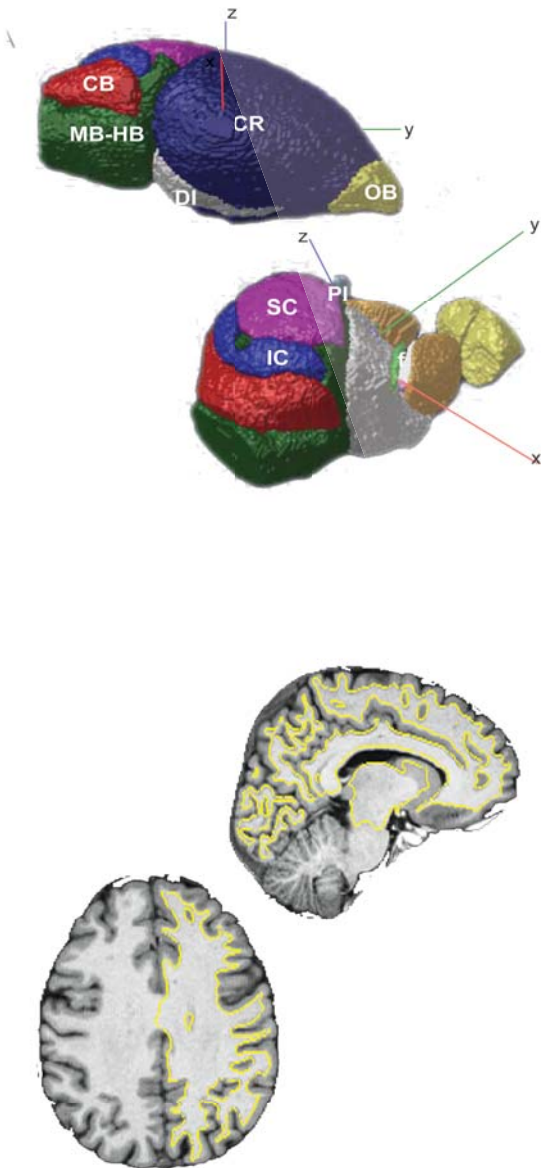


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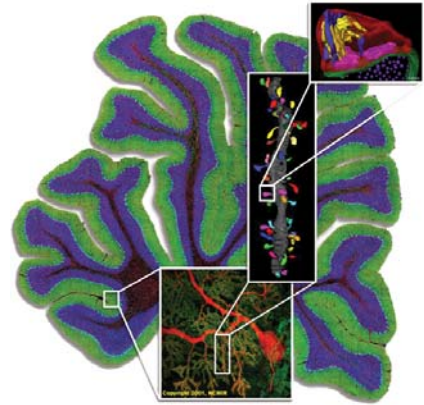
BIOMEDICAL INFORMATICS RESEARCH NETWORK



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BIRN Provides a Useful Suite of Research Tools and Datasets

The Biomedical Informatics Research Network is committed to an open source policy. In every case of tool development, BIRN developers produce open source software tools which will be made available without restrictions. Data will also be openly shared and made available with no restrictions other than subject confidentiality. The following are the current suite of BIRN tools and data available to researchers.

Tools

Data Acquisition Protocols and Best Practices

Eprime Programs Phase I Traveling Subjects (Function BIRN)

- Used during the 2003 Function BIRN traveling subjects study.
- Require purchase and availability of Eprime from Psychology Software Tools, Inc. (<http://www.pstnet.com/products/eprime/>).
- Paradigms include: sensorimotor task, breathhold task, program for resting scans, Serial Item Recognition Paradigm (Sternberg, or SIRP), and Mismatch Negativity or MMN paradigm.

Function BIRN Stability Phantom Quality Assurance (QA) Procedures

- QA scans performed on a routine basis.
- Used to verify and measure scanner stability during a typical fMRI scanning sequence.
 - Performed on a 17cm spherical phantom filled with an agar gel.
 - Consist of 200 separate image volumes captured over roughly a ten-minute interval.
 - Post acquisition analyses consist of mean

and standard deviation measurements, drift and percent fluctuation in signal, signal-to-noise (SNR), and signal-to-fluctuation-noise (SFNR) ratios calculated over all volumes.

Data Management

XML-Based Clinical Experiment Data Exchange Schema (XCEDE)

An extensive metadata hierarchy for describing and documenting research and clinical studies.

XCEDE SPM Toolbox

Captures the results from activation maps using the XCEDE schema.

- Supports both SPM99 and SPM2 statistical structures.
- Tested on SUN, LINUX, and Microsoft Windows operating systems.
- Used to capture PET and fMRI analysis results and the associated analysis model specifications.

BXH/XCEDE Toolbox

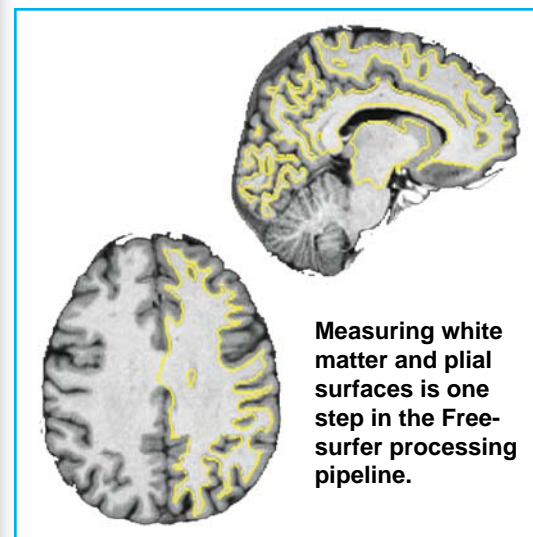
Suite of tools designed to read, write and manipulate XML descriptors using the BXH or XCEDE schemas.

- Descriptors are “wrappers” of the original, unadulterated image data files.
- Provides standard interface to image data and other metadata extracted from image headers.
- Includes tools to create and use XML “event” descriptors for representing stimulus presentation and other time-based data.

Human Imaging Database (HID)

Developed to address problems associated with managing increasingly large and diverse datasets collected throughout clinical and imaging communities. The HID is an extensible database management system comprised of three core components:

- *Human Imaging Database Schema*
Designed to be customized and extended



(Continued on page 3)

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BIRN Provides a Useful Suite of Research Tools...

