



BIRNing Issues

BIRN Quarterly Newsletter

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BIRNing Issues welcomes feedback. Please send comments to:
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Generating a Bioinformatics Toolbox Networks Can Be Greater Than the Sum of Their Nodes

By Judy Vaitukaitis, M.D., National Institutes of Health

As research becomes more complex, the tools, expertise, and approaches to effectively conduct that research must change. Over the past few years, informatics has become more prominent as high-throughput technologies and advanced imaging instrumentation for targets, ranging from molecules to the whole organism, generate vast data sets. These enormous sets create challenging problems that increase the need for tighter collaboration and communication between researchers. Progressively more investigators require access to the equivalent of a “bioinformatics toolbox” that includes a wide range of communication, analysis, and shared visualization tools that exploit access to teraflop and greater computing and to high-speed, next-generation networking. This toolbox allows construction of a research network that is “greater than the sum of its parts,” and it is this principle that inspired the recently initiated Biomedical Informatics Research Network (BIRN).



BIRN Defines the Tools

The BIRN will facilitate the implementation of investigator-identified elements for important networking, computational, and social infrastructure that will enable collaborative science. The infrastructure is significant not only because of its direct impact on the neuroscience research of the several NCRR Neuroimaging Centers and General Clinical Research Centers participating in the testbed, but also because the framework that it is defining is a prototype for the infrastructure that will underlie all of biomedical science in the coming years. The initial effort of BIRN focuses on neuroscience, but future “BIRNs” may concen-

trate on, for example, diabetes mellitus, autoimmune diseases, and cell biology. The research enhancements for one BIRN will be adopted for another. In essence, a set of reusable tools will be generated, and the toolbox will continue to grow and to become more robust providing a cost-effective approach for constructing a flexible national research infrastructure that facilitates a wide range of research.

NIH Provides the Support

The NIH has increased its support of collaborative research and data sharing (see http://grants1.nih.gov/grants/policy/data_sharing/index.htm). But meeting requirements for data availability will not necessarily foster full utilization of the data. Innovative tools—new approaches to infrastructure—are needed so that the computer science and information technology that make data sharing possible, also make it practical in a way that is transparent to

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Highlights

Look sharp at your next brain meeting with new BIRN golf shirts by Ace's Embroidery.Pg. 2

They came by plane, by car, by foot. Their intent? To improve the way research will be donePg. 3



BIRN-CC Actively Responds to Your Needs

by Mark James, UCSD

As new neuroscience research sites join the BIRN, users have discussed the need for increased storage, security and speed. Your requests encouraged the Coordinating Center (BIRN-CC) to continue to examine technological improvements, including rack architecture, the Storage Resource Broker (SRB) and portal architecture.

Rack Technology

To ensure the availability of the most updated rack technology, BIRN-CC keeps in continuing contact with our corporate partners. One of the most enthusiastic is Hewlett Packard (HP). HP manufactures the rack structures that provide BIRN with a stable architecture that allows us to grow with technology and still provide compatibility with the previously fielded racks. In 2002, the first set of racks came with 36 GB disk drives and dual 1.2 GHz CPU processors - the most advanced at the time. Now, for the same money, BIRN racks are configured with 72 GB disk drives and dual 2.8 GHz processors.

The first generation of racks were shipped with a Network Attached

Storage (NAS) configured as Raid 0+1 to provide for continuous access to your data even in the event of a disk failure while still providing optimum performance and throughput. However, this configuration is only 50% space efficient.

By switching to a Linux NAS from Windows 2000, we are now able to use Raid 5. (See *Join the Great RAID Migration*, page 7.) This will significantly increase storage and nearly match the performance provided by Raid 0+1.

Storage Resource Broker

Your user requirements are also driving improvements for the Storage Resource Broker (SRB). Release 2.0 improves the security requirements of the metadata catalog so that researchers can see only those fields (with their corresponding files) in the metadata catalog for which they have authorization. In the past, file information in the metadata catalog data was available to everyone. SRB has also improved the speed of uploading files through multi-threading (e.g. parallelization of data streams). This allows large collections of files to be

sent as one bulk upload instead of sending each file singly. The metadata catalog is accessed only once and is updated for all files sent. Improvements have also been made to give us visibility in the auditing of data sets so we can comply with all HIPAA regulations.

