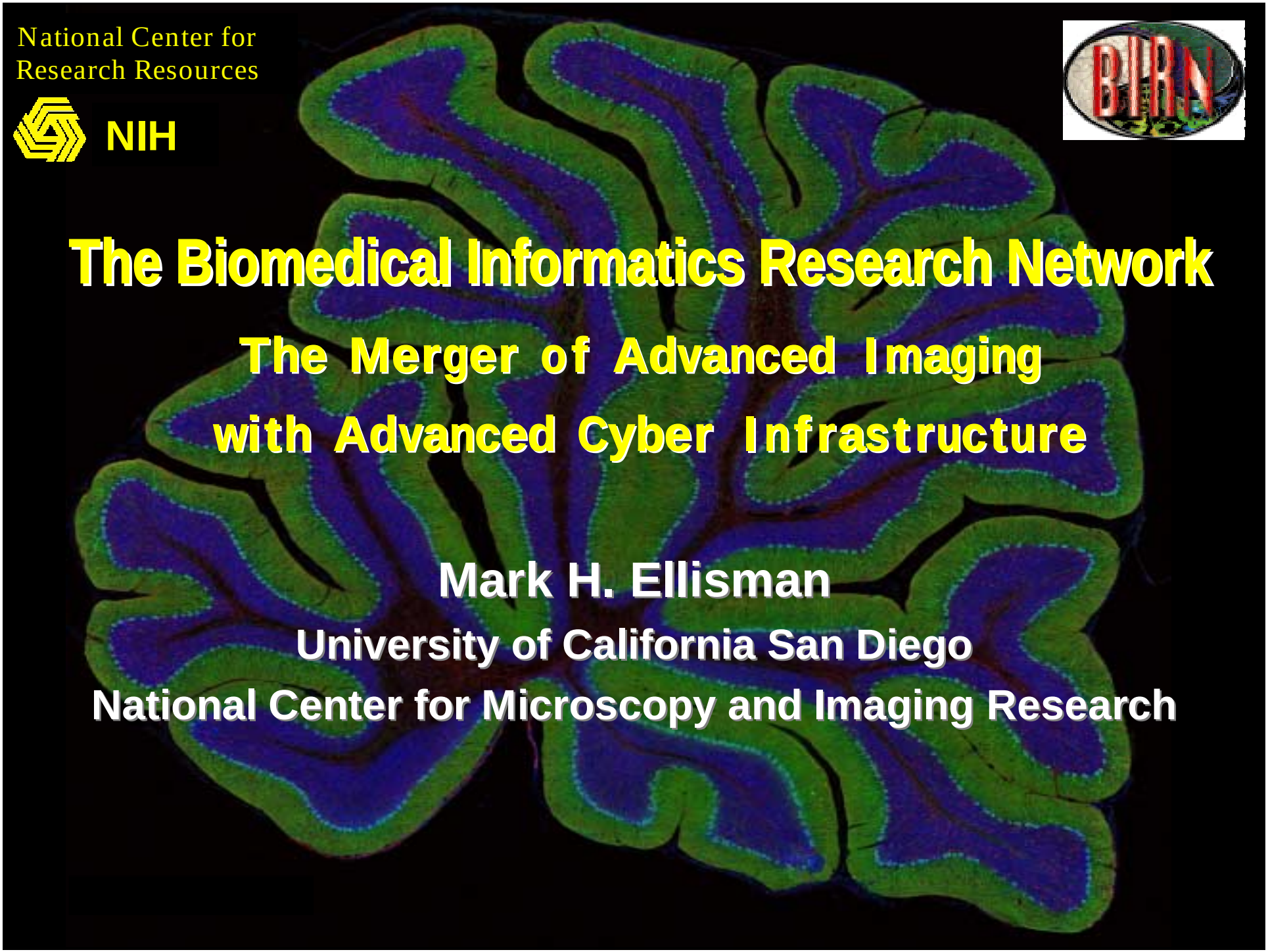
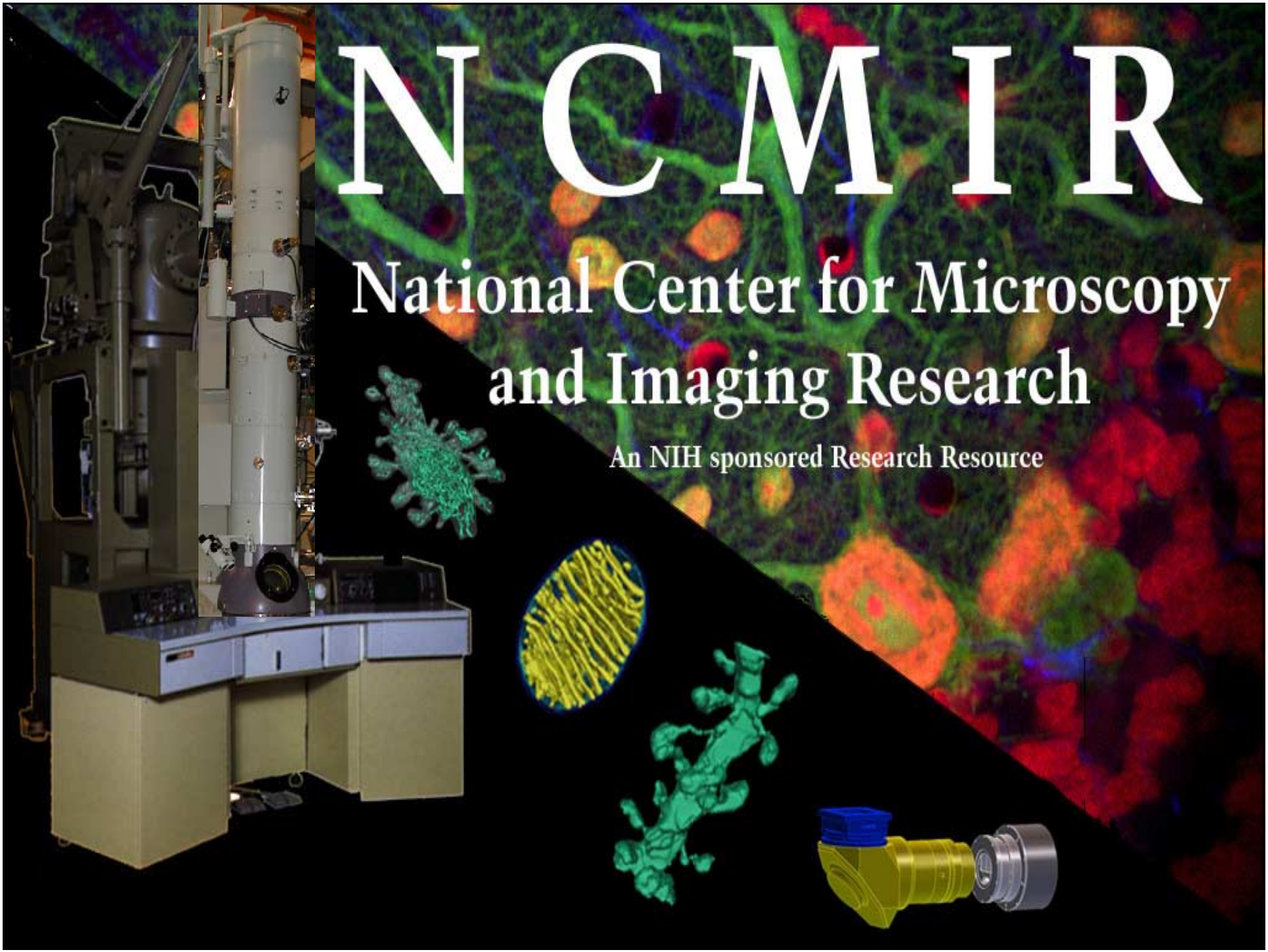

National Center for
Research Resources
NIH
BIRN
The Biomedical Informatics Research Network
The Merger of Advanced Imaging
with Advanced Cyber Infrastructure
Mark H. Ellisman
University of California San Diego
National Center for Microscopy and Imaging Research


NCMIR
National Center for Microscopy
and Imaging Research
An NIH sponsored Research Resource

Modern 3D Transmission Electron Microscope

extreme penetration!

Ultra High Voltage EM @ Osaka Univ.

- **3 Million Electron Volts**
- **15 Meters Tall**
- **140 Tons**
- **$$$ > 50M US Dollars**
- **only one of these**

Synchrotrons

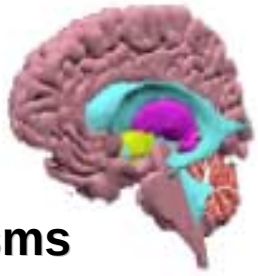
Molecules

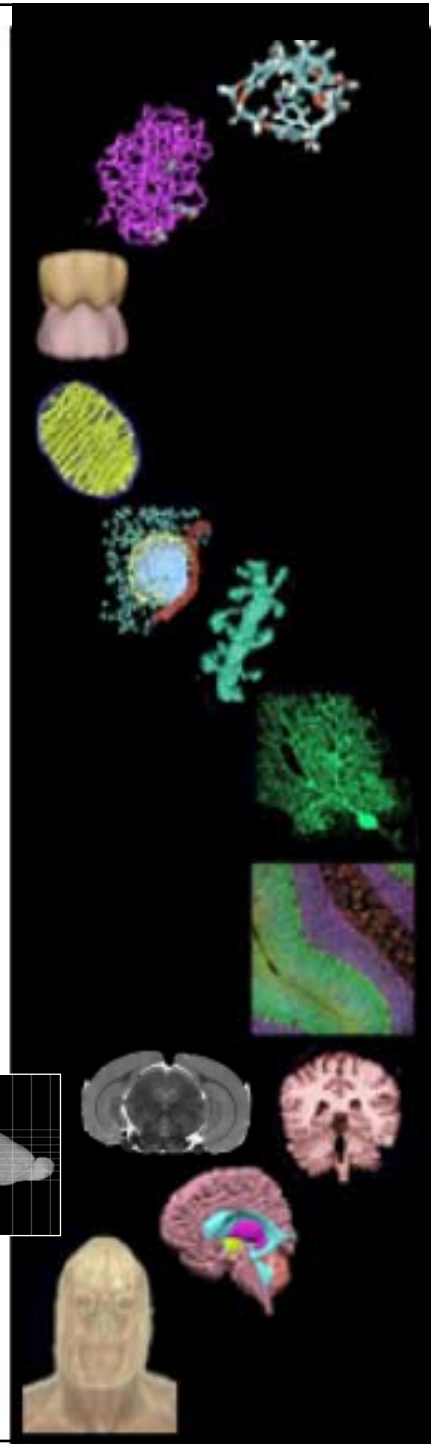
Microscopes

Macromolecular Complexes, Organelles, Cells

Magnetic Resonance Imagers

Organs, Organ Systems, Organisms

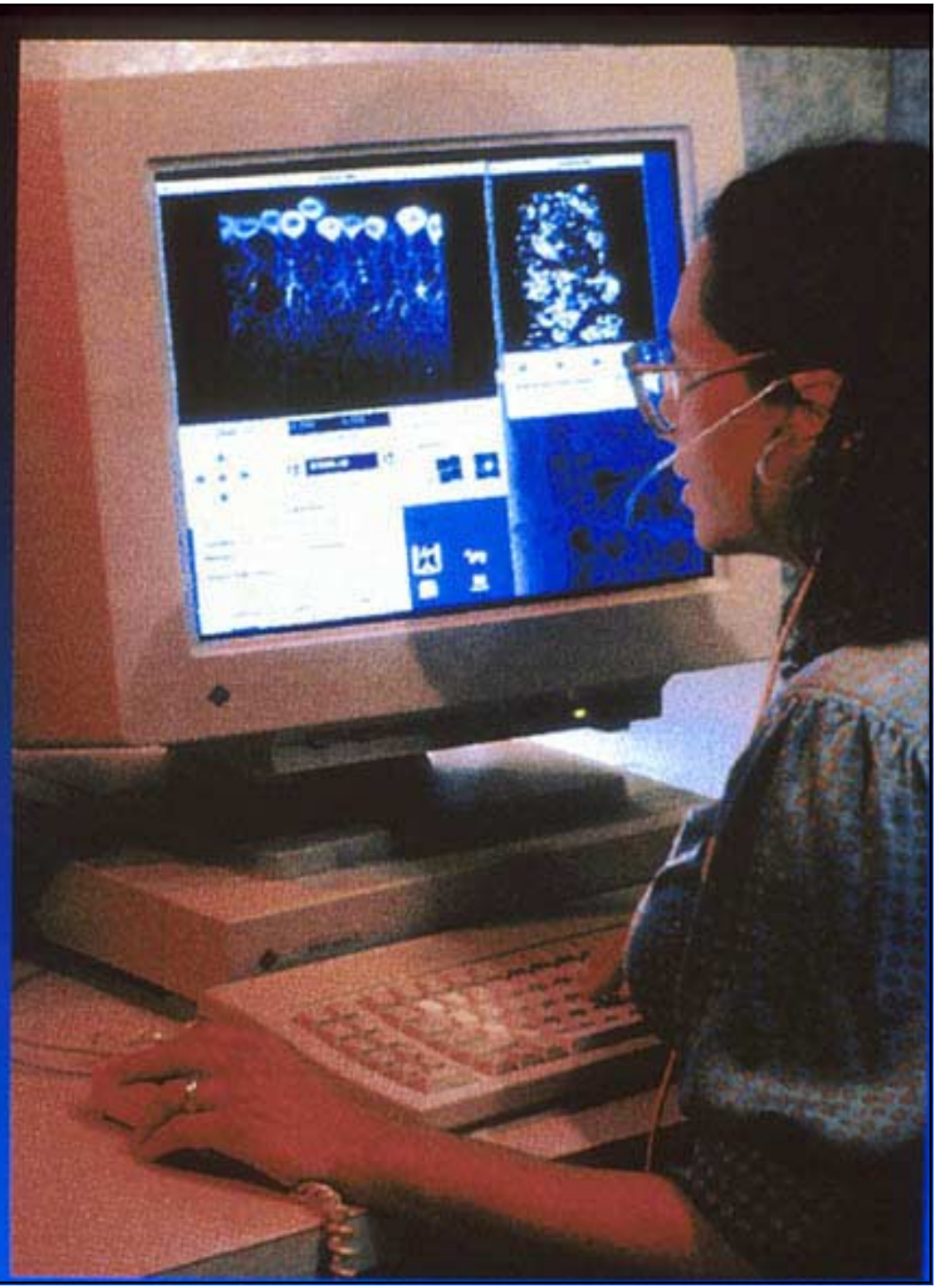




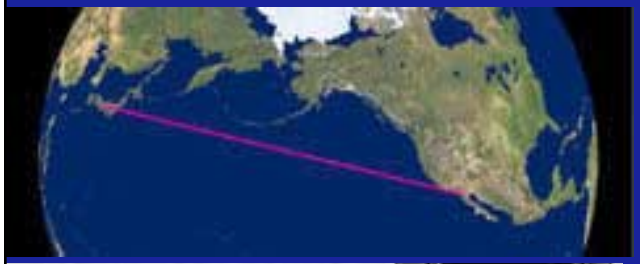
Telemicroscopy

First Demonstration of "Telemicroscopy" was between NCMIR at San Diego and Chicago at the Super Computing Convention in 1992

It involved remote use of the IVEM at UCSD and the Cray YMP at the San Diego Supercomputer Center



Trans-Pacific Telemicroscopy



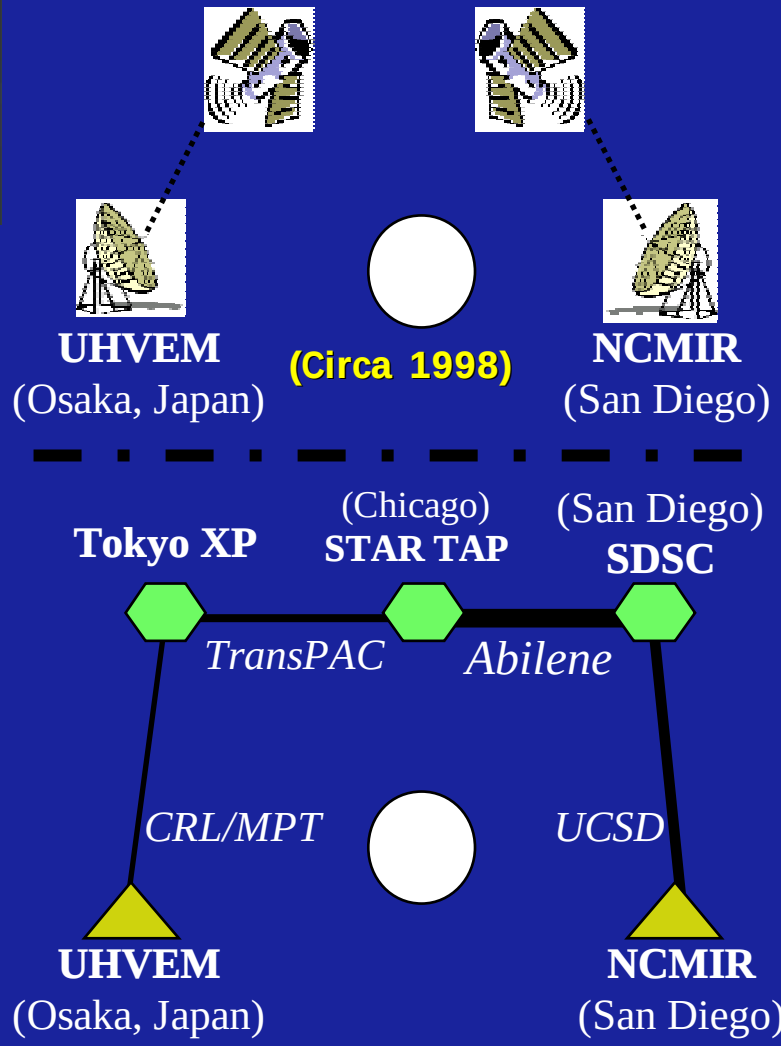
NET NEWS

Microscopy Across an Ocean

A big push by biologists to use computer networks to operate rare instruments from afar passed a major milestone on 25 June: Scientists took a spin on the world's most powerful electron microscope in Japan—while sitting 6000 kilometers away in California.

Six years ago, University of California, San Diego, neuroscientist Mark Ellisman thrilled audiences at a conference in Chicago by using the Internet to control an electron microscope in San Diego. Several U.S. agencies jumped in to fund projects for operating microscopes by remote control, and by now at least a dozen groups are doing so in the United States. Ellisman's team has since moved on to the Mount Everest of microscopes: Osaka University's Ultra High Voltage Electron Microscope, a 3,000,000-volt behemoth that can create three-dimensional images from much thicker samples (such as biological cells) than ordinary microscopes can. Ellisman and his U.S. and Japanese colleagues wondered if they could operate this instrument's roomful of controls from across the Pacific Ocean.

They showed they could. Over 5 hours, San Diego scientists imaged nerve cells from a rat and a frog without setting foot in Japan, controlling things like focus and specimen position across a private data line while the images came in across a satellite video link. Ellisman says this lays the groundwork for researchers all over the United States and Japan to borrow each others' specialized microscopes, probably via a high-speed Internet link, "within a year or two."