(Continued from page 2)

to contain relevant information from sites without requiring schema modification. Information can consist of:

- Data concerning the research subjects.
 - Subject assessments and demographics.
 - Experimental data.
 - Experimental protocols.
 - Annotations or statistics (metadata) normally included with an experiment or study.
- **Clinical Assessment Layout Manager**
Facilitates the preparation and incorporation of an online clinical assessment entry forms.
 - **Human Imaging Database User Interface** Allows for management of research subjects and experiments.

Data Analysis

3D Slicer

Open-source application that assists with visualization, registration, segmentation, and quantification of medical image data.

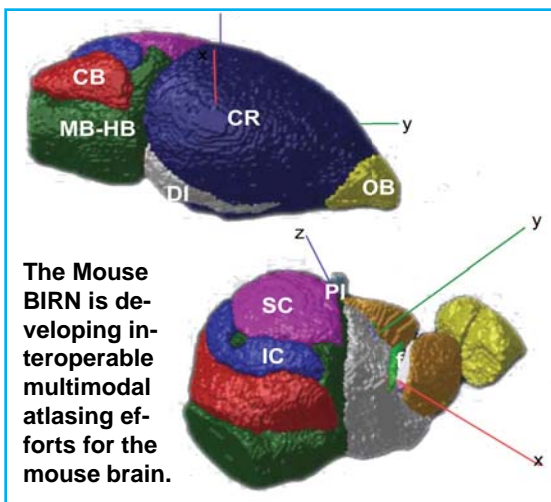
- Ongoing collaboration between MIT Artificial Intelligence Lab and Surgical Planning Lab at Brigham & Women's Hospital, an affiliate of Harvard Medical School.

FreeSurfer

Set of semi-automated tools for reconstruction of brain cortical surface and overlay of functional data onto that surface.

LONI Pipeline

Visual programming interface that allows researchers to link many independently developed analysis programs into a processing



“pipeline.”

B0 and Eddy Current Correction Code for Diffusion MRI

Software tool (executable and source code) and recommendations for acquisition protocols to correct distortions in diffusion MR images that are generated by main magnetic field inhomogeneities and eddy current generated from the direction-dependent diffusion encoding gradients.

Defacer for Structural MRI

Algorithm for removing identifiable facial features (eyes, nose, and mouth).

- Still in validation phase.
- Does not disturb brain tissue.
- Works on T1-weighted structural MRI.
- Produces a defaced structural image, and an image of applied mask.
- Code `mri_deface` produces a facial mask, which is used to apply mask to original volume, resulting in a defaced structural image.
- For images in other modalities, mask can be co-registered to the image before application.

Large Diffeomorphic Deformation Metric Mapping (LDDMM) and Tutorials

Assigns metric distances on the space of anatomical images in Computational Anatomy thereby allowing for the direct comparison and quantization of morphometric changes in shapes.

- As part of these efforts the Center for Imaging Science at Johns Hopkins University develop techniques to compare images and to visualize the changes and differences.

Gradient Non-linearity Distortion Correction

Provides 3D correction of image distortions in MRI data due to non-linearity of the magnetic fields from imaging gradient coils.

Data

Calibration

Function BIRN Multi-Site Quality Assurance (QA) Data

Routinely performed QA scans used to verify and measure scanner stability during a typical fMRI scanning sequence.

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For more information, visit:
<http://www.nbirn.net>

BIRN Provides a Useful Suite of Research Tools and Datasets...

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- Scans are performed on a 17cm spherical phantom filled with an agar gel.
- 200 separate image volumes captured over a ten minute interval.

Mouse

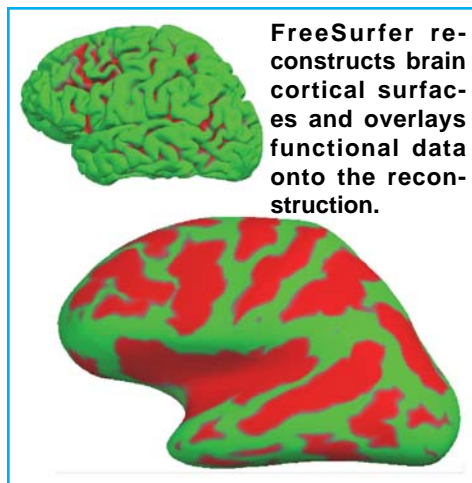
Mouse 3D Atlas

Atlas based on a magnetic resonance microscopy (MRM) image diffusion-weighted in the Z-direction acquired from a normal, 100-day old male C57BL/6J mouse.

- Comprised of a diffusion-weighted image volume, label volume, mask volume, and label index.

Mouse Shiverer DTI

High-resolution (80um isotropic) contrast-enhanced diffusion tensor data



acquired from six background control (C3HeB) and six dysmyelinating shiverer (C3Fe.SWV shi/shi) mouse brains.

- Data consists of nominally unweighted and diffusion weighted images with optimized icosahedral sampling.

Cerebellum Large Scale Mosaic

High resolution, large scale multiphoton microscopy mosaic image from cerebellum of C57BL/6H normal mouse. A high resolution multiphoton microscopy mosaic image of a cerebellar distribution of cell bodies (Hoescht 33342; blue) and alpha-synuclein (green) from a non-transgenic animal.

Hippocampus Large Scale Mosaic

Large scale multiphoton microscopy

mosaic image from hippocampus of C57BL/6H D-line transgenic mouse overexpressing alpha-synuclein. A high resolution multiphoton microscopy mosaic image of distribution of cell bodies (Hoescht 33342; blue) and alpha-synuclein (green) from a D-line transgenic animal overexpressing alpha-synuclein under the PDGF promoter.

Mouse Common Specimen

Single fixed specimen using MRM from Duke's CIVM, Diffusion Weighted MR from Caltech's Beckman Institute, and Optical Histology and Staining from UCLA's LONI. UCSD's NCMIR performed Multiphoton Microscopy using tissue from an animal of the same strain.

Human

Open Access Structural Imaging Series (OASIS)

Series of structural MRI data sets available for study and analysis.

