Building the BIRN Image Database

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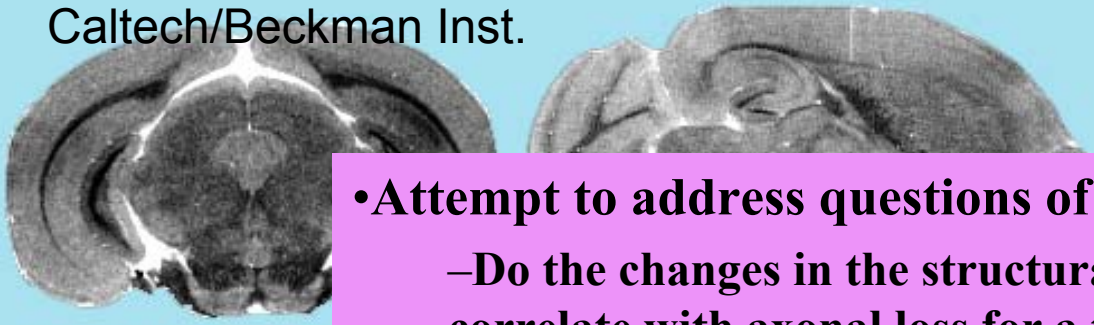
Brain Morphometry BIRN

- Clinical Specific Aims
- Attempt to address questions of the following type:
  - Do structural differences contribute to specific symptoms such as memory dysfunction or depression independent of diagnosis?
  - Do specific structural differences distinguish specific diagnostic categories?

- Technological Specific 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.
  - Make the above happen

The Mouse BIRN

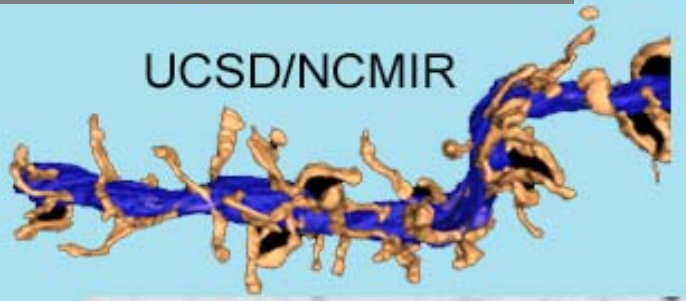
Caltech/Beckman Inst.



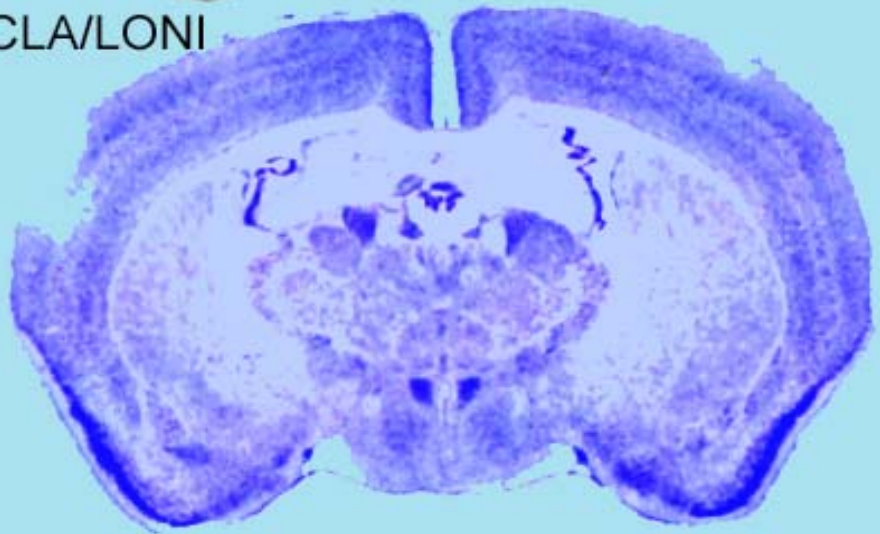
- **Attempt to address questions of the following type:**
  - **Do the changes in the structural properties of astrocytes correlate with axonal loss for a transgenic mouse at the time when the first volume reduction is observed in the MRI?**

Duke/CIVM

UCSD/NCMIR



UCLA/LONI



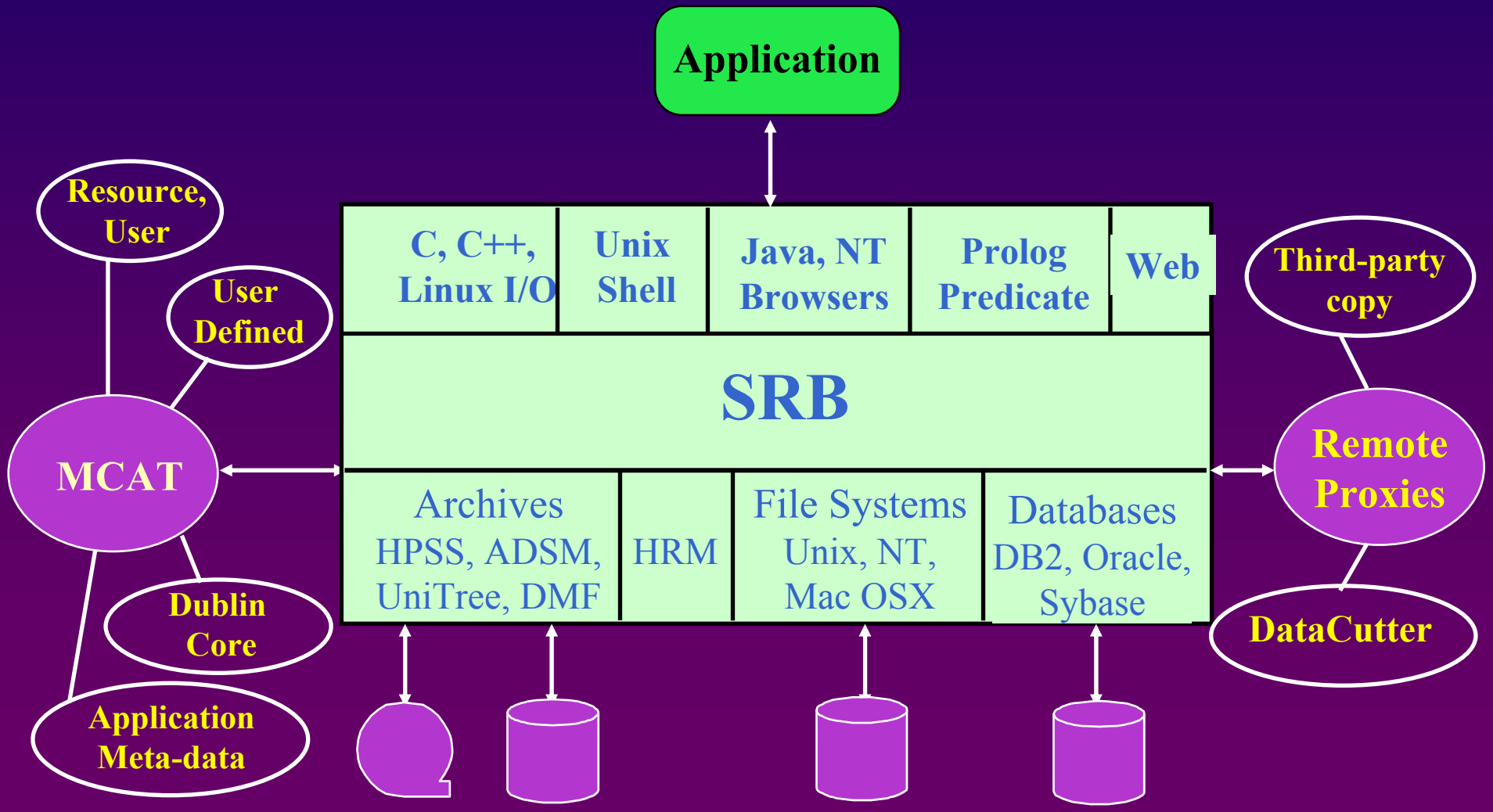
Images in BIRN

- BIRN needs to deal with a wide variety of images
  - MRI images for human and mouse
  - Functional MRI images for human
  - Diffusion Tensor Imaging for mouse
  - Histological Sections of mouse brain slices with different stains
  - High-resolution Confocal Microscopy images for protein localization
  - Electron Tomographic Reconstructions of ultrastructures
  - Derived images (e.g., atlases)

