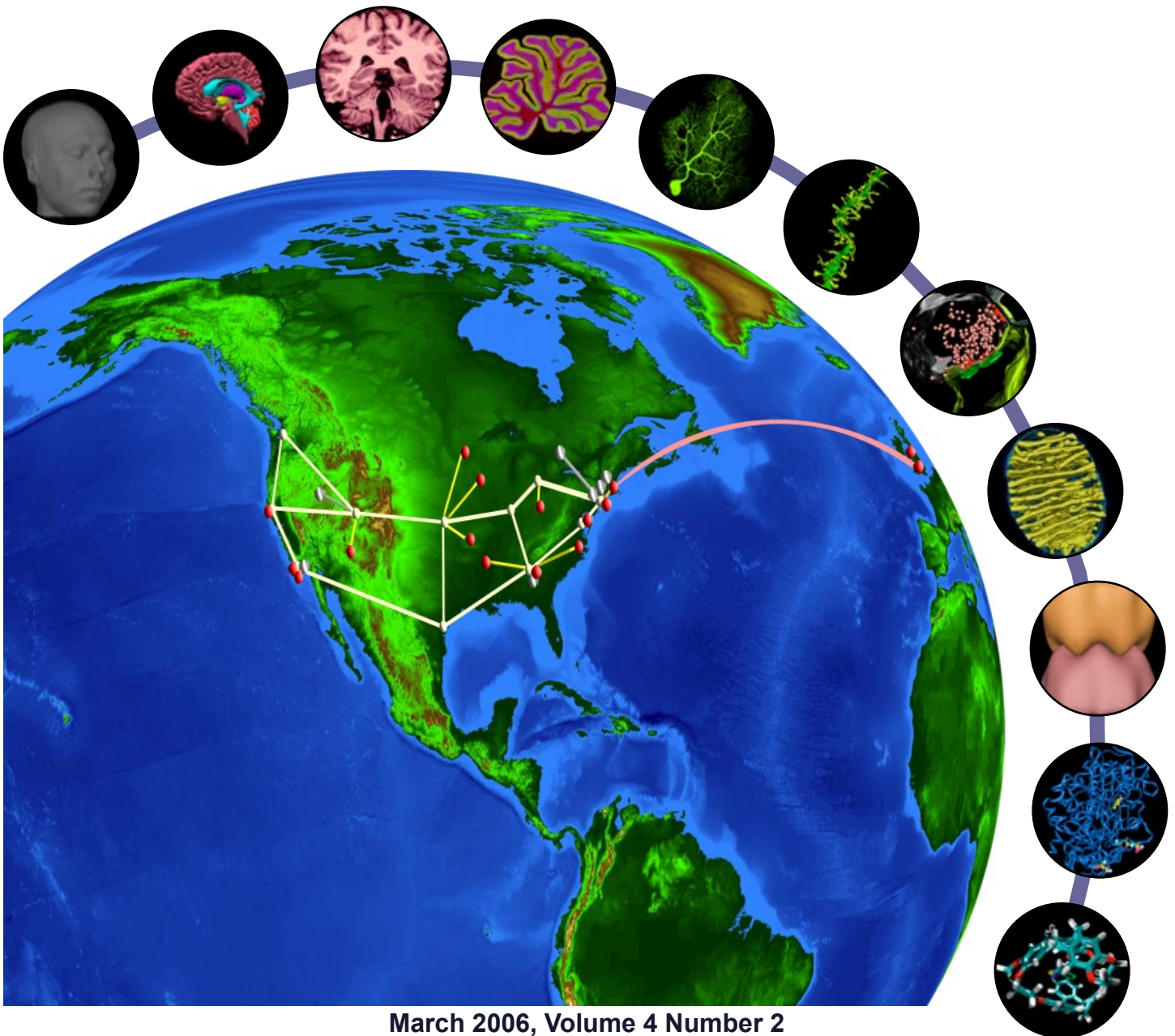


BIRNing issues

BIOMEDICAL INFORMATICS RESEARCH NETWORK



March 2006, Volume 4 Number 2

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Ontology Boot Camp

by Maryann Martone and Skip Cynar

The first of several Ontology Boot Camps was hosted at the BIRN Coordinating Center at UCSD's School of Medicine January 26-27, 2006. Thirteen scientists from UC Irvine, UCLA, Stanford, UCSD, Duke, University of Tennessee Memphis, University of Texas Health Science Center San Antonio, the NIH, and Drexel University participated in person and by video teleconference with more than a dozen scientists and programmers from UCSD. BIRN's Ontology mapping software, Bonfire, was an integral part of the camp. The overarching goal of boot camp: Make BIRN databases and data understandable to human and machine!