- Cross-sectional collection of 400 subjects covering the adult life span.
- Three or 4 individual T1-weighted MRI scans obtained in single scan sessions.
- Subjects are all right-handed and approximately equally divided by gender.
- 100 subjects over the age of 60 have been diagnosed with very mild to mild dementia of the Alzheimer's type (DAT).
- Additional reliability data set of images obtained from 20 of the non-demented subjects on a subsequent visit.

Structural MRI Calibration Data

Structural MRI data from 5 healthy volunteers scanned multiple times on multiple sites having different 1.5T systems (Siemens, GE, Picker).

- For each subject, four multi-spectral structural scans were obtained in a single scan session, from which tissue proton density and T1 maps can be derived.
- Data acquired to investigate various

metrics of within-site and across-site reproducibility.

Diffusion MRI Calibration Data

Database contains structural and diffusion MRI data from two healthy volunteers scanned multiple times on a 1.5T Philips system to investigate reproducibility of diffusion-derived metrics, such as fractional anisotropy maps.

Function BIRN Phase I Traveling Subjects Dataset

Phase I subject pool consisted of six right-handed healthy male subjects tested twice at each Function BIRN site on successive days.

- Scanned in each MRI scanner at least twice using the calibration and cognitive protocols to produce a dataset to measure intersite, intersubject, and intersession variance.

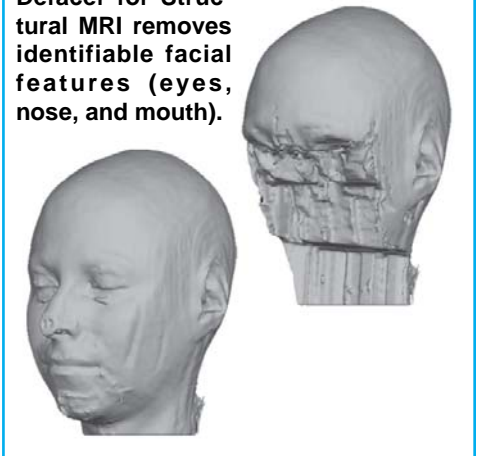
Tools utilized by BIRN participants

SRB

Client-server middleware designed for managing file collections in a heterogeneous, distributed environment.

ImageJ

Defacer for Structural MRI removes identifiable facial features (eyes, nose, and mouth).



Pure Java image processing application, currently able to open DICOM, JPG, GIF, and TIFF images directly from BIRN Portal.

J viewer

Simple 3D viewer that reads and displays Microbrightfield's Neurolucida V3 ASCII, XVtrace, and Synu.

BIRN-CC Update: All Hands Meeting 2005

by Skip Cynar, UCSD

The annual BIRN All Hands Meeting (AHM) was hosted at the University of California's San Diego campus the week of October 17-20. The four-day meeting, consisting of working group meetings, training sessions, and status meetings, engaged more than 200 national participants in presentations, brain-storming workshops, and problem-solving discussions. "Official registrants totaled 201, an increase of approximately 40 over the 2004 AHM," according to Mark James, chair of the local organizing team within the BIRN-CC. The main theme of the meeting was on seeking ways to expand and improve how BIRN's test-bed discovery-science can be shared with other researchers in the neurosciences for the benefit of our society.

The meeting was held in the newly completed California Institute for Telecommunications and Information Technology (Cal(IT)²) building, within the Jacobs School of Engineering. On Monday, the first day of the AHM, the BIRN test bed participants (Mouse, Function, and Morphometry) met to solidify plans and key goals for the next 3, 6, and 12 months.

Steven Potkin chaired Tuesday morning's 'Welcome Session', organized around BIRN's main theme of 'collaborative tools enabling scientific discovery.' Following the afternoon's five breakout sessions, Timothy Killeen, Director of the National



BIRN Coordinating Center Director Mark Ellisman, Keynote Speaker and Director of the National Center for Atmospheric Research Timothy Killeen, and NCRR Director Barbara Alving attended the AHM.



Morphometry BIRN members found ample time to meet and discuss research needs, processes and goals for the coming year.

Center for Atmospheric Research, delivered the keynote address, entitled "Cyberinfrastructure and Earth System Science." Following the talk, many participants enjoyed dinner and cocktails at UCSD's Birch Aquarium overlooking the Pacific. Hewlett Packard's generous support in helping to sponsor this social

event is gratefully acknowledged.

Wednesday morning was dedicated to working groups focused on portal and visualization (Jason Novotny), Ontologies (Maryann Martone and Carol Bean), Databases and Integration (Jeffrey Grethe), and Workflows (Shawn Murphy). The Test Beds and Working Groups delivered closing summary presentations on their efforts late in the afternoon. This was followed up with closing remarks from members of the BIRN Executive Committee.

Thursday morning members of the BIRN Executive Committee held a planning session for the Society for Neuroscience Conference. Three concurrent workshops focusing on atlases (Jyl Boline), portal development (Jason Novotny), and FreeSurfer/3D Slicer (Randy Gollub) were taught for both BIRN and non-BIRN participants. The AHM concluded Thursday afternoon. Many of the speakers indicated that their Power Point slide presentations would be made available on the BIRN website.

We value your impressions of the 2005 AHM. If you haven't already done so, please take a minute to complete the AHM survey e-mailed to registrants on 28-October. All information provided will be anonymous unless you choose to identify yourself. Survey URL: <http://www.nbirn.net/AU/Events/AHM2005/index.htm>



More than 200 BIRN members from across the nation participated in presentations, brain-storming workshops, and problem-solving discussions at the BIRN All Hands Meeting.

