National Alliance for Medical Image Computing
Annual Research Progress Report - 2007
Contents

NATIONAL ALLIANCE FOR MEDICAL IMAGE COMPUTING
THIRD ANNUAL RESEARCH PROGRESS REPORT
2007

1 Introduction

The National Alliance for Medical Imaging Computing (NA-MIC) is now in its third year. This Center is comprised of a multi-institutional, interdisciplinary team of computer scientists, software engineers, and medical investigators who have come together to develop and apply computational tools for the analysis and visualization of medical imaging data. A further purpose of the Center is to provide infrastructure and environmental support for the development of computational algorithms and open source technologies, and to oversee the training and dissemination of these tools to the medical research community. The driving biological projects (DBPs) for the first three years of the Center came from schizophrenia, although the methods and tools developed are clearly applicable to many other diseases.

In the first year of this endeavor, our main focus was to develop alliances among the many cores to increase awareness of the kinds of tools needed for specific imaging applications. Our first annual report and All-hands meeting reflected this emphasis on cores, which was necessary to bring together members of an interdisciplinary team of scientists with such diverse expertise and interests. In the second year of the Center our emphasis shifted from the integration of cores to the identification of themes that cut across cores and were driven by the requirements of the DBPs. We saw this shift as a natural evolution, given that the development and application of computational tools became more closely aligned with specific clinical applications. This change in emphasis was reflected in the Center's four main themes, which included Diffusion Tensor Analysis, Structural Analysis, Functional MRI Analysis, and the integration of newly developed tools into the NA-MIC Tool Kit. In the third year of the Center, collaborative efforts have continued along each of these themes among computer scientists, clinical core counterparts, and engineering partners. We are thus quite pleased with the focus on themes, and we also note that not only has our progress continued but also more projects have come to fruition with respect to publications and presentations from NA-MIC investigators, which are listed on our publications page.

Below, in the next section (Section 2), we summarize our progress over the last year using the same four central themes to organize the progress report. These four themes include Diffusion Image Analysis (Section 2.1), Structural Analysis (Section 2.2), Functional MRI Analysis (Section 2.3), and the NA-MIC toolkit (Section 2.4). Section 3 highlights four important accomplishments of the third year: advanced algorithm development in Shape and DTI analysis, the newly architected open source application platform, Slicer3, and our outreach and technology transfer efforts. Section 4 summarizes the impact and value of our work to the biocomputing community at three different levels: within the center, within the NIH-funded research community, and externally to a national and international community. The final section of this report, Section 5, provides a timeline of Center activities.

In addition, the end of the first three years of the Center marks a transition from the first set of DBPs that were focused entirely on schizophrenia to a new set that spans a wider range of biological problems. The new DBPs continue to include neuropsychiatric disorders such as systemic lupus erythematosis (MIND Institute, University of New Mexico), schizophrenia (Harvard), and autism (University of North Carolina, Chapel Hill), and additionally adopt a direction that is new but synergistic for NA-MIC: prostate interventions (Johns Hopkins University). Funding for the second round of DBPs starts in the next cycle, but the PIs were able to attend the recent All-hands meeting and start developing plans for their future research in NA-MIC.

Finally, we note that Core 3.1 (Shenton and Saykin) is in the process of applying for a Collaborative R01 to expand current research with NA-MIC, which ends on July 31, 2007. Both Drs. Shenton and Saykin have worked for three years to drive tool development for shape measures, DTI tools, and path analysis measures for fMRI as part of the driving biological project in NA-MIC. They now plan to expand this research in a Collaborative R01 working closely with Drs. Westin, Miller, Pieper, and Wells, to design, assess, implement, and apply tools that will enable the integration of MRI, DTI, and fMRI in individual subjects. They will also develop an atlas of functional networks and circuits that are based on a DTI atlas (i.e., structural connectivity), which will be integrated with a network of functional connectivity that will be identified from fMRI probes of attention, memory, emotion, and semantic processing. We mention this here because this will be, to our knowledge, the first DBP to apply for further funding to continue critical work begun with NA-MIC.

(Please note that this report is available on the NA-MIC wiki at the following url: http://www.na-mic.org/Wiki/index.php/2007_Annual_Scientific_Report)

2 Four Main Themes

This year's activities focus on four main themes: Diffusion Image Analysis, Structural Analysis, Functional MRI Analysis, and the NA-MIC Kit. Each of the following sections begins with an overview of the theme, provides a progress update and list of key investigators, and concludes with a set of links to additional information for individual projects in that theme.

These thematic activities involve scientists from each of the 7 NA-MIC cores (Appendix).

- Core 1 Algorithms-Ross Whitaker PI
  http://www.na-mic.org/Wiki/index.php/Algorithm:Main
- Core 2 Engineering-Will Schroeder PI
  http://www.na-mic.org/Wiki/index.php/Engineering:Main
- Core 3 Driving Biological Problems DBP1-Martha Shenton PI / DBP2-Andy Saykin PI / DBP3-Steven Potkin PI
  http://www.na-mic.org/Wiki/index.php/DBP:Main
- Core 4 Service-Will Schroeder PI
  http://www.na-mic.org/Wiki/index.php/Service:Main

- Core 5 Training-Randy Gollub PI
  http://www.na-mic.org/Wiki/index.php/Training:Main
- Core 6 Dissemination-Tina Kapur Co-PI; Steve Pieper Co-PI
  http://www.na-mic.org/Wiki/index.php/Dissemination:Main
- Core 7 Leadership-Ron Kikinis
  http://www.na-mic.org/Wiki/index.php/Leadership:Main

2.1 Diffusion Image Analysis Theme

Progress

Over the past year, we have continued to develop a number of tools relevant to diffusion tensor estimation, fiber tractography, and geometric and statistical diffusion tensor analysis. Some of these tools have already been integrated into diffusion dedicated software (e.g., Fiber Viewer-UNC) and into the Slicer platform. Various groups focus on more sophisticated methodologies as alternatives to conventional tractography for more robust extraction of fiber bundles (Georgia Tech, Utah). Others combine tractography results from individuals into fiber cluster atlases (MIT). In addition, UNC started developing brain mapping tools for group data analysis, such as white matter atlases and tools for data integration, that would combine and interface among different imaging modalities (such as structural, fMRI, and DTI) to better estimate anatomical and functional connectivity. The current reporting period is clearly characterized by a significantly improved effort towards application of NA-MIC DTI tools developed by Core-1 partners to clinical data provided by Core-3 DBPs used in multiple clinical projects involving several psychiatric populations. Below we provide detailed progress in the area of diffusion image analysis.

Fiber Tract Extraction and Analysis

- Since last year, all of the algorithms for fiber tractography and anisotropy estimation have been implemented in both the “Fiber Viewer” and “Slicer” packages, and now the resulting methods are being applied to clinical studies. The FiberViewer tool and its application in a large clinical UNC DTI study have been published in journals. Utah recently extended the tractography-based concept with a new approach based on solving a PDE, thus replacing the tractography-based extraction of fiber bundles by a fully volumetric process. Characterization of bundles is then approached by a new regression method (IPMI'07). In a similar spirit, the BWH/MIT/UNC groups applied diffusion measures along a specific fiber bundle of inerest, parametrized by arc-length, to the cingulum bundle. Georgia Tech develops a method called "Finsler Active Contour DWI", a mathematically more sophisticated approach to standard tractography methods that makes use of Finsler geometry and solves a new anisotropic energy function for extraction of 3D curves from tensor data.

Preliminary applications to the cinculum bundle in the PNL schizophrenia dataset of our Core-3 partner are very promising.

