

Advanced Cyberinfrastructure to enable Multi-scale and Multi-site Brain Research

Mark Ellisman

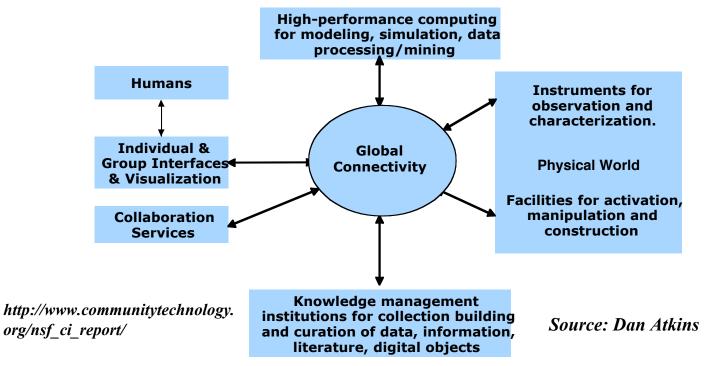
Professor of Neurosciences and Bioengineering, University of California San Diego, and Director of the Center for Research in Biological Systems



"CYBERINFRASTRUCTURE" What is a Grid? What do we mean?

GRID technologies bring remote resources together

A broad, systemic, strategic conceptualization Components of Cyberinfrastructure (Grid)-enabled science & engineering

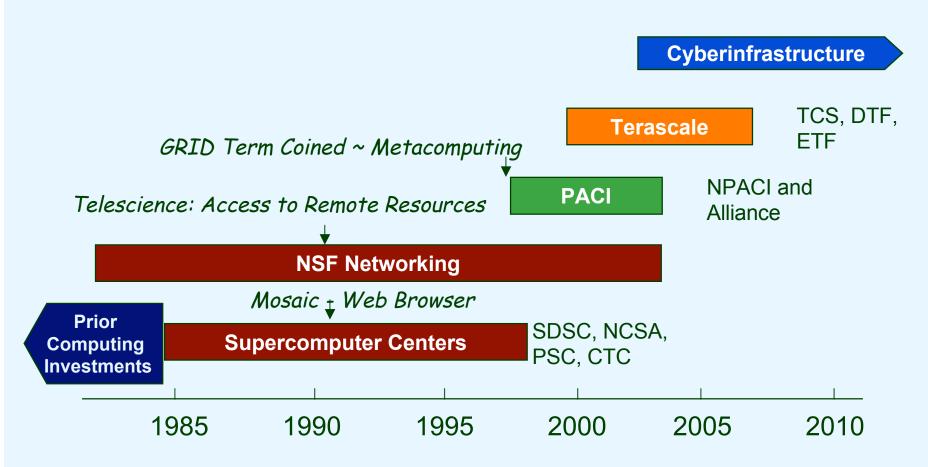


Grid implies global (international) system for collaboration



Evolution of the Computational Infrastructure

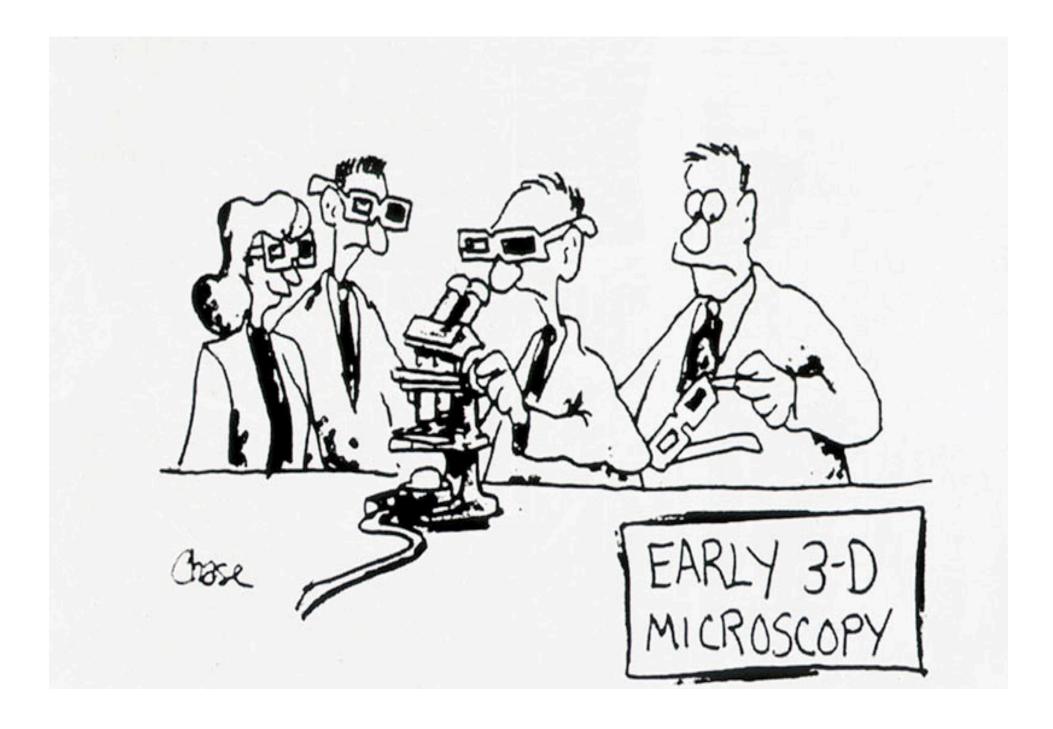
Investments in the US Source: Dr. Deborah Crawford Chair, NSF CyberInfrastructure Working Group (CIWG)

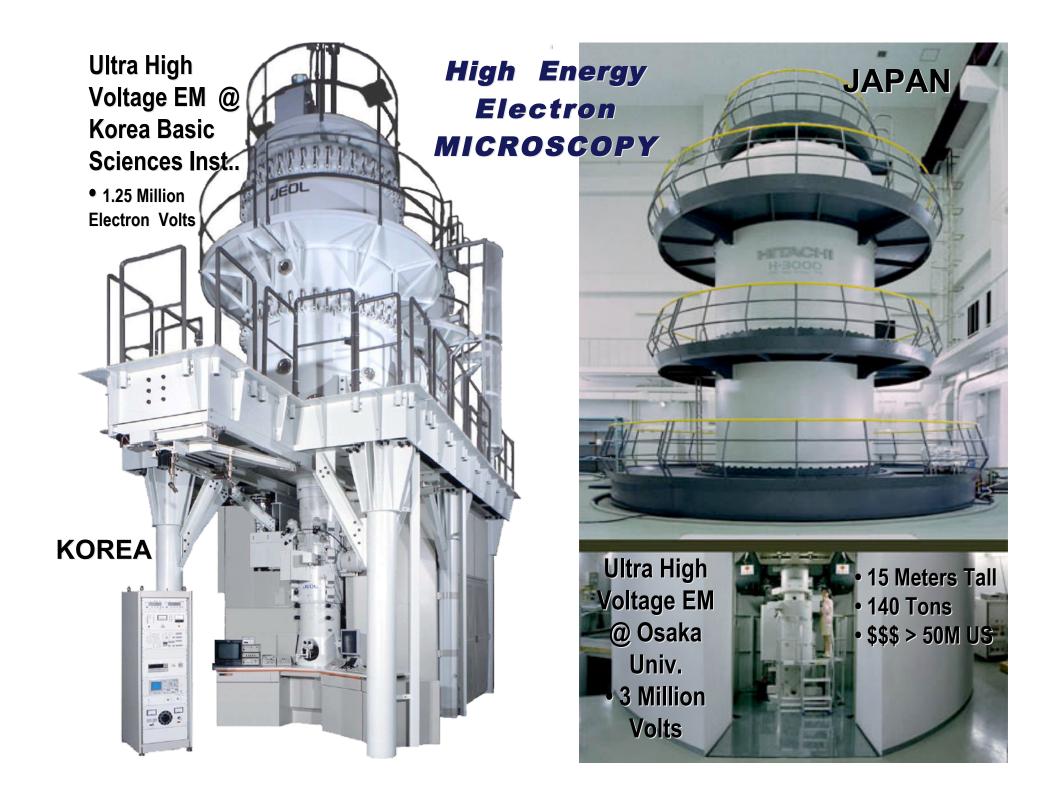


A timeline from the Computational Infrastructure Division of the US National Science Foundation

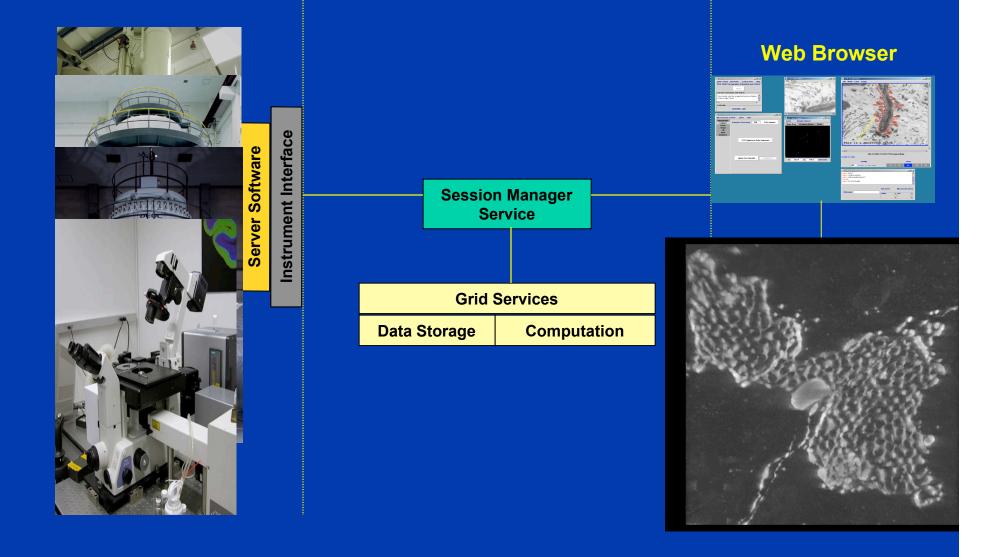
National Center for Microscopy and Imaging Research

An NIH sponsored Research Resource

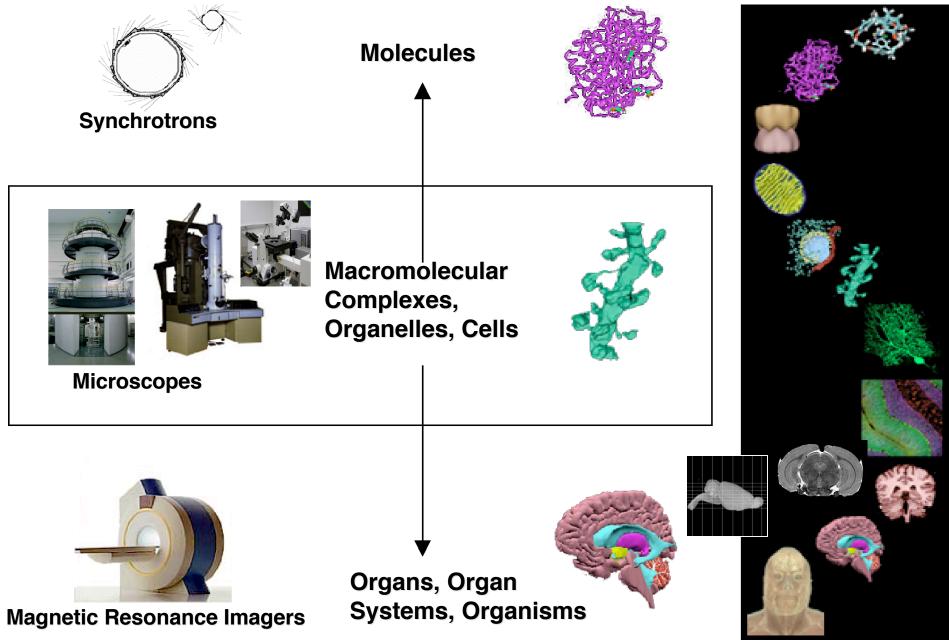




TELEMICROSCOPY & CYBERINFRASTRUCTURE *REMOTE ACCESS FOR DATA ACQUISITION, GRID COMPUTING AND DISTRIBUTED DATABASES*



Synchrotrons, Microscopes and MRI's: Tools for the Nano, "Meso" and Macro Scales of Biological Systems