The Ontology Task Force (Carol Bean, Maryann Martone, co-chairs; Bill Bug, Jeff Grethe, Amarnath Gupta, Christine Fennema-Notestine, Jessica Turner) organized the two day boot camp. Maryann offered inspirational words to the group during the opening session:

This [mapping to an ontology] isn't an easy process. If it were, we would have this done. I don't think we are going to get it perfectly, but it will help.

Given the complexity of implementing consensus-derived solutions over just two days, the boot camp was a surprising success. The following are some highlights of the meeting.



Members of the Function and Morphometry test beds made progress in mapping terms to the Unified Medical Language System (UMLS). They identified key concerns and limitations in using several UMLS concepts for generic human experimental descriptions and used trial and error to define "best practices" for submitting new concepts. A goal was set to demonstrate a semantic query via the mediator at the FBIRN All Hands Meeting, held March 13-14 at UC Irvine. This goal was met. Follow-up meetings are scheduled with BrainMap collaborators regarding cognitive terms and concepts.

The Human Imaging Database table names and fields were identified. The task of defining each one was initiated. Function and Morphometry test bed members assigned mapping tasks for remaining schema and contents.

Mouse BIRN Ontology members began mapping anatomical terms from the mouse atlas to the structural hierarchy provided by Neuronames. They established a standard schema for entering species, strain, genotype and phenotype information on subjects.



Ontologists are encouraged to investigate the Foundational Model of Anatomies (FMA) knowledge base. The

FMA is a domain ontology representing a coherent body of declarative knowledge about human anatomy. For a trial period, it will join the UMLS and Neuronames databases available through BONFIRE, BIRN's ontology editing environment. Following the initial trial period, the BIRN-CC will evaluate an option to secure a long-term license. Additional information about FMA is available on the University of Washington's FMA Web site. <http://sig.biostr.washington.edu/projects/fm>


Ontology Boot Camp



January 26-27 – Members of the Ontology Boot Camp hard at work in the BIRN-CC conference room in La Jolla, Calif.

All terms mapped by the sources to UMLS will be provided on the BIRN ontology page as “BIRNLex”. Maryann and Jeff will assemble all of the newly edited terms from the boot camp and post to the BIRN’s ontology page. This list will serve as the basis for developing curatorial procedures for BIRN.

At the beginning of the boot camp, Bill Bug of Drexel University, who is credited with the inspiration behind the camp, quipped, “This is the first meeting, so even the process is a work-in-progress.” The significant outcomes of the meeting, given this starting point, attest to the dedication and hard work by all of the boot camp participants. ■



Feb 28–Mar 1. Elaine Collier and Bret Peterson of NIH-NCRR joined the BIRN Ontology Task Force members in an ontology tutorial at Stanford University’s Medical School. Hosted by the National Center for Biomedical Ontology (NCBio), the two day workshop featured presentations and discussions with NCBio collaborators, including Daniel L Rubin (Stanford), Mark Musen (Stanford), Barry Smith (University of Buffalo), and Suzanna Lewis (Lawrence Berkeley Natl. Labs). An overview of the NIH sponsored Center for Biomedical Ontology is available at <http://bioontology.org/overview.html>.



From organism to macromolecules, neuroscience research spans several orders of magnitude. The BIRN is on the forefront of building an infrastructure of data integration standards and other emerging technologies, to link data across these scales and pave the way for biomedical researchers to transform the treatment of disease.