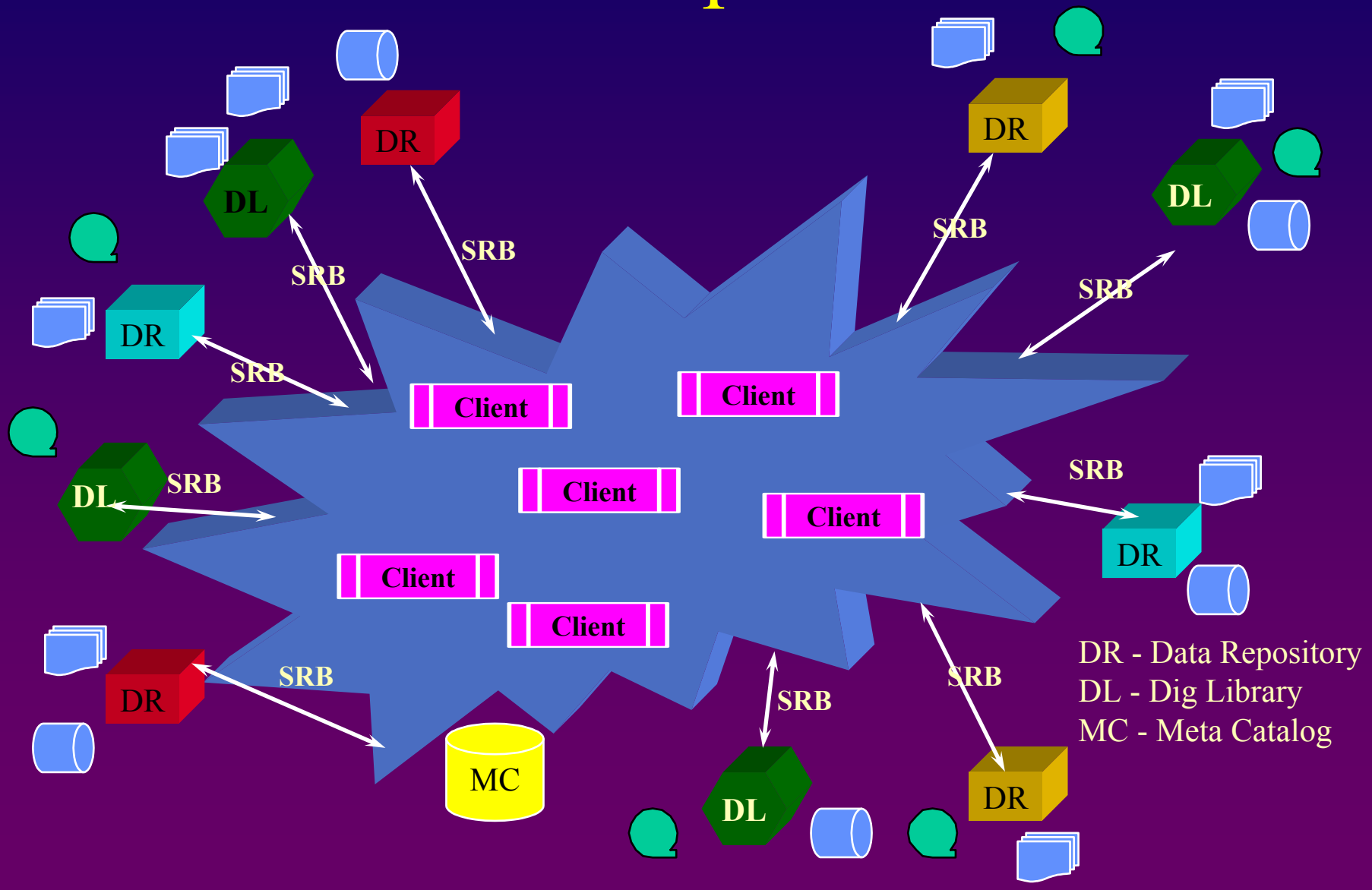
Some General Goals

- **Share images**
- **Form distributed image collections and find images in the collections by patient and image acquisition parameters**
- **Correlate images of the same subject across resolutions and time-points**
- **Compare images of different subjects that satisfy certain conditions**
- **Correlate image information to those obtained from other experimental data (EEG, cognitive tasks, …)**
- **Send images to different analysis tools, then take the products of analysis and put them back in the database for further comparison and querying**
- **Formulate a scientific question as a "workflow" consisting of queries, computation and visualization**

Storage Resource Broker and Metadata Catalog



SRB Space


DR
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DR
MC
DR - Data Repository
DL - Dig Library
MC - Meta Catalog

Image Metadata in BIRN

- Each image produced in BIRN comes with a set of metadata
  - subject-related (age, weight, diagnosis, treatment, …)
  - instrument-related (instrument type, lens details, mag…)
  - protocol-related (specimen preparation, stain properties, weightings for imaging, cognitive activities…)
  - processing-related (segmentation algorithms, image manipulation parameters, clustering thresholds…)
  - …
- Some of these metadata are available in a standard form like DICOM and can be automatically extracted by SRB proxies

Using the Metadata

- Scientist's Question:
  - I obse B. I need to find if ages were genera
- In other
  - Using ce in which different parts of the metadata were produced, perform a "progressive diff" of the *lineages* of the two images
- Why this can be complicated
  - An initial difference may be removed by a subsequent processing step (e.g., distortion correction for MRI)
  - Presence of "equivalence classes":
    - A sequence of steps, although different, may not *semantically* contribute to any difference in the outcome
  - …

We "really" need to know the use of the metadata to determine the appropriate way to model the application

Mike Vannier's Poster Query

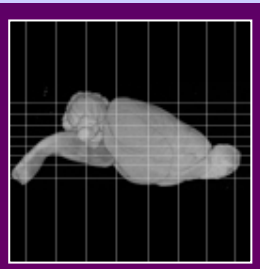
Are changes in axon diameter and/or number present in the optic nerve of EAE animals before the development of gross structural changes?