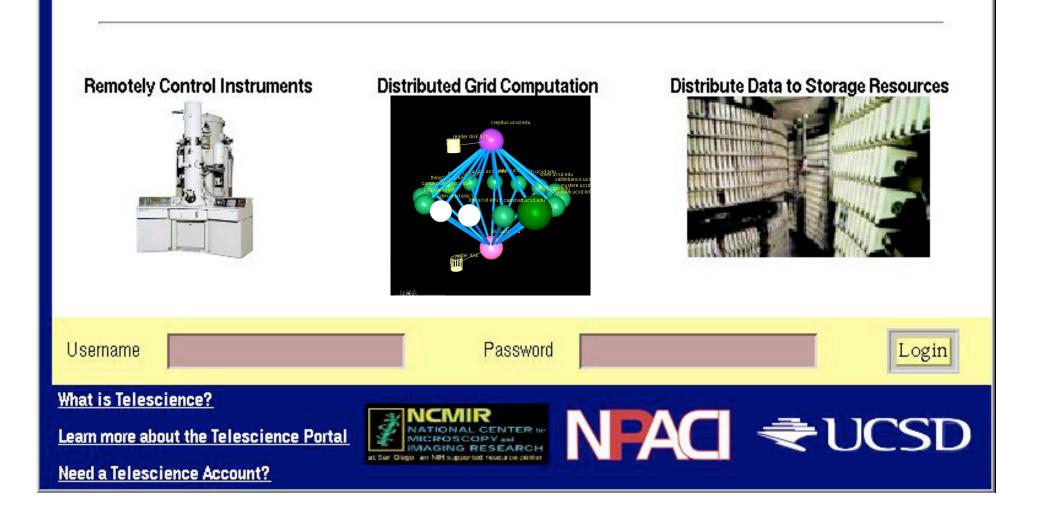


The Login Page: The Entrance into the Portal

Single login grants authenticated access to all applications, resources, and services

telescience

for advanced tomography applications

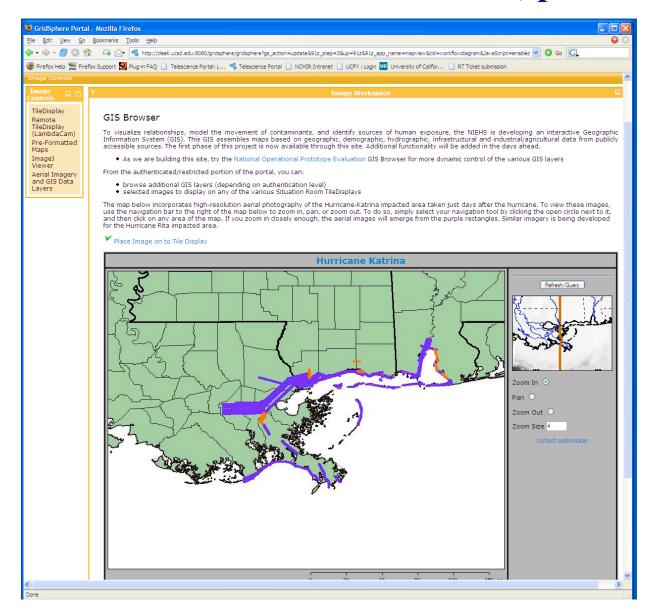


Telescience/ BIRN Portal Technology used as SARS Portal for Taiwan

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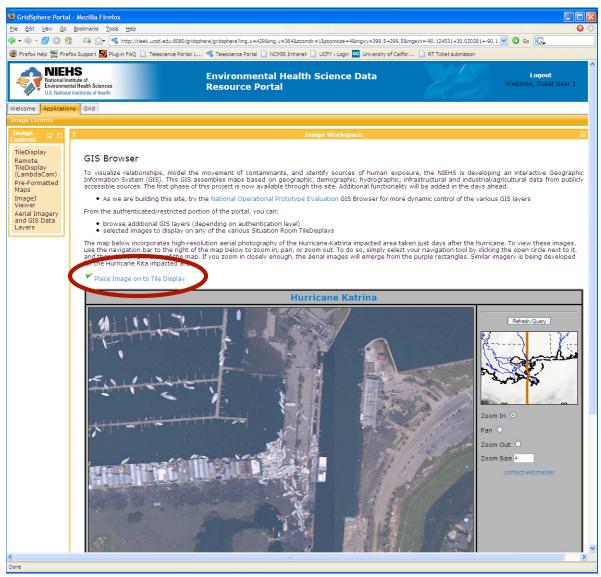
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Site Browser	Hurricanes Katrina and Rita					
NIEHS Natural Disaster Response About the GIS Site Pre-Formatted Maps	NIEHS Katrina/Rita Response Portal This GIS site is intended to provide tools and information for those who are addressing the consequences of natural disasters such as Hurricanes Katrina and Rita by supporting the decision-making process related to:					
Aerial Imagery and GIS Data Layers Restricted Data	 Identifying sources and routes of contaminants Evaluating the potential for future exposures Assessing human exposures that occurred in the immediate aftermath of the hurricanes Assessing the immediate and longer term health impacts associated with these exposures This site contains pre-formatted or ready-made maps of potential sources of environmental contaminants in the hurricane-affected					
areas. It also contains aerial photography images of the areas affected by Hurricane Katrina and we are compiling aerial images with Hurricane Rita. We are also working to provide a functional set of GIS data layers that will allow users to cons tailored to individual needs. We will continually update this site as we obtain and process additional information to meet challenges that arise a proceeds. Send GIS-related comments and questions: hurricanegis@niehs.nih.gov						
						NIEHS Home Accessibility Disclaimers Privacy
	U.S. Department of Health & Human Services Vertices National Institutes of Health National Institute of Environmental Health Sciences	telescience				
Done						

Integrated GIS Browser: View High Resolution Satellite Data, part 1



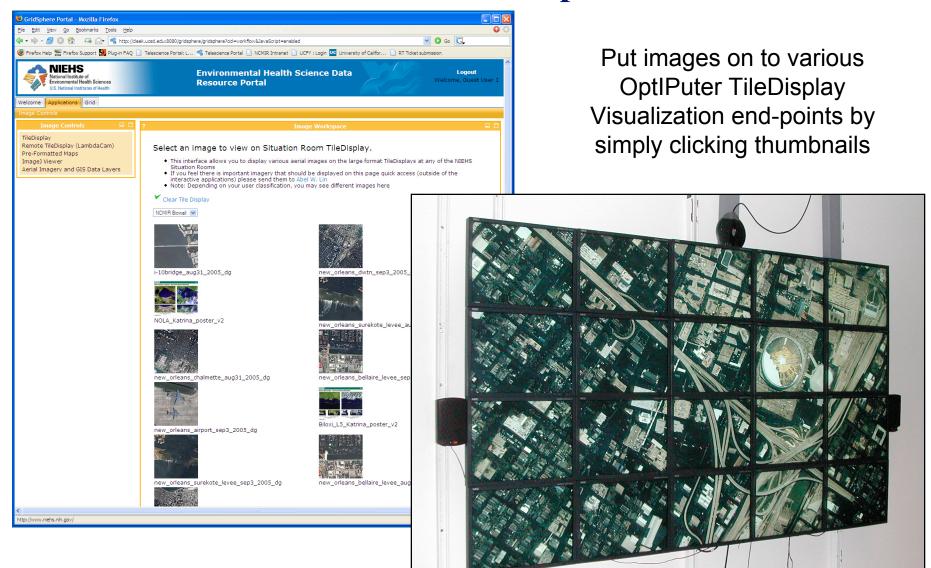
Integrated Browser to scan integrated satellite imagery

Integrated GIS Browser: View High Resolution Satellite Data, part 2

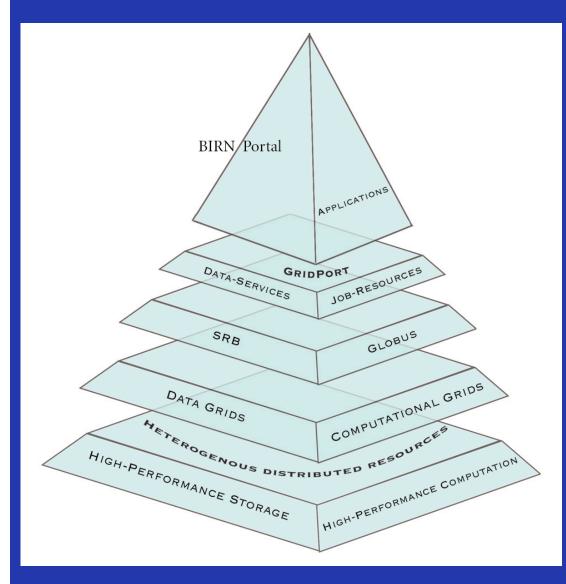


Can also Place GIS Image on TileDisplay for large format viewing

Launch images to large format TileDisplay visualization end-points



Layered Architecture

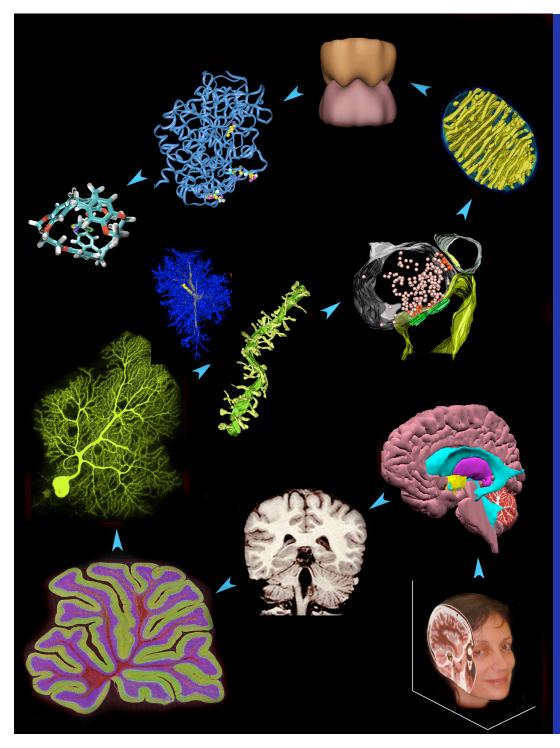


• The Telescience Portal is composed of many "layers"

• Layers are modular, allowing for extension of any layer without great disruption to the entire system

• Every Layer has its own complexity and administration that was previously passed on to the end-user

 Portal centralizes all administrative details of each layer into a single username and pass phrase



Team Science Applied to Stretch Goals

Enable new understanding of the brain by linking data about macroscopic brain function to its molecular and cellular underpinnings

Federate Distributed Multiscale
 Brain Map Data

Accommodate associated Large
 Scale Computational Challenges

 Provide Infrastructure for Construction of more Accurate Models and more Realistic Simulations of Brain Activity

Origins of IT Infrastructure used to build the BIRN:

Initiatives like the NSF - National Partnership for Advanced Computational Infrastructure (NPACI)

> NSF Network Linked Brain Mapping Data Caches

@ Wash U. & UCLA With Supercomputing at UCSD

- ~50 partner sites
- Shared compute resources
- High-speed networks
- Computational science
 efforts in ...
 - Neuroscience
 - Molecular Science
 - Earth Systems Science
 - Engineering
- Enabling Technologies:
 - Resources (TeraFlops, High Performance Networks, Data Caches)

Leading-edge Site
Compute Resource Partners

Associate Partners

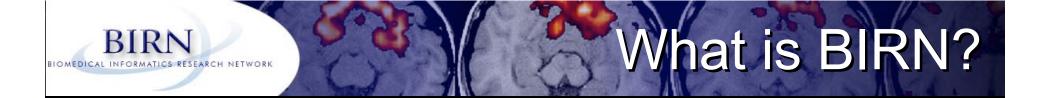
Data Resource Partners

Development and Education Partners

- Metacomputing (Grid Tools Middleware)
- Interaction Environments (Visualization Science Portals)
- Data-Intensive Computing (Databases Data Integration)

The NSF PACI Program Started in 1995 Current Program is "Cyberinfrastructure"





- Testbed for a biomedical knowledge infrastructure
- Creation and support federated bioscience databases
- Data integration
- Interoperable analysis tools
- Datamining software
- ✓ Scalable and extensible
- Driven by research needs pull, not technology push

We Began with Standard Hardware

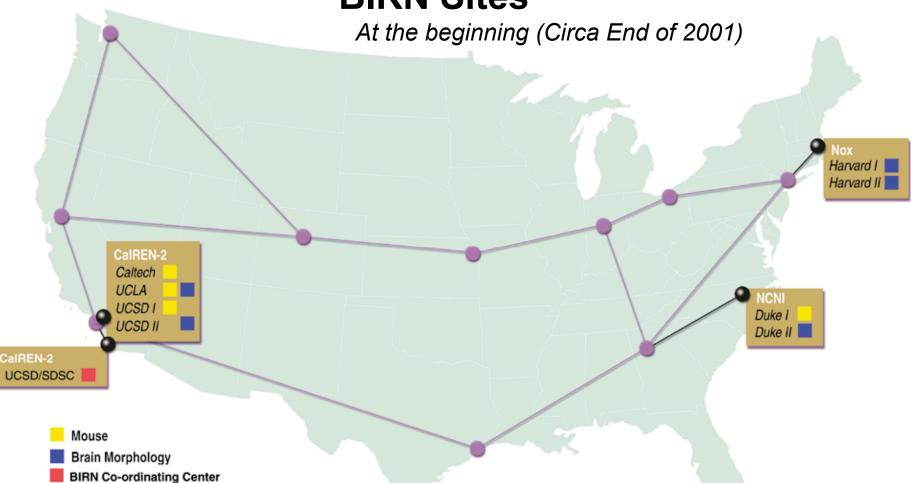


- This jumpstarted BIRN for functionality
- Software footprint is managed from the BIRN Coordinating Center
- Integration of domain tools, middleware, OS, updates, and more
- BIRN expansion/upgrade of existing sites has a more generic (and less expensive) hardware footprint