In addition to clinical studies, teams have been working on other methods to define and estimate brain connectivity. The most important developments in this regard include volumetric connectivity and stochastic tractography measures. For volumetric connectivity, a PDE-based approach to white matter connectivity from DTI has been developed. This approach is founded on the principal of minimal paths through the tensor volume. This method computes a volumetric representation of a white matter tract given two endpoint regions. In addition, statistical methods for quantifying the full tensor data along these pathways have been also developed. Directional PDE-based flows have been proposed and implemented for a similar purpose. Further, an approach called "stochastic tractography," has been developed to calculate the probability of two regions being connected by the fiber tract. This should be especially useful when the tract must traverse through regions characterized by low diffusion anisotropy.

- Some initial attempts have been made in the population-based analysis of DT-MRI. One method in development by UNC in collaboration with Utah is based on the unbiased non-rigid registration of a population to a common coordinate system. The registration jointly produces an average DTI atlas, which is unbiased with respect to the choice of a template image, along with a diffeomorphic correspondence for each image. The method includes calculation of features driving non-linear, population-based diffeomorphic deformation to an average template, nonlinear mapping of tensor fields, and a statistical framework for region-based and tract-based analysis of the whole population not only in the geometry of the atlas space but also in the respective space of the original MR-DWI. The anatomically significant correspondence provides a basis for comparison of tensor features and fiber tract geometry in clinical studies. This development is in response to the need of the clinical community for efficient, automatic analysis of large populations of images as an alternative to case-by-case user-supervised processing, similarly to the SPM package used for fMRI analysis. A different route is taken in a project by MIT/BWH: Tractography applied to the whole brain of a population of subjects is used to create a model (atlas) of fiber tract clusters. This method can be applied to subdivide the corpus callosum left-right tracts into smaller entities that connect particular subareas of the cortex. A key issue of this research is a geometric characterization of bundles of streamlines obtained by tractography.

- Validation of DTI tools is pursued via a joint collaboration between UCI, MGH, UNC, and MIT. Initial work used the DTI Studio method provided by Susumo Mori. Extension of this validation to include Slicer was difficult due to incompatibility of data, thick-slice DTI data available for the preliminary

analysis, and the use of very different formats not yet fully integrated into ITK. This effort will have priority for the Core-5 training group, which will integrate validation of methods as a key part into their training workshop activities.

Fractional Anisotropy Analysis

- We have applied tools developed last year to our population of chronic schizophrenia subjects to investigate two fiber tracts: the cingulum bundle and the corpus callosum. In the case of cingulum bundle, manually drawn regions of interest and Finsler geometry were used to extract the entire cingulum bundle fiber tract, and FA was estimated along the tract and compared between groups. The cross-sectional area of the corpus callosum and its probabilistic subdivisions were determined automatically from the structural MRI scans using a model-based deformable contour segmentation. The structural scan was then co-registered with the DTI scan and the anatomical corpus callosum subdivisions were propagated to the associated FA map, and compared between groups, demonstrating deficient interhemispheric communication in schizophrenia.

Please see a summary of clinical applications below.

Integration of fMRI and DTI, Path-of-Interest Analysis

- Progress has been also made in the development of a tool that would successfully combine and integrate functional and anatomical information. The Optimal Path Analysis method has been applied to the Harvard-BWH fMRI data set, and anatomical connections between regions active during the fMRI experiment have been extracted for each subject. The connectivity has been calculated and compared between groups. This tool is now being ported to Slicer3.

Summary of NA-MIC Clinical DWI Applications

The current reporting period is clearly characterized by a significant increase in the application of tools to the clinical DWI data provided by the Core-3 DBP groups. There are two main reasons for this increase. First, several new tools are ready for application to image data sets. Second, we now have high-resolution DTI data from the 3-Tesla scanners that are more appropriate for these new tools than older, highly non-isotropic voxel data.

- The application of NA-MIC DTI tools jointly with our Core-3 partners includes the ongoing study of inferior frontotemporal connections (BWH/MIT) by applying fiber tractography to extract the uncinate fasciculus and occipito-frontal fasciculus in a study of 27 chronic schizophrenics and 34 controls. The same group studies corpus callosum clustering in the new 3-Tesla data set provided by PNL (24 subjects, 12

chronic schizophrenics and 12 matched control subjects). Preliminary results show reduced FA and reduced volume in two different clusters.

- A collaboration between Harvard PNL, MIT, and BWH is studying diffusion properties of the fornix, an interconnection between the frontal and temporal lobes that is likely implicated in schizophrenia. Tractography tools were used to extract the left and right fornix in 34 chronic schizophrenia subjects and 40 matched controls.

- The atlas-based analysis of DWI in development by UNC has been applied to the 3-Tesla schizophrenia DTI data of Harvard PNL (n=24 subjects). Key structures like the fornix, cingulum, or uncinate fasciculus can be efficiently extracted from the tensor atlas and thus immediately applied to all data sets of the population. Statistical analysis of regions or tracts of interest that are relevant to the study of schizophrenia is currently performed jointly with the Core-3 partner PNL.

- Dartmouth, in collaboration with BWH and UNC, is applying corpus callosum regional analysis to the chronic schizophrenia data. BWH, together with MIT and Dartmouth, are currently working on FA analysis of the corpus callosum and the anterior commissure. The same groups also study the uncinate fasciculus bundle in schizophrenia and bipolar disease, a study that attempts to replicate previous user-guided ROI analysis with application of new NA-MIC tools.

- The cinculum bundle in the PNL 3-Tesla schizophrenia data set is being analyzed by Georgia Tech, using the newly developed "Finsler Active Contour DWI" method.

- Corpus callosum probabilistic subdivision and quantitative analysis, originally developed by the UNC shape analysis group, is now being applied to a clinical study of 32 schizophrenic subjects and 42 controls, a joint collaboration between Harvard PNL, BWH and UNC.

- The path of interest method has been successfully tested by Dartmouth to map uncinate fasciculus and arcuate fasciculus in a healthy adult. They will continue to study the fronto-temporal circuitry in the Darthmouth schizophrenia study. Anatomical connectivity of regions of functional activation, using the "optimal path analysis" method, is currently being applied by BWH, PNL, and MIT to study anatomical connectivity between regions demonstrating functional activation.

- A clinical project between Toronto and BWH still in the recruitment phase is planning a DTI and genetic study of psychosis across the life-span.

Key Investigators

- BWH: Martha Shenton, Marek Kubicki, Marc Niethammer, Sylvain Bouix, Jennifer Fitzsimmons, Katarina Quintis, Doug Markant, Kate Smith, Georgia Bushell, Mark Dreusicke, Carl-Fredrik Westin, Raul San Jose, Gordon Kindlmann
- MGH: Bruce Fischl, Denis Jen, David Kennedy
- MIT: Lauren O'Donnell, Polina Golland, Tri Ngo
- UCI: James Fallon, Martina Panzenboeck
- UNC: Guido Gerig, Isabelle Corouge, Casey Goodlett, Martin Styner
- Utah: Tom Fletcher, Ross Whitaker, Saurav Basu, Davis McKay
- GA Tech: Eric Pichon, John Melonakos, Xavier LaFaucheur, Vandana Mohan, Allen Tannenbaum
- Dartmouth: John West, Andrew Saykin, Laura Flashman, Paul Wang, Heather Pixley, Robert Roth
- Isomics: Steve Pieper
- Kitware: Luis Ibanez

Additional Information

For details of each of the projects in this theme, please see NA-MIC Projects on Diffusion Image Analysis http://www.na-mic.org/Wiki/index.php/NA-MIC_Collaborations

2.2 Structural Analysis Theme

Progress

Within NAMIC's structural analysis theme, the main topics of interest are structural segmentation, registration, and shape analysis. These topics are of course intertwined, e.g., segmentation or registration can directly deliver structural correspondence used in shape analysis, and in turn, shape modeling is necessary for good structural segmentations. Here is a selection of progress highlights in the structural analysis theme.

