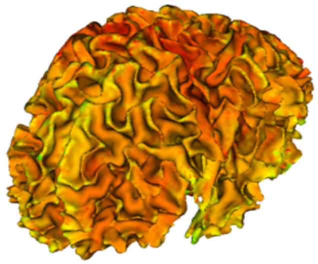
NA-MIC
National Alliance for Medical Image Computing
http://na-mic.org

Cortical Thickness Analysis with Slicer



Martin Styner

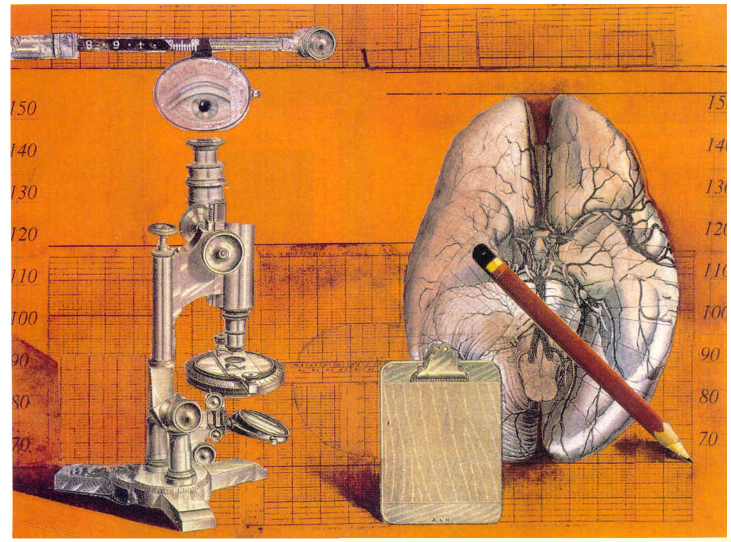
UNC - Departments of Computer Science and Psychiatry

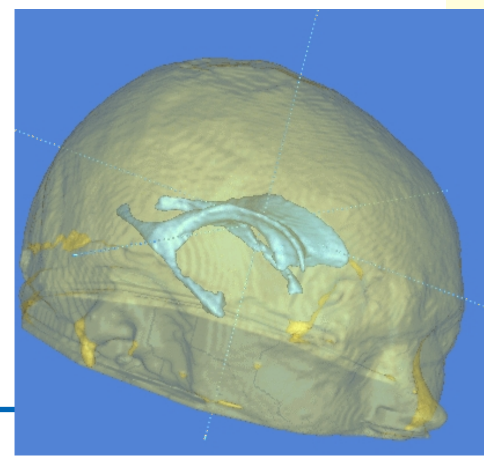
NIRAL, UNC IDDRC

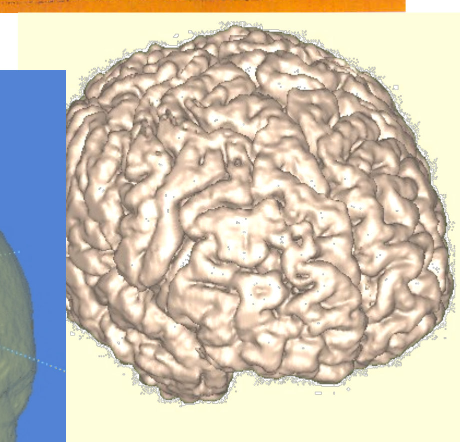
Guido Gerig, Ipek Oguz, Josh Cates, Clement Vachet, Cedric Mathieu, Marc Niethammer

Motivation Neuroimaging

- Brain imaging in healthy & pathology
- Morphometry, Connectivity ⇔ Pathology
- Schizophrenia
- Autism, Fragile-X
- MPS, Krabbe
- Normal Development
- High risk offspring
- Fitness & Aging



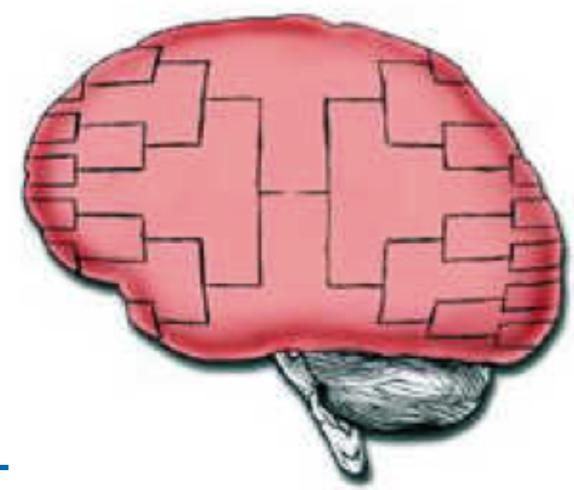




TOC

- Cortical thickness examples
- Existing methods for cortical thickness
- NAMIC methods & modules
- Future work

