1 NCRR Progress Report

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR RESEARCH RESOURCES
BIOMEDICAL TECHNOLOGY AREA
ANNUAL PROGRESS REPORT

1. PHS Grant Number: 1P41RR12553-03A1
2. Name of Recipient Institution: University Of Utah
3. Reporting Period:
   A. From - September 1, 2003
   B. To - June 30, 2004
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9. Was Patent or Copyright awarded this grant year: No
10. Total % of effort related to AIDS research: None
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2 Narrative Description
2.1 Summary of Research Progress

2.1.1 Center Overview

The overall goal of the NCRR Center for Bioelectric Field Modeling, Simulation, and Visualization is to develop and disseminate new methods, algorithms, and programs for use in the study of experimental, clinical, and computational bioelectric field problems.

2.1.2 Scientific Focus

1. Develop and implement techniques and software for the efficient manipulation and processing of bioelectric field data: geometric model generation and manipulation, bioelectric field simulation, and scalar and vector field visualization.

2. To use the resulting techniques and software in supporting research projects within the Center and in combination with Center collaborators in computational, clinical, and basic electrocardiology and electroencephalography.

3. Develop an integrated, extensible, problem solving environment that features a computational steering framework for interactive modeling, simulating, and visualizing of bioelectric field problems.

4. Incorporate the techniques and software modules developed within the Center into the problem solving environment. Disseminate state-of-the-art software for geometric modeling, simulation, and visualization in basic and clinical bioelectric field research. Specific software tools include:

   (a) Modeling tools: semi-automatic segmentation, surface generation, automatic mesh generation, parametric representations of surfaces and volumes, and a set of CAD-type tools for viewing and editing models.

   (b) Finite element, finite difference, and boundary element, techniques for the numerical solution of bioelectric field problems.

   (c) Regularization techniques to constrain the effects of the ill-posed nature of the ECG, EEG, and MEG inverse problems. Techniques will include singular value decomposition, Tikhonov, Twomey, admissible solution approaches, frequency domain, and maximum entropy methods.

   (d) Adaptive refinement techniques for forward and inverse approximation methods.

   (e) Visualization tools: interactive scalar field display, isocontour and isosurface extraction, volume and surface rendering, vector field visualization, methods for the characterization, representation, and presentation of error and uncertainty due to modeling, simulation, and visualization methods, and line integral convolution.

5. Provide an on-line database consisting of a test suite of geometric models and simulation data to bioelectric field researchers for use in testing and comparing new methods and results.

6. Conduct workshops on the use of the software tools and instruct and aid researchers in incorporating their own programs into the BioPSE software system.

7. Make available to other bioelectric field researchers, via the world wide web (WWW), the software infrastructure developed within the Center.
2.1 Summary of Research Progress

The overall development focus of the Center in the past years has been to extend the utility and functionality of BioPSE and *map3d* so as to increase its impact in the biomedical research community. This is the continuation of a shift away from developing core infrastructure for the software to adding user-level capabilities and targeting specific communities. Our research thrusts have remained centered around the solution of bioelectrical field problems in both the cardiac and brain research areas.

Specific topics of progress include the following:

**BioPSE usability** We have carried out a number of technical improvements to BioPSE to improve its ease of use at all levels. The user of the network editor will find a host of new tools to facilitate the creation and editing of network diagrams (the programming language of BioPSE) including extensive annotation support for modules and datapipes as well as the ability to merge multiple modules into "subnetworks" that then appear as a single unit in the network diagram.

To further simplify access to BioPSE functionality, we have developed dedicated “PowerApps”, which consist of a network of BioPSE modules with a customized user interface providing access to the control variables relevant to that application. We have released two powerapps to date, one for computing the solution to bioelectric forward problems and the other for reading diffusion weighted magnetic resonance data, extracting the resulting diffusion tensors, and displaying them in very flexible formats.

**Extending BioPSE:** In order to facilitate wider acceptance and use of BioPSE, we have added the Apple Mac/OSX platform to the supported systems to the existing SGI Linux and Linux versions of the program.

A persistent challenge to using any new program is getting it to read the data files and formats that are in local use. Each laboratory tends to have its own formats so that conversions between (and among) them quickly becomes a daunting problem. For BioPSE, we have developed a generalized module for reading data files that has a plug-in structure, much like a web browser allows third party converters to plug into the browser and provide I/O extensibility. The first instance of expanded data reading we have included in BioPSE is for MATLAB files, which will also greatly simplify the steps for users to get their data into the BioPSE framework. Plug-ins for other formats will follow as we identify collaborators and their file needs.

**map3d:** The recent developments with *map3d* have also included increased accessibility by developing a version of the program for Mac/OSX and adding support for reading MATLAB files for both geometry and time-signal data. We have also improved usability by adopting a completely new window management and interface system called GTK as the basis for the program. This has resulted in new widgets and interface elements and thus more flexibility in operating the program. We have also added support for saving program state and layout to files that the user can use to launch the program again into the same state.

**Brain source localization:** We have made improvements in the computation of source localization (inverse) problems in both magnetic (MEG) and electric (EEG) fields in the brain. In the MEG domain, we have investigated the effects of conductivity changes in the recovered sources. In the EEG inverse problem, we have built on past research in computing lead fields and greatly augmented it through Dr. Carsten Wolters joining the group. He has brought a new set of numerical techniques and software tools that we look forward to integrating into BioPSE.

**Cardiac simulation:** We have made considerable progress in the modeling of cardiac electrophysiology in two different contexts. In a collaboration with Dr. Craig Henriquez, we have secured additional funding for a project to simulate discrete cardiac tissue and to develop efficient software to simulate electrocardiography in the mouse. This project will require merging of existing dedicated software
for simulating the electrical behavior of myocardial tissue with BioPSE. In a separate but related project, we have developed whole-heart models that are capable of simulating myocardial ischemia and have used this work to create a new biophysical theory of the electrocardiographic features of subendocardial ischemia.

Medical image processing and visualization: An emerging new theme for the Center is the development of techniques to process, manipulate, and visualize data from medical imaging modalities. In one example of this thrust, we have created novel approaches to the visualization of diffusion weighted MRI data through a collaboration with Dr. Elliot McVeigh and his group of image acquisition specialists. We have also developed algorithms for segmentation of medical data from MRI and confocal optical imaging and will create a PowerApp with this focus in the coming year. We have also contributed to fundamental research in MRI post processing with the goals of accelerated acquisition and reconstruction as well as distortion correction.

Education and User Support: We have continued to develop new mechanisms to educate and support users of our software and research data. We held a second 3-day workshop that was attended by both beginning users and advanced developers of BioPSE. We also developed tutorials for the powerapps and continued to expand our already extensive documentation of the software. We have also used both BioPSE and map3d to aid in teaching courses in electrophysiology at the graduate level. The feedback from workshop participants and students is especially valuable in helping to improve the usability and functionality of the software.
2.2 Highlights

2.2.1 BioPSE

Over the past year we have continued to enhance the Biomedical Problem Solving Environment (BioPSE). The most recent major BioPSE projects have been driven by user requests for increased ease-of-use, more powerful modeling tools, direct data import/export mechanisms, increased stability, and support for the Macintosh OSX platform. We have made these new features available through two major releases of our software over this past year: BioPSE 1.20 and 1.22, released in October 2003 and July 2004, respectively.

In the following sections we detail our progress in the areas of usability, extensibility, and stability.

2.2.1.1 Usability

Historically, one of the major hurdles to SCIRun becoming a tool for the scientist as well as the engineer has been SCIRun’s dataflow interface. While visual programming is natural for computer scientists and engineers, who are accustomed to writing software and building algorithmic pipelines, it is overly cumbersome for application scientists. Even when a dataflow network implements a specific application (such as the forward bioelectric field simulation network provided with BioPSE and detailed in the BioPSE Tutorial), the user interface (UI) components of the network are presented to the user in separate UI windows, without any semantic context for their settings. For example, SCIRun provides file browser user interfaces for reading in data. However, on the dataflow network all of the file browsers have the same generic presentation. Historically, there has not been a way to present the filename entries in their semantic context, for example to indicate that one entry should identify the electrodes input file and another should identify the finite element mesh file.

While this interface shortcoming has long been identified, it has only recently been addressed. With the 1.20 release of BioPSE/SCIRun (in October 2003), we introduced PowerApps. A PowerApp is a customized interface built atop a dataflow application network. The dataflow network controls the execution and synchronization of the modules that comprise the application, but the generic user interface windows are replaced with entries that are placed in the context of a single application-specific interface window.

With the 1.20 release of BioPSE, we released a PowerApp called BioFEM. BioFEM has been built atop the dataflow network shown in Figure 2.1, and provides a useful example for demonstrating the differences between the dataflow and PowerApp views of the same functionality. In Figure 2.1, the dataflow version of the application is shown: the user has separate interface windows for controlling different aspects of the simulation and visualization. In contrast, the PowerApp version is shown in Figure 2.2: here, the application has been wrapped up into a single interface window, with logically arranged and semantically-labelled user interface elements composed within panels and notetabs.