Segmentation

- *Wavelet-based Structural Segmentation:* We have developed a spherical wavelet-based framework for the segmentation of selected brain structures, such as the hippocampus or the caudate nucleus. An automated segmentation of such structures must be highly accurate and include high frequency variations in the surface. Since shape representation is a key component of the segmentation, it must be rich enough to express shape variations at various frequency levels, from low harmonics to sharp edges. Medical object segmentation with deformable models and statistical shape modeling may be combined to obtain a more robust and accurate segmentation. To address this issue, a decomposable spherical wavelet-based shape representation targeted to the population seems

natural, where the shape parameters are separated into groups that describe independent global and/or local biological variations in the population, and a prior induced over each group explicitly encodes these variations. This work presents three novel contributions for shape representation, multiscale prior probability estimation, and segmentation.

- *Directional Based Segmentation:* We have proposed an image segmentation technique based on augmenting the conformal (or geodesic) active contour framework with directional information. In the classical case, the Euclidean metric is locally multiplied by a scalar conformal factor (based on image information) such that the weighted length of curves lying on points of interest (typically edges) is small. We propose to add directionality to the factor, and show that one gets a well-defined minimization problem in the case that the factor defines a Finsler metric. Optimal curves may be obtained using the calculus of variations or dynamic programming. This methodology also makes connections to the important technique of graph-cuts.

- *Statistical PDE Methods for Segmentation in Shape Space:* This past year, we have proposed another method to perform shape-driven segmentation. In our approach, shapes are represented using binary maps, and linear PCA is utilized to provide shape priors for segmentation. Intensity-based probability distributions are then employed to convert the given volume into a binary map representation, and a new energy functional is formulated whose minimization is performed using a parametric model for surface evolution in the shape space. Our algorithm is then applied to the segmentation of brain caudate nucleus and hippocampus from MRI data. Our validation shows that the proposed algorithm outperforms the log-likelihood-based energy, converges in less than 5 iterations, and is very robust to initialization. The overall algorithm illustrates the potential for segmentation in shape space.

- *Rule-based Segmentation Methods:* We have continued this past year to develop segmentation methods based on heuristic rules provided to us by our Core 3 partners for segmenting various brain regions of interest in schizophrenia, e.g. the DLPFC and the striatum. The idea is to try to semi-automate these rules in order to forge an interactive tool for segmentation which can greatly shorten the time necessary for manual segmentation. Typically, these methods are used in conjunction with some Bayesian classifier which further aids to automating and in speeding up the given segmentation methodology.

- *Tissue and Structural Segmentation via EM Segmenter:* Standard image based segmentation approaches perform poorly when there is little or no contrast along boundaries of different regions. In such cases segmentation is mostly performed manually using prior knowledge of the shape and relative location of the

underlying structures combined with partially discernible boundaries. We have developed an automated approach guided by covariant shape deformations of neighboring structures, which is an additional source of prior knowledge. Captured by a shape atlas, these deformations are transformed into a statistical model using the logistic function. The mapping between atlas and image space, structure boundaries, anatomical labels, and image inhomogeneities are estimated simultaneously within an Expectation-Maximization formulation of the Maximum A posteriori Probability (MAP) estimation problem. These results are then fed into an Active Mean Field approach, which views the results as priors to a Mean Field approximation with a curve length prior. This segmentation framework has been ported into the NAMIC-toolkit and a first version of the tool is distributed with Slicer 3.

Shape Analysis

- *Wavelet-based Shape Analysis:* A shape representation that encodes variations at multiple scales can be useful as a rich feature set for shape analysis and classification. Combining tools from the existing shape analysis toolset, we extended it to include spherical wavelet coefficients (SWC) as features and compared the results obtained to shape analysis using a SPHARM-PDM representation. The rich SWC feature set allows the differentiation of shape differences at various scales as well as highly correlates with the existing SPHARM-PDM analysis but with increased statistical sensitivity. Wavelet coefficient shrinkage and dimension reduction are well-understood and have been widely researched for traditional types of wavelet decompositions but not much explored for the second generation wavelets. During the past year, we have developed a Bayesian model on our specific wavelet structure based on a population of surfaces. For each shape, the deviation from the mean is computed and is modeled as the sum of an unknown signal and a noise. This deviation is encoded by the wavelet transform and our goal is to estimate the wavelet coefficients belonging to the noiseless signal.

- *Surface Flattening for Shape Analysis:* Flattened representations of undulated surfaces constitute an active area of research in the field of medical imaging and visualization, owing to their extensive use for registration and shape analysis of various structures of interest. We have presented a method for flattening anatomical surfaces in an area-preserving manner, while minimizing the geometrical distortion. This method is based on the theory of optimal mass transport and conformal mapping of surfaces. The key idea here is the use of a multiresolution scheme for the solution of optimal mass transport gradient descent equations, which allows a fast and stable solution for optimal transport. The method has been implemented on a GPU, allowing us to flatten a 128 x 128 x 128 volume in about 5 seconds on a standard workstation.

- *Curvature-based Population Correspondence:* We have extended the Minimum Description Length population-based correspondence framework to include curvature-based measurements, such as the Koenderink Shape Index S and Curvedness C in combination with the standard location information. Current methodology in population-based correspondence is based mainly on minimizing distribution properties of surface point locations and is thus not invariant to alignment. We have favorably compared our combined "Curvature + Location" MDL to the standard MDL, as well as to the SPHARM approach, in complex structures, such as the striatal brain structure (composed of caudate, nucleus accumbens, and putamen).

- *Shape Analysis Toolset:* A considerable amount of work was spent on the development aspect of the shape analysis tools. The distributed set of tools is continuously enhanced and the population-based correspondence framework has been released as open source. All the tools including the visualization tool, KWMeshVisu, can be called directly from Slicer3. The visualization tool allows the overlay of scalar, vector, and ellipsoid data onto surfaces via versatile colormaps. The attributed surfaces are then visible within Slicer3. This lean visualization tool fills a niche and is also used in our cortical thickness analysis tool. Also, while it is entirely possible to run all shape analysis steps by calling the individual modules, this is highly inefficient in a larger study. As a result we are developing a separate shape pipeline Slicer module that uses Batchmake to run the shape analysis pipeline as a distributed background process. The whole shape analysis pipeline will thus become entirely encapsulated and accessible to the trained clinical collaborator.

- *Particle-based Correspondence:* We have developed a method for a multi-object correspondence optimization, and have applied it successfully to a proof-of-concept application for the analysis of brain structure complexes from a longitudinal study of pediatric autism. This new method for constructing compact statistical point-based models of ensembles of similar shapes does not rely on any specific surface parameterization, requires little preprocessing or parameter tuning, and is applicable to a wider range of problems than existing methods, including non-manifold surfaces and objects of arbitrary topology. The method uses a dynamic particle system to optimize correspondence point positions across all structures by simultaneously maximizing both the geometric accuracy and the statistical simplicity of the model.

Key Investigators

- MIT: Kilian Pohl, Sandy Wells, Eric Grimson
- UNC: Martin Styner, Ipek Oguz, Guido Gerig, Xavier Barbero

- Utah: Ross Whitaker, Suyash Awate, Tolga Tasdizen, Tom Fletcher, Joshua Cates, Miriah Meyer
- GaTech: Allen Tannenbaum, John Melonakos, Tauseef ur Rehman, Shawn Lankton, Ramsey Al-Hakim, Eric Pichon, Delphine Nain, Oleg Michailovich, Yogesh Rathi, James Malcolm
- Isomics: Steve Pieper
- GE: Bill Lorensen, Jim Miller
- Kitware: Luis Ibanez, Karthik Krishnan,
- UCLA: Michael J. Pan, Jagadeeswaran Rajendiran
- BWH: Sylvain Bouix, Motoaki Nakamura, Min-Seong Koo, Martha Shenton, Marc Niethammer, Jim Levitt
- Dartmouth: Andrew Saykin
- UCI: James Fallon

Additional Information

For details of each of the projects in this theme, please see NA-MIC Projects on Structural Image Analysis. http://www.na-mic.org/Wiki/index.php/NA-MIC_Collaborations

2.3 Functional MRI Analysis Theme

Progress

During this year, the focus of the algorithms and the engineering cores has been on the structural and DTI analysis. While we continued to expand the methods and the infrastructure in NAMIC-kit to support fMRI analysis, as well as using the analysis tools to perform clinical studies, the emphasis of the work this year has been on integrating the fMRI analysis with other modalities and supporting other modalities.

