7 Introduction

7.1 Overview

This proposal describes our plans for the third renewal of the Center for Integrated Biomedical Computing (CIBC), hosted by the Scientific Computing and Imaging (SCI) Institute at the University of Utah. The CIBC is a research resource that produces open-source software tools for biomedical image-based modeling, biomedical simulation and estimation, and the visualization of biomedical data. The software tools created by the Center are supported by a critical mass of research in scientific computing housed within the SCI Institute (see Section 4.1 for more details). These software tools, the research that underlies them, and the driving biological projects and collaborations that motivate their development are unified by a single vision: to develop the role of image-based modeling and analysis in biomedical science and clinical practice.

The overarching goal of this proposal is to advance the state of practice in biomedical computing and its applications both to biomedical science and to the translation of this science to clinical practice. We seek to achieve this goal by making advanced computation tools, tailored to the specific domains of image-based modeling, simulation, estimation, and visualization, accessible to scientists, engineers, and physicians by releasing readily usable, open-source software. We work closely with these users of our software, providing advice, technical support, workshops, and education to enhance their success with the tools we provide. Our long-term vision is to make scientific computing so useful and user friendly a tool, that it becomes a transparent and ubiquitous aspect of clinical and scientific practice.

Our commitment to empowering researchers through scientific computing is apparent in the number and breadth of the driving biological projects (DBPs) we wish to pursue and in the central role these projects play in all decisions within the Center. Many of our DBPs now have a very clinical focus. Consider, for instance, Dr. John Triedman, MD, a practicing pediatric cardiac electrophysiologist at the Children’s Hospital Boston. The shared goal of our project with Dr. Triedman is to create a validated methodology capable of generating unbiased predictions about cardiac defibrillation techniques using patient-specific finite element models. The successful development of such a methodology will have a profound impact on daily clinical practice for cardiologists and also influence commercial device design and optimization. To achieve this success, we must rely on a seamless integration of sophisticated tools for the segmentation of three-dimensional images (e.g., CT or MRI), for rapid generation of high-quality geometric models, and for the creation of accurate simulations, performed at interactive speeds on desktop computers. This proposal describes recent progress, current technology, and concrete plans for future developments that are crucial to this and other projects sharing our ambition to use computing to improve the care of patients.

In this next funding period, we propose to reach beyond our past exclusive focus on bioelectric fields and expand into new areas in which advanced computing can achieve breakthroughs. For example, the goal of the DBP with Dr. Jeff Weiss of the Department of Bioengineering at the University of Utah is to develop statistical shape models in concert with biomechanical simulations to characterize those aspects of hip shape and function that give rise to dysplasia. Dr. Weiss works closely with orthopedic surgeons who will one day use two- and three-dimensional images, databases of hip geometries and outcomes, and an extended set of software tools developed in part at the Center to carry out holistic analyses of hip shape and function in order to plan surgeries and predict treatment outcomes. Dr. Roy Bloebaum, Ph.D., from the Orthopedics Department at the VA Medical Center in Salt Lake City, will also use computational tools for improved treatment of bone disorders in patients. In this case, however, the goal is to facilitate and accelerate the implantation of metallic anchors in the residual limbs of young, healthy amputees to improve the functionality of prosthetic devices. Dr. Bloebaum and his team, who have done research suggesting that low-voltage electrical stimulation can enhance bone growth, will use Center software and low-voltage, electrical stimulation systems to simulate electric fields in the limbs of these patients. Center software will enable researchers to optimize the stimulation parameters and thus...
shorten the time required for the implants to stabilize from almost two years to several months, critical time in the rehabilitation phase of a victim of explosive ordinance in battle among other amputees.

The driving biological projects and collaborations driving this proposal vary by field and their application to medicine, and include genetics, cancer, neurology, cardiology, and orthopedics. They also span the full spectrum of biological science, from that engaged with studying basic physiology to clinical activities such as treatment planning and intervention. We now place a heavier emphasis on translation and clinical utility than in any previous period in the Center's history.

The origins of our success in developing widely used software tools lie in a set of strategies for algorithm research and software development. One strategy has been the production of software tools with low barriers to entry. This entails the release of documented, tested, complete applications that do not entail learning new programming languages or complex, architecture-specific build environments. This strategy is reflected in the complete merging of SCIRun and BioPSE, problem-solving environments that were first released as separate pieces of source code in the initial phase of the Center. Now, the Center has taken over all SCIRun development and support, has merged into SCIRun the full functionality of BioPSE, and released the result as a binary application for the dominant operating systems (Windows and Mac/OSX) and either source code or binary RPMs for Linux. We also continue to follow an initiative proposed in the previous renewal to create a suite of lightweight, stand-alone applications, also single binary-file releases, directed at specific tasks of great interest across a wide set of disciplines. The result is a set of programs, ImageVis3D and Seg3D, which have joined map3d as applications with large and growing user bases.

Implementing this strategy with the limited resources of a P41 Center has required the development of algorithms that are robust, general purpose, and designed to operate in a wide variety of scenarios while remaining easily customized for particular fields or settings. The same need for efficiency drives another important aspect of our strategy, which is the development of an integrated software infrastructure that allows the same basic algorithms and associated software modules to be used either together as part of a user-defined workflow (SCIRun) or separately and in combination with software from other sources (Seg3D, ImageVis3D, and map3d). We have yet to achieve a completely interchangeable architecture for this versatile integration; this is a major goal of the next funding period.

An overarching goal in the process of algorithm and software creation is achieving computational acceleration in order to expand the space of solvable biomedical problems. This strategy has been a major focus of the SCI Institute since its inception in 1994 and of this NCRR P41 Center since its beginning in 1999. Over the intervening years since the founding of these two efforts, the technology has changed rapidly, and we have embraced this change. In the first phases of the Center, our focus was on large, multiprocessor, shared memory computers; during the second phase, we began to include multiprocessor, distributed memory, computer clusters. In our most recent research, we have continued to respond to developing technology by moving to multiple, relatively small shared memory clusters. By doing so, we have achieved significant performance at dramatically reduced costs. Now, we are shifting our attention to streaming architectures, with an eye toward commodity processing available in the form of inexpensive graphics processing units (GPUs). This evolving strategy is representative of the agility that has solidified the SCI Institute's position as a technology leader in high-performance computing.