Normal Brain

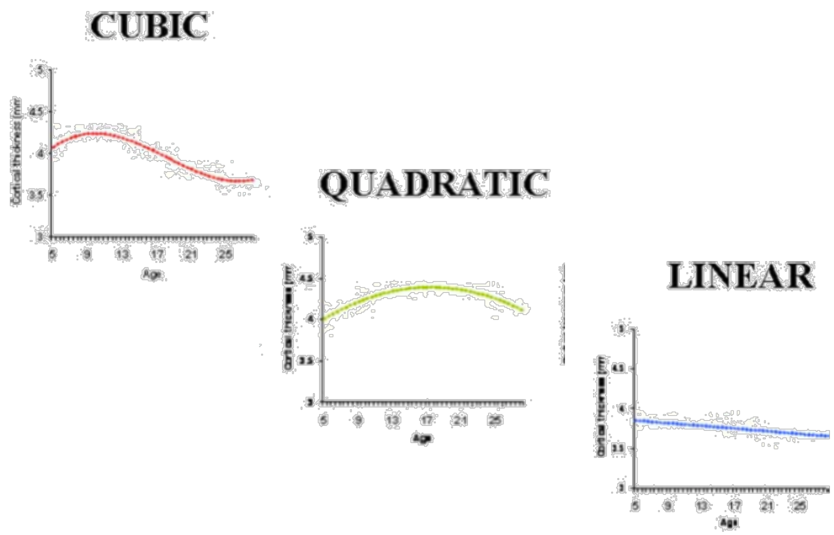


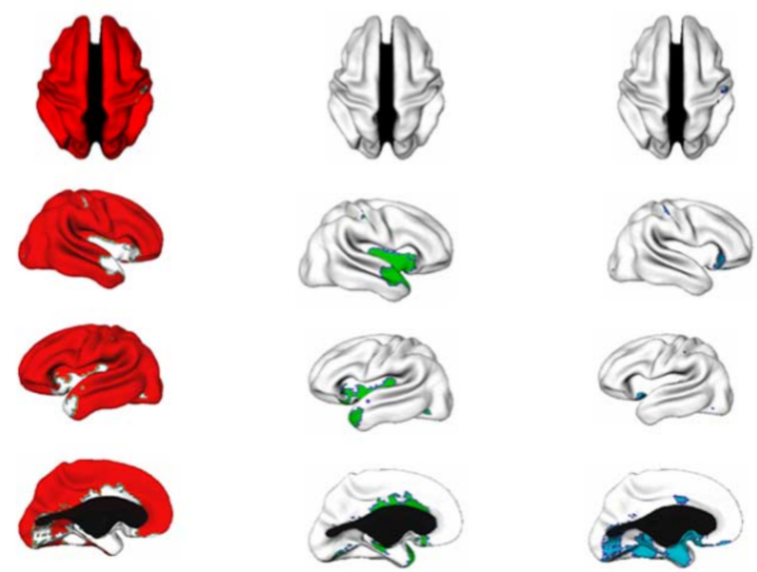
March Madness Brain

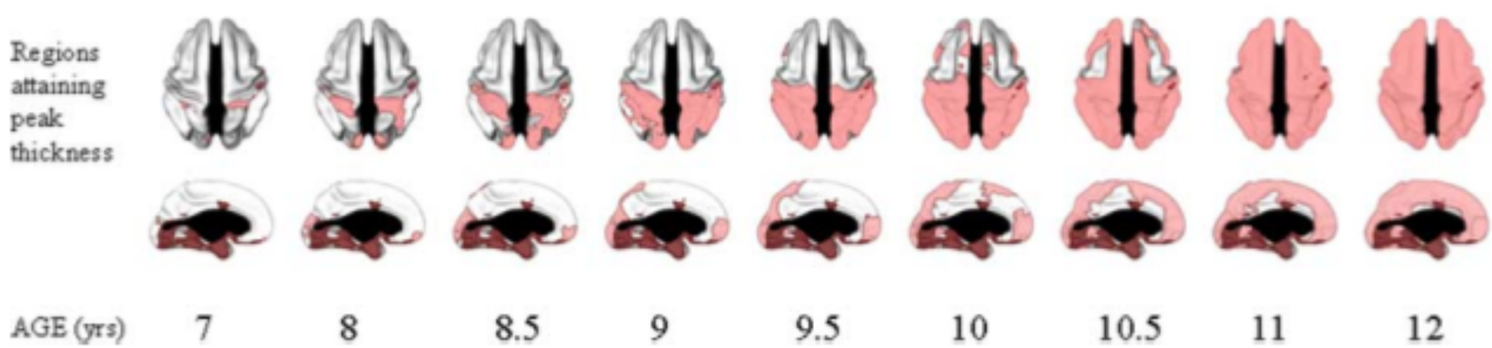
Neurodevelopmental Trajectories of the Human Cerebral Cortex

Philip Shaw,[1] Noor J. Kabani,[3] Jason P. Lerch,[4] Kristen Eckstrand,[1] Rhoshel Lenroot,[1] Nitin Gogtay,[1] Deanna Greenstein,[1] Liv Clasen,[1] Alan Evans,[4] Judith L. Rapoport,[1] Jay N. Giedd,[1] and Steve P. Wise[2]

[1]Child Psychiatry Branch and [2]Laboratory of Systems Neuroscience, National Institute of Mental Health, Bethesda, Maryland 20892, [3]Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada M4N 3N1, and [4]Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada H3A 2B4



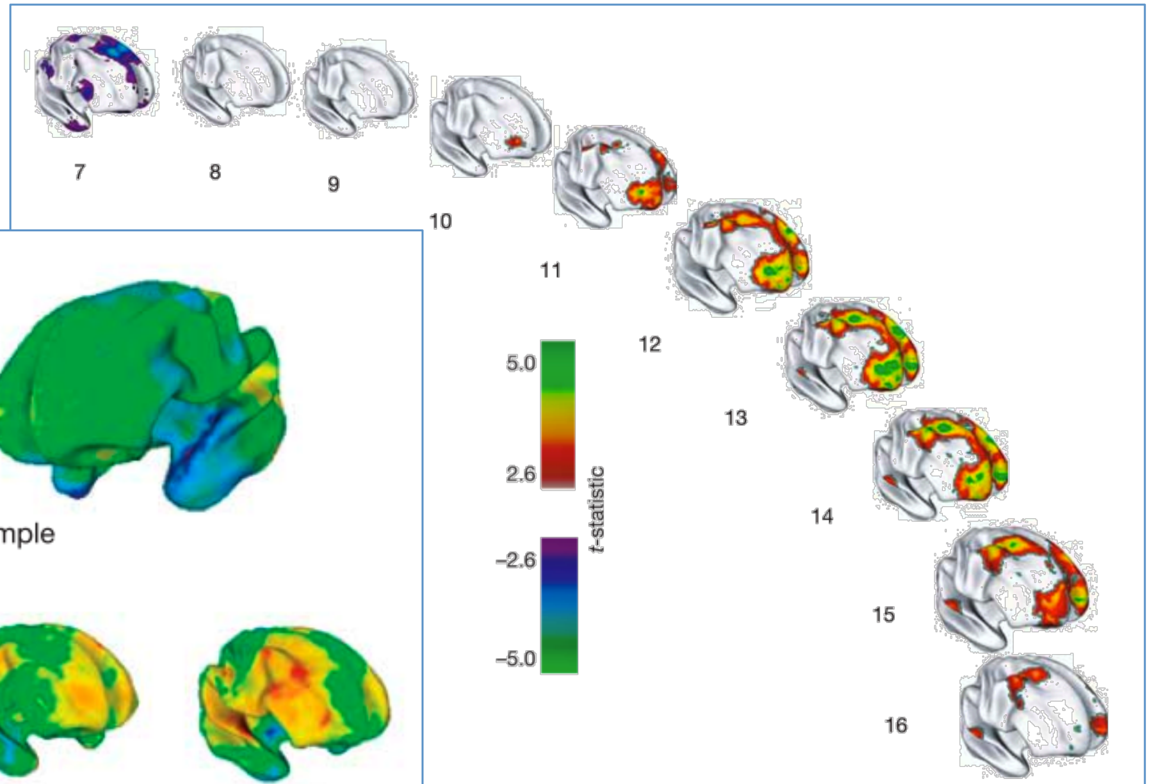


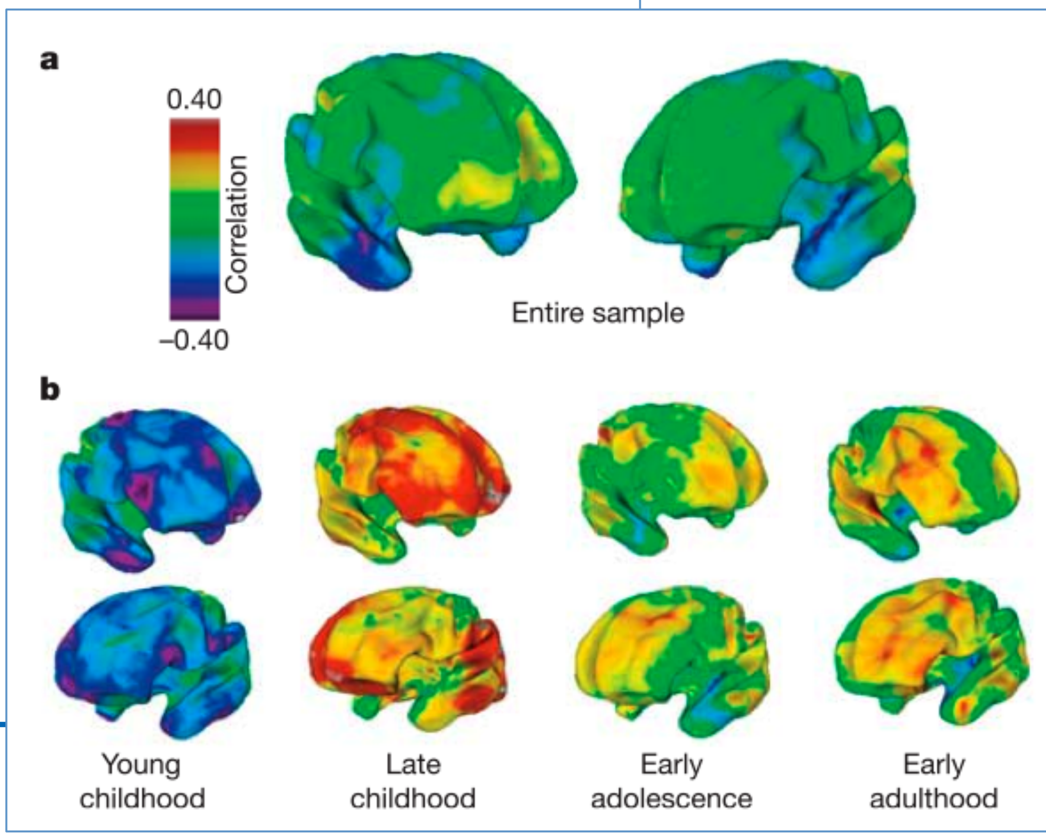


nature Vol 440|30 March 2006|doi:10.1038/nature04513

Intellectual ability and cortical development in children and adolescents

P. Shaw[1], D. Greenstein[1], J. Lerch[2], L. Clasen[1], R. Lenroot[1], N. Gogtay[1], A. Evans[2], J. Rapoport[1] & J. Giedd[1]