Clinical Studies

We would like to highlight several clinical studies within NAMIC that focused on fMRI data and its relationship with other imaging modalities:

- *Imaging Phenotypes in Schizophrenics and Controls*: Functional connectivity of the DLPFC by genotype was investigated employing partial least squares (PLS) correlation analysis. PLS is a multivariate analytical technique used to summarize large neuroimaging data sets in such a way as to correlate patterns of activation with a variable(s) of interest (i.e., DLPFC activity). In the most recent analysis, the DRD1 genotype was used as a grouping variable. This analysis has been submitted for publication (Tura, Turner, Fallon, Kennedy, and Potkin. *Genetic Impact on Functional Connectivity in Schizophrenics During a Working Memory Task*). Working memory performance did not differ significantly

between the two cohorts. However, imaging-genetic analysis showed a significant difference ($P < 0.05$) between the circuitry engaged by each group. Significance and reliability of the resulting imaging-behavioral patterns within each genotype were assessed by 200 bootstrap and 500 permutation tests, respectively. In one group, the circuitry included the temporal pole, the insula, the dorsolateral prefrontal cortex, and the Brodmann Areas (BA) 1,2,3,4,6,11 and 21, while the other group showed a network comprising the tectum, precuneus retroplenial, vermis, substantia nigra, BA 22,39,8, and 9. The DRD1 polymorphic site may characterize circuitry differences in schizophrenic patients.

- *Path-Of-Interest Analysis (joint DTI/fMRI modeling)*: We collected preliminary data using an application of the "optimal path analysis." In this analysis, we extracted group fMRI activation due to the Stroop effect (an attentional experiment where incongruent color, in which the word is written, competes with name of the color itself, activating areas responding to conflict monitoring and selection) separately for controls and schizophrenics. This resulted in three clusters of activation, one in the right Dorsolateral Prefrontal Cortex, a second in the Anterior Cingulate Gyrus, and a third in the Medial Parietal Lobe. In the next step, we placed activation clusters in each individual space, by reversing normalization parameters used during fMRI analysis. Finally, EPI fMRI scans were co-registered to DTI scans, and the same registration parameters were applied to activation maps (fMRI results). Regions of activation were used as start and destination points for optimal path analysis, which resulted in three separate paths of optimal connectivity for each subject. The probability of the connections was then calculated for each path and each subject and compared between groups. In our preliminary analysis, we included 10 control subjects and 10 chronic schizophrenics. Our results demonstrated a relationship between Stroop Effect fMRI activation in the medial parietal area and optimal path connectivity between parietal and cingulate activation sites in schizophrenics ($rho=-0.56$; $p=0.047$), which was not observed in controls. These findings suggest that decreased connectivity may result in schizophrenics relying more on posterior parts of the executive attentional network during performance of the Stroop task.

- *Hippocampal and Frontal Memory Circuitry Abnormalities in Schizophrenia: Relation of Diffusion, Morphometric, and fMRI Markers*: We performed a combined DTI, fMRI, and morphometric study on 13 patients with schizophrenia (SZ) and 14 HC. We identified areas of increased trace diffusivity (TD) in the hippocampal and insular regions as well as areas of reduced fractional anisotropy (FA) in left frontal white matter in SZ relative to HC ($p<.01$). Voxel-based morphometry analyses in a subset of these subjects showed corresponding reductions in gray matter density in hippocampal and insular regions in patients relative to controls ($p<.01$). Analysis of fMRI results from the novel vs. repeated word contrast from the event-related auditory verbal episodic memory encoding/retrieval task in a

subset of the subjects indicated reduced activation in frontal and temporal regions, as well as increased activation in posterior cingulate, retrosplenial, and thalamic regions in SZ relative to HC ($p<.05$). Further analysis showed that left frontal white matter FA was associated with activation in the left and right hippocampi as well as other frontal and temporal regions, but inversely related to activation in the retrosplenial/posterior cingulate region ($p<.05$). These initial findings indicate a pattern of relationships between of structural and functional brain abnormalities in schizophrenia and demonstrate the feasibility of integrated quantitative analyses across modalities.

Methods

During this year, we continued methodological development along two directions:

- *Improving fMRI detectors by incorporating Markov priors on the activation state.* We integrated the improved detector into Slicer and performed substantial validation of the methods using fBIRN data provided by the UC Irvine group. A journal paper on the method has been submitted to IEEE TMI.

- *Improving registration of EPI images to anatomical scans through modeling of the EPI distortions.* We demonstrated an initial model that uses segmentation of the structural scan to predict the distortions in the EPI images. The preliminary results are quite encouraging.

Key Investigators

- MIT: Polina Golland, Sandy Wells, Wanmei Ou, Claire Poynton
- BWH: Martha Shenton, Marek Kubicki
- Dartmouth: Andy Saykin
- UCI: Jessica Turner, Stephen Potkin
- Toronto: Jim Kennedy

Additional Information

For details of each of the projects in this theme, please see NA-MIC Projects on fMRI Analysis. [http://www.na-mic.org/Wiki/index.php/NA-MIC_Collaborations]

2.4 NA-MIC Kit Theme

Progress

The continuing vision of the NA-MIC Kit is to provide an open source set of software tools and methodologies that will serve as the foundation for medical image computing projects for both academic and commercial use. Key elements of this vision are:

1. *Unrestrictive License.* Users of the Kit are free to distribute their derived works under any license suitable to their needs.
2. *Cross Platform.* This software set can be adapted to the best available price-performance computer systems for any particular use.
3. *Extensible Application Framework.* New techniques and algorithms can be quickly integrated into a working system. Sophisticated user interfaces can be generated easily through automated processes. Sophisticated toolsets such as ITK, VTK, and KWWidgets are available to create and deploy applications quickly.
4. *Quality Software Process.* Developers and users can rely on accurate and well documented behavior from all the parts of the Kit.
5. *Sustainable Community.* Users are actively involved in the design process of the Kit. Documentation, training materials, and hands-on sessions are available and well publicized to the community.

Slicer3

A major focus of the third year was the implementation of the Slicer3 in the NAMIC Kit. This effort addressed Item #3 above *Extensible Application Framework.* The previous two years of the NAMIC project, which entailed gathering requirements from Cores 1 and 3, and developing the computational foundation, toolsets, and software process, came together in the Slicer3 application platform.
Core 2 worked hard to insure that the Slicer 3 application serves, and will continue to serve, as a productive technology deployment platform. The application framework was designed carefully to provide ease-of-use, both in terms of interaction and software integration. Advanced capabilities, including the ability to launch large-scale grid computing, were designed into the application. Some of the key features of the Slicer3 application completed in the third year include the following.

- Advanced application framework including a tuned GUI for ease of use, undo/redo capabilities, 2D/3D view windows, and support for advanced interaction techniques such as 3D widgets. The application provides viewers for displaying slices, volumes, and models including the ability to edit properties. A built in transformation pipeline enables users to confidently import, edit and display data in a consistent coordinate system.

- The application is data-driven based on the next generation MRML scene description file format. Backward compatibility to Slicer 2.x MRML files is preserved.