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Jason Novotny: GridSphere Architect

by Skip Cynar, UCSD

Jason Novotny is one of the nation's leading portal architects for Grid computing and the chief architect of the GridSphere portal framework. Working out of the BIRN-CC in La Jolla, Jason is overseeing the development of the production research portal for the BIRN. Jason has been involved in distributed computing research and Grid computing since 1999, authoring the Grid Portal Development Kit (GSDK) and co-authoring the MyProxy online credential repository software. His interests include distributed computing frameworks and middleware, distributed system security, high performance networking, and tools for developing distributed computing applications using Java. Jason has been involved with developing and deploying distributed applications and Grid middleware for the U.S. Dept. of Energy's Science Grid, the NCSA/Alliance Virtual Machine Room (VMR), and the NASA Information Power Grid (IPG), and he has been an active participant in Grid Forum since its inception. He is a member of the Expert Group for JSR-286, the Java Portlet Specification.

Q. What is your current role in the BIRN-CC?

A. I'm leading a team of programmers to develop the new BIRN Portal. It is our goal to develop a standards-based Portlet framework for BIRN's Portal and create new Portlet Web applications to provide an enhanced Grid portal development solution. The BIRN Portal provides a terrific opportunity to test and expand GridSphere robustness and collaborative capabilities in the BIRN test beds.

Q. How did you get started in developing software for Grid Portals?

A. I've been working in the area of Grid portals since 1999 and started one of the first portals for accessing grid services while I was working at NASA Ames for the Information Power Grid (IPG) Project, one of the early grid deployment efforts.



Jason Novotny, BIRN-CC Portal Architect

The IPG deployed infrastructure at all of the NASA Centers and developed end-user environments, or portals, for accessing those resources. That is how I got involved in developing what became the Grid Portal Development Kit, GSDK. That took off and I was amazed at how many downloads we were getting from folks interested in doing the very same thing. It proved that what we were doing at the time was not some wild, pie-in-the-sky idea, but something that a lot of people around the world were trying to achieve.

Q. How did you come to co-found GridSphere?

A. In 2002, Grid computing was beginning to take off. My mentor, Edward Seidel of the National Center for Supercomputing Applications (NCSA), became the leader of the European Union's GridLab project. I left the Lawrence Berkeley National Labs and joined his group at the Albert Einstein Institute in Berlin, Germany. One of the key objectives of the GridLab project was the development of a portal that would allow astrophysicists to launch numerical relativity computer simulations. My colleagues, Michael Russell and Oliver Wehrens, and I set ourselves the task of finding a Grid portal framework that would provide a seamless environment for doing this. At the time, one of the best open-source portals was JetSpeed, who coined the popular Portlet concept for those small pieces of screen real estate able to serve up specific functionality. Even IBM adopted the Portlet concept within their WebSphere application server. We thought

there was a good chance that Portlets were on their way to becoming a *de facto* standard. We couldn't find any such software, so we accepted the challenge of developing our own from scratch.

We analyzed IBM's WebSphere functionality in developing our own open-source portal, targeting the needs of the GridLab community. I wrote the first line of code in August 2002. Submerged in a grandiose vision of developing a robust framework that could be applied to other application communities beyond astrophysics, we opted to channel our efforts using

standards and emerging standards. Several months of hard work into the GridLab project, the project leaders asked us to show them what we were doing. Proud of our systematic effort to create a standardized code base, we were expecting a few words of praise. Instead we received strong criticism regarding the lack of a deliverable portal. Ed Seidel scolded me, "I would fire you but we don't even have a portal yet." Now there is irony.

We were vindicated later in building software that would garner thousands of downloads from all over the world. When we officially released GridSphere 1.0 in September 2003, there was not yet an official Portlet standard. The Java Specification Request (JSR) 168 Portlet API was ratified in October 2003, marking a major turning point for GridSphere, when all of the major applications vendors, such as Sun, Oracle, IBM, HP and others agreed to a common standard. We were excited because we were one of the first open-source providers of portal software. After the Portlet standard came out, it took us only five more months to have a compliant implementation of GridSphere, passing all 370 tests in the JSR-168 Technology Compatibility Kit. This was an incredible win for us, claiming compliance in early 2004. We realized our goal—providing a turn-key grid portal solution for the academic community.

