Shape Analysis of Dendritic Spines from the CCDB

Lisa Fong

Eric Cochran

Stephen Tang

Dominic Pisano

Dr. Tilak Ratnanather

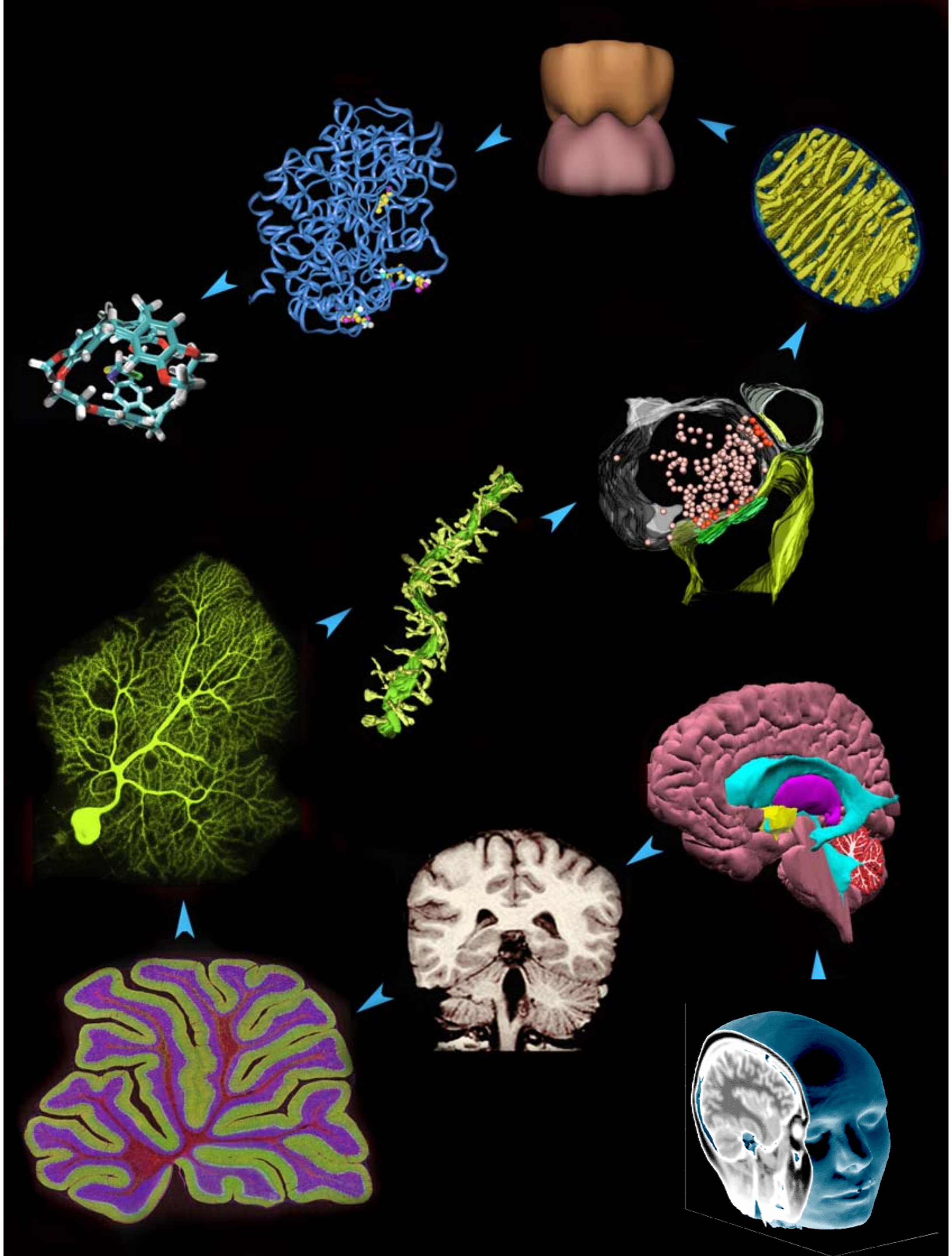
Center for IMAGING SCIENCE

JOHNS HOPKINS UNIVERSITY

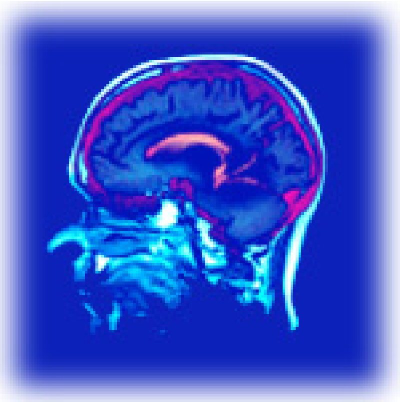
NPACI

BUILDING THE COMPUTATIONAL INFRASTRUCTURE FOR TOMORROW'S SCIENTIFIC DISCOVERY

Scales of neuroscience data from Maryann Martone

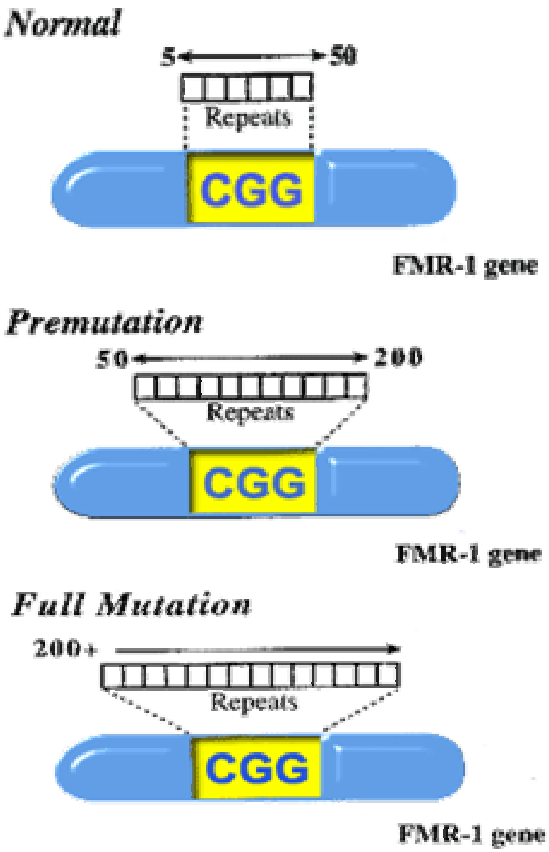


Neuron and Spine Biology of Fragile X Syndrome



Oxford University Press 2004
http://www3.oup.co.uk/jnls/fields/neuroscience/default.html

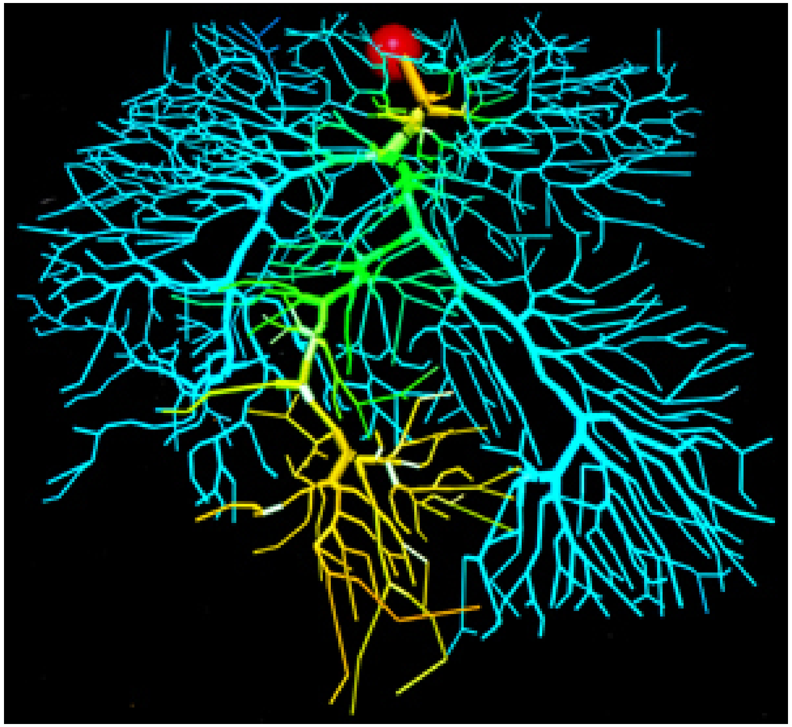
Fragile X Syndrome



Conquer Fragile X Foundation
http://www.conquerfragilex.org/what_is_fragile_x.html

Fragile X syndrome, the most common form of mental retardation, is caused by the duplication of the CGG sequence on the FMR-1 gene. This lengthened region is susceptible to DNA methylation. Severity of symptoms varies with the number of repeats of this sequence, and can range from mild learning disability to severe mental retardation. Though it is X-linked, the pattern of inheritance is not fully understood and does not follow the order of Mendelian genetics. For example, one-fifth of males with the mutated form of the FMR-1 gene are unaffected.

Dendrite Structure



University of Southern Carolina Neurobiology
www.biol.sc.edu/~vogt/courses/neuro/neuro.html

Dendrite Arbor – the treelike area of the neuron, there are many different arborization patterns.

Dendritic Shaft – the “branches” of the dendritic arbor on which there are dendritic spines.

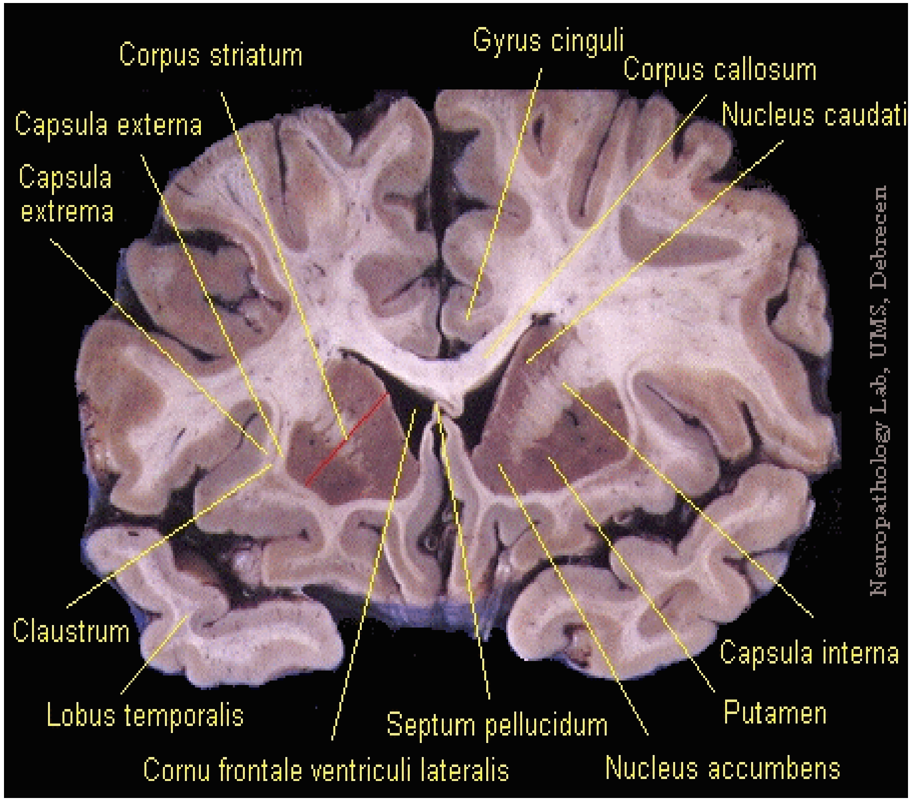
Dendritic Spines – extensions from the dendritic shaft that have been known to change shape.

Spine Composition

Spines have actin-based cytoskeletons that allow for rapid changes in spine structure. They are composed of cytoplasm and contain SER. Larger spines, often mushroom spines, also contain microtubules and in rare cases mitochondria. Calcium is used to send neurotransmitters across the synaptic cleft and on dendrites calcium functions to induce changes in dendritic spine shape.

Neostriatum

The spines we are using for our project came from the dorsal part of the neostriatum which is composed of the caudate nucleus and the putamen. The common arborization pattern in this part of the brain is the spherical radiation pattern in which dendrites radiate in all directions from the soma. Aproximately 8 percent of the spines in the striatum have second synapses on their necks.



Katalin Hegedus, Scilinks
http://www.neuropat.dote.hu/brain.htm

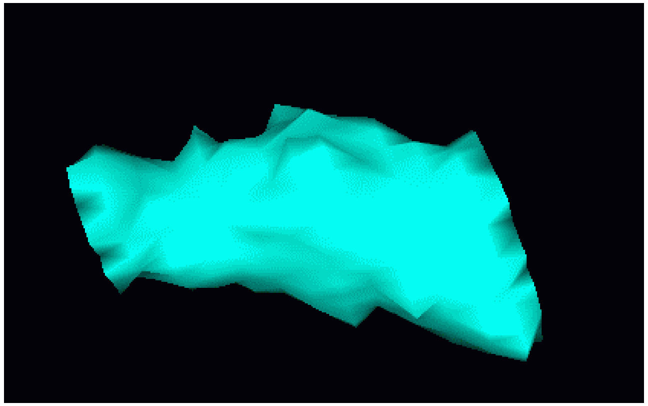
Spine Shapes

Sessile Spines

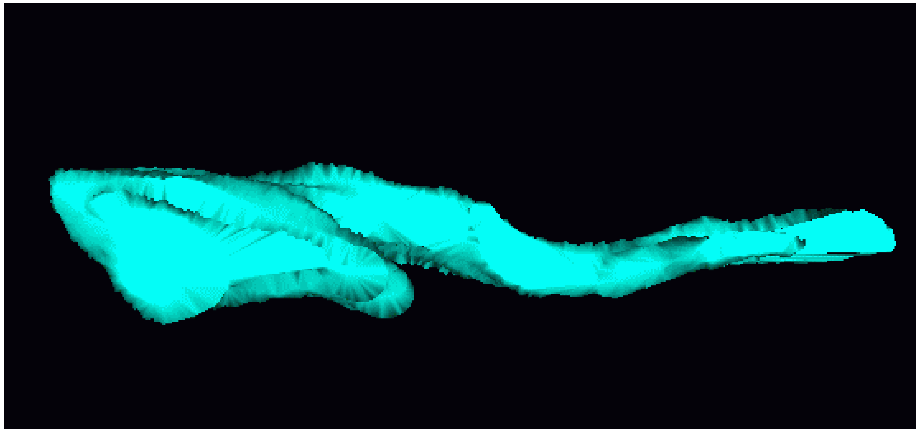
Also called stubby spines, sessile spines do not have significant neck constriction. The length of the spine may be less than or equal to the width.

Pedunculated Spines

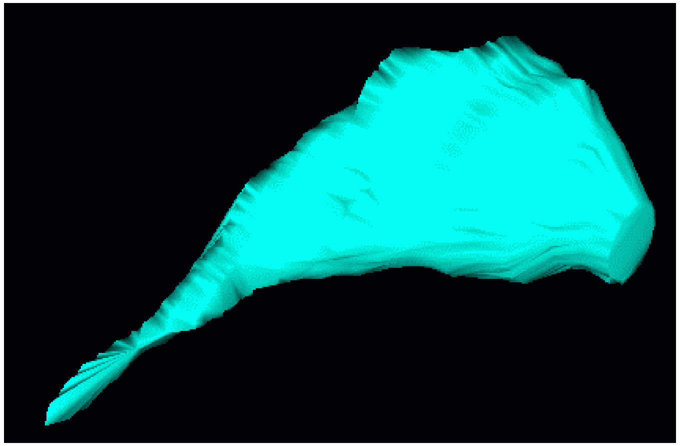
These spines attach to dendrites through thin necks. There are two types: thin spines and mushroom spines. Thin spines are those with small heads. Mushroom spines are those with spine head diameter greater than 0.6 micrometers.