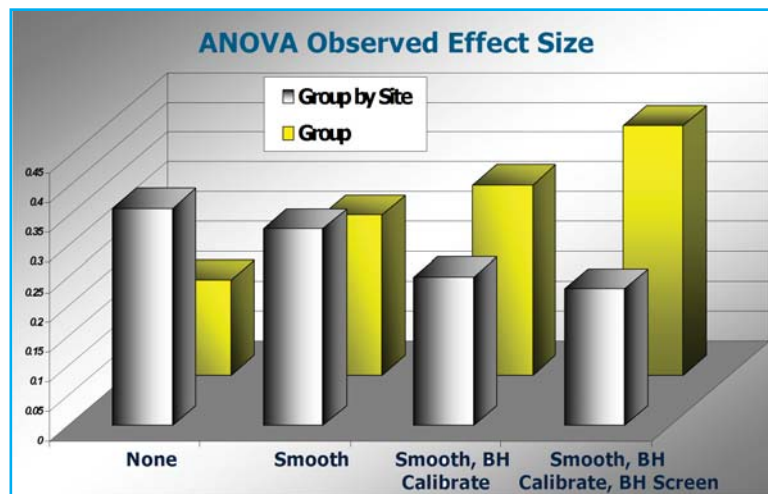
Function BIRN Update

by Jessica Turner and Liv Trondsen, UCI

The summer of 2005 has been a rich and productive time-window for Function-BIRN (FBIRN) researchers. We've been able to fully exploit the collaborative environment and physical infrastructure that we've developed and deployed over the past three years. FBIRN expects to meet their recruitment target of 300 subjects by November 2005. With this substantial dataset, the FBIRN will achieve a key goal of the project by the creation of a large, well-characterized, de-identified neuroimaging dataset available to the scientific community. Accelerating discovery-science through multi-site collaborations and publicly available datasets has been a driving force for the BIRN project and continues to fuel the FBIRN in its research aims.

Calibration progress

A central mission of the FBIRN program is to develop methods to provide for robust multi-site fMRI studies, by reducing the surprisingly large impact of scanner differences across imagers. New analyses done by the FBIRN, principally focusing on the general patterns of the BOLD signal in fMRI, confirmed that variability among imaging sites can exceed variability among subjects, thereby greatly limiting the value of multi-site imaging studies. Figure 1 illustrates the inter-site variability from a group of subjects traveling among all of the FBIRN sites for the first study: imaging the same brain at the different



ANOVA results comparing the effect of 4 different calibration conditions on the relative sensitivity to the diagnostic group effect (in yellow) and the inter-site variability (foreground, in gray). From left to right: No-calibration correction, the inter-site variability overshadows the difference between patients and controls; smoothing; calibration-by-breathholding; and finally using the breathholding response to filter out implausible physiological responses. There is an increasing sensitivity to the diagnostic group differences, and a decrease in the unwanted interaction term.

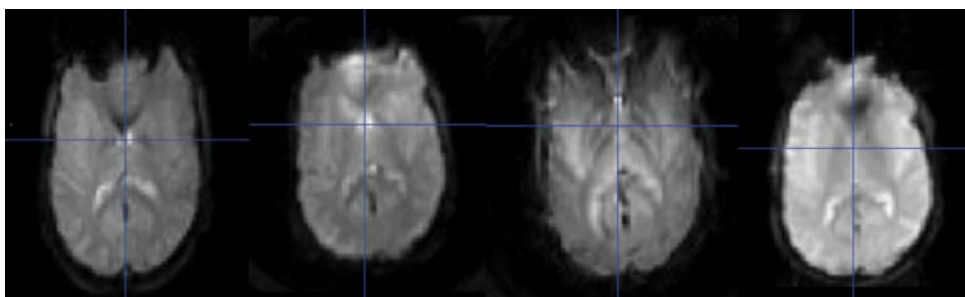
imaging sites generated wildly different images. This clearly demonstrates the need to reduce inter-site variability in order to improve the power of multi-site datasets. Since June, FBIRN has worked to reduce inter-site variability by 54% through their collaborative analytical efforts.

Using a subset of the FBIRN multi-site dataset from subjects with schizophrenia plus age-matched controls, we systematically compared four calibration methods (1) no-calibration, 2) smooth-to-calibration, 3) proportional scaling, 4) combined calibration) using ANOVA. Our study performed an analysis of variance (ANOVA) on fMRI data from 30 schizophrenic and healthy subjects

acquired at three imaging sites (above) in order to investigate differences in brain function between subjects with and without schizophrenia (Diagnostic Group effect). The no-calibration condition (1) was associated with a small Diagnostic Group effect relative to the large Group-by-Site interaction. The Group-by-Site interaction indicates that the difference between the subject groups is not the same from site to site, which reduces the overall sensitivity to the group difference. The smooth-to calibration method (2) increased the effect of group and

reduced the impact of the group-by-site effect, two desirable results. Adding proportional scaling based on the vasoreactive response to breath holding, (3) to the calibration pathway further improved the results. Once outliers (three subjects) were identified based on their unusual vasoreactive responses, the combined calibration method (4) revealed a better discrimination between schizophrenic and non-schizophrenic subjects. Using these combined methods, the group differences in the data were robust, and the variation across scanner and site was minimized. This is successfully paving the way for robust integration of the imaging data in this multi-site study.

Although the calibration methods described above improved the sensitivity of multi-site imaging datasets to the effect under study, there is still work to be done. While these methods reduced the undesirable inter-site variation, it remains moderately large. The calibration methods proposed for the FBIRN project will further reduce this variation and improve methods for determining more subtle differences in neuro-circuitry.



Examples of 4 fMRI scans of a single subject acquired at 4 different imaging sites. The variability across imaging sites from the same subject is evident.

ZOLA - Yerkes National Primate Research Center

Stuart Zola, PhD is one of the nation's leading neuroscientists and a champion for communicating science and research to the public. As the director of the Yerkes National Primate Research Center, Dr. Zola oversees diverse research programs addressing infectious diseases, childhood visual deficits, organ transplantation and cognitive development. Yerkes is one of eight National Primate Research Centers funded by the National Institutes of Health and is recognized as an international leader in biomedical and behavioral studies with nonhuman primates.



Stuart Zola

Dr. Zola's own research focuses on memory, its formation, consolidation, and retrieval; he has contributed valuable insights into the brain's organization of memory and how this relates to amnesia and other memory problems. In addition to his leadership role at Yerkes, Zola is a Professor of Psychiatry and Behavioral Sciences at Emory's School of Medicine, and a Senior Research Career Scientist at Atlanta's VA Medical Center.

Q. What is your current role within the BIRN?

A. I'm coordinating the development of the non-human primate BIRN test bed. The National Center for Research Resources ([NCRR](#)) approached me with an interest in evaluating the feasibility of a non-human primate BIRN. I suggested the NCRR-funded [Yerkes National Primate Research Center](#) at Emory University in Atlanta would be a good seed project to begin building this test bed.