BIRN Must Accommodate Growth

BIRN Sites



10+ Distinct Installations, ~ 100 Individual Machines



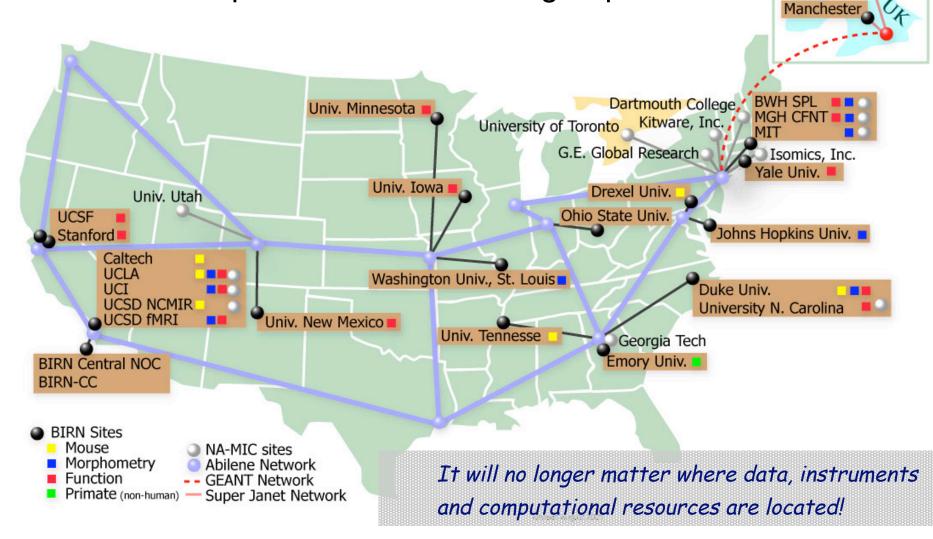
Abilene Backbone

From the Expanding the BIRN Meeting @ NCRR: December. 6 & 7, 2001)

The BIRN Collaboratory Today

Edinburgh

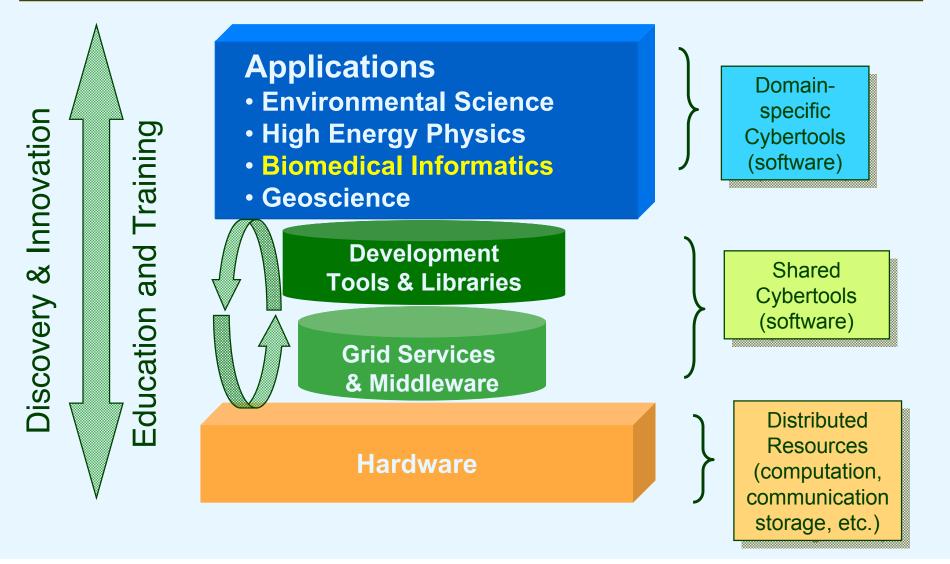
Enabling collaborative research at 28 research institutions comprised of 37 research groups.





Integrated Cyberinfrastructure System meeting the needs of multiple communities

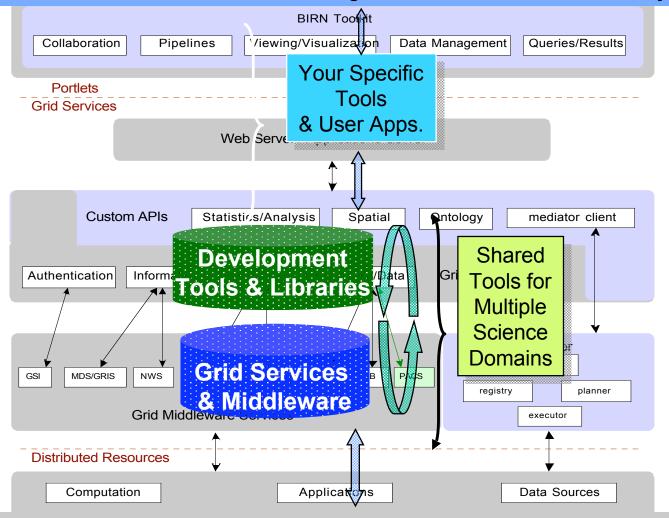
Source: Dr. Deborah Crawford, Chair, NSF CyberInfrastructure Working Group



BIRN Core Software Infrastructure

Friendly Work Facilitating Portals

Authentication - Authorization - Auditing - Workflows - Visualization - Analysis



• BIRN builds on evolving community standards for middleware

 Adds new capabilities required by projects

•Does System Integration of domain-specific tools building a distributed infrastructure

• Utilizes commodity hardware and stable networks for baseline connectivity

Distributed Computing, Instruments and Data Resources

Software Problem in a Nutshell

Vetwork

CPU

Security

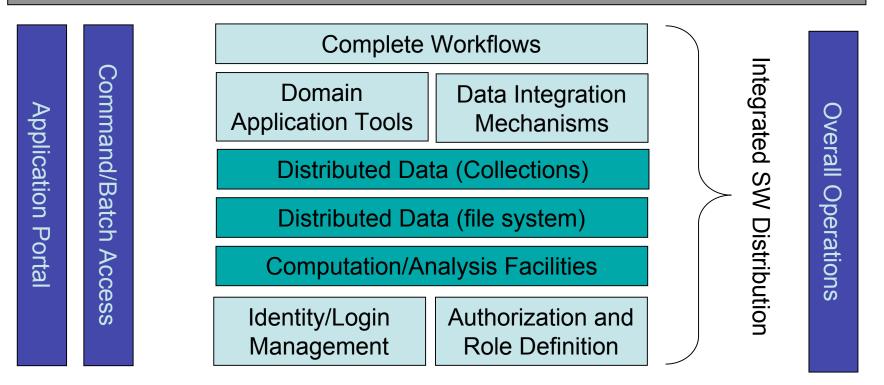
Data

- Enable Analysis of Distributed Biomedical Data in a National-Scale Production Facility
 - Data sets are large Data sets are many
 - Enable new queries that integrate multiple sources
 - Specialized application codes (from Test Beds) need to work on BIRN-accessible data
- Some analysis pipelines require significant computation
 - Privacy, patient anonymity required
 - Institutional ownership of originals

Easily Replicate Entire Software Stack (Including Centralized Services) for other Groups

Major System Components

Collaborating Groups of Biomedical Researchers

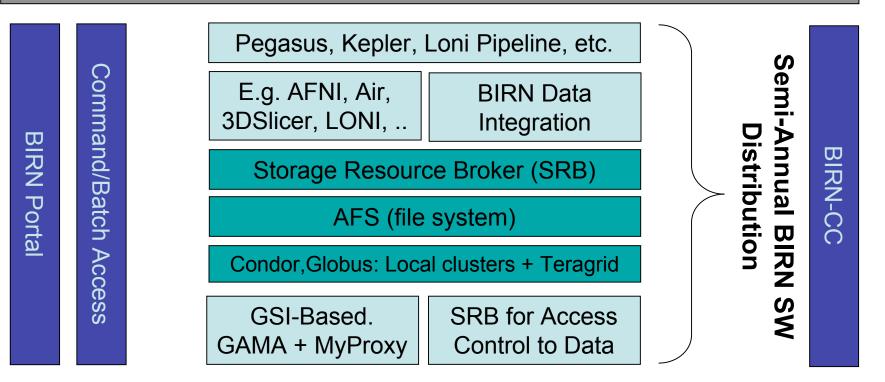


Note: Similar Structure to Many Other Grids

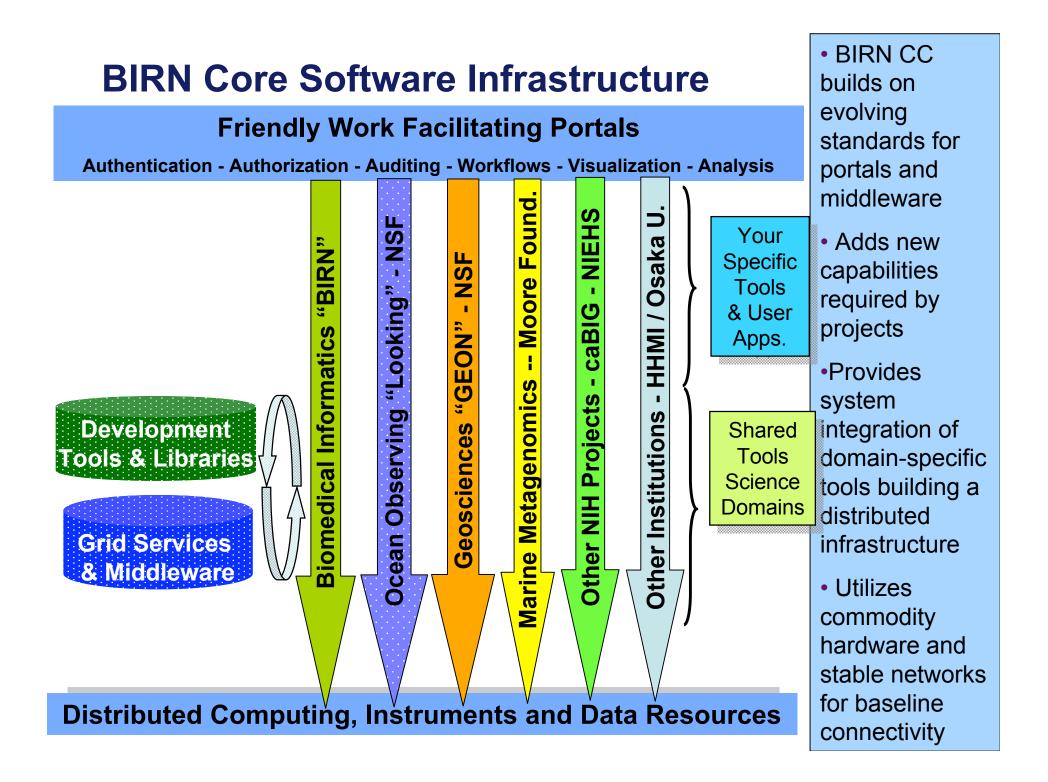
BIOMEDICAL INFORMATICS RESEARCH NETWORK

Specific Implementations

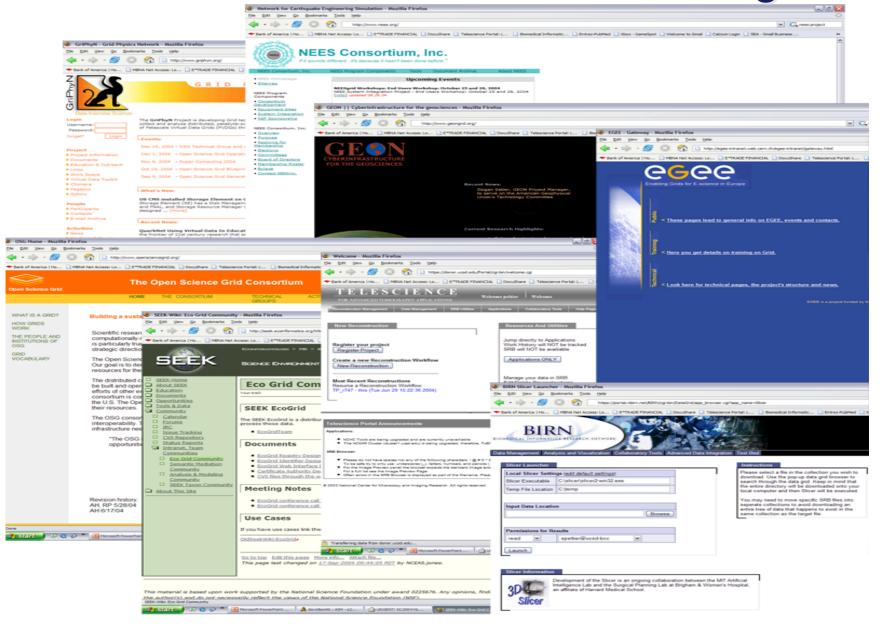
Mouse, Function, Morphometry (+ New Areas and Users)



Note: Similar Structure as Many Other Grids

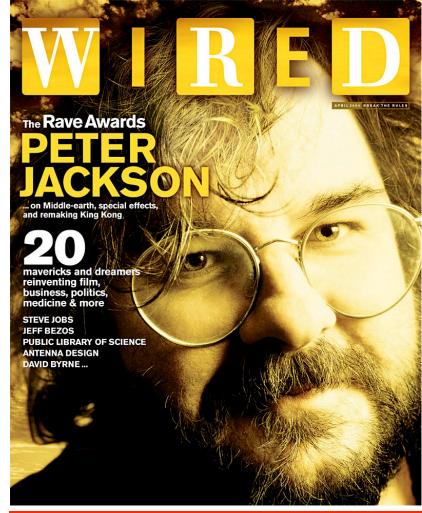


The Grid is becoming the backbone for collaborative science and data sharing



Grid Infrastructure in Action

- The Grid is already having an impact...
 - Many projects in many subjects:
 - Life sciences
 - Medicine
 - Environment
 - Engineering
 - Materials
 - Chemistry
 - Physics
 - BIRN embodies the most innovative use of data, metadata & portals



BIRN cited as successful model of grid computing.