Portal Architecture

Over the past few months, the BIRN-CC has been putting greater emphasis on the portal architecture and has been devising more convenient ways to launch the applications you are accustomed to using. We also have acquired an application server that will be able to support Web services as well as our growing Concurrent Versions Systems (CVS) library - a vital resource in helping our development teams maintain an orderly upgrade release cycle.

New Ontologies

BIRN-CC acquired licenses for the use of ontologies like the Unified Medical Language Systems (UMLS) and Neuronames Brain Hierarchy. You will be able to access these tools via the BIRN Portal when integration

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BIRN golf shirts now available for purchase

Be the Envy of the "Neuro" Crowd

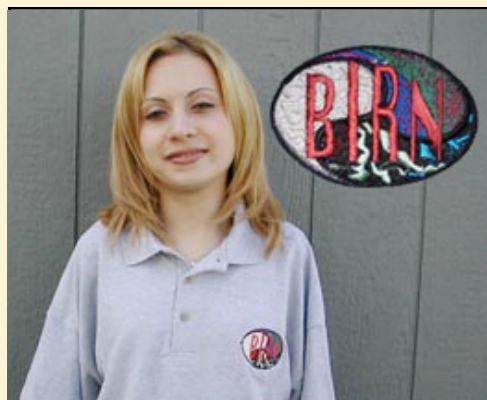
BIRN-CC has made a deal with Ace's Embroidery to provide high quality golf shirts, embroidered with the BIRN logo, at an affordable price. Two fabric types are available, both in the color of ash with taped welt cotton collars and cuffs and three wood tone buttons.

Option 1) #06499 is 90% cotton and 10% polyester. S-XL \$17.50 / 2X \$19.50/ 3X \$21.50.

Option 2) #06497 is 99% cotton and 1% polyester. S-XL \$15.00, 2X \$17.00.

Ace's Embroidery accepts Visa, Master Card, Discover Card, A/X and checks. Contact: Bruce Adler, 9059 East Alondra Blvd., Bellflower, CA 90706. Phone: (562) 461-8088 or e-mail: deyfrey@yahoo.com.

Include an additional \$5.00 for shipping and handling. This is a flat rate and applies to all orders, no matter how large the order is. Be sure to specify that you want the BIRN logo on the shirt.



Nora Makhsudova, BIRN-CC's petite first contact, models an extra large version of the new golf shirt. Out-take is a sample of the double stitched BIRN logo.

All-Hands Held at UCSD BIRN Center

by Jorge Jovicich, Harvard

On February 5-7, 2003, the Morphometry BIRN held an all hands meeting to identify and prioritize key issues that will allow testing of clinical specific hypotheses by October 2003 using BIRN enabled processing tools and data. Approximately 40 Brain Morphometry, Function, Mouse and BIRN CC members from all over the country participated in the two-day retreat followed by a half-day workshop. Attendees felt that the ability to conduct discussions with all members allowed them to make informed decisions as well as design strategies to move the project forward.

The retreat was organized as a large group discussion to define potential publishable manuscripts by October 2003. The workshop allowed the working groups to separately refine their specific tasks.

Documenting BIRN Progress

Documenting validation methods in peer-reviewed journals is important for legitimizing the BIRN project. Through a series of discussions and demonstrations, participants identified ten potential reports of required work with high probability of being published. The papers address three main topics, listed in priority order to reflect their dependencies:

- ▶ Technical specific aims (HIPAA compliant data de-identification, multi-site MRI calibration, network enabled processing)
- ▶ Clinical specific aims (subcortical processing of multi-site retrospective AD & Controls data)
- ▶ Cross-species integration between Human- and Mouse BIRN (integration of processing tools and queries)

The final outcome of some of these reports will depend on the results produced by all work groups.

The recommended strategy is for the working groups to focus first on the deliverables that are absolutely necessary for creating the reports in the shortest possible time. The role of the group leaders will be crucial for keeping the big picture in mind when allocating resources to solve specific tasks. Some of the solutions we find may go through iterations of improvements, so spending too much time to generate *final general* solutions may be not be adequate at this stage.

New Work Groups Developed

The main issues concerning the different working groups were discussed, and actions for each group

were devised. Three additional work groups were created to fill identified gaps in the project progress. These work groups include the BIRN Portal, to focus on portal development; Statistical Analysis, to focus on the long-term need for a Grid Enabled Volumetric Parametric Map calculation environment for doing the large-scale population analyses; and Grid Computation, which has a goal of running large (multi-hundred) brain studies on SDSC computer resources.