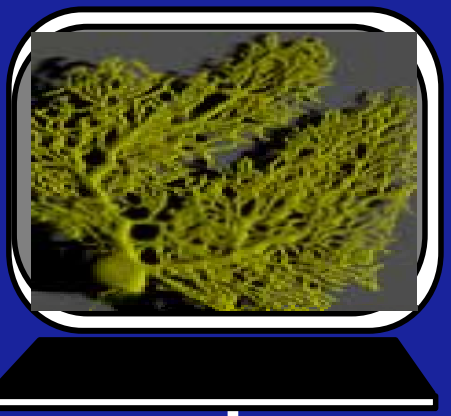


Now part of a production environment using IPv6

TELEMICROSCOPY & GRID - BASED COMPUTING
REMOTE ACCESS FOR DATA ACQUISITION AND ANALYSIS

DATA ACQUISITION

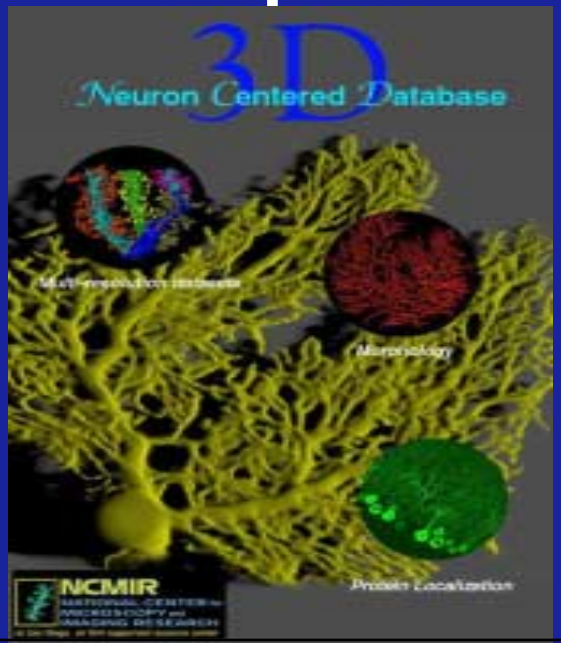
DATA ANALYSIS



ADVANCED COMPUTER GRAPHICS

NETWORK

QuickTime™ and a YUV420 codec decompressor are needed to see this picture.



MULTI-SCALE DATA-BASES

IMAGING INSTRUMENTS

COMPUTATIONAL RESOURCES

The Login Page: The Entrance into the Portal

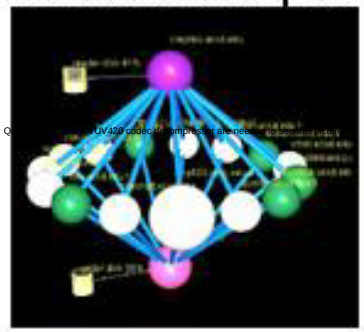
Single login grants authenticated access to all applications, resources, and services

telescience

for advanced tomography applications

Remotely Control Instruments

Distributed Grid Computation



Distribute Data to Storage Resources

Username

Password

Login

What is Telescience?

Learn more about the Telescience Portal

Need a Telescience Account?

NCMIR NATIONAL CENTER for MICROSCOPY and IMAGING RESEARCH at San Diego, an NIH-supported research center

NPACI

UCSD

What is the Telescience Portal ?

→ **Centralized access** to ALL tools/applications necessary for electron tomography with a **Single Login** from any Internet capable location

→ Telescience Portal Login provides:

- **Globus** authentication to distributed **Grid Computing**
- Login to the **Storage** Resource Broker - **Data Grid**
- Login to the Cell Centered **Federated Database**

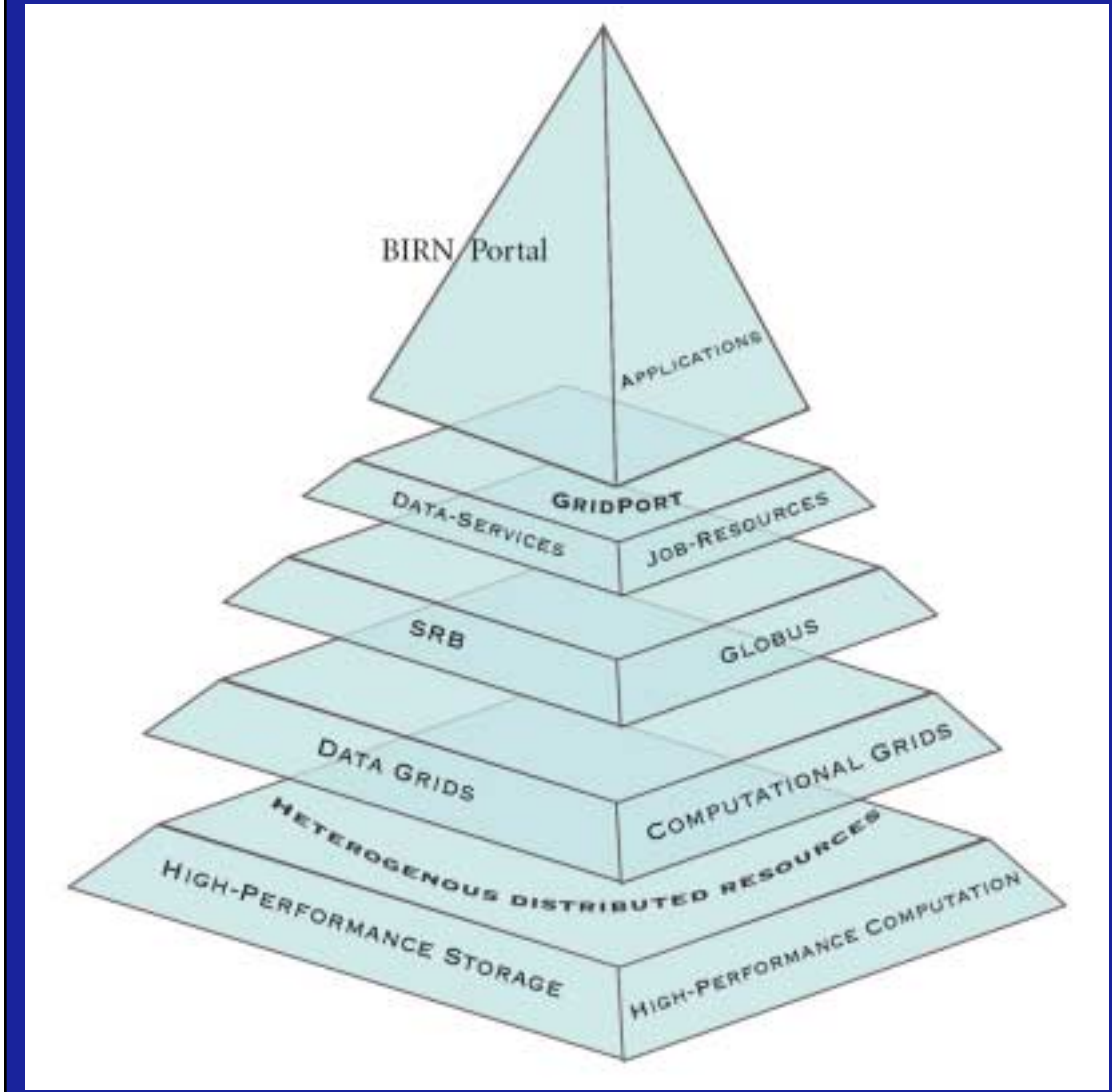
→ Provides simple, intuitive access to sophisticated instrumentation and Grid resources for data storage and computation

→ Provides a framework for future needs of high-throughput electron tomography

The Telescience Portal Provides Access to Tools and Workflows

- → Telemicroscopy for remote instrumentation and data acquisition
- → Parallel tomographic reconstruction using distributed, heterogeneous platforms and grid computing domains from a point-and-click interface
- → Tools for Visualization, Segmentation, and Image processing
- → Management & Access to distributed file/data systems
- → Transparent deposition of data products into Databases
- → Collaborative telecommunication utilities
  - Shared “whiteboard" image annotations
  - “Chatting” between multiple remote researchers
  - HDTV-based real-time image sharing

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

Telescience Portal Welcome Page

telescience
for advanced tomography applications

Welcome to the Telescience Portal

hello abel

Click here to create a
new Reconstruction Workflow

New Reconstruction

Manage your data in SRB
Edit/Delete Reconstructions
View Images/Movies

Manage Work and Files

Collaborate with Other
Telescience Researchers

Collaboratory TOOLS

Most Recent Reconstructions
Resume a Reconstruction Workflow:

TP_r750 - THIS (Wed Apr 17 15:29:54 2002)
TP_r709 - Phaeo (Wed Apr 17 15:30:02 2002)
TP_r800 - demo3 (Wed Apr 24 13:16:34 2002)
TP_r708 - Spiny Dendrites (Fri Apr 26 11:44:03 2002)

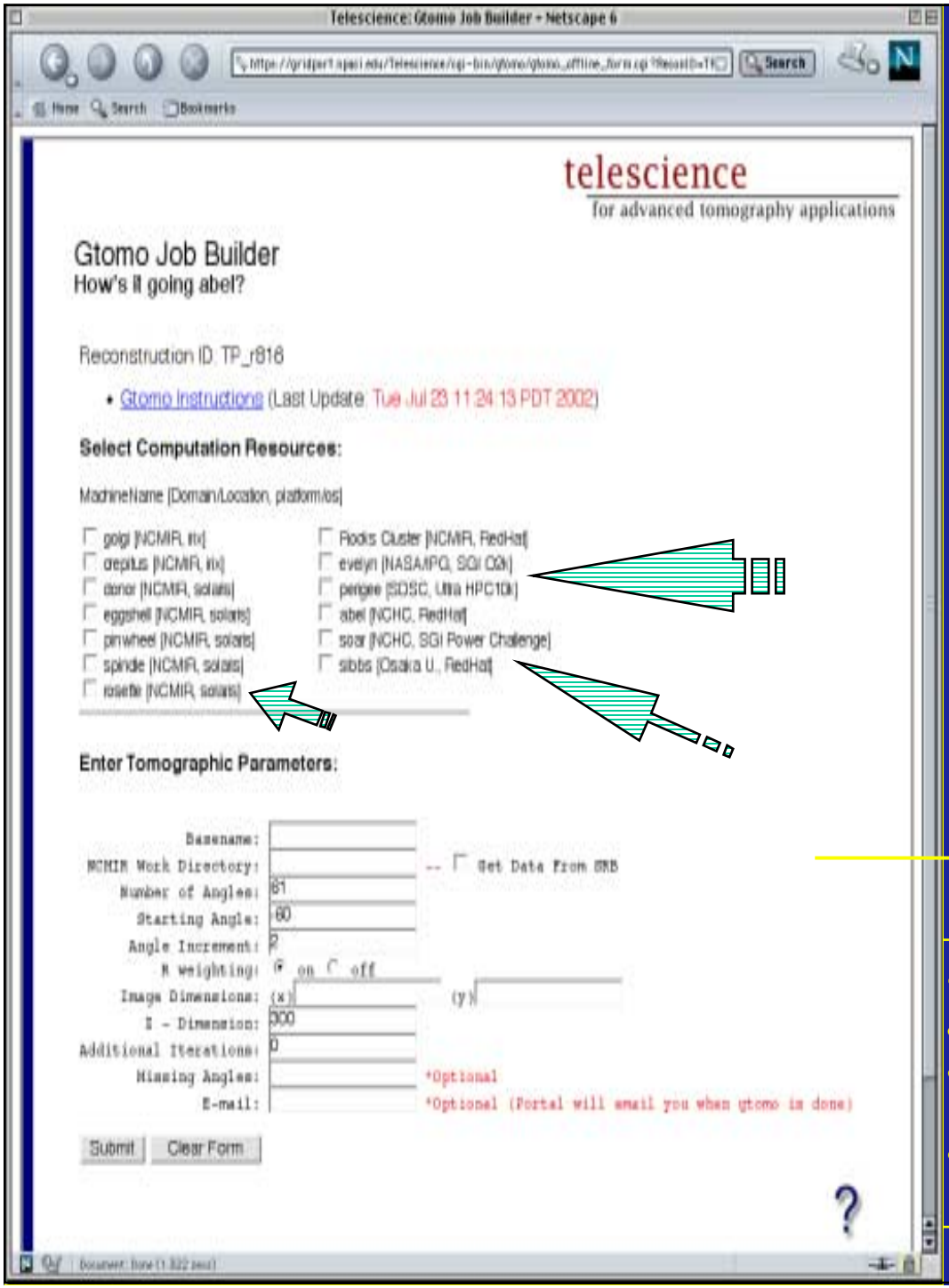
Jump directly to Applications
Work History will NOT be tracked
SRB will NOT be availiable

Applications ONLY

LOGOUT

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

NPACI



Globus Enabled Tomography (Gtomo)

Seleted Resource (s):
NCMIR NPACI NASA/IPG
NCHC Osaka U.

Gtomo Reader

Gtomo Writer

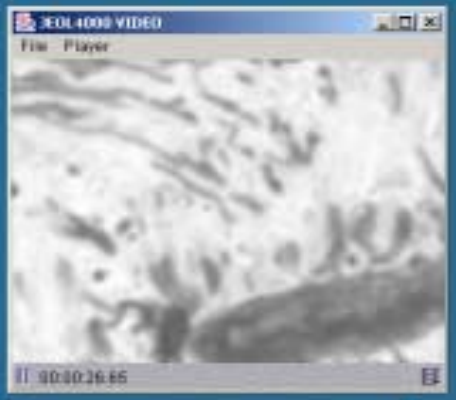
Data Input

Data Output

Gtomo Driver

- Complete Abstraction of Grid
- No need to manage Globus Certificates
- Simply click resource(s) to use and enter biological parameters
- Resources are transparently cross-platform, cross-domain

Telemicroscopy via VidCon2

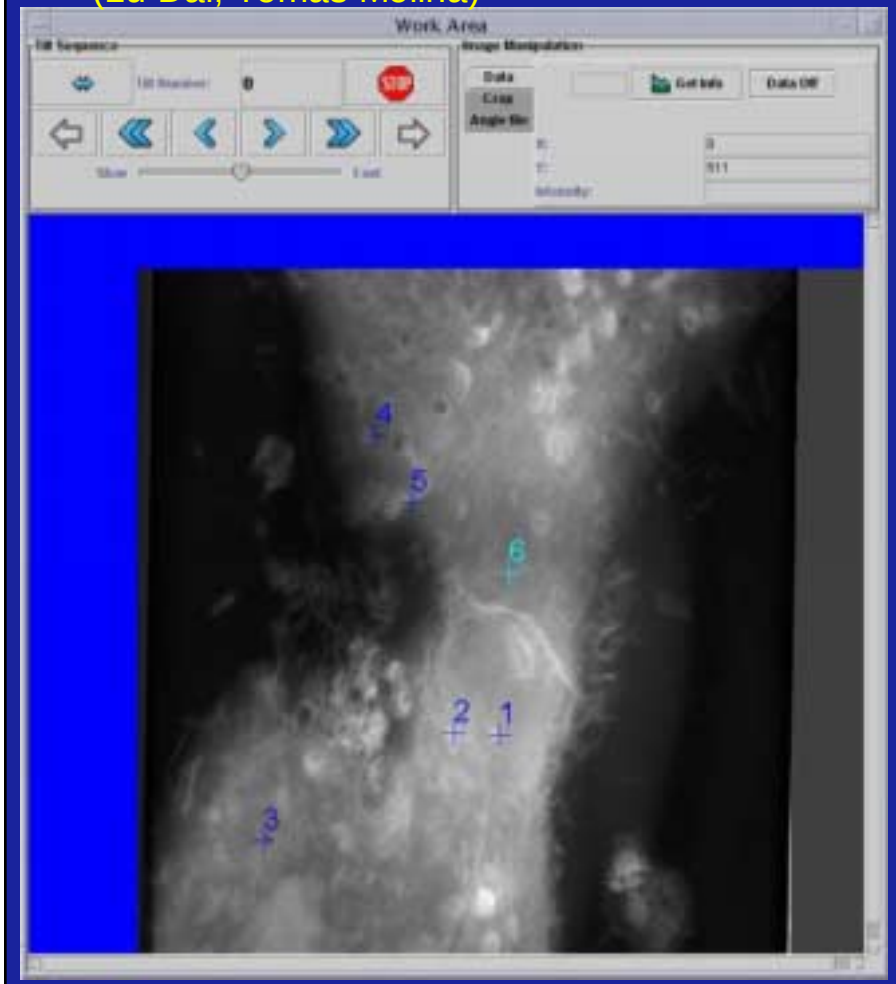


- **Video Based Instrument Controller**
- **Client-Server Java Application**

More Applications

JFido

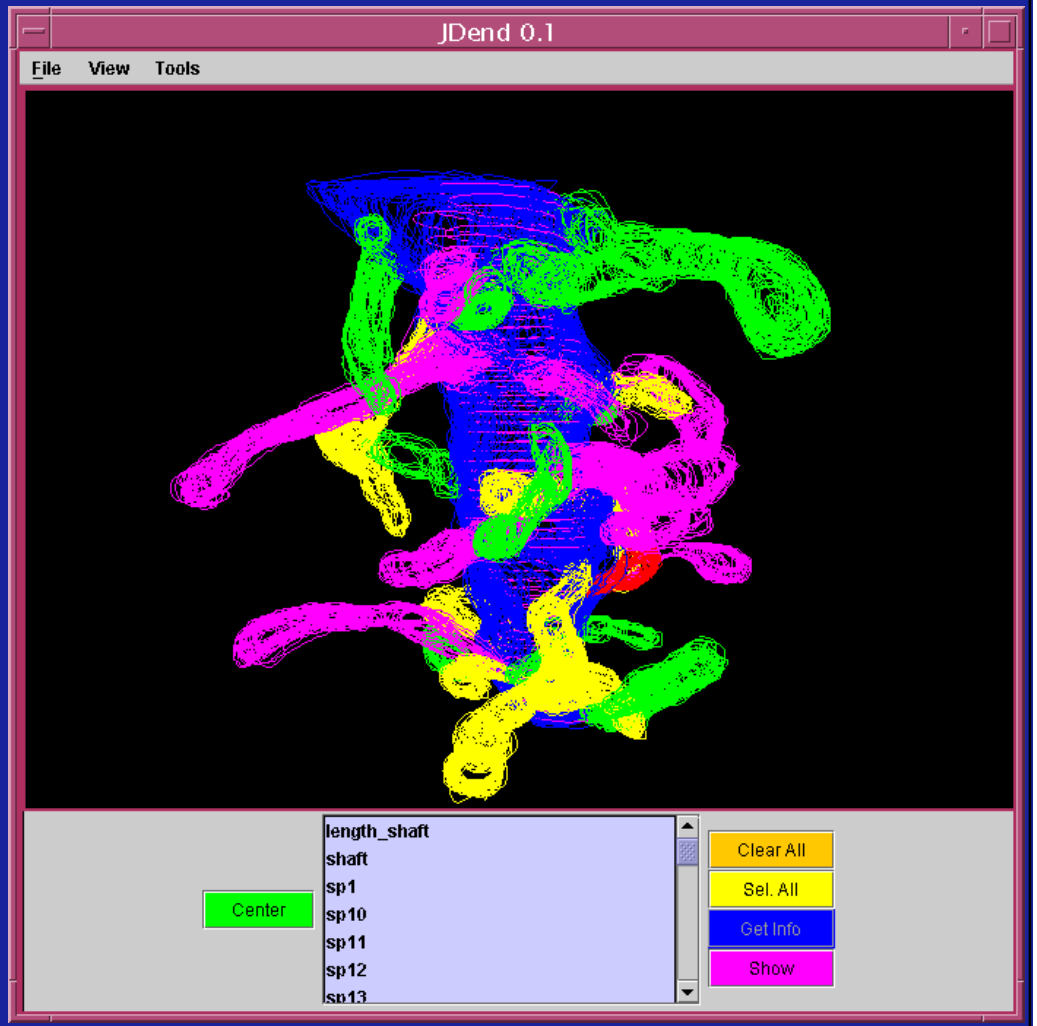
(Lu Dai, Tomas Molina)