Q. What are some of the most urgent challenges in your current grid portal development?

A. We face a lot of issues involving scalability and robustness, for example, how many concurrent BIRN portal users we can support. We don't have the answers to those questions yet. Part of the problem with component design is the unexpected inter-

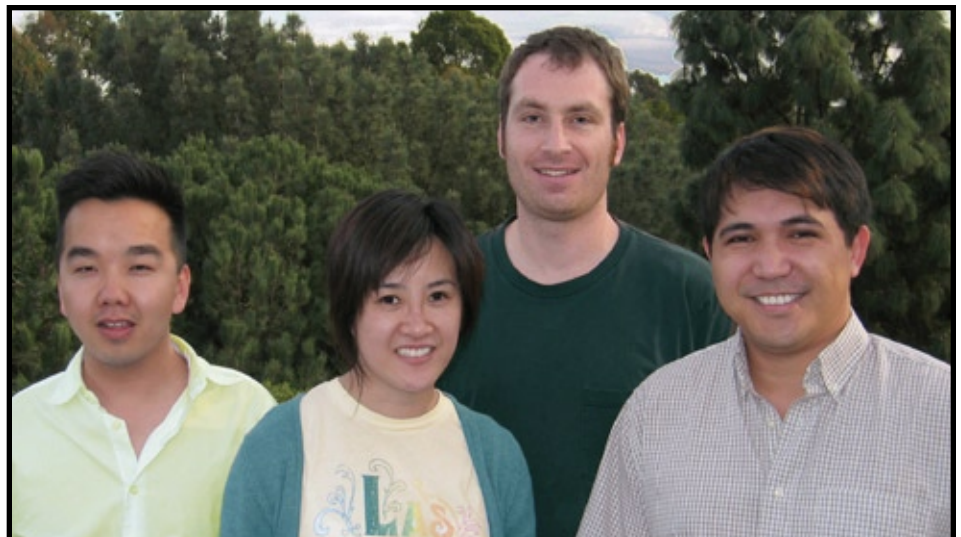
actions or collisions among components. My most pressing concern is making the transition from the present BIRN portal sans standards to GridSphere's standards-compliant environment. Quite a bit of development has gone in just to get to the point where we are now. We're at a pre-alpha stage. Our Portals team is making solid progress on retaining much of the original functionality.

Thien Nguyen and Ramil Manansala are doing a remarkable amount of work to develop the functionality planned for the BIRN Portal. In addition, Jana Nguyen is focused on security, deployment, and database setup. One of the big advantages of adopting a Portlets approach is that each programmer can focus on a unique piece of the puzzle without worrying about how his work will fit together with other programmers' work. Ramil is currently developing the Storage Resource Broker (SRB) file browser Portlet so that BIRN users will have improved access to the SRB to download and upload their data. Thien has recently been developing collaboration Portlets so that scientists may initiate new projects

and allow others to subscribe, allowing communities to be created on the fly. The Portal will be thoroughly tested in-house before we release it to the biomedical community. We are getting close to a point where we can begin rolling out a beta version of the new BIRN Portal.

Q. Any advice for students considering a career in computer science?

A. Remember that developing software is like playing a game. There are lots of puzzles to solve and new challenges around every corner. Software is never really finished. There is always a bug to fix or a new feature to develop. Part of the fun of research is that I'm always playing with new ideas. You are working on questions that no one may have an answer to. In the words of Einstein, "If we knew what we were doing, it would not be called research." ■



BIRN-CC Portal team: Thien Nguyen, Jana Nguyen, Jason Novotny and Ramil Manansala

Compute Cluster contributes to Morph BIRN study on morphometric changes in mild cognitive impairment.

BIRN's 64 processors AMD/Opteron compute cluster is getting plenty of use by Anthony Kolasny (Johns Hopkins University). He has been using the Large Deformation Diffeomorphic Metric Mapping (LDDMM) tool, an application to assign metric distances onto anatomical images in order to permit direct comparison and quantification of morphometric changes in shapes for the analysis of shape change. To date, Anthony has processed over 1,500 jobs. The BIRN resource compute cluster is a dedicated resource and available to all sites for their computation-intensive processing.