In addition to bioelectric field problems, the BioPSE system can also be used to investigate other biomedical applications. For example, we have wrapped the tensor and raster data processing functionality of the Teem toolkit into the Teem package of BioPSE, and we have used that increased functionality to develop the BioTensor PowerApp, as seen in Figure 2.3. BioTensor presents a customized interface to a 140 module dataflow network. With BioTensor the user can visualize diffusion weighted imaging (DWI) datasets in order to investigate the anisotropic structure of biological tissues. The application supports the import of DICOM and Analyze datasets, and implements the latest diffusion tensor visualization techniques, including superquadric glyphs\textsuperscript{6} and tensorlines\textsuperscript{20} (both shown).

The other major usability hurdle that we have addressed with our most recent releases is the complexity of dataflow programming. In order to make SCIRun dataflow a more complete, easy to use language for application development and rapid prototyping, we have added comments, variable names, and functions / abstractions to the dataflow vocabulary. We have also increased dataflow usability through the addition of NetworkEditing options for clone, insert, replace, and undo.

These enhancements are depicted in Figures 2.4, 2.5, 2.6, and 2.7.
Figure 2.1: BioPSE dataflow interface to the forward bioelectric field application. The underlying dataflow network implements the application with inter-connected components called modules. Data are passed between the modules as input and output parameters to the algorithms. While this is a useful interface for prototyping, it is nonintuitive for end-users; it is confusing to have a separate user interface window to control the settings for each module. Moreover, the entries in the user interface windows fail to provide semantic context for their settings. For example, the text-entry field on the SampleField user interface that is labelled “Maximum number of samples” is controlling the number of electric field streamlines that are produced for the visualization.

Figure 2.2: The BioFEM custom interface. Though the application is functionality equivalent to the dataflow version shown in Figure 2.1, this PowerApp version provides an easier-to-use custom interface. Everything is contained within a single window; the user is lead through the steps of loading and visualizing the data with the tabs on the right; generic control settings have been replaced with contextually appropriate labels; and application-specific tooltips (not shown) appear when the user places the cursor over any user interface element.
2.2 Highlights

GRANT NUMBER 1P41RR12553-04A1
REPORT PD: (09/1/2002 - 06/30/2003)

Figure 2.3: The BioTensor PowerApp. Just as with BioFEM, we have wrapped up a complicated dataflow network into a custom application. In the left panel, the user is guided through the stages of loading the data, co-registering the diffusion weighted images, and constructing diffusion tensors. On the right panel, the user has controls for setting the visualization options. In the rendering window in the middle, the user can render and interact with the dataset.

Figure 2.4: Text labels used for adding comments and variable names to the components of a dataflow network. With the addition of these elements, the network becomes much more readable.
Figure 2.5: Functional Decomposition. Analyzing this network, we define groups of modules that are gathered to provide higher-level functionality. For example, the group at the bottom right implements potential-mapped streamline advection. Each group is a candidate for a “subnetwork” - a logical grouping mechanism for organizing dataflow networks and building libraries of reusable functionality.

Figure 2.6: The groups from Figure 2.5 have been transformed into subnetworks. Each subnetwork has its own canvas (shown on the sides), and is represented on the main dataflow canvas as a single module.
2.2 Highlights

Figure 2.7: The use of higher-order functions (subnetworks) allows the reduction of the dataflow graph to a relatively simple program that can be understood or “read” without much effort.

2.2.1.2 Extensibility

BioPSE has been designed to be extensible: other software and other data formats should be able to integrate directly into our system, rather than forcing users to re-write everything natively in our framework. Over the past year we have continued to improve the extensibility of our system through the introduction of a plug-in import/export architecture for loading and storing data files in other formats, and by adding a socket library to allow other programs to communicate with and control a SCIRun session.

We have extended the SCIRun data Readers and Writers to read data that formerly had to be converted to SCIRun data types with external commandline converter programs. We have implemented this new functionality as a flexible plug-in system, whereby users can create functions to translate their file formats into SCIRun data formats, and the system automatically adds those translators into the Reader and Writer modules.

To make SCIRun more interoperable with other applications, we have also added a socket library. This socket library has already been leveraged to create a “server” mode for SCIRun: when enabled, SCIRun opens a telnet socket at start-up, through which other programs can issue commands to control the user interface options and dataflow execution of SCIRun. In the coming months, this socket mechanism will be further leveraged to provide richer scripting capabilities for SCIRun, as well as for streaming data into and out of SCIRun Readers and Writers.

For BioPSE to be most useful to computational scientists, it is critical that the system natively support a wide range of mesh types, data types, and a flexible mapping between the two. SCIRun currently supports a wide variety of mesh topologies and data types that can be defined over those meshes. However, our design was initially limited to only constant and linear variations of data values over those elements.

Adding support in SCIRun/BioPSE for elements of order greater than one (“higher order elements”) poses substantial challenges because of the very general nature of the computations that it supports. In SCIRun, a user should be able to apply the same computational steps on any type of mesh with any order of basis function e.g., interpolation must be supported with linear, quadratic, or other order elements. Thus to implement higher order elements requires complete support for any data type and for all of the tasks currently supported for linear elements. We have developed a solution to this problem that adds
an additional degree of flexibility in the description of elements; in addition to specifying data type of an element, the user may also specify element order and the underlying class structure will accommodate by creating the necessary source code, compiling it on demand, and then linking the result into the running program, a process we have already developed called “dynamic compilation”\(^2\). We have submitted a description of this approach to the upcoming IEEE Engineering in Medicine and Biology Conference\(^1\).

### 2.2.1.3 Stability

As the SCIRun user base has grown, and we have continued to add greater functionality and more supported platforms to the system, the need for robust software engineering has become ever-more important. To address this need, we have developed an automated regression testing system. This system automatically runs a suite of SCIRun networks every night across a variety of hardware and operating system platforms, automatically submits the results back to a central web server, automatically determines a measure for how successful each regression test was (through comparison to a past “ground-truth” solution), and automatically collates these results into an easy-to-read web page. Through this automated process we have been able to reduce the number of bugs that are introduced unnoticed into our code base. The long-term advantages of this regression testing suite will be more frequent and more robust major releases: this will reduce the lag time between when new features are developed and when they are made available to the public, and will also greatly increase the quality and stability of the first version of major releases.
2.2.2 map3d

Once again, we have released two new versions of map3d in the past year with a number of additions in features and functions. The main advances in the past year have been in the area of user interface, made possible by a wholesale move to a new window management system. This system, known as “GTK”, is the basis for a number of public domain software packages, most notably the gimp toolkit, an image processing system. It allows for much more flexible creation of user interface elements and much more powerful control of all aspects of the window placement and management than our original system, which was based on the GL User Tools (GLUT).

With GTK available, we have added an array of new user interface elements, including one that manages, at a glance, all the files for geometry and data and the surfaces to which map3d attaches them. There are also menus for setting colors and sizes that appear in a number of contexts to allow the user to tailor the display.

Figure 2.8: Sample composite figure from map3d. Here we see two surface geometries and associated scalar potential time series measurements. The left-hand surface is from the epicardium of an in situ dog heart and the right-hand surface is from a multielectrode basket catheter placed in the left ventricle of the same dog. Also visible is the new surfaces window that allows the user to review and select surface geometries and associated data files. Colored spheres indicate the locations of all the recording electrodes in both electrode arrays. The figure reveals the location of initial activation from both the epicardial and endocardial surfaces, indicated by the blue region of negative potential in both panels.

We have also added the capability to read files in MATLAB format into map3d and thus greatly facilitated other users porting their results and data into the program. This addition required the creation of a MATLAB library that permits any C/C++ program to read and manage MATLAB data files. We have used this library both in map3d and in SCIRun/BioPSE. Figure 2.8 contains an example of data read from MATLAB files as well as the new file interface window. These data came from a collaborative project with Dr. Elliot McVeigh at NIH, who is using map3d to examine results from his experiments in cardiac electrophysiology.

Another important improvement is that map3d is now available for the Apple Mac/OSX platform so that we now have coverage of all the major systems including Linux, Windows, Mac OSX, and SGI/Irix.
2.2 Highlights

When working on a large set of data files, one often wishes to save the state of a program and then return to that same point later. To provide this support for \textit{map3d}, we have added extensive state-saving capabilities in two forms. In the first, we have defined a \texttt{.map3drc} files that contains the state of the program and all the default settings for the program. The user can create such a file with a single button click, then edit it to modify settings, and have it read again the next time the program launches. The second form of state saving is a script (or batch in Windows) file that contains the placement and layout of all the windows currently open, including their contents. This file is meant to provide a template for script files that the user will create to automate the launching of complex arrangements of windows and data files in subsequent work sessions. The user can easily edit the scripts, add control variable that become command-line arguments at execution time, and then facilitate using \textit{map3d} to look at large series of data with common features and organization.

The list of projects planned includes such things as:

**File I/O:** We are nearing completion of a project to broaden the scope of files that \textit{map3d} will read from the CVRTI time series data files (tsdf) to a much more versatile container file system that can include access to an infinite number of tsdf files. We have completed the support for MATLAB files and are just completing the support for hierarchical data files in the CVRTI \texttt{graphicsio} format. This will allow display of time signals and derived parameters from them in the same framework. One example that is driving this development is the ability to display both time series of potentials and the activation and recovery maps that one can derive from them. We will also target some of the file formats that come from commercial mapping systems such as the CARTO\textsuperscript{13}, Endocardial Solutions\textsuperscript{23}, and EGI\textsuperscript{16}.