Pre-processing Utilities (ie. Fiducial marking, cropping, normalization)
general 2D image viewer

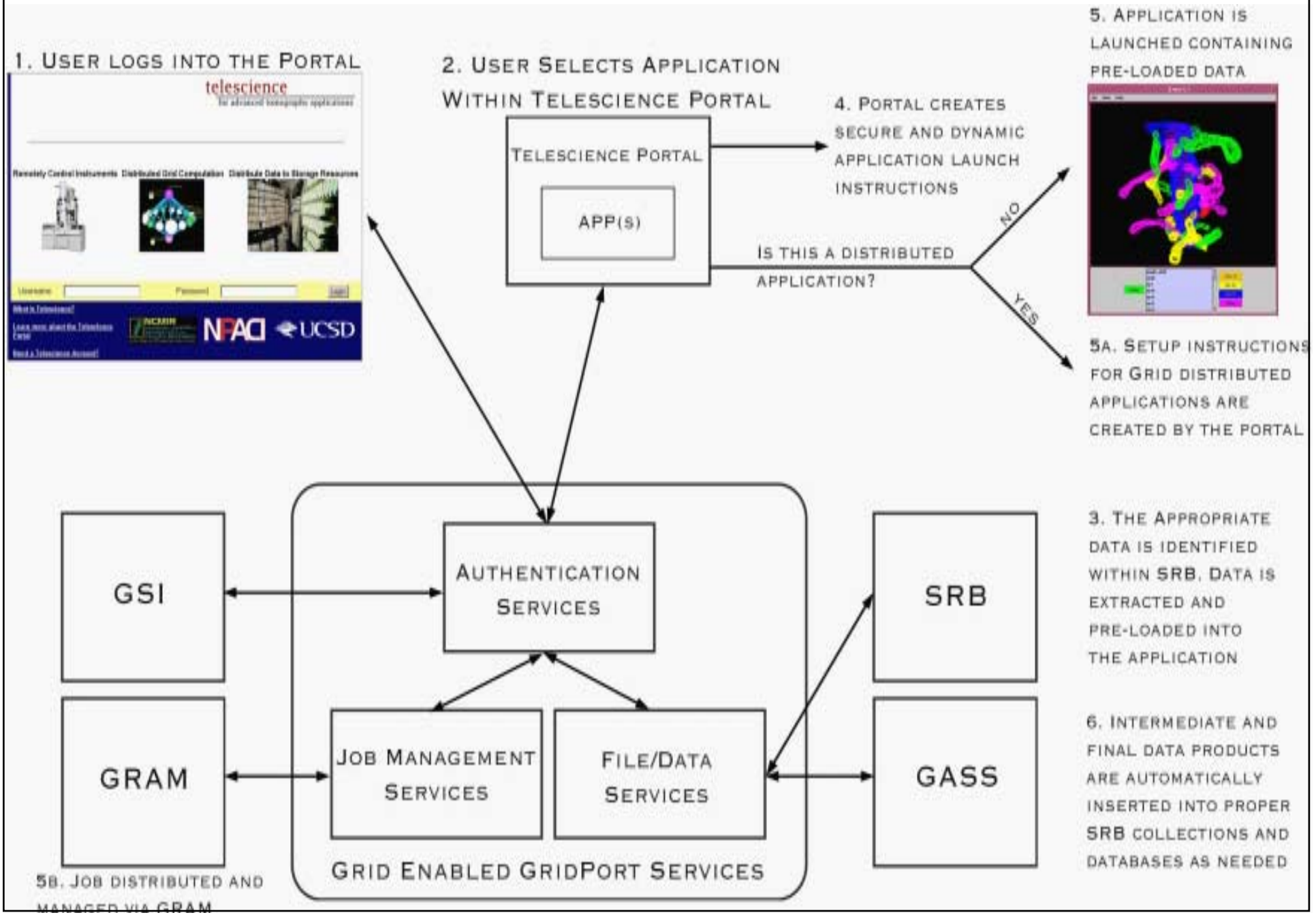
JViewer

(Mona Wong)



3D contour visualization
morphological measurements

Grid Services



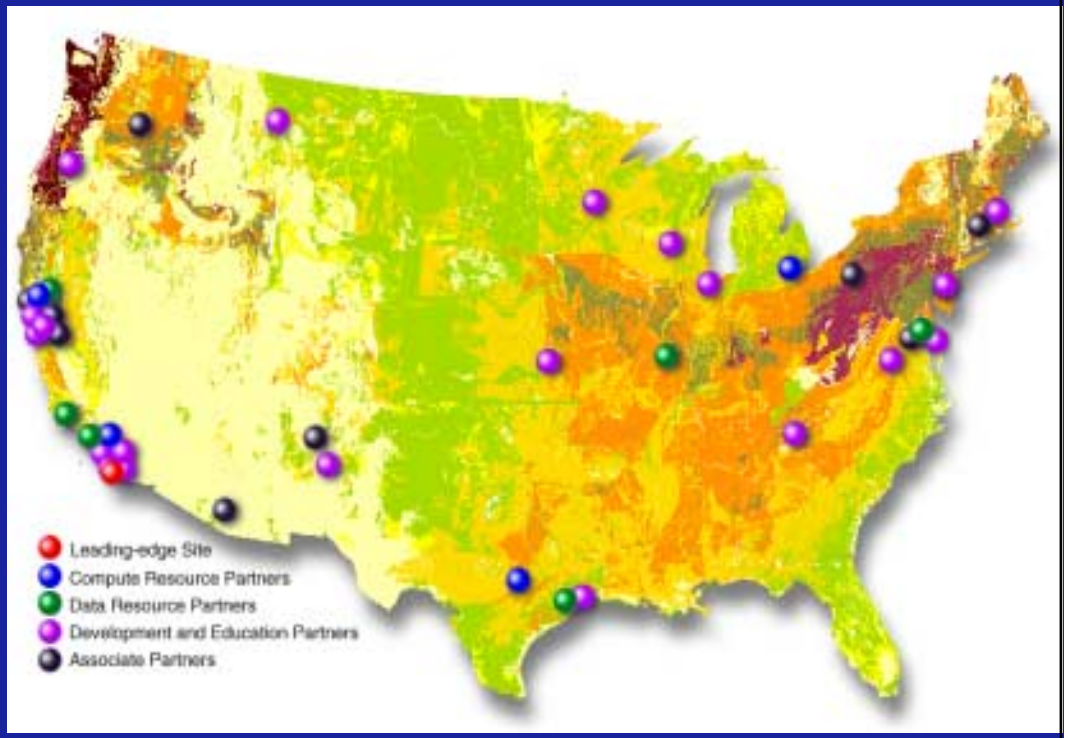
The Telescience Project: Integrated Cyber Infrastructure

Telescience Portal was Quickly Adapted to a SARS Portal for Taiwan

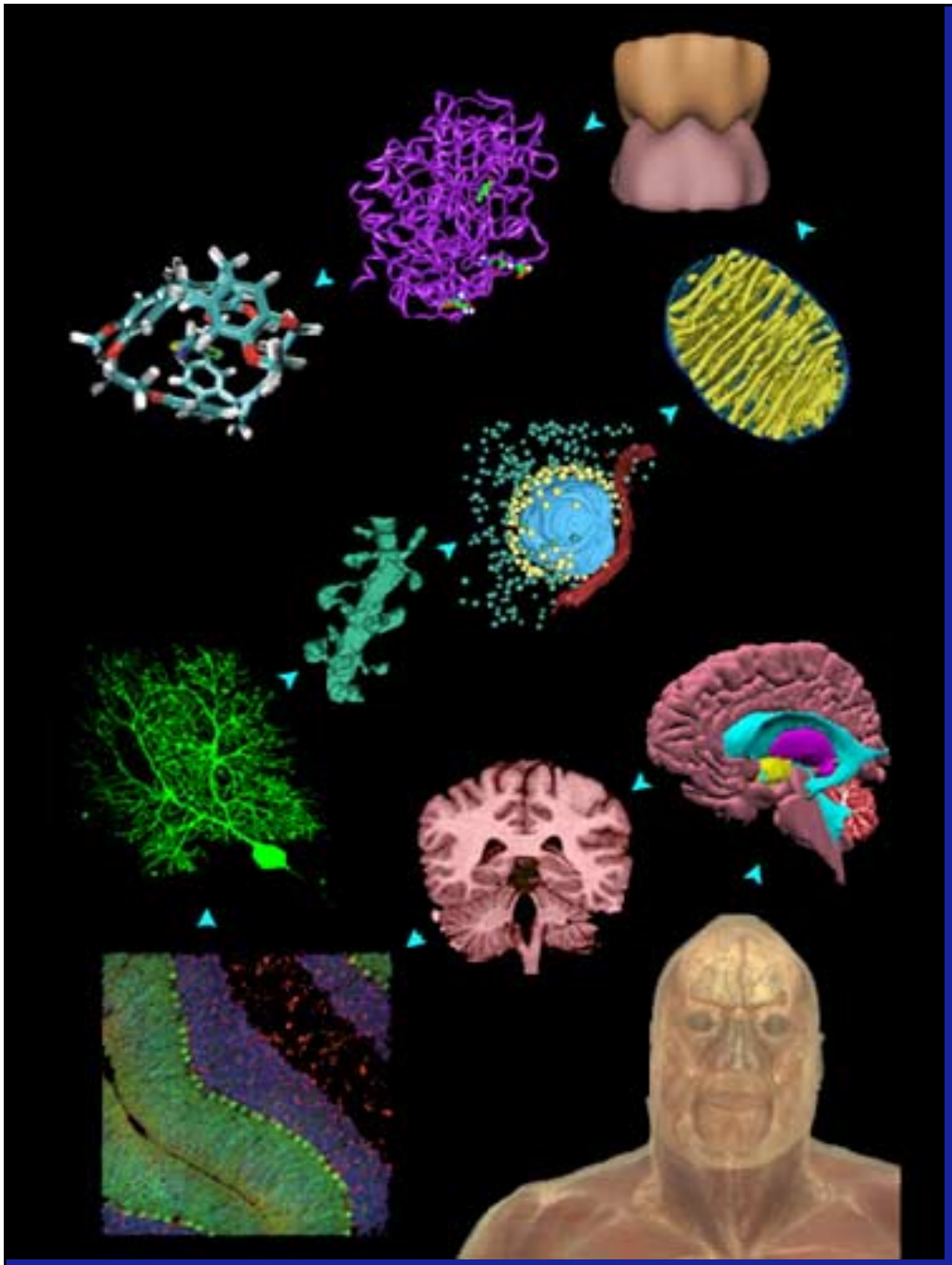
QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

NPACI - The National Partnership for Advanced Computational Infrastructure (NSF)

- ~50 Partner Sites
- Shared Compute Resources -> Grid
- High-speed Networks
- Computational Science Efforts in "Thrusts"
  - *Neuroscience*
  - Molecular Science
  - Earth Systems Science
  - Engineering



- Enabling Technology Thrusts
  - Resources (TeraFlops, High Performance Networks, Data Caches)
  - Metacomputing (Grid Tools - Middleware)
  - Interaction Environments (Visualization - Science Portals)
  - *Data-Intensive Computing (Databases - Data Migration - Knowledge Engineering)*

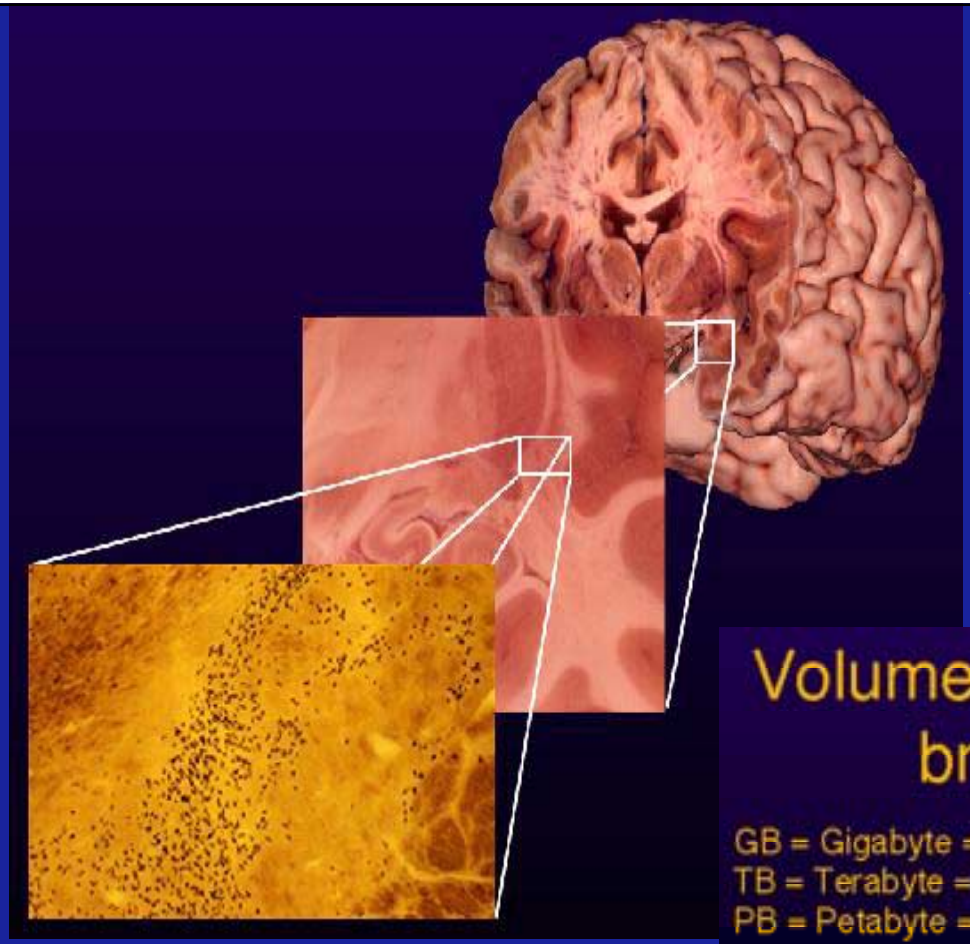


Scales of NS data from Maryann Martone

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*



EACH BRAIN REPRESENTS A LOT OF DATA

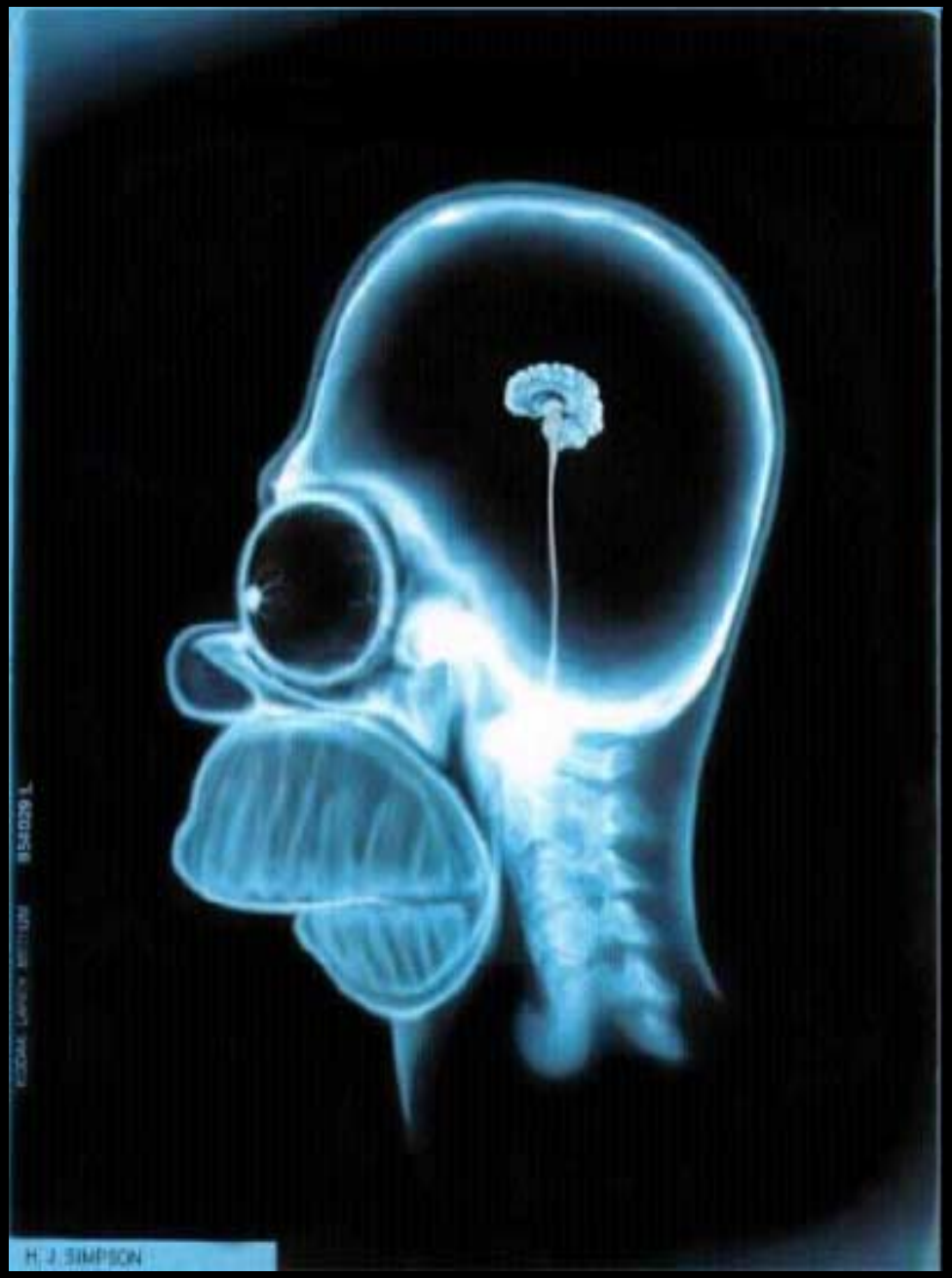
Volume sizes by resolution - brain = 1500 cm^3

GB = Gigabyte = 10^9
TB = Terabyte = 10^{12}
PB = Petabyte = 10^{15}

Voxel size	B&W (1 B/p)	High res (2 B/p)	Color (3 B/p)
cm	1.5 KB	3 KB	4.5 KB
mm	1.5 MB	3 MB	4.5 MB
10 μm	1.5 TB	3 TB	4.5 TB
μm	1.5 PB	3 PB	4.5 PB