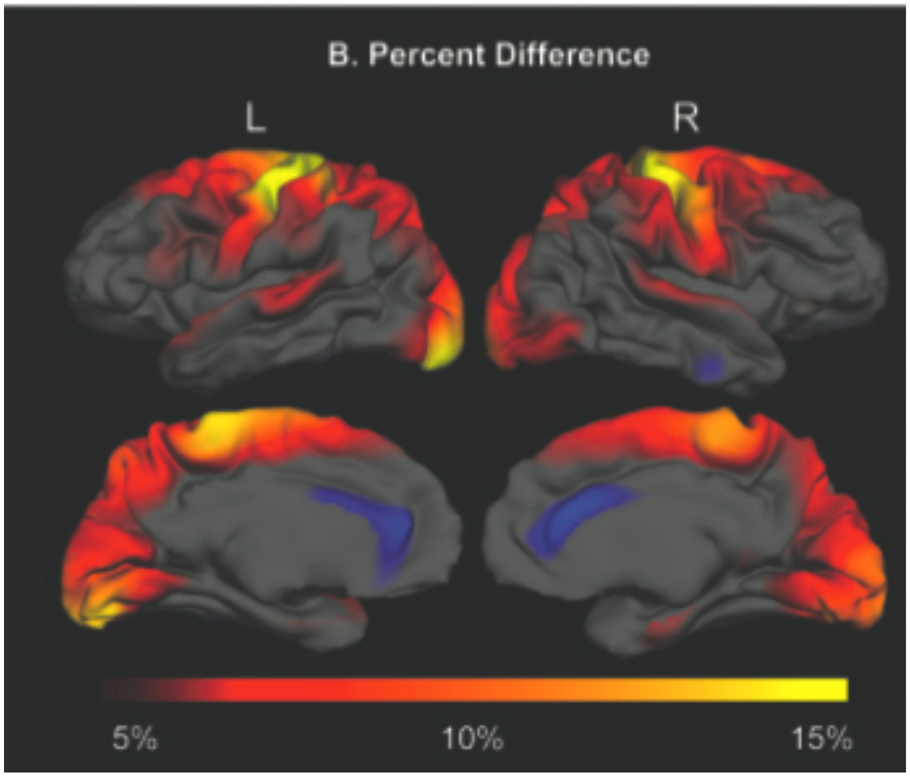




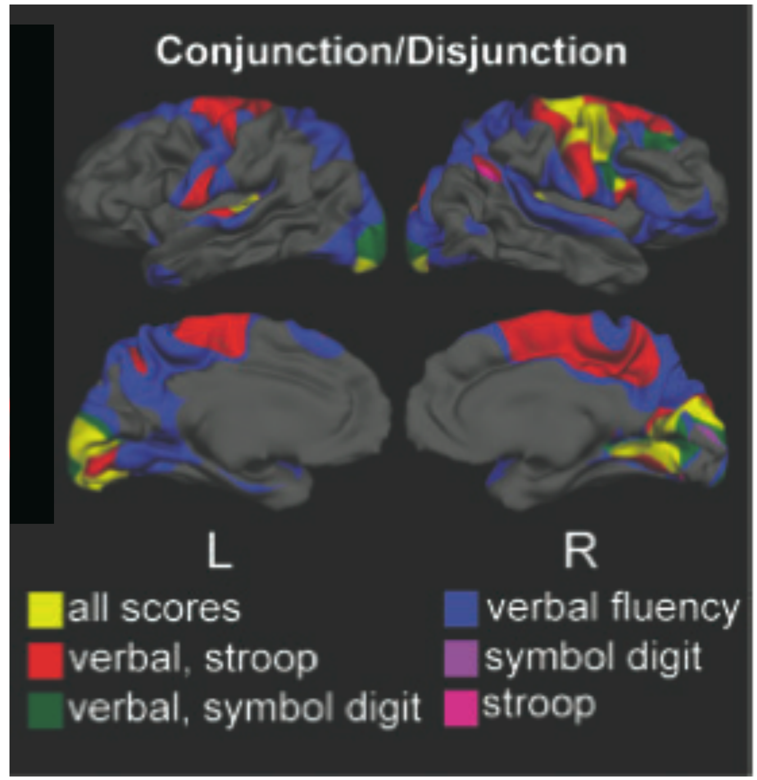
doi:10.1093/brain/awn025
Brain (2008), **131**, 1057–1068

Cerebral cortex and the clinical expression of Huntington's disease: complexity and heterogeneity

H. Diana Rosas,[1,2,3] David H. Salat,[2,3] Stephanie Y. Lee,[1,2,3] Alexandra K. Zaleta,[1,2,3] Vasanth Pappu,[1,2,3] Bruce Fischl,[3,4] Doug Greve,[3,4] Nathanael Hevelone[5] and Steven M. Hersch[1]



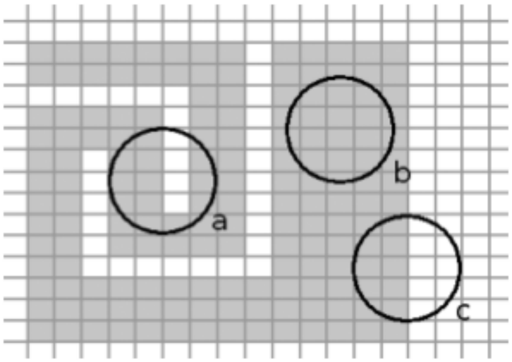
Cortical thinning

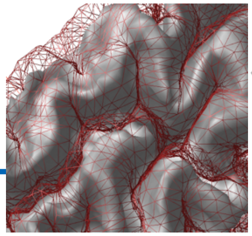


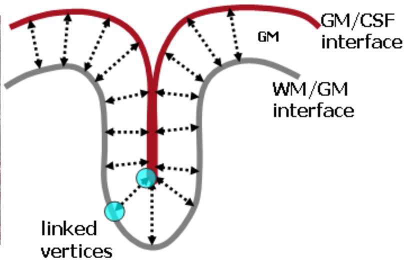
Correlation with cortical thinning

Existing Methods

- Cortical thickness ≠ Graymatter density
  - M Chung, TMI 2007, negatively correl.
- Major methods
  - BrainVoyager, Goebel
    - Commercialized, Brain Innovation
  - CLASP, Evans et al (MNI)
  - FreeSurfer, Fischl et al (MGH)
  - CRUISE, Tosun et al (JHU,UCLA,UCSF)