BIRN has the Advantage of having Developed an "End-to-End" Infrastructure: <u>Built around research</u> projects with geographically distributed data.

- Consists of all the components required to effectively share and collaboratively explore data
 - The BIRN Rack (BIRN site infrastructure)
 - The BIRN Portal
 - The BIRN Virtual Data Grid
 - The BIRN Data Integration Infrastructure
 - The BIRN Computational GRID
- The system integration, development, deployment and management of this infrastructure is the main focus of activities within the BIRN Coordinating Center



The BIRN Portal

)	BIRN BIOMEDICAL INFORMATICS RESEARCH NETWORK	Username: Password: login	
	Home Account Request	Style Help	
d			

Login Information

BIRN Portal Login	
Enter your username/password	
Username:	
Password:	
Login	
<u>Request</u> a BIRN account (must be a BIRN participant) <u>Email</u> BIRN Portal admins	

Portal Requirements

You must have cookies enabled to login to the BIRN Portal, in addition, Javascript is highly recommended but not required.

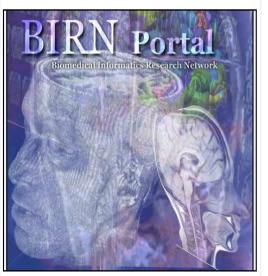
The latest version of Java will be required to access *some* of the applications.

For optimal browsing please use <u>Mozilla</u>, Netscape or Internet Explorer.

There are known problems with Safari that prevent proper authentication with the portal, as a result, Safari users will have to chose an alternative browser to access the BIRN Portal.

Welcome to the BIRN Portal

The Biomedical Informatics Research Network (BIRN) Portal provides BIRN members with a single sign on web portal to access data grid files, computation grid resources and a variety of collaboration tools to facilitate the scientific needs of BIRN researchers. Non-BIRN participants may access the portal through a guest registration.



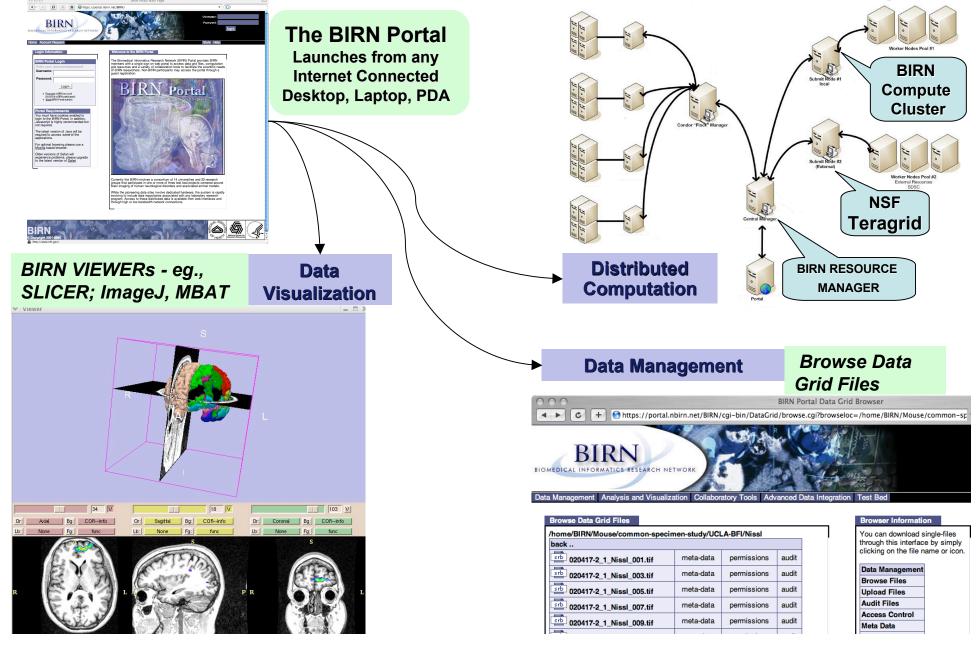
Currently the BIRN involves a consortium of 14 universities and 22 research groups that participate in one or more of three test bed projects centered around brain imaging of human neurological disorders and associated animal models.

•Application environment that provides transparent and pervasive access to the BIRN infrastructure (i.e. tools, applications, resources) with a **Single Login** from any Internet capable location

•Provides simple, intuitive access to distributed resources for data storage, distributed computation, and visualization

•Provides a scalable interface for users of all backgrounds and levels of expertise

The BIRN Portal Provides an Intuitive Interface to Software Tools, Data and Computational Resources in the BIRN Collaboratory



BIRN is a Leader in Portal Technology

- The BIRN-CC is supporting development of the leading open-source standards-based grid portal
- Application environment that provides transparent and pervasive access to the BIRN infrastructure (i.e. tools, applications, resources) with a Single Login from any Internet capable location
- Support for dynamic collaborative projects

BIRN

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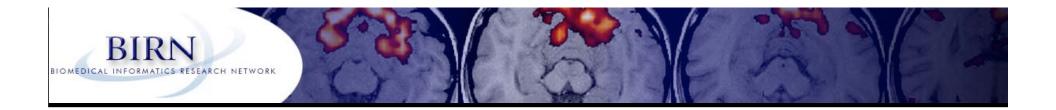
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Benefits of a Data Grid

- Uniform interface for connecting to heterogeneous distributed data resources
 - Allows for any "grid enabled" tool to interact with data no matter where it is located or what it is located on
- Allows for the seamless creation and management of distributed data sets
 - Distributed data appear as a single managed collection both to users and tools
- Access is Managed using GRID Authentication through BIRN Portal





- BIRN Coordinating Center (UCSD)
- BIRN Test Bed Projects
 - Morphometry BIRN
 - Function BIRN
 - Mouse BIRN

Clinical Aims

RIRN

IOMEDICAL INFORMATICS

 Do structural differences contribute to specific symptoms such as memory dysfunction or depression?

Brain Morphometry BIRN

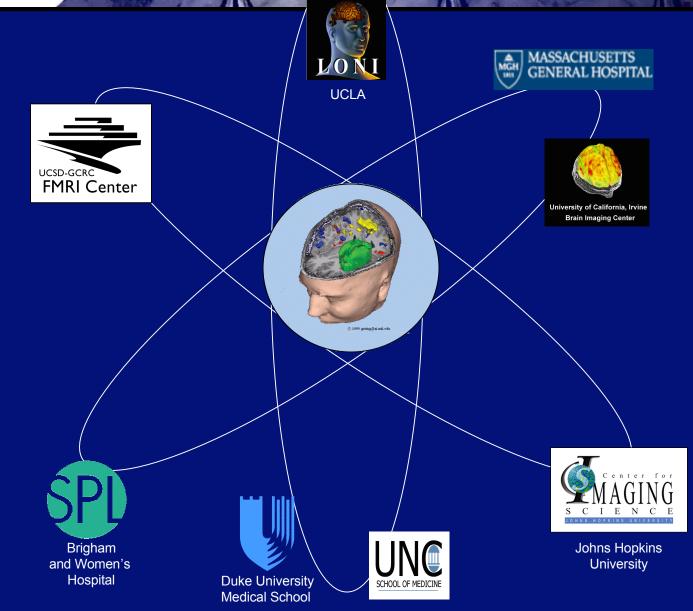
Do specific structural differences distinguish specific diagnostic categories?

Technological Aims

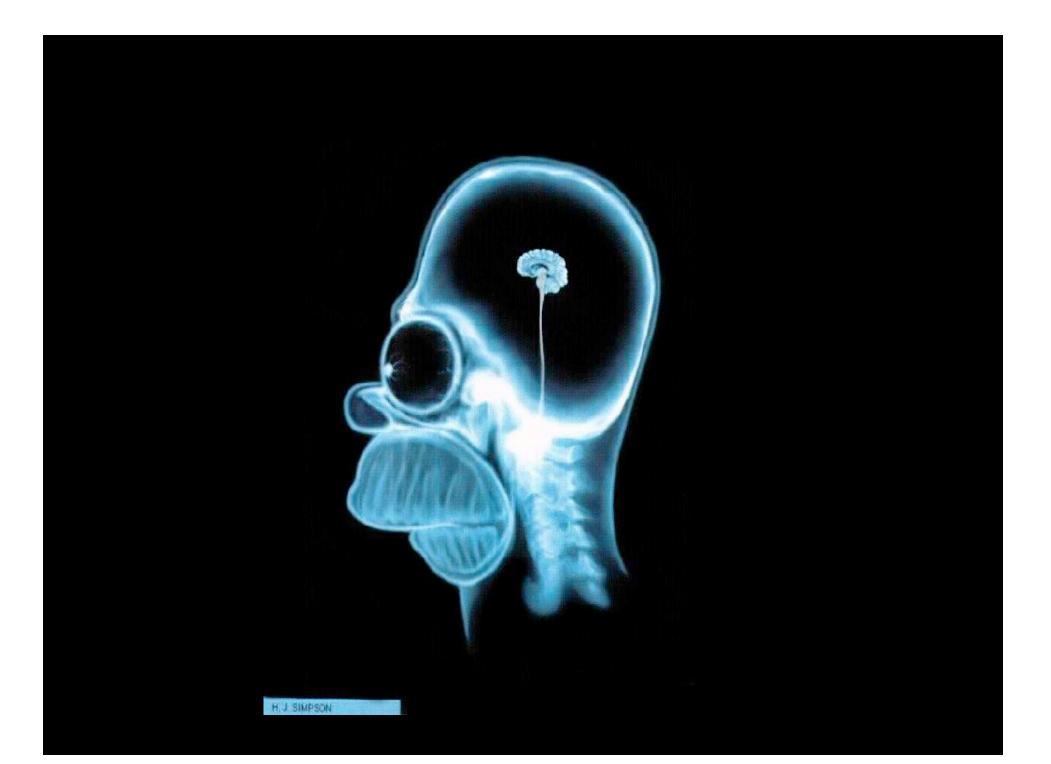
 Attempt to overcome obstacles to the use of neuroimaging data as quantitative outcome measures for clinical investigation including the issues raised by longitudinal and multi-site studies.



Morph BIRN



BIRN BIOMEDICAL INFORMATICS RESEARCH NETWORK



Human Subjects Considerations

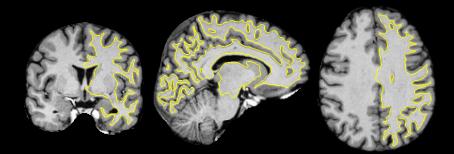
- High-resolution structural images can be used as an identifier.
 - Reconstruction of face from raw anatomical data might be able to be used to identify subject
 - Some members of BIRN require/desire unaltered raw data
 - BIRN has received approval from local IRBs to allow for the sharing of raw anatomical data from prospective subjects with current authorized BIRN members (i.e. fBIRN Human Phantoms)
- BIRN must conform to multiple overlapping regulations
 - Common Rule
 - HIPAA

RIRN

- State Law

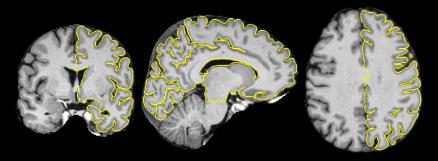


Cortical Thickness Estimation with Sub-Voxel Accuracy



Gray-white boundary

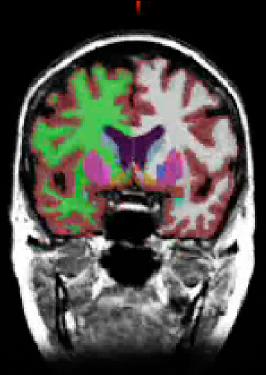




Pial surface

From Anders Dale / Mass General Hospital - Harvard

Automated Whole-Brain Segmentation



Part of Free Surfer By Bruce Fishl and Anders Dale (MGH)

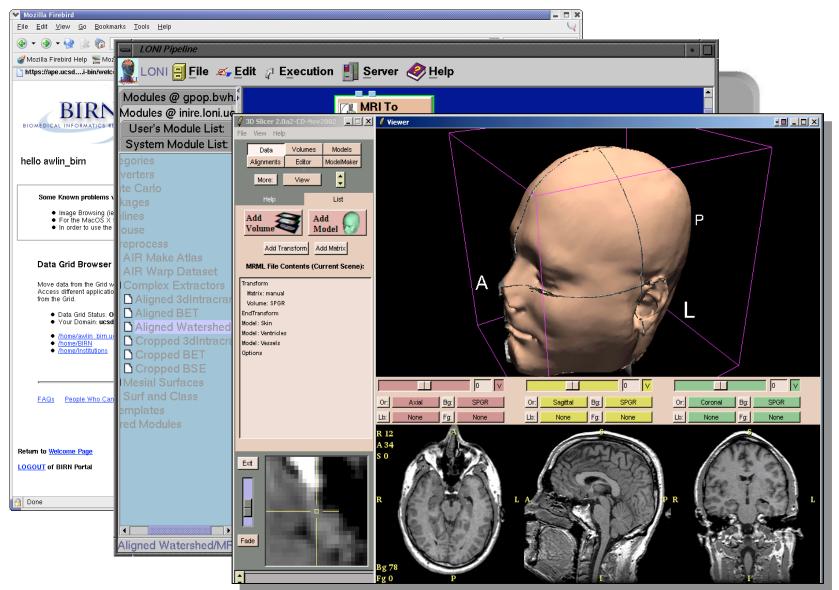
Cerebellar cortex
 Cerebellar WM
 4th ventricle
 RH cerebral WM