Another important strategy for software development is to make our tools relevant for the broader community by building and testing them in close collaboration with specific, high-profile biomedical groups. These practicing scientists and physicians educate us to achieve an appropriate level of generality to impact the largest group possible at the same time that our close collaborations with them help us to define and solve specific, relevant biomedical problems. These collaborators also inform us about other tools that investigators are using, this helping us to ensure that our software fills a clear need in the community and remains at (or ahead of) the state of the art. And, since the proof of the effectiveness of the Center is in the success of our users, this collaboration strategy and the high profile of our collaborators has also proven to be a mechanism for dissemination of tools.

An important, complementary strategy to ensure wide usage is to freely release all tools and data as open source. In this way, users need not be concerned with licensing restrictions and they can, if need be, modify or verify the implementations of specific components. This open science approach to dissemination also allows the community at large to reproduce the results of the Center and its collaborators.

These software strategies dovetail with a set of scientific goals and strategies that are important to the success of the Center. One goal is to enable more widespread use of personalized or individualized medicine and bioscience by developing and providing access to the necessary tools. Our hypothesis is that sufficient access to imaging capabilities and other patient-specific functional and anatomical measurements, combined
with computational tools for analysis and simulation, will allow clinicians to make better treatment decisions leading to lower costs and better patient outcomes. The same assumptions apply to furthering fundamental discovery of physiological and pathophysiological processes.

A second goal is to take on technical problems and challenges that are truly barriers to biomedical research. This goal is achieved by selecting collaborators and DBP partners who are at the leading edge of their fields and making them early adopters of the most important, influential technology developments in computing, many of which are being discovered and shaped within the SCI Institute. We also pursue close interactions with these collaborators in order to ensure that we are responsive to their ideas and computational needs.

7.2 History of the Current Center

The NIH Center for Bioelectric Field Modeling, Simulation, and Visualization officially began on September 15, 1999 (see the time line shown in Figure 7.1). During the first five years, the Center focused on creating an extensible, scalable, scientific problem-solving environment (PSE) and on developing corresponding research to solve real-world problems relating to bioelectric fields. To accomplish this goal, we conducted research and development in advanced modeling, simulation, and visualization methods for solving bioelectric field problems; we also created BioPSE, an extension to the existing SCIRun, which is a modular, extensible, integrated software problem-solving environment for bioelectric field problems1. The SCIRun software supported interaction among the modeling, computation, and visualization phases of bioelectric field simulation with BioPSE providing specific extensions for the Center.

The structure of SCIRun resembles the dataflow structure originally developed in a variety of visualization applications (e.g., AVS, Khoros, and Data Explorer), and at the time if its development represented a new approach to addressing the much broader range of computation needs in biomedical research. We imagined SCIRun as a “computational workbench,” in which a user selects tools (software modules) from a set of drawers (categories) and connects them to create a workflow (a network) that performs all the necessary steps. Each tool has different settings by which a researcher may adjust it to the specific task or object at hand. Such flexibility means that a researcher may even keep multiple copies of a particular tool, each with a different purpose and setting. Just as a skilled craftsman may design and fabricate new tools when the complexity of the task so requires, a skilled developer of SCIRun workflows may develop new software modules (or consolidate existing ones into “meta-modules”) and thus add as desired to the capabilities of the system. Ultimately, we felt that good tools are most properly modified and refined by the people who use and need them, rather than by the people who designed them. Thus, biomedical scientists should be able to adopt SCIRun and adapt it themselves, to suit their own needs, without relying on specialized computer programmers.

Thousands of users have downloaded the SCIRun and BioPSE software and used it in their bioelectric field research. Their topics of investigation include cardiac electro-mechanical simulation, ECG and EEG forward and inverse calculations, modeling of deep brain stimulation, electromyography calculation, and determination

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1BioPSE, pronounced “Bio”-“P”-“S”-“E”, derives its name from Biomedical Problem Solving Environment
of the electrical conductivity of anisotropic heart tissue. Users have also employed SCIRun for the visualization of breast tumor brachytherapy, computer aided surgery, teaching, and a number of non-biomedical applications.

Creating and disseminating this integrated, efficient, modular, extensible problem-solving environment for bioelectric field problems was a tremendous challenge, but it is one that we successfully met by 2003 (see the timeline). After successfully releasing SCIRun and BioPSE, we began to learn from researchers how they were using these tools and what additional capabilities they required. Feedback from users indicated that the dataflow system of modules connected to each other by data pipes was too complicated for some biomedical researchers, who were used to typical desktop application programs with simple pull-down-menu interfaces. At our 2003 External Advisory Board (EAB) meeting, we proposed new approaches to reduce the complexity of the SCIRun interface in order to expand our user base and impact. By 2004 we had created easy-to-use, application-specific software programs based upon SCIRun. We called these programs “PowerApps”.

PowerApps looked like dedicated applications but were essentially wrappers around pieces of an underlying dataflow network, as illustrated in Figure 7.2. The user saw only the parameters relevant to the task and in a context that could be as domain specific as necessary. Users reported that their productivity improved because of the lack of distractions and the natural mapping of workflow to user interface. However, the workflow was driven by the underlying dataflow, a process architecture that provides many advantages but also presents some challenges. In order to overcome these challenges, in 2005 the Center redesigned the package, moving away from a strict link to dataflow and developing in its place truly independent, standalone applications. As part of this move to more independent applications, the Center also re-engineered SCIRun to separate the underlying filters or modules from the dataflow interface. In this way the basic algorithms and data structures in SCIRun remain accessible in libraries that can then form the basis of new applications, independent from data flow.

During this time, the Center has also integrated third-party packages into its tools. One example is the Insight Toolkit (ITK), a public-domain library of image processing tools created by a consortium and funded by the National Library of Medicine and NIH. Prof. Whitaker is a founding member of the Insight Consortium and active in ITK development through his participation in the NAMIC and in the National Center for Biomedical Computing (PI—R. Kikinis, Harvard University). ITK file I/O, data structures, and processing filters are used...
extensively in this latest generation of applications, and the interactions between these software centers are mutually beneficial. For instance the NRRD file format (nearly raw raster data) and associated command line tools for manipulating multidimensional images (TEEM), which were developed within the CIBC, are now an integral part of ITK and of the NAMIC Toolkit.