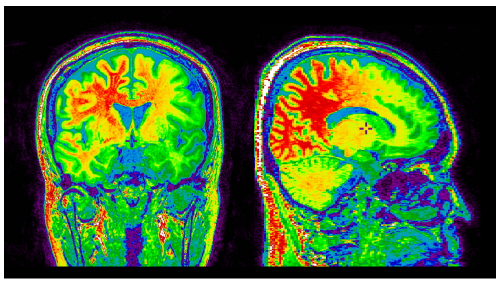


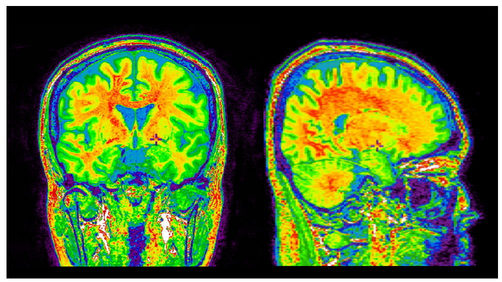


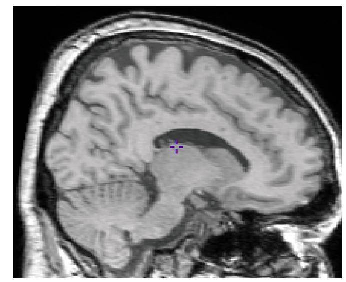
CLASP - MNI

- **Image preprocessing & Cortical surface extraction**

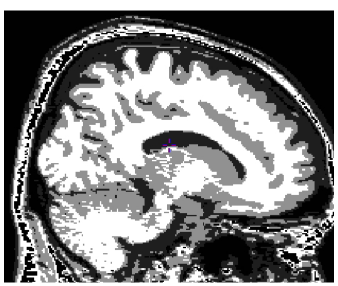
Native MR image → Intensity Non-uniformity Correction → Spatial Normalization to stereotaxic space →

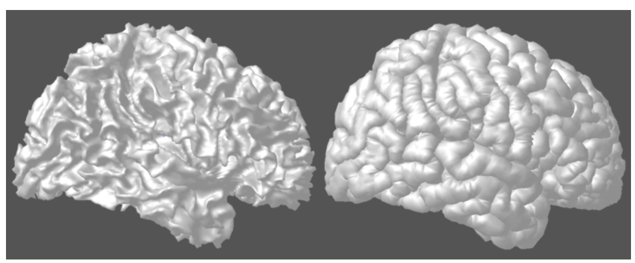


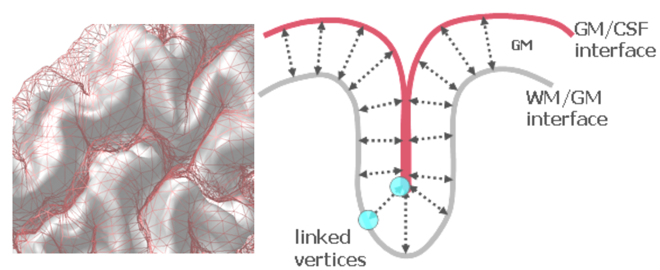




Tissue Classification → Cortical Surface Extraction (CLASP algorithm) → Cortical thickness measurement

