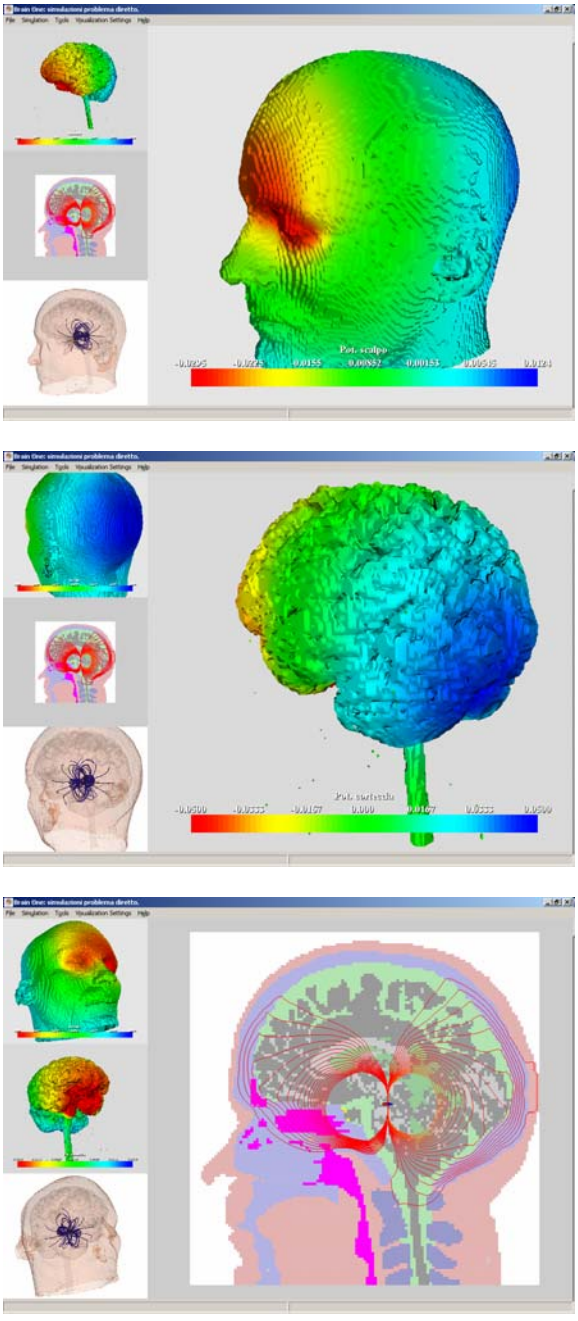


Figure 5: (Top) Scalp surface with electric potential color-map; (Middle) Cortex surface with electric potential color-map.; (Bottom) Tissues cut plane with potential iso-lines.

developed using VTK libraries (Schroeder, Martin, and Lorensen 1996). The hardware stereo support used for testing is an auto-stereo display DTI 2015XLS Virtual Window (Dimension Technologies Inc.) based on Parallax Illumination technology.

The visualization module of TEBAM focused on visualization techniques useful to help data analysis in the context of anatomo-functional integration. The objective in developing these visualization instruments was to have a tool for a better "intuitive" understanding of the 3D EEG source reconstruction procedures, both for research purpose and for future users or developers of TEBAM tools. Visualization output is divided in 4 panels (see Fig. 5), each with a different rendering showing different features.

This multimodal data presentation helps understanding the link between functional and anatomical data. In all the four graphics visualizations, the user can freely "navigate" the model using the mouse to rotate, zoom and pan. The main rendering panel may be switched to stereo 3D mode to improve comprehension of complex configurations adding the depth clues. Most visualization parameters may be changed at will by the user, to allow a deep and meaningful "neuro-navigation".

7. CONCLUSION

The TEBAM original simulation framework presented in this paper is a powerful tool to model and simulate brain activity with high spatio-temporal resolution and accuracy.

TEBAM's features allow overcoming many important limits of several scientific and commercial software. Qualifying features are: flexibility in computational methods, flexibility in modeling to accurately conforming to the specific patient's head, scalability from PC to HPC, multimodal stereo visualization.

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