BIRN Portal Development

Starting with the BIRN 3.0 release, the BIRN Portal environment will run in GridSphere, an open-source Portlet-based Web portal (see related profile of Jason Novotny, co-founder of Gridsphere, p. 4). The new BIRN Portal will feature several standard Portlets for enhancing the user's collaborative work environment, including Portlets to:

- Allow users an easy way to create public and private projects
- Create discussion forums among BIRN individuals or groups
- Send E-mail within a handy stand-alone client
- Set up automated notification via RSS feed
- Manage lists—e.g., to-do lists, contact lists, etc.
- Keep expanded member profiles—e.g., contacts manager
- Store and share photos
- Blog, for anyone wishing an alternative to discussion forums

All standard SRB processing features are converted to run under GridSphere. The incorporation of icons to represent routine tasks in the new graphical user environment will facilitate uploading, downloading, assignment of metadata, permissions processing and auditing.

New BIRN Sites

The BIRN welcomes two new sites that have recently become operational:

- Emory University, Yerkes National Primate Research Center
- NIH—Center for Information Technology, National Database for Autism Research (NDAR)

Secure communication options available through the new BIRN Wiki

The BIRN community requested that a secure wiki be made available (i.e., password protected sections). This wiki environment is for communication among BIRN researchers. Current BIRN participants have been utilizing an open access Wiki (the NA-MIC Wiki). In order to provide seamless access to Wiki functionality within the BIRN infrastructure, the BIRN-CC has reviewed candidate Wiki tools and selected a communication tool that would also meet the expectations of the BIRN community and the requirements of operating within the BIRN portal.

The BIRN xWiki environment is available to all BIRN Portal users (within the Collaboration Tools menu tab). In addition, xWiki permits users to create and control permissions to sections of the Wiki. This feature will allow working groups to secure portions of their Wiki space. ■



What is a Wiki? — A Wiki is a simplified system of generating Web content that records and catalogues revisions, so entries may be reverted to a previous state. Wikis enable collaborative document authoring using any Web browser. BIRN's new xWiki is a professional version with features for enterprise-level application. XWiki is written in Java and uses an underlying relational database management system.

Morphometry BIRN Update

by Karl Helmer and Randy Gollub

Karl Helmer has assumed the position of the Morphometry BIRN Project Manager as of February 1, 2006. Previously he was a Research Assistant Professor in the Department of Biomedical Engineering at Worcester Polytechnic Institute, where he focused on determining structural changes in tissue brought about by disease or therapeutic intervention using diffusion-weighted imaging (DWI) and the optimization of DWI contrast. His interest in image protocol standardization and the effects of changes in scanner hardware on image quality began when he was part of an fMRI study in which he suffered through three software upgrades and one vendor change. He can be reached at 671.726.8626 and by e-mail at helmer@nmr.mgh.harvard.edu.



Karl Helmer, Ph.D.,
Mass. General Hospital

Morphometry BIRN at Spring Brain Conference

Christine Fennema-Notestine, Ph.D. will present a talk entitled "Morphometry BIRN: Structural MRI provides a myriad of information to advance our understanding of neurodegenerative disease" at the Spring Brain Conference in Sedona, AZ as part of an invited workshop led by Randy



Christine Fennema-Notestine, Ph.D.,
UCSF Department of Psychiatry

Gollub, M.D., Ph.D. Chris will discuss active projects on multi-site calibration and emphasize recent work pooling valuable, well-curated legacy and prospectively gathered data sets from structural MRI studies of Alzheimer's disease. This talk has the goal of disseminating the Morphometry BIRN's approaches, methods, and results to the larger scientific community. The URL for the conference is www.springbrain.org.

Sedona Meeting

The Morphometry BIRN All-Hands-Meeting will be held March 19-21, 2006 in Sedona, Ariz. The agenda for the meeting is posted at www.na-mic.org/Wiki/index.php/Mbirn:Spring-Conference2006. Three significant pieces of software will be introduced to the Morphometry BIRN community during the meeting. First is the new eXtensible Neuroimaging Archive Toolkit (XNAT) release which will be presented by Dan Marcus (Washington University, St. Louis). XNAT is an environment for developing experimental data archives in which relational databases can be used to query non-imaging data and imaging data can be stored in standardized directory structures. Second is a demonstration of functioning workflows from the BIRN portal, presented by

Shawn Murphy (Harvard-MGH). This will allow the launching of workflows from mature pipelines such as LONI. Third, Steve Pieper will present the MBIRN-wide deployment of the BIRND-UP de-identification software tools and lead a hands-on workshop to train investigators.