**User interface development:** We will continue to add more user interface in the form elements of GTK widgets and dialog windows.

**Generating animations:** A key feature of \textit{map3d} is the ability to visualize in a dynamic way time-dependent data and we will soon have the ability to capture these dynamics from the program in the form of digital movie files. This way, the user can create animated sequences for inclusion in presentations or dissemination in video formats.
2.2.3 Applications

A principal mandate of our NCRR Center is to provide examples and support to help users integrate BioPSE into their scientific research. To support this mission, we continue to interact closely with our Center collaborators and researchers within the SCI Institute and the CVRTI. These collaborations are a microcosm of our growing user base, and have provided excellent opportunities for us to evaluate and extend the breadth of our tools, as well as to develop user-support strategies and mechanisms. Through these collaborations, we have developed an array of applications, many of which are already available to the bioelectric field research community.

Over the past year, we have moved our software focus away from developing core functionality and towards developing interfaces and applications targeted at the needs of our collaborators. As a direct result of this effort, we currently have a number of successful ongoing collaborations. Here, we report on the current status of those applications and describe some emerging developments.

2.2.3.1 Inverse MEG Simulation

In the past year, we have investigated the affects of conductivity on magnetic field calculations and MEG source localization problems\(^{19,18}\). The influence of head tissue conductivity on MEG was investigated by comparing the normal component of the magnetic field calculated at 61 detectors and the localization accuracy of realistic head finite element method (FEM) models using dipolar sources and containing altered scalp, skull, cerebrospinal fluid, gray, and white matter conductivities to the results obtained using a FEM realistic head model with the same dipolar sources but containing published baseline conductivity values. In the models containing altered conductivity values, the tissue conductivity values were varied, one at a time, between 10% and 200% of their baseline values, and then varied simultaneously. Although changes in conductivity values for a single tissue layer often altered the calculated magnetic field and source localization accuracy only slightly, varying multiple conductivity layers simultaneously caused significant discrepancies in calculated results. The conductivity of scalp, and to a lesser extent that of white and gray matter, appears especially influential in determining the magnetic field. Comparing the results obtained from models containing the baseline conductivity values to the results obtained using other published conductivity values suggests that inaccuracies can occur depending upon which tissue conductivity values are employed. We show the importance of accurate head tissue conductivities for MEG source localization in human brain, especially for deep dipole sources or when an accuracy greater than 1.4 cm is needed.

2.2.3.2 Source localization in the brain

We are very pleased to have Carsten Wolters recently from the Max Plank Institut in Leipzig, Germany, join the Center as a post doctoral fellow. Dr. Wolters brings considerable knowledge and experience in the area of Algorithms of Finite-Element-Method based Electroencephalography/Magnetoencephalography source reconstruction in the human brain. He has made substantial progress already on three separate projects, some of which originated in Germany, but all of which are now active projects within the Center.

**Efficient Computation of Lead Field Bases and Influence Matrix**

The inverse problem in EEG and MEG aims at reconstructing the underlying current distribution in the human brain. The simulation of EEG and MEG fields for a given dipolar source in the brain using a volume-conduction model of the head is called the forward problem. The Finite Element (FE) method, used for the forward problem, is able to realistically model tissue conductivity inhomogeneities and anisotropies, which is crucial for an accurate reconstruction of the current distribution. So far, the computational complexity is quite large when using the necessary high resolution FE models. It is already known that the so-called reciprocity principle can strongly reduce this complexity in EEG. We have derived new algorithms for the efficient computation of EEG and MEG lead field bases which exploit the fact that the number of sensors is generally much smaller than the number of reasonable dipolar sources \(^{21}\). The state-of-the-art forward
approach is sped up substantially for a realistic number of sensors and sources. Our approaches can be applied to inverse reconstruction algorithms in both continuous and discrete source parameter space for EEG and MEG. In combination with algebraic multigrid solvers and multiple right hand side treatment, the presented approach leads to a highly efficient solution of FE-based source reconstruction problems.

The new lead field bases approach was tested by means of an influence matrix computation, which is the basis for all current density reconstruction methods. Nevertheless, the presented approach can be used for all inverse algorithms in discrete and also continuous parameter space such as MUSIC, dipole fitting etc. For the following cases, we chose an anisotropic tetrahedral FE head model with 892,119 elements and 147,287 nodes. The brain surface was represented by a triangular mesh with 2mm mesh resolution, resulting in an influence space with 19,106 triangles and 9,555 nodes. We chose a 71 electrode EEG configuration and a 147 channel whole head BTI MEG. The influence matrices were computed without normal constraint but with a tangential constraint for the MEG, so that 9,555×3=28,665 forward computations were necessary for the EEG influence matrix and 9,555×2=19,110 for the MEG. We performed the simulations on two platforms, a 3.2GHz Pentium 4 PC with 2GB main and 1024 KB cache memory running Red-Hat Linux and a 1GHz G4 Apple Macintosh PowerBook with 1GB main and 512 KB cache memory running OSX. We compared the new lead field bases approach with the standard approach in FEM source reconstruction, i.e., solving a large sparse FE equation system for each dipole in the influence space.

<table>
<thead>
<tr>
<th>Platform</th>
<th>Method</th>
<th>Solver method</th>
<th>Setup time</th>
<th>RHS # Mons</th>
<th>Influence matrix</th>
<th>Max. memory (in MB)</th>
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</table>

Figure 2.9: Comparing the computational complexity between the lead field bases approach and the standard approach in an influence matrix computation.

The iterative FE solver method is indicated in column 3 of Figure 2.9. The setup time, column 4 in Figure 2.9, only occurs once per head model. Simulations concerning the computational complexity for the influence matrix were performed for both, a blurred and a mathematical dipole (see \textsuperscript{22,9}). This is indicated in column 5 of Table 1 through the number of non-zeros of the FE Right-Hand Side (RHS) indicating n_{cz} the amount of blurring and N being the mathematical dipole. We also indicate the maximal memory necessary for the current implementation in our FE based source reconstruction software NeuroFEM.

**Algebraic MultiGrid for Efficient Computation of EEG and MEG Lead Field Bases**

Iterative solver techniques are used for the computation of EEG and MEG lead field bases for finite element method based volume conductor modeling. As a separate project, we developed and implemented a new efficiency strategy: the algebraic multigrid preconditioned conjugate gradient method with simultaneous treatment of multiple right-hand sides. We have shown that this solver leads to a much higher cache hit rate, which speeds the computation by more than a factor of 2. Together with the concept of the EEG and MEG lead field bases, the complexity of realistic high resolution anisotropic finite element forward modeling within the EEG/MEG inverse problem is significantly reduced and can now be performed in approximately the same time as boundary element head modeling.

As a basis for our computations, we chose a realistic anisotropic tetrahedral FE model with 147,287 nodes and 892,115 elements, and a 147 channel MEG configuration. We compared the computation time for the construction of the MEG lead field bases for the Jakobi-preconditioned CG (J-CG), the symmetric Incomplete Cholesky preconditioned CG without fill-in (symIC(0)-CG) and the AMG-CG with the new MultiRHS-AMG-CG while varying the number of simultaneously treated RHSs. Speedup tests were
2.2 Highlights

Figure 2.10: The results for AMG-CG and MultiRHS-AMG-CG for MEG. The computation time for a specific number of simultaneous RHS’s is indicated above the curves.

...performed on three different platforms, a Mac-OSX with PowerBook G4 proc (1Ghz, 512 KB cache), a Red-Hat Linux PC with Xeon proc (2.4Ghz, 512 KB cache) and a Red-Hat Linux PC with Pentium 4 proc (3.2 Ghz, 1024 KB cache). The computation time for the MEG lead field bases with J-CG (symIC(0)-CG) on those three platforms were 13,361 sec. (7,261 sec.), 4,061 sec. (2,089 sec.) and 2,512 sec. (1,322 sec.) Figure 2.10 shows results from these simulations.

**STR: A new Spatio-Temporal Approach for Accurate and Efficient Current Density Reconstruction**

We have developed a new and fast regularization procedure for reconstructing current densities based on EEG and/or MEG measurements. It was our goal to achieve a stabilization of the solution which is superior to known procedures: our approach not only considers spatial smoothness but also temporal smoothness of activation curves as a-priori information. We state an appropriate minimization problem which expands known Tikhonov-based methods based on spatial smoothness operators as known from LORETA and others. Trying to solve the resulting minimization problem with standard tools from linear algebra, one encounters efficiency problems which result in computation times ranging from several days to some weeks. The STR algorithm that we developed leads to an immense speedup, reconstructions can be computed on standard desktop computers, the solution time ranges from seconds to a few minutes depending on the number of time steps and influence nodes considered. We prove that the STR algorithm can be decomposed into filtering followed by inversion. But, in contrast to known smoothing techniques, the filter induced by STR is adopted to the underlying model and cannot be decomposed into spatial and temporal filtering. So STR is different to applying temporal filters as a preprocessing step to known spatial regularization procedures. Simulations show the distinct improvement of spatial and temporal accuracy of current density reconstructions in the presence of noise.
2.2 Highlights

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Figure 2.11: Left: setup of the simulation. Middle: current densities calculated from temporally uncoupled Tikhonov-Phillips solution. Right: current densities calculated from STR reconstruction.