An example of such an application, with the Center since the beginning, is map3d, a tool for analysis and visualization of bioelectric fields. map3d was built as a stand-alone, end-user application for engineers, physiologists, and clinicians and maintains a steady rate of downloads and a dedicated user group who regularly publish images created using map3d. More recent examples include ImageVis3D (Figure 7.3), a program that provides interactive volume visualization of very large datasets, up to hundreds of gigabytes—far too big to fit into dynamic memory. Like map3d and all the other applications we have developed, ImageVis3D makes heavy use of standards of user interface, file formats, and modular software developed within the SCI Institute, in this case, a volume-rendering engine called TUVOK.

Another example of a highly successful application from the Center is Seg3D, which performs user-guided image processing and segmentation (See Figure 7.4). Seg3D is also based on the Insight Toolkit and presents through a simple user interface the appropriate filters and segmentation algorithms with some settings pre-selected based on our experience with data sets from our collaborators. By providing interactive access to the relevant parameters with experience-based guidelines and constraints imposed, Seg3D seeks to make available to biomedical users a powerful set of capabilities in a form that is inviting and easy yet efficient to use.

Yet another example of recent progress in focused application development is BioMesh3D, a set of interactive and off-line tools for constructing triangle and tetrahedral meshes from three-dimensional images for subsequent finite-element simulations. BioMesh3D combines in-house research developments with SCIRun modules and third-party packages in a coherent, reusable, tunable pipeline. Another application released within the past month is called ShapeWorks, a pipeline of off-line and interactive tools for statistical shape analysis (see Figure 7.5). While each tool is important in its own right, the tools are even more powerful as a suite sharing a common look and feel, a common research vision, and a common set of file formats. Such integrated tools, which are flexible and easy to use, are essential to our vision of scientific computing as essential to developing personalized medicine and leading edge science.
In large part, the software strategies for the Center have developed in response to the growing breadth of application domains and technology foci. During the first phase of the Center, when we focused primarily on bioelectric field simulation and visualization, we learned that the generation of geometric models was a significant obstacle to the development of patient-specific simulations and analysis. Until this obstacle could be overcome, bioelectric field simulation would remain of peripheral interest, especially for the clinician. This need then motivated in the second phase of the grant new developments directed toward better tools for image preprocessing and geometric modeling generation. The results included many additions to SCIRun that allow, for example, flexible creation of realistic models of cardiac myocytes and tissue. Combining these technical advances with our new strategy for software design then led to the creation of Seg3D and BioMesh3D, applications that form essential components of the modeling pipeline described in more detail in Section 11.

Creating new software tools also allowed us to broaden the impact domains of those tools. From simulating bioelectric fields generated by the heart, we expanded into computing the fields generated by defibrillators, then into deep brain stimulation, and then into applying electric fields to enhance bone growth. Examining the shapes that emerged from segmentation and mesh generation allowed us to assist another collaborator to quantify the effects of shape on joint function and clinical management of patients with hip joint irregularities. New imaging and visualization tools like Seg3D and ImageVis3D have allowed us to explore the domain of image-based phenotyping and, through our new collaborators, we have begun to work on applications for use in cancer research and treatment and in research in developmental biology. There are many more examples of the ways in which a push from science may create a pull from the technology, and vice-versa, leading to a highly productive cycle of growth and impact.

As committed as we are to the values of responsiveness, and collaboration, we also highly value the important original research that has come out of the Center. We have made significant advances in the area of bioelectric field simulation, modeling, and visualization. We have created new approaches to the solution of forward and inverse problems in both cardiology and neurology and have used SCIRun both to carry out this research and as a repository for its products. We have developed several new methods for the visualization of three-dimensional data sets, some of which change rapidly in time, and we have translated award-winning, cutting-edge visualization research into working capabilities in SCIRun, map3d, Seg3D, and ImageVis3D. We have published new techniques in geometric model generation and helped collaborators to generate specific models of the heads, hearts, and thoraxes of different species. And because we believe that the ability of researchers to directly compare their new ideas, techniques, and data with those of other researchers is crucial to scientific progress, we have gathered high-quality data sets and made them freely available to the scientific community. To this end, we have released a set of images and associated geometric models, from which we have computed simulations and prepared visualizations. In other words, we have made every aspect of our research—
images, geometric models, simulation results, and visualization results—available to other researchers for validation and comparison of their own methods. We believe providing such resources will accelerate progress in biomedical computing and biomedical science in general.

Perhaps the most important measure of the Center's success is the number of scientists using the resources we provide. Since our last renewal in 2005, there have been over 11,000 downloads of SCIRun, more than 8000 downloads of BioPSE (all from outside the Center and our affiliate institutions), over 7000 downloads of BioImage and Seg3D, and almost 4000 downloads of the CIBC data sets. Since December 2008, there have already been more than 2000 downloads of ImageVis3D. Since the year 2000, over 200 papers published by scientists outside the Center have included at least one reference to CIBC software or the underlying SCIRun infrastructure. During the same time, members of the Center have been listed among the authors of over 175 publications related to biomedical computing in a wide range of technical and biomedical journals and conference proceedings.

### 7.3 Goals for the Center

Each component of the Center has developed an extensive set of specific aims covering both research and development. These aims will provide the framework for the next five years of our growth. Summarized very generally, the goals for the Center as a whole are as follows:

1. To create the appropriate infrastructure of computer software, computer hardware, and technical expertise to provide our driving biological problems, collaborators, and the field at large with state-of-the-art computational tools that will result in demonstrable improvements in clinical and biomedical science.

2. To develop a modular pipeline, with interchangeable software components, for generating high-quality, subject-specific, geometric and statistical models from three-dimensional images for use in simulation and data analysis.

3. To extend the Center’s simulation capabilities to include endogenous bioelectric sources, electric stimulation, and the electrophysiological behavior of cardiac and neural membranes, cells, tissues, and organs.

4. To increase the breadth and sophistication of visualization technologies available to biomedical researchers by both leveraging existing expertise within the SCI Institute to develop and then implement advanced, high-performance algorithms and software for visualizing large, spatially distributed and/or time varying data sets.