Sessile Spine



Thin Spine



Mushroom Spine

Synaptogenesis

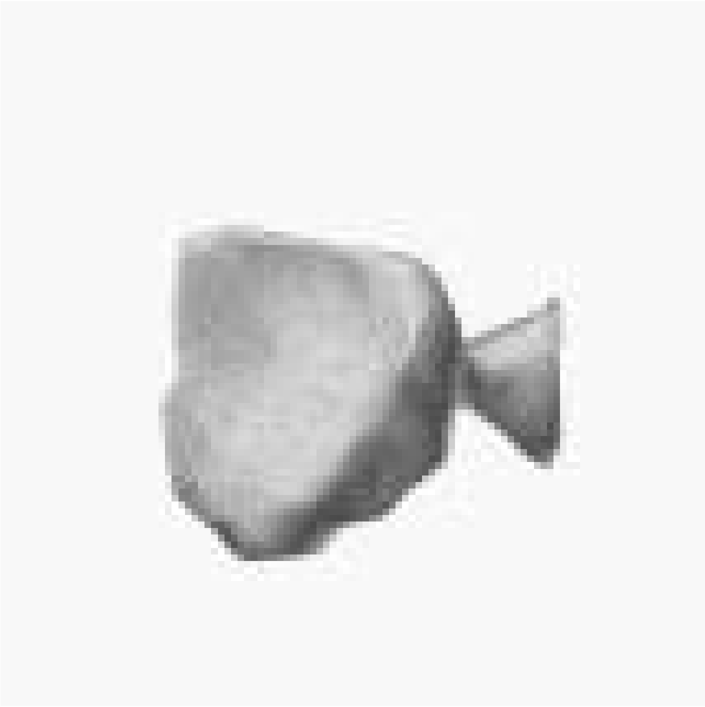
Spine development is activity-dependant. As a dendrite receives inputs, the shapes and lengths of its spines can change and dendrites can form new synapses. This is an example of neuroplasticity. Dendrites that receive more excitatory inputs have greater spine densities along their dendrite shafts.

Also, dendrite shafts can increase in length and in number as a result of synaptic activity.

Kristen Harris, Medical College of Georgia
http://synapses.mcg.edu/lab/harris/kristen.htm

Spine Maturity

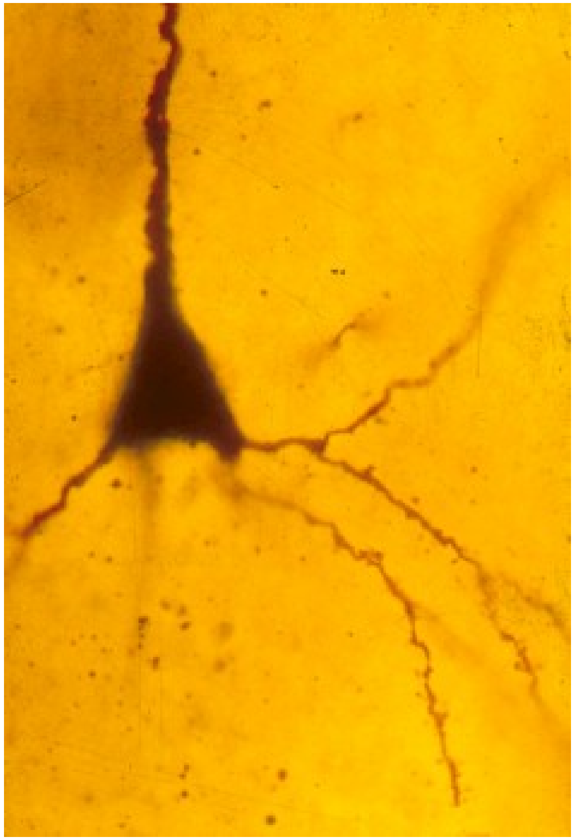
There is a greater number of long, thin spines on fragile X brain tissue than on normal tissue and a greater number of mushroom and sessile spines on normal brain tissue than on fragile X brain tissue. This reduces the area of synaptic contact on fragile X dendrites. The long, thin shape is characteristic of less developed tissue (Horner, 1993).



Synapse Web
http://synapses.mcg.edu/anatomy/Ca1pyrmd/radiatum/k18/spines/sp6_3D.stm

Related Studies

- Many studies over the past half decade have been performed on Fragile-X subjects
- More specifically, the studies have looked specifically at the effect of Fragile-X on the neurological development in patients
- Observations have been made on the length, shape/morphology and density of dendritic spines.



Courtesy of NeuroStructoral Laboratories, Tampa FL

Spine Length

- Many studies over the past four years have made similar observations on the length of dendritic spines of human and mice subjects.
- In general, the length of dendritic spines in Fragile-X subjects were found to be **longer** than that of the control subjects. More specifically, a greater number of abnormally long spines were found on the dendrites of Fragile-X subjects.

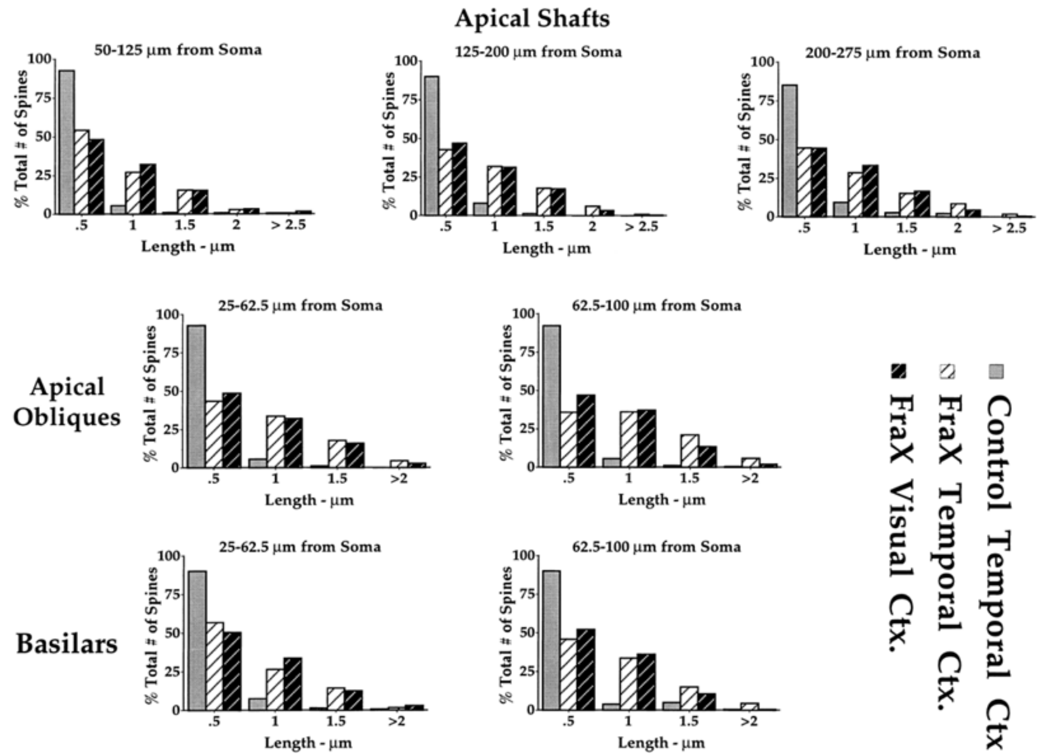


Figure 4. "Abnormal Dendritic Spine Characteristics in the Temporal and Visual Cortices of Patients with Fragile-X Syndrome: A Quantitative Examination" by Scott Irwin et. Al. 2001

Spine shape and morphology

- Many of these same studies have also made similar observations on the shape and morphology of these dendritic spines found in human and mouse subjects.
- Spine morphologies were determined using arbitrary shape categorization schemes. In general, the longer and thinner the spines were, the less mature they were.
- All studies noted that **more immature** spine shapes and **fewer mature** shapes were observed in the cortices of Fragile-X patients, both human and mouse.

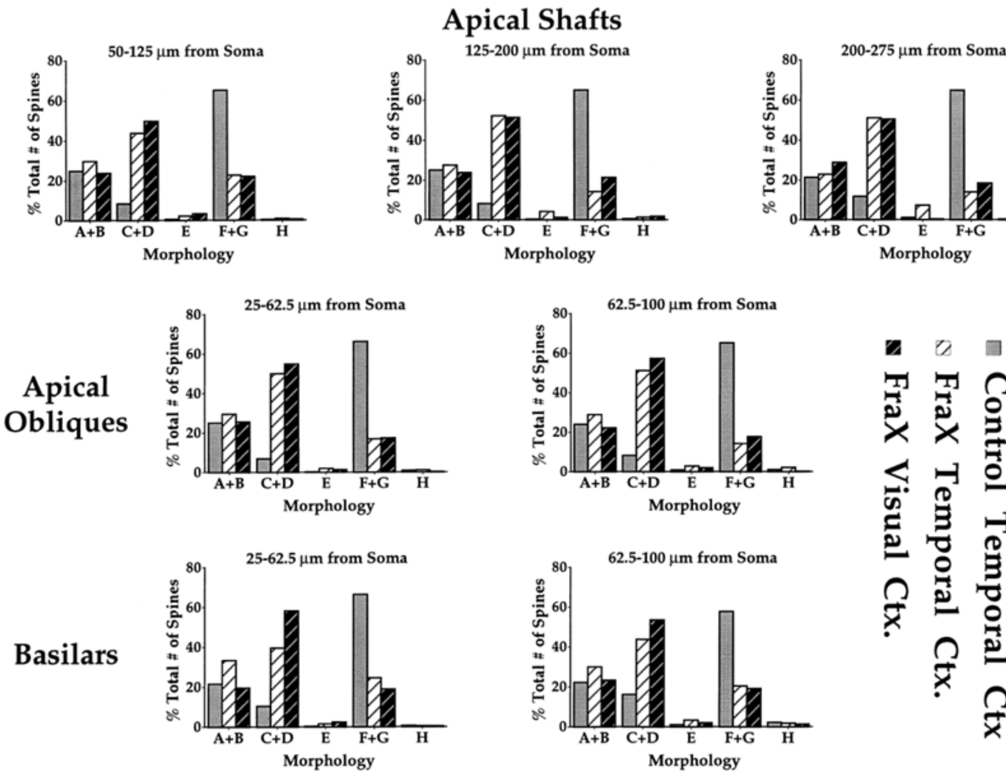


Figure 5. “Abnormal Dendritic Spine Characteristics in the Temporal and Visual Cortices of Patients with Fragile-X Syndrome: A Quantitative Examination” by Scott Irwin et. Al. 2001

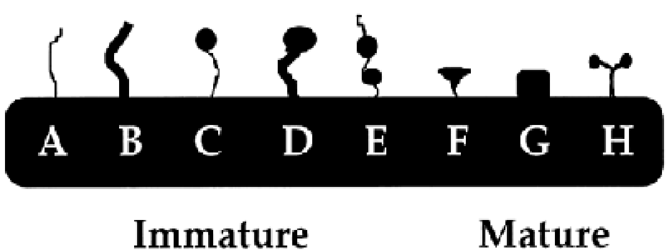


Figure 4A, “Synaptic regulation of protein synthesis and the Fragile-X protein” by Greenough, et. Al. 2001

Distribution of Spines

- Distribution of the spines is another important characteristic of the Fragile-X dendrite, for reasons pertaining to neurological development, more specifically the synaptic maturation process.
- It was suggested that Fragile-X may affect the process that eliminates lesser-used dendritic spines, basically causing a failure of the "weeding out" process.
- In general, the dendritic shafts of Fragile-X human patients have been shown to contain remarkably **higher densities** of dendritic spines, especially the less immature types characterized by its length.

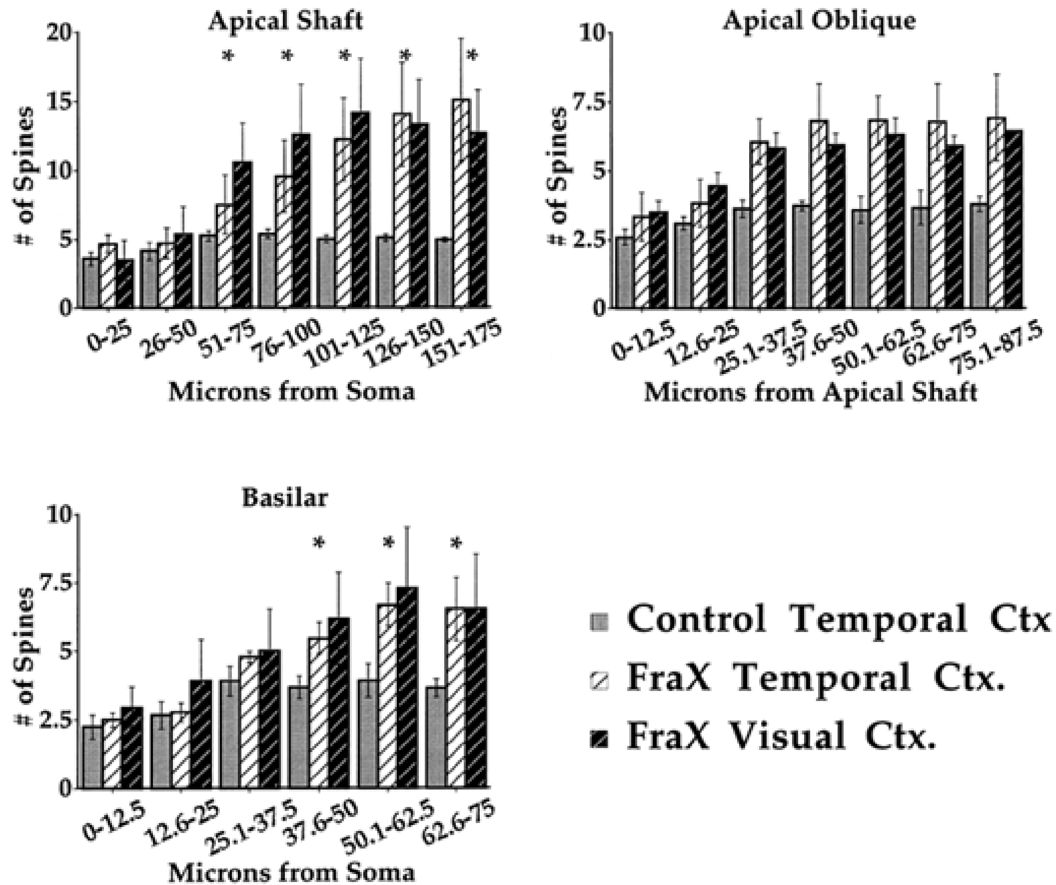
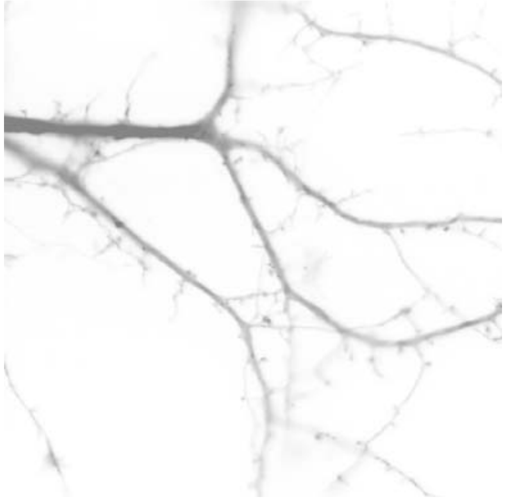


Figure 6. "Abnormal Dendritic Spine Characteristics in the Temporal and Visual Cortices of Patients with Fragile-X Syndrome: A Quantitative Examination" by Scott Irwin et. Al. 2001

Conclusions

- The results and observations of these recent studies set a basis for the current project which will analyze the shapes of dendritic spines, specifically in Fragile-X subjects, using computer-based methods.
- All of the results suggest that Fragile-X affects the neurological development in the dendrites of affected subjects, which results in a higher density of immature spines, which might play a role in some of the symptoms involved in Fragile-X.