AND COMPARISONS MUST BE MADE BETWEEN MANY

Slide courtesy of Arthur Toga / UCLA


H. J. SIMPSON

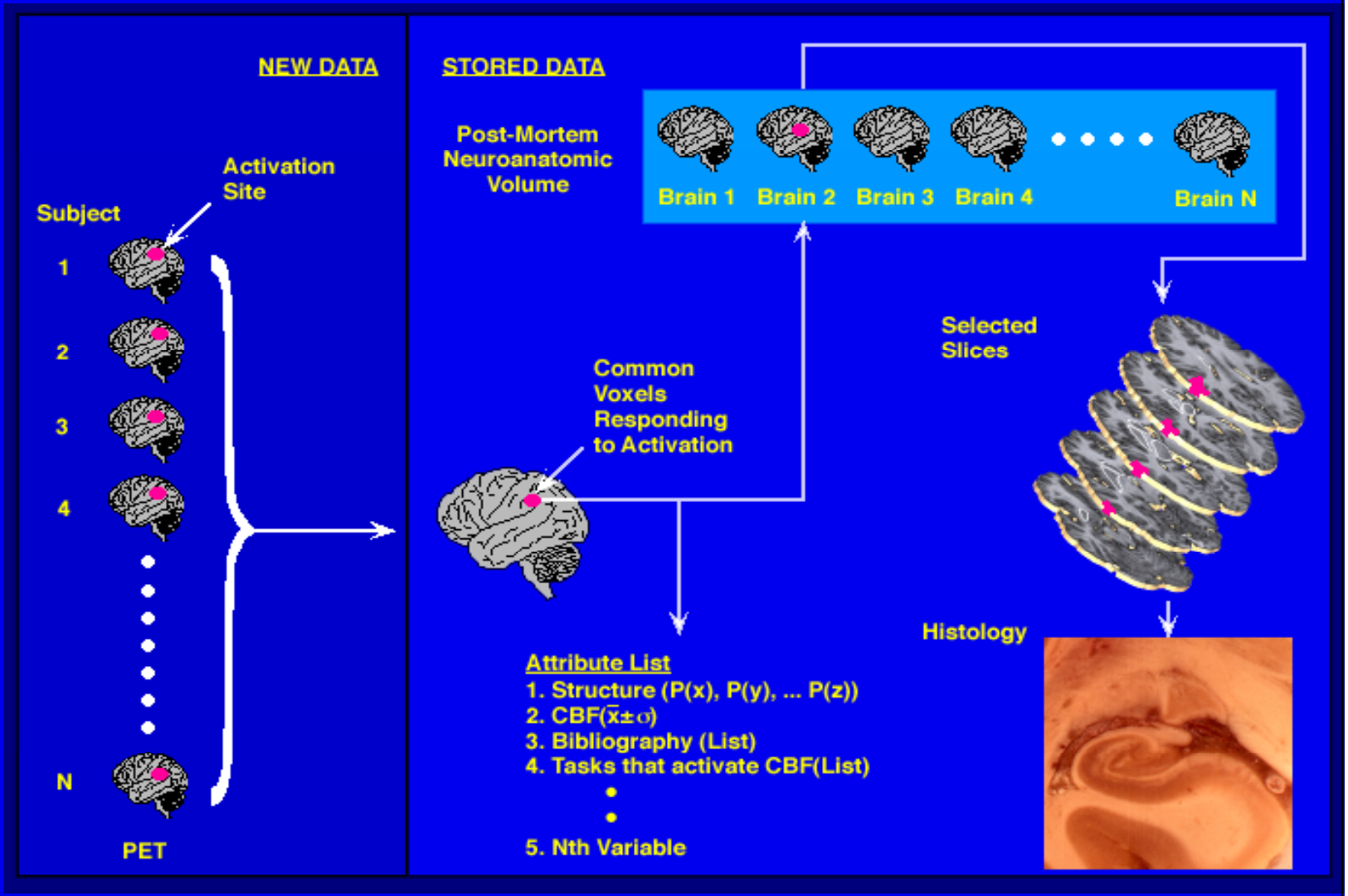
Federate Emerging Databases

Infrastructure to relate, combine & produce meta data

Deformation

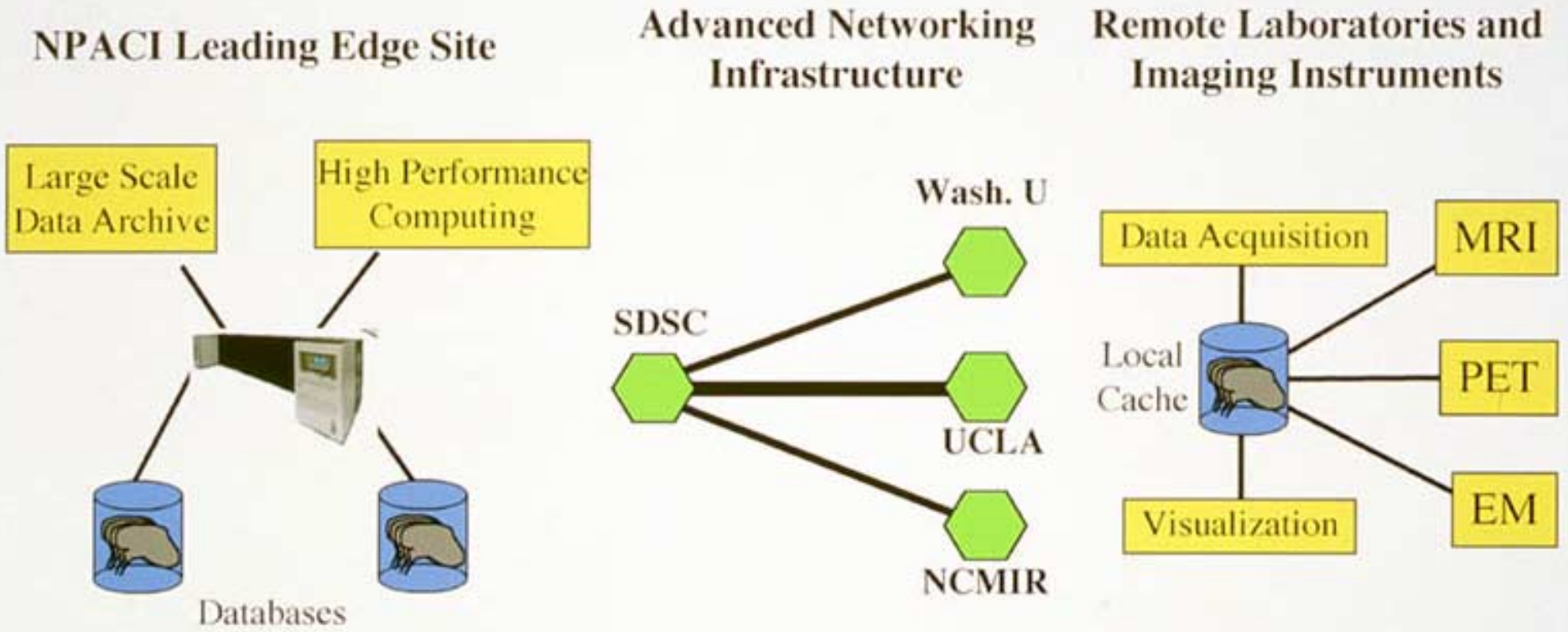
Segmentation

Quantification



Slide courtesy of Arthur Toga / UCLA

Federating Brain Data



Biomedical Informatics Research Network

Test-beds for biomedical knowledge infrastructure

National Center for Research Resources

... IS NPACI Powered !

BIRN Project Objectives

- Establish a stable, high performance network linking key Biotechnology Centers and Clinical Research Centers
- Establish distributed and linked data collections with partnering groups -
- Facilitate the use of computational GRID infrastructure and integrate BIRN with other middleware projects -
- Enable data mining from multiple data collections or databases on neuroimaging and bioinformatics -
- Build a stable software and hardware infrastructure that will allow centers to coordinate efforts to accumulate larger studies than can be carried out at one site.

BIRN 'Test-Beds" have very clear technical and scientific goals!

BIRN Test-beds *(1) Mouse Models of Disease; (2) Human Brain Morphometrics; (3) Functional Imaging of Schizophrenic Humans*

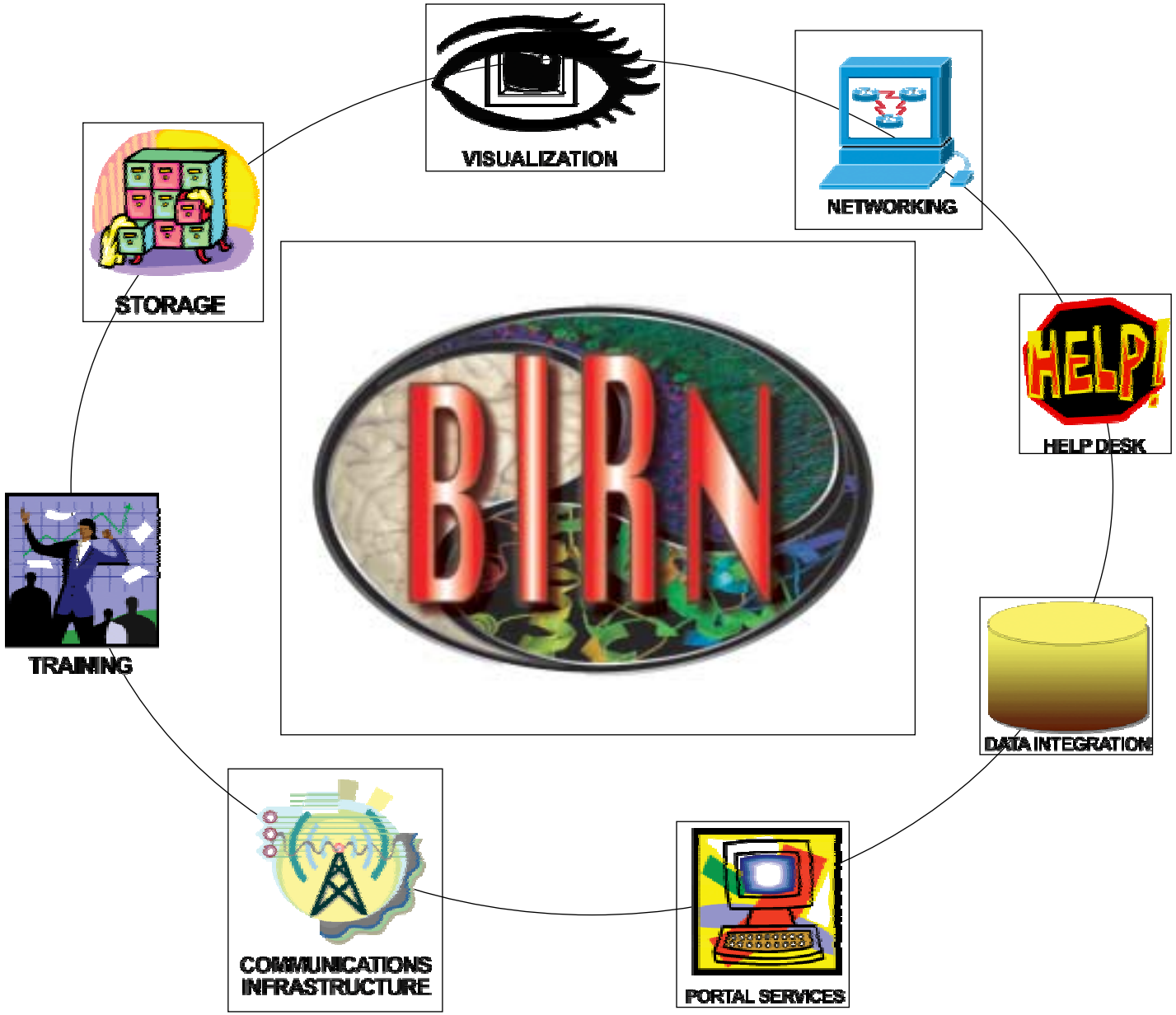
Biomedical Informatics Research Network

Test-beds for biomedical knowledge infrastructure

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

National Center for Research Resources

BIRN



BIRN Coordinating Center

BIRN Coordinating Center

- Deploying a network infrastructure capable of quickly moving large amounts of data between BIRN sites across the US
- Creating federated databases pertaining to the BIRN scientific test-beds
- Developing software to find, compare, and analyze complex neurological imaging data
- Ensure regulatory compliance (e.g., patient privacy) without inhibiting collaboration
- UC San Diego

BIRN CC Services

- Network Monitoring
- Statistics & Measurement
- 7 x 24 Help Desk
- Problem Tracking
- High Level Project Management
- Portal Services & Tools Integration
- Training
- Data Integration
- Visualization Tools
- Documentation – web site, best practices, lessons learned, checklists

BIRN Network Operations Center (NOC)

Logical Description with Standardized Site Rack

24x7 Operations Monitoring

BIRN NOC Monitoring

UCSD/SDSC Network

Internet 2

GB Switches

BIRN Network Management

- Network Switch
- BIRN Statistics
- BIRN Network Probe
- Network Attached Storage –
- Grid POP/ SRB, Globus
- General purpose (eg., encryption)
- UPS for Rack

NCRR

Cisco 4006

DL380 - Network Stats

GigE Net Probe

N2400 NAS 1 - 10 TB

DL380 Grid POP

DL380

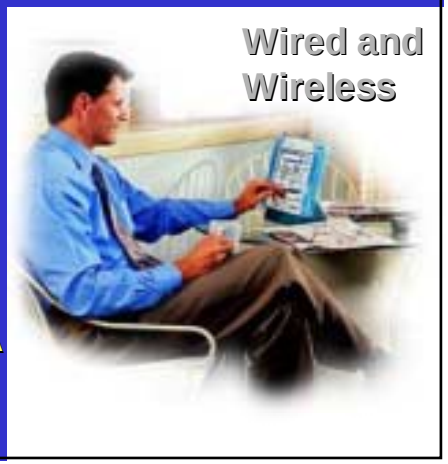
APC UPS

BIRN Site Rack

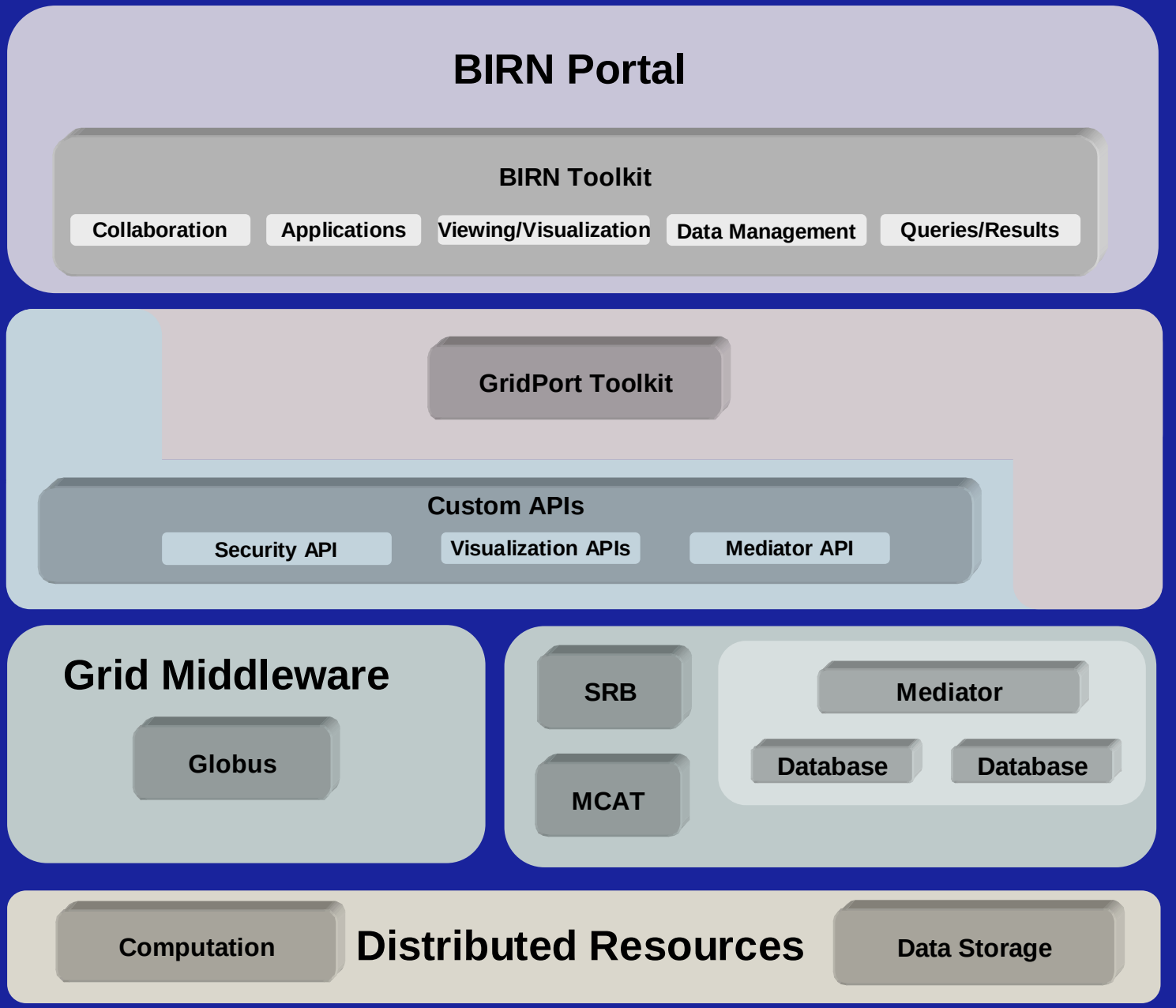
Gigabit Network Probes

NOC Servers and Testers/Analyzers

Ultimately, Access from Anywhere to BIRN DATA Everywhere



BIRN Grid Infrastructure

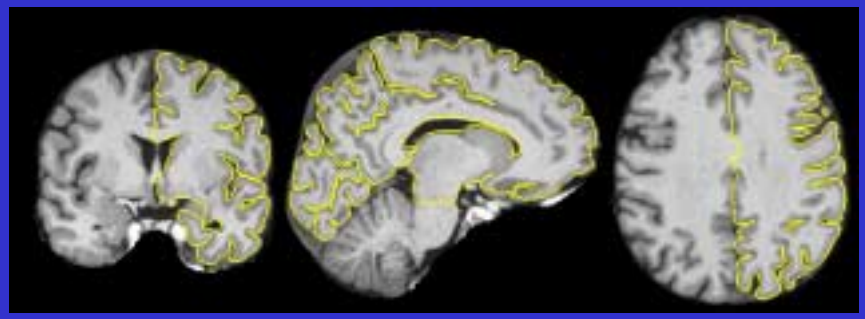


Brain Morphometry BIRN

- Clinical Aims
  - Do structural differences contribute to specific symptoms such as memory dysfunction or depression?
  - 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.