FreeSurfer 3.0

Release 3.0 of FreeSurfer, a brain imaging analysis tool developed by Morphometry BIRN collaborators at the Massachusetts General Hospital in Boston was released on March 5, 2006. Features of the latest version include:

- Online tutorial for workflows
- Simplified distribution, download, and installation
- Support for 64bit Linux and Mac OS X platforms
- Fully updated wiki-based documentation (<https://surfer.nmr.mgh.harvard.edu/fswiki/Free-SurferWiki>)
- Subcortical segmentations (Fig.1)
- Automated filling of ventricles and basal ganglia
- Improved skull-stripping and cutting plane definition
- Surface-based General Linear Model analysis ■

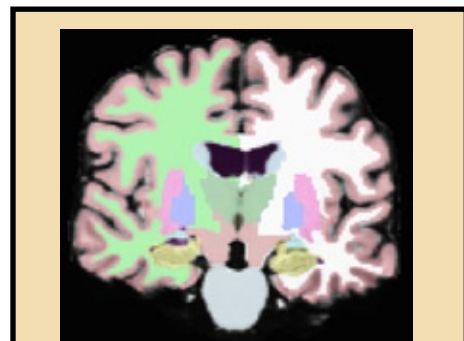


Fig. 1 — An example of FreeSurfer's new subcortical segmentation functionality. The structures identified include: caudate, putamen, pallidum, amygdala, hippocampus, thalamus, ventricles, cortex, and white matter. FreeSurfer also generates volume statistics, allowing group analysis.

Mouse BIRN Update

by Jyl Boline and Diana Price

BIRN's Mouse Test Bed experienced several exciting developments this past quarter, including advances in several core areas and new opportunities for distributing Mouse BIRN tool and data resources. Here is a summary of these highlights.

Mouse BIRN Resources at Annual Society for Neuroscience (SfN) Meeting

Mouse BIRN representatives distributed a package of resources at the SfN meeting last fall. These resources were detailed in the November 2005 issue of BIRN's Newsletter at <http://nbirn.net/Publications/Newsletter/index.htm>. In brief, they included the beta release of the Mouse BIRN Atlasing Toolkit (MBAT), access to multiple datasets, and other resources shared by the group. CDs containing MBAT and how to access these new resources were distributed at the meeting and can be found at www.nbirn.net/Resources/Downloads. Information about the mouse BIRN and demonstrations of MBAT were met with enthusiasm by a number of SfN attendees. Since then, members of the mouse BIRN group have been contacted by several people interested in the work of our group and our resources.

Advances in Data Acquisition

Researchers at the National Center for Microscopy and Imaging Research have developed a method for imaging large regions of brain at close to the resolution limit of light microscopy using a mosaic imaging technique in conjunction with multiphoton microscopy. These maps are being used to characterize Parkinson's Disease (PD) related proteins in the central nervous system of the alpha-synuclein transgenic mouse

model. These data fill in the information "gap" in the mouse BIRN multi-scale imaging techniques of whole brain MR and electron microscopy (Fig. 1).

A manuscript detailing the practical and application aspects of this imaging technique is scheduled for publication in a Spring 2006 Special Issue of *Neuroinformatics*.

Price DL, Chow SK, MacLean NAB, Hako-zaki H, Peltier S, Martone ME, Ellisman MH (2006) High-resolution large-scale mosaic imaging using multiphoton microscopy to characterize transgenic mouse models of human neurological disorders. *Neuroinformatics* 4(1):65-80.

Digital archives of the cerebellum and hippocampus mouse brain datasets are available for online viewing and download through the Cell Centered Database and the Biomedical Informatics Research Network (BIRN) at www.nBIRN.net. The Cell Centered Database is an online resource for 3D Light and electron microscopic data (www.ncmir.ucsd.edu/CCDB).