Figure 2.12: Left: activation curves of the two dipoles used for generating synthetic data. Middle: activation curves based on temporally uncoupled Tikhonov-Phillips solutions. Right: activation curves calculated from STR reconstruction.

For studying the general behavior of STR, we used a simple setup, see Figure 2.11. The influence space is a 10x10 grid in two dimensions. Nine sensors are placed in a planar array above the grid with center (5.5, 5.5, 2). The center of the influence space is (5.5, 5.5, 0). We assume constant conductivity in the whole space, so the leadfield matrix can be computed analytically. Two equally oriented dipoles with moment (0,0,1) at x=3, 8 both at y=5 are placed on the 10x10 grid.

Gaussian dipole-strength time series are assigned to each dipole, they are drawn in Figure 2.12. We generated synthetic data and added 30% uniform noise. All methods use the identity matrix as the regularization matrix. We calculated temporally uncoupled Tikhonov-Phillips solutions and STR solutions. The first used temporal smoothed data (Savitzky-Golay filter of order three and length five). Based on these results, Figure 2.11 shows current density reconstructions, in Figure 2.12 reconstructed activation curves are drawn. The improved stability in presence of noise is apparent.

2.2.3.3 Mouse heart simulation

In last year’s progress report, we described a collaboration with Craig Henriquez at Duke University in which we generated a three-dimensional simulation of mouse heart activation and extracardiac potentials. We carried out this project by using SCIRun/BioPSE to create the geometric model and visualize the results of the simulation and Dr. Henriquez’s Cardiowave software to perform the simulations.

Based on these and other preliminary data, we successfully submitted a joint grant application to expand on this research by creating detailed models of cardiac tissue at the (microscopic) level of individual cells. The goals of this project are two-fold. The first is to advance computer simulation of the heart by providing users a unified problem-solving environment to simulate impulse propagation at both the microscopic and macroscopic scales. The second is to develop a complete model of mouse electrophysiology, to complement the experimental use of transgenic mice to study the molecular basis of cardiac disease.
A novel feature of the problem-solving environment will be the ability to rapidly create preparation-specific models of cellular structure and heart anatomy directly from image data and to manipulate and assign properties in three dimensions. To implement these goals, Dr. Henriquez proposes to link the existing Cardiowave software of his group into the SCIRun and BioPSE framework of the Utah group. The Center will play a key role in the project by developing the shared computational infrastructure that will allow SCIRun/BioPSE and Cardiowave to integrate more tightly in a way that includes the strengths of both systems. Figure 2.13 shows the schematic diagram of the integrated software, named “CardioPSE”, as well as the input data it will require. The grant will fund a post doctoral fellow, Dr. Jeroen Stinstra, who has spent the past two years working with Dr. MacLeod on a separate project, the goals of which were to develop models of myocardium with which to compute tissue conductivity; results of these simulations led directly to the simulations of ischemia described in Section 2.2.3.5.

2.2.3.4 Cardiac forward problems using the Boundary Element Method

In the current grant year, we developed a new version of the BioPSE modules for BEM forward modeling for electrocardiography and similar bioelectric problems with potential source boundary conditions and potential measurements on the outer surface. In particular, we:

- Rewrote the BioPSE integration routines to incorporate more accurate methods of quadrature integration, in particular for the difficult cases where the integrals are singular that arise in BEM solutions of this type.
- Modified the modules’ code to improve computational efficiency.
- Working with SCI personnel, restructured the BEM modules to allow a flexible number of surfaces in the BEM geometry. The user can also specify on which surface to compute the potentials. The module automatically determined the geometric relationship between the surfaces so that the user does not need to specify it.
2.2 Highlights

- Tested the BEM models we compute against experimental data acquired by our CVRTI collaborators in their special tank using their double-dog experimental techniques.

- As a first step to developing BEM models for electrical impedance tomography (EIT), we used BioPSE to perform some geometric modeling and for visualization.

Two conference publications (one accepted for IEEE EMBS conference and the other submitted to the Asilomar Signals and Systems Conference) have come from this work, and a first journal paper is in preparation.

2.2.3.5 Simulating myocardial ischemia

Simulation of cardiac electric fields from a heart undergoing myocardial ischemia is the goal of a project that is housed at the CVRTI and makes use of NCRR resources. Ischemia results from inadequate blood supply to the heart and the resulting heterogeneities in tissue properties provide a source of current between healthy and ischemic parts of the heart. Detection and proper characterization of these currents from body surface ECG measurements is the basis of clinical diagnoses, however, there are considerable errors in this process that accurate simulation should improve.

This project also receives support from two other grants; the Center provides computational resources and software expertise. The goal of the current simulations is to determine the sensitivity of the ischemic potential distributions to changes in parameter values such as myocardial fiber orientation, cardiac geometry, and conductivity. The output of the simulations are extracellular potentials over the surface of the heart from a given cardiac geometry, including fiber orientation data, and a source distribution of transmembrane potentials. The heart geometry consists of a regular grid mesh of the entire heart; the choice of a regular grid facilitates the simulation, data analysis, and visualization compared to irregular meshes. Emulation of ischemia occurs through the selection of the source potentials.

Results from this project have resulted in two publications in the past year, one in press\(^5\) and the other currently in review\(^4\). Figure 2.14 contains images of the geometric model used for these simulations, the left hand panel showing the epicardial and endocardial surfaces as well as the ischemic region within and the right hand panel showing the local fiber orientation for the same geometry.

Figure 2.14: A model of the canine ventricles used for simulating ischemia. Left-hand panel shows the epicardial and left ventricular endocardial surfaces of the model. The yellow colored patch indicates the outline of the ischemic region which began at the endocardium and penetrated to varying degrees through the left ventricular wall. The right-hand panel shows the local fiber orientation for the same geometry.
2.2 Highlights

Figure 2.15: Simulation results from myocardial ischemia. Epicardial potentials are color coded such that blue corresponds to the lowest value, red the largest, and green shades the values in between. Results are (from left to right) for ischemia regions that extended 40%, 70%, and 90% of the distance from endocardium to epicardium.

2.2.3.6 Bayesian Constraints in Electrocardiographic Inverse Problems

Due to attenuation and spatial smoothing that occurs in the conducting media, the bioelectric inverse problem of estimating sources from remote measurements is ill-posed and solution requires regularization. The most common approach to this problem is deterministic “regularization” (also known as Tikhonov regularization), where the solution is a trade-off between the estimate that best represents the data and fidelity to an a priori regularization constraint imposed on the solution. Recent studies have described Bayesian approaches to the bioelectric inverse problem. In addition to providing a more general way to formulate physiological constraints, these approaches also offer statistical performance evaluation tools that are not generally available with deterministic approaches. However, the Bayesian methods rely on the choice of prior probability density function (pdf); the better the prior model fits the epicardial potentials, the greater the reliability of the Bayesian estimates.

In one study, we employed Bayesian methods, and presented the mathematical framework for incorporating additional information in the form of prior statistics, and extra measurements. We applied the methods to inverse electrocardiography problem, in which we had torso measurements and a forward model as the primary information, and sparse epicardial measurements, and a training set of epicardial potential maps as additional information. We compared performances of deterministic and Bayesian methods that employ one or more of these information sources. We also used Bayesian error metrics to evaluate the reconstructions. The results showed that it is possible to improve the reconstructions by including extra information, and that Bayesian error metrics are useful in evaluating the results. A journal publication based on an expanded version of these results has been accepted with minor revisions to the IEEE Transactions on Biomedical Engineering.

In another study, a complement to the first reporting of Bayesian approach, we examined the effect of the number and location of epicardial measurements used in the Bayesian approach. We also illustrated the use of the Bayesian predicted error covariance to quantify this effect. The ultimate goal was to recommend practices for venous catheter mapping that together with body surface potential measurements would allow accurate reconstruction of epicardial potentials. The results showed that we obtain better reconstructions as we increase the number of epicardial measurements included in the Bayesian solution.

Our previous studies on Bayesian MAP estimation applied to the inverse ECG problem have shown that it was important to use a “good” prior model in order to increase the reliability of the Bayesian reconstructions. In a subsequent study, we used Bayesian evidence and examined a very simple prior selection scenario, with only three prior models. Even by using this simple simulation, we obtained results that support the hypothesis that the prior model that maximizes the evidence is a good choice of prior. The results of this proof-of-concept study show that it is feasible to use the Bayesian evidence in a prior
2.2.3.7 Tensor Visualization

We have continued to investigate a fundamental problem in visualization: the design of glyphs, or icons, for effectively displaying multi-variate data. Tensor data, such as arises from diffusion tensor magnetic resonance imaging (DT-MRI), is traditionally displayed with an ellipsoid. The ellipsoid glyph is defined by mapping a sphere geometry through the linear transform defined tensor. While the mathematical simplicity of the ellipsoid glyph is compelling, its perceptual characteristics are significantly lacking. The smooth surface of the ellipsoid makes it difficult to discern details about tensor shape and orientation, which are fundamental to understanding structure and trends in tensor fields.

![Ellipsoidal glyphs suffer from visual ambiguity.](image1)

Figure 2.16: Ellipsoidal glyphs suffer from visual ambiguity.

![Superquadric glyphs differentiate shape and convey orientation more clearly than do ellipsoids.](image2)

Figure 2.17: Superquadric glyphs differentiate shape and convey orientation more clearly than do ellipsoids.