We intend to grow it by bringing other sites into a consortium in order to take advantage of the aggregate of distributed data and pooled subjects. The BIRN provides an information technology infrastructure that facilitates collaboration—especially where the data come from different groups, different technologies and across geographic sites. It is important to recognize that the BIRN's creation of a public repository of data and shared tools is a significant step towards open access of published data.

Q. What inspired your interest in human cognition and emotional development?

A. When I first started my graduate studies, it was in social psychology. Initially, I was interested in being a clinician and therapist. During my first year of study, I took a course about the brain, taught by Professor Helen Mahut. Before that I'd never studied the brain, I was more of a behaviorist. During her course, I suddenly understood a new powerful approach to providing insights about behavior. That very semester I decided to switch my graduate program to physiological psychology, which today we call neuroscience. Prof. Mahut's brain course inspired my career; she became my PhD advisor in graduate school.

Q. What are some of the most urgent challenges in your research?

A. My research program is focused on memory, brain function, and how memory is organized in the brain. We have used nonhuman primate models for many years and during the course of that work, we uncovered a memory system for the brain--a group of interrelated structures in the temporal lobe of the brain. This development laid the groundwork for much of the work to come. The question was, how do these structures interact?--presumably they are not all doing the same thing. Each component is doing a different computational process in the service of memory. The focus became, how do we sort out what each component contributes. This has turned out to be a fairly difficult problem, largely in part because the structures are interconnected.

We have begun to develop new ways of assessing the roles of specific interconnections, such as chilling down select portions of the brain so that we can reversibly

disable a portion of the brain and later bring it back on line. One of the difficulties in our research field is that if you make permanent lesions to the brain then you can't go back and ask the question of what would happen now to the learning that went on without the structure being in place. But with reversible lesions you can actually do that. You can shut off a system for a period of time, such as either during the encoding process or during the consolidation process or during the retrieval process and you can ask 'What is the role of that structure during any of these different components of learning?' That has turned out to be the biggest challenge for us--how to begin to delineate the contributions of individual structures at different times in the processes of learning and memory.

Q. How will the Biomedical Informatics Research Network help advance this research?

A. BIRN will be very helpful; the framework of our proposed research with the BIRN will build on this area of research. The BIRN will allow us to integrate related avenues of research, such as imaging, the analysis of cDNA microarrays, and sophisticated behavioral assessments, such as infrared eye tracking. We have techniques now by which we can track what an individual is actually looking at on a monitor that

(Continued on page 8)

Mouse BIRN Update

by Jyl Boline, UCLA, Anjum Ali, Duke University

The Mouse BIRN is building multi-scale, multimodal brain atlases of mouse models of neurodegenerative disease, along with a set of associated tools for registering data to this framework and querying spatially linked data. The first major release of a multi-scale brain atlas is scheduled for November, with additional data, improved methods, and new workflows will also be released.

Participating researchers at five universities are acquiring data from normal mice and mouse models of multiple sclerosis and Parkinson's disease and registering this data to the mouse BIRN framework. Plans for the near future include extending this collaboration to include an Alzheimer's disease model. Protocols have been developed to image the animals at two or more sites using a combination of high

resolution magnetic resonance microscopy, diffusion weighted MRI, histology, and high resolution light and electron

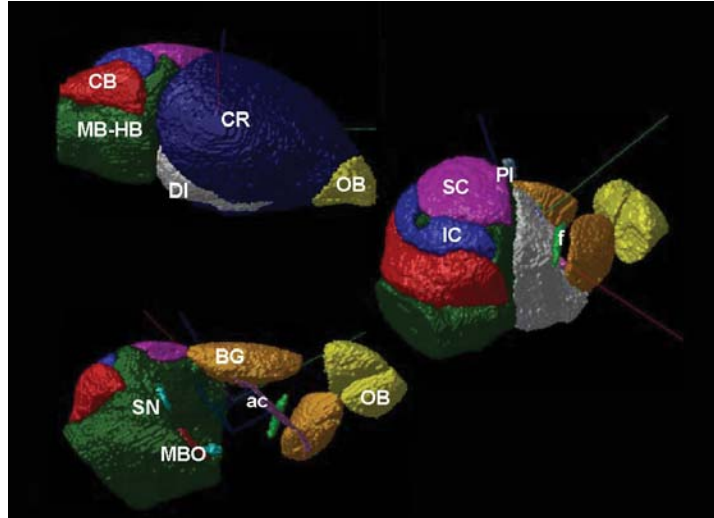
microscopy. Microarray analyses are being used in conjunction with these image-based techniques. Guided by

a vision of open-access to diverse, distributed data and the interoperability of software and data resources, the Mouse-BIRN team will continue to develop protocols to enable neuroscientists to mine multiple, disparate, and distributed resources from their desktop.

Advances in the Atlasing Toolkit

The atlasing efforts of the mouse BIRN rely on spatially registering several types of data into a common framework. The BIRN infrastructure provides a unique opportunity to coordinate the registration efforts of separate sites and their atlas data sets, which include a 3D Nissl-stained brain (Drexel); a 3D MRI at-

(Continued on page 9)



Lower threshold (62.5%) reconstructions of surface models retrieved from the probability anatomic map. Abbreviations: OLF olfactory bulb. CR cerebrum. DI diencephalon. MBHB midbrain-hindbrain. CB cerebellum. SC superior colliculus. IC inferior colliculus. CP+GP striatum nuclei. SN substantia nigra. MB mammillary body. PI pineal gland. Middle: surface of cerebrum removed. Bottom: both surfaces of cerebrum and diencephalon removed.

ZOLA - Yerkes National Primate Research Center...

(Continued from page 7)

they are viewing and watch how they are processing that visual information. When combined, these data require a daunting amount of data analysis, and data translation.

The BIRN promises to supply this integration from a number of different platforms, including positron emission tomography (PET) and magnetic resonance imaging (MRI). Each provides unique information that are critically important. With the enormous amount of genomic information flowing in from microarrays, such as the chimpanzee, human, and rhesus genomes, we have the opportunity of asking questions about learning and memory across different species. Linking together diverse genomic data with imaging information and behavioral observations will be the extraordinary challenge. And the BIRN technology is the best opportunity we

have to integrate this information from diverse platforms and locations.