LH cerebral WM
 Hippocampus
 LH pallidum

Thalamus

- Cerebral cortex
 Misc.
- Lateral ventricle
- Caudate

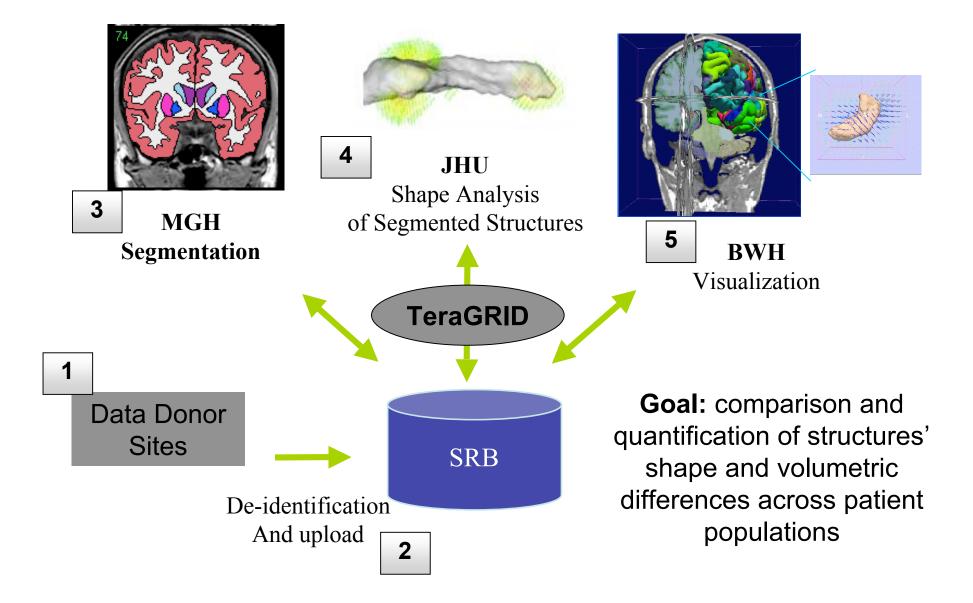
BIRN Portal: Launches Scientific Workflow

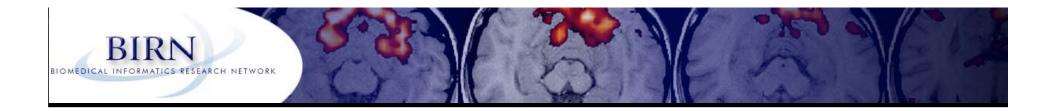


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SASHA Project





- A team of eleven universities studying regional brain dysfunctions related to the progression and treatment of schizophrenia.
 - Prefrontal Cortex (executive dysfunction)
 - Temporal Lobe (auditory processing)

Clinical Aims

BIRM

NOMEDICAL INFOR

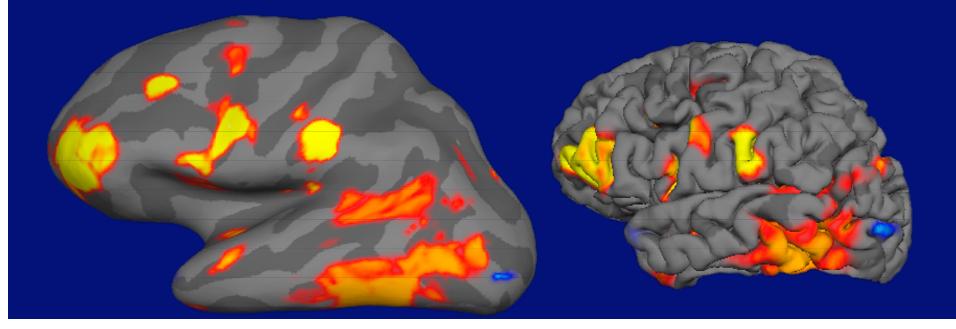
Is Frontal and Temporal Lobe Dysfunction the Cause of Schizophrenia?

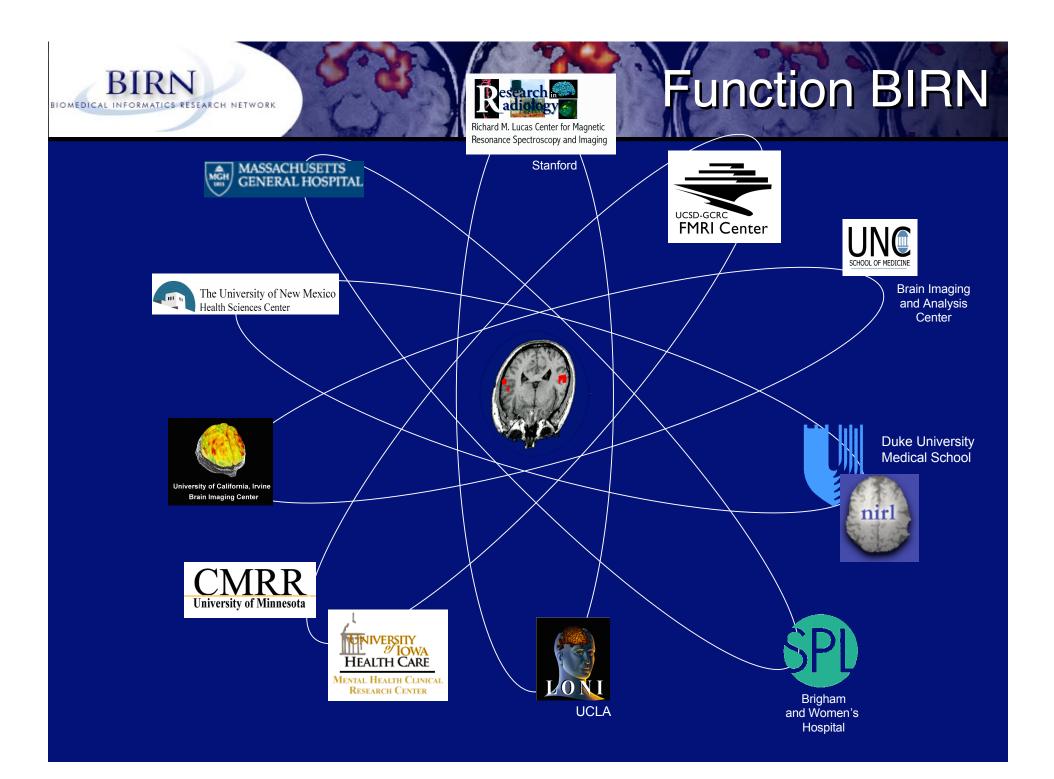
Functional Imaging

How can Treatment Reverse this Dysfunction?

Technological Aims

- Integration of 4D Data from Multiple Sites Acquired with Different Non-Invasive Imaging Devices
- Integration of Information Obtained with Different Brain Activation Tasks.





Traveling Humans Study





BIOMEDICAL INFORM

- Subjects traveled around the country to be scanned at all Function BIRN sites
- Unique dataset: (Subject) x (site) interactions can be measured for the first time

Mouse **BIRN**

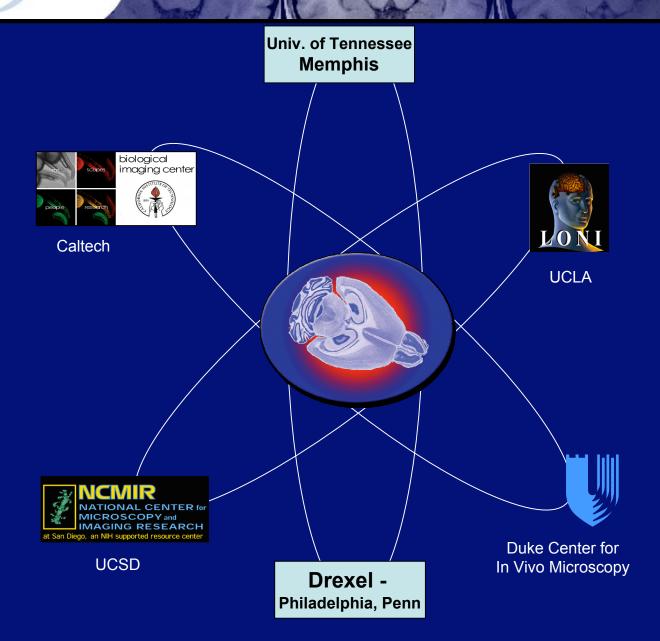
Studying animal models of disease across dimensional scales to test hypothesis with human neurological disorders

RIBN

IOMEDICAL INFORMATICS RESEARCH NETWOR

- Experimental Allergic Encephalomyelitis (EAE) mouse models (both chemically induced and transgenic) exhibit episodic weakness and demyelination characteristic of Multiple Sclerosis (MS)
- Dopamine Transporter (DAT) knockout mouse for studies of schizophrenia, attention-deficit hyperactivity disorder (ADHD), Tourette's disorder, and substance abuse
- Using an alpha-synuclein mouse to model the symptoms/pathology of Parkinson's Disease
- Cancer animal models consortium with astrocytoma mouse model: NCI supported with Terry Van Dyke @ Duke

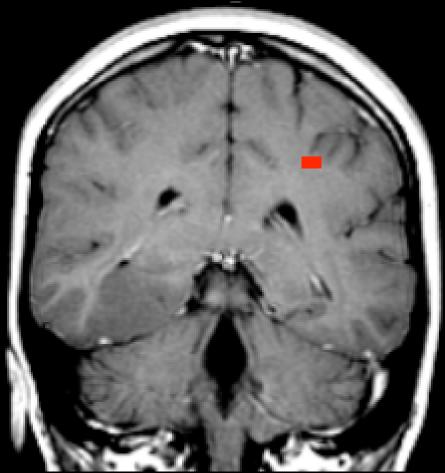
Mouse **BIRN**



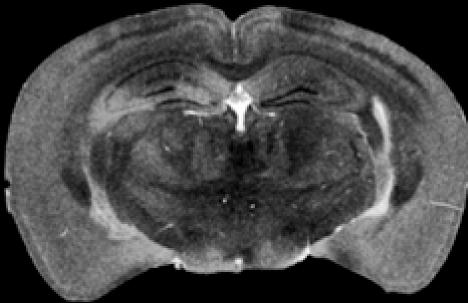
BIRN BIOMEDICAL INFORMATICS RESEARCH NETWORK