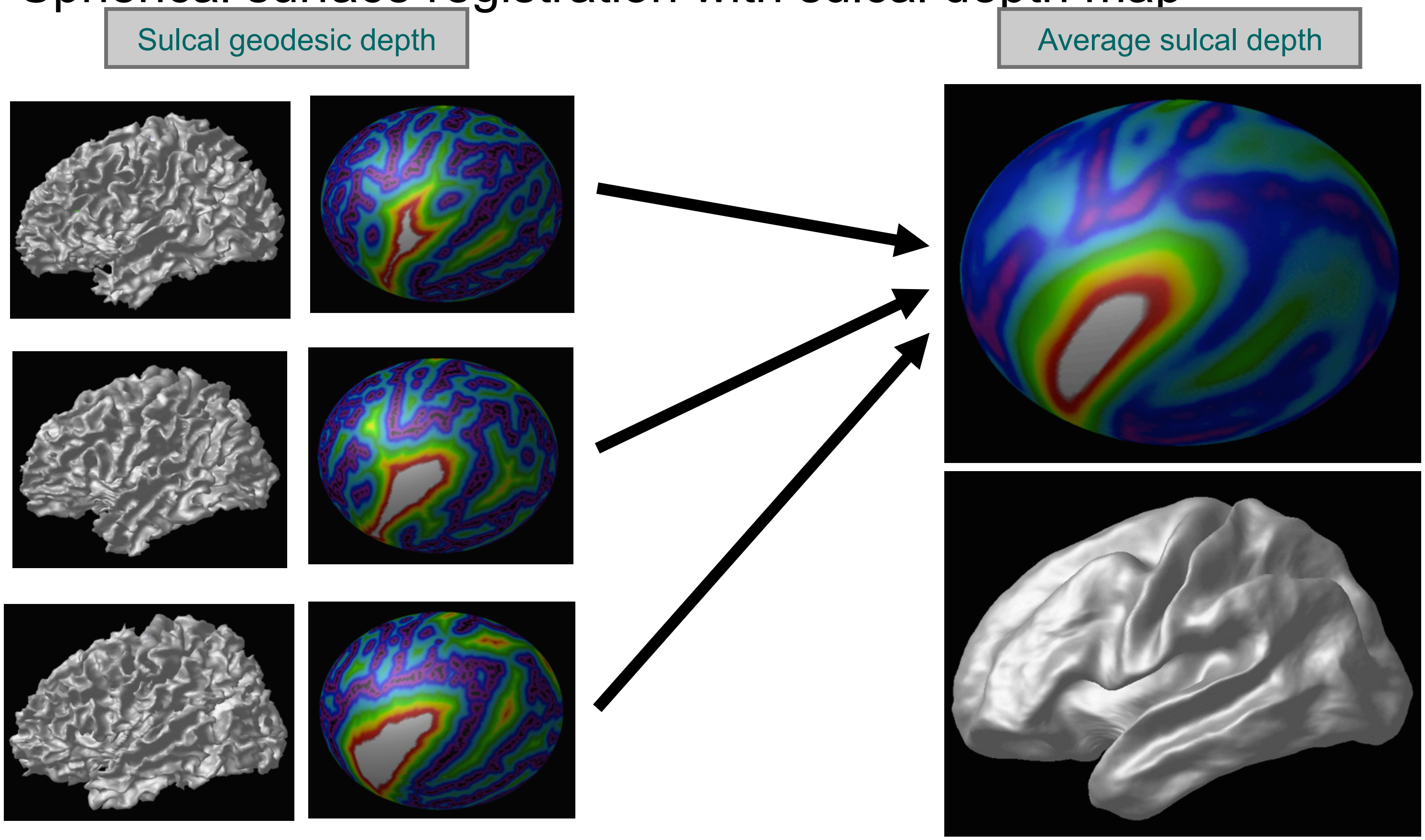






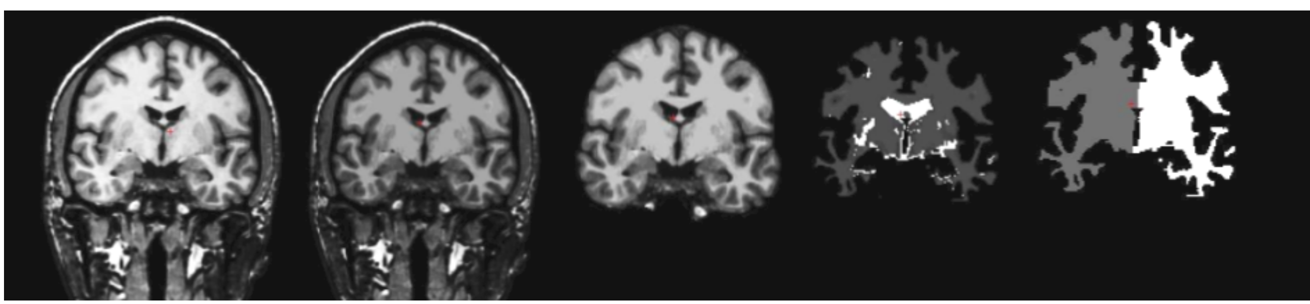
CLASP Correspondence

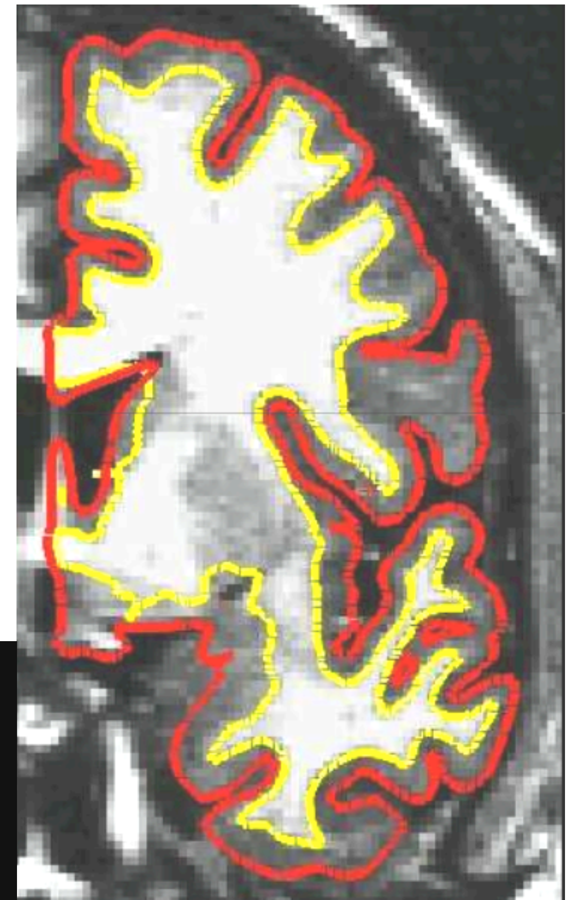
- Nonlinear registration on 2D sphere surfaces
- Spherical surface registration with sulcal depth map



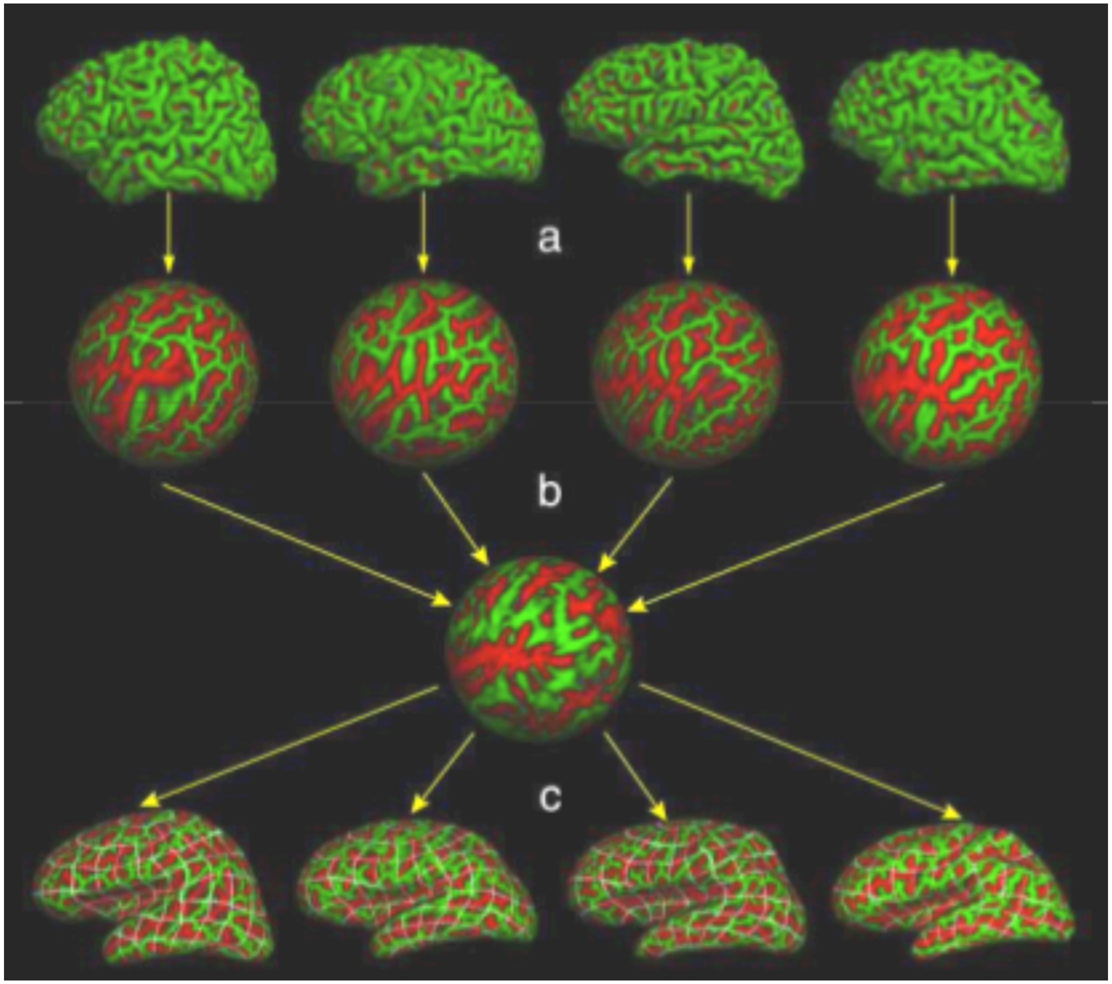
FreeSurfer

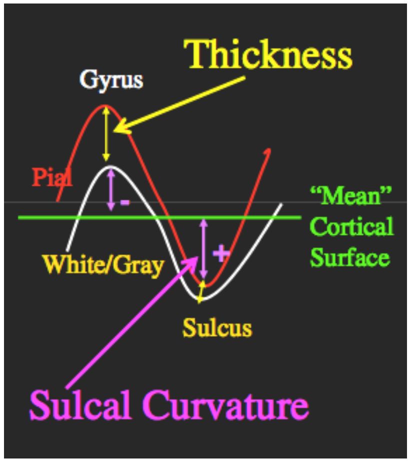
- Similar preprocessing
  - Different order of steps
- WM from segmentation and topology correction
- GM surface from evolution along T1 intensity gradient