Governance Document Revision

The P.I.s continued to discuss governance issues related to the use of BIRN tools and database images, and future growth of the project. The results of those discussions will be used to revise the draft Governance Document.

Future meetings

The next Brain Morphometry BIRN PI-CoPI meeting will be held prior to Human Brain Mapping Conference, New York (tentatively 11:30-13:30, June 17, 2003). This should include Function BIRN members. (See page 7 for upcoming meeting info.)

The next BIRN Governance Meeting will be held on October 2003 during the BIRN All Hands Meeting.



More than 40 members of various BIRN groups joined the Brain Morphometry meeting at UCSD's BIRN-CC building. So many brilliant minds in one place... Did anyone think to ask about the load capacity of the deck?

We Make the Most Out of What Little Brains We Have

by Maryann Martone, UCSD and Michael Fehnel, Duke

One of the issues that the Mouse BIRN project needed to address was how to make the best use of the SRB and the BIRN Data Grid capabilities during the time that databases and supporting tools were being developed. To enhance the collaborations through the use of the Grid and SRB, we decided to:

- ▶ Define the collections hierarchy within the SRB to deposit datasets associated with particular studies.
- ▶ Define a critical set of metadata that would accompany each dataset loaded onto the SRB.
- ▶ Each institution would request that their external collaborators use the SRB for exchanging data.

The definition of the storage hierarchy and the critical metadata to be associated with each dataset has

been completed. An XML schema is being developed to define the document structure and data elements that make up the metadata for each dataset. This document can be parsed with software and the data loaded into the MCAT so that it can be queried from within the SRB browser and the BIRN Portal.

Additionally, at Caltech, Edriss Merchant has developed a script for ImageJ that will parse their image data and produce a center slice as a jpeg thumbnail. This script is called from his web server application to display the image to the user.

Scientific Collaborations

The Mouse BIRN has established working collaborations on several projects. Diana Price of UCSD (see photo) and Aki Laakso of Duke have begun cell-level imaging on the dopamine transporter

knock out mouse. Dr. Laakso visited UCSD in January to perform some experiments. Dr. Price has also completed all of the necessary paperwork to begin sending the Parkinson's disease model mice from UCSD to Duke.

In a cross-over study with the Human Morphometric BIRN, Duke and UCSD are collaborating with Harvard on adapting the FreeSurfer automated segmentation routines for human MRI data for use with the mouse MRM datasets produced by Duke. Al Johnson and graduate student Anjum Ali, both at Duke, are collaborating with Anders Dale at Harvard and Maryann Martone at UCSD on this project. Duke has

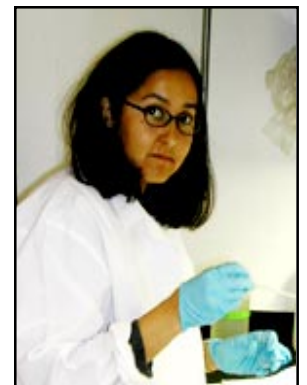
already provided two MRM datasets of normal mouse brain, one with a contrast enhancing agent and one without. Dr. Martone is performing a manual segmentation of anatomical structures in the mouse brain (see figure on this page). These datasets will be used as teaching templates by FreeSurfer to create automated routines. The ability to segment large numbers of brain structures automatically will be of tremendous benefit to the study of animal models of neurological disease.

At the recent Human Morphometry BIRN meeting at UCSD, Steve Pieper (see opposite page) of Harvard and Maryann Martone



Maryann Martone

outlined strategies for linking queries launched from 3D human data viewed in Slicer to the mouse data being assembled by the Mouse BIRN. Slicer is also being integrated into the BIRN portal and can be used to view both mouse and human data. Allan MacKenzie-Graham and Karen Crawford of UCLA have been working with the Data Mediation Group of the BIRN-CC on linking data taken at UCLA to the mediator and on implementing the necessary knowledge bases for linking mouse and human data. They have established the "Coffee Bean" in Tustin as the ideal meeting place half-way between UCLA and UCSD.