Figure 2.16 shows the space of tensor shapes with ellipsoid glyphs, and shows how variations in shape are not clearly distinguished. Figure 2.17 shows the same tensor shapes with our novel superquadric glyph geometry. The work defining the superquadric tensor glyph geometry has been recently published.

Ongoing collaborations have applied the superquadric glyph visualization technique in two separate areas. In collaboration with Drs. Elliot McVeigh and Dan Ennis at NIH and Johns Hopkins University, the new glyph method has improved the visualization of both diffusion and strain tensors acquired via MRI in the canine myocardium. The superquadric glyphs proved effective at displaying structural features of the diffusion tensor fields that had previously not been visualized from DT-MRI, such as an increase in orthotropy in the midwall of the myocardium. The principal diffusivity direction indicates myofiber orientation, but the tensor shape has a planar component, consistently oriented, which may be indicating myocardial laminae or sheets. In visualizing strain tensors, the superquadric glyphs convey the transmural...
2.2 Highlights

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gradient in radial thickening, as well as the torsion in the primary contractile direction. This collaborative
work was presented at the most recent ISMRM conference.

The other application of superquadric glyphs has been in the visualization of anatomical covariance
tensors calculated from human brain mapping. Drs. Art Toga and Paul Thompson, of the Laboratory of
NeuroImaging (LONI), UCLA School of Medicine, are interested in understanding the extent and nature
of anatomical variability on the cortical surface of the human brain. Using cortical models extracted from
MRI scans of individuals in a population of interest (healthy volunteers, Alzheimer’s patients), deformable
registration methods generate, for each point in the surface mesh, a covariance tensor representing the
anatomic variation in the location of the underlying feature. Visualizing the features and trends in the
covariance tensor field can enable insight into the biological dimensions of anatomic variability, with the
compelling possibility of characterizing disease states in terms of deviations from normal anatomical pat-
terns. The visualization tools also provide a direct way of evaluating the algorithms required to generate
the data.

In Figure 2.18, the covariance tensors are shown with superquadric glyphs raised above the cortical
surface mesh. On the surface mesh is mapped, by a grayscale map, the level of anisotropy in the covariance
tensors, which quantifies how non-spherical the tensors are. The glyphs themselves are colored according
to the skewness of the eigenvalues, which quantifies whether the pattern of anisotropy is more linear or
planar in shape. These images indicate that the temporal and occipital lobes are the areas of highest high
anatomic variability.

2.2.3.8 Segmentation

Segmentation of medical imaging data is typically the first step in creating geometric models and requires
the identification of boundaries between regions with different tissue characteristics. We have continued
to pursue our research on segmenting medical image data. A complete description of this project has been
published as a University of Utah Technical Report.

The segmentation algorithm we designed is based on three principles: (i) a combination of scalar and
multispectral Expectation-Maximization clustering stages provides fast, unsupervised statistical analysis,
(ii) a modest amount of prior anatomical knowledge can help resolve statistical ambiguities, and (iii) a
top-down modular approach that breaks the problem into smaller logical pieces leads to efficient solutions.

In Figure 2.19, the top and bottom rows show non-brain tissue classification and the brain tissues and
sinuses for the same slices, respectively. The classification in column 1, row 1 demonstrates several tissue
types: the eyes, orbital fat around the eyes, the skull and the temporalis muscle on either side of the head,
as well as muscle in the forehead between the eyes. In the second row, the superior sagittal sinus has been
detected at the top as have cerebral arteries below the center of the brain. Some noise is present in the
classification between white and gray matter. As part of our future work, spatial continuity constraints
will be introduced into the multi-spectral EM classifier using Markov Random Fields. The classification
in column 2, row 1 shows that air pockets inside the frontal bone of the skull, i.e., the frontal sinuses have
been successfully separated from the bone. The classification in column 4, row 1 illustrates the separation
between bone and bone marrow.

Another segmentation project that we have continued to investigate is the automatic segmentation
of Virtual Cell data. The Virtual Cell software allows users to set up models of biochemical reaction
pathways and membrane transport kinetics that apply to two- or three-dimensional models of real cells.
The source information for such models typically comes from confocal microscope datasets, which the user
must first process and prepare in order to convert the gray-scale images into volume compartments based
on cell features (e.g., nucleus, cytoplasm, extracellular space, etc.). The main component of this process
is segmentation, i.e., the definition of boundaries between cell compartments, and currently users perform
this operation with commercial software outside the Virtual Cell. Although commodity software such
as Adobe Photoshop provides support for constructing two-dimensional segmentations, three-dimensional
segmentations based on confocal stacks requires specialized and expensive software (e.g., Imaris by Bitplane
at a single installation license cost of $15,000). Such software is not accessible to most VC users and also requires a steep learning curve. Thus, a simple three-dimensional segmentation tool that could be integrated with the VC software environment would be highly beneficial.

The technical approach we have pursued involves the same steps as the whole-head segmentation described above, i.e., investigating both statistical and morphological algorithms to achieve robust segmentations. These preliminary investigations provide the groundwork for a PowerApp that will guide the user through the segmentation process, providing both a variety of complete protocols (examples) and access to the individual component algorithms.

Figure 2.20 contains preliminary results using what are known as “k-means cluster” and “watershed” segmentations. The top row shows five gray-scale slices from the original confocal data of a cell. Our first approach to segmenting this data was a k-means clustering method in which we found three clusters in the histogram of the data, corresponding roughly to background, nucleus, and cytoplasm. We then applied a morphological opening operator to identify the neurites independently from the cell body. The results of this classification are shown in the middle panel. We also applied a user-guided watershed segmentation approach, shown in the lower panel. The left-hand image is the result of global watershed segmentation, and the right-hand image shows the result of manual interaction to group these classifications into fewer regions, overlayed on the original data.

2.2.3.9 MRI image post processing

Another area of progress in the last year has been on developing advanced methods for acquisition, reconstruction, and post processing of MRI data. The primary target of our efforts was the development of advanced parallel MRI techniques. Parallel Magnetic Resonance Imaging (P-MRI) provides significant speedup of the data collection process by utilizing differences in sensitivities of multiple receivers. One application of P-MRI is to increase spatial and temporal resolution for the existing acquisition sequences. Existing P-MRI systems may provide an increase of 8-16 fold in spatial/temporal resolution for improved imaging of brain function, DT measurements, cardiovascular imaging, etc. Such improved data may prove very important for building realistic models. A drawback of P-MRI is the associated reduction in image quality, which limits the application of P-MRI for highly accelerated imaging. P-MRI is still vulnerable to many imaging artifacts.

We have developed a new fast iterative method for the reconstruction of P-MRI data. Based on Projections Onto Convex Sets (POCS), the new method, POCSENSE, includes a priori knowledge in the form of reconstruction constraints. We have demonstrated that such flexibility may provide high image quality for highly accelerated MRI, and push the acquisition speedup above that of traditional P-MRI, which is limited by the number of coil receivers. One example of reconstruction of data acquired using partial Fourier P-MRI approach is shown in Figure 2.21.

We have also developed two practical applications of POCSENSE for reconstruction of Fast Spin Echo (FSE) MRI data. The new methods take advantage of the unique image phase properties of FSE data. Our new methods may allow significant image error reduction (up to 15 dB in our experiments) and additional speedup (up to 150% of regular speedup) in certain FSE P-MRI applications. Finally, we have created a method for correcting MR image corrupted by motion artifacts using developed POCSENSE formalism. The new method may eliminate motion-related ghosting and blurring in a fast and efficient way. The new artifact correction approach reduced image error more than 2 times in comparison with the related methods. The new artifact correction procedure performs post-acquisition data correction and thereby avoids data reacquisition, which may save time in time critical clinical situations. An example of motion artifact correction is shown in Figure 2.22.
2.2.4 Volume Rendering

In May 2004, we were granted funding for a supplementary project to improve the Volume Rendering capabilities in SCIRun. Volume Rendering is a powerful visualization technique for investigating volumetric datasets such as MRI and CT. Though we are less than two months into this one year project, we have already generated preliminary results from this work, and are now beginning to provide alpha versions of the software to our collaborators for early adoption and feedback.

2.2.4.1 Lighting and Shading

Lighting and shading models can be incorporated into volume rendering to provide spatial cues similar to those found in surface rendering. A surface that is directly facing a light appears brighter than a surface illuminated by light from a glancing angle. This concept extends to volumetric objects through the computation of local “orientation” for each voxel in the volume. A voxel which is at the boundary between two materials with different gray scale values will have a local orientation (“gradient”) that points in the direction of greatest change across the boundary.

We have extended SCIRun to add lighting and shading to volume rendering, and have made the rendering process highly interactive by writing custom volume rendering software that runs directly on the graphics processing unit (GPU). In Figures 2.23 and 2.24 we demonstrate the improvements in the volume rendering image quality due to added lighting and shading effects.