Integrated View

Integrated View Definition

Mediator

Wrapper

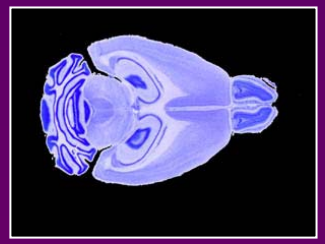


MRI

Wrapper

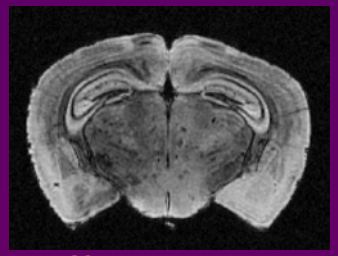
Electron microscopy

Wrapper



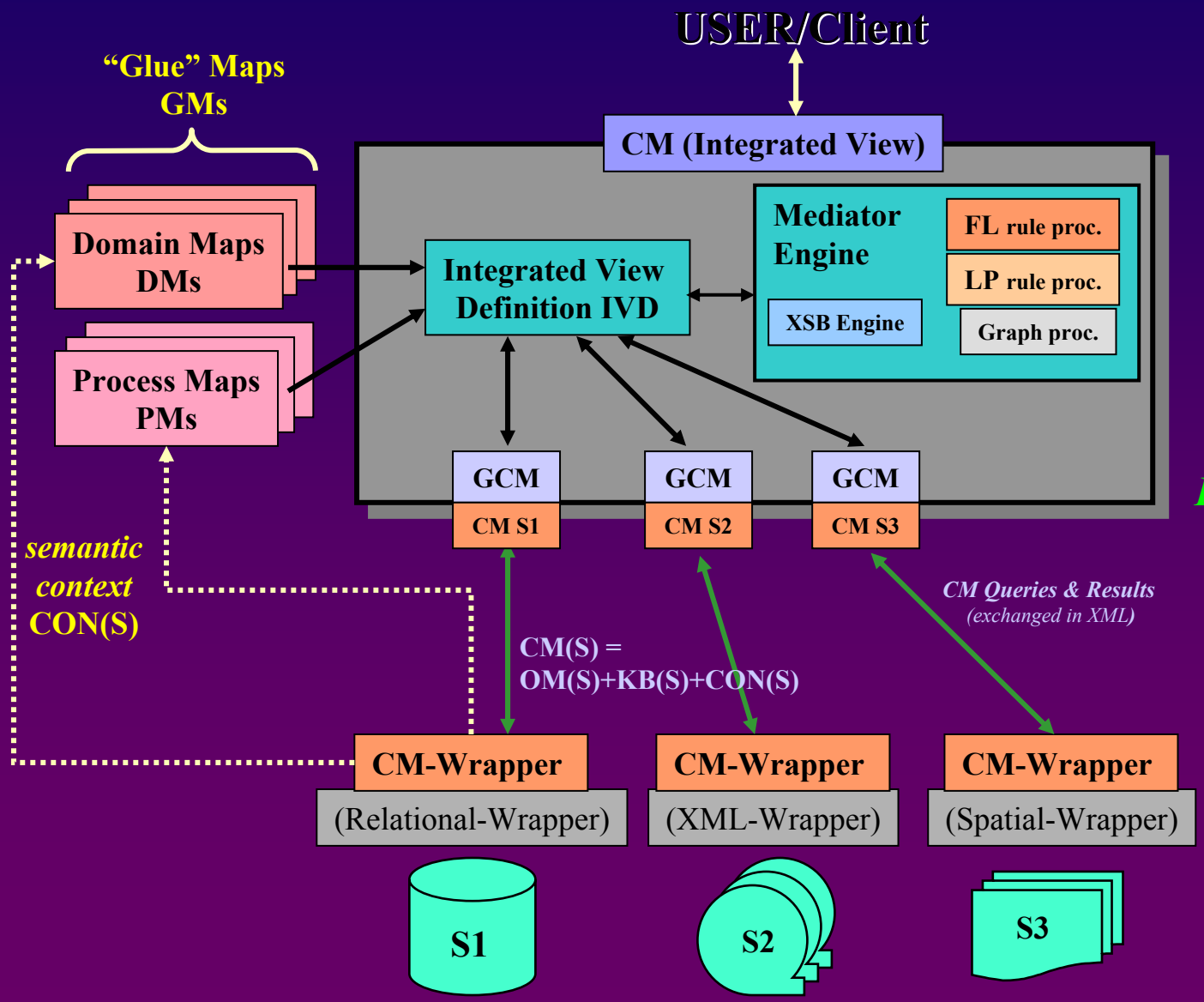
Histology

Wrapper



Diffusion Tensor

Model-Based Mediator Architecture

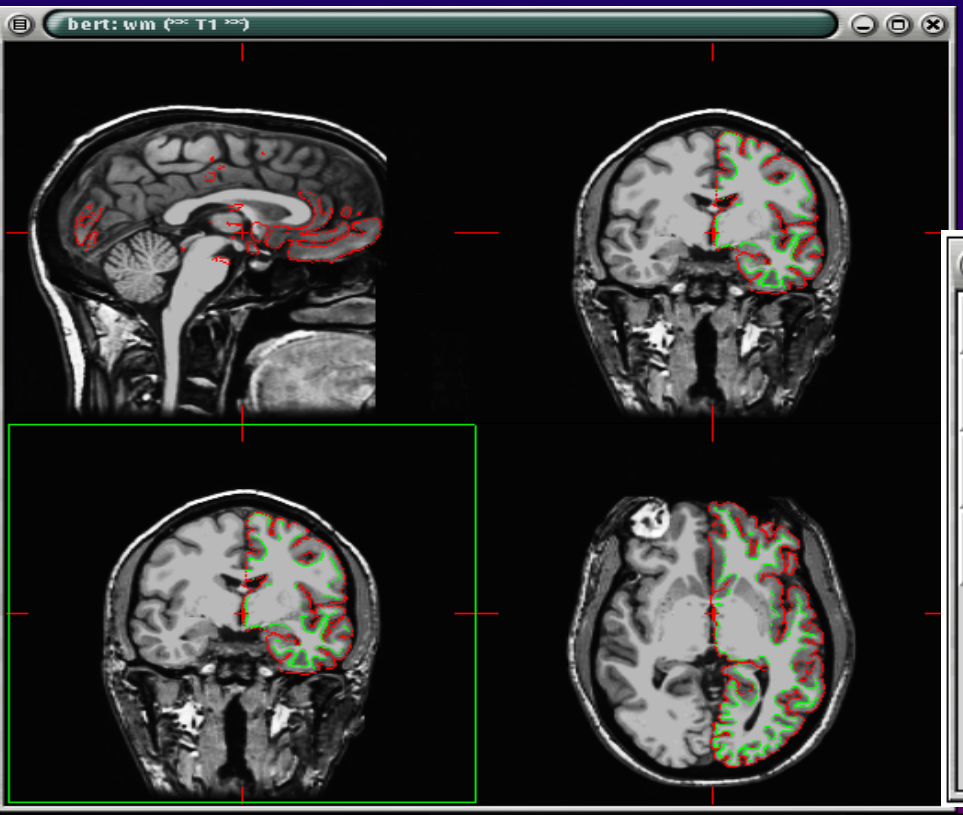


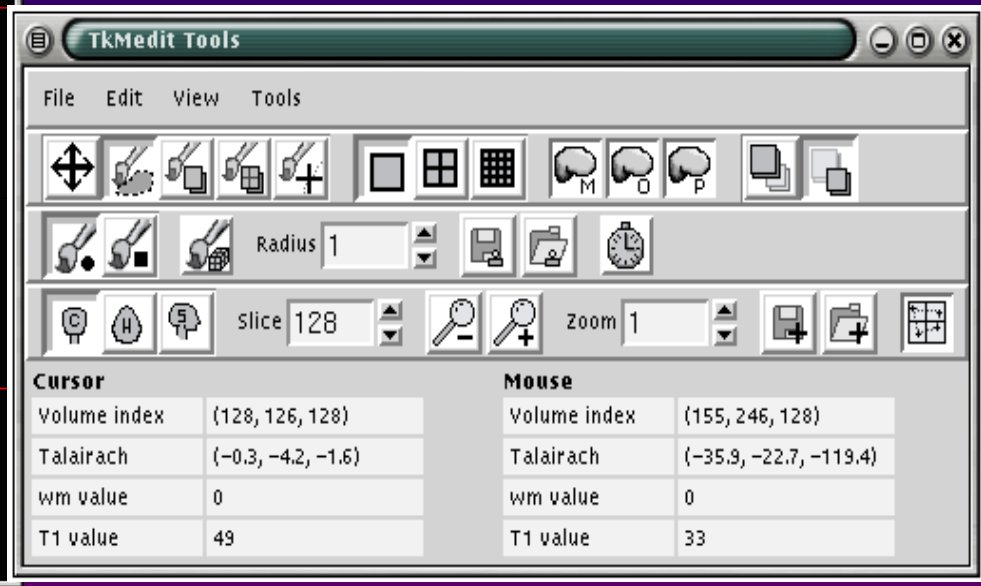
First results & Demos:
KIND prototype, formal DM semantics, PMs
[SSDBM00] [VLDB00] [ICDE01] [NIH-HB01]