Courtesy of Millerm, Brandeis University

- To be more specific, as a subject matures, he/she/it will create new neural pathways involving the synapses, which in turn involve the dendritic spines in the subject's neurons. As new neural pathways are created, the pathways not being used are “pruned” off and eliminated. This is neuroplasticity at work.
- The fact that there are higher densities of said immature spines suggests a failure of normal spine development. In any case, the project involves analysis of the shapes and lengths of dendrite spines, which should assist in future study of the syndrome as well as in many different applications.

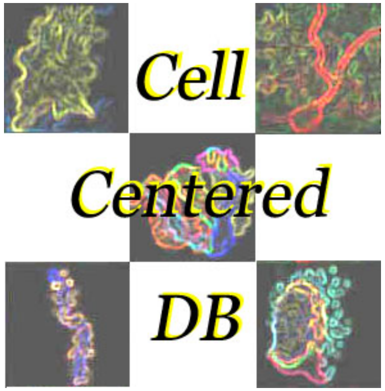
Objectives

- Main Purpose: to compare spine morphologies between two populations:
  - FragileX (Knock Out) mice
  - Control (Wild Type) mice

1. Acquire the data via the SRB
2. Convert the raw data into readable formats
3. Ensure correct topology of the spines
4. Landmark the spines
5. Register the spines into a standard coordinate system
6. Create binary images
7. Apply the LDDMM (Large Deformation Diffeomorphic Metric Mapping)
8. Perform a statistical analysis of the spines – analyze intrapoint distances and vector fields

The Data

- Data received from the Cell Centered Database (CCDB) at the National Partnership for Advanced Computational Infrastructure (NPACI) at UCSD
  - A database that contains structural and protein distribution information from confocal, multiphoton, and electron microscopy.
  - Segmentation done at UCSD by Masako Terada
  - Dendrites from medium spiny neurons of the dorsal region of the neostriatum area of the brain
- Subjects: Mus musculus (3) – Adult males
  - 2 from Knock Out (2 cells)
    - Cell 1: 5 dendrites – 244 spines
    - Cell 2: 6 dendrites – 198 spines
  - 1 from Wild Type (2 cells)
    - Cell 1: 3 dendrites – 47 spines
    - Cell 2: 3 dendrites – 53 spines
  - Original Spine Total: 542 spines
- Format:
  - 3D Volume Analyze images of whole spines
  - Triangulated graphs of the spines
    - Constructed by Steve Lamont at UCSD
    - Received in *.synu format, converted to *.byu format readable in BrainWorks



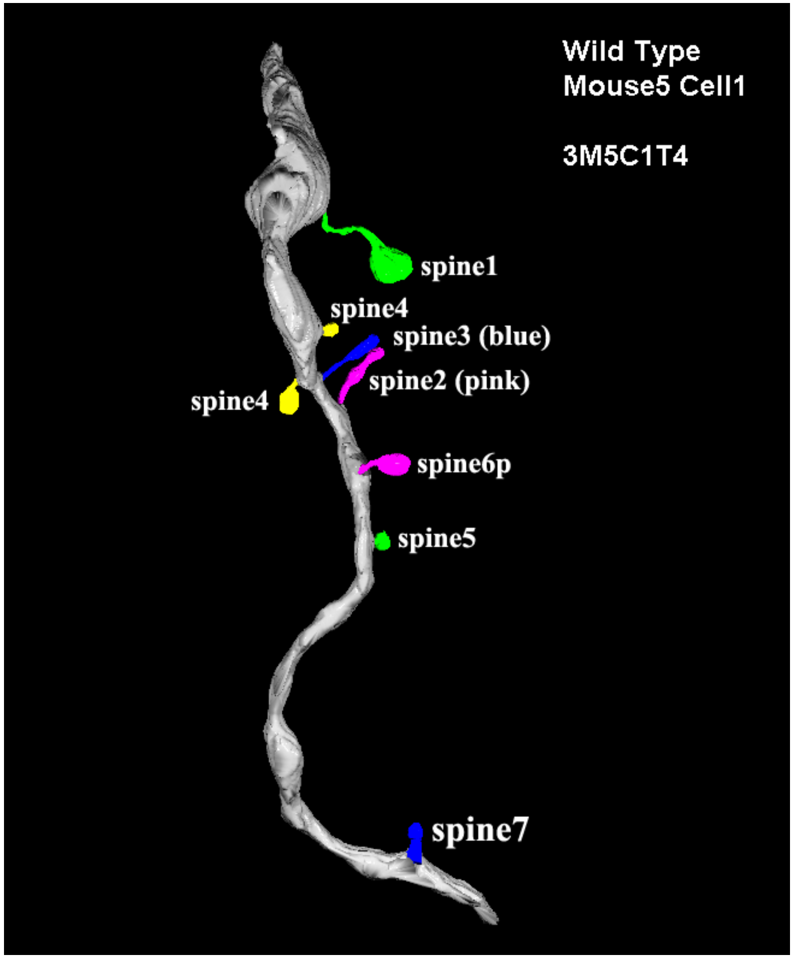
3D Volume Images

(axial views)

4M5C2T2

5M5C2T3

Image Maps


Wild Type
Mouse5 Cell1
3M5C1T4
spine1
spine4
spine3 (blue)
spine2 (pink)
spine4
spine6p
spine5
spine7

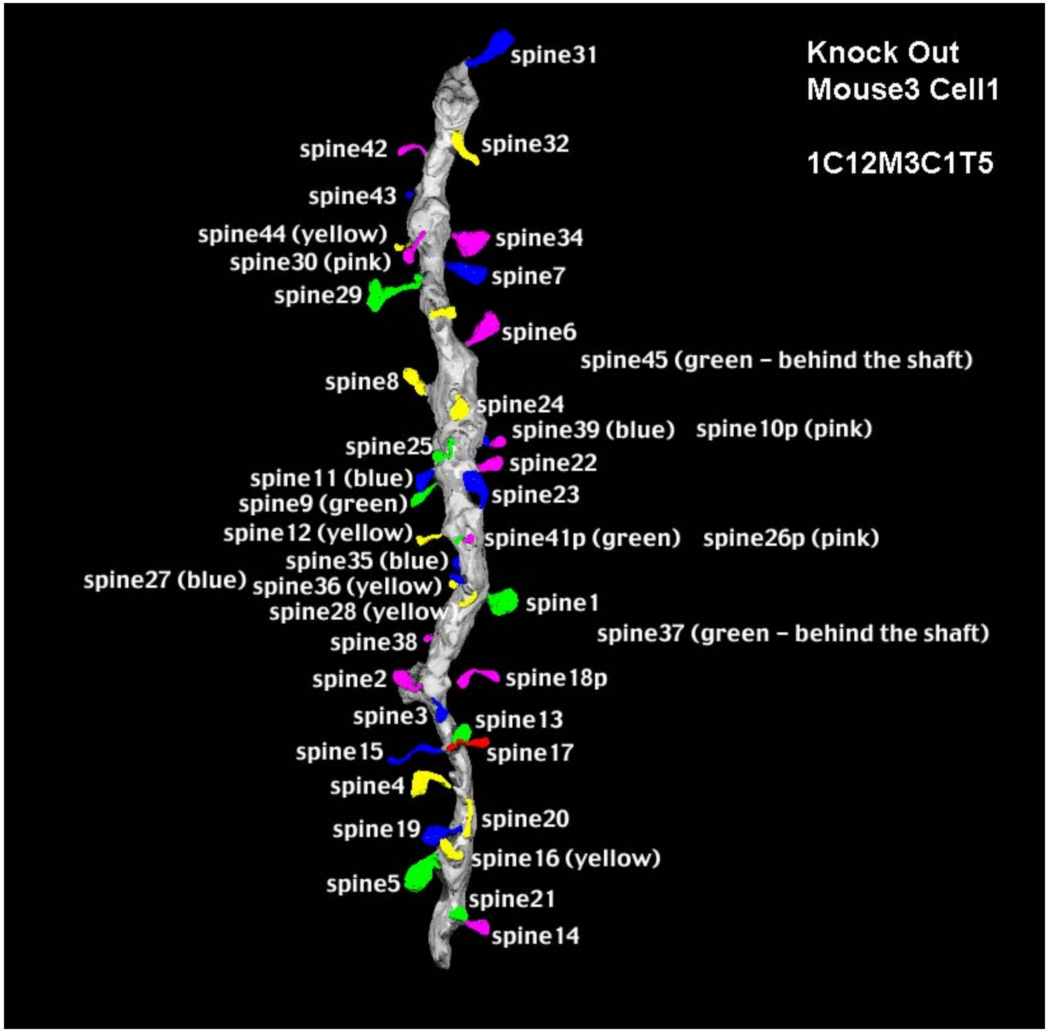
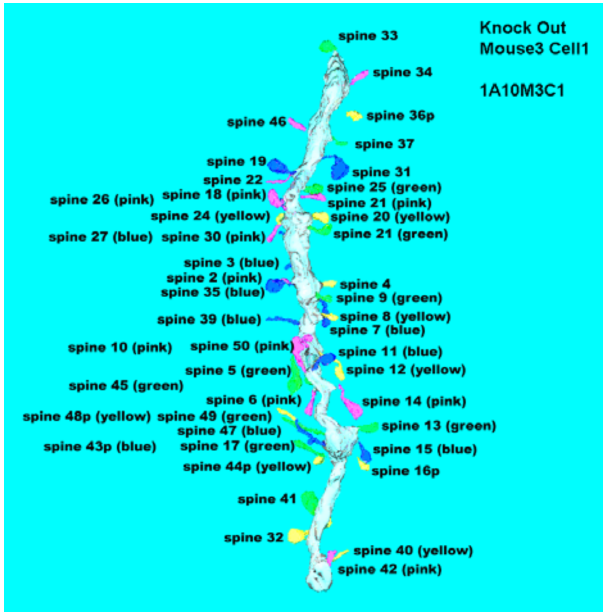
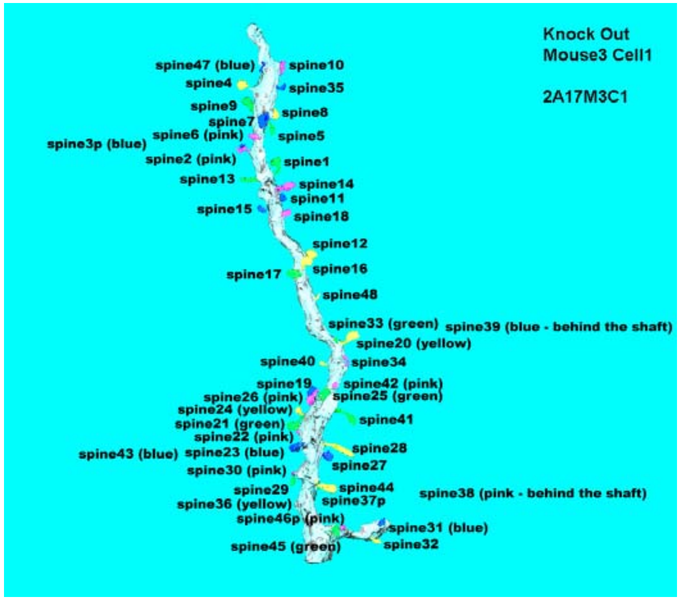

Knock Out
Mouse3 Cell1
1C12M3C1T5
spine31
spine42
spine32
spine43
spine44 (yellow)
spine34
spine30 (pink)
spine7
spine29
spine6
spine45 (green – behind the shaft)
spine8
spine24
spine39 (blue)
spine10p (pink)
spine25
spine22
spine11 (blue)
spine23
spine9 (green)
spine12 (yellow)
spine41p (green)
spine26p (pink)
spine35 (blue)
spine27 (blue)
spine36 (yellow)
spine28 (yellow)
spine1
spine37 (green – behind the shaft)
spine38
spine2
spine18p
spine3
spine13
spine15
spine17
spine4
spine20
spine19
spine16 (yellow)
spine5
spine21
spine14

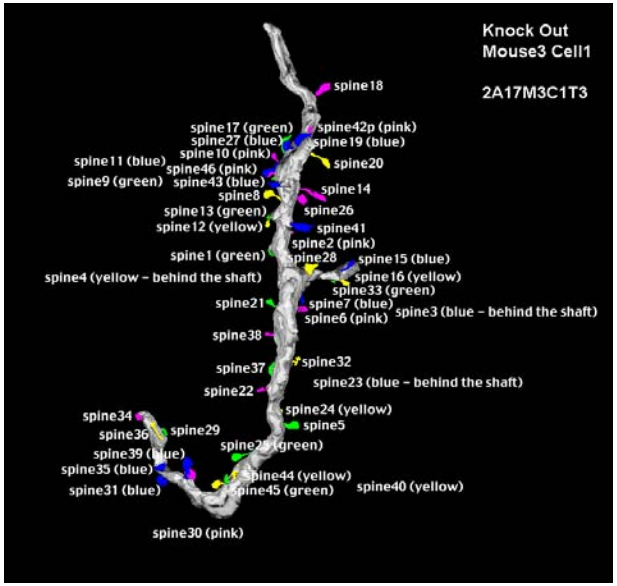
Image Maps



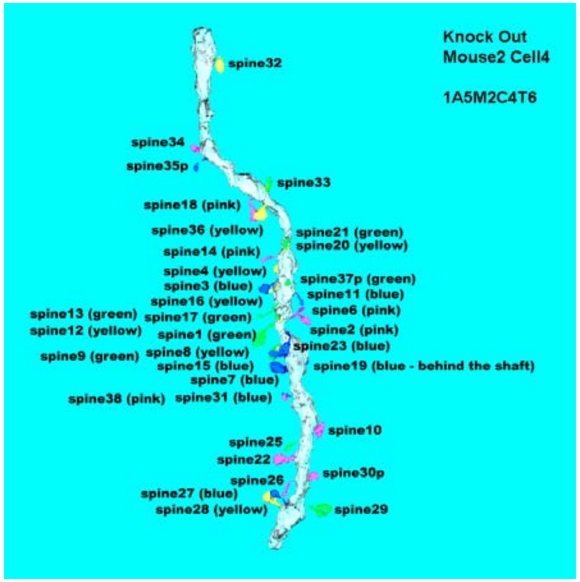
Knock Out
Mouse3 Cell1
1A10M3C1
spine 33
spine 34
spine 46
spine 36p
spine 37
spine 19
spine 31
spine 22
spine 25 (green)
spine 26 (pink)
spine 18 (pink)
spine 21 (pink)
spine 24 (yellow)
spine 20 (yellow)
spine 27 (blue)
spine 30 (pink)
spine 21 (green)
spine 3 (blue)
spine 2 (pink)
spine 4
spine 35 (blue)
spine 9 (green)
spine 39 (blue)
spine 8 (yellow)
spine 7 (blue)
spine 10 (pink)
spine 50 (pink)
spine 11 (blue)
spine 5 (green)
spine 12 (yellow)
spine 45 (green)
spine 6 (pink)
spine 14 (pink)
spine 48p (yellow)
spine 49 (green)
spine 47 (blue)
spine 13 (green)
spine 43p (blue)
spine 17 (green)
spine 15 (blue)
spine 44p (yellow)
spine 16p
spine 41
spine 32
spine 40 (yellow)
spine 42 (pink)