2.2.4.2 Multi-Dimensional Transfer Functions

The second major enhancement that we have added to the SCIRun volume rendering engine is support for multi-dimensional transfer functions. Transfer functions are used to assign color and opacity to each voxel of a volumetric dataset (such as MRI or CT). Typically this assignment is based solely on the local gray-scale value associated with each voxel. Such a transfer function can be described as “one-dimensional”. However, for medical datasets it is often useful to look at the two-dimensional histogram defined by both the local gray-scale value at each voxel, and the local “gradient magnitude” at each voxel. The gradient magnitude is a measure of how similar the voxel’s value is to the values of its immediate neighbors. If the gradient magnitude is low, the voxel is very similar to its neighbors. However, if the gradient magnitude is high, then the voxel has a value which is different from its neighbors, which is often indicative of a boundary. By plotting the two-dimensional histogram of a CT dataset, such as the tooth shown in Figure 2.25, we see a large clusters of points (representing many voxels from the volume) in the lower portion of the graph. These voxels have low gradient magnitudes and correspond to the interior regions of the model. The cluster are connected by arcs, which correspond to the interfaces between those regions of the model. By inspecting the two-dimensional histogram and assigning colors and opacities to those voxels that make up the arcs (while leaving all other voxels completely transparent) the user is able to visualize the boundaries of the model, as shown in Figures 2.26 and 2.27. As with lighting and shading, this improved volume rendering technique can only be made interactive by specifying custom programs that implement this rendering technique and run directly on the GPU.

We have completed preliminary SCIRun implementations of both lighting/shading and multi-dimensional histograms for volume rendering. We are now making these enhancements available to a subset of our collaborators for alpha testing and refinement. We will be making a PowerApp version available as part of our next major release. A preliminary mock-up of this BioImage PowerApp is shown in Figure 2.28.
2.2 Highlights

2.2.5 Administration, Personnel, and Training

1. Personnel Activity - The grant period of 2003-2004 was very stable for the center personnel, in general. We have continued to take advantage of the staff building and training done during the 2000-2003 period. There was no turnover in our software development team during the last year and we have continued to operate with the software engineering management consolidated under Mr. Dav de St. Germain. The stability in development staff, which is mirrored by the entire center, has in turn produced a more stable software package and more stable user-developer relationships. With substantial difficulty we have recruited a post-doctoral fellow for modeling research and inverse problem research. Specifically, we have hired Dr. Carsten Wolters from the University of Leipzig, see section 2.2.3.2. Additionally, Dr. Tolga Tasdizen was also recruited as a post-doctoral fellow during the 2003-2004 grant period and performed research on automated segmentation algorithms, see section 2.2.3.8. This work was directed by Dr. Weinstein, the center Technical Manager.

2. NCRR Seminars -
As in previous years, the NCRR seminar series of 2003-2004 consisted of a variety of presentations from local, national, and international presenters.

- Jul 07, 2003 Colin Davey and Kevin Glass – The Application of SCIRun to Source-Localization Products and Head-Tissue-Conductivity Estimation Technology
- Jul 10, 2003 Carsten Wolters – Influence of Tissue Conductivity Inhomogeneity and Anisotropy on EEG/MEG based Source Localization in the Human Brain
- Jul 11, 2003 PD Dr.-Ing. Frank B. Sachse – Modeling of Cardiac Electro-Mechanics
- Sep 12, 2003 Greg Worrell – Medically Intractable Neocortical Epilepsy
- Sep 12, 2003 Irina Ionescu – Finite Element Analysis of an Implanted Human Tibia Under Normal Gait Loading
- Sep 26, 2003 Gordon Kindlmann – Curvature-Based Transfer Functions for Direct Volume Rendering: Methods and Applications
- Oct 10, 2003 Joe Kniss – Gaussian Transfer Functions for Multi-Field Volume Visualization
- Oct 24, 2003 Alexey Chernyavskiy – Calibration and Tracking Using Low-parameter Geometric Shapes
- Oct 28, 2003 David Banks – Counting Cases in Substitope Algorithms
- Nov 14, 2003 Natalia Trayanova – Cardiac Defibrillation: Virtually Shocking
- Nov 20, 2003 Marc Droske – Gradient flow methods for morphological image registration and level set Willmore flow
- Nov 21, 2003 Robert Johnson – Visualizing to Understand Complexity
- Mar 05, 2004 Carsten Wolters – Efficient Computation of Lead Field Bases for the FEM-based EEG and MEG Inverse Problem, the Treatment of the Potential Singularity and new Spatio-Temporal Regularization Methods
- Mar 12, 2004 Prasad Saripalli – Visualization as Computation: Knowledge Discovery Using Visualization of Complex Biological and Physico-chemical Systems
- Apr 22, 2004 Tom Fletcher – Statistics on Curved Spaces: Applications to Diffusion Tensor Imaging and Statistical Shape Analysis
- Jul 19, 2004 Craig Henriques – Tridomain Models of Cardiac Tissue: Modeling Propagation in 3D Cardiac Ultrastructure
2.2 Highlights

Figure 2.18: Eigenvalue skew colormapped on glyphs, fractional anisotropy on cortical surface.

Figure 2.19: Top row: Bone (magenta), marrow (gray), fat (black), muscle (brown), eyes (gray), air (green). 2nd row: CSF (magenta), WM (gray), GM (black), sinuses (brown).
2.2 Highlights

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Figure 2.20: Top: confocal data slices of virtual cell data; middle: k-means clustering segmentation results; bottom: watershed segmentation.

Figure 2.21: Comparison of different approaches for reconstruction of partial Fourier P-MRI data (total acceleration is 3.2). Top row: images reconstructed using direct Fourier inversion, standard approach (rms=0.165), and our method (rms=0.095), respectively. Bottom row: corresponding error images.
2.2 Highlights

Figure 2.22: Correction of brain data corrupted by real motion. a: initial, corrupted image. b: image after three iterations of the newly developed correction procedure. c: difference between (a) and (b).

Figure 2.23: Traditional volume rendering of a skull from CT data, without lighting or shading.

Figure 2.24: Volume rendering of CT skull with gradient-based shading. Using the gradient as a local normal, and applying a standard surface shading model, the shape of the skull becomes more clearly visible.
Figure 2.25: Scatter plot, or 2D histogram derived from a computed tomography scan of a human tooth. The clusters at the bottom represent the distinct material region of the dataset e.g., dentin, pulp, enamel, etc. and the arches between the clusters represent the material boundaries.

Figure 2.26: Transfer Function Editor. The user can add triangular and rectangular “widgets” overlayed on the 2D histogram from Figure 2.25. Each widget specifies the color and opacity for the voxels underneath it. Adding and manipulating widgets in the transfer function editor is completely interactive.

Figure 2.27: Volume rendering of a computed tomography scan of a human tooth produced using the transfer function specified in Figure 2.26. By assigning opacity and distinct colors to the portions of the arcs in the 2D histogram, we are able to uniquely identify all of the boundaries in the model.
Figure 2.28: Preliminary mock-up of the BioImage PowerApp. Users will be able to load and process medical scans through the interface options in the left panel. On the right panel the user will control the rendering options for the 3D visualization. In the middle panel the user can visualize both orthogonal views (slices) of the data, as well as a 3D volume rendering.
3 Description of Program Activities
3.1 Scientific Subprojects

3.1.1 BioPSE

BTA UNIT: T
TITLE: BioPSE
KEYWORDS: bioelectric fields, problem solving environments, software, scientific computing
AXIS I: 9
AXIS II: 42 52 92 - Software Development
INVEST1: Rob MacLeod
DEGREE1: Ph.D.
DEPT1: Bioengineering
NONHOST1:
INVEST2: Christopher R. Johnson
DEGREE2: Ph.D.
DEPT2: Computer Science
NONHOST2:
INVEST3: Chuck Hansen
DEGREE3: Ph.D.
DEPT3: Computer
NONHOST3:
INVEST4:
DEGREE4:
DEPT4:
NONHOST4:
% BRTP $: 40%
% BTA $ for AIDS: 0%

ABSTRACT: Over the past year we have continued to enhance the Biomedical Problem Solving Environment (BioPSE). The most recent major BioPSE projects have been driven by user requests for increased ease-of-use, more powerful modeling tools, direct data import/export mechanisms, increased stability, and support for the Macintosh OSX platform. We have made these new features available through two major releases of our software over this past year: BioPSE 1.20 and 1.22, released in October 2003 and July 2004, respectively.

In the Highlights section we detail our progress in the areas of usability, extensibility, and stability. Following we preview the work done in these areas.

3.1.1.1 Usability

With the 1.20 release of BioPSE/SCIRun (in October 2003), we introduced ”PowerApps”. A PowerApp is a customized user interface built atop a dataflow application network. With the 1.20 release of BioPSE, we released a PowerApps called BioFEM and BioTensor.

The other major usability hurdle that we have addressed with our most recent releases is the complexity of dataflow programming. In order to make SCIRun dataflow a more complete, easy to use language for application development and rapid prototyping, we have added comments, variable names, and functions / abstractions to the dataflow vocabulary. We have also increased dataflow usability through the addition of NetworkEditing options for clone, insert, replace, and undo.
3.1.1.2 Extensibility

BioPSE has been designed to be extensible: other software and other data formats should be able to integrate directly into our system, rather than forcing users to re-write everything natively in our framework. Over the past year we have continued to improve the extensibility of our system through the introduction of a plug-in import/export architecture for loading and storing data files in other formats, and by adding a socket library to allow other programs to communicate with and control a SCIRun session.