HARVARD x 2

UCLA

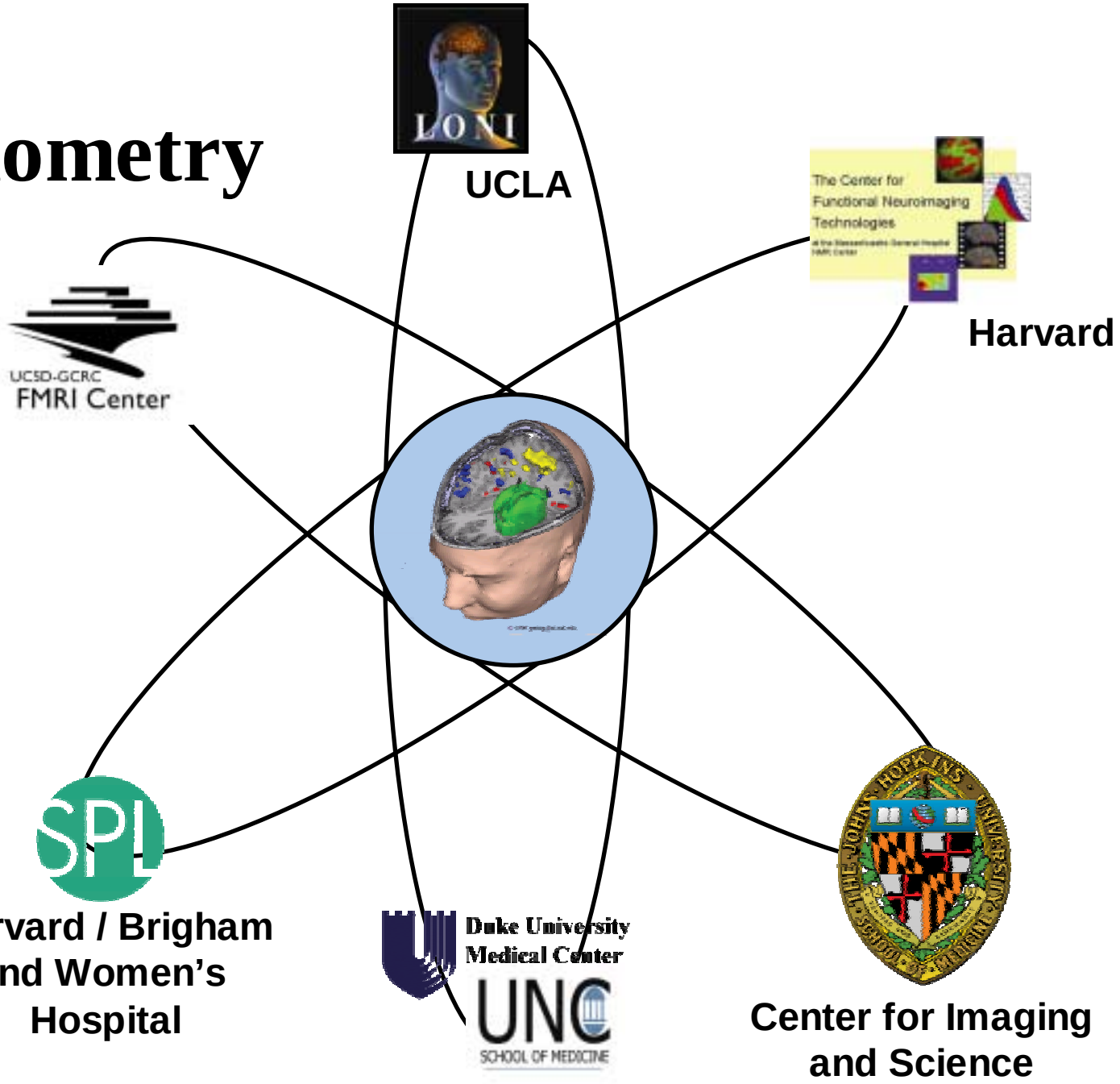


Johns Hopkins U.

Duke

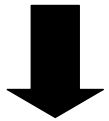
UCSD

Brain Morphometry BIRN

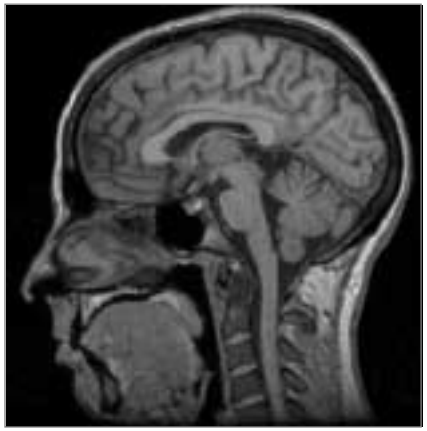


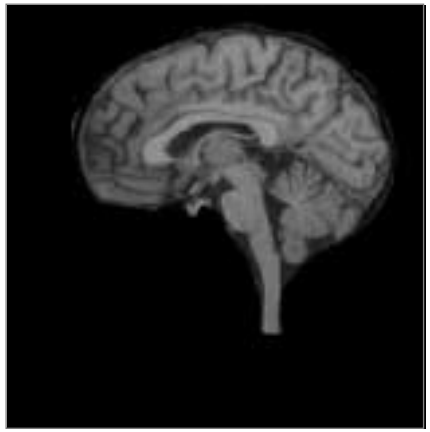
Important Considerations

- **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 will provide both raw and skull stripped data**
  - **BIRN is working with local IRBs to allow for the sharing of raw anatomical data for authorized BIRN members**
- **BIRN must conform to multiple overlapping regulations**
  - **Common Rule**
  - **HIPAA**
  - **State Law**



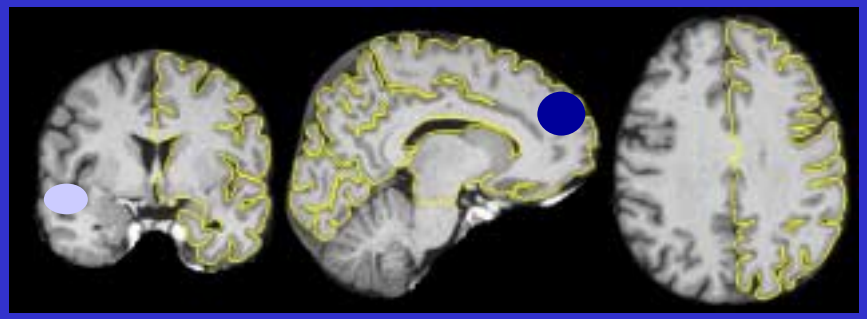


Raw Skull Stripped

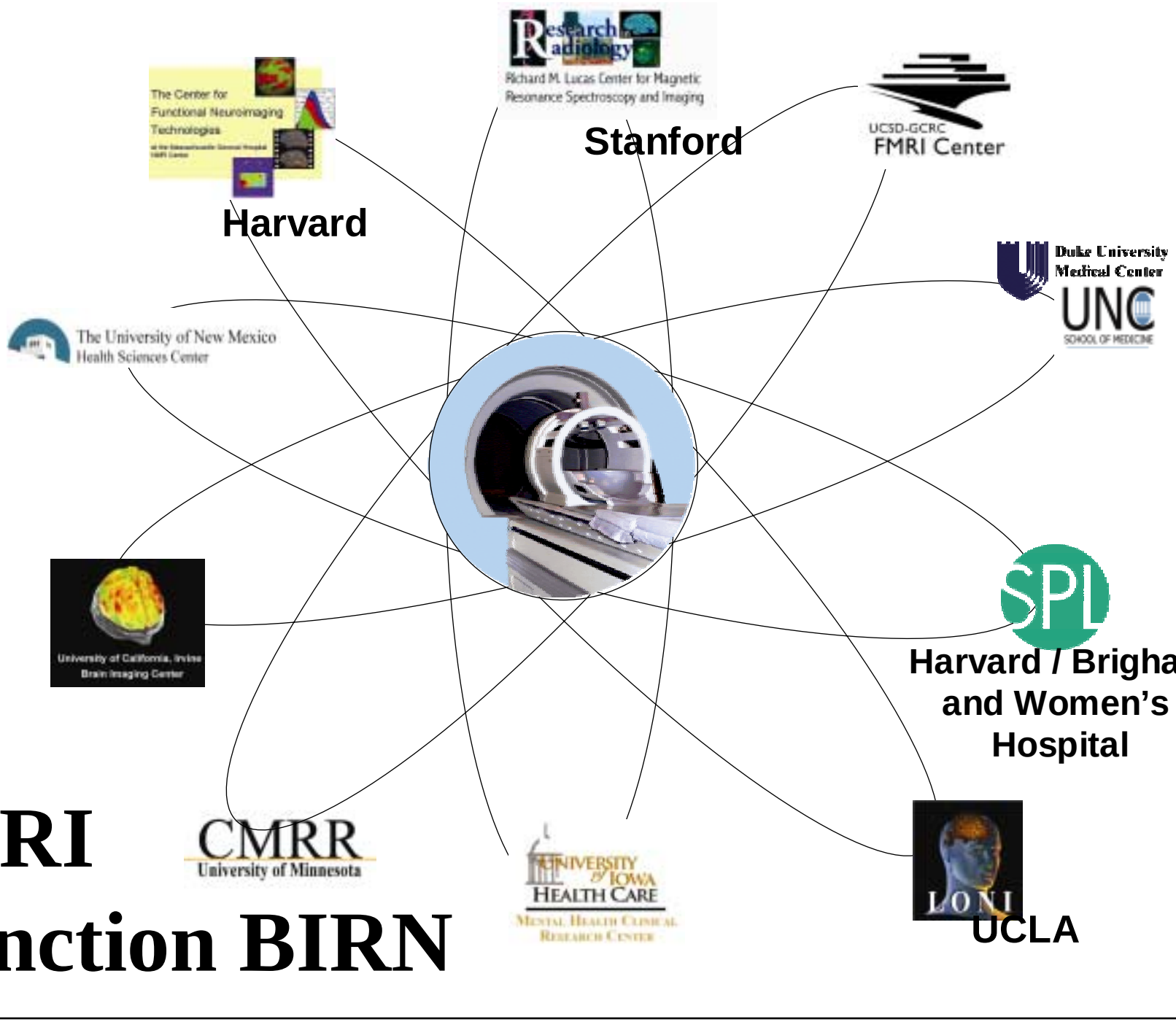
Functional Imaging BIRN

- Clinical Aims
  - Is Frontal and Temporal Lobe Dysfunction the Cause of Schizophrenia?
  - 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.

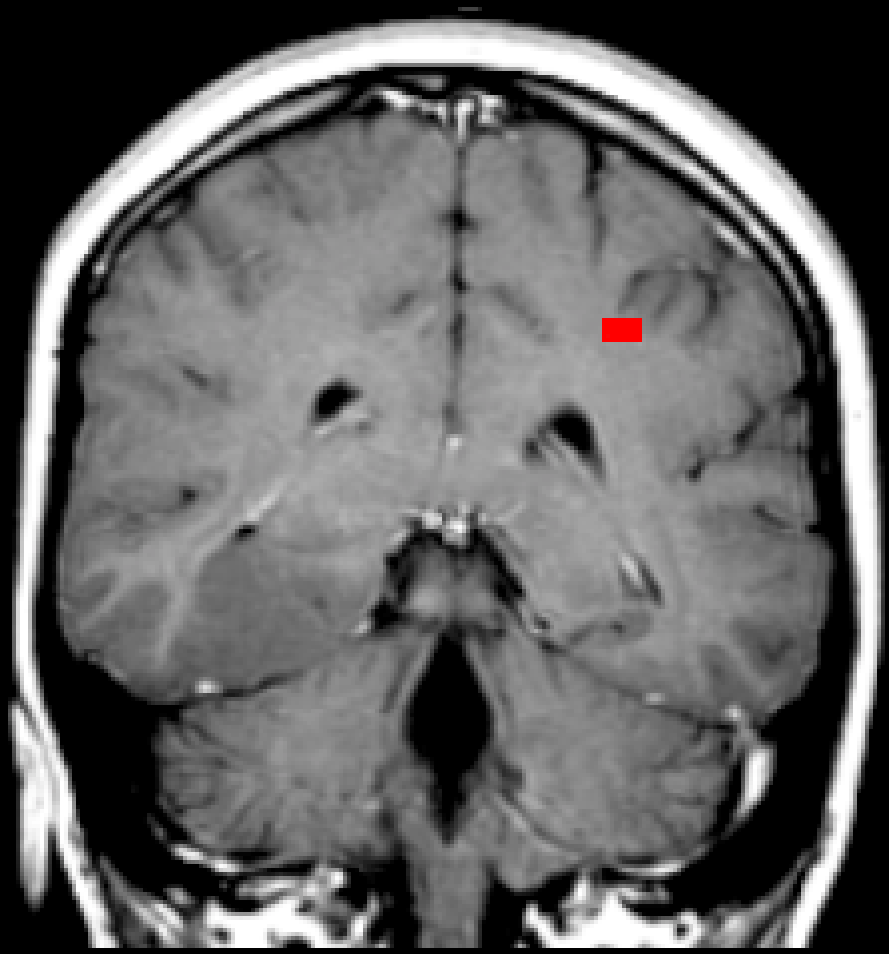
Duke
New Mexico
UCLA
Iowa
UNC



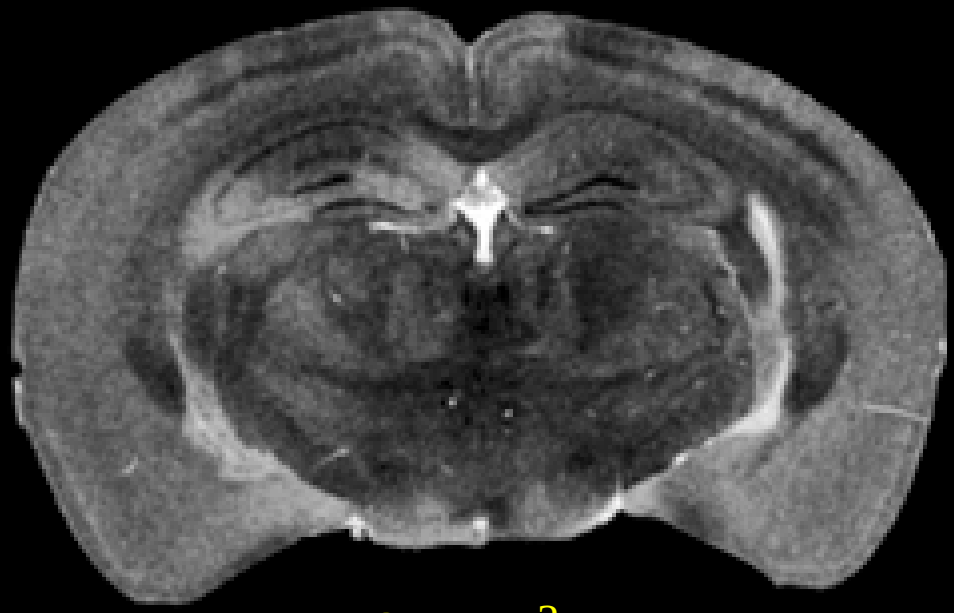
Stanford
Harvard x 2
Minn
UCSD
UCIrvine


The Center for Functional Neuroimaging Technologies
Harvard
Research Radiology
Richard M. Lucas Center for Magnetic Resonance Spectroscopy and Imaging
Stanford
UCSD-GCRC
FMRI Center
Duke University Medical Center
UNC
SCHOOL OF MEDICINE
The University of New Mexico Health Sciences Center
University of California, Irvine
Brain Imaging Center
SPL
Harvard / Brigham and Women's Hospital
CMRR
University of Minnesota
University of Iowa Health Care
Mental Health Clinical Research Center
LONI
UCLA
fMRI
Function BIRN