Diana Price

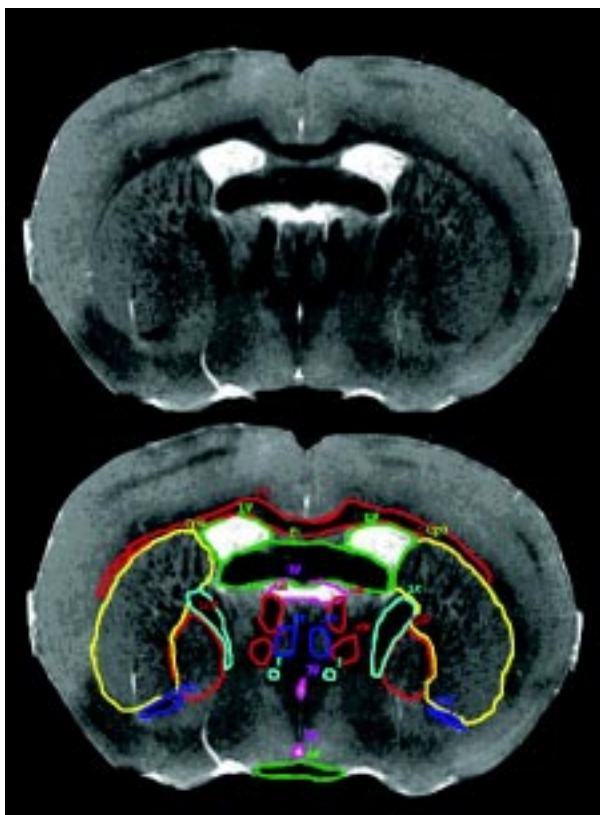


Figure Legend: MRM of normal mouse brain segmented (bottom) using Xvoxtrace, a segmentation tool developed for electron tomography at UCSD.

Steve Pieper: a Man Embracing a Challenge

Steve Pieper is the Neuro Analysis Center's BIRN PI and a Computer Scientist at the Surgical Planning Laboratory, Brigham and Women's Hospital, Boston. He is also responsible for the ongoing architectural development and maintenance of the 3D Slicer, the SPL's flagship software system.

Q. Where are you from?

A. I was born in Omaha, Nebraska, and lived in Lincoln, Nebraska, through high school.

Q. Where did you go to college?

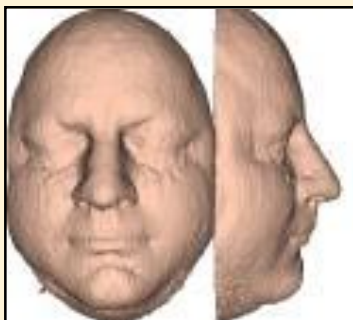
A. I got my undergraduate degree in Computer Science at UC Berkeley. After working at AMD in the Silicon Valley for a while on chip design for 3D Graphics, I went to MIT and got my Masters and PhD from the Media Lab. I worked on FEM and 3D graphics interactive simulators and planning tools for plastic surgery.

Q. What attracted you to the BIRN project?

A. Fun people and the chance to travel! Okay, seriously I like the challenge of a big project.

Q. Do you think the BIRN project will help advance scientific research?

A. I think it's already been helpful to several of us at Brigham and Women's simply because it's brought us together with a community of like-minded researchers from various institutions. This helps us better understand how science is done from other perspectives.



Self-created MRI image of Pieper

Q. How do you think BIRN can be valuable/useful to the neuroscience research community?

A. As a large reference database of images and clinical data together with software optimized to work with the data. I know several researchers who are really looking forward to working with the BIRN as a proving ground for new hypotheses and analysis techniques.

Q. Technologies are often developed with one purpose in mind, but adopted for another. How do you think the BIRN will be used?

A. Our first incarnation is very specific to our needs, but ultimately I think a coordinated set of BIRN technologies and techniques will be very valuable in domains requiring controlled sharing. For example, I know researchers who have large collections of data they would like to share, but the logistical hurdles including not just technical infrastructure, but complex issues like IRB/HIPAA policies. If we can provide a turn-key solution for controlled sharing I think a lot of people will be happy to participate.

Q. Collaboration is invaluable, but it often creates additional hurdles. What are some of the challenges you have experienced working with different groups?

A. Frankly the biggest issue I see arises when people's time is split too finely between many projects at their institutions. As a result, their contributions to the BIRN effort aren't adequately focused and we don't get the full benefit of their participation.