Advanced Imaging - Correlating Human and Mouse







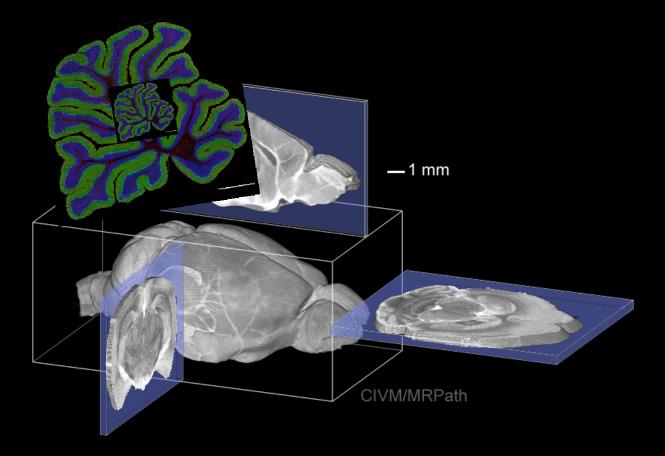


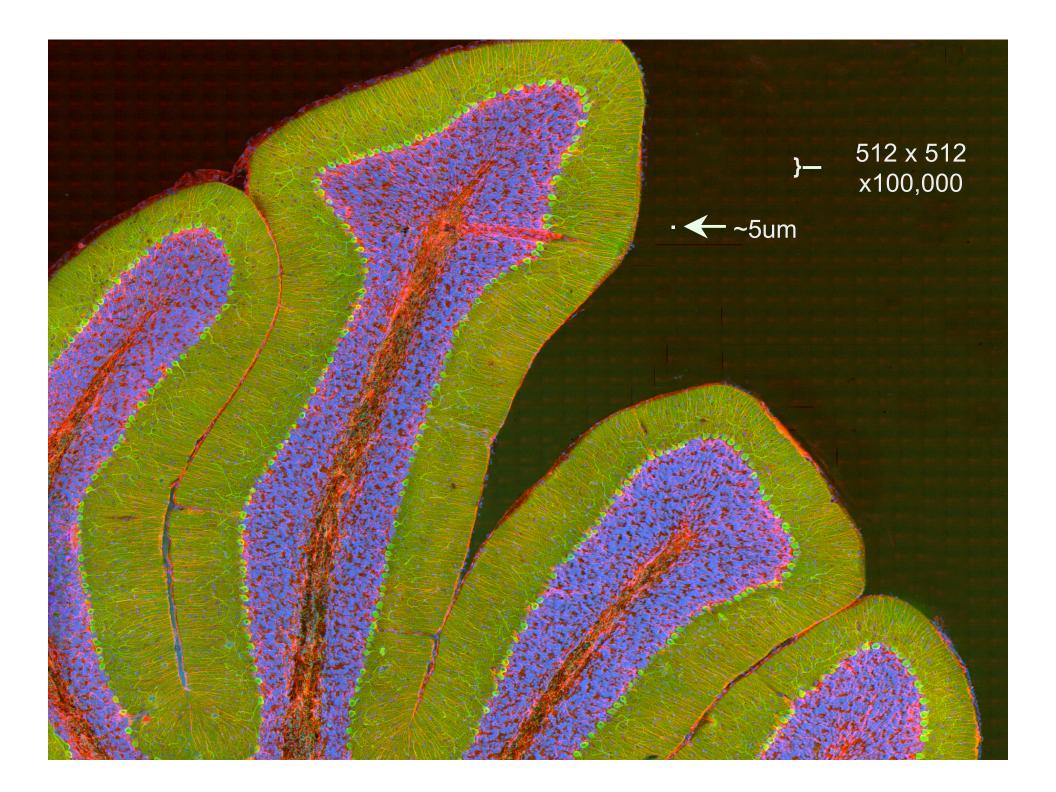
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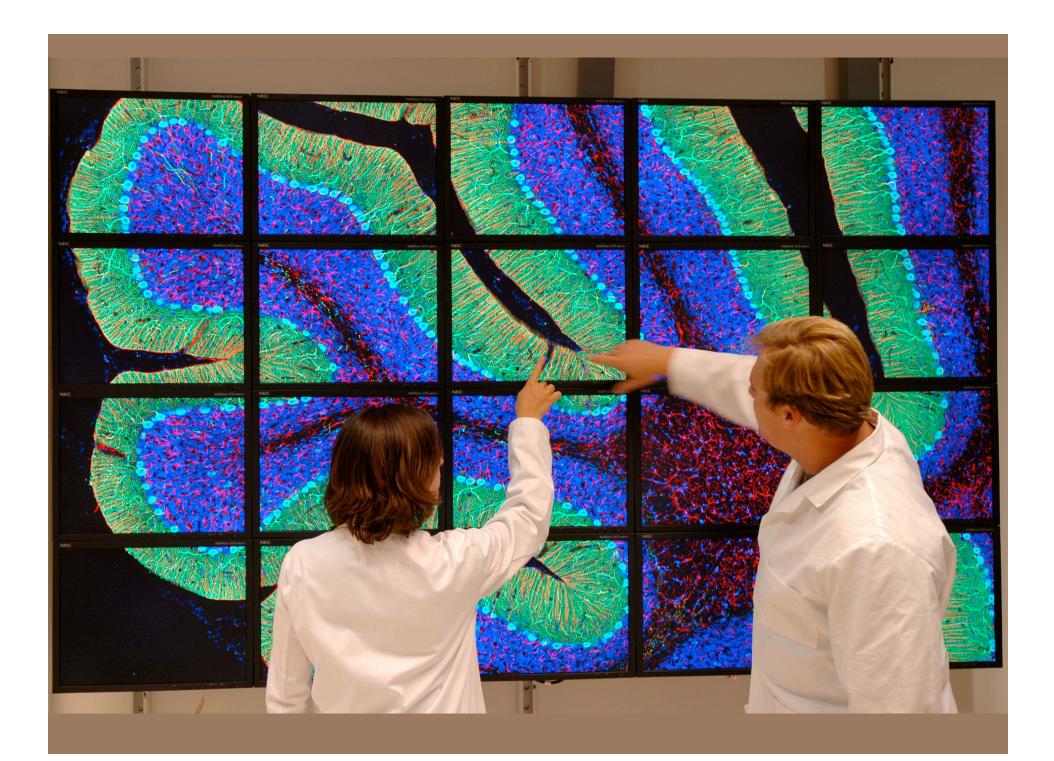
Center for in vivo Microscopy J.A. Johnson - Duke Univ.

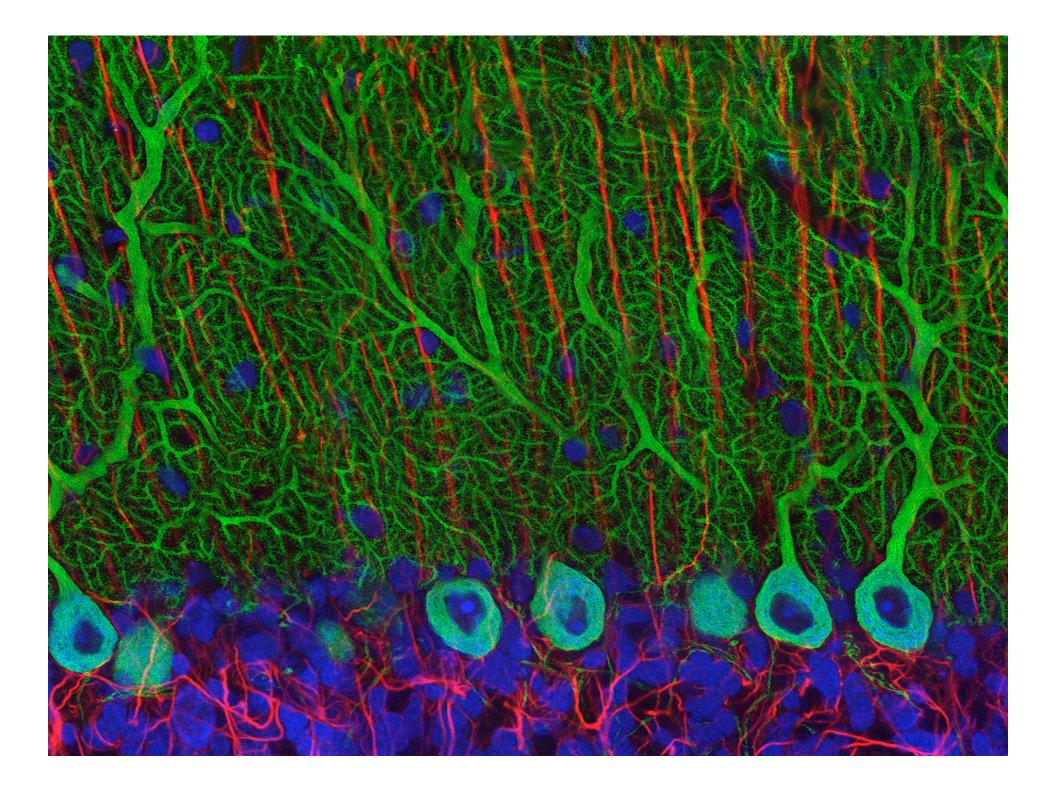
Integration of Multi-resolution data

Mouse BIRN - Duke, Caltech, UCLA, U. Tenn. Memphis, Drexel, UCSD

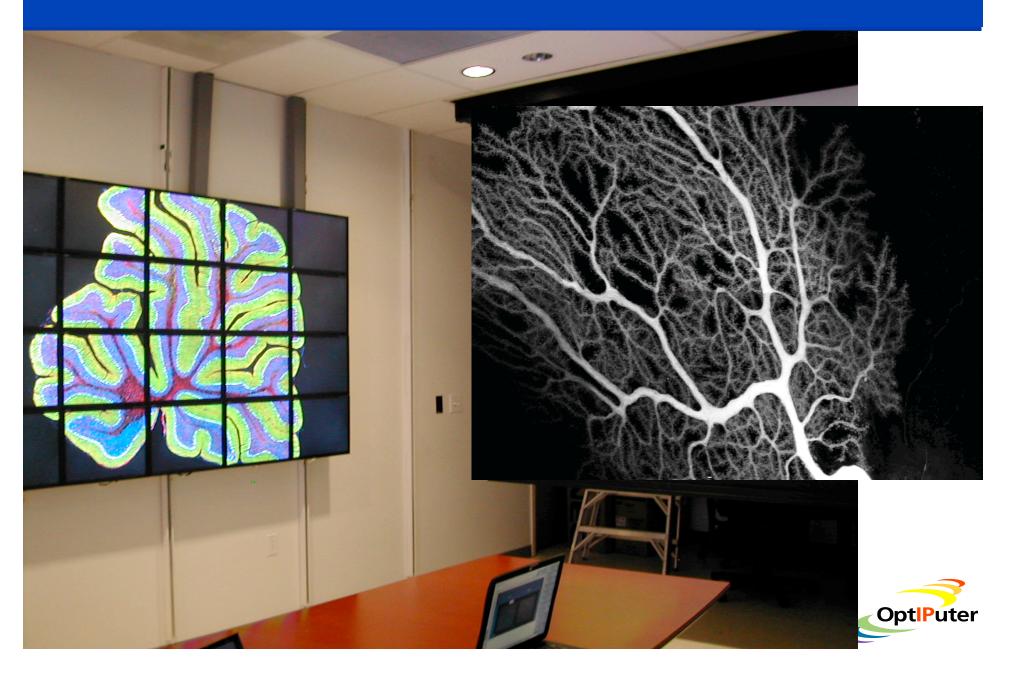




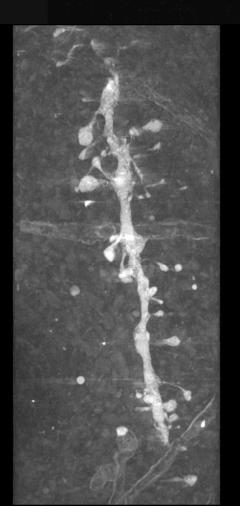


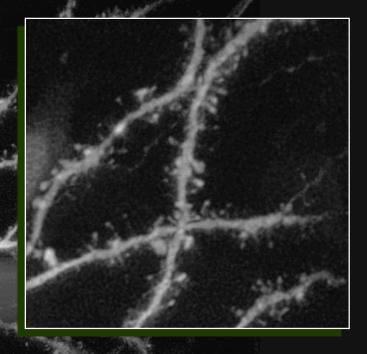


OptIPuter Visualization Environments at NCMIR



Single Cell Reconstructions



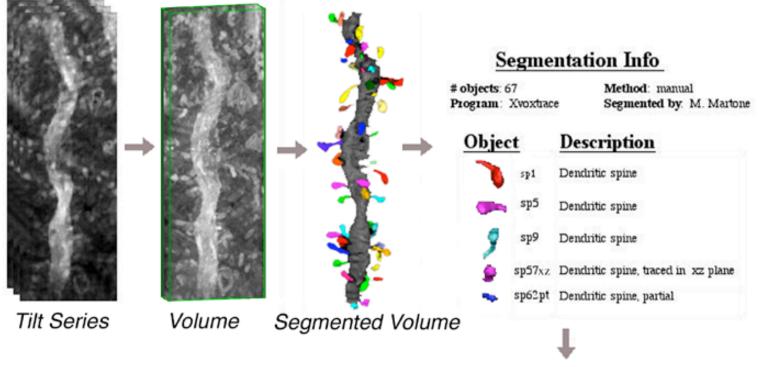


Hiroyuki Hakozaki: BioRad Radiance, deconvolution with Autoquant

NATIONAL CENTER for MICROSCOPY and IMAGING RESEARCH

at San Diego, an NIH supported resource center

Data Modeling and Deposition in the Cell Centered Data Base (CCDB)



Measurements

1

1

1

1 na

measurement muv						
Measurement	Programs Used		De .	SA	Vol	Length
SA	Analyze	1 [sp 1	1.1	0.05	1.2
Vol	Analyze	1. [sp5	0.4	0.01	0.8
Length	Xdend	end 📃	sp9	1.53	0.05	1.0
Number	Manual		sp57xz	1.36	0.05	1.2
Number	Ivianual		sp62pt	na	na	na

Measurement Info

Units=µm

from Maryann Martone, Amarnath Gupta, Bertram Ludaescher, Naoko Yamada and Mona Wong

A Federated Distributed Database for Neuroscience

- A Multimode & Multiscale "DataGrid"
- Interoperates with Gene and Protein databases & "brain map" databases of brain anatomy

From:

Maryann Martone, Amarnath Gupta, Bertram Ludaescher, Naoko Yamada, Yujun Wang, Julia Sun, and Mona Wong

The Cell Centered Database "CCDB"