FreeSurfer Correspondence



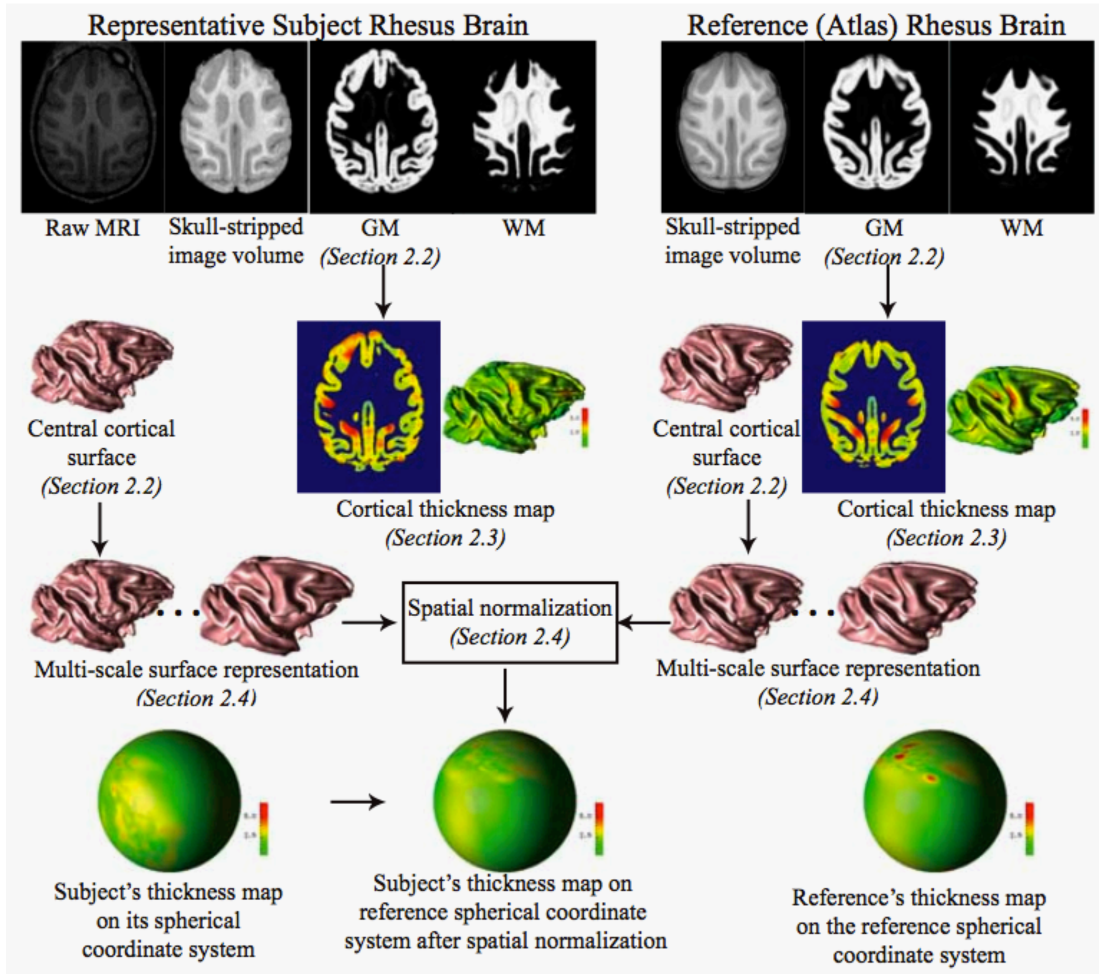


Sulcal depth

Surface registration to atlas

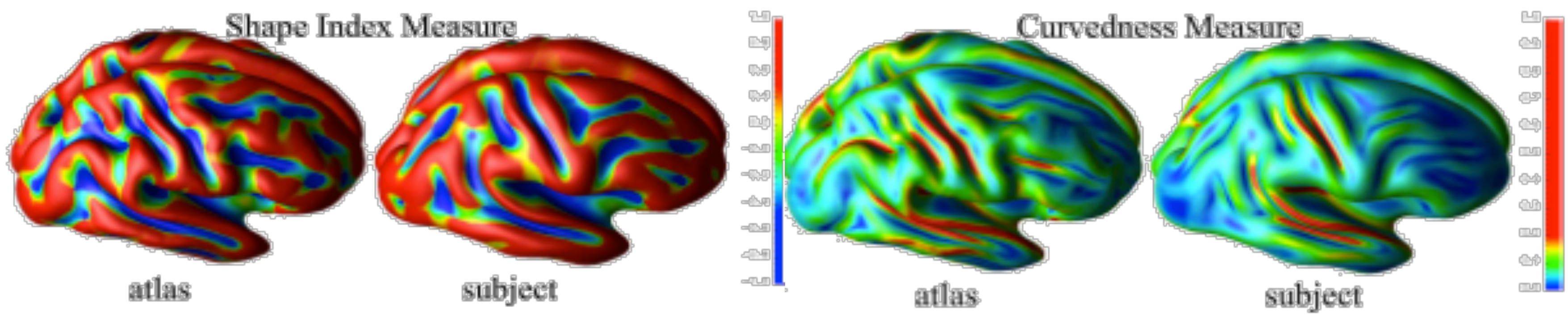
CRUISE Cortical Reconstruction Using Implicit Surface Evolution

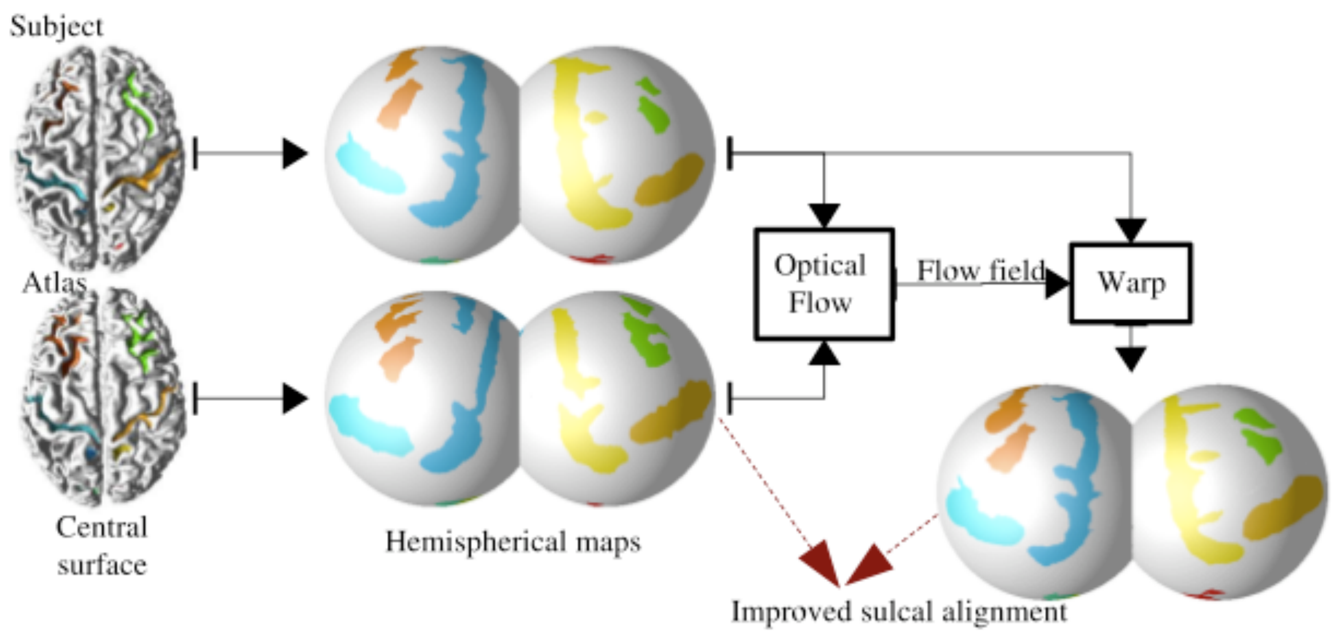
Laplacian based
Cortical Thickness



CRUISE Correspondence

Koenderink Shape Measures





Major Differences

- Cortical topology
  - Spherical topology needed?
  - During or After WM/GM segmentation
- Thickness measurement
  - Closest point, skeleton based, deformation based and laplacian solution based
- Cortical correspondence
  - Many based on sulcal depth based
  - But template? Population based? Parametrization? Uni vs Bi-hemispheric?