Q. What are some of the major challenges in the horizon?

A. We need to deliver results to the NIH that justify the investment of resources. Some of this is in
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Generating a Bioinformatics Toolbox...

Continued from cover

distributed groups of biomedical researchers, allowing them to focus solely on the scientific questions at hand. This technical challenge is formidable but critical to the future of biomedical research.

The BIRN will lead the way in showing that a toolbox full of such seamless technologies can result in accomplishments that combine and magnify the strengths of individual laboratories and institutions.

It is this nonlinear payoff that makes networks, and infrastructure in general, so powerful and a critical investment. In order to succeed, the BIRN must generate networks that are greater than the sum of their nodes.

Function BIRN Takes Its FIRST Steps

by Jessica Turner, UCI

In its first months of funding, the Functional Imaging Research In Schizophrenia Testbed (FIRST) BIRN made its initial progress in organizing the consortium, acquiring hardware and software, setting up working groups and determining its milestones. With the goal of building on the Mouse and "Morph" BIRN structures, the Function BIRN has the unique challenges of incorporating cognitive and sensory tasks, along with the added dimensions of time and human behavior, into the BIRN database.

The Calibration Working Group

The issues of multisite calibration for the functional studies include the need to calibrate the static MRI images and the cortical/subcortical activity signal (as a result of the experimental paradigm). The *calibration working group* has finalized the sensorimotor calibration tasks, the stimulus presentation and response devices, and strategies for human phan-

tom studies. The use of normal volunteers, who can be imaged at all sites, has replaced the rotating engi-



neers strategy in order to ensure timely completion of the initial calibration testing phase. A version of the sensorimotor stimuli program, which includes the capability to either trigger the MRI or receive a trigger from it, allowing precise timing of the functional scans using the same method across sites, is being developed by this group, chaired by Gary Glover (Stanford).

The Cognitive Task Development Workgroup

A major challenge for the Function BIRN is to test both basic sensory-attention processing with a cognitive working memory task in a manner that gives robust, reliable brain activity within the short scanning time. The

cognitive task development workgroup (chaired by Stephen Heckers, Harvard MGH) has reviewed cognitive activation tasks relevant to the designated subject population and will be updating those in more detail in future meetings. This group has collected and reviewed pilot data comparing different versions of the sensory task for the most reliable results, as collected and presented by Cindy Wible (Harvard BWH). Stephen Heckers has presented information to the effect that the working memory task will fit in the time allotted.

Database development group

The *database development group* has a great deal of overlap with the Morphometry BIRN's working group, *Continued on page 8*

Function BIRN Latest!

February 14, 2003 - The first of the second generation racks went online at UC Irvine.

BIRN-CC Responds to Your Needs...

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is complete. UMLS will be used in conjunction with the Mediator to allow for intelligent queries across the various data sources

Next Steps

The BIRN-CC is actively listening to your requests. The next months of development effort will be devoted to:

- ▶ Bringing more tools online (LONI pipeline, FreeSurfer, etc.)
- ▶ Enhancing the portal user interface
- ▶ Completion of the mediator

- ▶ Launching queries from the portal

It is heartening to see the level of cooperation between researchers and research sites. The interoperability and sharing of data files allows for a level of cooperation rarely seen in collaborative neuroscience projects. For example, researchers can now view mouse data using a human species tool like 3D Slicer. The integration of tools from each site allows researchers to explore their data in exciting new ways.

Function BIRN Has a New Project Manager

As the new project manager, let me introduce myself to those who have not met me yet. My background is in the cognitive sciences, initially in visual perception; I come to the project from the Long Beach, California VA hospital, having been the head of fMRI for Research there for the past three years, working with a group studying motor learning, cortical



Jessica Turner

plasticity, and motor representations following spinal cord injury or amputation. The BIRN ideas and vision are very exciting, and I am looking forward to working with everyone in the various BIRN groups to move these projects forward.

Join the Great RAID Migration

by Chuck Lane, BIRN Coordinating Center

In the beginning, computer scientists created the BIRN racks, and NAS was provided for the users. And the creators looked upon them and saw that they were good.