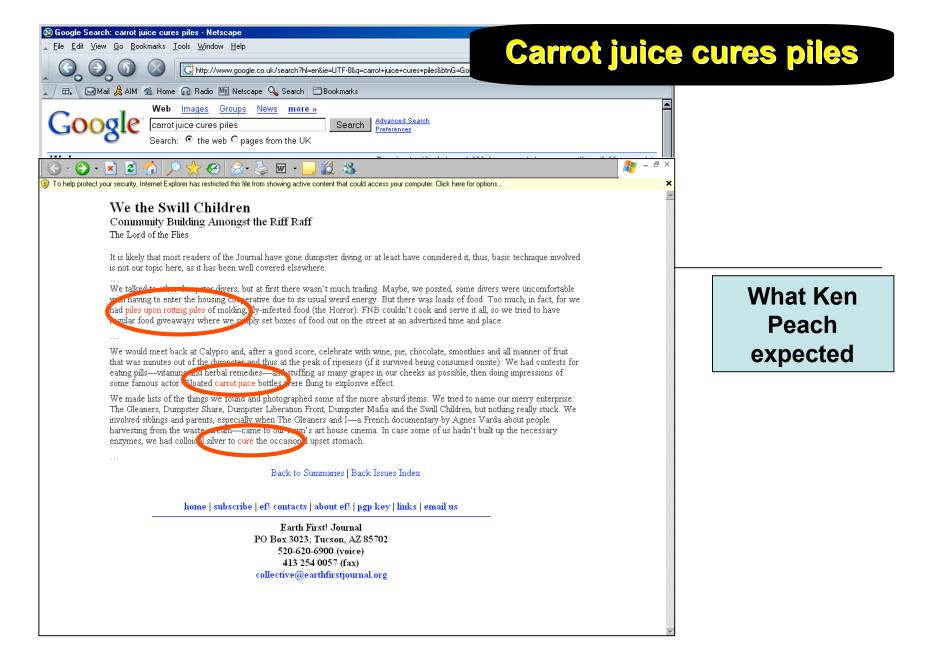
Multi-resolution datasets

Morphology

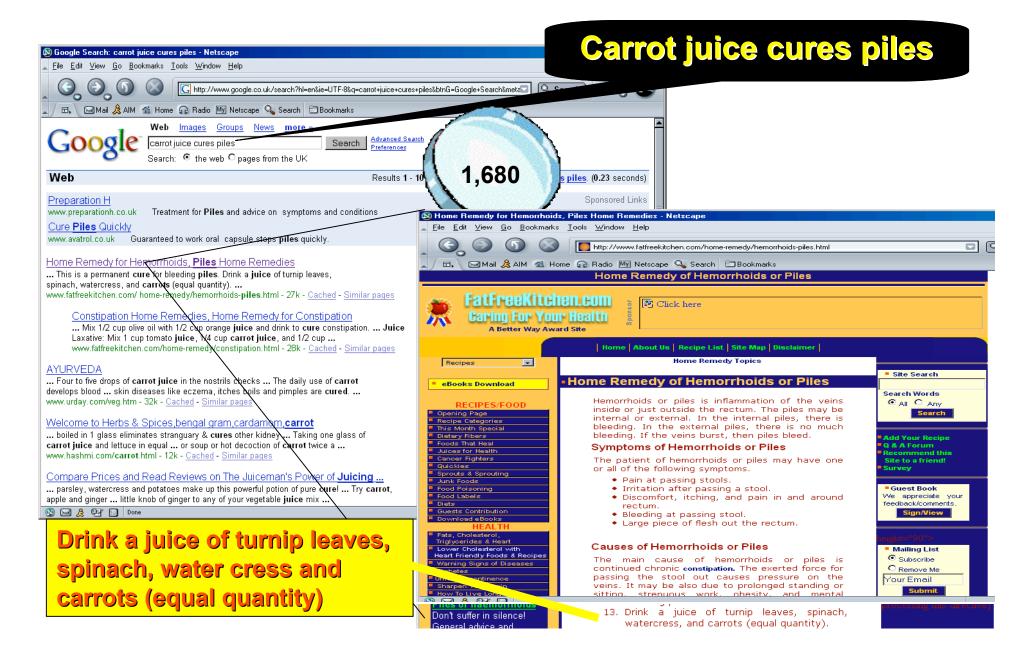
ATIONAL CENTER for MICROSCOPY and IMAGING RESEARCH at San Diego, an NIH supported resource center

Protein Localization

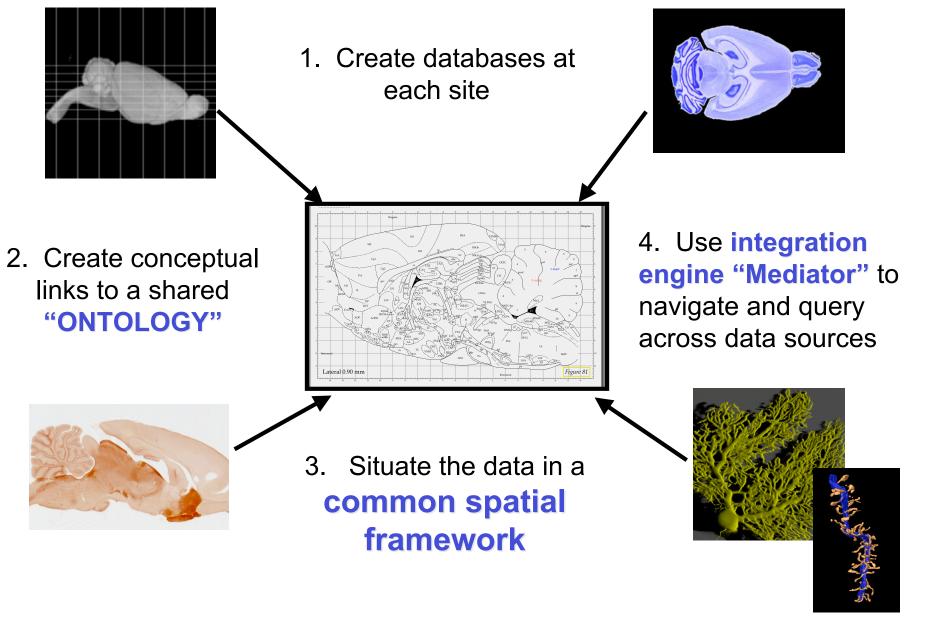
Google is not a portal



What he did not expect



BIRN Data Integration: An example of federation of Multi-scale, Multi-modal data from Mouse BIRN



DATA MODELS: Frameworks to Integrate Databases

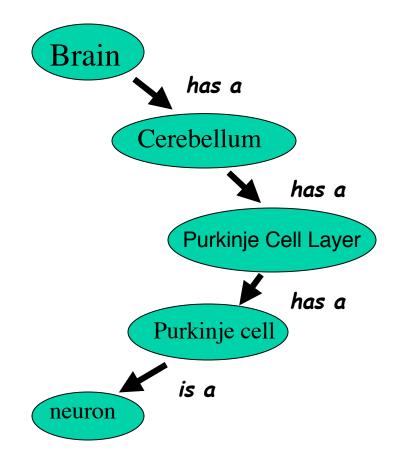
BIRN uses "Integrated Views" based on "Ontologies"

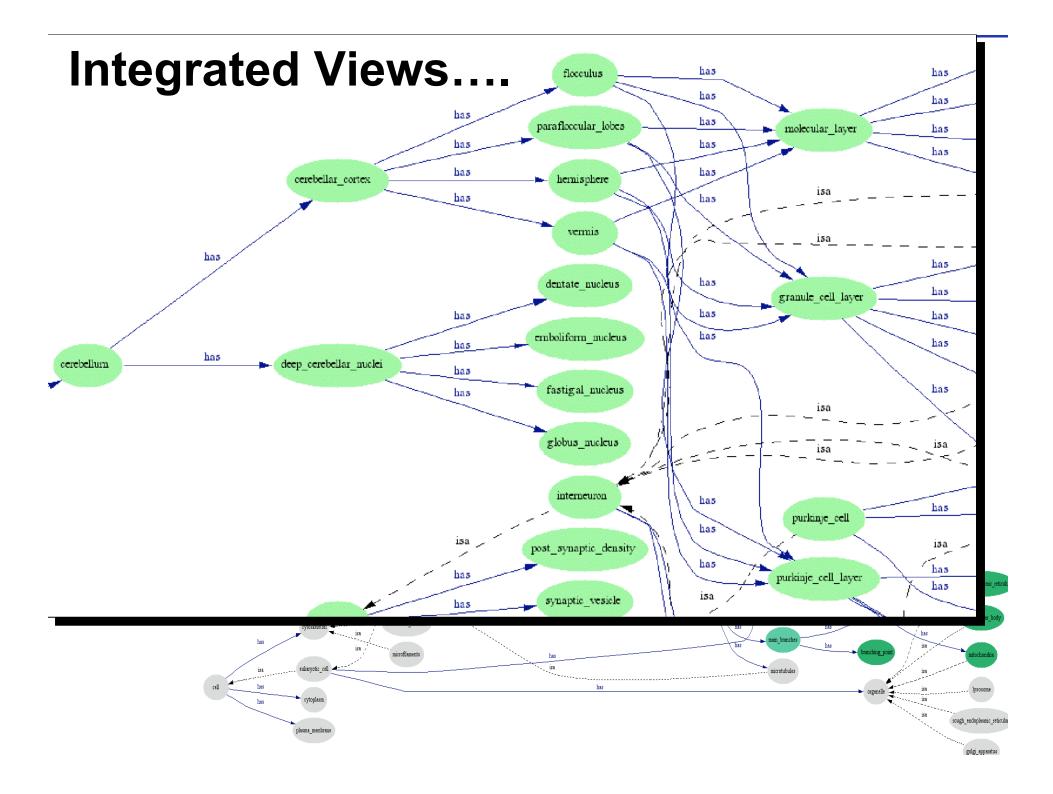
What is an **Ontology**?

- a way to represent and communicate a shared understanding of a field
- representation of terminological knowledge
- explicit specification of a conceptualization
- concept hierarchy ("*is-a*")
- further semantic relationships between concepts ("is part of", "causes", etc.)

Examples:

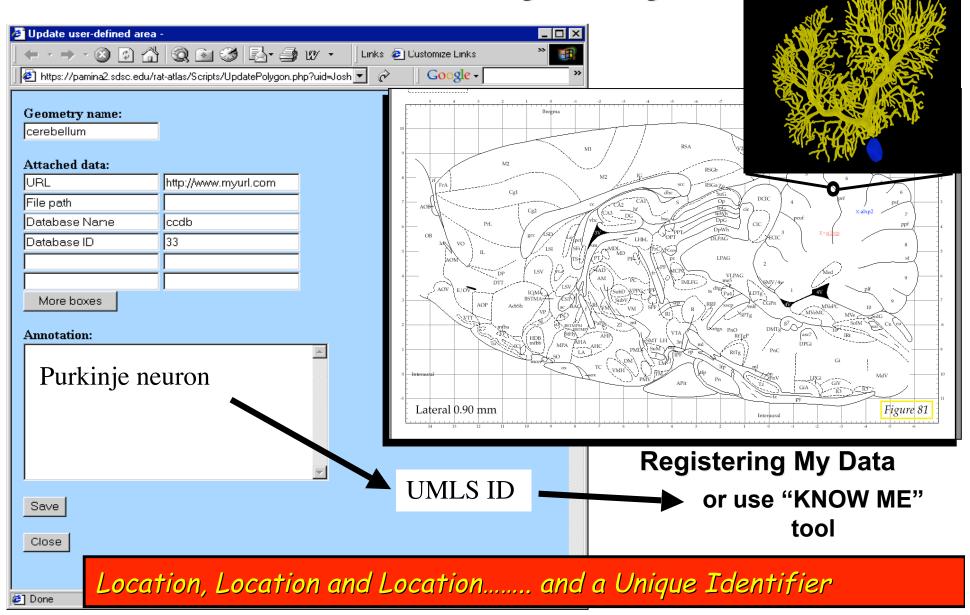
- NCMIR ANATOM
- GO (Gene Ontology)
- UMLS (Unified Medical Language System)
- CYC



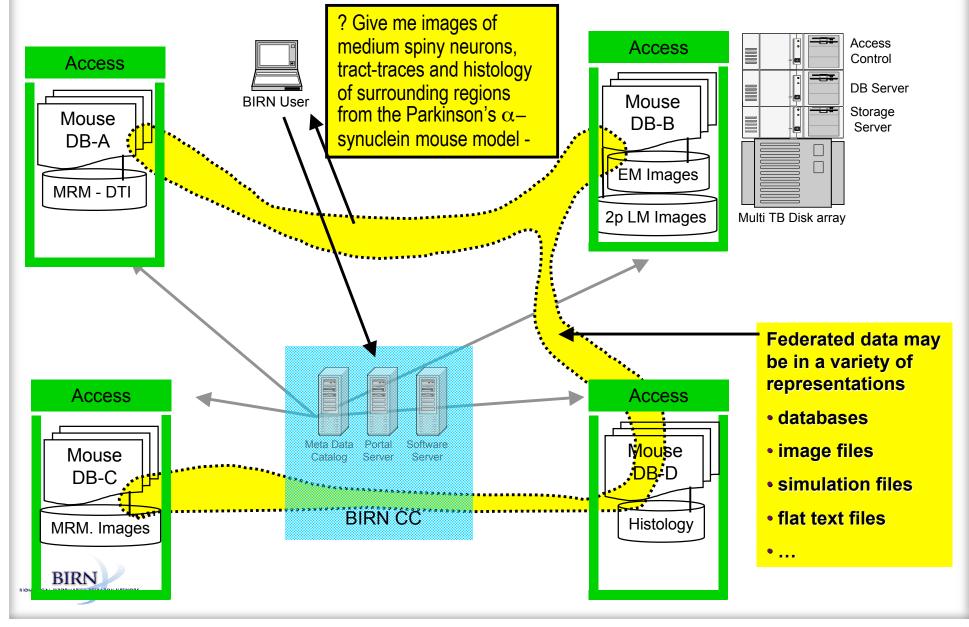


Atlas-based Spatial Reference Systems: Multi-Scale and

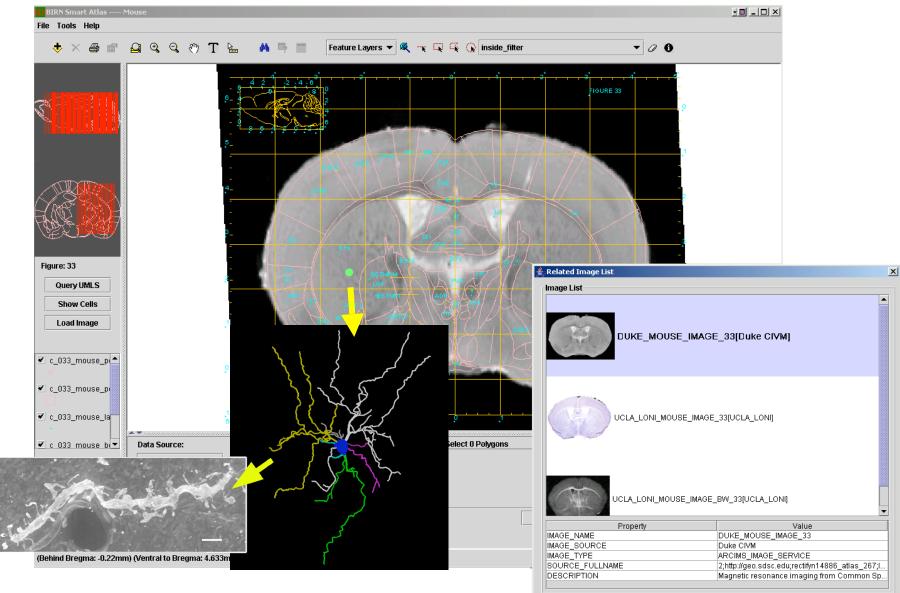
Multi-Modal Data are Connected through Ontologies