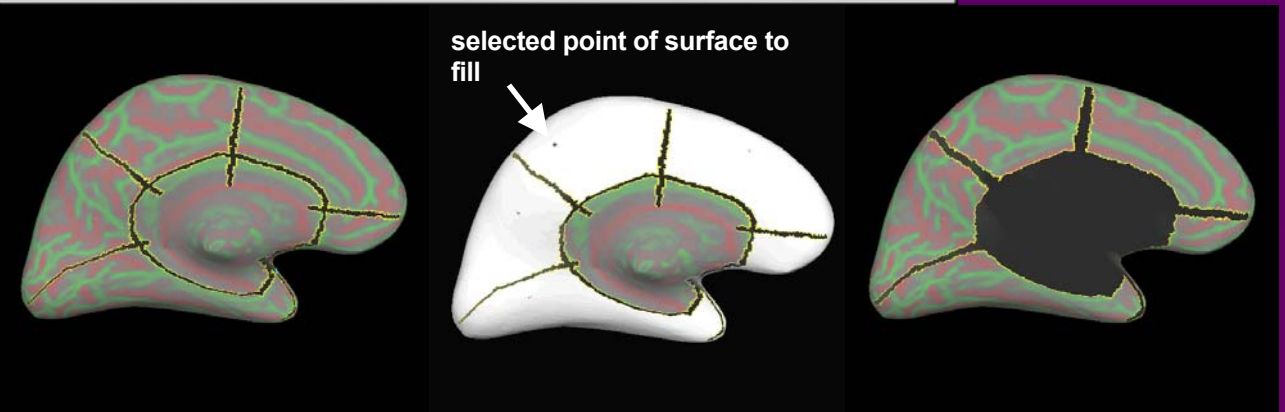
Integrated View Definition and Query Planning at the Mediator

- An ultra-Simple Definition for "Gross Structural Change"
  - Volume change found in MRI (not vol. change in electron tomography)
  - Shape change found in MRI or in histology images
  - This means
    - We need a source which either records the volumes directly or computes the volumes
    - Either this source can also detect changes (i.e., a difference across successive time points) or this computation has to be done in the "mediator" software
    - We need a "shape feature" that adequately describes the shape and a feature difference metric that characterizes the shape – these will differ between the MRI and the histology sections
    - If the sources do not provide it, we need to compute this at the mediator

A Typical Source: FreeSurfer

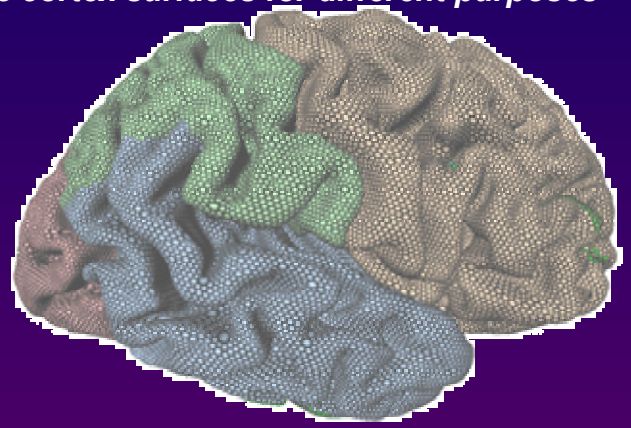


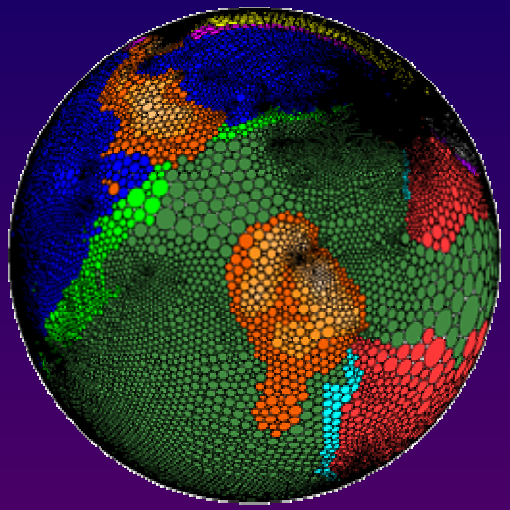




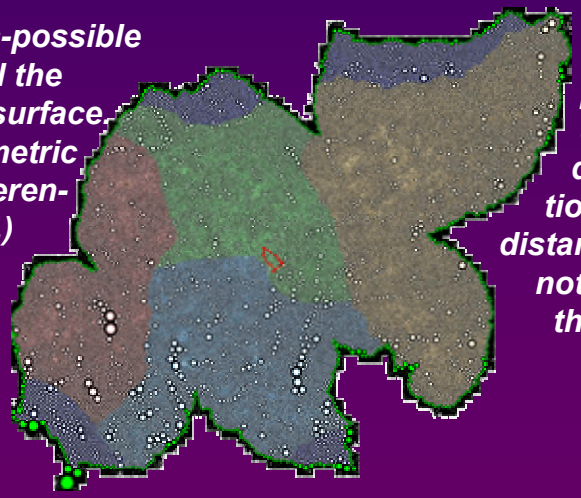
Surface Representations

Neuroscientists use different representations of the cortex surfaces for different purposes





Fiducial representation: as-exact-as-possible representation of the cortex, with all the folds and the creases of the actual surface. Allows the measurement of all geometric quantities of interest, including differential properties (Gaussian curvature..) but most quantities are difficult to compute, as they require the integration of the local properties of the surface.



Spherical map: the cortex can be projected on the surface of a sphere in a way that preserves (approximately) the distances between points. This represnta-tion affords the efficient computation of distances,areas, and topological relations, but not of properties related to the curvature of the surface.

flat map: preserves the area of the regions, but introduces cuts so that distances and topological properties can't be coputed

All these representations are stored in the database, but scientists ask questions on a conceptual model based on the fiducial representation. How can we rewrite the query to make optimal use of the available representations?

Query Rewriting for Geometric Data

$R(\alpha, \beta)$

Replace if:
The current representation has efficiency less than α ***AND*** *there is a representation with efficiency at least β*

	Fiducial	Spherical	Flat
Gauss	6	8	1
Area	2	5	8
Connectivity	5	6	0

Query:

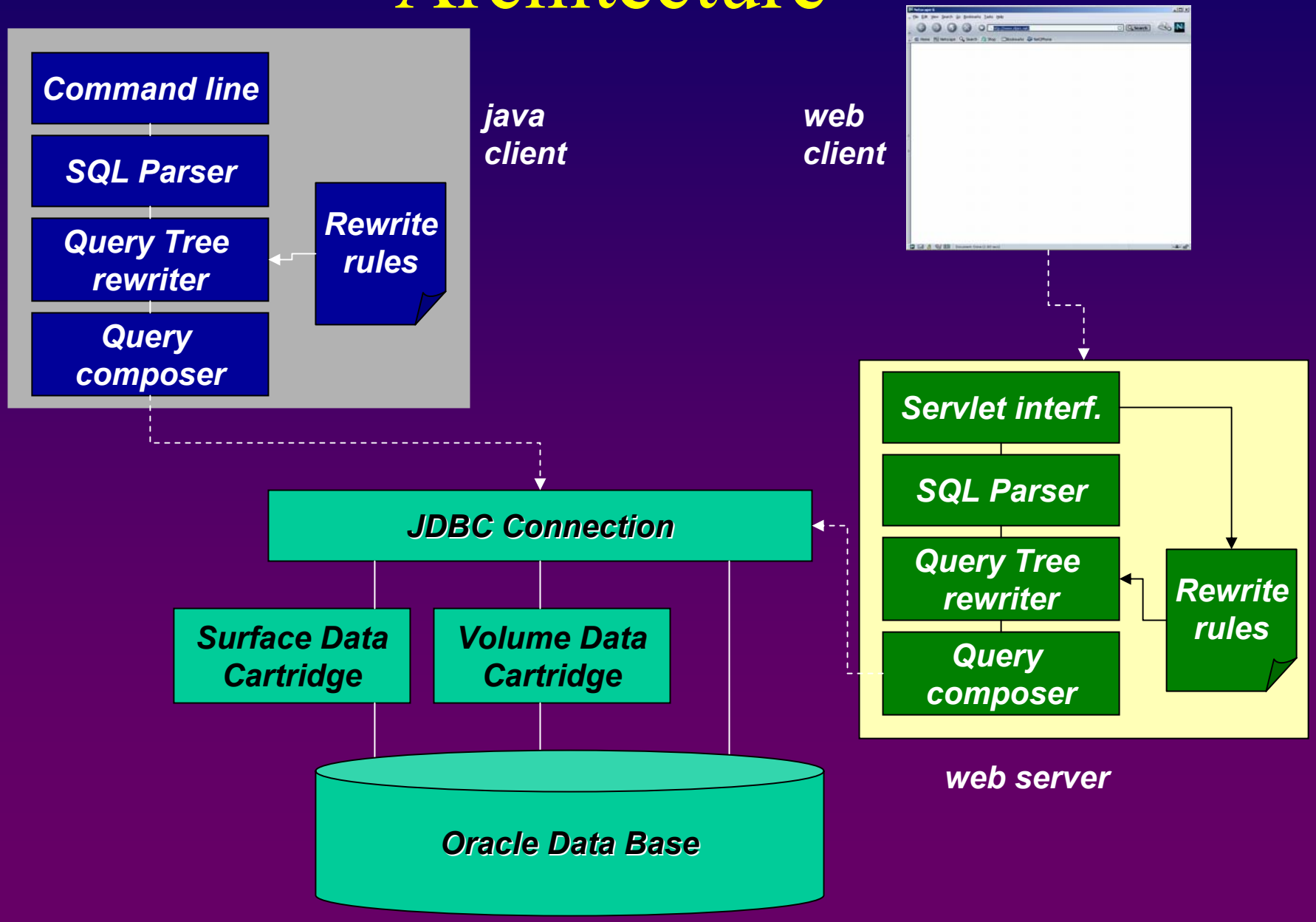
```
select *
from Cortex c
where (Connectivity(c.TOPO) = 2 AND Gauss(c.PEAKS) < 2)
        AND Area(c.PTS) < 100
```

Strategy 1:
1. R(3,3): Area -> Flat

Strategy 2:
1. R(8,8): Gauss -> Spherical, Area->Flat

Strategy 3:
1. R(8,8): Gauss -> Spherical, Area->Flat
2. C:
3. R(6,6): Connectivity -> Spherical

Architecture



Modeling Brain Data

Brain

Structure$_1$ (volume)

Structure$_2$ (surface)

Structure$_3$ (segment)

Multidimensional Array With (Nested) Relational Labels

Hierarchical Adjacency Graph With Relational Nodes

Orthogonal Sets of Layered Geometric Objects

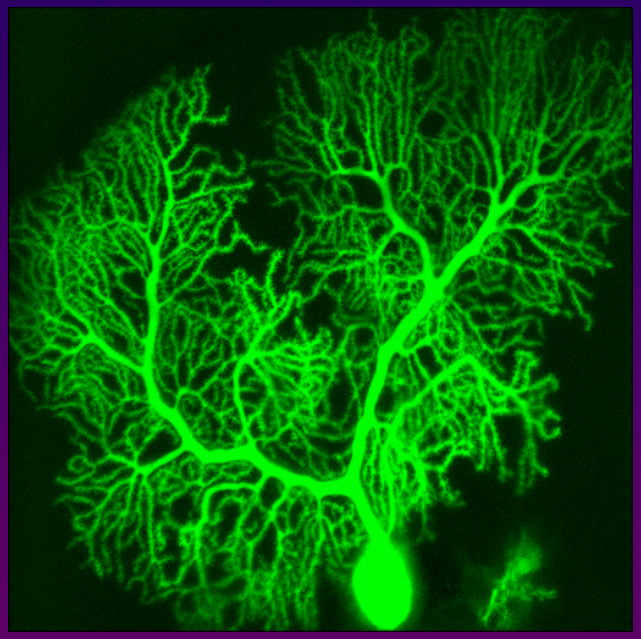
Reference Representation

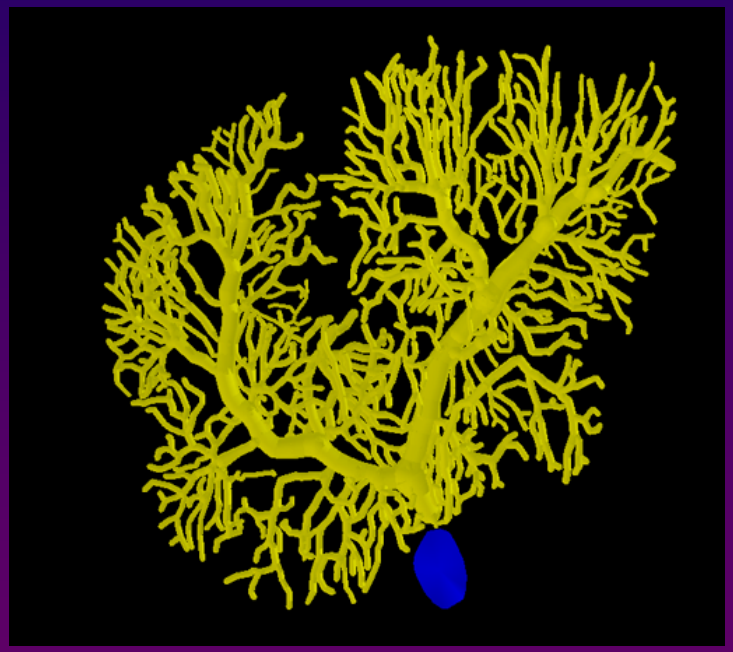
Deformation Representation

Conformally Transformed Representation

Non-Conformally Transformed Representation

Modeling of Neuronal Branching Data





- Tree structures are traced using Neurolucida
- Quantitative data on branch length, diameter, order and spine density are stored in the database