Knock Out
Mouse3 Cell1
2A17M3C1
spine47 (blue)
spine10
spine4
spine35
spine9
spine8
spine7
spine6 (pink)
spine5
spine3p (blue)
spine2 (pink)
spine1
spine13
spine14
spine11
spine15
spine18
spine12
spine16
spine17
spine48
spine33 (green)
spine39 (blue - behind the shaft)
spine20 (yellow)
spine40
spine34
spine19
spine42 (pink)
spine26 (pink)
spine25 (green)
spine24 (yellow)
spine21 (green)
spine41
spine22 (pink)
spine43 (blue)
spine23 (blue)
spine28
spine30 (pink)
spine27
spine29
spine44
spine38 (pink - behind the shaft)
spine36 (yellow)
spine37p
spine46p (pink)
spine31 (blue)
spine45 (green)
spine32

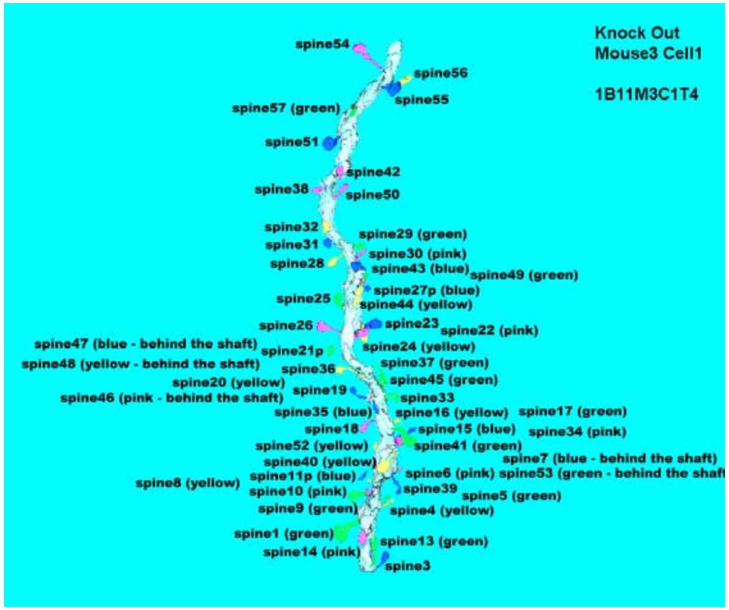


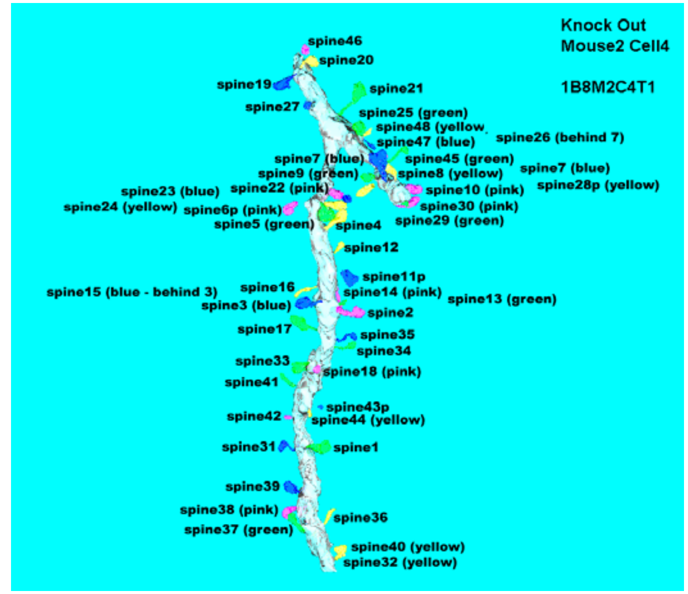
Knock Out
Mouse3 Cell1
2A17M3C1T3
spine18
spine17 (green)
spine42p (pink)
spine27 (blue)
spine19 (blue)
spine10 (pink)
spine11 (blue)
spine20
spine46 (pink)
spine9 (green)
spine43 (blue)
spine14
spine8
spine13 (green)
spine26
spine12 (yellow)
spine41
spine2 (pink)
spine1 (green)
spine28
spine15 (blue)
spine4 (yellow – behind the shaft)
spine16 (yellow)
spine33 (green)
spine21
spine7 (blue)
spine3 (blue – behind the shaft)
spine6 (pink)
spine38
spine32
spine37
spine23 (blue – behind the shaft)
spine22
spine24 (yellow)
spine34
spine5
spine36
spine29
spine25 (green)
spine39 (blue)
spine35 (blue)
spine44 (yellow)
spine31 (blue)
spine45 (green)
spine40 (yellow)
spine30 (pink)

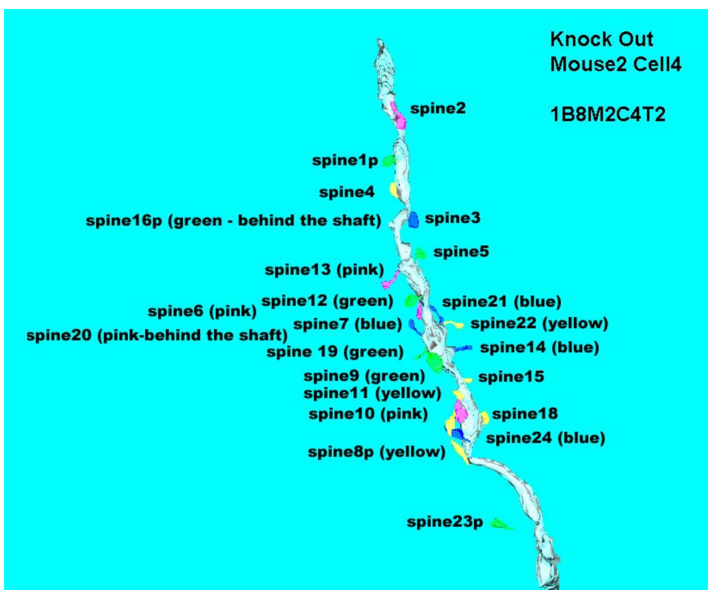


Knock Out
Mouse2 Cell4
1A5M2C4T6
spine32
spine34
spine35p
spine33
spine18 (pink)
spine36 (yellow)
spine21 (green)
spine20 (yellow)
spine14 (pink)
spine4 (yellow)
spine37p (green)
spine3 (blue)
spine11 (blue)
spine16 (yellow)
spine6 (pink)
spine13 (green)
spine17 (green)
spine12 (yellow)
spine1 (green)
spine2 (pink)
spine23 (blue)
spine9 (green)
spine8 (yellow)
spine15 (blue)
spine19 (blue - behind the shaft)
spine7 (blue)
spine38 (pink)
spine31 (blue)
spine10
spine25
spine22
spine30p
spine26
spine27 (blue)
spine28 (yellow)
spine29

Image Maps


Knock Out
Mouse3 Cell1
1B11M3C1T4
spine54
spine56
spine55
spine57 (green)
spine51
spine42
spine38
spine50
spine32
spine29 (green)
spine31
spine30 (pink)
spine28
spine43 (blue)
spine49 (green)
spine27p (blue)
spine25
spine44 (yellow)
spine26
spine23
spine22 (pink)
spine47 (blue - behind the shaft)
spine21p
spine24 (yellow)
spine48 (yellow - behind the shaft)
spine36
spine37 (green)
spine20 (yellow)
spine45 (green)
spine19
spine46 (pink - behind the shaft)
spine33
spine35 (blue)
spine16 (yellow)
spine17 (green)
spine18
spine15 (blue)
spine34 (pink)
spine52 (yellow)
spine41 (green)
spine40 (yellow)
spine7 (blue - behind the shaft)
spine11p (blue)
spine6 (pink)
spine53 (green - behind the shaft
spine8 (yellow)
spine10 (pink)
spine39
spine5 (green)
spine9 (green)
spine4 (yellow)
spine1 (green)
spine13 (green)
spine14 (pink)
spine3


Knock Out
Mouse2 Cell4
1B8M2C4T1
spine46
spine20
spine19
spine21
spine27
spine25 (green)
spine48 (yellow
spine47 (blue)
spine26 (behind 7)
spine7 (blue)
spine45 (green)
spine7 (blue)
spine9 (green)
spine8 (yellow)
spine28p (yellow)
spine23 (blue)
spine22 (pink)
spine10 (pink)
spine24 (yellow)
spine6p (pink)
spine30 (pink)
spine5 (green)
spine4
spine29 (green)
spine12
spine11p
spine16
spine14 (pink)
spine15 (blue - behind 3)
spine13 (green)
spine3 (blue)
spine2
spine17
spine35
spine34
spine33
spine18 (pink)
spine41
spine43p
spine42
spine44 (yellow)
spine31
spine1
spine39
spine38 (pink)
spine36
spine37 (green)
spine40 (yellow)
spine32 (yellow)


Knock Out
Mouse2 Cell4
1B8M2C4T2
spine2
spine1p
spine4
spine16p (green - behind the shaft)
spine3
spine5
spine13 (pink)
spine6 (pink)
spine12 (green)
spine21 (blue)
spine7 (blue)
spine22 (yellow)
spine20 (pink-behind the shaft)
spine 19 (green)
spine14 (blue)
spine9 (green)
spine15
spine11 (yellow)
spine10 (pink)
spine18
spine24 (blue)
spine8p (yellow)
spine23p

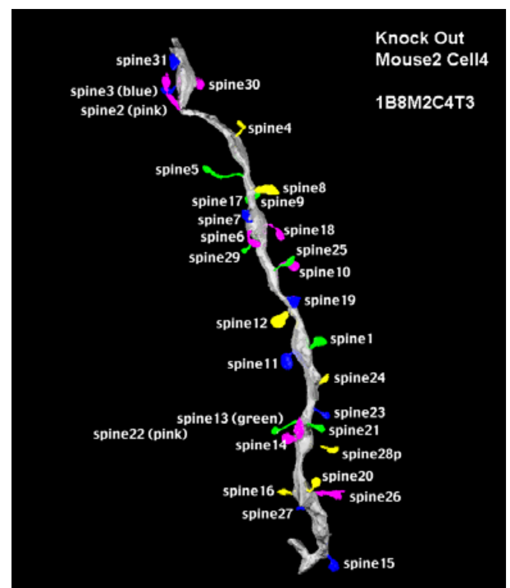
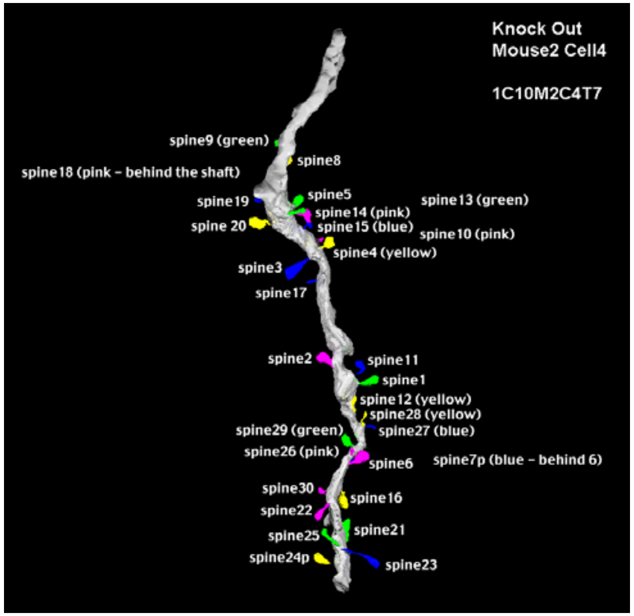
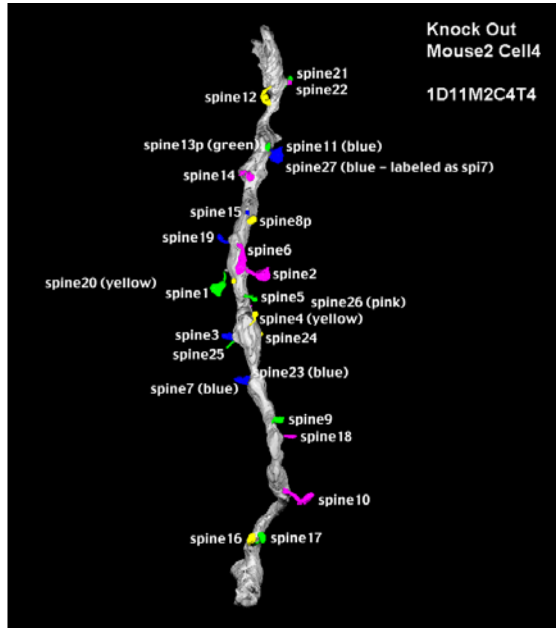
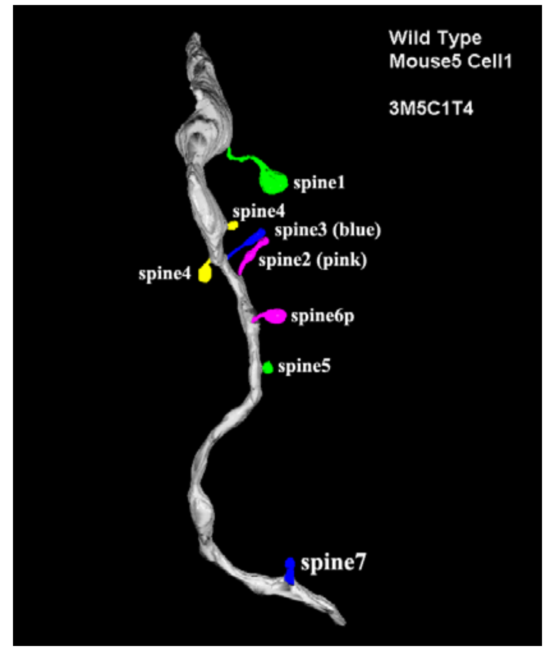
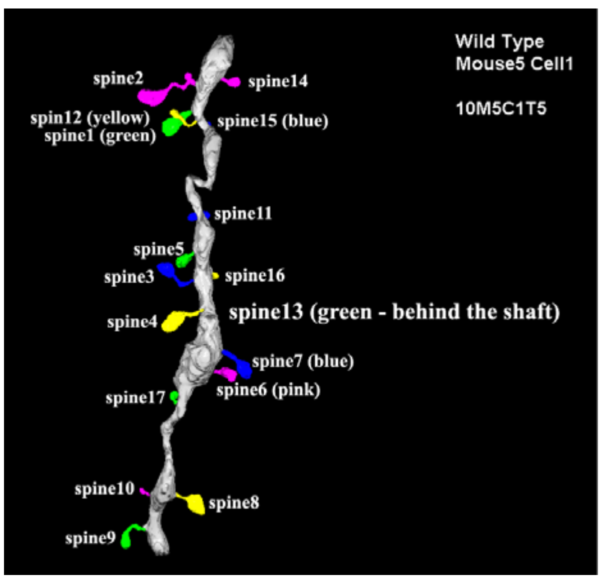