5. To further expand our service role through workshops, tutorials, presentations, and booths at international conferences, with the goal of bringing biomedical scientists together with computational specialists to develop sophisticated solutions to critical questions in biomedicine.

### 7.4 Frequently asked questions

Past experience has suggested a set of questions that often arise with regard to the Center, our technology, and our organization. We hope that answering them here will facilitate review of the proposal.

1. **What is the relationship between BioPSE and SCIRun?**
   
   *In the past, BioPSE was a special set of modules that integrated into the SCIRun problems solving environment; however, now all the functionality of BioPSE has been absorbed and enhanced in SCIRun and the Center is the sole developer and distributor of SCIRun.*

2. **What is the relationship between the Center and other NCRR Resources?**
   
   *Our Center has numerous ongoing collaborations with other NCRR Resources, including:*
   
   - National Center for Microscopy and Imaging Research, University of California, San Diego: Collaboration with Center PI Mark Ellisman and Steve Peltier.
   
   - National Resource for Cell Analysis and Modeling, University of Connecticut Health Center: Collaboration with Center PI Les Loew*
• National Biomedical Computation Resource, University of California, San Diego: Collaboration with Center PI Peter Arzberger.
• Laboratory of Neuro Imaging Resource, UCLA School of Medicine: Collaboration with Center PI Art Toga and researcher Paul Thompson.
• Neuroimaging Analysis Center, Brigham and Women’s Hospital: Collaboration with numerous investigators including Ron Kikinis, Carl Fredrick Westin, and Simon Warfield.

3. What is the relationship of the Center to the new centers in the National Centers for Biomedical Computing?

The SCI Institute is a formal collaborator on two of the four recently awarded NIH National Centers for Biomedical Computing. Dr. Chris Johnson is part of a technological research and development project with the Center for Computational Anatomy (UCLA, Dr. Art Toga), and Dr. Ross Whitaker is one of the imaging researchers in the National Alliance for Medical Image Computing (Harvard Medical School, Dr. Ron Kikinis). NCBC projects emphasize the development and integration of software (e.g. SCIRun, LONI pipeline, and ITK). The proposed work compliments the goals of these other centers, and this project will leverage our work with these NCBCs to deliver a better level of technological support to our collaborators and the community at large.
7.5  Selected Quotes from the submitted letters of support

7.5.1 Resource – general

...For example, your groundbreaking computer software SCIRun, which uses sophisticated mathematics to convert two-dimensional image data into detailed three-dimensional pictures, that can be rotated and viewed from different angles, has essentially opened new research fields in anatomy and surgery as well as genomics.

With your colleague and Nobel Laureate in Medicine and Physiology Mario R. Capecchi ...you used SCIRun to generate high-resolution virtual histology for phenotypic assessment of mouse embryos. This bold new effort to understand the genomics of brain development by disrupting every gene in the mouse genome, and correlating the genomic information with the SCIRun’s 3D assessments of brain phenotype is certain to influence the way researchers bring genomics to bear on medicine!

- Orly Alter, Assistant Professor, Department of Biomedical, Engineering, and Fellow, Institute for Cellular and Molecular Biology, Cockrell School of Engineering, The University of Texas at Austin

...In particular, ImageVis3D and Seg3D have great promise as key tools for important steps in the workflow of our patient-specific cardiac modeling research. Indeed, three new R01 grants recently awarded by NHLBI all involving patient-specific modeling will benefit from the continued development and improvement of these tools.

...In addition, we will continue to interact with the CIBC through the activities of our own P41, the National Biomedical Computation Resource (P41 RR08605), which has very effective synergies with the technology research and development efforts at your center.

- Andrew D. McCulloch, Professor and Vice Chair, Department of Bioengineering, The Whitaker Institute for Biomedical Engineering, Cardiac Mechanics Research Group, University of California, San Diego

As you know, we have our own NCRR Resource grant entitled “National Resource for Cell Analysis and Modeling”. ...We have great needs for visualizing multi-variable dynamic 3D simulations and plan to use the software components that you are developing for this purpose. We also will use your tools for 3D image segmentation. We have already evaluated Seg3D for this purpose and it contains exactly the technology our users need.

- Leslie M. Loew, Boehringer Ingelheim Chair in Cell Sciences, Professor of Cell Biology, Professor of Computer Science and Engineering, Director Berlin Center for Cell Analysis and Modeling, University of Connecticut Health Center

I am pleased to support your proposal to renew your NIH NCRR. I feel that your continued efforts to develop robust biomedical computing and visualization software will continue to complement our NIH NCBC, “The National Alliance for Medical Imaging Computing (NAMIC)”. Your ability to integrate software programs and components will help us leverage the software we are creating.

- Ron Kikinis, Director Surgical Planning Laboratory Director NIH NCBC National Alliance for Medical Imaging Computing Brigham and Women’s Hospital, Harvard Medical School

...[W]e are impressed with your state-of-the-art open-source software and its flexibility to meet our needs and those of other researchers in biomedical computing. Our students found the software flexible and particularly well-suited to our research environment...
Charles A. DiMarzio, Associate Professor, Electrical and Computer Engineering, Northeastern University

The combination of open source software at SCI and the strong support resources at the SCI Institute have made our work with SCIRun extremely productive. The sophistication of the SCI software provides us with a realistic demonstration of the benefits of checkpointing graphics applications.

Gene Cooperman, High Performance Computing Laboratory, College of Computer and Information Science, Northeastern University

Recent years have seen a phenomenal growth in this field and computation tools are seen as a key to its success. Your role in this activity is likely to continue to play an important part in forthcoming years.

Simon Arridge, Professor of Image Processing, Department of Computer Science, University College London

The SCIRun, Seg3D and ImageVis3D software tools from the CIBC are likely to provide a powerful tool for visualization, segmentation and classification of tissue morphology for pathology-type analyses. Thus, such tools may synergistically complement confocal microscopy (as well as other imaging technologies) and pathology to accelerate translation into the clinic for routine use on patients.