NAMIC Approach for CT

- 2 separate module pipelines

1. Regional/image based CT analysis:
   – Template based registration, simple but stable, good for regional analysis
2. Local/surface based CT analysis
   – Spherical topology, but tolerance against violations
   – Group-wise correspondence
   – Extensible generic framework that easily incorporates landmarks, connectivity, vessels, functional
   – Full framework in open source, NAMIC Kit

Regional CT – Pipeline

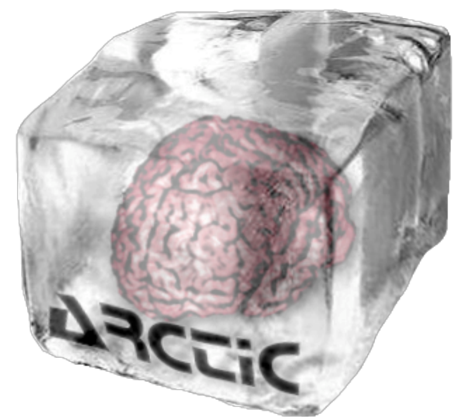
Slicer external module (loadable via extension manager)

ARCTIC (Automatic Regional Cortical ThICkness)

Input: raw data (T1-w, T2-w, PD-w images)

Three steps in the pipeline:

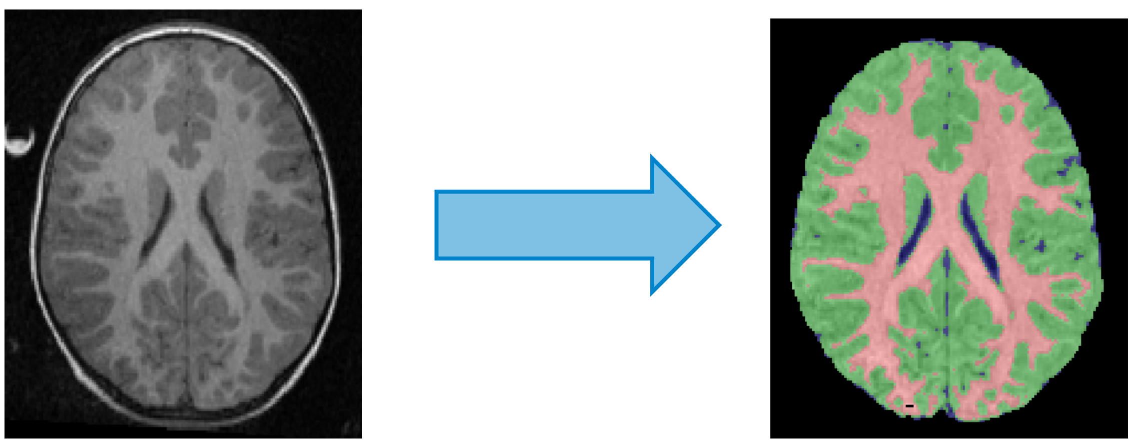
1. **Tissue segmentation**
2. **Regional atlas deformable registration**
3. **Cortical Thickness**



ARCTIC pipeline

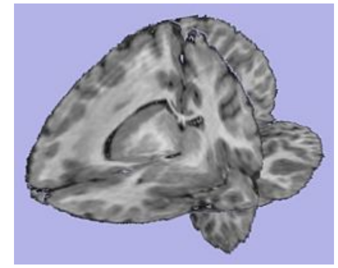
Step 1: Tissue segmentation

- Probabilistic atlas-based automatic tissue segmentation via an Expectation-Maximization scheme
- Tool: itkEMS or ABC (Automatic Brain Classification on NITRC, UNC & UUtah)



ARCTIC pipeline (2)

Step 2. Regional atlas deformable registration



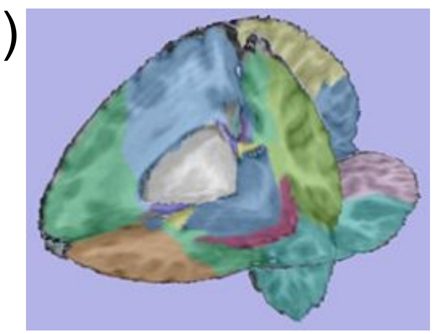
• **2.1** Skull stripping using previously computed tissue

segmentation label image

Tool: SegPostProcess (UNC Slicer3 external module)

•**2.2** T1-weighted atlas deformable registration using a B-spline pipeline registration

Tool: RegisterImages or BrainsFit (Slicer3 modules)



•**2.3** Applying transformation to the parcellation map

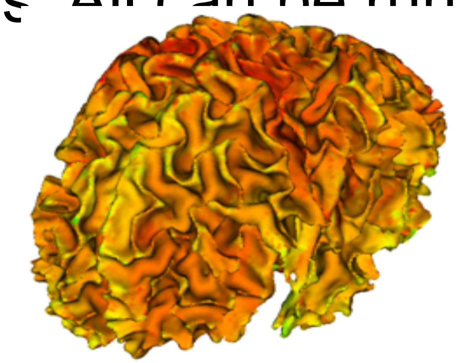
Tool: ResampleVolume2 (Slicer3 module)

ARCTIC pipeline (3)

Step 3. Cortical Thickness

- Sparse asymmetric local cortical thickness
- Uses distance map based local maxima to correct for CSF/GM errors (akin to skeleton based CT)
- Tool: CortThick (UNC Slicer3 module)

Note: All the tools used in the pipeline are Slicer3 modules, some of them being UNC external modules. All can be run as command line and thus are scriptable



ARCTIC Validation

ARCTIC vs. Freesurfer:

FreeSurfer's tutorial dataset consisting of 40 healthy subjects, ranging in age from 18 to 93, Pearson correlation of the mean lobar CT's

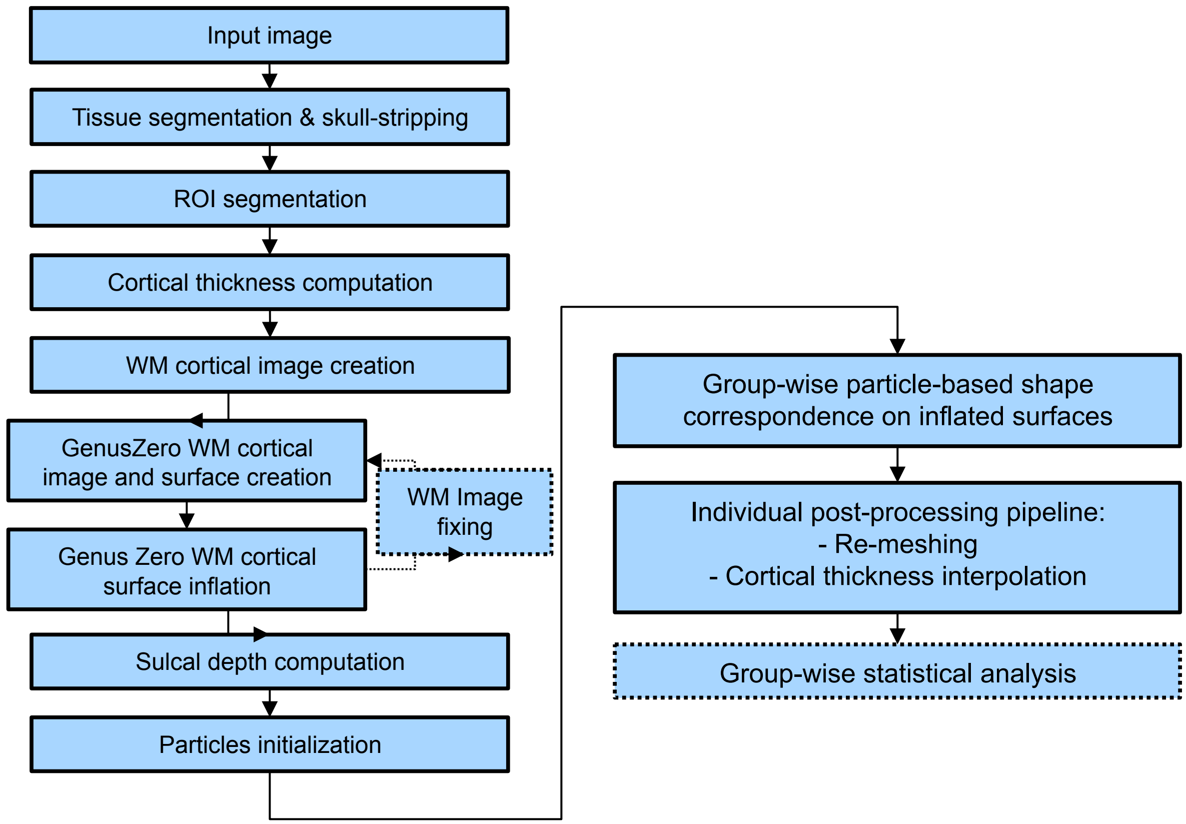
- As is: Good correlation for parietal lobe, other lobes $r < 0.7$
- When using Freesurfer's WM/GM segmentation: all lobes $r > 0.75$
- Also using Fressurfer's parcellation: all lobes $r > 0.85$