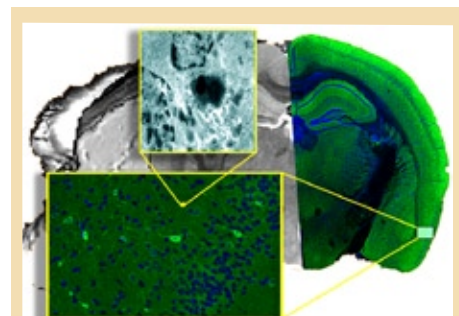


Fig. 1. Large scale mosaic used in conjunction with 3D MRI volume from collaborator Duke-CIVM, and electron microscopic analysis from UCSD-NCMIR. The area sampled by the mosaic was directed by the MRI and shows detailed views of cellular and subcellular structure which directed the location of the EM sample.

Global Conceptual Schema

All of the Mouse BIRN participants have been working with the BIRN-CC on data mediation on a Global Conceptual Schema (GCS) that can be readily queried to access the multi-modal mouse BIRN data types. Major changes have recently been made to extend the GCS to accommodate genetic and genomic resources with the help of the group at The University of Tennessee Health Science Center (Rob Williams, Hongqiang Li, and Jintao Wang).

Mapping to the BIRN Mediator

Mouse BIRN in conjunction with the BIRN-CC has begun mapping site databases to the BIRN Mediator using ontologies. These ontological tags will identify tables, fields, or views within the database. Initiated at the Ontology Boot Camp on January 26-27, 2006 (see page 2), we began to create a set of mappings to be referenced during this process.

Linking Ontologies and Atlasing

Several members of the Mouse BIRN participated in the Ontology Boot Camp. Much of our focus was on mapping anatomical terms used by members of Mouse BIRN in their mouse atlases to structural hierarchies within BIRN's Bonfire Ontology editor. Once these extensions are committed to Bonfire, this knowledge base will be used to map between and across structural hierarchies. Our goal is to access and view these new hierarchies using the Mouse BIRN Atlasing Toolkit (MBAT). To date, we added 41 new terms of neuroanatomy and experimental methodology and linked another 40 anatomical terms into the NeuroNames hierarchy. ■

Function BIRN: The Next Phase of Multi-site Neuroimaging Methods

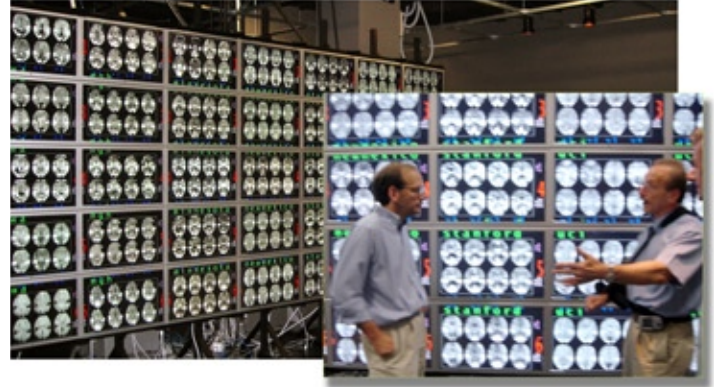
by Jessica Turner

As of December 1 2005, Function BIRN has entered a new phase of research. In its first three years, from 2002 to 2005, the consortium developed several multi-site neuroimaging protocols, tested them by scanning a group of traveling volunteers at each of several research sites, revised the protocols based on these data, and subsequently used the improved protocols to acquire imaging, behavioral, and clinical data on over 200 subjects across all the sites. In this process, many calibration methods and multiple correction techniques were tested. The Human Imaging Database schema was conceived, implemented, redesigned, and re-deployed on two popular platforms, Oracle and Postgres, at multiple sites, and most recently, populated with imaging and demographic data across all the sites. The Phase I traveling subject data is now available to the research community on the BIRN portal. The Human Imaging Database schema has been disseminated as an extensible method for storing imaging experiments. Our Quality Assurance (QA) methods for scanners have been made public with the agar phantoms for the QA methods becoming a popular item. fMRI sites are using the tools to assess the scan quality. FBIRN methods are helping several other multi-site imaging consortia to embark on their own unique studies.