Milind Rajadhyaksha, Ph.D., Associate Member in Dermatology, PI of Optical Imaging Laboratory, Memorial Sloan Kettering Cancer Center, New York, NY

A major part of our group's ability to advance the fields of orthopaedics and computational biomechanics requires that we quickly, but accurately, discretize joint geometries from medical image data. The SCI Institute has been a leader in visualization and image processing and I would expect that your group will continue to develop efficient, user-friendly tools to fulfill this objective.

Andrew Anderson, Ph.D., Research Assistant Professor, Department of Orthopaedics, University of Utah

I have no doubt that our collaboration with you to apply the most modern tools for data analysis to ongoing clinical research projects within the Utah CTSA will help transform our clinical and translational science projects.

Don McClain, M.D. Ph.D., Director, NIH CTSA Center for Clinical and Translational Science, Professor of Medicine and of Biochemistry, University of Utah

...At NLM, we have relied on the SCI Institute to be full participants in NLM-sponsored programs in open-source software development...

...In my annual participation in the NA-MIC allhands meetings, I observe that Utah is one of the major contributors to this effort...

Terry S. Yoo, Ph.D., HPCC Project Officer, NLM, National Institutes of Health

I enthusiastically support the renewal of your NCRR Center and look forward to continuing our collaboration with you on software for biomedical computing and visualization. I feel that your proposed software efforts complement our NIH NCBC by allowing us to link our LONI pipeline to your SCIRun software environment such that we can take advantage of a large number of the modeling and simulation programs.
linking computational approaches to experimental approaches is essential for addressing the complexity of systems biology, and I am excited by the techniques and software tools your NIH Center has created in visualization and image analysis.

- Leroy Hood, M.D. Ph.D., President Institute for Systems Biology

Thus, in total, we expect to provide the SCI Institute with well in excess of $5 million in matching support over the five-year period of this award to ensure that the project is a major success. We are willing to make a commitment of this magnitude because of the caliber of the faculty involved and because of the centrality of this proposed effort to the strategic plan of the University.

- David W. Pershing, Ph.D., Chief Academic Officer, Sr. Vice President for Academic Affairs, University of Utah

Therefore, your new 3D meshing algorithms whose output is used as input in MEG/EEG forward modeling techniques are especially valuable in our research...

- Matti Hamalainen, Ph.D., Director, Magnetoencephalography Core, Athinoula A. Martinos Center For Biomedical Imaging, Harvard Medical School

7.5.2 Direct impact

The multi-disciplinary collaborations we established have fundamentally changed the scope of my laboratory’s research, making imaging an essential part of our studies of mouse models of disease. As you can see from the list of 9 publications listed at the end of this letter, our direct collaborations or the crnc software tools made available to us have made it possible to qualitatively and quantitatively convey the results of our studies in ways not otherwise possible.

- Charles Keller, M.D., Assistant Professor, Department of Cellular & Structural Biology Investigator, Developmental Cancer Genetics and Therapeutics Leader, Pediatric Preclinical Testing Initiative Greehey Children’s Cancer Research Institute University of Texas Health Science Center, San Antonio

Our lab has begun to use the software produced by the SCI Institute (SCIRun, Seg3D, ImageVis3d) and has found it extremely useful in both the visualization and quantification of 3D MIMS data. This software has allowed us to examine things such as quantified protein turnover or nutrient localization at a sub-cellular scale. This has and should continue to open up important avenues of research.

- Claude Lechene, M.D., Director National Resource for Imaging Mass Spectrometry, Brigham and Women's Hospital, Harvard Medical School, Massachusetts Institute of Technology

Your Center’s tools are a key component in our image processing, visualization, and analysis arsenal: we literally use SCIRun and Seg3D on a daily basis. We have experimented with a wide range of alternative software packages, including GE’s MicroView, Mercury’s Amira, and MathWorks’ MATLAB: we always come back to your Center's software because of its breadth of functionality, its modular extensibility, and its ease-of-use.

- Michael A. Beeuwsaert, President & CEO, Numira Biosciences
...In particular I would like to mention the program map3d which we have used extensively in our work. We have recently had two editorialized papers published in Heart Rhythm, the premier subspecialty journal in our field (2007 and 2008). One of these was a paper of the year at the International Heart Rhythm meeting in 2008. Both used map3d extensively in the figures. Without map3d, these works could not have been communicated well and probably would not have been accepted in the prestigious journal they were published in.

- Edward J. Ciaccio, Ph.D., Associate Research Scientist, Dept. of Pharmacology and Biomedical Engineering, Columbia University

As you know from our ongoing collaboration, the research work at EGI and the UO NeuroInformatics Center has benefited greatly from the Utah NCRR. The maturity of your Center has led to highly stable software resources, and also a technical staff that can provide valuable consultation to scientific researchers in a variety of disciplines.

- Don M. Tucker, Ph.D., Professor of Psychology, Associate Director NeuroInformatics Center, University of Oregon, CEO, Chief Scientist, Electrical Geodesics, Inc.

In particular, I am very interested in using any extensions of your particle based shape correspondence software package, as I am currently applying these to my studies of brain structure shape differences in a variety of neurodevelopmental diseases, such as Autism, Fragile X and Schizophrenia. Your software package is furthermore a crucial, central module in our own analysis pipeline for studying cortical thickness in the pediatric neurodevelopment as it allows us to compute cortical correspondence in an efficient, group wise fashion that provides enhanced anatomical correctness and stability. Your particle based correspondence software tools truly are indispensable to our research projects.

- Martin Styner, Ph.D., Assistant Professor Departments of Psychiatry and Computer Science, The University of North Carolina at Chapel Hill

The time at SCI and CIBC allowed me to explore this new area of my research and over the past two years has resulted in seven conference presentations (all with undergraduate authors) and two journal articles in preparation (also with undergraduate authors).

- Joseph Tranquillo, Ph.D., Assistant Professor of Biomedical and Electrical Engineering, Bucknell University

The computational resources developed by your Center are an important aid to CCI’s research enterprise. In particular, I look forward to using CIBC software and tools as CCI conducts novel integrative in silico experiments to study brain tumors at our recently awarded caBIG(R) In Silico Brain Tumor Research Center.