- A module plug-in architecture and execution model that enables researchers to package and integrate their software into the Slicer3 framework. Plug-in modules can be implemented in a variety of programming languages, and are described using a simple XML description. These modules, when located and loaded into

Slicer3, have the capability to automatically generate their user interface, which is seamlessly integrated into the Slicer3 GUI.

- Support for editing and marking data including support for fudicials, paint and draw editors.

- The creation of several simple plug-in modules, including the conversion of previous Slicer 2.x modules to the new Slicer3 architecture.

EM Segment

As an application framework, Slicer3 provides tools for loading, viewing, measuring, editing, and saving data. To support advanced medical image analysis, plug-in modules are required in conjunction with the Slicer3 core. To demonstrate the capabilities of the framework we implemented the EM Segment module [http://www.na-mic.org/Wiki/index.php/Slicer3:EM], a sophisticated and proven method for automatically segmenting complex anatomical structures. To use this module, users specify parameters defining the image protocol and the anatomical structures of interests. This process results in a template that the module uses to automatically segment large data sets. The template is composed of atlas data and a non-trivial collection of parameters for the EM Segment algorithm (Pohl et al.). Once the parameters are specified, the target images are segmented using the algorithm; if the results are satisfactory, the template is saved and can be used later to segment new images (via the GUI or batch processing). If the results are unsatisfactory, the parameters can be modified and the segmentation re-run. Besides successfully demonstrating the use of complex algorithms in the Slicer3 framework, this effort also led us to develop tools, including modifications to the underlying KWWidgets GUI toolkit, to support module workflow. With these tools, it is possible to simplify complex modules by dividing the complicated template specification task into a number of smaller, intuitive steps. These steps are enforced by the GUI and reduce the potential for user error, while improving the overall user interface.

Quality Software Process

Building on last year's success with the KDE community [http://lwn.net/Articles/188693/] the NAMIC community continued to extend its world-class open source software process tools CMake, DART, CTest and DART. These tools form the core of a quality-oriented, test-driven development (TDD) software process. In particular, the CPack system is now able to automatically package and distribute code, libraries, executables, and installers across all of NAMIC's supported platforms (i.e., Linux, Windows, Mac). This enables the NAMIC developer community to rapidly deploy software tools to the user community.

Key Investigators

- GE: Bill Lorensen, Jim Miller, Xiaodong Tao, Dan Blezek
- Isomics: Steve Pieper, Alex Yarmarkovich
- Kitware: Will Schroeder, Luis Ibanez, Brad Davis, Andy Cedilnik, Sebastien Barre, Bill Hoffman
- UCLA: Mike Pan, Jagadeeswaran Rajendiran
- UCSD: Neil Jones, Jeffrey Grethe, Mark Ellisman
- BWH: Nicole Aucoin, Katie Hayes, Wendy Plesniak, Mike Halle, Gordon Kindlmann, Raul San Jose Estepar, Haiying Liu, Ron Kikinis
- MIT: Lauren O'Donnell, Kilian Pohl

Additional Information

For details of each of the projects in this theme, please see NA-MIC Kit Projects. [http://www.na-mic.org/Wiki/index.php/NA-MIC_Collaborations]

3. Highlights

The third year of the NAMIC project saw continued development and dissemination of medical image analysis software. With the release of the first version of Slicer3, the transfer of this technology is accelerating. Because of NAMIC's strong ties with several large open source communities, such as ITK, VTK, and CMake, NAMIC continues to make significant impact on the nation's broader biocomputing infrastructure. The following are just a few of the many highlights from the third year of the NAMIC effort.

3.1 Advanced Algorithms

Core 1 continues to lead the biomedical community in DTI and shape analysis.

- NAMIC published an open source framework for shape analysis, including providing access to the open source software repository. Shape analysis has become of increasing relevance to the neuroimaging community due to its potential to precisely locate morphological changes between healthy and pathological structures. The software has been downloaded many times since the first online publication in October 2006, and is now used by several prestigious image analysis groups.
- The spherical based wavelet shape analysis package has been integrated into ITK, and in the next few months the multi-scale segmentation work will be incorporated as well.
- The NAMIC community has implemented a very fast method for the optimal transport approach to elastic image registration, which is currently being added to ITK.

- The conformal flattening algorithm has been implemented as an ITK filter and is in the NAMIC Sandbox in preparation for formal acceptance into the NAMIC Kit.

3.2 Technology Deployment Platform: Slicer3

Core 2 in conjunction with Algorithms (Core 1) and DBP (Core 3) are creating new tools to accelerate the transition of technology to the biomedical imaging community.

- One of the year's major achievements was the release of the first viable version of the Slicer3 application, which evolved from concept to a full-featured application. The second beta version of Slicer3 was released in April 2007. The application provides a full range of functionality for loading, viewing, editing, and saving models, volumes, transforms, fiducials, and other common medical data types. Slicer3 also includes a powerful execution model that enables Core 1 developers (and other in the NAMIC community) to easily deploy algorithms to Core 2 and other biocomputing clients.
- Slicer3's execution model supports plug-in modules. These modules can be run stand alone or integrated into the Slicer3 framework. When integrated, the GUI to the module can be automatically generated from an associated XML file describing input parameters to the module. A variety of modules were created, ranging from simple image processing algorithms, to complex, multi-step segmentation procedures.
- To stress test Slicer3's architecture and demonstrate its capabilities, the EM Segment module (http://wiki.na-mic.org/Wiki/index.php/Slicer3:EM) was created and added to Slicer's library of modules. EM Segment is an automatic segmentation algorithm for medical images and represents a collaborative effort between the NAMIC engineering, algorithms, and biological problem cores. The EM Segment module enables users to quickly configure the algorithm to a variety of imaging protocols as well as anatomical structures through a wizard-style, workflow interface. The workflow tools have been integrated into the NAMIC Kit, and are now available to all other modules built on the Slicer3 framework.

3.3 Outreach and Technology Transfer

Cores 4-5-6 continue to support, train and disseminate to the NAMIC community, and the broader biomedical computing community.

- NAMIC continues to practice the best of collaborative science through its bi-annual Project Week events. These events, which gather key representatives from Cores 1-7 and external collaborators, are organized to gather experts from a variety of domains to address current research problems. This year's first Project Week (http://wiki.na-mic.org/Wiki/index.php/2007_Project_Half_Week) was held in January and hosted by the University of Utah. It saw several significant

accomplishments including the first beta release of the next generation Slicer3 computing platform. The second Project Week is scheduled for June in Boston, MA. (http://wiki.na-mic.org/Wiki/index.php/2007_Programming/Project_Week_MIT)

- Twelve NAMIC-supported papers were published in high-quality peer reviewed conference proceedings (four papers in MICCAI alone). Another paper on the NAMIC software process was published in *IEEE Software.* All three DTI papers presented at MICCAI last year were NAMIC associated.
- Several workshops through the year were held at various institutions. This includes the DTI workshop at UNC, the MICCAI Open Source Workshop, and the NA-MIC Training Workshop at the Harvard Center for Neurodegeneration and Repair.

4. Impact and Value to Biocomputing

In NA-MIC's third year, it is evident that NA-MIC is developing a culture, environment, and resources to foster and incite collaborative research in medical image analysis that draws together mathematicians, computer scientists, software engineers, and clinical researchers. These artifacts of NA-MIC impact how NA-MIC operates, make NA-MIC a fulcrum for NIH funded research, and draws new collaborators from across the country and around the world to NA-MIC.