Knock Out
Mouse2 Cell4
1B8M2C4T3
spine31
spine30
spine3 (blue)
spine2 (pink)
spine4
spine5
spine8
spine17
spine9
spine7
spine18
spine6
spine25
spine29
spine10
spine19
spine12
spine1
spine11
spine24
spine23
spine13 (green)
spine21
spine22 (pink)
spine14
spine28p
spine20
spine16
spine26
spine27
spine15

Image Maps


Knock Out
Mouse2 Cell4
1C10M2C4T7
spine9 (green)
spine8
spine18 (pink – behind the shaft)
spine5
spine19
spine14 (pink)
spine13 (green)
spine 20
spine15 (blue)
spine10 (pink)
spine4 (yellow)
spine3
spine17
spine2
spine11
spine1
spine12 (yellow)
spine28 (yellow)
spine29 (green)
spine27 (blue)
spine26 (pink)
spine6
spine7p (blue – behind 6)
spine30
spine16
spine22
spine21
spine25
spine24p
spine23


Knock Out
Mouse2 Cell4
1D11M2C4T4
spine21
spine22
spine12
spine13p (green)
spine11 (blue)
spine27 (blue – labeled as spi7)
spine14
spine15
spine8p
spine19
spine6
spine2
spine20 (yellow)
spine1
spine5
spine26 (pink)
spine4 (yellow)
spine3
spine24
spine25
spine23 (blue)
spine7 (blue)
spine9
spine18
spine10
spine16
spine17


Wild Type
Mouse5 Cell1
3M5C1T4
spine1
spine4
spine3 (blue)
spine2 (pink)
spine4
spine6p
spine5
spine7


Wild Type
Mouse5 Cell1
10M5C1T5
spine2
spine14
spin12 (yellow)
spine1 (green)
spine15 (blue)
spine11
spine5
spine3
spine16
spine4
spine13 (green - behind the shaft)
spine7 (blue)
spine6 (pink)
spine17
spine10
spine8
spine9

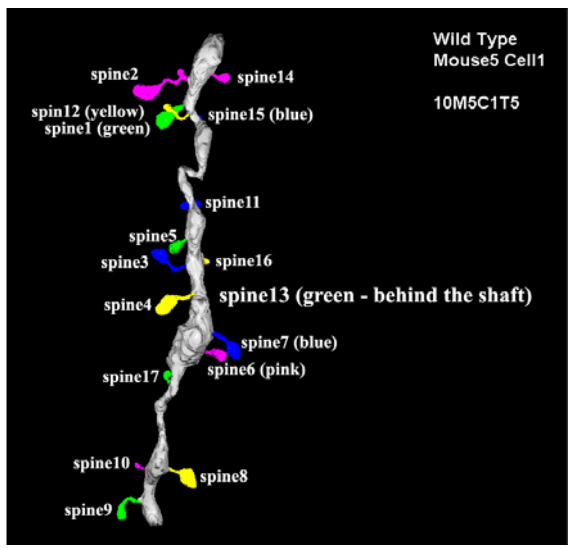
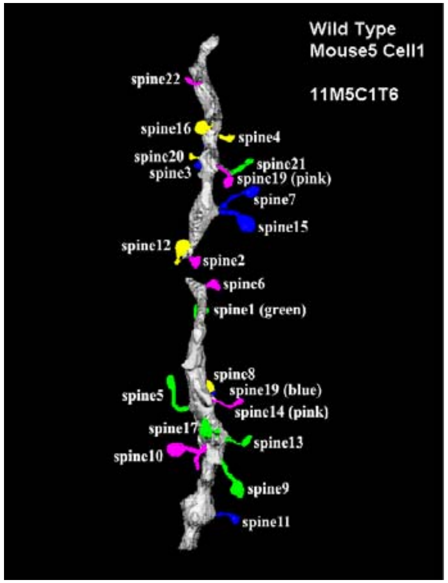
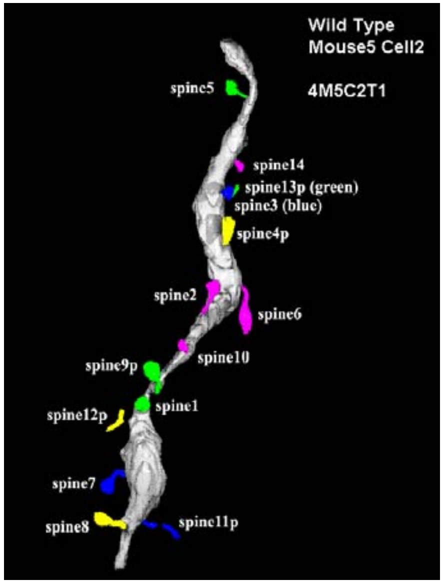
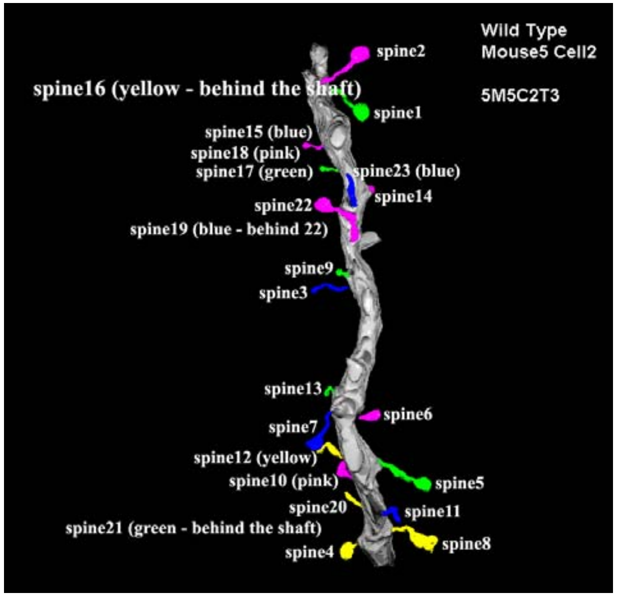
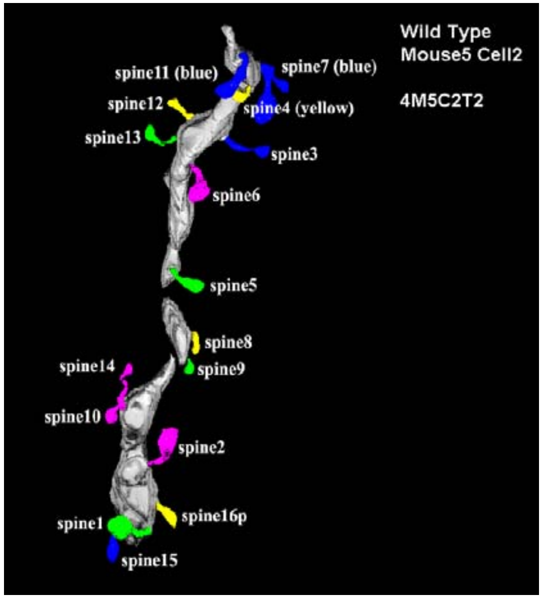

Wild Type
Mouse5 Cell1
10M5C1T5
spine2
spine14
spin12 (yellow)
spine1 (green)
spine15 (blue)
spine11
spine5
spine3
spine16
spine4
spine13 (green - behind the shaft)
spine7 (blue)
spine6 (pink)
spine17
spine10
spine8
spine9

Image Maps


Wild Type
Mouse5 Cell1
11M5C1T6
spine22
spine16
spine4
spine20
spine3
spine21
spine19 (pink)
spine7
spine15
spine12
spine2
spine6
spine1 (green)
spine8
spine5
spine19 (blue)
spine14 (pink)
spine17
spine13
spine10
spine9
spine11

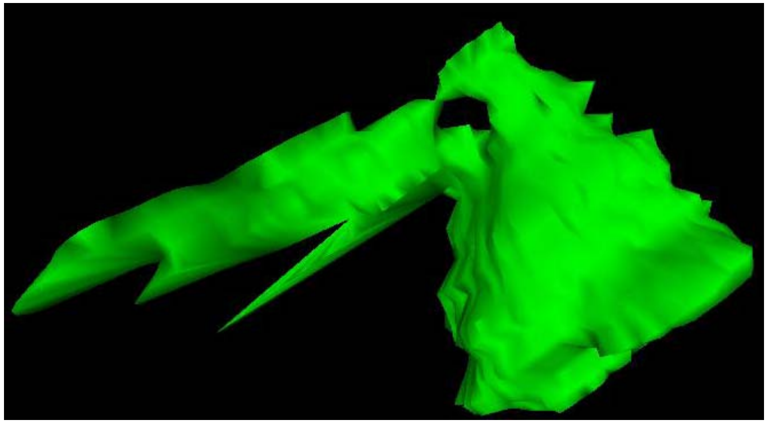

Wild Type
Mouse5 Cell2
4M5C2T1
spine5
spine14
spine13p (green)
spine3 (blue)
spine4p
spine2
spine6
spine10
spine9p
spine1
spine12p
spine7
spine8
spine11p


Wild Type
Mouse5 Cell2
5M5C2T3
spine2
spine16 (yellow - behind the shaft)
spine1
spine15 (blue)
spine18 (pink)
spine17 (green)
spine23 (blue)
spine14
spine22
spine19 (blue - behind 22)
spine9
spine3
spine13
spine6
spine7
spine12 (yellow)
spine10 (pink)
spine5
spine20
spine11
spine21 (green - behind the shaft)
spine8
spine4


Wild Type
Mouse5 Cell2
4M5C2T2
spine11 (blue)
spine7 (blue)
spine12
spine4 (yellow)
spine13
spine3
spine6
spine5
spine8
spine14
spine9
spine10
spine2
spine16p
spine1
spine15

Topologically Correct

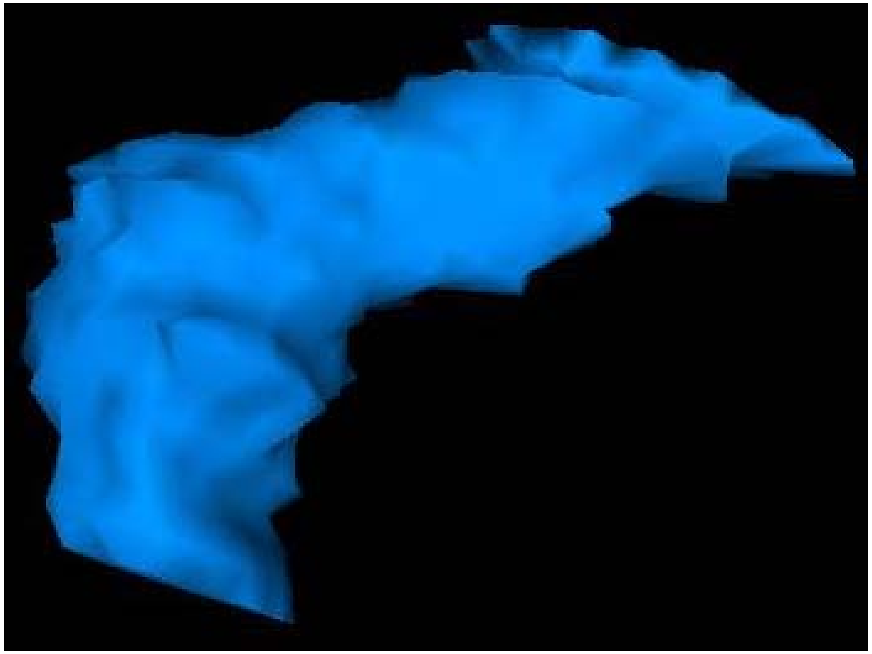
- Only spines with correct topology used
  - Euler number = 2
    - Euler number = V – E + F
      - V = number of vertices
      - E = number of edges
      - F = number of triangular faces
  - Closed volumes



Topologically Incorrect

• Euler number: 1

• Volume: not closed



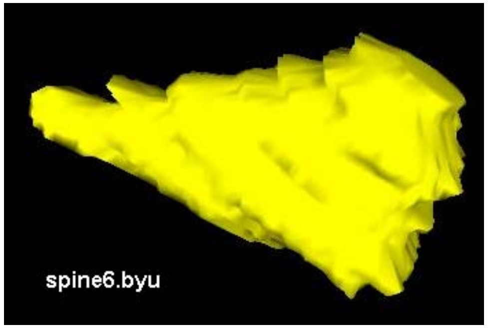
Topologically Correct

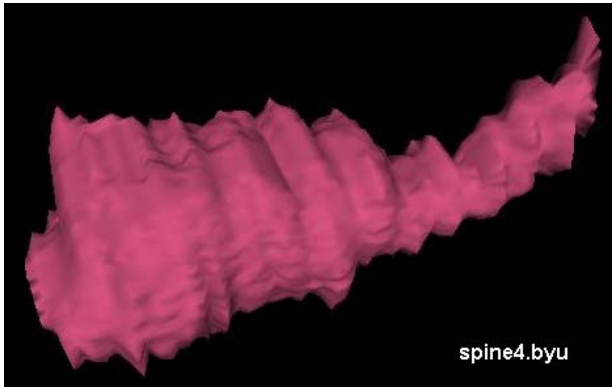
• Euler number: 2

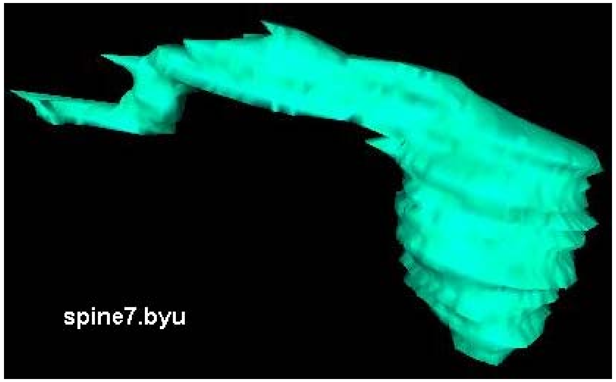
• Volume: closed

Revised Dataset

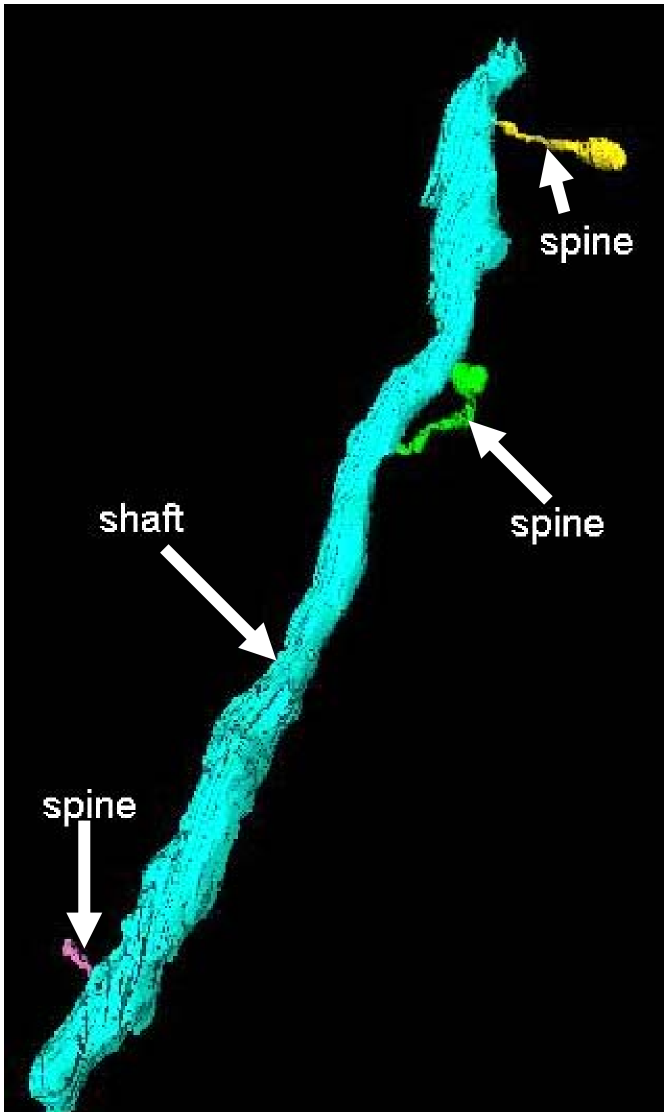
- Knock Out (2 cells)
  - Cell 1: 5 dendrites – 140 spines
  - Cell 2: 6 dendrites – 118 spines
- Wild Type (2 cells)
  - Cell 1: 3 dendrites – 33 spines
  - Cell 2: 3 dendrites – 37 spines
- New spine total after checking topology: 328 spines
- Resolution: 1.0 X 1.0 X 1.0 mm/voxel
- Spine shapes vary