3.1.1.3 Stability

As the SCIRun user base has grown, and we have continued to add greater functionality and more supported platforms to the system, the need for robust software engineering has become ever-more important. To address this need, we have developed an automated regression testing system. The long-term advantages of this regression testing suite will be more frequent and more robust major releases: this will reduce the lag time between when new features are developed and when they are made available to the public, and will also greatly increase the quality and stability of the first version of major releases.
3.1.2 Applications

BTA UNIT: T
TITLE: Applications
KEYWORDS: AXIS I: 9 13 21
AXIS II: 39 42 52 63 77
INVEST1: Christopher R. Johnson
DEGREE1: Ph.D.
DEPT1: Computer Science
NONHOST1:
INVEST2: Rob MacLeod
DEGREE2: Ph.D.
DEPT2: Bioengineering
NONHOST2:
INVEST3:
DEGREE3:
DEPT3:
NONHOST3:
INVEST4:
DEGREE4:
DEPT4:
NONHOST4:
% BRTP $: 30%
% BTA $ for AIDS: 0%

ABSTRACT: A principal mandate of our NCRR Center is to provide examples and support to help users integrate BioPSE into their scientific research. To support this mission, we continue to interact closely with our Center collaborators and researchers within the SCI Institute and the CVRTI. These collaborations are a microcosm of our growing user base, and have provided excellent opportunities for us to evaluate and extend the breadth of our tools, as well as to develop user-support strategies and mechanisms. Through these collaborations, we have developed an array of applications, many of which are already available to the bioelectric field research community.

Over the past year, we have moved our software focus away from developing core functionality and towards developing interfaces and applications targeted at the needs of our collaborators. As a direct result of this effort, we currently have a number of successful ongoing collaborations. In the highlights section we offer a detailed report on the current status of those applications and describe some emerging developments. In this abstract we offer a brief synopsis of these applications and developments.

3.1.2.1 Inverse MEG Simulation

In the past year, we have investigated the affects of conductivity on magnetic field calculations and MEG source localization problems. The influence of head tissue conductivity on MEG was investigated by comparing the normal component of the magnetic field calculated at 61 detectors and the localization accuracy of realistic head finite element method (FEM) models using dipolar sources and containing altered scalp, skull, cerebrospinal fluid, gray, and white matter conductivities to the results obtained using a FEM realistic head model with the same dipolar sources but containing published baseline conductivity values.
In this work, we show the importance of accurate head tissue conductivities for MEG source localization in human brain, especially for deep dipole sources.

### 3.1.2.2 Source localization in the brain

We are very pleased to have Carsten Wolters recently from the Max Plank Institut in Leipzig, Germany, join the Center as a post doctoral fellow. Dr. Wolters brings considerable knowledge and experience in the area of Algorithm Development for Finite-Element-Method based Electroencephalography/Magnetoencephalography source reconstruction in the human brain. He has made substantial progress already on three separate projects, some of which originated in Germany, but all of which are now active projects within the Center: 1)Efficient Computation of Lead Field Bases and Influence Matrix; 2) Algebraic MultiGrid for Efficient Computation of EEG and MEG Lead Field Bases; and 3) STR: A new Spatio-Temporal Approach for Accurate and Efficient Current Density Reconstruction.

### 3.1.2.3 Mouse heart simulation

In the progress report for 2002-2003, we described a collaboration with Craig Henriquez at Duke University in which we generated a three-dimensional simulation of mouse heart activation and extracardiac potentials. We carried out this project by using SCIRun/BioPSE to create the geometric model and visualize the results of the simulation and Dr. Henriquez’s Cardiowave software to perform the simulations.

Based on these and other preliminary data, we successfully submitted a joint grant application to expand on this research by creating detailed models of cardiac tissue at the (microscopic) level of individual cells. The goals of this project are two-fold. The first is to advance computer simulation of the heart by providing users a unified problem-solving environment to simulate impulse propagation at both the microscopic and macroscopic scales. The second is to develop a complete model of mouse electrophysiology, to complement the experimental use of transgenic mice to study the molecular basis of cardiac disease.

The grant will fund a post doctoral fellow, Dr. Jeroen Stinstra, who has spent the past two years working with Dr. MacLeod on a separate project, the goals of which were to develop models of myocardium with which to compute tissue conductivity; results of these simulations led directly to the simulations of ischemia described below and in further detail in the highlights section.

### 3.1.2.4 Cardiac forward problems using the Boundary Element Method

In the current grant year, we developed a new version of the BioPSE modules for BEM forward modeling for electrocardiography and similar bioelectric problems with potential source boundary conditions and potential measurements on the outer surface. Two conference publications (one accepted for IEEE EMBS conference and the other submitted to the Asilomar Signals and Systems Conference) have come from this work, and a first journal paper is in preparation.

### 3.1.2.5 Simulating myocardial ischemia

Simulation of cardiac electric fields from a heart undergoing myocardial ischemia is the goal of a project that is housed at the CVRTI and makes use of NCRR resources. Ischemia results from inadequate blood supply to the heart and the resulting heterogeneities in tissue properties provide a source of current between healthy and ischemic parts of the heart. Detection and proper characterization of these currents from body surface ECG measurements is the basis of clinical diagnoses, however, there are considerable errors in this process that accurate simulation should improve. This project also receives support from two other grants; the Center provides computational resources and software expertise.
3.1.2.6 Bayesian Constraints in Electrocardiographic Inverse Problems

Due to attenuation and spatial smoothing that occurs in the conducting media, the bioelectric inverse problem of estimating sources from remote measurements is ill-posed and solution requires regularization. The most common approach to this problem is deterministic “regularization” (also known as Tikhonov regularization), where the solution is a trade-off between the estimate that best represents the data and fidelity to an a priori regularization constraint imposed on the solution. Recent studies have described Bayesian approaches to the bioelectric inverse problem. In addition to providing a more general way to formulate physiological constraints, these approaches also offer statistical performance evaluation tools that are not generally available with deterministic approaches. However, the Bayesian methods rely on the choice of prior probability density function (pdf); the better the prior model fits the epicardial potentials, the greater the reliability of the Bayesian estimates.

3.1.2.7 Tensor Visualization

We have continued to investigate a fundamental problem in visualization: the design of glyphs, or icons, for effectively displaying multi-variate data. Tensor data, such as arises from diffusion tensor magnetic resonance imaging (DT-MRI), is traditionally displayed with an ellipsoid. The ellipsoid glyph is defined by mapping a sphere geometry through the linear transform defined tensor. While the mathematical simplicity of the ellipsoid glyph is compelling, its perceptual characteristics are significantly lacking. The smooth surface of the ellipsoid makes it difficult to discern details about tensor shape and orientation, which are fundamental to understanding structure and trends in tensor fields.

In collaboration with Drs. Elliot McVeigh and Dan Ennis at NIH and Johns Hopkins University, the new glyph method has improved the visualization of both diffusion and strain tensors acquired via MRI in the canine myocardium. This collaborative work was presented at the most recent ISMRM conference.

The other application of superquadric glyphs has been in the visualization of anatomical covariance tensors calculated from human brain mapping. Drs. Art Toga and Paul Thompson, of the Laboratory of NeuroImaging (LONI), UCLA School of Medicine, are interested in understanding the extent and nature of anatomical variability on the cortical surface of the human brain. Using cortical models extracted from MRI scans of individuals in a population of interest (healthy volunteers, Alzheimer’s patients), deformable registration methods generate, for each point in the surface mesh, a covariance tensor representing the anatomic variation in the location of the underlying feature. Visualizing the features and trends in the covariance tensor field can enable insight into the biological dimensions of anatomic variability, with the compelling possibility of characterizing disease states in terms of deviations from normal anatomical patterns. The visualization tools also provide a direct way of evaluating the algorithms required to generate the data.

3.1.2.8 Segmentation

Segmentation of medical imaging data is typically the first step in creating geometric models and requires the identification of boundaries between regions with different tissue characteristics. We have continued to pursue our research on segmenting medical image data. A complete description of this project has been published as a University of Utah Technical Report.

The segmentation algorithm we designed is based on three principles: (i) a combination of scalar and multispectral Expectation-Maximization clustering stages provides fast, unsupervised statistical analysis, (ii) a modest amount of prior anatomical knowledge can help resolve statistical ambiguities, and (iii) a top-down modular approach that breaks the problem into smaller logical pieces leads to efficient solutions.
3.1.2.9 MRI image post processing

Another area of progress in the last year has been on developing advanced methods for acquisition, reconstruction, and post processing of MRI data. The primary target of our efforts was the development of advanced parallel MRI techniques. Parallel Magnetic Resonance Imaging (P-MRI) provides significant speedup of the data collection process by utilizing differences in sensitivities of multiple receivers. One application of P-MRI is to increase spatial and temporal resolution for the existing acquisition sequences. Existing P-MRI systems may provide an increase of 8-16 fold in spatial/temporal resolution for improved imaging of brain function, DT measurements, cardiovascular imaging, etc. Such improved data may prove very important for building realistic models. A drawback of P-MRI is the associated reduction in image quality, which limits the application of P-MRI for highly accelerated imaging.
3.1.3  map3d

BTA UNIT: T
TITLE: map3d
KEYWORDS: bioelectric fields, visualization, multi-platform
AXIS I: 9
AXIS II: 42 52 92 - Software Development
INVEST1: Rob MacLeod
DEGREE1: Ph.D.
DEPT1: Bioengineering
NONHOST1:
INVEST2: Christopher R. Johnson
DEGREE2: Ph.D.
DEPT2: Computer Science
NONHOST2:
INVEST3:
DEGREE3:
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INVEST4:
DEGREE4:
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NONHOST4:
% BRTP $: 15%
% BTA $ for AIDS: 0%

ABSTRACT: Once again, we have released two new versions of map3d in the past year with a number of additions in features and functions. The main advances in the past year have been in the area of user interface, made possible by a wholesale move to a new window management system. This system, know as “GTK”, is the basis for a number of public domain software packages, most notably the gimp toolkit, an image processing system. It allows for much more flexible creation of user interface elements and much more powerful control of all aspects of the window placement and management than our original system, which was based on the GL User Tools (GLUT).