- Joel Saltz, MD, Ph.D., Director Center for Comprehensive Informatics, Professor Departments of Pathology, Biostatistics and Bioinformatics, Mathematics and Computer Science, Chief Medical Information Officer, Emory Healthcare, Georgia Research Alliance Eminent Scholar, Emory University

As a recent user of the software produced by your NIH NCRR Center, I want to extend my enthusiastic support for the renewal of your Center... The close collaboration between your NIH NCRR Center staff and the Oak Ridge National Laboratory visualization staff was very important to the success of [the] DARPA [Virtual Soldier] Project.

...The flexibility and utility of the SCI Institute’s SCIRun software proved to be of enormous benefit to our previous project.
We have a critical need for improved methods of epileptogenic brain localization in epilepsy surgery, and are convinced that the computational tools that will be developed in our collaboration will help us achieve this goal. Being able to accurately, and non-invasively, localize epileptogenic brain in patients with medically intractable epilepsy may lead to improved surgical treatments. Additionally, this effort is a critical component of Mayo Clinic’s ongoing epilepsy research program.

My laboratory is forever indebted to the software produced by your NIH NCRR Center. We use the image processing, visualization, and simulation tools on a daily basis in our research on Deep Brain Stimulations (DBS). ...[We have many NIH grants that] are directly aided by the developments of your center... In addition, the training and support your center provides is of the utmost importance for introducing new students and fellows to your powerful technology.

As a current user of the software produced by your NIH NCRR Center for Integrative Biomedical Computing, I want to extend my strong support for the renewal of your Center. The tools that have emerged from our interactions with your center have been catalytic in our recent work in neural connectomics. We would not have gotten where we are without you.

As daily users of the Scientific Computing and Imagining (SCI) Institute’s open source software packages, my lab and I rely heavily on these novel tools for visualization, image processing and simulation research. The software platforms developed by your team provides invaluable support for our research which is focused on improving prosthetic technology for wounded servicemen and women returning from overseas combat.

...Our research drastically depends on the software tools created at the SCI institute. By utilizing the Seg3D, SCIRun and ImageVis3d platforms, we have been able to accurately reconstruct amputee residual limbs and use finite element analysis to provide proof of concept for novel device development.

As you know, we recently published collaborative work with David Weinstein and other members of your SCI Institute, creating cutting-edge visualizations of brain imaging data. These visualizations help us significantly in our research. We deal with complex brain imaging data, typically with millions of variables describing the anatomic variability of the human brain.

- Richard C. Ward, Senior R&D Staff Member, Modeling and Simulation Group, Computational Sciences and Engineering Division, Oak Ridge National Laboratory

- Gregory A. Worrell, M.D., Ph.D., Associate Professor of Neurology, Division of Epilepsy and Section of Electroencephalography, Mayo Clinic

- Cameron C. McIntyre, Ph.D., Associate Professor, Cleveland Clinic Lerner College of Medicine Case Western Reserve University

- Robert E. Marc, Ph.D., Mary H. Boesche Professor of Ophthalmology, Director of Research, John A. Moran Eye Center, Unviersity of Utah

- Paul Thompson, Ph.D., Professor of Neurology, UCLA School of Medicine, Laboratory of Neuro Imaging Department of Neurology, UCLA
Your software platform SCIRun was a central component of our successful DARPA Virtual Soldier Project demonstration as well as our NIH Visible Human Project activities. I can tell you that your willingness to integrate other “standard” NIH computing platforms such as the NLM Imaging Tool Kit (ITK) and the University of Michigan’s Edgewarp into your system is giving the community unprecedented capability to process, visualize and understand complex biomedical image datasets...

...The excitement that your work is creating at the University of Michigan, one of the nation’s premier sites for NIH research activities, is real and growing.

...My team loves working with your team at Utah. You and your Center “make things happen”. It is without a doubt that your Center has become a national treasure, and it is well deserving of the “National Center” status.

...As the designated leader of Academic Informatics at the University of Michigan Medical School, I want to say that we look up to you and your Center as an example of professionalism and cutting-edge science and technology.

- Brian D. Athey, Ph.D., Professor, Biomedical Informatics (Medical School)
  Chair Designate, University of Michigan Computational Medicine and Bioinformatics (CM&B) Department Director, Academic Informatics Medical School Co-Chair, National CTSA Operations Committee Principal Investigator, National Center for Integrative Biomedical Informatics (NCIBI)

I am especially excited about our proposed collaborative project to enable improved pediatric epilepsy surgical planning. Being able to utilize [the SCI Institute’s] sophisticated image analysis, bioelectromagnetic field simulation and visualization software tools will enable us to dramatically improve our insight into the abnormal electrical activity in the pediatric epilepsy patients that we see.

- Simon K. Warfield, Ph.D., Associate Professor of Radiology, Director of Radiology Research Harvard Medical School,

We have found that using your software to examine basal ganglia shape in our images of toddlers with autism is proving to be quite interesting and of potential significance.

- Joseph Piven, M.D., Professor of Psychiatry, Pediatrics and Psychology, University of North Carolina at Chapel Hill

Being able to non-invasively and effectively reconstruct estimated potential distributions on the cardiac surfaces (through SCIRun, Seg3d, and Map3d) and prospectively also throughout the entire heart muscle during rhythm disturbances, will help significantly advance my research goals.

- Petr Stovicek, MD, Ph.D., Cardiac Arrhythmia Consultant, Department of Cardiology and Angiology, Charles University, Prague, Czech Republic

...Chris Johnson, Director of the SCI Institute was chosen as the Chair of the Executive Committee for the NIH/NSF Visualization Research Challenges Workshops. He led an international team of experts from across industry, government, and academics and headed the executive committee that drafted the final report in 2006. We relied on his leadership and his judgment to help plan for the future of this vital area...

- Terry S. Yoo, Ph.D., HPCC Project Officer, NLM, National Institutes of Health

Thus, the interdisciplinary partnership you have established at Utah between world-class computer scientists, biomedical computing experts, and software engineers, and your focus on delivering research results via high-quality open source software, have already had a strong positive impact on biomedical research at the University of Chicago.
- Dr. Ian Foster, Director, Computation Institute, The University of Chicago & Argonne National Laboratory

All of these software tools will support and enhance the research underway at the Drexel Geometric Biomedical Computing Group in the areas of breast cancer diagnosis via histology scan examination, breast tumor reconstruction and bone scan analysis. Your tools are an invaluable resource that will significantly advance my work.