The non-human primate test bed will address several challenging problems facing NIH researchers working on non-human primate models of disease. The new test bed will fit nicely between the mouse and human test beds currently in BIRN. Linking different platforms together will be extremely useful for advancing our understanding of the relationship between performance, genetics, and the structural changes we track with imaging. The BIRN is an unique opportunity to address these important questions (and daunting challenges) in an effective way--that is an aspect of the BIRN program that excites me!

Q. Would you like to offer advice to students embarking on a research career?

A. I'd tell them two things. First, remain

flexible about how you are looking at things in your science and career. Nothing is in concrete; decisions you make can be changed. Second, try and figure out what really gets you up and going in the morning. I can't think of a more exciting time for the neurosciences. We are really on an exciting and creative pathway for understanding brain functions and realizing important translational accomplishments. So if I was a youngster, I'd be heading into the field of genomics. I see the opportunities there in terms of technology and organizations, like BIRN, being able to bring all of these pieces together for achieving breakthroughs. This will be an era of accomplishment in terms of brain science. It is really an exciting time for all of us.

For more information on the Non-human Primate BIRN, see page 11.

Mouse BIRN Update...

(Continued from page 8)

las (UCLA), and a 2D set of atlas plates with the Paxinos and Franklin (2001) brain delineations (UCSD). Researchers among this group are working to first achieve a common spatial framework between these efforts, and then to standardize the process of registering new data to fit this framework. The BIRN infrastructure provides the means to tie these atlases together.

At the recent BIRN All Hands Meeting, Mouse BIRN researchers demonstrated significant progress in establishing a common framework across the individual atlases. In this system, a user can open two or more atlases, and as they navigate through one, the display of the other is updated concurrently--achieving coordinated navigation through multiple atlases.

A beta version of this interoperable atlas environment, the Mouse BIRN Atlas Tool (MBAT) is scheduled for release in November. Both a stand-alone and a portal-enabled version will be released. More information about this project, and access to the tools can be found at <http://www.nbirn.net>. (See figure, below)

Advances in data acquisition

Members of the Mouse-BIRN have been pushing the limits of MRI data acquisition in the mouse brain, resulting in remarkably detailed, high resolution images of mouse brain morphology. This is largely due to an enhanced T2 weighted acquisition protocol for the 'actively stained' mouse developed by Anjum Ali at Duke's Center for in vivo Microscopy (CIVM).

Accurate T2 measurements and subsequent T2 weighted images are a difficult challenge at high fields due to the combined effects of diffusion mediated losses and large susceptibility variation. Furthermore, in the presence of paramagnetic contrast

agents, mouse brain-tissue-T2s decrease significantly.

This protocol is capable of producing 43 micron, isotropic, 16 echo volumes with a minimum echo spacing of 7ms in an acquisition time of 4 hrs. The pulse sequence consists of a 3D volume imaging implementation of the multi-echo, Carr Purcell Meiboom Gill sequence. T2 weighted images are computed by taking a Fourier Transform of the echo volumes in the temporal dimension. This produces enhanced T2 weighted contrast with a significant gain in signal-to-noise ratio.

Images obtained using this protocol reveal detailed mouse brain morphology such as multiple layers of the cortex, groups of thalamic nuclei, layers of the inferior and superior colliculus, and molecular and granular layers of the cerebellum with a high degree of definition and contrast not reported before in T2-weighted acquisitions at high fields.

Advances in mouse atlas development

Brain atlases may provide stereotaxic coordinates that define brain position and orientation within grid systems. Since gene expression changes rapidly during development, correlating expression to

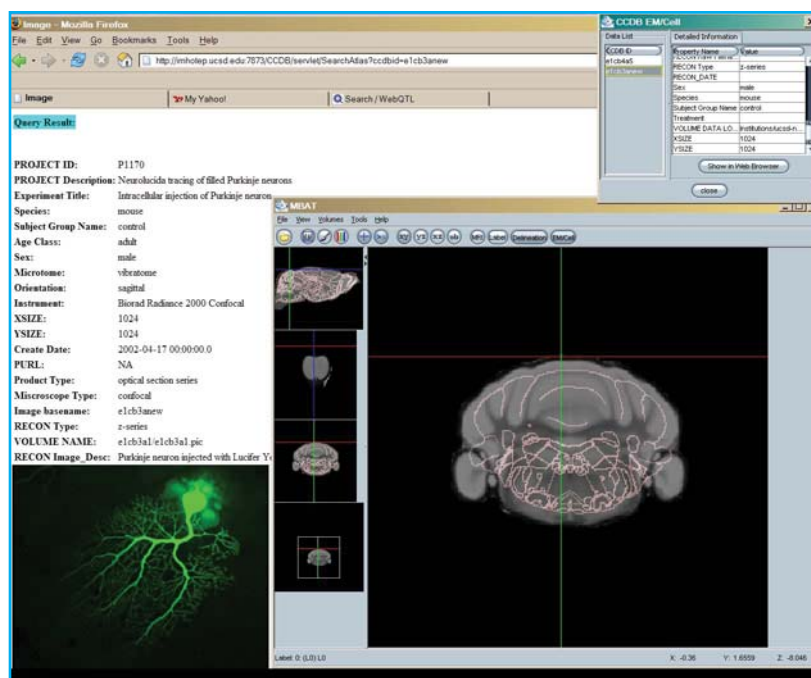
anatomy can be quite difficult without such a coordinate system for each developmental stage. However, until recently this has not been constructed for the developing mouse brain. Recently, in *Anatomy and Embryology* (14-Oct-2005;:1-19), Erh-Fang Lee and colleagues at the Laboratory of Neuro Imaging (LONI-UCLA), constructed just such an atlas for the neonatal (P0) mouse brain. This atlas helps structure the data, enabling comparison and ensuring consistency across different laboratories, a central objective of the Mouse-BIRN.

This atlas was constructed from the mean brain shape obtained from the MR image volumes of 8 mice. Anatomic labels were described that enabled feature-based registration. Variations in the atlas space provided a spatial range for probability maps of several important anatomic structures. The atlas was tested using both MR images from a test brain and a reconstructed high resolution histological image volume.

By selecting a threshold of the probability map, anatomic space for each structure with various confidence intervals can be reconstructed for different purposes;

restrictive thresholds provide more accurate mapping, while looser thresholds provide more labeling throughout. This suggests that the proposed anatomic space provides an accurate map when an appropriate registration strategy takes into account the intended purpose.