Spine Anatomy: Neck and Head



Neck: point closest to dendrite shaft

Head: point furthest from dendrite shaft

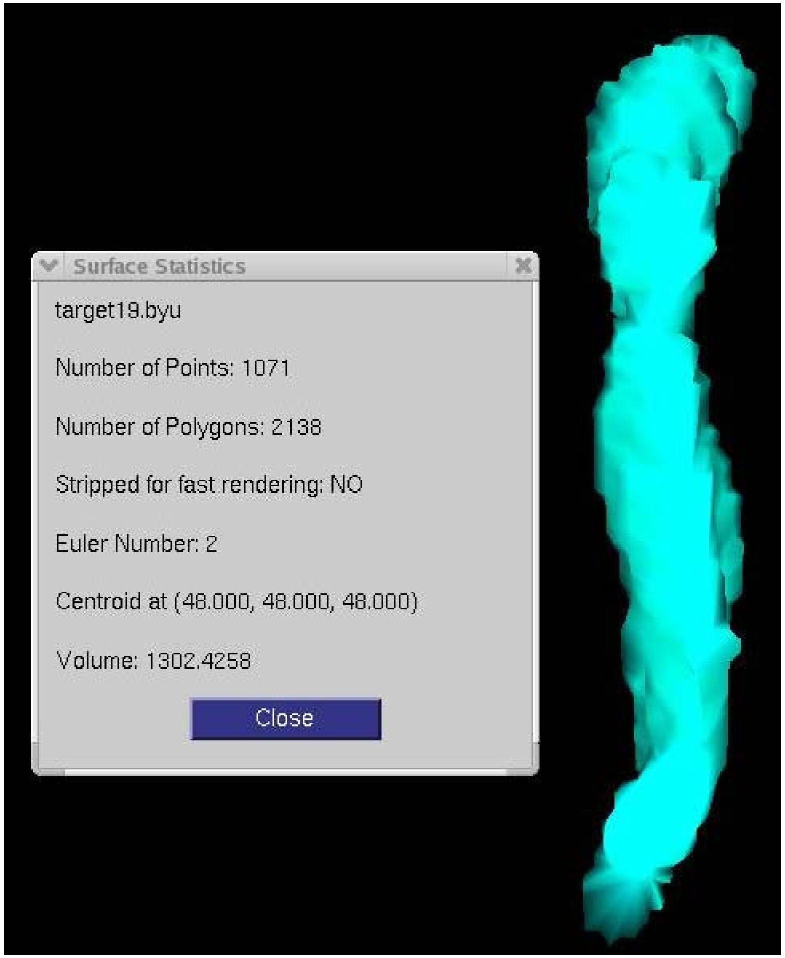
Superimposed each spine on the shaft

- ones that did not touch shaft were discarded – segmentation errors?

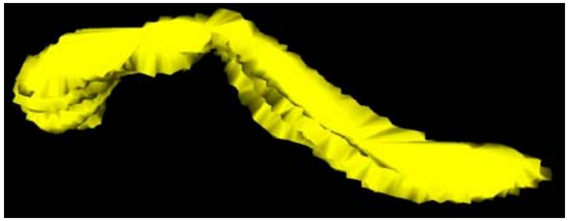
- New spine total: 287 spines

Registration of the Spines

- register 286 spines to a chosen target spine surface, which is placed in a standard 96.0 X 96.0 X 96.0 coordinate system
  - Target spine: intermediate in length
  - Target spine translated by changing the centroid to (48.0, 48.0, 48.0)

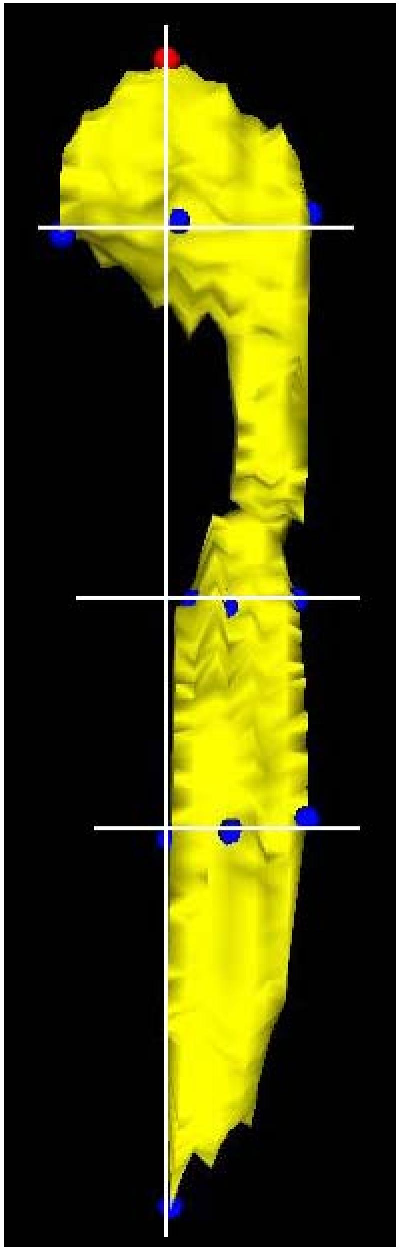


Landmarking



Landmark Number	Description
1	Neck
2	Head
3 - 6	Upper section
7 - 10	Medial section
11 - 14	Lower section

- 14 landmarks placed on each surface
- Neck and head used as main reference points – aligned vertically
- 3 imaginary lines drawn to separate spine into 4 sections
- Landmarks evenly distributed



runSim and applySimByu

- 2 versions of runSim were used, thus providing us with 2 datasets
  1. Scaling
  2. No scaling

- runSim computes the rotation, translation, and scale (optional) needed to transform a set of template landmarks into a target set of landmarks
  - This is saved as an Rts file

- runSim gives a transformed set of landmarks that register with the target set of landmarks

- applySimByu then applies the Rts file to the template *.byu surface to generate a new *.byu surface, which is correctly registered with the target surface

Registering Spines

- 2 sets of points x_i and y_i are given in a 3-dimensional space
- The lowest value of the mean squared error is calculated using the transformation parameters (rotation, translation, and scaling)

$$\min_{R,t,s} \sum_{i=1}^{n} \| sR(x_i) + t - y_i \|^2$$

R = rotation matrix

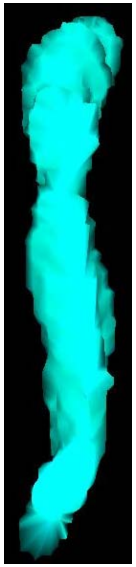
t = translation vector

s = scale factor

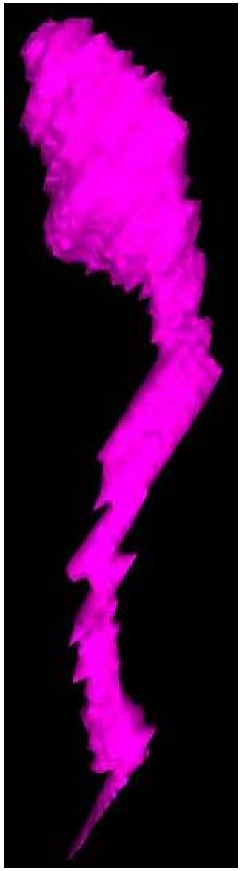
where $\|x\| = \sqrt{x_1^2 + \ldots + x_n^2}$

Umeyama, Shinji. "Least-Square Estimation of Transformation Parameters Between Two Point Patterns" (1991)

Example – Before Registration



target

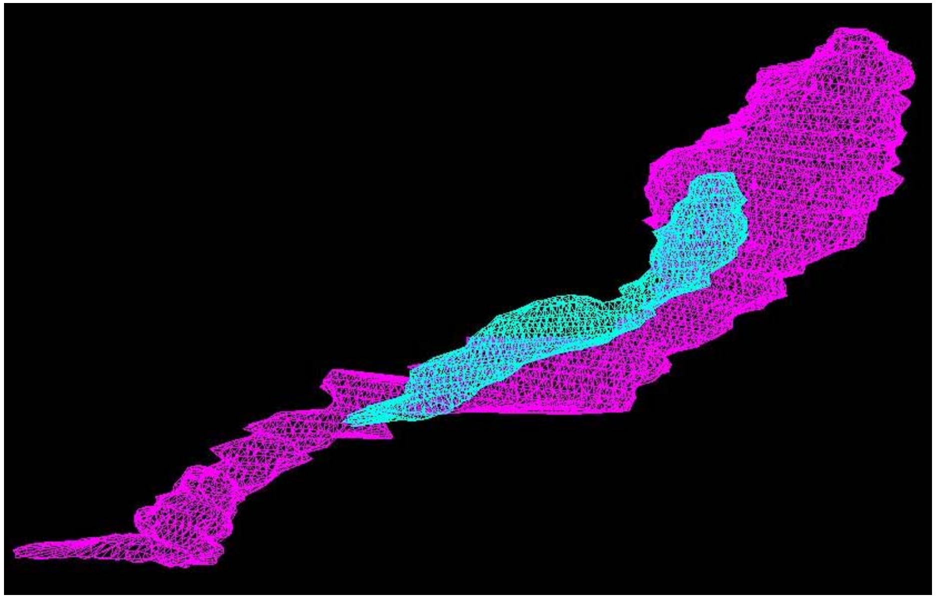


template

spines don’t superimpose

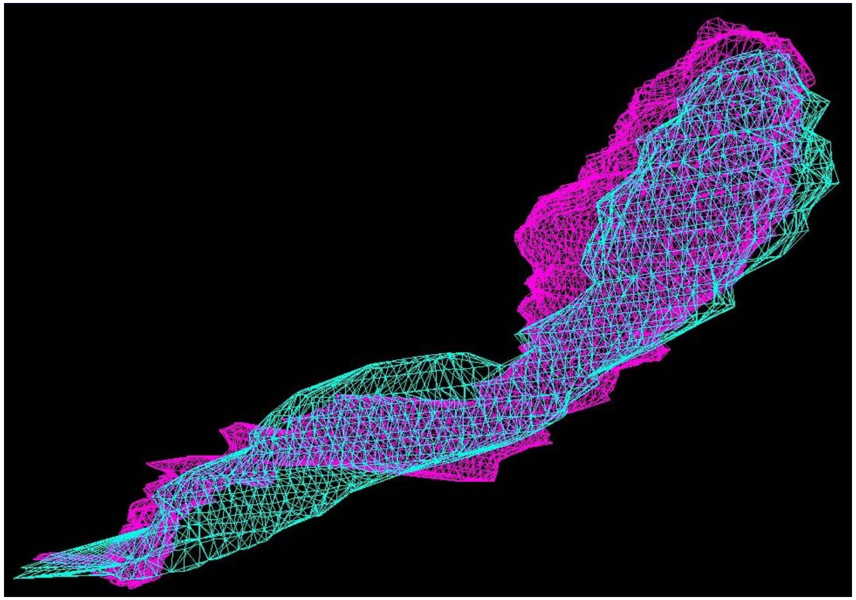
Example – After Registration

No scaling



96 X 96 X 96

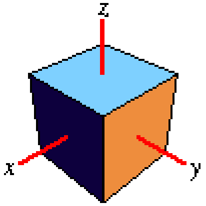
Scaling



96 X 96 X 96

Blue = target
Pink = template

Transformation Matrices



- Multidimensional array
- Can concatenate many math operations into a single matrix
- Used to translate, rotate, and scale the surfaces into the standard coordinate system
  - 3 most common types of transformation – only ones that don't distort the object (i.e. a straight line will remain straight)
- Each point in the surface gets multiplied by the matrix
  - Each point represented as a 4X1 matrix:
  - The points/vertices are homogeneous coordinates

$$\begin{bmatrix} x \\ y \\ z \\ 1 \end{bmatrix}$$

  - Result: each point gets transformed by the matrix so that a transformed surface is generated, which fits into our standard coordinate system

Rotations about each axis

- In a clockwise direction, when looking toward the origin :

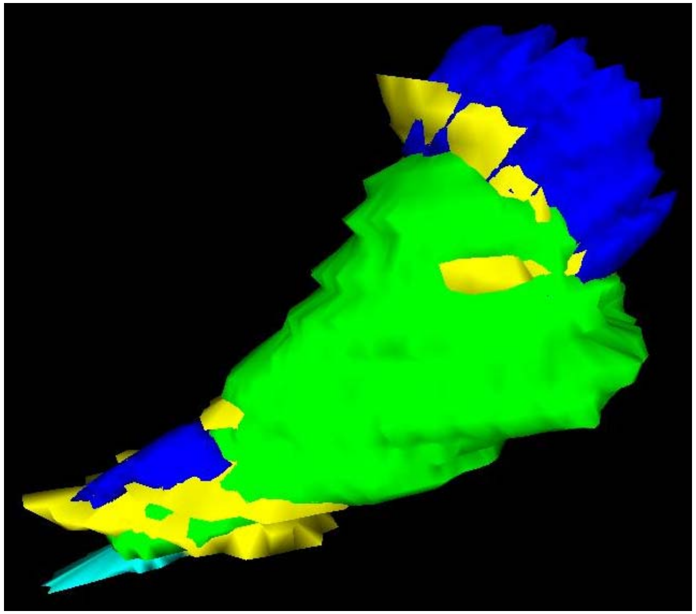
$$R_X(\alpha) = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\alpha & \sin\alpha \\ 0 & -\sin\alpha & \cos\alpha \end{bmatrix} \quad R_y(\beta) = \begin{bmatrix} \cos\beta & 0 & -\sin\beta \\ 0 & 1 & 0 \\ \sin\beta & 0 & \cos\beta \end{bmatrix} \quad R_z(\gamma) = \begin{bmatrix} \cos\gamma & \sin\gamma & 0 \\ -\sin\gamma & \cos\gamma & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

- Any rotation can be given as a composition of rotations about three axes and can be portrayed in a 3 X 3 matrix:

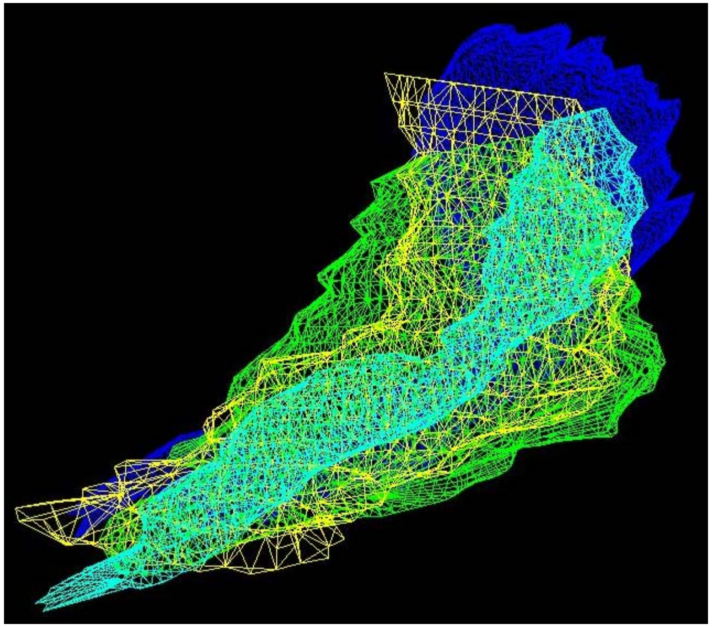
$$\begin{bmatrix} x'_1 \\ x'_2 \\ x'_3 \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix}$$

Visualization

Each of the transformed surfaces were then superimposed on the target surface to ensure correct registration



Solid View
Light blue = target



Wireframe View
Light blue = target

Scaled dataset:

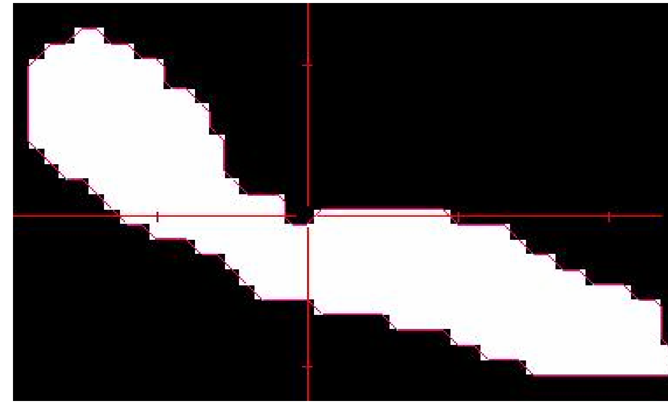
- 2 incorrectly registered (discarded)
- New spine count: 285

Non scaled dataset:

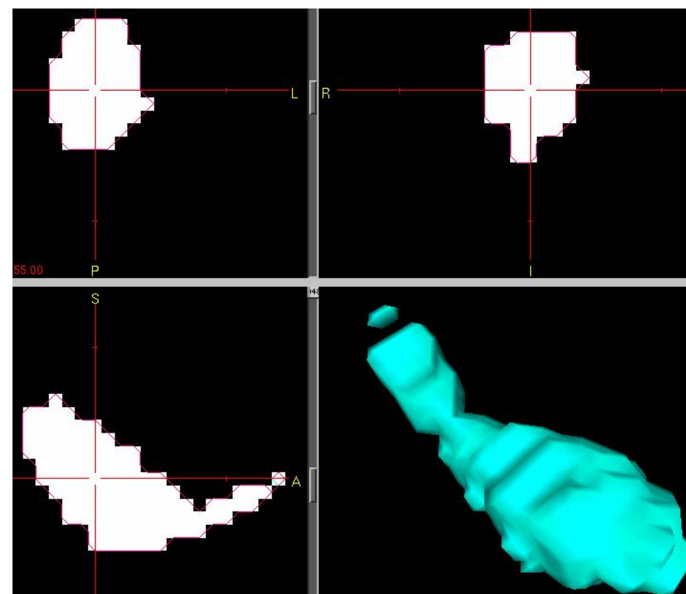
- 3 incorrectly registered (discarded)
- New spine count: 284

Binary Images

- Created directly from the newly transformed surface files
- Created by using a simple function in BrainWorks
  - Placed into a 96 X 96 X 96 coordinate system
- Surfaces of each binary image was viewed to ensure correct topology (no holes or small separate pieces)
  - Scaled dataset: 3 with incorrect topology
    - Number of images used: 282
  - Non scaled dataset: 3 with incorrect topology
    - Number of images used: 281



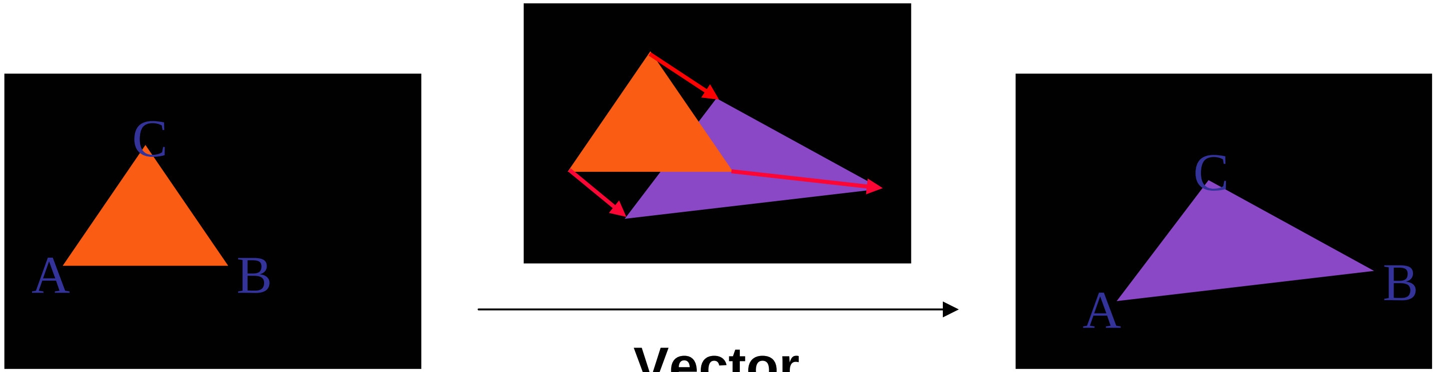
Target image (sagittal view)



Problematic image (K1_3_spine43.img)

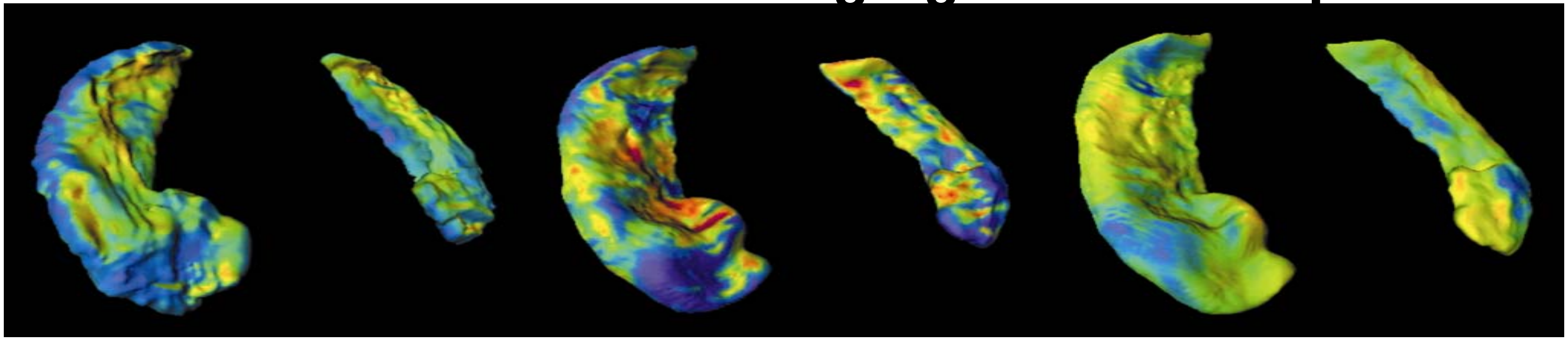
CA: shape analysis (Grenander & Miller, 1998)

- anatomy is a collection of shapes (images) or coordinate systems
- anatomies compared by vector transformations



Object 1 **Vector Transformation** **Object 2**

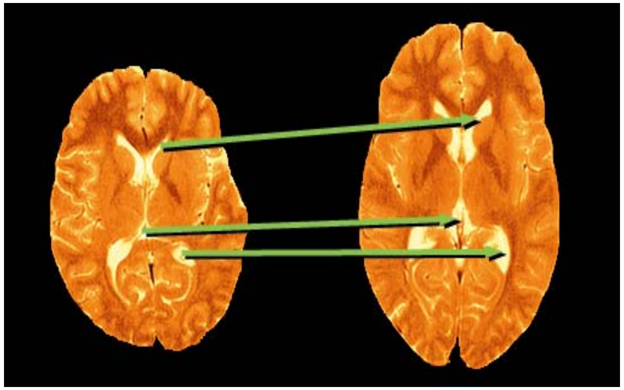
Alzheimer's **Normal Aging** **Schizophrenia**



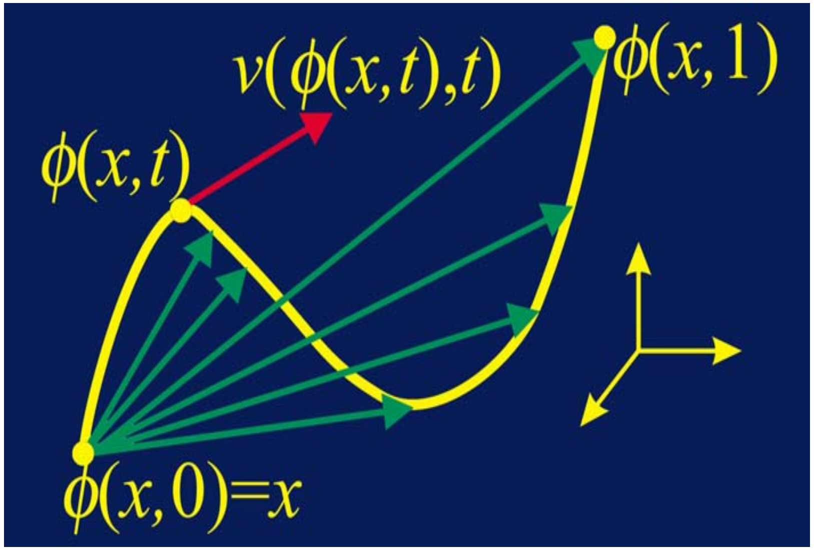
- quantification: Csernansky et al, PNAS 1998; Am J Psych 2002, 2003, 2004; Neurology 2001

Computational Anatomy: A study of geodesic diffeomorphisms i.e. metric distances

I_0: Template I_1:Target



ϕ



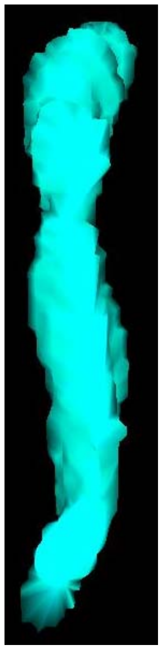
$$\frac{\partial}{\partial t}(Lv)^t + (\nabla^t.v)(Lv)^t + (v.\nabla^t)(Lv)^t + (Lv)^t\nabla^t v = 0$$

$$d(I_0, I_1) = \sqrt{\int_0^1 \|Lv\|_2^2 \, dt}$$

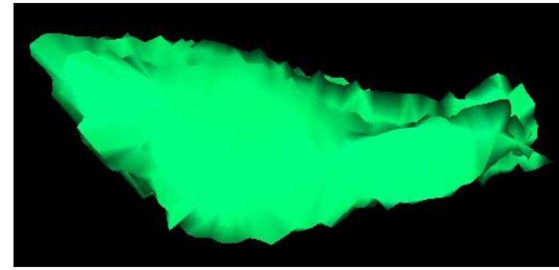
Miller, Trouvé, Younes: Ann. Rev. Biomed Engng. (2002)

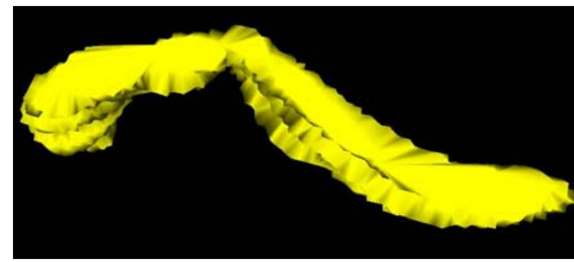
Shape analysis on anatomical image databases via the Internet

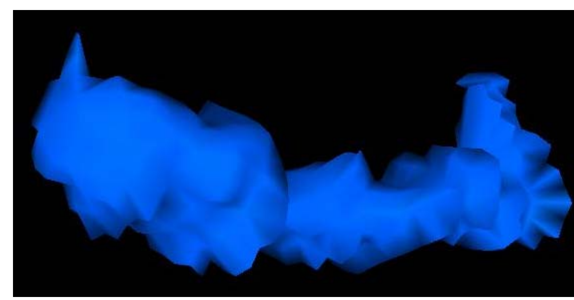
$$d(I_0, I_1) = \sqrt{\int_0^1 \|Lv\|_2^2 \, dt}$$



SDSC
SRB
Storage Resource Broker







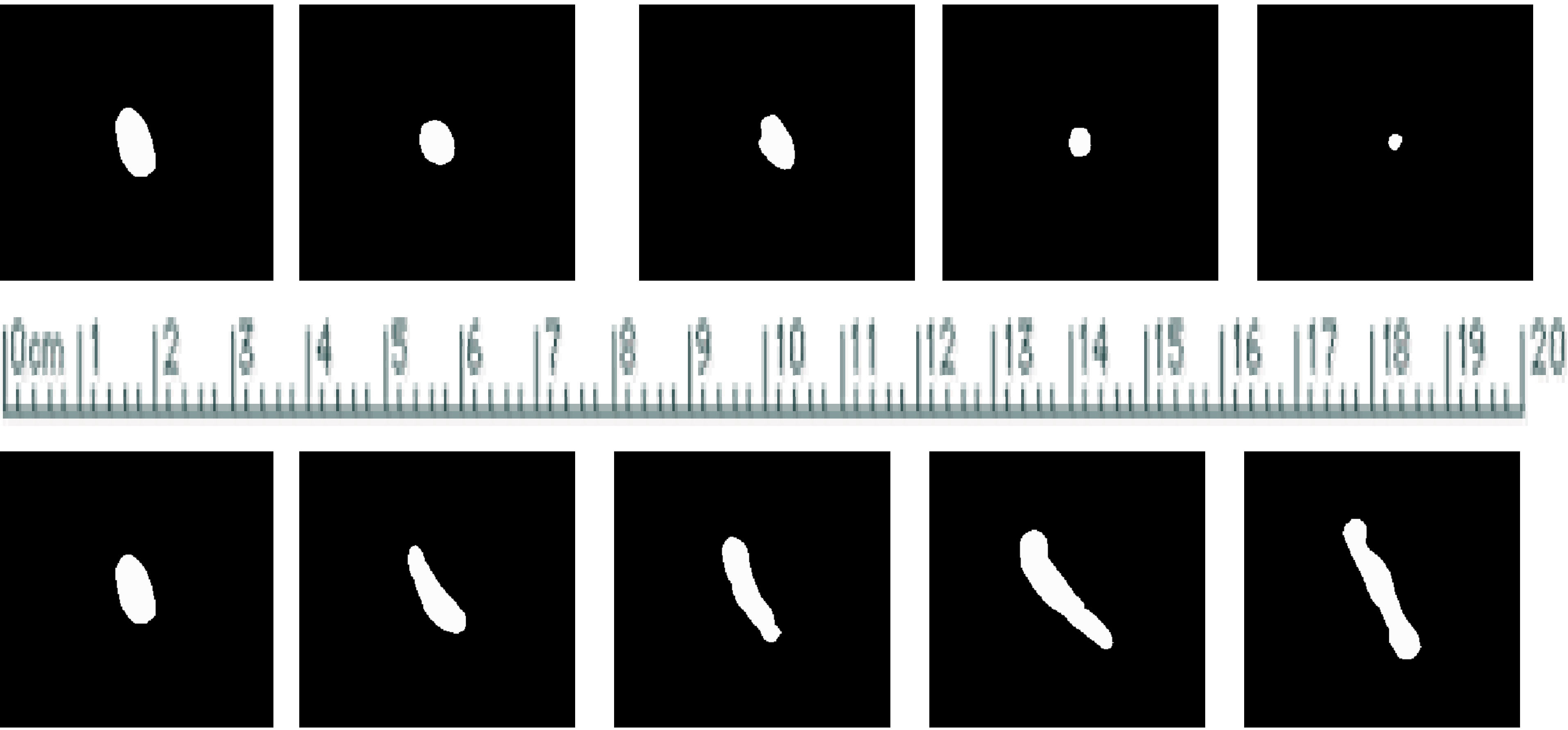
Neuroanatomist asks: "Is there evidence for shape differences?"