Advanced Imaging - Correlating Human and Mouse



$5mm^3$

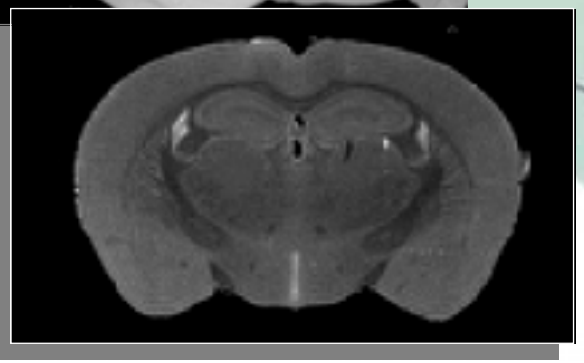


$25um^3$

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

Mouse BIRN: Protocols for correlated imaging

Cryosectioning: UCLA

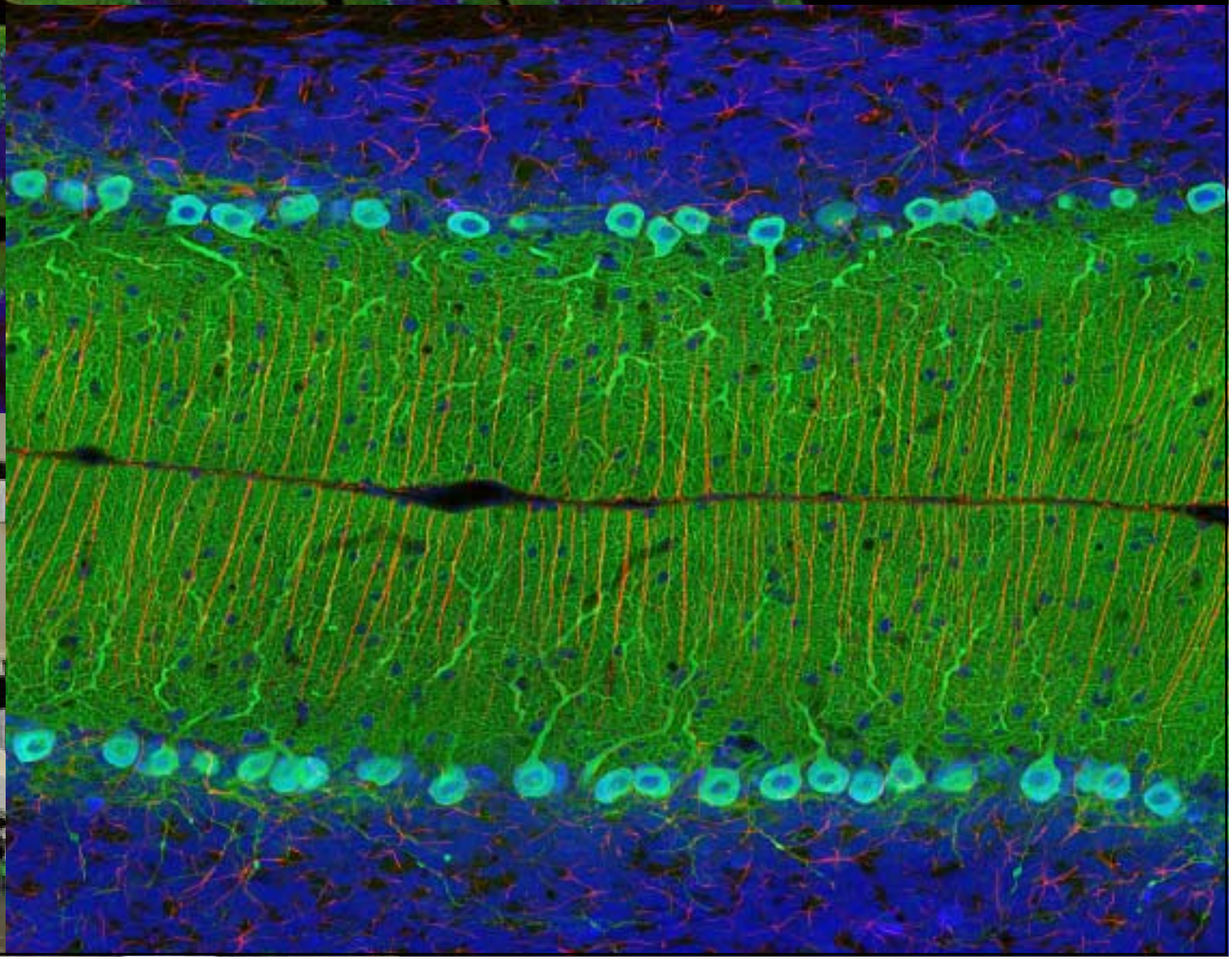


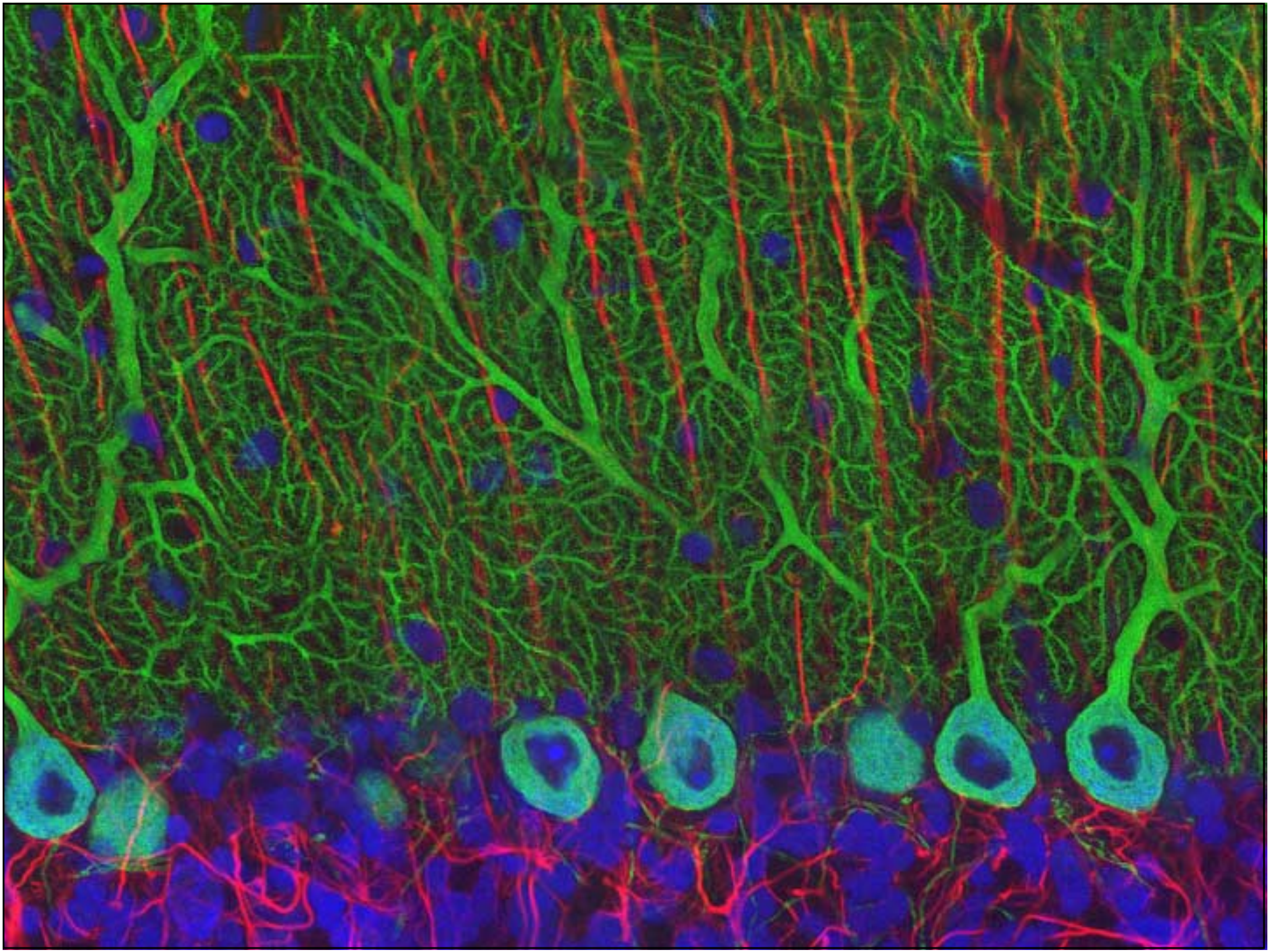
Diffusion Tensor
Imaging: Cal Tech

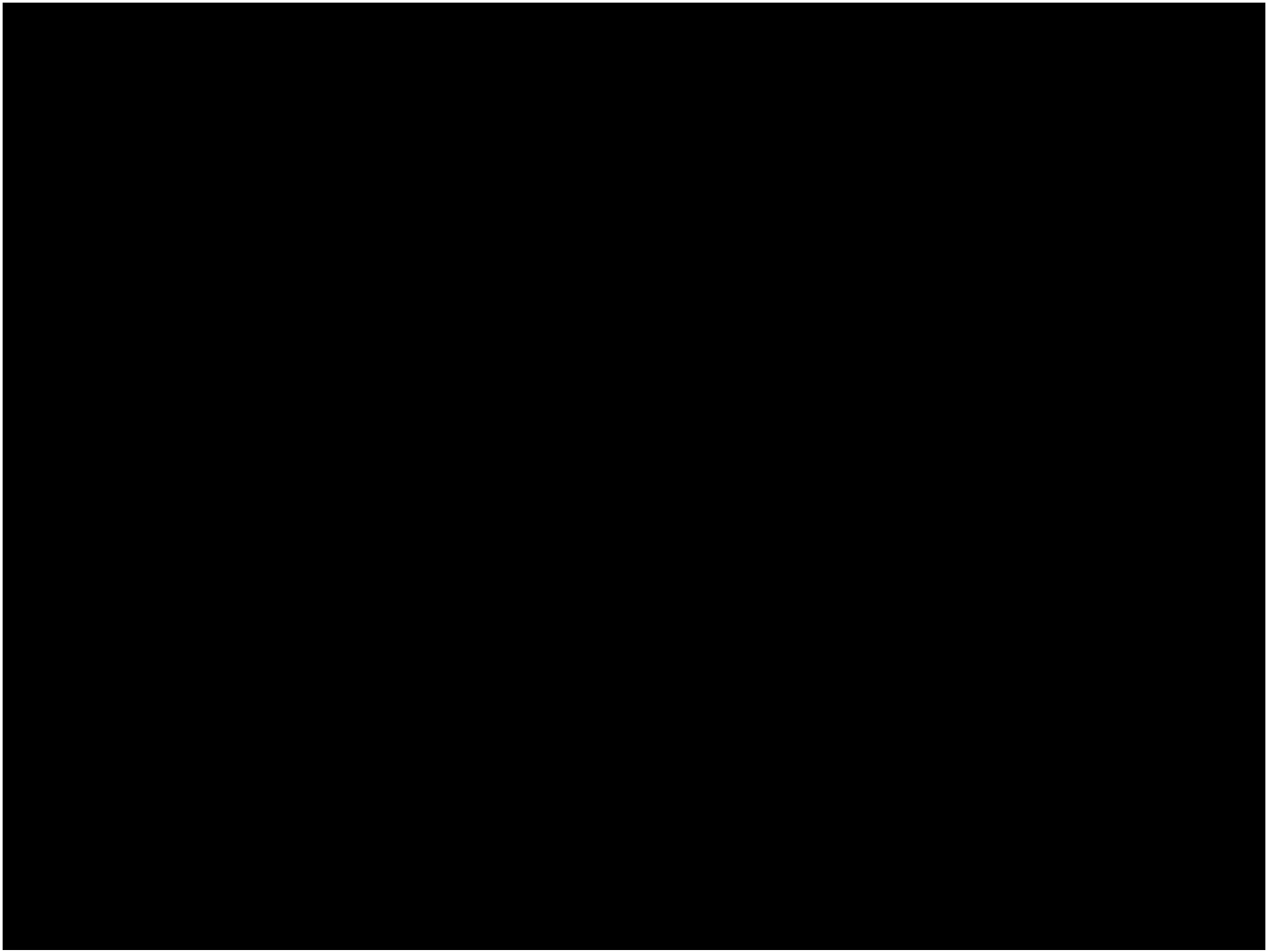
Magnetic Resonance
Microscopy: Duke

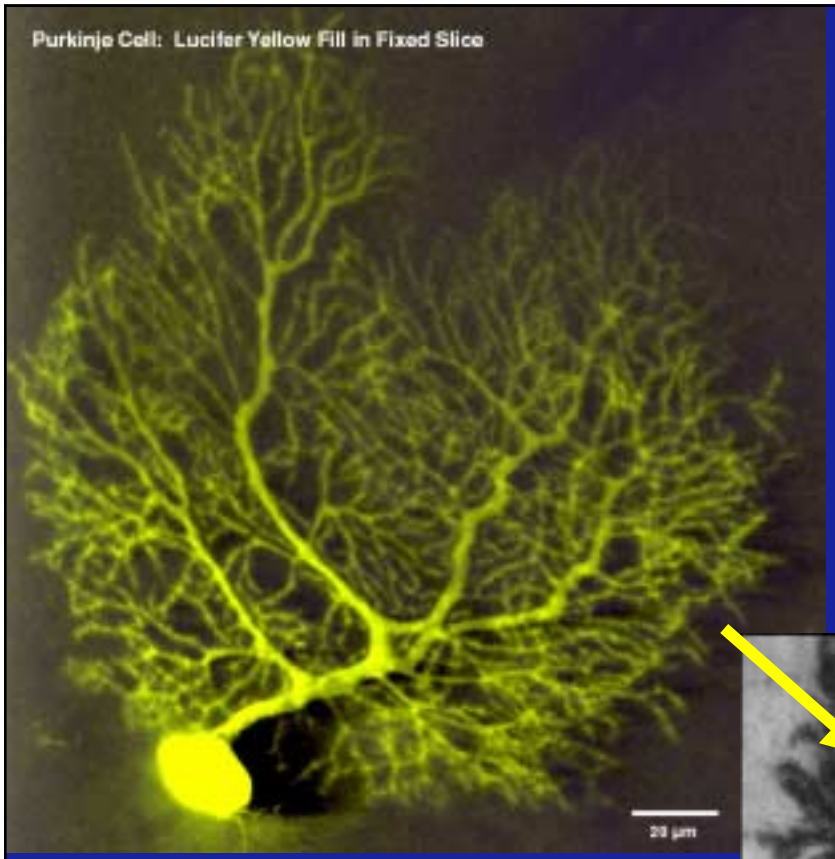
Large Scale Brain Maps / NCMIR

- Custom high-speed multi-photon auto montaging 3 & 4D imaging system



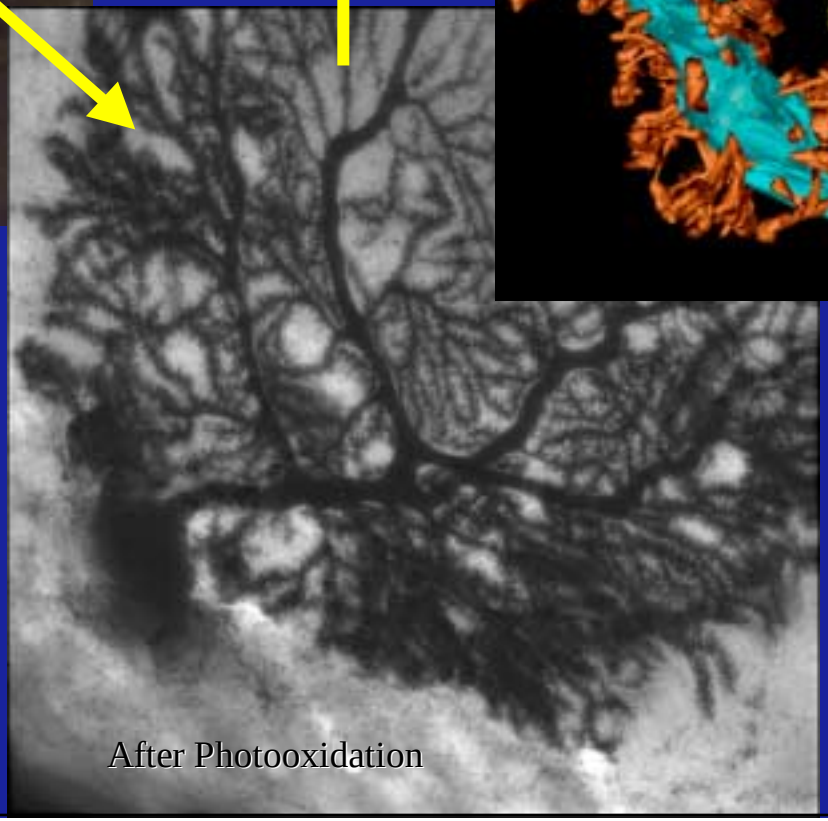






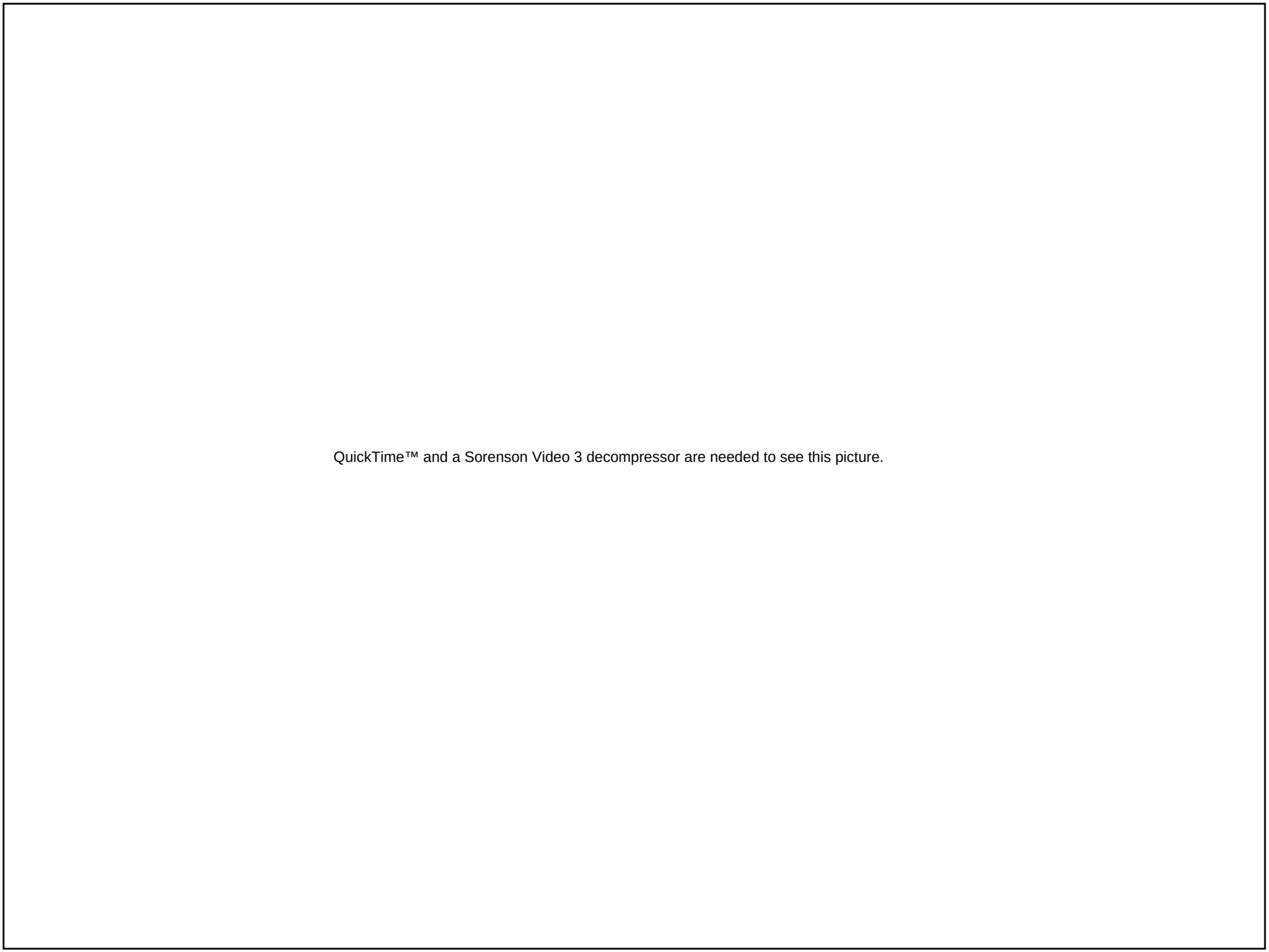
•UHVEM

Photooxidation of Neuron Filled with Lucifer Yellow

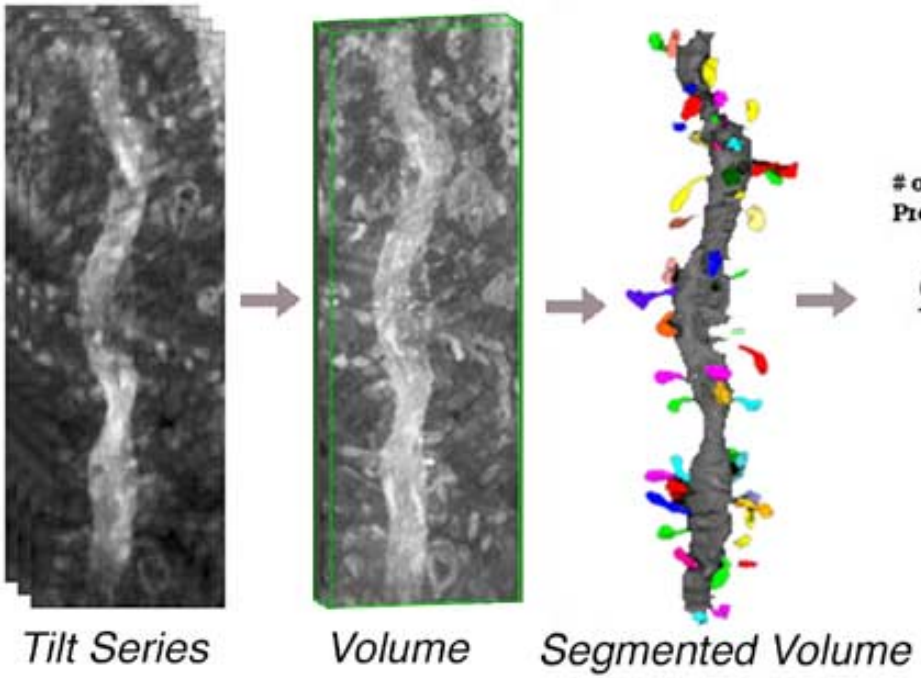


Tomographic Volume

From M. Martone E. Bushong and N. Yamada


QuickTime™ and a Sorenson Video 3 decompressor are needed to see this picture.