Modeling Branched Structures

```
( (Color Yellow)  ; [10,1]
  (Dendrite)
  (    5.04    -44.40    -89.00      1.32)  ; Root
  (    3.39    -44.40    -89.00      1.32)  ; R, 1
  (
    (    2.81    -45.10    -90.00      0.91)  ; R-1, 1
    (    2.81    -45.18    -90.00      0.91)  ; R-1, 2
    (    1.90    -46.01    -90.00      0.91)  ; R-1, 3
    (    1.82    -46.09    -90.00      0.91)  ; R-1, 4
    (    0.91    -46.59    -90.00      0.91)  ; R-1, 5
    (    0.41    -46.83    -92.50      0.91)  ; R-1, 6
    (
      (   -0.66    -46.92    -88.50      0.74)  ; R-1-1, 1
      (   -0.74    -46.92    -88.50      0.74)  ; R-1-1, 2
      (   -2.15    -47.25    -88.00      0.74)  ; R-1-1, 3
      (   -2.15    -47.33    -88.00      0.74)  ; R-1-1, 4
      (   -3.06    -47.00    -87.00      0.74)  ; R-1-1, 5
      (   -4.05    -46.92    -86.00      0.74)  ; R-1-1, 6
```

children

nd for each type there is a relational table

m

tree

nodes	spines	segments	…

cellbody

tree_id	perimeter	area	…

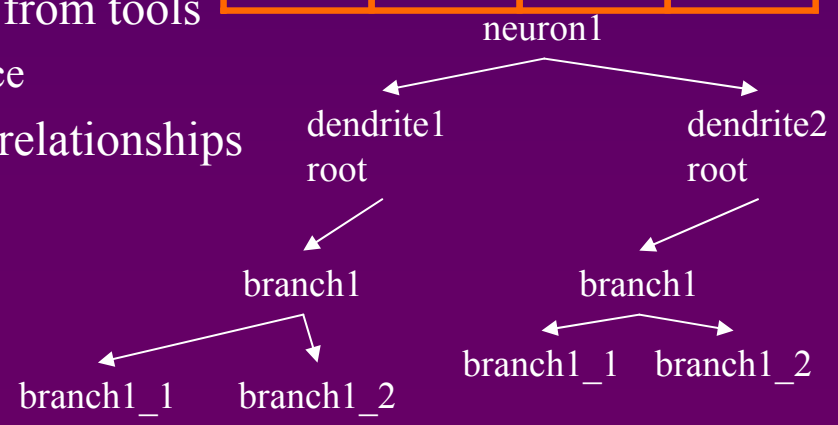
dendrite

tree_id	length	diameter	…

erties from tools

- Neurolucida, Analyze, XVoxTrace

- Operations for deriving geometric relationships
  - gap analysis
  - spatial interdigitation
  - …



Querying Branched Structures

Query Result

4 records were found!

Record : 1

oject: P1170

ption: Neurolucida tracing of filled Purkinje neurons

ecies: mouse

stem: CNS

rgan: brain

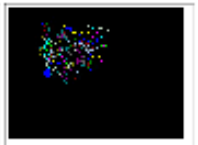
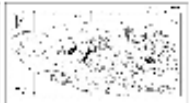
egion: cerebellum

type: Purkinje

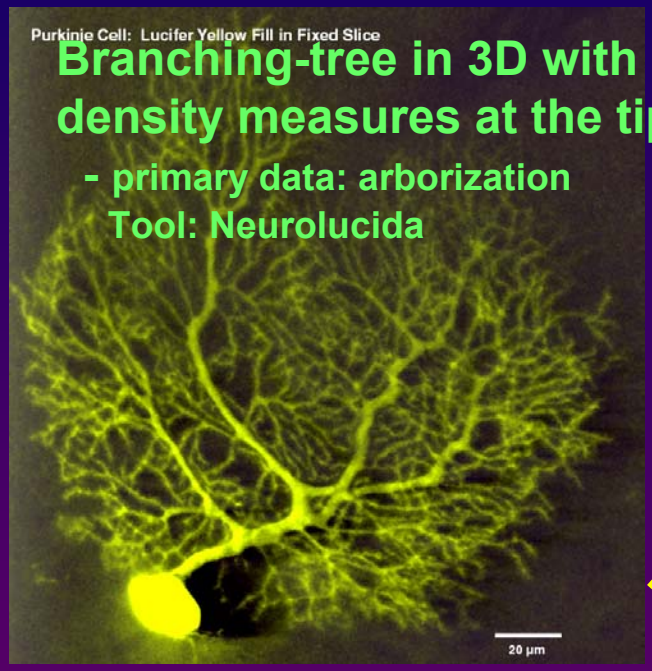
ment: BioRad Radiance

View Detail

Feedback

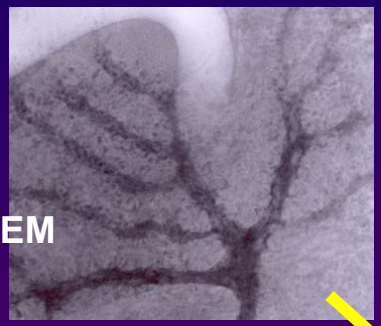
Volume	Segmented File	Animation	Atlas Map
Down load!	 Download!	click here to obtain the image, click on the image to view the animation	

Modeling Across Resolution Boundaries



Branching-tree in 3D with density measures at the tips

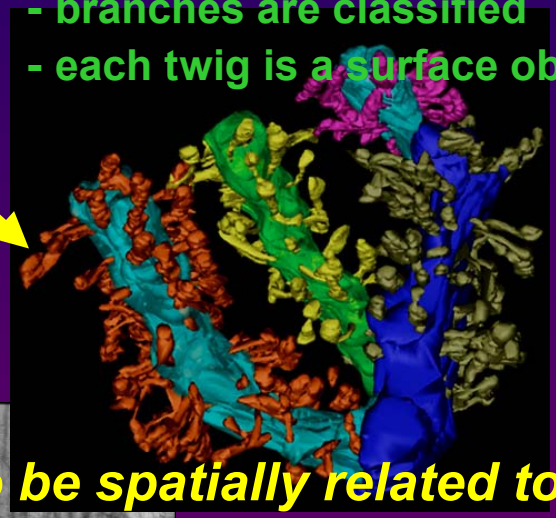
- primary data: arborization
  Tool: Neurolucida



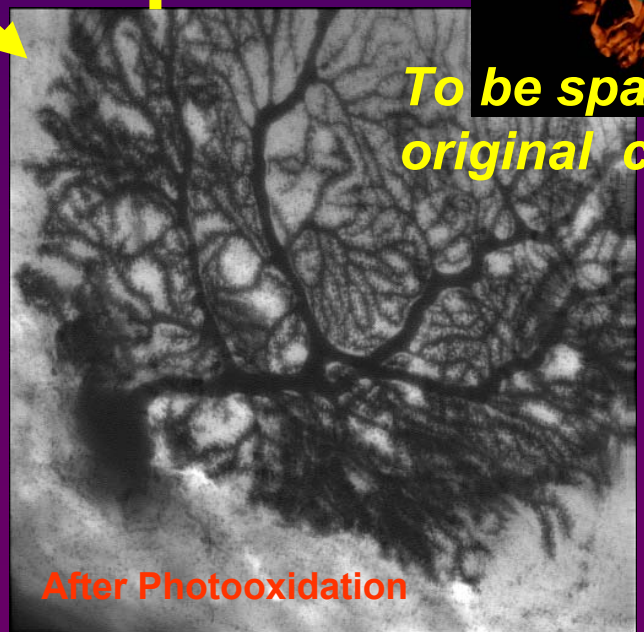
HVEM

Branching-tree in 3D with density measures at the tips

- more detailed measurements
- branches are classified
- each twig is a surface object