In their wisdom, the creators then said "Let us use RAID 5, for it offers a balance of capacity, performance and reliability." However, the implementation in Windows was slothful and none could abide its performance. Thus, the initial racks were sent out onto the grid in the configuration of RAID 0+1. Although the performance was good, soon the users began to cry out "Deliver us from RAID 0+1, for it wastes half of its capacity."

Linux conversion

Rest assured that the needs of the BIRN community did not go unheard. We have done significant NAS testing under Linux and dem-

onstrated that RAID 5 offers comparable read and write performance to RAID 0+1 for file sizes up to 1Gb. Our survey of the various BIRN sites indicates that most files (not collections) are less than 1 Mb. Thus, we can increase the effective capacity of each NAS by more than 70% without significantly impacting storage perfor-

"...we can increase the effective capacity of each NAS by more than 70% without significantly impacting storage performance."

mance.

The timing of this activity is particularly propitious owing to the release of SRB 2.0. With this new release, SRB

can be configured to manage multiple file systems as a single logical volume. This means that files will be uploaded to each mounted file system on a rotating basis, rather than being copied to all of them concurrently. Thus, we can set up each NAS storage shelf (14 drives) as a RAID 5 file system and present a rack with up to 4 of these shelves (3.5 TB) as a single pool of storage to the BIRN community.

Upgrades

After all sites have upgraded to SRB 2.0, the BIRN-CC will assist everyone with a RAID 0+1 to RAID 5 migration. To prepare for this, all sites should confirm that they can reliably back up and restore the existing data on their local NAS.

Expect to be contacted within the next quarter with additional details... *And it will be good.*

Upcoming Meetings of Interest

March 18-21, 2003

NPACI All-Hands Meeting. UC San Diego.

<http://www.npaci.edu/ahm2003/index.html>

March 29 - April 2, 2003

International Congress on Schizophrenia Research. Broadmoor Hotel in Colorado Springs, Colorado.

<http://www.schizophreniacongress.org/>

March 30 - April 1, 2003

Cognitive Neuroscience Meeting. New York City Marriott Marquis Hotel

<http://sssa091.ucdavis.edu/>

June 18-22, 2003

USA Organization for Human Brain Mapping. New York.

(952) 646-2029

<http://www.humanbrainmapping.org/NYC2003>

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Communications/People/
list_participant.msq](http://www.nbirn.net/Communications/People/list_participant.msq)

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the science we do to address our clinical aims and some is in the computer technologies we bring to bear. But the biggest — and toughest — result will be to show that we have a viable methodology for knowledge creation on an ongoing basis.

Q. Is there anything else you would like to add?

A. I think we're all very lucky to be involved in a well supported project like this.

Contact Steve at: (617) 596-2719 or e-mail him: pieper@bwh.harvard.edu



Function BIRN Takes Its FIRST Steps...

Continued from page 6

because the two BIRNs share many of the same challenges in structuring the database. They are determining which clinical database fields will accommodate the various patient characteristics that different sites collect. Nancy Andreasen and the *MIND group* are providing collaborative feedback so the resulting database can serve an even wider range of needs.

Imaging Database Working Group

The *imaging database working group* is determining the best schema for the imaging data.

Identification Regulations

IRB and HIPAA regulations have been discussed and their database implications are being negotiated. The question of de-identification,

which was covered by the Morphometry BIRN in the October 2002 issue of the newsletter, is equally relevant to the Function BIRN data. Sample IRB language has been circulated to each of the sites' IRB and legal representatives. Feedback from the sites has been coordinated with the Morphometry BIRN and a joint template for IRB submission of these projects is being developed, spearheaded by Randy Gollub, Harvard MGH; Jeff Grethe, BIRN-CC; and Jessica Turner, UCI.

The Function BIRN is also attacking the problems of statistical analysis and visualization of functional MRI results across sites. This requires interaction with both database design and the IRB approvals for uploading protected data, as well

as the network group, to assure that the necessary clinical and behavioral data can be shared, and that the very large datasets and heavy computational loads can be handled across sites.

A satellite workshop for the Statistics and Visualization Workgroup is being scheduled to coincide with the meeting of the Organization for Human Brain Mapping in New York this June.

The Function BIRN project was presented as a poster at the American College of Neuropsychopharmacology in Puerto Rico in December 2002, and will be described in a short presentation at the upcoming International Conference on Schizophrenia Research. (*See Upcoming Meetings on page 7 for more information.*)