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



Segmentation Info

 # objects: 67 **Method**: manual
Program: Xvoxtrace **Segmented by**: M. Martone

Object	Description
sp1	Dendritic spine
sp5	Dendritic spine
sp9	Dendritic spine
sp57xz	Dendritic spine, traced in xz plane
sp62pt	Dendritic spine, partial

Measurement Info

Measurement	Programs Used
SA	Analyze
Vol	Analyze
Length	Xdend
Number	Manual

Measurements

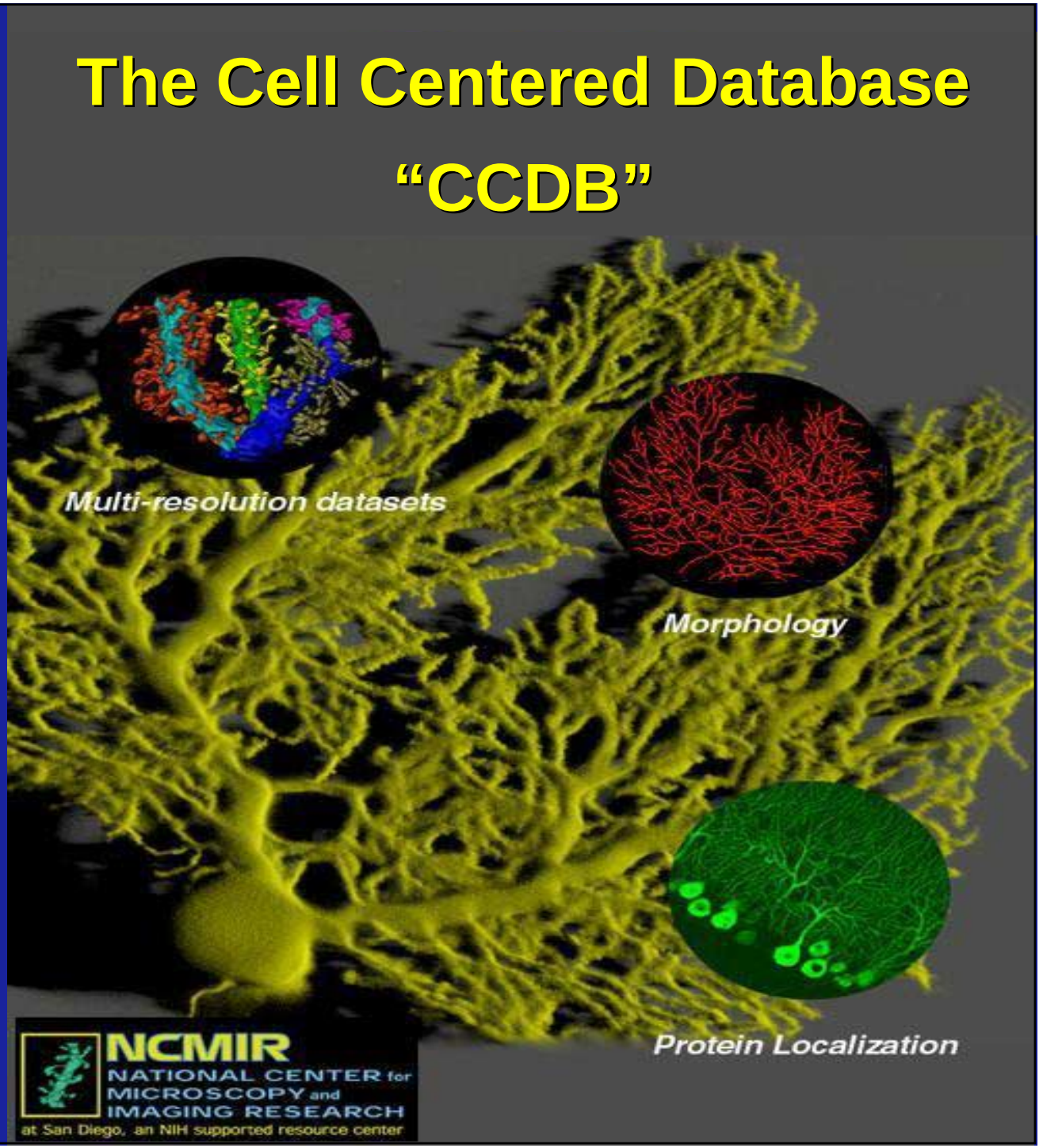
	SA	Vol	Length	#
sp1	1.1	0.05	1.2	1
sp5	0.4	0.01	0.8	1
sp9	1.53	0.05	1.0	1
sp57xz	1.36	0.05	1.2	1
sp62pt	na	na	na	na

Units=μm

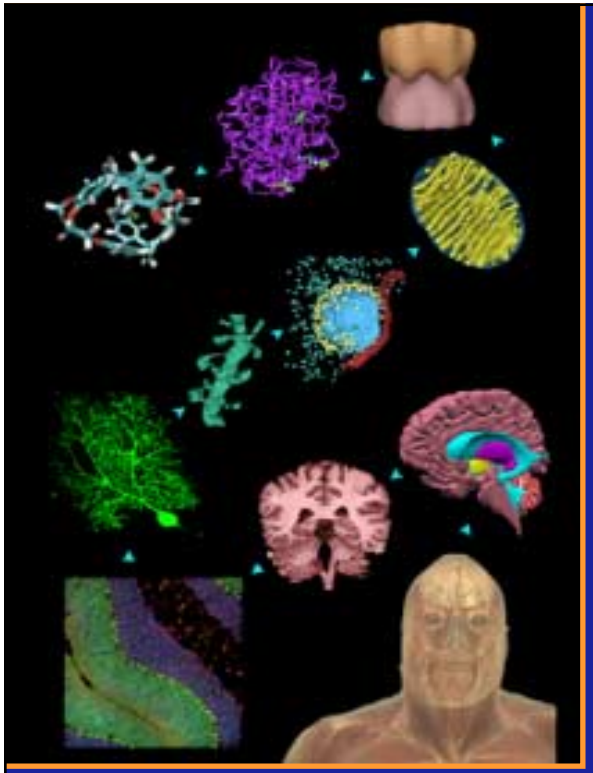
from Maryann Martone, Amarnath Gupta, Bertram Ludaescher, Naoko Yamada and Mona Wong

The Cell Centered Database "CCDB"

- A Federated Distributed Database for Neuroscience
- A Multimode & Multiscale "DataGrid"
- Interoperates with Gene and Protein databases & "brain map" databases of brain anatomy

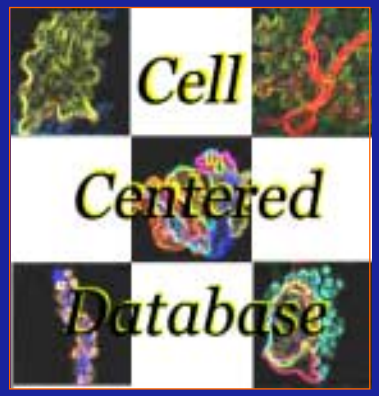


from
Maryann Martone, Amarnath Gupta, Bertram Ludaescher, Naoko Yamada and Mona Wong



Federation of Brain Data

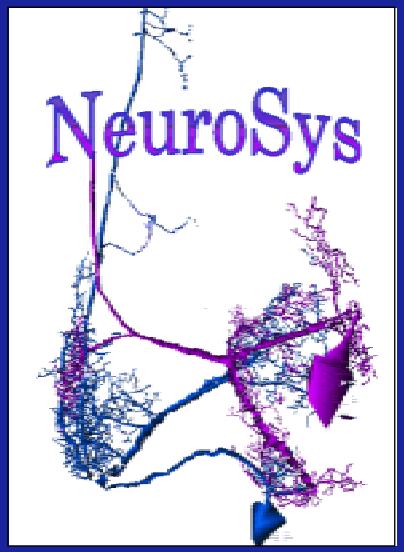
- National Partnership for Advanced Computational Infrastructure
- Integrating brain data across scales and disciplines



UCSD

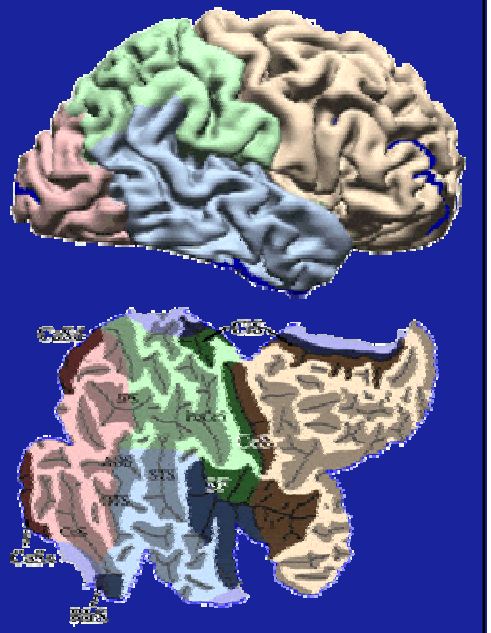
UCLA

Art Toga



Montana State Univ

Gwen Jacobs



Washington Univ

David Van Essen

Database Mediation for BIRN

Find animal models of movement disorders where the volume of basal ganglia structures are decreased and where loss of spines from medium spiny neurons is observed.

Integrated View

Integrated View Definition

Mediator

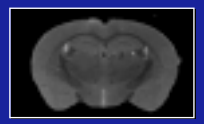
Wrapper

Wrapper

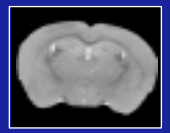
Wrapper

Wrapper

UCSD



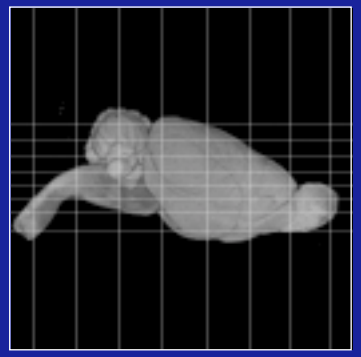
Cal Tech



Duke

UCLA

Mouse BIRN Data Integration Framework

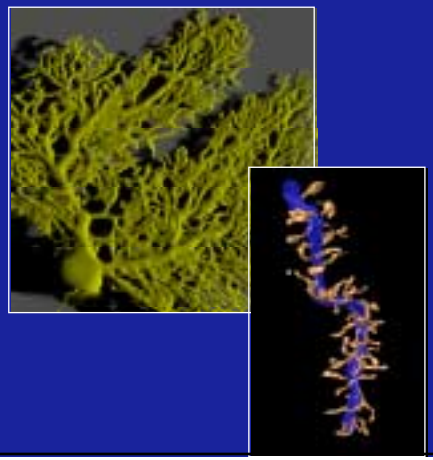


1. Create databases at each site

2. Create conceptual links to a shared ontology

4. Use mediator to navigate and query across data sources

3. Situate the data in a common spatial framework



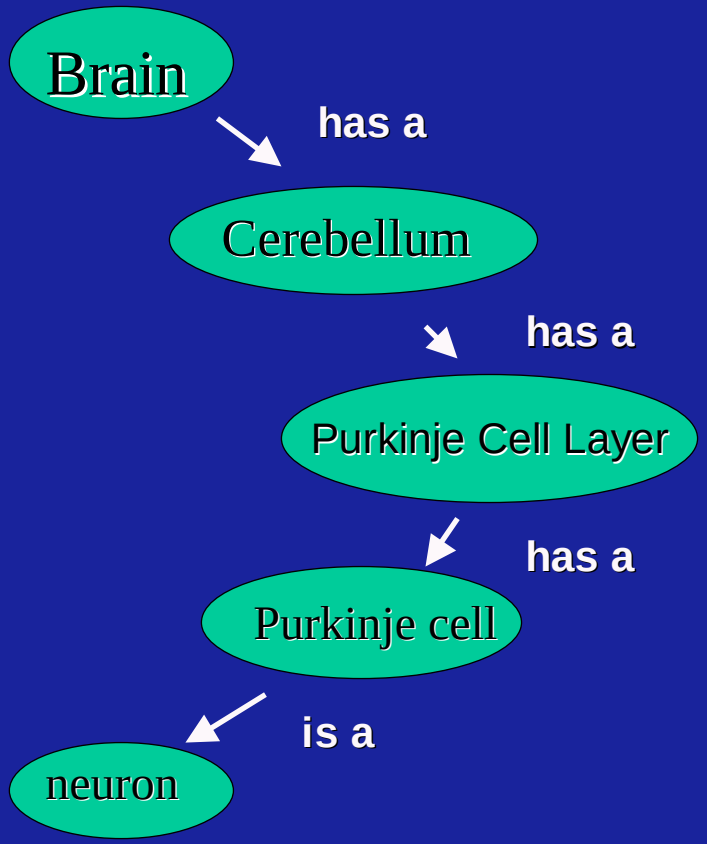
Ontologies

What is an Ontology?

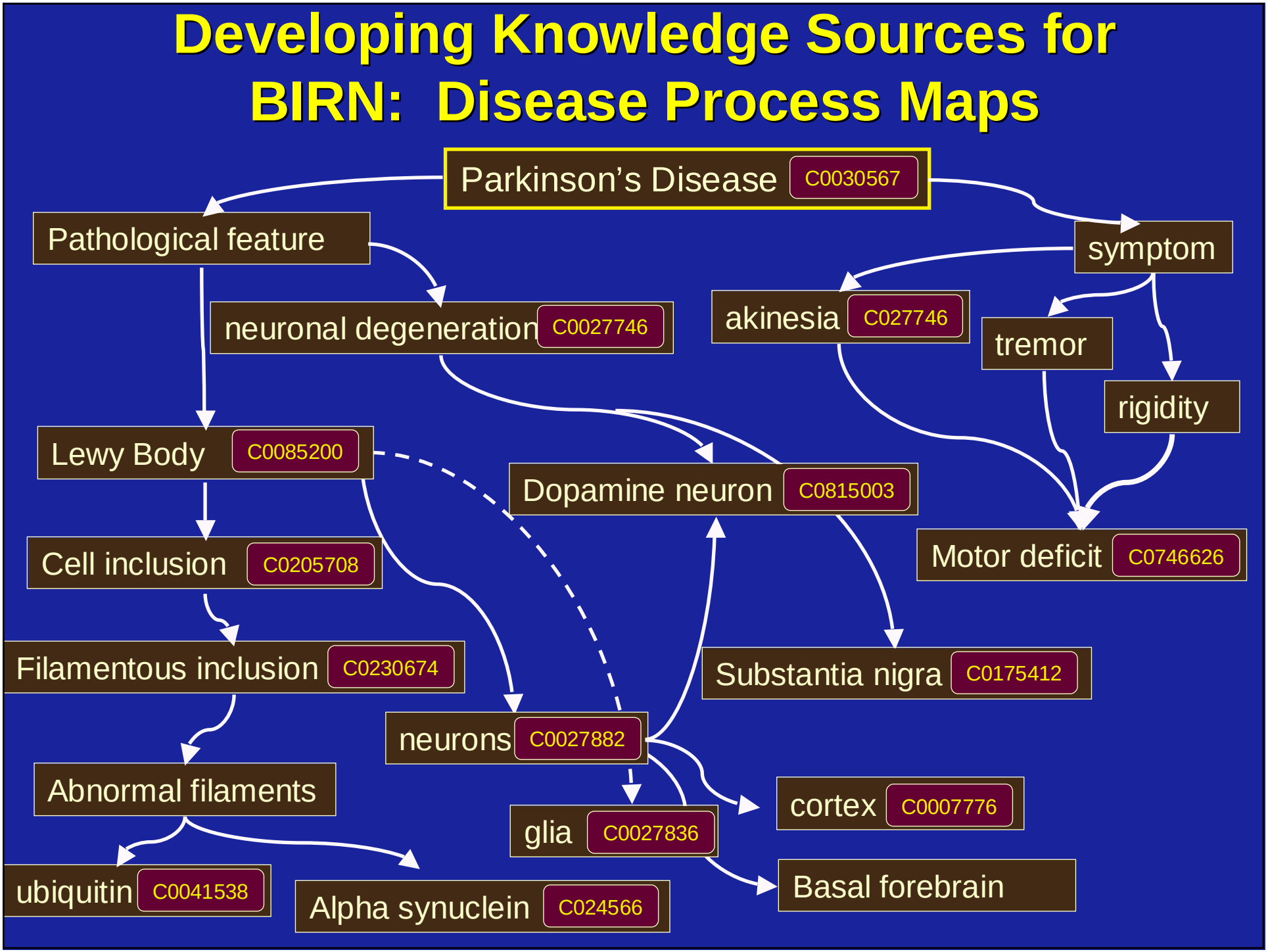
- Way to communicate a shared understanding of a field
- representation of terminological knowledge
- explicit specification of a conceptualization
- concept hierarchy ("is-a")
- further semantic relationships between concepts ("is part of", "causes" etc.)