- Dr. David E. Breen, Drexel University

I especially appreciate your leadership in helping define a vision for large-scale biomedical computing and visualization for the DOE and the next generation of computational biologists.

- Rick L. Stevens, Associate Laboratory Director for Computing, Environment and Life Sciences Argonne National Laboratory Professor, Department of Computer Science, University of Chicago

The tools developed by the center were instrumental throughout my career in biomedical research. The map3d software, which is still actively maintained and supported by the NCRR center, was an essential tool in my investigation.

These progresses provide direct input to improve current implantable cardioverter defibrillator (ICD), new direction that may have profound impact on patient care in the future.

- Quan Ni, Ph.D., Senior Director of Research, Inspire Medical Systems

In summary, the technical and software resources provided by the CIBC have been and will continue to be a critical component of defibrillation modeling research, an area which we feel will have direct and immediate value to engineers and clinicians developing innovative defibrillation strategies.

- John K. Triedman, M.D., Senior Associate in Cardiology, Children’s Hospital Boston, Associate Professor of Pediatrics, Harvard Medical School

In our work at the Neuroinformatics Center (NIC) at the University of Oregon, where I am the Director, we have benefited greatly from both the research results generated by the scientists in SCI/CIBC, as well as by the cutting-edge open source software you have produced.

- Dr. Allen D. Malony, Director Neuroinformatics Center, University of Oregon

...we have benefited hugely from the collaboration with Dr. Allen Sanderson of SCI in the implementation of graphics-processor based (GPU) supercomputing. With Allen’s direction, we successfully implemented this revolutionary development and are seeing dramatic speedups in our large-scale simulations. (Our publication “Acceleration of cardiac tissue simulation with graphic processing units” appeared last month in Med Biol Eng Comput.)

- Alan Garfinkel, Ph.D., Professor of Medicine (Cardiology) and Physiological Science, UCLA

You have assembled a group of international super-stars in visualization and image analysis and created an environment that supports effective interdisciplinary collaboration. You’ve even figured out a way to produce high quality software in an academic environment. The SCI Institute is probably one of the very few academic research institutes in the world that can lay claim to such strong interdisciplinary research and strong software development in visualization and image analysis.
Over the last five years I have used the software tools created by this center to generate results and visualizations for 15 peer reviewed papers and numerous conference presentations. And these tools have allowed us to focus our energy on research rather than software development, which we lack the expertise to do effectively.

- Christoper Butson, Ph.D., Departments of Neurology & Neurosurgery, Medical College of Wisconsin.

Using GPU-based rendering, a flexible yet easy-to-use set of rendering parameters, and an optimized user interface, [your software] allows us to go from raw datasets to useful visualizations at least severalfold faster than previously. Furthermore, features that are being added now will allow us to batch-process large 3D datasets and also 4D (dynamic) datasets. In SCI’s admirable tradition, [the software] is now being distributed freely, and we have had a great deal of interest from other neurobiology laboratories.

- Chi-Bin Chien, Associate Professor, Neurobiology and Anatomy, University of Utah

7.5.3 Students/faculty

The Finnish Centre of Excellence in Inverse Problems Research, supported by the Academy of Finland, is a consortium comprising the best inverse problems research groups within Finland. It is the only center of excellence in applied mathematics in the whole country. Because the SCI Institute is internationally known for its research excellence in inverse problems, imaging, and visualization research and software development, we chose you [Dr. Chris Johnson] to be one of two Scientific Advisory Board members to both advise our national center and to report to the Academy of Finland on our progress.

- Lassi Paivarinta, Director Finnish Centre of Excellence in Inverse Problems ResearchPresident Finnish Inverse Problem Society, Professor of Applied Mathematics, University of Helsinki

CIBC researchers are among the preeminent scientists in computer vision and biomedical image analysis, their brilliant work is extensively cited, and each is a consummate professional. Their seminal and continuing software contributions, including active leadership in the Insight Software Consortium responsible for the acclaimed Insight Segmentation and Registration Toolkit, reflect the Center’s deep devotion to advancing open-source software development. Building on a peerless record of research excellence, CIBC investigators continue to pioneer highly original, theoretically rigorous and efficient approaches to a range of challenging problems in biomedical image computing and computer vision, and the biomedical research community will be extremely well served by the renewal of the CIBC.

- James C. Gee, Ph.D., Associate Professor of Radiologic Science and Computer and Information Science, Director, HHMI-NIBIB Interfaces Program in Biomedical Imaging and Informational Sciences, Co-Director, Translational Biomedical Imaging Center, University of Pennsylvania

In my opinion, the SCI Institute has the best combination of visualization, imaging, and scientific computing researches in the world.

- Anne Trefethen, Professor and Director, Oxford e-Research Center, Oxford University
...Furthermore, I have actively sought to hire graduates and alumni of the SCI Institute programs...

- Terry S. Yoo, Ph.D., HPCC Project Officer, NLM, National Institutes of Health

Because of the quality of the Utah researchers when I was editor of the IEEE Transactions on Visualization and Computer Graphics, I chose several Utah visualization faculty to serve on the TVCG editorial board... Your record for training graduate students and postdoctoral fellows in visualization is excellent, which is why Utah was selected to partner in our International Graduate School funded by the German Research Foundation.

- Dr. Hans Hagen, University of Kaiserslautern

As one more piece of evidence of our interest in your center and our high regard for its work, I want to mention that our group at MGH recently hired one of your recent crnc Ph.D. graduates, Dr. Seok Lew, to work with us on our brain imaging research.

- Dr. David A. Boas, Harvard Medical School

I am now establishing my own research laboratory at the DFKI, the German Institute for Artificial Intelligence, and I am keen on continuing our collaborations. At the SCI Institute and through the CIBC, I will have access to biological and clinical data that will help drive additional research and development within ImageVis3D. In addition, the SCI Institute has several of the best visualization researchers in the world, and I value working with SCI Institute faculty on basic visualization research problems. As you know, I have already started such research collaborations with Professors Claudio Silva, Juliana Freire, and Chuck Hansen. As such, I plan to spend significant amounts of time, approximately 8 weeks per year, at the SCI Institute.

I look forward to continuing our productive collaborations!