Databases Of Shapes

NPACI

The Pyschophysics of Metric Space of Biological Shapes

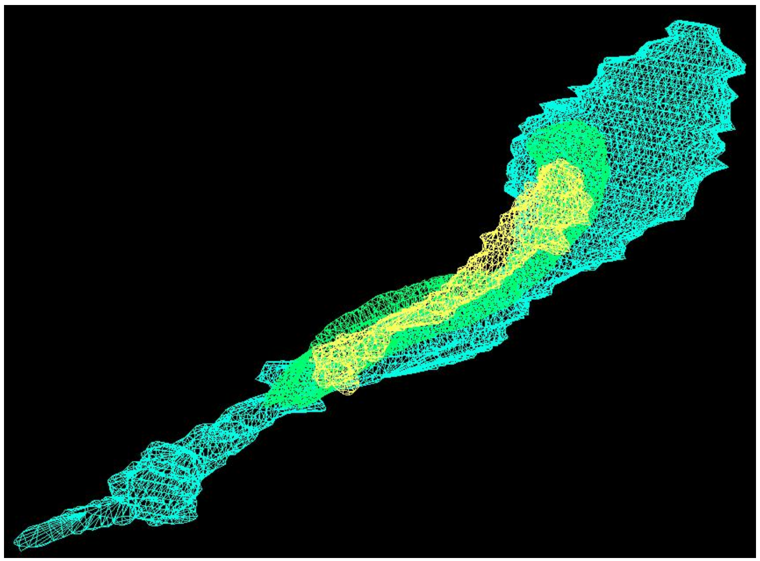
0 | 0.845 | 1.747 | 2.568 | 4.410



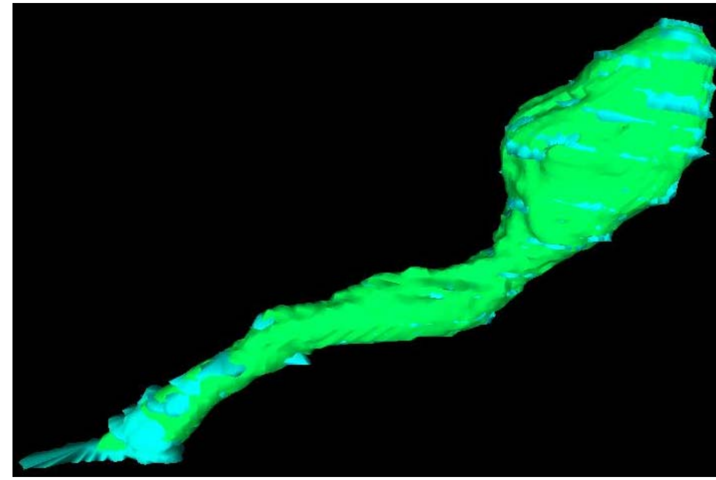
0 | 2.579 | 2.918 | 5.596 | 5.989

Miller, Trouvé, Younes: Ann. Rev. Biomed Engng. (2002)

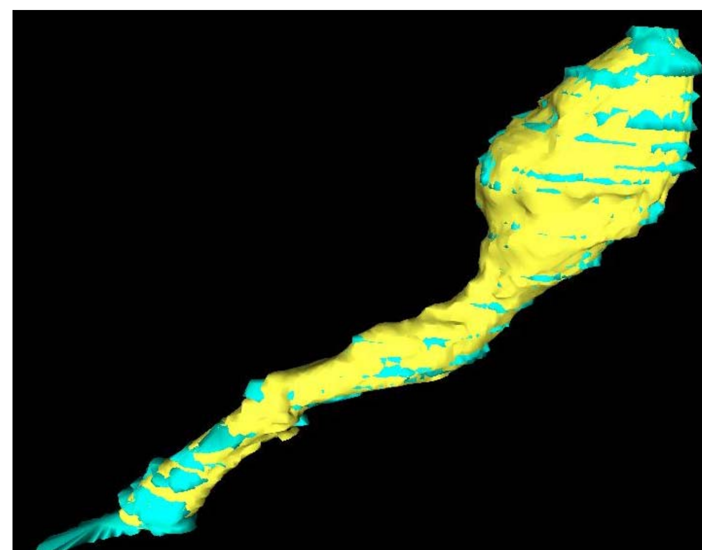
Results



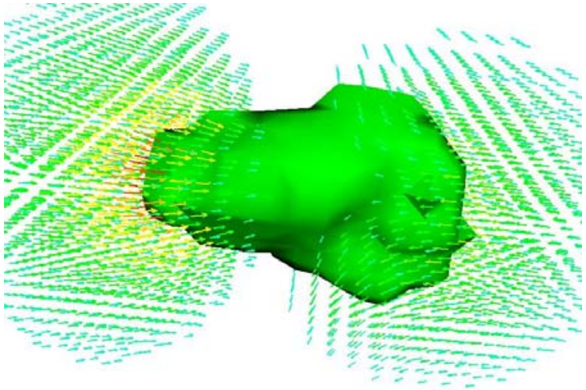
Registered surfaces



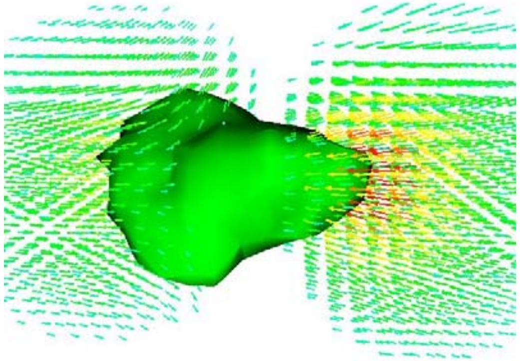
Deformed surfaces



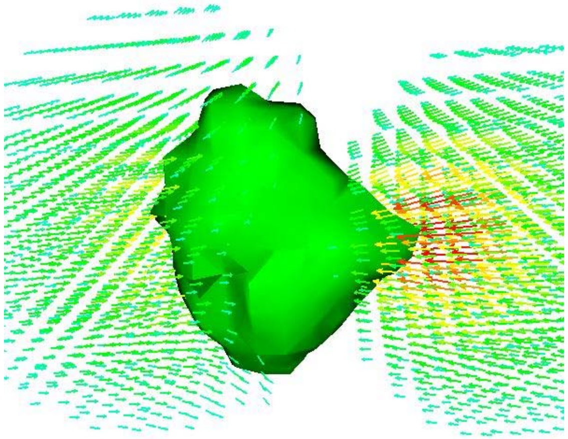
Progression of LDDMM



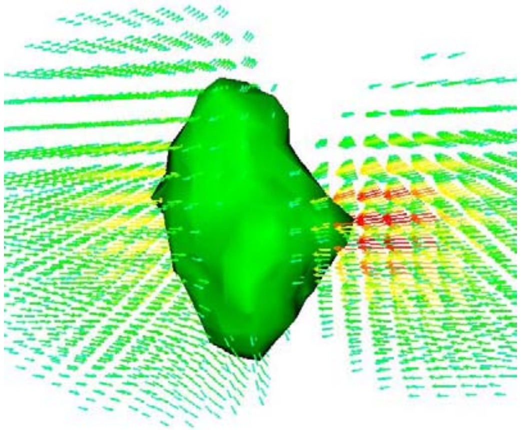
Timestep 1



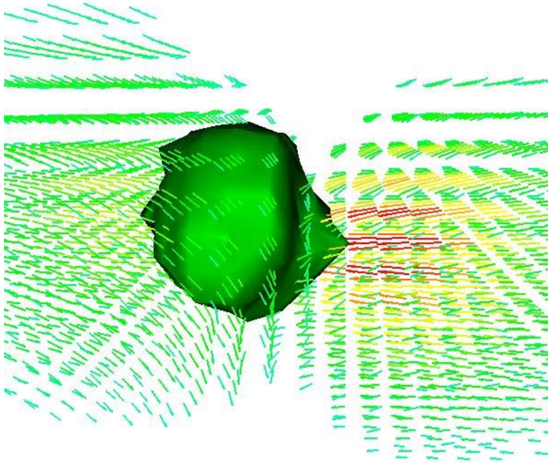
Timestep 3



Timestep 5



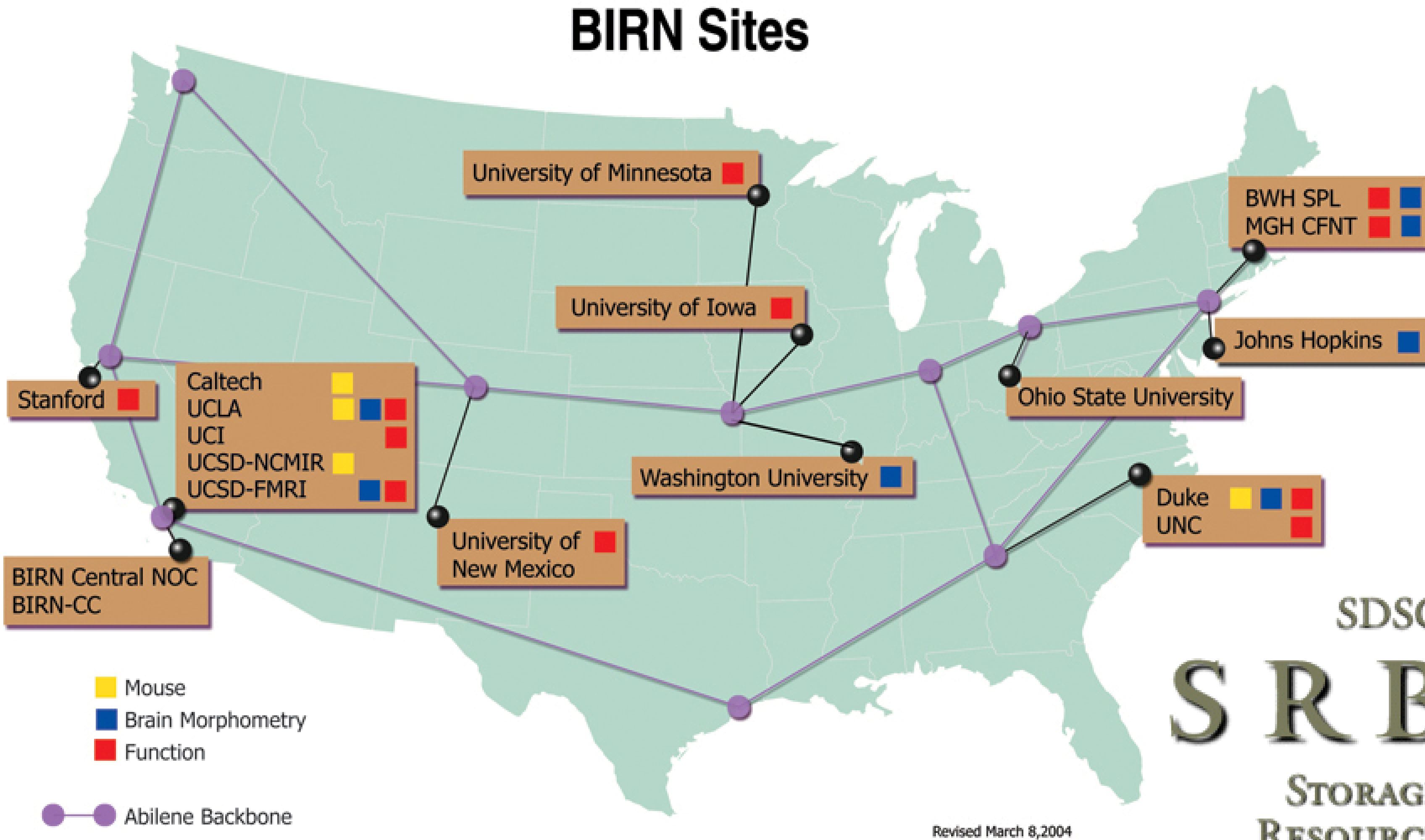
Timestep 7



Timestep 9

Frisby, R. http://www.cis.jhu.edu/~rfrisby

Biomedical Informatics Research Network: a new paradigm for neuroscience research

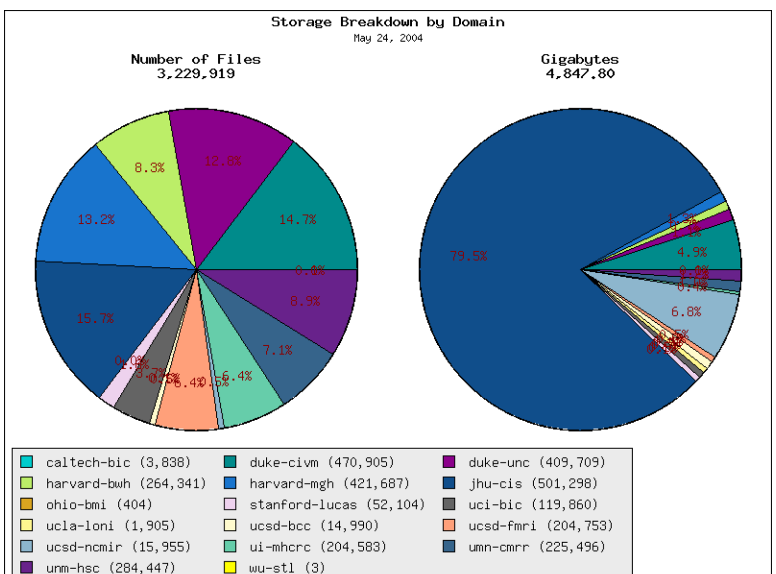


SDSC
SRB
STORAGE
RESOURCE
BROKER

Large Deformation Diffeomorphic Metric Mapping (LDDMM)

- Measures the distance between a template and a target image via metrics
- Notion of how close and far shapes are relative to template
- Teragrid used to significantly speed up the process

Single PC	TeraGrid
1 comparison	60 comparisons simultaneously
~431 days	~7 days



- Each LDDMM takes about 3 to 8 hours for a hippocampus
- JHU CIS - largest user of BIRN storage and computing infrastructure for hippocampus mappings

Future work: statistical analysis of shape analysis

- perform statistical analysis of metric distances i.e. demonstrate that metric distances can be used to distinguish or classify shapes

- perform statistical analysis of vector fields i.e. localize subtle anatomical differences in spines

Acknowledgements

- Dr. Tilak Ratnanather
- USCD collaborators: Maryann Martone, Masako Terada, and Julia Sun
- James Churchill – Saint Louis University
- Can Ceritoglu
- Marc Vaillant
- Elvan Ceyhan
- Anthony Kolasny
- Timothy Brown