4.1 Impact within the Center

Within the center, the NA-MIC organization, NA-MIC processes, and the NA-MIC calendar has permeated the research. The organization is nimble, forming ad hoc distributed teams within and between cores to address specific biocomputing tasks. Information is shared freely on the NA-MIC Wiki, on the weekly Engineering telephone conferences, and in the NA-MIC Subversion source code repository. The software engineering tools of CMake, Dart 2 and CTest, CPack, and KWWidgets facilitate a cross platform software environment for medical image analysis that be easily built, tested, and distributed to end-users. Core 2 has provided a platform, Slicer 3, that allows Core 1 to easily integrate new technology and deliver this technology in an end user application to Core 3. Core 1 has developed a host of techniques to apply to structural and diffusion analysis which are under evaluation by Core 3. Major NA-MIC events, such as the annual All Hands Meeting, the Summer Project Week, the Spring Algorithms meeting, and Engineering Teleconferences are avidly attended by NA-MIC researchers as opportunities to foster collaborations.

4.2 Impact within NIH Funded Research

Within NIH funded research, NA-MIC continues to forge relationships with other large NIH funded projects such as BIRN, caBIG, NAC, and IGT. Here, we are sharing the NA-MIC culture, engineering practices, and tools. BIRN hosts data for the NA-MIC

researchers and NA-MIC hosts BIRN wikis. caBIG lists the 3D Slicer among the applications available on the National Cancer Imaging Archive. NAC and IGT use the NA-MIC infrastructure and are involved in the development of the 3D Slicer. BIRN recently held an event modeled after the NA-MIC Project Week. NA-MIC has become a resource on open source licensing to the medical image analysis community.
NA-MIC is also attracting NIH funded collaborations. Two grants have been funded under PAR-05-063 to collaborate with NA-MIC: *Automated FE Mesh Development* and *Measuring Alcohol and Stress Interactions with Structural and Perfusion MRI*. Five additional applications to collaborate with NA-MIC via the NCBC collaborative grant mechanism are under consideration. Additional grant applications submitted under other calls are planning to use and extend the NA-MIC tools.

4.3 National and International Impact

NA-MIC events and tools garner national and international interest. There were nearly 100 participants at the NA-MIC All Hands Meeting in January 2007, with many of these participants from outside of NA-MIC. Several researchers from outside the NA-MIC community have attended the Summer Project Weeks and the Winter Project Half-Weeks to gain access to the NA-MIC tools and people. These external researchers are contributing ideas and technology back into NA-MIC.
Components of the NA-MIC kit are used globally. The software engineering tools of CMake, Dart 2 and CTest are used by many open source projects and commercial applications. For example, the K Desktop Environment (KDE) for Linux and Unix workstations uses CMake and Dart. KDE is one of the largest open source projects in the world. Many open source projects and commercial products are benefiting from the NA-MIC related contributions to ITK and VTK. Finally, Slicer 3 is being used as an image analysis platform in several fields outside of medical image analysis, in particular, biological image analysis, astronomy, and industrial inspection.
NA-MIC co-sponsored the *Workshop on Open Science* at the Medical Image Computing and Computer-Assisted Intervention (MICCAI) 2006 conference. The proceedings of the workshop are published on the electronic Insight Journal, another NIH-funded activity. Over 50 NA-MIC related publications have been produced since the inception of the center.

5. NA-MIC Timeline

This section provides a table of NAMIC timelines from the original proposal that graphically depicts completed tasks/goals in years 1, 2, and 3 and tasks/goals to be completed in years 4-5. Changes to the original timelines have also been described.
2007 Scientific Report Timeline

Core 1: Algorithms

Timelines and Milestones

Group	Aim	Milestone	Proposed time of completion	Status
MIT	1	**Shape-based segmentation**		
MIT	1.1	Methods to learn shape representations	Year 2	Completed
MIT	1.2	Shape in atlas-driven segmentation	Year 4	Completed
MIT	1.3	Validate and refine approach	Year 5	In Progress
MIT	2	**Shape analysis**		
MIT	2.1	Methods to compute statistics of shapes	Year 4	Completed
MIT	2.3	Validation of shape methods on application data	Year 5	In progress
MIT	3	**Analysis of DTI data**		
MIT	3.1	Fiber geometry	Year 3	Completed
MIT	3.2	Fiber statistics	Year 5	Completed, new developments ongoing
MIT	3.3	Validation on real data	Year 5	Ongoing
Utah	1	**Processing of DTI data**		
Utah	1.1	Filtering of DTI	Year 2	Completed
Utah	1.2	Quantitative analysis of DTI	Year 3	Completed partially, ongoing
Utah	1.3	Segmentation of cortex/WM	Year 3	Completed partially, ongoing
Utah	1.4	Segmentation analysis of white matter tracts	Year 3	Algorithms complete/published, refining and applying to Core 3 data.
Utah	2	Nonparametric Shape Analysis	Year 5	Incomplete, ongoing.
Utah	2.1	Framework in place	Year 3	Complete
Utah	2.2	Demonstration on shape of neuroanatomy (from Core 3)	Year 4	Complete
Utah	2.3	Development for multi-object complexes	Year 4	Complete

Utah	2.4	Demonstration of NP shape representations on clinical hypotheses from Core 3	Year 5	Incomplete, ongoing
UNC	1	**Statistical shape analysis**		
UNC	1.1	Comparative anal. of shape anal. schemes	Year 2	Completed
UNC	1.3	Statistical shape analysis incl. patient variable	Year 5	Incomplete, ongoing
UNC	2	**Structural analysis of DW-MRI**		
UNC	2.1	DTI tractography tools	Year 4	Completed
UNC	2.2	Geometric characterization of fiber tracts	Year 5	Completed
UNC	2.3	Quant. anal. of diffusion along fiber tracts	Year 5	Completed
GaTech	1.1	ITK Implementation of PDEs	Year 2	Completed
GaTech	1.1	Applications to Core 3 data	Year 4	Completed
GaTech	1.2	New statistic models	Year 4	Completed
GaTech	1.2	Shape analysis	Year 4	Preliminary results and ongoing
GaTech	2.0	Integration in to Slicer	Year 4-5	Preliminary results and ongoing
MGH	1	**Registration**		
MGH	1.1	Collect DTI/QBALL data	Year 2	Completed
MGH	1.2	Develop registration method	Year 2	Completed
MGH	1.3	Test/optimize registration method	Year 3	In Progress
MGH	1.4	Apply registration on core 3 data	Year 5	In Queue
MGH	2	**Group DTI Statistics**		
MGH	2.1	Develop group statistic method	Year 2	Partially Complete
MGH	2.2	Apply on core 3 data	Year 5	In Queue
MGH	3	**Diffusion Segmentation**		
MGH	3.1	Collect DTI/QBALL data	Year 2	Completed
MGH	3.2	Develop/optimize segmentation algorithm	Year 3	In Progress
MGH	3.3	Integrate w/ tractography	Year 4	In Progress
MGH	3.4	Apply on core 3 data	Year 5	In Queue

MGH	4	**Group Morphometry Statistics**		
MGH	4.1	Develop/optimize statistics algorithms	Year 3	Complete
MGH	4.2	Develop GUI for Linux	Year 3	Partially Complete
MGH	4.3	Slicer integration	Year 3	In Queue
MGH	4.4	Compile application on Windows	Year 4	In Queue