FBIRN now begins its second phase. Analyses are underway on the huge imaging dataset of schizophrenia subjects collected in our national effort. How well do our calibration and correction methods work to reduce the ever present yet undesirable inter-site differences observed in the scanning data? Which ones work best?

Of our automated methods for processing terabytes of imaging data, which methods are the most efficient and the most accurate? For the most discriminating analyses, what differences can we discern between patient and non-patient data and what does that tell us about the disease? These are some of the questions many FBIRN collaborators will be asking as we evaluate our findings and gear up for the next round of traveling subjects.

We are busy developing new ways of discriminating subject from site differences in fMRI data using Arterial Spin Labeling (ASL). ASL refers to the magnetic labeling of the arterial blood flow in order to induce a different magnetic state of the blood that will contrast with the magnetic state of the brain tissue. Current efforts are focused on testing new cognitive tasks for exploring brain function more thoroughly, improving how federated databases interact with the HID and the Storage Resource Broker for sharing and retrieving many datasets, and refining the tools to automate analysis. Database concepts are being mapped to standard terms in the Unified Medical Language System (UMLS). With this mapping, common queries across both FBIRN and other databases with a completely different organization, such as BrainMap (www.brainmap.org), are easily performed.



A recent and animated discussion between Steven Potkin, FBIRN PI, and Hal Stern, Statistics Working Group Co-Chair, regarding FBIRN traveling subject data.

FBIRN held its annual All Hands Meeting on March 13 and 14 at the National Academy of Sciences' Beckman Center on the campus of the University of California, Irvine. Progress across FBIRN's efforts was presented and future milestones were scheduled. This meeting was an exciting and productive time as we made progress developing the next generation of multi-site functional neuroimaging tools and methods.

Recent publications

Keator DB, Gadde S, Grethe J, Taylor D, BIRN F and Potkin SA. General XML schema and associated SPM toolbox for storage and retrieval of neuroimaging results and anatomical labels. *Neuroinformatics*. In press

Magnotta VA, Friedman L and BIRN F. Measurement of signal-to-noise and contrast-to-noise in the FBIRN multi-center imaging study. *Journal of Digital Imaging*. In press.

Thomason ME, Foland LC and Glover GH. Calibration of BOLD fMRI using breath-holding reduces group variance during a cognitive task. *Human Brain Mapping*. In press. ■

What is the BIRN?

The Biomedical Informatics Research Network Growing Collaborative Biomedical Research Through Technological Advances

Drawing upon the expertise and technologies available at numerous institutions, the Biomedical Informatics Research Network (BIRN) is building an infrastructure of networked high-performance computers, data integration standards, and other emerging technologies, to pave the way for medical researchers to transform the treatment of disease.

Launched in 2001 as an initiative of the National Institutes of Health's National Center for Research Resources, the BIRN is prototyping a collaborative environment for biomedical research and clinical information management.

A central component of the BIRN is its Coordinating Center, overseeing the networking, distributed storage, and software development needs of the three neuroimaging test beds.

The Function BIRN Test Bed is employing functional neuroimaging to explore the underlying causes of schizophrenia and to subsequently assess the impact of new

treatments on functional brain abnormalities.

The Brain Morphometry Test Bed is focused on pooling acquired data across neuroimaging sites to investigate if specific anatomical differences are diagnostic of specific memory dysfunctions, such as depression, mild Alzheimer's disease, and mild cognitive impairment.

Collaborators in the Mouse BIRN Test Bed are utilizing multi-modal and multi-scale imaging data from mouse models of neurological disorders to better understand schizophrenia, Parkinson's disease, multiple sclerosis, attention-deficit hyperactivity disorder, and

brain cancer.

The newest test bed is the Non-human Primate BIRN. The Yerkes National Primate Research Center will participate in the development of a new test bed for linking brain imaging, behavior, and molecular informatics in preclinical models of neurodegenerative disease. ■



The growing BIRN infrastructure is enabling fundamentally new capabilities in large-scale studies of human disorders. Currently, 31 universities and hospitals and 39 research groups participate in one or more of the four test beds and associated collaborative projects. Print and Web versions of the up-to-date map as well as other images are available for download at <http://nbirn.net/Publications/Articles/press-temp.htm>.