- Jens Kruger, Ph.D., Research Group Leader, MMCI Saarbrucken, Senior Researcher, DFKI Saarbrucken, Adjunct Faculty Member, Scientific Computing and Imaging Institute, University of Utah

7.5.4 Infrastructure

From my perspective, the work performed at the Center and in the SCI Institute is an incomparable balance of research and application. While there are many excellent institutions of education and research, it is extremely rare to find institutions that combine both research excellence with the delivery of useful, leading-edge computational systems such as ImageVis3D, Seg3D, and ShapeWorks.

- William J. Schroeder, Ph.D., President, Kitware Inc.

In addition, I am fortunate to have had the opportunity to see how you manage the Center, and how the Center team members work together. I can state unequivocally that this is the most well managed, productive Centers that I know of. The scientific and technical team is of extraordinary caliber. Team members work extremely well together. You deserve great credit for creating a highly positive and effective environment for the Center faculty and staff. This is a major reason why your Center has been so successful.

When we switched to Seg3D, the segmentation time was reduced by a factor of 4 relative to these other applications. This has tremendously accelerated our work, making the shape analysis possible.

- Raimond L. Winslow, Director Institute for Computational Medicine & The Center for Cardiovascular Bioinformatics and Modeling, Professor Biomedical Engineering, Computer Science, Electrical & Computer Engineering, Health Care Informatics and Medicine, Johns Hopkins University
I remain a staunch supporter of your layered approach to software development for biomedical computing applications...

...In addition, I already use some of your other software (BioFEM and Bio3D) in a core curriculum class for students pursuing a Ph.D. in Computational Biology. With your software and some of your datasets, the students are able to study the heart as a bioelectric dipole embedded in a human torso, and to visualize surface electrodes and electric field lines through the tissues.

- Joel R. Stiles, MD, Ph.D., Director National Resource for Biomedical Supercomputing, Pittsburgh Supercomputing Center, Associate Professor, Department of Biological Sciences, Carnegie Mellon University

In summary, I value tremendously our past collaboration. The SCI [Institute] mission serves an important national purpose in that it will provide tools and methods for a broad community of researchers in both medical imaging as well as in other domains of subsurface non-invasive imaging. It is without hesitation that I enthusiastically endorse your renewal application to NIH.

- Michael B. Silevitch, Robert D. Black Professor of Engineering, Director The Bernard M. Gordon Center for Subsurface Sensing and Imaging Systems, Co-Director Awareness & Localization of Explosives-Related Threats (ALERT), Northeastern University

...I have been impressed by the high quality of both the software developed by your group and the scientific foundations on which the software is based.

- Thom F. Oostendorp, Ph.D., Research Professor, Donders Center for Neuroscience, Radboud University Nijmegen

We also believe that software tools should be shared – a philosophy you have articulated well in your proposal and in your center’s practice.

... Last but not the least, I want to complement you and your resource for the very early agreement with me to work with NBCR and other computational research resources in creating a joint booth for NCRR projects, at technical meetings such as the Supercomputing Conference, as well as scientific meetings of the Neuroscience, the American Chemical, and the Biophysical societies. Your early support helped transform the idea into a vibrant showcase of the NCRR projects at these meetings.

- Sinan Muftu, Associate Professor, Department of Mechanical and Industrial Engineering, Northeastern University

We have found your web-page that distributes the software to be impressive and very professionally designed and better than many commercial sites. The software is nicely packaged and easy to install. The programs have several features and are very easy to use. It is a great tool for people to perform quick visualization of volume data and useful to visualize large image data sets of CT or MRI.

... Your software has also been very helpful as tutorials for our students and post doctoral fellows to learn new techniques in software development and their application. Most of your software development is written in C/C++ using well known libraries. The software is open source which allows our students and postdocs to study the code and learn techniques in code development.
Importantly, the CIBC acutely understands that biomedical computing research does not begin and end with developing new methodology. The Center has consistently demonstrated an ability to collaborate productively with biomedical and clinical researchers, to put forward credible hypotheses about various disorders and conditions, and to shape its research vision around these hypotheses accordingly. Another distinguishing aspect of the CIBC is its commitment to translating research accomplishments into software applications that are aimed at a broad base of users. These open-source tools have significantly accelerated research in the biomedical image computing field in general and in our laboratory in particular.

- James C. Gee, Ph.D., Associate Professor of Radiologic Science and Computer and Information Science, Director, HHMI-NIBIB Interfaces Program in Biomedical Imaging and Informational Sciences, Co-Director, Translational Biomedical Imaging Center, University of Pennsylvania

Rather than focus on the development of our own one-off tools, we have committed to partnering with computer science leaders like yourself to field a flexible array of the most advanced tools available and to provide the necessary mesoscopic biological drivers to your more appropriately scaled team of visualization experts to collaboratively extend these tools. Over the past four years, this model of “technology push and biomedical science pull” has allowed us to rapidly field at NCMIR your leading edge applications for volume segmentation, 3D visualization and surface meshing (Seg3D, ImageVis3D and the Biomesh3D pipeline, respectively).

...I’m thrilled at the prospect of more closely coupling our research centers and amplifying the progress we’ve made.

- Mark H. Ellisman, Ph.D., Professor of Neurosciences and Bioengineering, Director, Center for Research in Biological Systems and the National Center for Microscopy and Imaging Research, University of California, San Diego School of Medicine

...I am particularly impressed with how you have been able to move research results into open source software that is widely used by the research community.

- Anne Trefethen, Professor and Director, Oxford e-Research Center, Oxford University

We, and others in our field, do not often have the capacity to develop such packages and rely on the constant development and availability of these excellent tools through centres like CIBC to further our research.

- Don McNaughton, Australian Professorial Fellow, Director, Centre for Biospectroscopy School of Chemistry, Monash University, Clayton, Victoria, Australia

As members of both the Presidents Information Technology Advisory Committee (PITAC) for Computational Science and the NSF Cyberinfrastructure Task Force on Software, I know you understand the need for investing in research software infrastructure and I strongly encourage the NIH NCRR to continue to support important efforts such as your Center for Integrative Biomedical Computing.

- Jack Dongarra, Ph.D., University Distinguished Professor, University of Tennessee, Director, Innovative Computing Laboratory