Timeline Modifications

Group	**Aim**	**Milestone**	**Modification**
MIT	2.2	Methods to compare shape statistics	Removed, the effort refocused on registration necessary for population studies
MIT	2.4	Software infrastructure to integrate shape analysis tools into the pipeline for population studies.	New, partially completed
MIT	4	fMRI analysis including local and atlas-based priors for quantifying activation.	New, partially completed
Utah	2.2 (removed)	Feature-based brain image registration.	Shift emphasis to shape-based analysis/registration
Utah	2.1 (removed)	Cortical filtering and feature detection	Effort is subsumed by other Core 1 partners (e.g. see MGH/Freesurfer)
Utah	3.0 (removed)	Fast implementations of PDEs	Real-time filtering is de-emphasized in favor of shape/DTI analysis
Utah	2.1-2.3 (added, in place of cortical analysis)	Shape analysis	Nonparametric shape analysis added to address needs of core 3.
UNC	1.2	Develop medially-based shape representation	Remove
UNC	1.4	Develop generic cortical correspondence framework (Years 3-5)	New
UNC	2.4	DTI Atlas Building (Years 2--4)	New
GaTech	2.1	FA analysis	New
MGH	4.1 - 4.4	Group morphometry statistics	New

	added		

Core 2: Engineering

Core 2 Timelines and Milestones

Group	Aim	Milestone	Proposed time of completion	Status
GE	1	**Define software architecture**		
GE	1	Object design	Yr 1	Completed
GE	1	Identify patterns	Yr 3	Patterns for processing scalar and vector images, models, fiducials complete. Patterns for diffusion weighted imagery and fMRI ongoing.
GE	1	Create frameworks	Yr 3	Frameworks for processing scalar and vector images, models, fiducials complete. Frameworks for diffusion weighted imagery and fMRI ongoing.
GE	2	**Software engineering process**		
GE	2	Extreme programming	Yr 1-5	On schedule, ongoing
GE	2	Process automation	Yr 3	On schedule, ongoing
GE	2	Refactoring	Yr 3	Complete
GE	3	**Automated quality system**		
GE	3	DART deployment	Yr 2	Complete
GE	3	Persistent testing system	Yr 5	Incomplete
GE	3	Automatic defect detection	Yr 5	Incomplete
Kitware	1	**Cross-platform development**		
Kitware	1	Deploy environment	Yr 1	Complete

		(CMake, CTest)		
Kitware	1	DART Integration and testing	Yr 1	Complete
Kitware	1	Documentation tools	Yr 2	Complete
Kitware	2	**Integration tools**		
Kitware	2	File Formats/IO facilities	Yr 2	Complete (ongoing)
Kitware	2	CableSWIG deployment	Yr 3	Complete (integration ongoing)
Kitware	2	Establish XML schema	Yr 4	Incomplete
Kitware	3	**Technology delivery**		
Kitware	3	Deploy applications	Yr 1	Complete (ongoing)
Kitware	3	Establish plug-in repository	Yr 2	Incomplete
Kitware	3	Cpack	Yr 4-5	Incomplete
Isomics	1	NAMIC builds of slicer	Years 2--5	Complete
Isomics	1	Schizophrenia and DBP interfaces	Year 3---5	Partially completed, ongoing
Isomics	2	ITK Integration tools	Year 1---3	Completed
Isomics	2	Experiment Control Interfaces	Year 2---5	Migration from LONI to BatchMake Underway
Isomics	2	fMRI/DTI algorithm support	Year 2---5	Completed DTI, fMRI Ongoing
Isomics	2	New DBP algorithm support	Year 2---5	Ongoing

Isomics	3	Compatible build process	Year 1---3	Completed
Isomics	3	Dart Integration	Year 1---2	Completed, upgrades ongoing
Isomics	3	Test scripts for new code	Year 2---5	Ongoing
UCSD	1	Grid computing--- base	Year 1	Completed
UCSD	1	Grid enabled algorithms	Year 3	First version (GWiz alpha) available - initial integration with Slicer3 and execution model.
UCSD	1	Testing infrastructure	Year 4	Initiated
UCSD	2	Data grid --- compatibility	Year 2	Completed
UCSD	2	Data grid --- slicer access	Year 2	Completed for version 2.6. In progress for Slicer3
UCSD	3	Data mediation --- deploy	Year 1	Incomplete (modification below)
UCLA	1	Debabeler functionality	Year 1	Continued Progress
UCLA	2	SLIPIE Interpretation (Layer 1)	Year 1-- Year2	In Progress
UCLA	3	SLIPIE Interpretation (Layer 2)	Year 1-- Year2	On Schedule
UCLA	3	Developing ITK Modules	Year2	In Progress
UCLA	4	Integrating SRB (GSI-enabled)	Year2	Completed
UCLA	5	Integrating IDA	Year2	Completed
UCLA	5	Integrating External Visualization Applications	Year2	Completed

Core 2 Timeline Modifications

Group	Aim	Milestone	Modification
Isomics	3	Data mediation	Delayed pending integration of databases into NAMIC infrastructure

Core 3: Driving Biological Problems

The Core 3 projects submitted R01 style proposals, as specified in the RFA, and did not submit timelines.

Core 4: Service

Core 4 Timelines and Milestones

Group	Aim	Milestone	Proposed time of completion	Status
Kitware	1	**Implement Development Farms**		
Kitware	1	Deploy platforms	Yrs 1	Complete
Kitware	1	Communications	Yrs 1	Complete, ongoing
Kitware	2	**Establish software process**		
Kitware	2	Secure developer database	Yr 1	Complete, ongoing
Kitware	2	Collect guidelines	Yr 1	Complete
Kitware	2	Manage software submission process	Yr 1	Complete
Kitware	2	Configure process tools	Yr 1	Complete
Kitware	2	Survey community	Yr 1	Complete
Kitware	3	**Deploy NAMIC Tools**		
Kitware	3	Toolkits	Yr 1	Complete
Kitware	3	Integration tools	Yr 1	Complete
Kitware	3	Applications	Yr 1	Complete
Kitware	3	Integrate new computing resources	Yr 1	Complete
Kitware	4	**Provide support**		
Kitware	4	Establish support infrastructure	Yrs 1--5	On schedule, ongoing
Kitware	4	NAMIC support	Yr 1	Complete
Kitware	5	Manage NAMIC Software Releases	Yrs 1--5	On schedule, ongoing

Core 4 Timeline Modifications

Group	Aim	Milestone	Modification
Kitware	2-5	Various	Refined/modified the sub aims

Core 5: Training

Core 5 Timelines and Milestones

Group	Aim	Milestone	Proposed time of completion	Status
Harvard	1	**Formal Training Guidelines**		
Harvard	1	Functional neuroanatomy	Yr 1	Complete
Harvard	1	Clinical correlations	Yr 1	Complete
Harvard	2	**Mentoring**		
Harvard	2	Programming workshops	Yrs 1-5	On schedule, ongoing
Harvard	2	One-on-one mentoring, Cores 1, 2, 3	Yrs 1-5	On schedule, ongoing
Harvard	3	**Collaborative work environment**		
Harvard	3	Wiki	Yrs 1	Complete
Harvard	3	Mailing lists	Yrs 1	Complete
Harvard	3	Regular telephone conferences	Yrs 1-5	On schedule, ongoing
Harvard	4	**Educational component for tools**		
Harvard	4	Slicer training modules	Yr 2-5	Many complete for Slicer 2.x, Slicer 3 ongoing
Harvard	5	**Demonstrations and hands-on training**		
Harvard	5	Various workshops and conferences	Yrs 1--5	On schedule, ongoing (see also link)

Core 5 Timeline Modifications

None.

Core 6: Dissemination

Core 6 Timelines and Milestones

Group	Aim	Milestone	Proposed time of completion	Status
Isomics	1	Create a collaboration methodology for NA-MIC		
Isomics	1.1	develop a selection process	Yr 1	Done
Isomics	1.2	guidelines to govern the collaborations	Yr 1-2	Done
Isomics	1.3	Provide on-site training	Yr 1-5	On Schedule
Isomics	1.4	develop a web site infrastructure	Yr 1	Done
Isomics	2	Facilitate communication between NA-MIC developers and wider research community		
Isomics	2.1	develop materials describing NAMIC technology	Yr 1-5	On Schedule
Isomics	2.2	participate in scientific meetings	Yr 2-5	On Schedule
Isomics	2.3	Document interactions with external researchers	Yr 2-5	On Schedule
Isomics	2.4	Coordinate publication strategies	Yr 3-5	On Schedule
Isomics	3	Develop a publicly accessible internet resource of data, software, documentation, and publication of new discoveries		
Isomics	3.1	On-line repository of NAMIC related publications and presentations	Yr 1-5	On Schedule
Isomics	3.2	On-line repository of NAMIC tutorial and training material	Yr 1-5	On Schedule
Isomics	3.3	Index and a searchable database	Yr 1-2	Done
Isomics	3.4	Automated feedback systems that track software downloads	Yr 3	Done

Core 6 Timeline Modifications

Group	Aim	Milestone	Modification
Isomics	3.1	On-line repository of NAMIC related publications and presentations	Duration of this extended to the full grant cycle.