Examples:

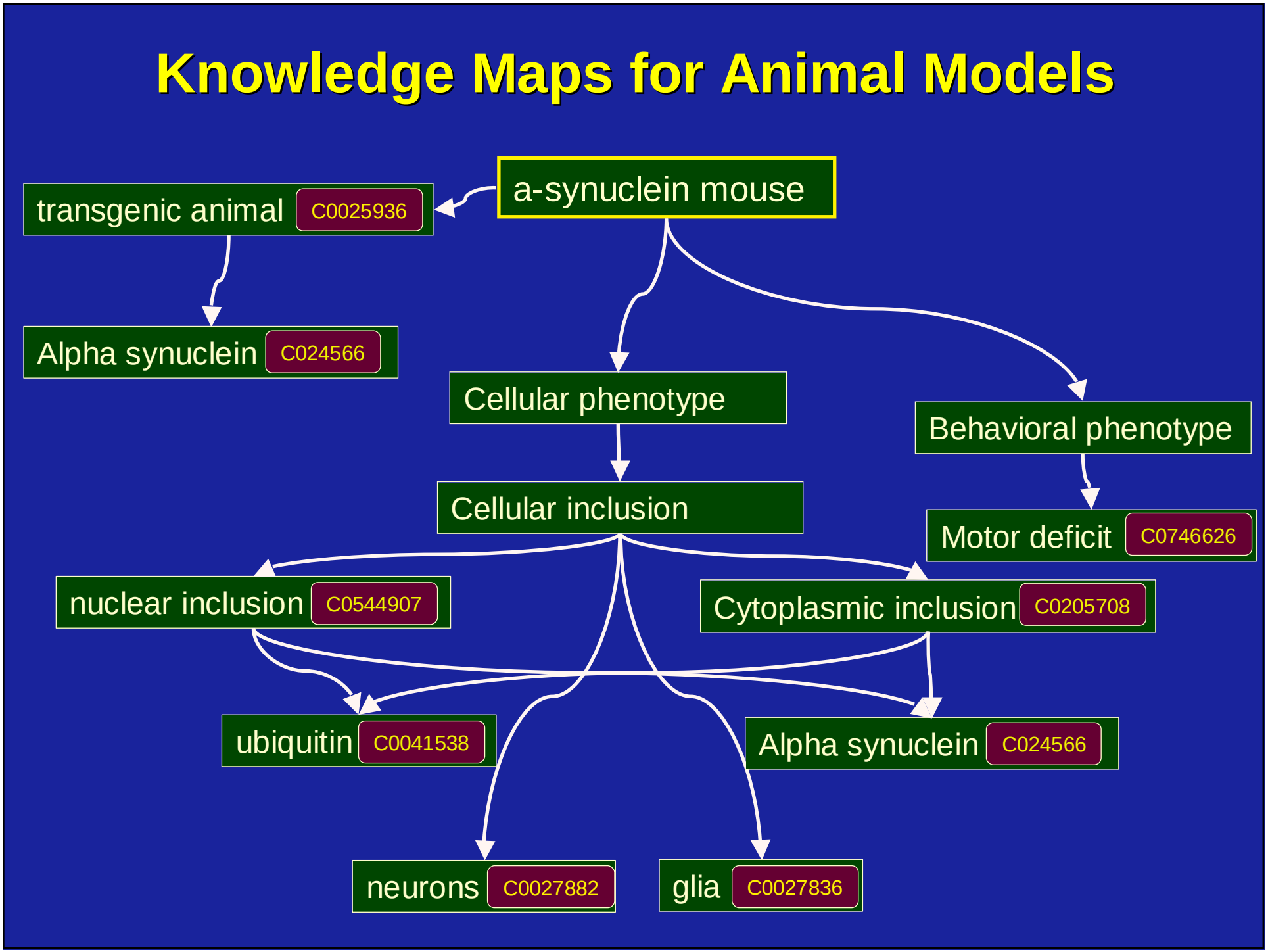
- NCMIR ANATOM
- GO (Gene Ontology)
- UMLS (Unified Medical Language System)
- CYC



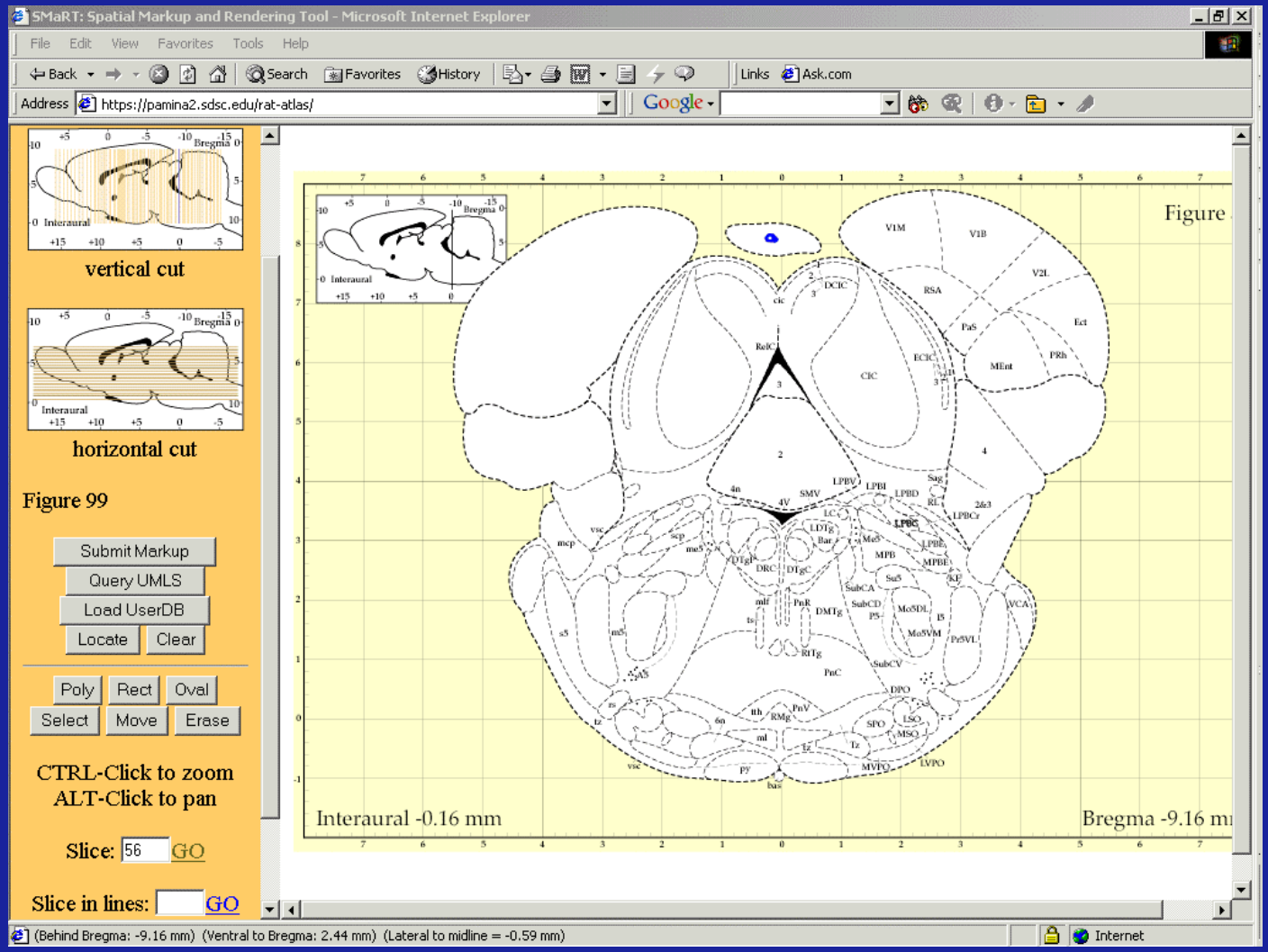
Developing Knowledge Sources for BIRN: Disease Process Maps



Knowledge Maps for Animal Models

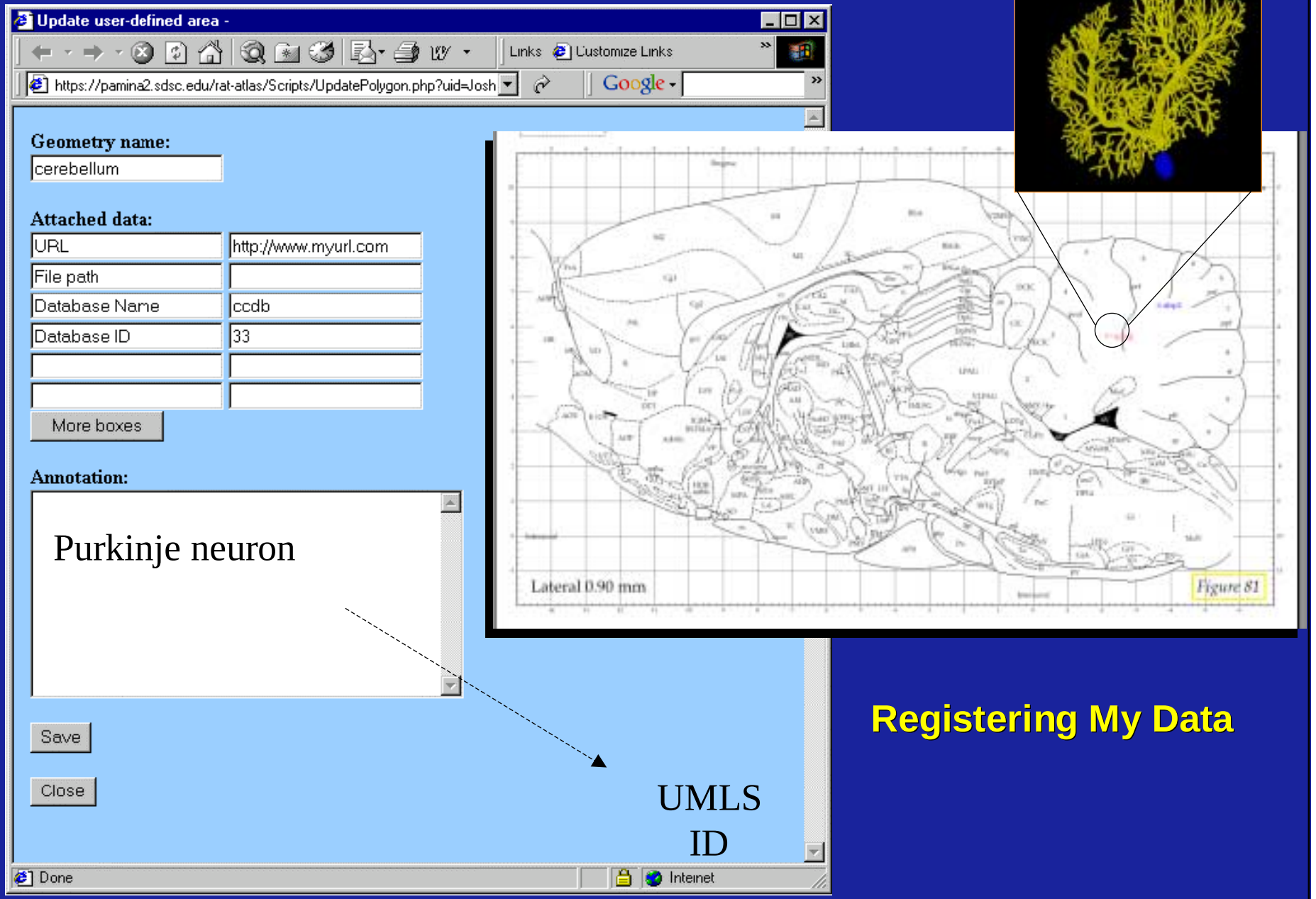


Spatial Registration of CCDB Data



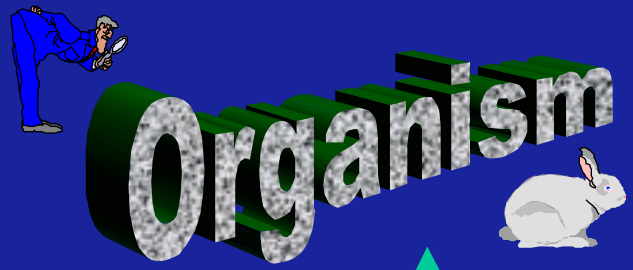
The Smart Atlas Tool: Ilya Zaslavsky and Haiyun He

- Provide a knowledge base of spatial relationships in the brain
- Provide tool for spatial registration of data
- Navigate through anatomical and semantic complexity of brain

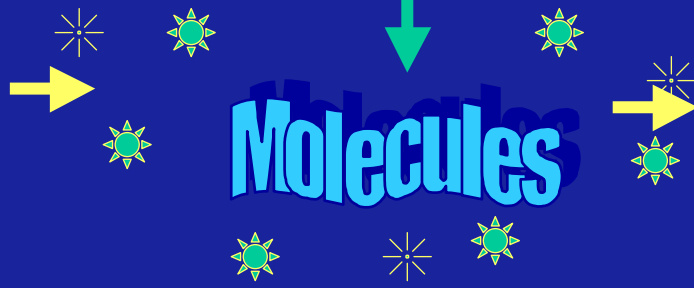


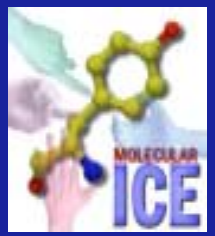
Registering My Data

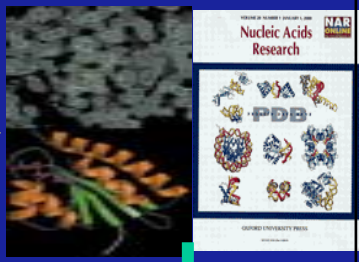
- Data Acquisition
- 3D or 4D Data Refinement
- Data Reduction
- Database Deposition



Macromolecular Complexes, Organelles & Cells







Genome DB's

• Data Acquisition

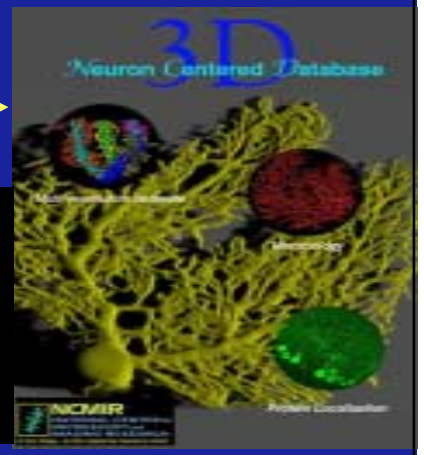
• 3D or 4D Data Refinement

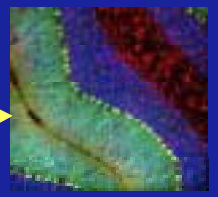
• Data Reduction

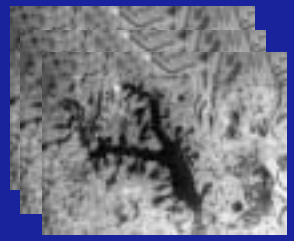
• Database Deposition

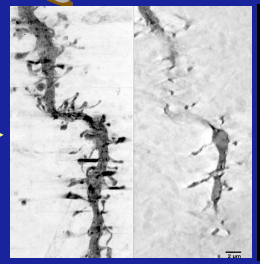
Organism

Macromolecular Complexes, Organelles & Cells

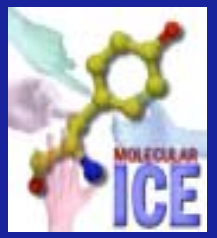


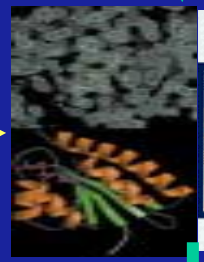






Molecules





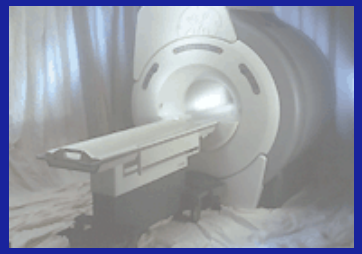
Genome DB's

• Data Acquisition

• 3D or 4D Data Refinement

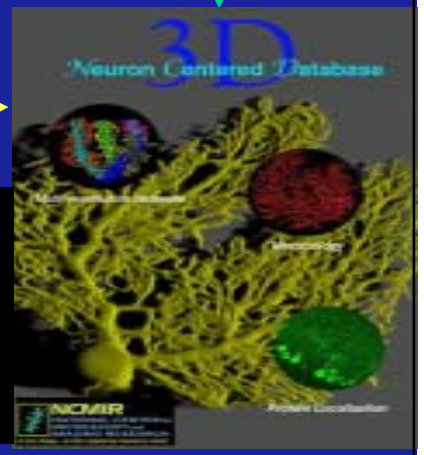
• Data Reduction

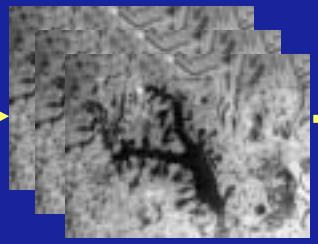
• Database Deposition

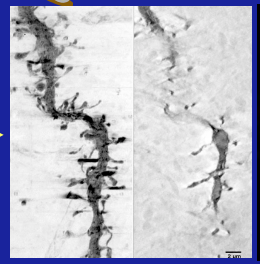


Organism

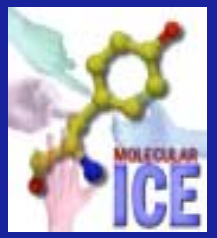
Macromolecular Complexes, Organelles & Cells



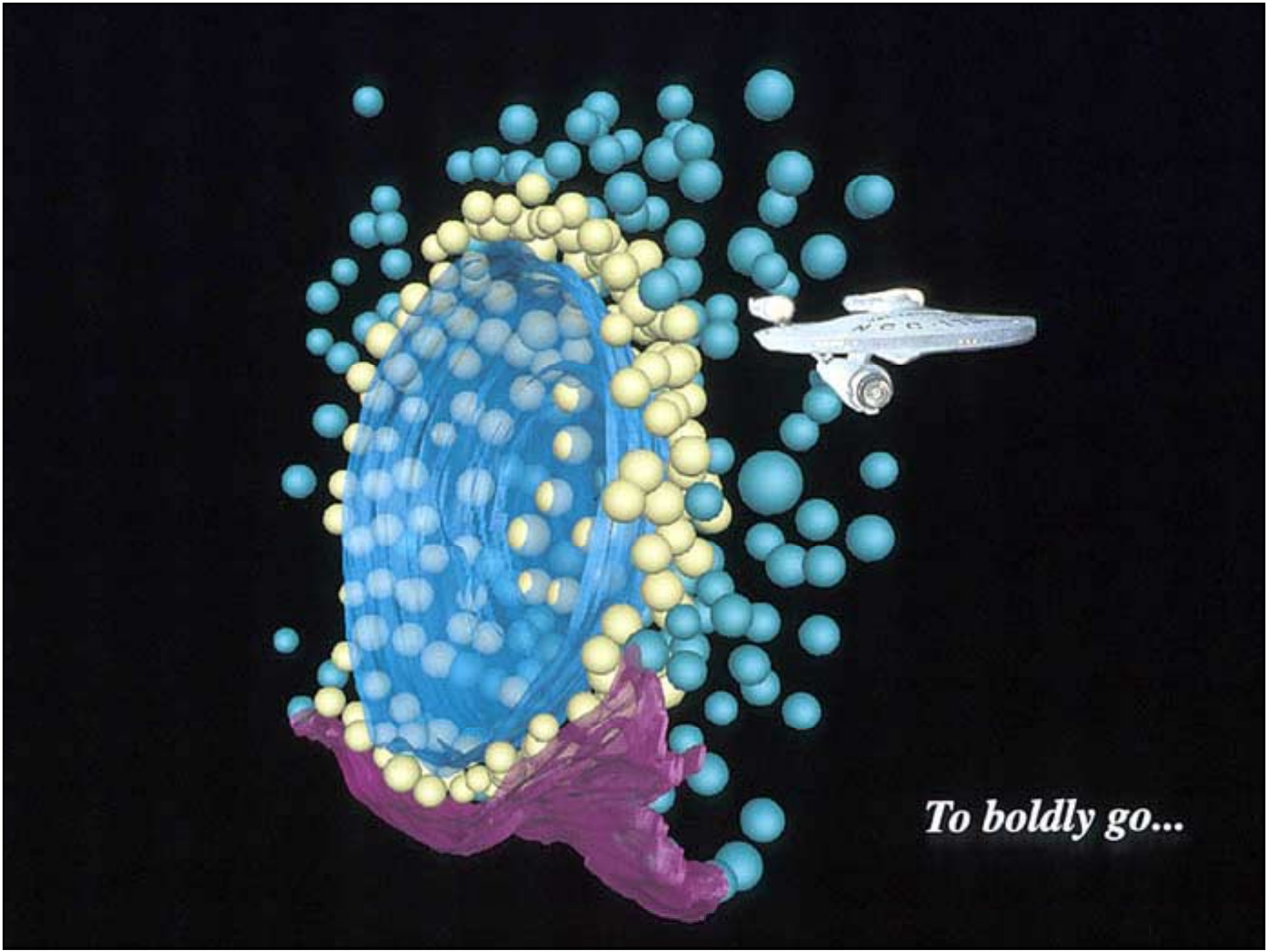




Molecules



Genome DB's


To boldly go...