Reference citation: Standard atlas space for C57BL/6J neonatal mouse brain, by E-F Lee, RE. Jacobs, I. Dinov, A. Leow, and AW. Toga in *Anatomy and Embryology* (Berl). 2005 Oct 14;:1-19 DOI: 10.1007/s00429-005-0048-y



Mouse BIRN is developing interoperable atlas environment, the Mouse BIRN Atlas Tool (MBAT) to enable data comparison and ensure consistency across different laboratories.

Morphometry BIRN Update

by Jorge Jovicich, MGH

Over the past few months the Morphometry test bed has been focused on attaining the goals set forth for the BIRN Annual All Hands Meeting (AHM, October 17-20, 2005, San Diego). A good part of this work has been finalizing the preparation of human imaging data and software tools for dissemination to the public at the Society for Neuroscience meeting, later this year (details below). We've been working with the other test beds to plan the 2005 AHM focusing on BIRN-wide interactions between the various working groups that address issues of common interest across all test beds. Here is a summary of Morphometry-BIRN's progress.

MRI system upgrade calibration: multi-site coordination

Later this year, the Massachusetts General Hospital (MGH) and Brigham and Women's Hospital (BWH) imaging facilities will have their 3T systems upgraded by Siemens and GE, respectively. Investigators from Morphometry and Function-BIRN test beds, as well as GCRC collaborators, are working together to coordinate a human and phantom calibration protocol that will enable us to characterize changes due

to the system upgrades. The new upgrades will enable improved spatial and temporal resolution through the use of multiple receiver channels with parallel acquisition factors.

3D Slicer Training

Together with our collaborators in the National Alliance for Medical Imaging Computing (NA-MIC), we prepared and offered a workshop providing hands-on training in using 3D Slicer, the neuroimaging data visualization software tool. Slicer's vtkFreeSurferReaders module allows interactive visualization and manipulation of the results of FreeSurfer analyses--the result of intense mBIRN interoperability development between MGH and BWH. Demand for this training course resulted in scheduling a second section. Details about this workshop and future training opportunities can be found at <http://www.na-mic.org/Wiki/index.php/Training:Main>

Morphometry test bed updates data and software tools

See page 2 for an outline of updated data and tools to be released at this November's Society for Neuroscience meeting.

Public dissemination deliverables

from Morphometry BIRN

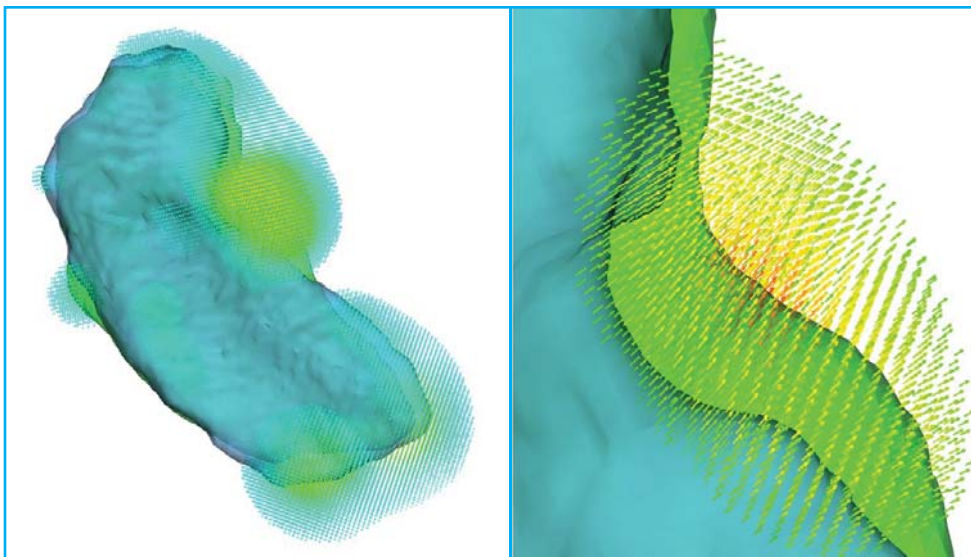
I Dissemination of human MRI data - Human Open Access Structural Imaging Series (OASIS)
OASIS is a series of structural MRI data sets publicly available for study and analysis. The initial data set consists of a cross-sectional collection of 400 adult subjects representative of an adult life span (ages 19 to 96). Three or 4 individual T1-weighted MRI scans from a single scan session are included for each subject. All subjects are right-handed and each gender is equally represented. One hundred subjects over the age of 60 have been diagnosed with very mild to mild dementia of the Alzheimer's type (DAT). Additionally, a replicated image scans of 20 of the non-demented subjects were acquired to assess data reliability. The data are amenable to a range of analytic approaches. Fundamental changes in brain structure between healthy and diseased subjects can be demonstrated by the comparison of analytic measures, such as the automated computations of whole brain volume and estimated total intracranial volume. Visualizing, exploring, and downloading the data is enabled through a web-based application.

Human structural MRI calibration data

In order to investigate various metrics of within-site and across-site reproducibility, structural MRI data from 5 volunteers was collected from multiple scans, multiple sites, and multiple 1.5T systems (Siemens, GE, and Philips). For each of the five healthy subjects, four multi-spectral structural scans were obtained during a single scan session. Tissue proton density and T1 maps were derived from these subjects.

Human diffusion MRI calibration data

We will distribute structural and diffusion MRI data from two healthy volunteers that were scanned multiple times on a 1.5T Philips system in order to investigate reproducibility of diffusion-derived



Left, two human hippocampi with the velocity vectors calculated by Large Deformation Diffeomorphic Metric Mapping (LDDMM). Right, the threshold of displayed velocities can be adjusted to display a narrow range of velocities (in this case the largest velocity vector, and hence deformation).