Appendix A Publications

http://www.na-mic.org/Wiki/index.php/Publications

Peer Reviewed Journal Papers

1. Nakamura M, McCarley RW, Kubicki M, Dickey CC, Niznikiewicz MA, Voglmaier MM, Seidman LJ, Maier SE, Westin CF, Kikinis R, Shenton ME. Fronto-temporal disconnectivity in schizotypal personality disorder: a diffusion tensor imaging study. Biol Psychiatry. 2005 Sep 15;58(6):468-478.

2. Tuch DS, Salat DH, Wisco JJ, Zaleta AK, Hevelone ND, Rosas HD. Choice reaction time performance correlates with diffusion anisotropy in white matter pathways supporting visuospatial attention. Proc Natl Acad Sci U S A. 2005 Aug 23;102(34):12212-7.

3. Tuch DS, Wisco JJ, Khachaturian MH, Ekstrom LB, Kotter R, Vanduffel W. Q-ball imaging of macaque white matter architecture. Philos Trans R Soc Lond B Biol Sci. 2005 May 29;360(1457):869-79.

4. Niethammer M, Vela P, Tannenbaum A. On the evolution of closed curves by means of vector distance functions. Int. Journal Computer Vision, 2006.

5. Niethammer M, Tannenbaum A, Angenent S. Dynamic active contours. IEEE Trans. Automatic Control. 2006; 51:562-579.

6. Turner JA, Smyth P, Macciardi F, Fallon JH, Kennedy JL, Potkin SG. Imaging phenotypes and genotypes in schizophrenia. Neuroinformatics. 2006;4(1):21-49. PDF

7. Cascio C, Styner M, Smith RG, Poe M, Gerig G, Hazlett H, Jomier M, Bammer R, Piven J. Reduced relationship to cortical white matter revealed by tractography-based segmentation of the corpus callosum in young children with developmental delay. Am J Psychiatry 163:12, December 2006.

8. Corouge I, Fletcher PT, Sarang J, Gouttard S, Gerig G. Fiber Tract-Oriented Statistics for Quantitative Diffusion Tensor MRI Analysis. Medical Image Analysis), 768-798.

9. Martin K, Hoffman B. An Open Source Approach to Developing Software in a Small Organization. IEEE Software. January/February 2007 (Vol. 24, No. 1).

In Press

1. Gilmore JH, Lin W, Corouge I, Vetsa Y, Sampath K, Smith JK, Kang C, Gu H, Hamer RM, Lieberman JA, Gerig G. Early postnatal development of corpus callosum and corticospinal white matter assessed with quantitative tractography, accepted AJNR-07-00044 (American Journal of Neuroradiology), in press, 2007.

2. Nain D, Haker S, Bobick A, Tannenbaum A. "Multiscale 3D Shape Representation and Segmentation using Spherical Wavelets", in press, IEEE Transactions on Medical Imaging Special issue on Computational Anatomy.

3. Liu T, Young G, Huang L, Chen N-K, Wong S. "76-space Analysis of Grey Matter Diffusivity: Methods and Applications," in press, NeuroImage.

4. O'Donnell L, Kubicki M, Shenton ME, Dreusicke MH, Grimson WEL, Westin CF. A method for clustering white matter fiber tracts. AJNR (In Press).

5. Koo MS, Levitt JJ, McCarley RW, Seidman LJ, Dickey CC, Niznikiewicz MA, Voglmaier MM, Zamani P, Long KL, Kim SS, Shenton ME. Reduction of caudate volume in neuroleptic-naive female subjects with schizotypal personality disorder. Biol Psychiatry (In Press).

6. Kuroki N, Kubicki M, Nestor PG, Salisbury DF, Park HJ, Levitt JJ, Woolston S, Frumin M, Niznikiewicz M, Westin CF, Maier SE, McCarley RW, Shenton ME. Fornix integrity and hippocampal volume in male schizophrenic patients. Biol Psychiatry (In Press).

7. Onitsuka T, Niznikiewicz MA, Spencer KM, Frumin M, Kuroki N, Lucia LC, Shenton ME, McCarley RW. Schizophrenia is associated with functional and structural deficits in brain regions subserving face processing. Am J Psychiatry (In Press).

8. Niethammer M, Tannenbaum A, Kalies W, Mischaikow K. Detecting simple points in higher dimensions. IEEE Image Processing, 2006. (In Press).

9. Rathi Y, Dambreville S, Tannenbaum A. Comparative analysis of kernel methods for statistical shape learning. CVAMIA'06, 2006. (In Press).

10. Roth RM, Koven, NS, Randolph JJ, Flashman LA, Pixley HS, Ricketts SM, Wishart HA, Saykin AJ. Event-Related fMRI study of Functional magnetic resonance imaging of executive control in bipolar disorder. NeuroReport, 2006 (In Press).

11. Pohl KM, Fisher J, Grimson WEL, Kikinis R, Wells WM. A bayesian model for joint segmentation and registration. NeuroImage, 2006 (In Press).

12. Fletcher PT, Joshi S. Riemannian Geometry for the Statistical Analysis of Diffusion Tensor Data. Signal Processing, 2006. (In Press).

Peer Reviewed Conference Proceedings

Conferences included here represent the major high quality conferences in medical image analysis (MICCAI, IPMI, MMBIA, ISBI). These conferences only accept submission of full papers and guarantee a peer review process by at least three reviewers and an area chair. Acceptance rates are below 40% for MICCAI, IPMI and MMBIA and around 50% for ISBI.

1. Maddah M, Wells WM, Warfield SK, Westin CF, Grimson WEL, Probabilistic Clustering and Quantitative Analysis of White Matter Fiber Tracts, IPMI 2007, Netherlands.

2. Styner M, Xu SC, El-Sayed M, Gerig G, Correspondence Evaluation in Local Shape Analysis and Structural Subdivision, IEEE Symposium on Biomedical Imaging ISBI 2007, in print

3. Zhou C, Park DC, Styner M, Wang YM, ROI Constrained Statistical Surface Morphometry, IEEE Symposium on Biomedical Imaging ISBI 2007, in print

4. Nain D, Styner M, Niethammer M, Levitt JJ, Shenton ME, Gerig G, Bobick A, Tannenbaum A. Statistical Shape Analysis of Brain Structures using Spherical Wavelets. Accepted in The Fourth IEEE International Symposium on Biomedical Imaging (ISBI '07), April 12-15, 2007, Washington DC, USA.

5. Kim S, Smyth P. Hierarchical Dirichlet processes with random effects. Advances in Neural Information Processing Systems 19, to appear, 2006.

6. Kim S, Smyth P, Stern H. A nonparametric Bayesian approach to detecting spatial activation patterns in fMRI data. To appear in MICCAI, Oct 2-5, 2006. PDF

7. Nain D, Haker S, Bobick A, Tannenbaum A. Shape-driven surface segmentation using spherical wavelets. MICCAI, LNCS 4190, Oct 2-5, 2006.

8. Goodlett C, Davis B, Jean R, Gilmore J, Gerig G. Improved Correspondence for DTI Population Studies via Unbiased Atlas Building. Proceedings of MICCAI, 2006. PDF

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