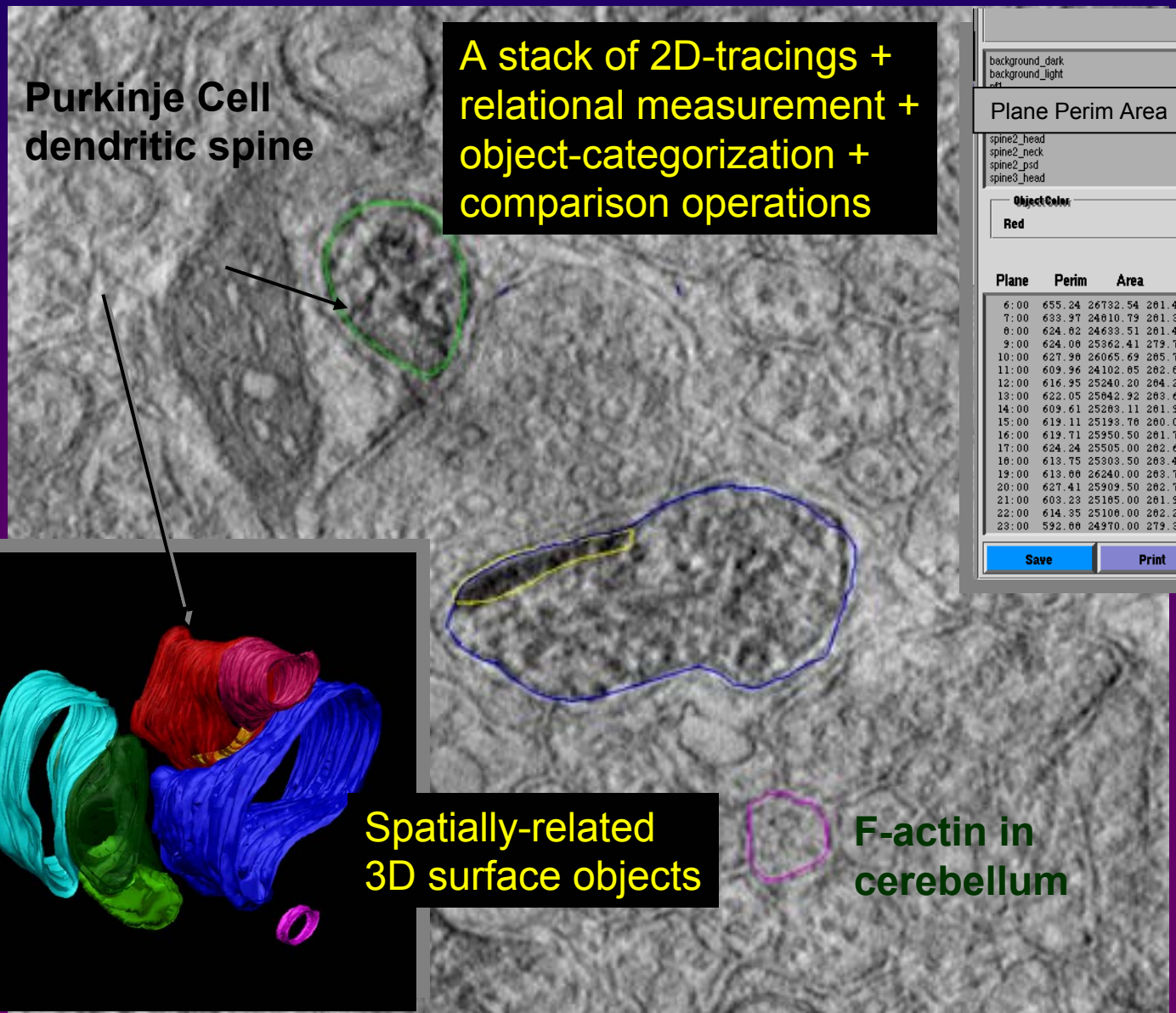
To be spatially related to original cell

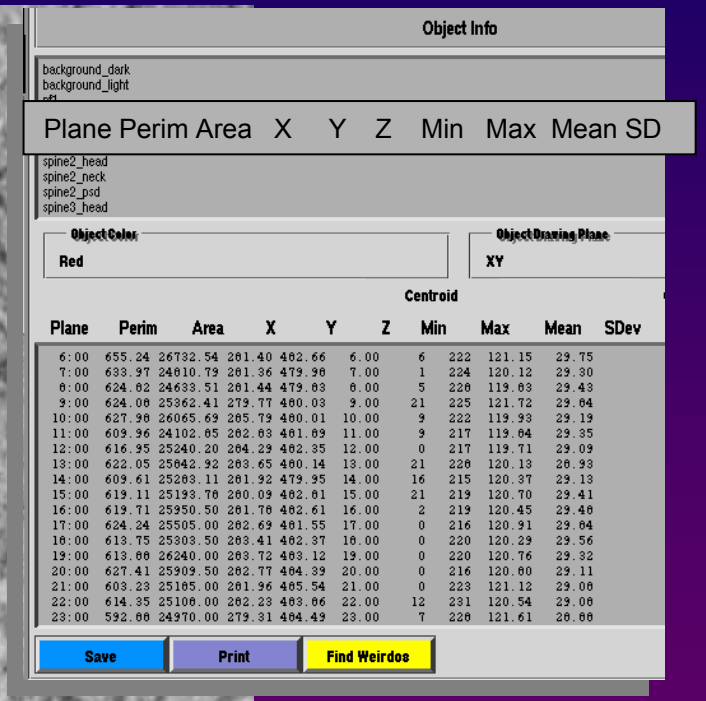


Tomographic Volume

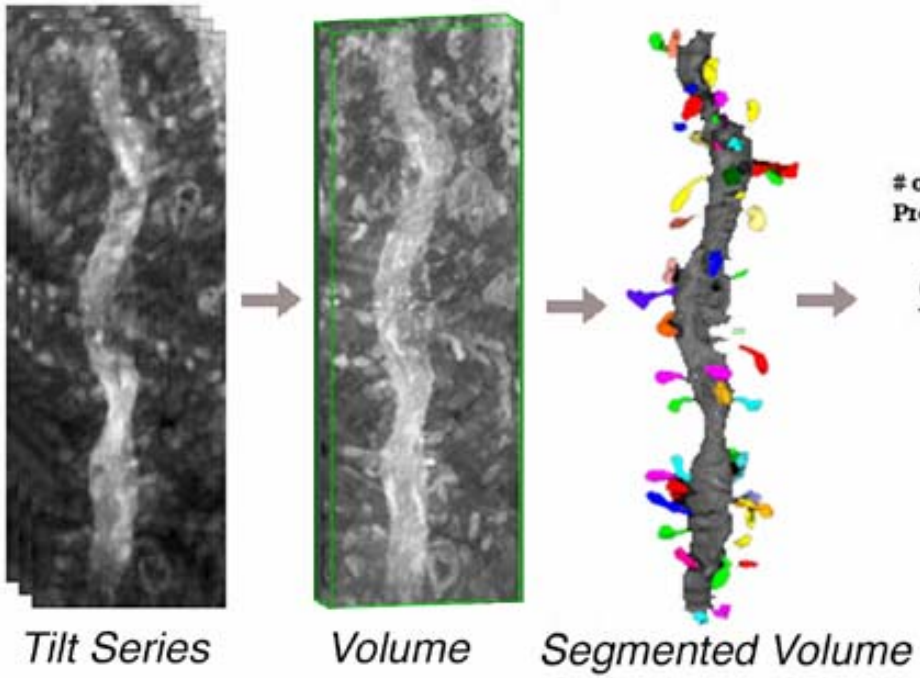
Photooxidation of Neuron Filled with Lucifer Yellow