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Introducing Non-human Primate BIRN

by Stuart Zola, Emory University

The Yerkes National Primate Research Center at Atlanta's Emory University is directing the development of a new BIRN test bed for linking brain imaging, behavior, and molecular informatics in non-human primate preclinical models of neurodegenerative disease. Our initial plan proposes to link three recently developed capabilities for research with monkeys: (1) structural and functional MRI and PET data from rhesus monkeys as animal models for Mild Cognitive Impairment (MCI, a risk factor in humans for subsequent onset of Alzheimer's Disease); (2) molecular informatics-based microarray technologies using the nearly completed monkey genome and rhesus gene chip, combined with microarrays being developed to assess material from

monkey brain biopsy samples; (3) new and sophisticated ways of assessing



New BIRN test bed participants. Rhesus monkey mother and infant at the Yerkes National Primate Research Center.

cognitive function in monkeys, (e.g., noninvasive infrared eye-tracking, paralleling work in humans, used with current functional brain imaging technology. This approach will clarify relationships between genetics and behavior, specifically the fundamental connection between genetic predispositions and the potential expression of neurodegenerative disease.

The non-human primate test bed will use the cyberinfrastructure of the BIRN project for data-sharing and linking the eight separate NCCR-supported primate centers, as well as other geographically distributed research groups. Many of the interdisciplinary groups participating in the non-human primate

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Morphometry BIRN Update...

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metrics, such as fractional anisotropy maps.

While we work to investigate how the reproducibility of diffusion derived metrics, like fractional anisotropy, depend on signal-to-noise ratio (SNR) and the number of gradient orientations. The database can be used for many other purposes, for example, investigating the reproducibility of tractography, as well as studying the effects of different tractography fitting routines on stability. The data is also a resource for processing and visualizing tool developments.

II. New software analyses and visualization tools released

Correction for distortions from gradient non-linearities

A software tool for correcting image distortions introduced by non-linearities in the imaging gradients.

Correction for direction-dependent distortions in diffusion Tensor Imaging

A software tool and acquisition protocol was developed for correcting diffusion

MR image distortions generated by inhomogeneities in the main magnetic field resulting from eddy currents generated from the diffusion encoding gradients.

Defacing tool for MRI data. A software tool for removing facial image pixels, without touching brain pixels, is now available for de-identifying high-resolution structural data.

FreeSurfer

FreeSurfer is a set of semi-automated imaging tools for reconstructing the brain's cortical surface from structural MRI data and thus providing a reconstructed surface for the overlay of functional MRI data (<https://surfer.nmr.mgh.harvard.edu/>)

3D Slicer

The 3D Slicer software tool is open-source software for the visualization, registration, segmentation, and quantification of medical data (<http://www.slicer.org/>)

Large Diffeomorphic Metric Mapping (LDDMM)

The LDDMM application assigns metric distances onto anatomical images

in support of computational anatomy. The LDDMM provides for the direct comparison and quantization of changes in brain morphometrics. The Center for Imaging Science at Johns Hopkins University is developing techniques to facilitate the comparison of images, including visualizing morphological changes and differences (<http://cis.jhu.edu/software/ldmm/>). This software is not yet available for distribution, but is currently available via the BIRN Portal.

Publications

Bin Chen; Hua Guo; Allen W. Song. Fast correction for direction-dependent distortions in diffusion tensor imaging using matched magnetic field maps, *NeuroImage* (in press)

Jorge Jovicich; Siter Czanner; Douglas Greve; Elizabeth Haley; Andre van der Kouwe; Randy Gollub; David Kennedy; Franz Schmitt; Gregory Brown; James MacFall; Bruce Fischl; Anders Dale. Reliability in multi-site structural MRI studies: Effects of gradient non-linearity correction on phantom and human data, *NeuroImage* (in press)

The Biomedical Informatics Research Network

Growing Collaborative Biomedical Research Through Technological Advances

The Biomedical Informatics Research Network (BIRN), a National Institutes of Health (NIH), National Centers for Research Resources (NCRR), and US Department of Health and Human Services (DHHS) supported initiative, is establishing a distributed information technology infrastructure to enable fundamentally new capabilities in large-scale studies of human disorders, such as Parkinson's, Alzheimer's, and mental retardation.

The BIRN involves a national consortium of 21 universities and 30 research groups, comprising three neuroimaging test bed projects that are conducting structural and func-

tional studies of neurological disease. Additional projects utilizing the BIRN infrastructure include the National Alliance for Medical Imaging Computing (NA-MIC) and the United Kingdom e-Science program.

The BIRN Coordinating Center was established in 2001 to create, support, and distribute essential cyberinfrastructure and to pioneer the model for a persistent, scalable architecture with application beyond neuroimaging.

This integrated cyberinfrastructure is being created upon technologies supported by the next generation Internet and the National Science



Foundation (NSF) Middleware Initiative, including high bandwidth, inter-institutional connectivity via Internet2, grid-based file management and computational services, software and techniques to federate databases, and shared processing, visualization, and analysis environments.

Introducing Non-human Primate BIRN...

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model test bed are also engaged in related BIRN-facilitated data integration activities, including the development of key PET ligands.

The rhesus monkey model studies will combine behavioral assessments with non-invasive imaging methods to genomic background information and direct (and invasive) gene expression analyses of CNS biochemical changes. We plan to link the non-human primate data to other NIH and BIRN test-bed investigators working on Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD). The work here will advance our understanding of treatments and interventions for MCI and AD, and will serve as a proof-of-concept for developing effective strategies for understanding other neurodegenerative disorders. In the long term, the software tools developed for integrating the imaging, behavioral and microarray data will be folded into the BIRN-enabled toolbox. In the short-term, our goal is the development of a tool to link the separate

data bases and analyses tools via the BIRN Portal.

The non-human primate test bed will nurture the development of core technology for data sharing while cultivating collaboration among investigators of the

eight geographically separate NCRR-supported National Primate Research Centers. Moreover, these new collaborations will disseminate BIRN's tools and methodology beyond BIRN's current test bed investigators.

Upcoming Meetings

November 12-16, 2005

**Society for Neuroscience
Washington, DC**

<http://web.sfn.org/am2005/>

**Booths: NCRR (#918) and
BIRN (#916)**

November 12-18

**Supercomputing
Seattle, WA**

<http://sc05.supercomputing.org>

January 8-10, 2006

**NA-MIC All Hands Meeting
Salt Lake City, UT**

[http://www.na-mic.org/Wiki/index.php/AHM_2006:
AHM_2006](http://www.na-mic.org/Wiki/index.php/AHM_2006:AHM_2006)