With GTK available, we have added an array of new user interface elements, including one that manages, at a glance, all the files for geometry and data and the surfaces to which map3d attaches them. There are also menus for setting colors and sizes that appear in a number of contexts to allow the user to tailor the display.

We have also added the capability to read files in MATLAB format into map3d and thus greatly facilitated other users porting their results and data into the program. This addition required the creation of a MATLAB library that permits any C/C++ program to read and manage MATLAB data files. We have used this library both in map3d and in SCIRun/BioPSE.

Another important improvement is that map3d is now available for the Apple Mac/OSX platform so that we now have coverage of all the major systems including Linux, Windows, Mac OSX, and SGI/Irix.
3.1.4 Administration, Personnel, and Training

ABSTRACT:

3.1.4.1 Personnel Activity

The grant period of 2003-2004 was very stable for the center personnel, in general. We have continued to take advantage of the staff building and training done during the 2000-2003 period. There was no turnover in our software development team during the last year and we have continued to operate with the software engineering management consolidated under Mr. Dav de St. Germain. The stability in development staff, which is mirrored by the entire center, has in turn produced a more stable software package and more stable user-developer relationships. With substantial difficulty we have recruited a post-doctoral fellow for modeling research and inverse problem research. Specifically, we have hired Dr. Carsten Wolters from the University of Leipzig. Additionally, Dr. Tolga Tasdizen was also recruited as a post-doctoral fellow during the 2003-2004 grant period and performed research on automated segmentation algorithms. This work was directed by Dr. Weinstein, the center Technical Manager.

3.1.4.2 NCRR Seminars

As in previous years, the NCRR seminar series of 2003-2004 consisted of a variety of presentations from local, national, and international presenters. A listing of these presenters is available in the highlights section.
3.1.5 Volume Rendering

ABSTRACT: In May 2004, we were granted funding for a supplementary project to improve the Volume Rendering capabilities in SCIRun. Volume Rendering is a powerful visualization technique for investigating volumetric datasets such as MRI and CT. Though we are less than two months into this one year project, we have already generated preliminary results from this work, and are now beginning to provide alpha versions of the software to our collaborators for early adoption and feedback.

3.1.5.1 Lighting and Shading

Lighting and shading models can be incorporated into volume rendering to provide spatial cues similar to those found in surface rendering. A surface that is directly facing a light appears brighter than a surface illuminated by light from a glancing angle. This concept extends to volumetric objects through the computation of local “orientation” for each voxel in the volume. A voxel which is at the boundary between two materials with different gray scale values will have a local orientation ("gradient") that points in the direction of greatest change across the boundary.
3.1.5.2 Multi-dimensional Transfer Functions

The second major enhancement that we have added to the SCIRun volume rendering engine is support for multi-dimensional transfer functions. Transfer functions are used to assign color and opacity to each voxel of a volumetric dataset (such as MRI or CT). Typically this assignment is based solely on the local gray-scale value associated with each voxel. Such a transfer function can be described as “one-dimensional”. However, for medical datasets it is often useful to look at the two-dimensional histogram defined by both the local gray-scale value at each voxel, and the local “gradient magnitude” at each voxel. The gradient magnitude is a measure of how similar the voxel’s value is to the values of its immediate neighbors. If the gradient magnitude is low, the voxel is very similar to its neighbors. However, if the gradient magnitude is high, then the voxel has a value which is different from its neighbors, which is often indicative of a boundary. By plotting the two-dimensional histogram of a dataset we see a large clusters of points (representing many voxels from the volume). The clusters are connected by arcs, which correspond to the interfaces between those regions of the model. By inspecting the two-dimensional histogram and assigning colors and opacities to those voxels that make up the arcs (while leaving all other voxels completely transparent) the user is able to visualize the boundaries of the model. As with lighting and shading, this improved volume rendering technique can only be made interactive by specifying custom programs that implement this rendering technique and run directly on the GPU.

We have completed preliminary SCIRun implementations of both lighting/shading and multi-dimensional histograms for volume rendering. We are now making these enhancements available to a subset of our collaborators for alpha testing and refinement. We will be making a PowerApp version available as part of our next major release.

3.2 Resource Summary

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3.3 Geographical Data

1. Chris R. Johnson, Ph.D.  UT
2. Rob MacLeod, Ph.D.  UT
3. Charles Hansen, Ph.D.  UT
3.4 Sources of Investigator Support

Technology Research and Development

<table>
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Collaborative Research and Service

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3.5 Books, Papers, and Abstracts


4 Advisory Committee Report
External Advisory Board Report 2004 for the NCRR Center

Members of the external advisory board are:
- Prof Jim Bower, Cajal Neuroscience Center, Univ. of Texas, San Antonio
- Dr. Mark Ellisman, Departments of Neurosciences and Bioengineering, University of California
- Dr John George, Los Alamos National Laboratory
- Dr. Andrew Pullen, Bioengineering Institute, University of Auckland, NZ
- Dr. Erik Voth, Endocardial Solutions Inc.
- Mr Bill Lorensen, (chair) Electronic Systems Lab, GE Corporate R&D Center, NY
- Dr. John Wikswo, Vanderbuilt University, Nashville, TN

4.1 Report

The External Advisory Board (EAB) has not yet convened for this year because of scheduling difficulties. The meeting with the EAB will be on August 5 and we will forward their report immediately after the visit.
5 Administrative Data

5.1 Allocation of Resource Access

In March, 2000, the NCRR Center for Bioelectric Field Modeling, Simulation, and Visualization at the University of Utah released the two primary software packages: map3d (section 2.2.2) and BioPSE (section 2.2.1). Both software packages were released under academic use only licensing (the University of Utah Public License UUPL). In July, 2004 the latest version of BioPSE was released as open source software under the MIT open source license allowing the non-warrantied, unlimited use of the software without fee. The latest version of map3d was released as binary code with a similar free use license. Update of both software packages and the accompanying documentation occurs on a regular development cycle. In support of the code that is readily available at the www.sci.utah.edu/ncrr website, complete documentation, sample datasets, and sample program networks are also available for download. Additionally, a user’s mailing list is available for support of both map3d and BioPSE. The functionality of the BioPSE and map3d software packages is covered elsewhere in this report.

NCRR Center resources are also allocated toward the aim of accomplishing research in bioelectric field modeling, simulation, and visualization. The Applications subproject (section 2.2.3) and BioPSE subproject (section 2.2.1) and the publication list (section 3.5) in this report describe the results of this aspect of Center activity.

The allocation of resources used in development of the Center software is strongly guided by both our External Advisory Board and the ongoing dialogue between the Center Director, Technical Manager, and investigators and the Center collaborators. This group of world class scientists provides suggestions, requests, and valuable feedback specific to the use of Center software for their research and clinical projects.

5.2 Dissemination of Information

Dissemination of the actual technology developed by this center—software, datasets, software support, and software documentation—occurs primarily through the center website www.sci.utah.edu/ncrr. The website also hosts a carefully designed collection of easily navigable web pages that highlight the Center’s mission, research and publications, results, and news and events. On a limited basis, we have also made the Center software available for distribution on CD-ROM.

An important aspect of the Center’s activities is creating awareness of the presence of the Center and especially the resources we provide to the community. Our primary method of awareness generation is via scientific conferences, using both presentations and tutorials to describe the resource and provide instruction in its use. In addition to presenting and demonstrating the software packages with examples of relevant applications, we also distribute flyers describing the capabilities of the BioPSE and map3d packages. We have received substantial attention through our presentations and positive feedback regarding the flyers. Conferences at which we have presented our NCRR Center resources and results include:

- Computational Bioimaging and Visualization, International Conference on Computer Graphics and Imaging, Kauai, Hawaii, August 2004 (Keynote Speaker).
Another method we have used to develop awareness is by word of mouth through a large network of collaborators, both official NCRR center collaborators and external collaborators. The sources of these collaborations span the spectrum from academic to industrial.

5.3 Training

User education and training for BioPSE has taken place in three modes:

1. direct one-on-one interaction with our collaborators;
2. using online documentation combined with email-based user group interactions (scirun-users@cs.utah.edu and map3d-users@cs.utah.edu), and
3. workshop and laboratory training.
   - 3-day BioPSE/map3d Workshop, Salt Lake City, Utah, December 2003
   - Two BioPSE/map3d labs for graduate Bioengineering physiology class, Spring, 2004

We have allocated and will continue to allocate considerable resources to training in all formats as we feel this is an essential aspect of our mission. Software with the complexity and power of BioPSE and map3d simply require extensive documentation and education. We will limit the costly one-on-one interactions as much as possible to those who are developing either new applications or new capabilities for the software.
A Cited References