Surface Models for Ultrastructures





Data Modeling for Ultrastructures



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

Measurements

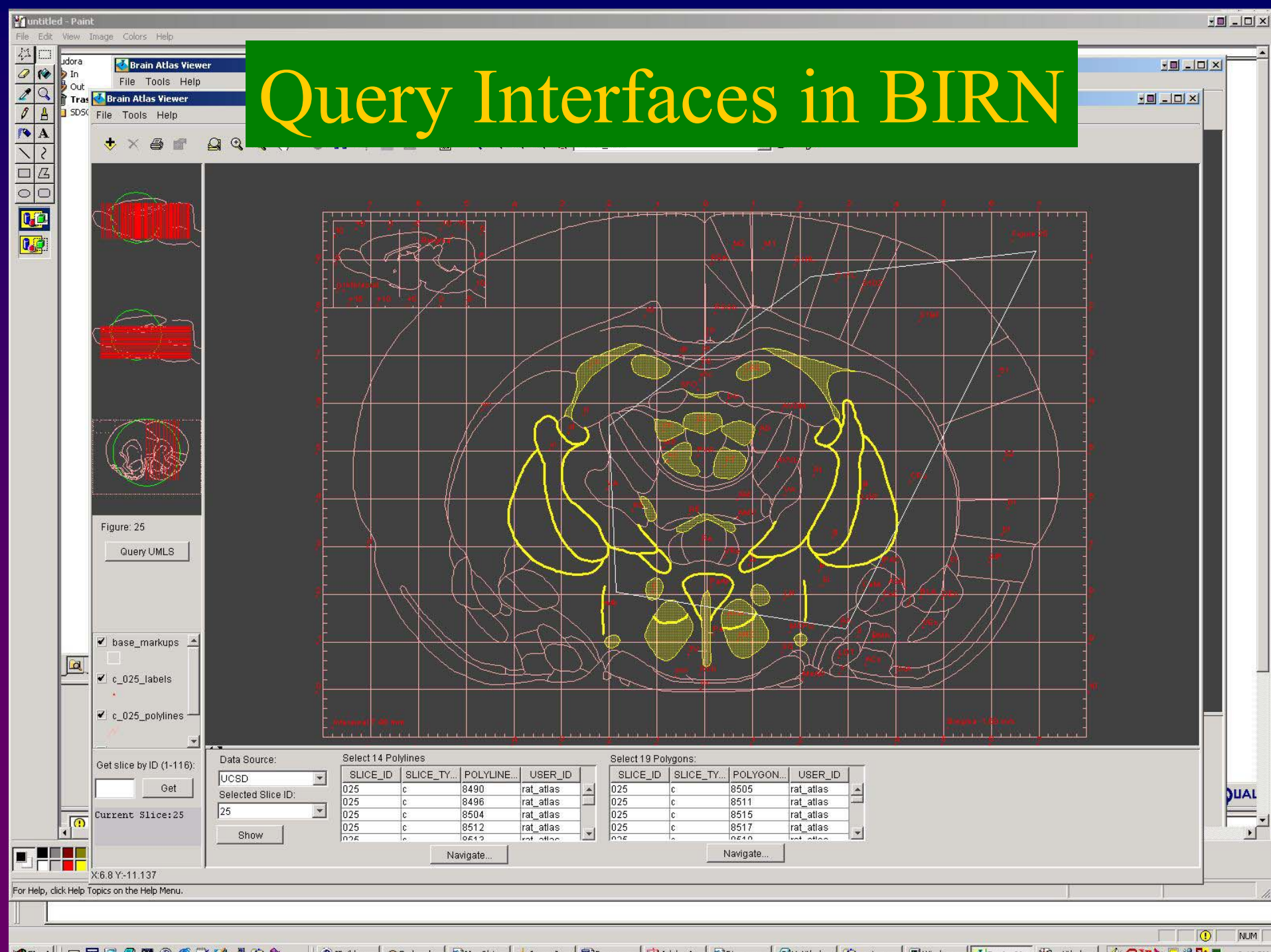
	SA	Vol	Length	#
sp1	1.1	0.05	1.2	1
sp5	0.4	0.01	0.8	1
sp9	1.53	0.05	1.0	1
sp57xz	1.36	0.05	1.2	1
sp62pt	na	na	na	na

Units=μm

Measurement Info

Measurement	Programs Used
SA	Analyze
Vol	Analyze
Length	Xdend
Number	Manual

Query Interfaces in BIRN



Domain-Sensitive Result Viewer PROTLOC-AxioMap

http://www.npaci.edu/DICE/Neuro/EM/main.htm - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Forward Stop Refresh Home Search Favorites History Mail Print Edit Related

Links home- Backflip It!

Address http://www.npaci.edu/DICE/Neuro/EM/main.htm Go

Calsequestrin

- __none__
- Average Intensity
- Minimum Intensity
- Maximum Intensity
- Standard Deviation
- Normalized to Background
- Rank

Compose | Query | Options

STRUCTURES

Map Navigation

zoom 2x IN | pan | zoom 2x OUT | open URL

Initial View

Help | Annotation

AxioMap

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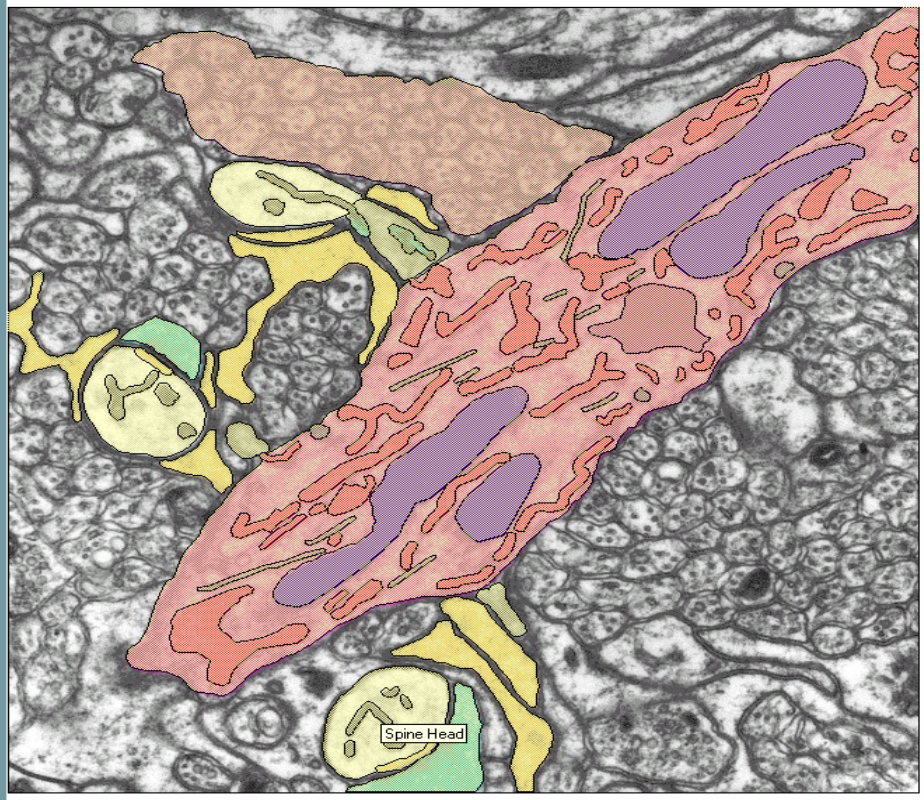
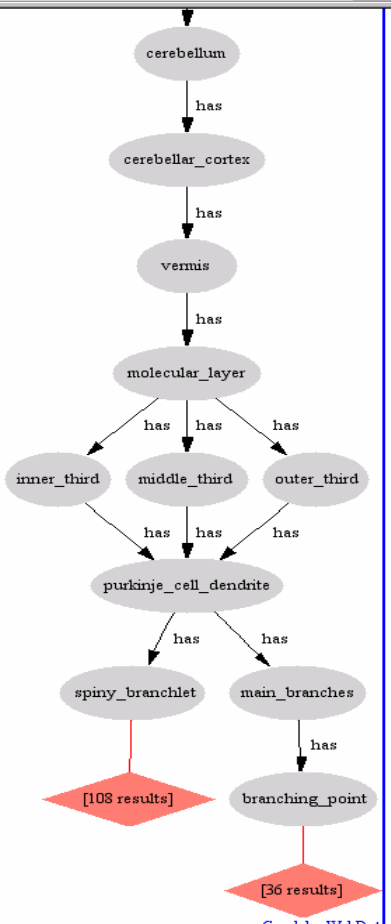
Electron Micrograph of Purkinje Cell Dendrite



Chick cerebellum, aged 1 day post hatch
Additional Metadata



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Conclusion

- Deep data modeling is important to handle deep scientific questions
- Knowledge-based information integration approach is proving to be useful
- The tools, techniques and approach used in BIRN are generally applicable to scientific information management infrastructure beyond Neuroscience

http://www.nbirn.net