BIRN Data Integration Environment Bridges Data Models When Users Explore Distributed Data

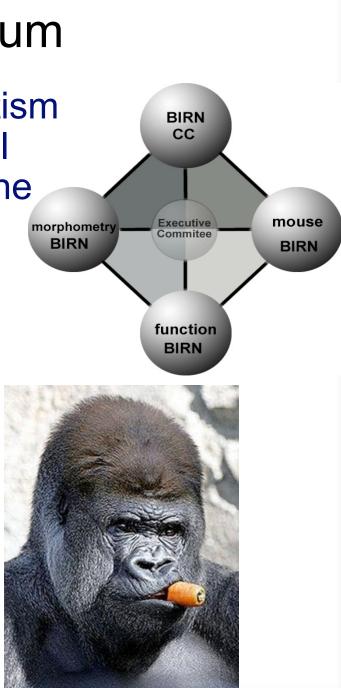


The BIRN Smart Atlas: An Example of a Data Grid-based GIS-like tool for spatial integration of multiscale distributed brain data. *Runs from BIRN Portal



BIRN is a Growing Consortium

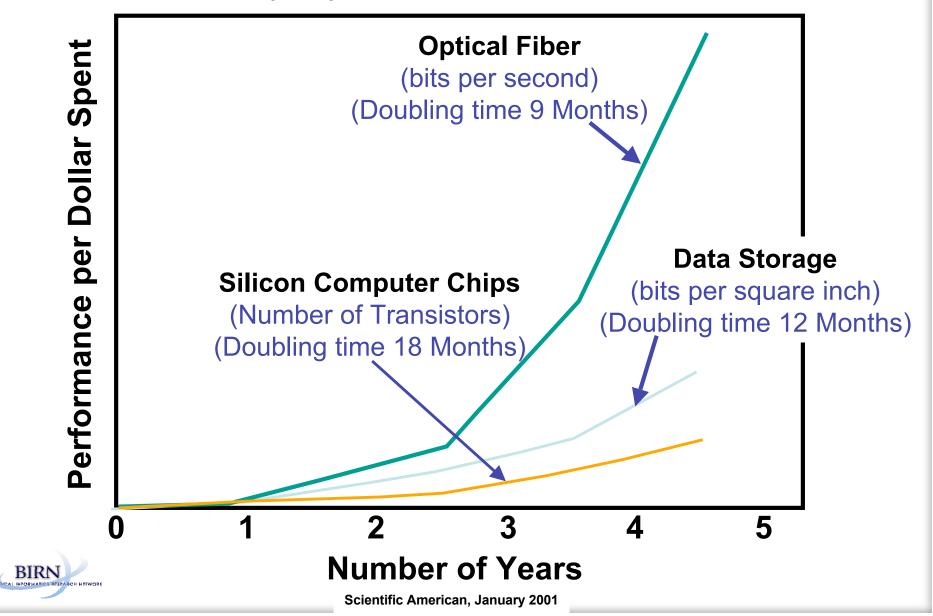
- NDAR National Database for Autism Research for the support of clinical and translational research within the autism research community
- Non-Human Primate Linking imaging, behavior, and molecular informatics in non-human primate pre-clinical models of disease
- UK e-Science Fostering collaborations with European cyberinfrastructure community



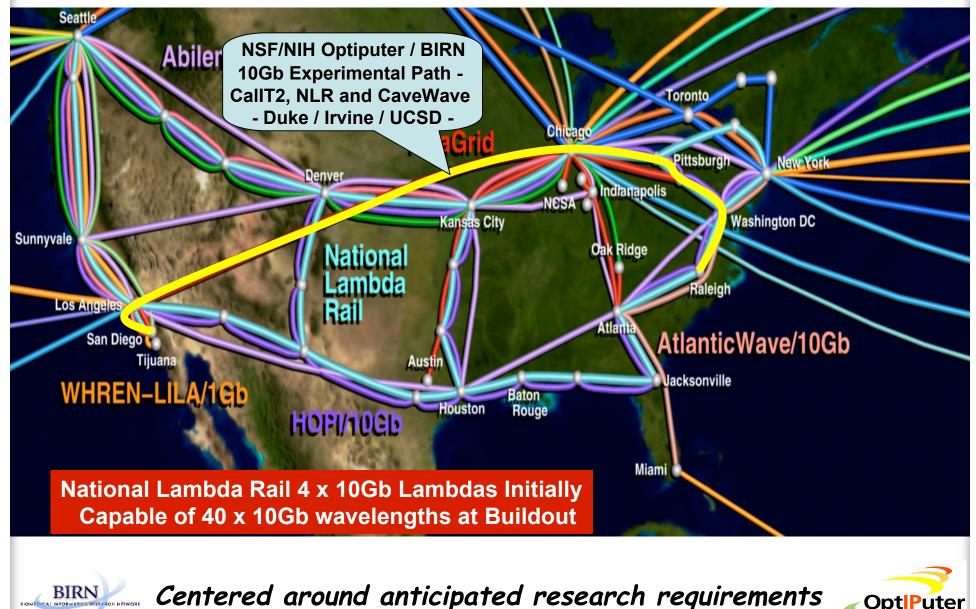


The BIRN Collaboratory Today Edinburgh Enabling collaborative research at 28 research institutions comprised of 37 research groups. Manchester **BWH SPL** Dartmouth College, Univ. Minnesota MGH CFNT University of Toronto Kitware, Inc. мтт G.E. Global Research Isomics, Inc. Yale Univ. Univ. Iowa Drexel Univ. Univ. Utah Ohio State Univ. UCSF Johns Hopkins Univ. Stanford Caltech UCLA Washington Univ., St. Louis Duke Univ. UCI UCSD NCMIR University N. Carolina UCSD fMRI Univ. New Mexico Univ. Tennesse Georgia Tech Emory Univ. **BIRN Central NOC BIRN-CC BIRN Sites** Mouse NA-MIC sites Morphometry Abilene Network Function - GEANT Network Primate (non-human) — Super Janet Network BIOM Revised August 2005

Optical Networks Are Becoming the 21st Century Cyberinfrastructure Driver



Building Bridges: NIH Research and Infrastructure Projects & NSF Advanced Network Research and Infrastructure Projects



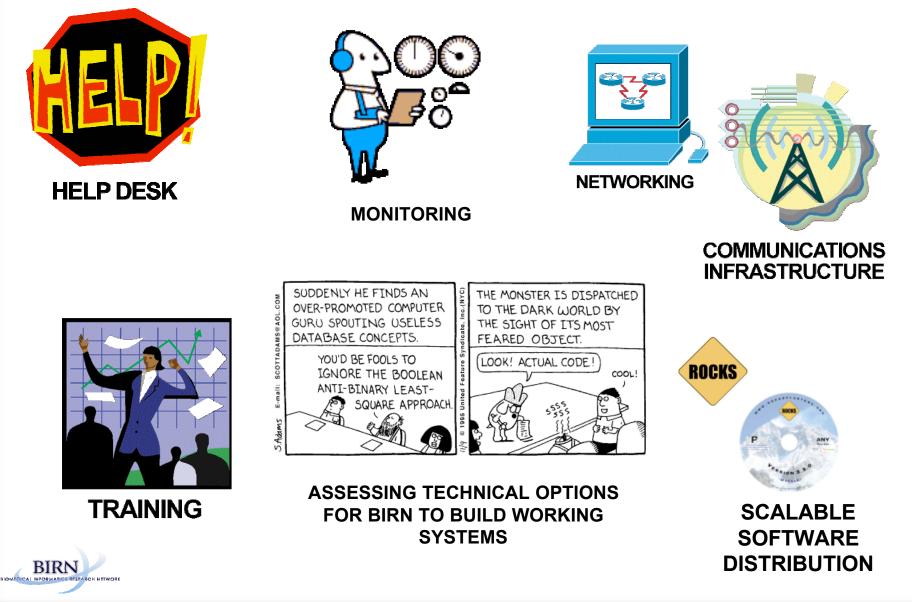
OptPuter

Removing Barriers to BIRN: Decreasing Cost of Entry & Increasing Scalability \$120K < \$20K < \$5K (2001)(Today) (~2011) 0 BIRN Cisco 3750 **BIRN** Portal <u>Elequest</u> a DEN account. In ast be a BEN participe Cisco 3002 VPN GridPOP E0 - 172.31.x.1/24 E2-10.0.2.1/24 E3 - Routed LO - 172.31.x.101/24 KVM Switch (reccommended) Gcomp E0 - 172.31.x.3/24 Flat Panel Monitor/Keuh E1 - Routed E2-10.0.2.3/24 LO - 172.31.x.103/24 Compaq DL380s Sun v20 Dell 2650 Prescribed or equivalent hardware NASO Storage Trays E0-172.31.x.4/24 (1-10TB) E2-10.0.2.4/24 LO - 172.31.x.104/24 jumpstarted BIRN for functionality Managed UPS Software solution for researchers to Support for **BIRN** "enable" multiple vendors local hardware BIRN BIOMEDICAL INFORMATICS RESEARCH NETWOR

BIRN is a Stable & Rapidly Evolving National Research Infrastructure

- ✓ Supporting collaborative activities of advanced biomedical research & clinical research centers in the US Serving as a model for programs everywhere.
- Ensuring a stable, robust, shared network environment across > 35 institutions today
 <u>High Bandwidth Connectivity</u> via Internet2.
- Developing hardware and software infrastructure for managing distributed data creation of the <u>BIRN Data GRID</u>.
- Providing secure and audited access to distributed data deployment of a <u>Uniform</u> <u>BIRN Security Model</u>.
- Exploring data using "intelligent" query engines that can make inferences upon locating "interesting" data – development of the <u>BIRN Data Integration Environment</u>.
- ✓ Integrating BIRN with middleware projects in academia & industry facilitating the use of <u>Computational GRID</u> infrastructure.
- <u>Providing</u> simple and intuitive <u>access</u> to a shared processing, visualization and analysis environment – BIRN is a leader in <u>GRID Portal</u> technology.
- ✓ Changing the use pattern for research <u>data</u> from the individual laboratory/project <u>to</u> <u>shared use</u>.
- Promoting <u>large-scale collaboration</u> among research scientists <u>across institutional</u> <u>boundaries</u>

The BIRN Coordinating Center is Supporting and Evolving the Deployed Infrastructure



5th Annual BIRN All-Hands Meeting



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.



October 2005 La Jolla, CA



http://www.nbirn.net

✓ ► ♂ + triangle http://www.nbirn.net/	 Q → Google
BIRN	Username: BIRN Portal Login Password:
BIOMEDICAL INFORMATICS RESEARCH NETWORK	Search This Site
About Us Resources Test Beds Publications BIRN is	Contact Us → Site Map → Help!
The <u>Biomedical Informatics Research Network</u> (BIRN), a <u>National Institutes of Health (NIH)-National Ce</u> for <u>Research Resources (NCRR)</u> -sponsored initiative, is establishing a distributed information technolog infrastructure to improve biomedical research. This evolving "cyberinfrastructure" will enable researchers throughout the United States to collaborate large-scale studies of human disease with unique, multi-resolution tools. <u>More ></u>	BY October 6, 2003 The newest BIRNing Issues, volume 2, issue 1, is online (PDF).
Research Focus Hot Topic	View the document as a <u>PDF</u> or <u>Microsoft Project</u> file.
The BIRN currently consists of three "test bed" projects that are conducting structural and functional studies of neurological disease: Function BIRN - studying regional brain dysfunctions related to the progression and treatment of schizophrenia. Morphometry BIRN - examining unipolar depression, mild Alzheimer's disease and mild cognitive impairment. Mouse BIRN - studying animal models of multiple sclerosis, schiziphrenia, Parkinson's disease, ADHD, Tourette's disorder, brain cancer.	ages from June 27, 2003 The June 2003 BIRNing Issues is now posted on the Web. (PDF) ent d Events angths 2003 All Hands Meeting, October 8-10 at UCSD.

•

• Breaking down the barriers

Mistrust

- Open sharing of information
- Who gets credit
- Commercial products
- Governance
- Incorporating processes for multi-site studies and sharing of human data
 - HIPPA Compliance
 - Patient confidentiality
 - Institutional Review Board (IRB) approvals

Challenges

- Developing guidelines for sharing data & authorship
- Integrating new participants
- Providing an architecture to allow for technology improvements with the existing infrastructure
- Guaranteeing security versus ease of use