Longitudinal autism study of 86 subject aged 2-4 years.

- FreeSurfer low success: <40% without, <70% manual intervention
- ARCTIC: 98% success rate

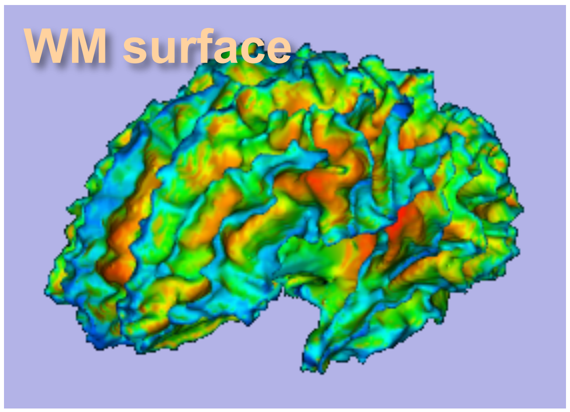
GAMBIT: local CT analysis

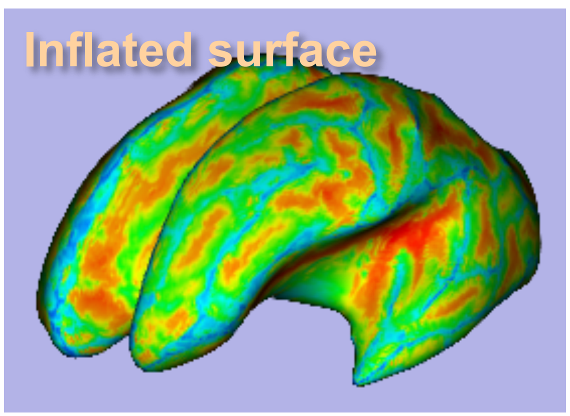
- Group-wise Automatic Mesh-Based Analysis of Cortical Thickness (GAMBIT)
- Similar processing to other local approaches



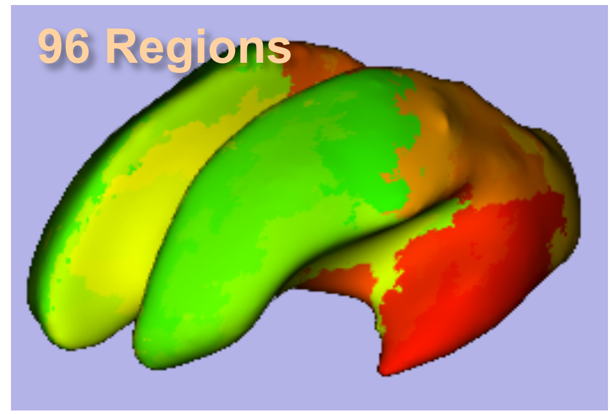
Inflation, Sulcal Depth and Particle Initialization

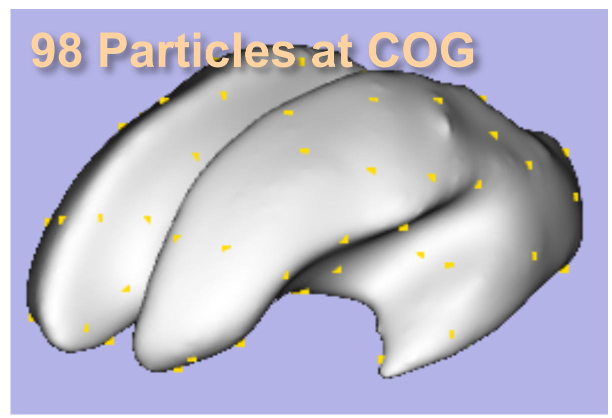
Sulcal Depthmap





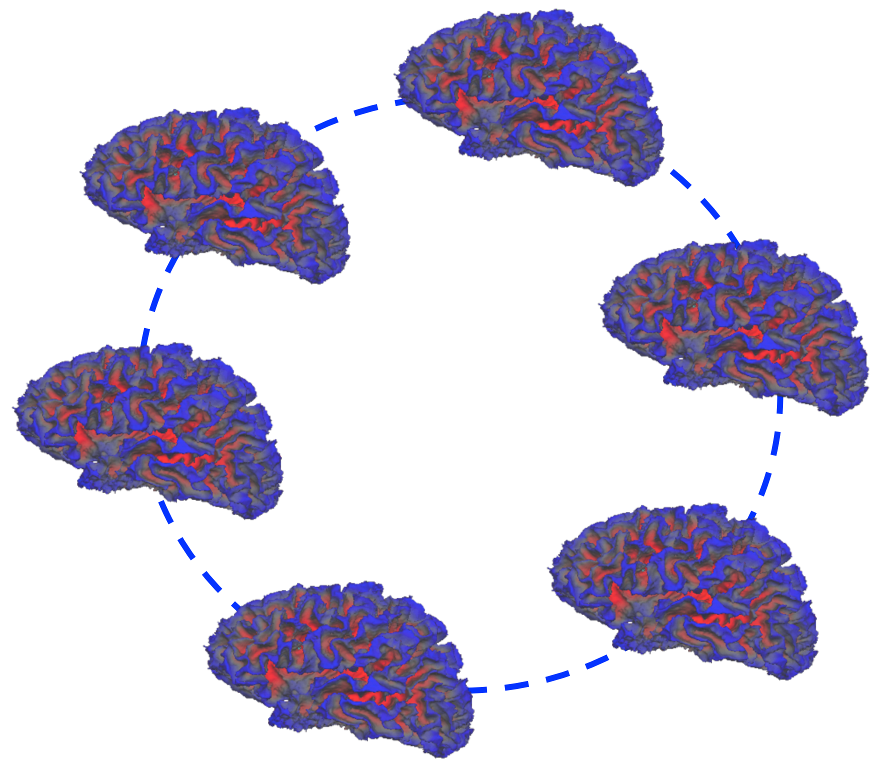
Particle Placement





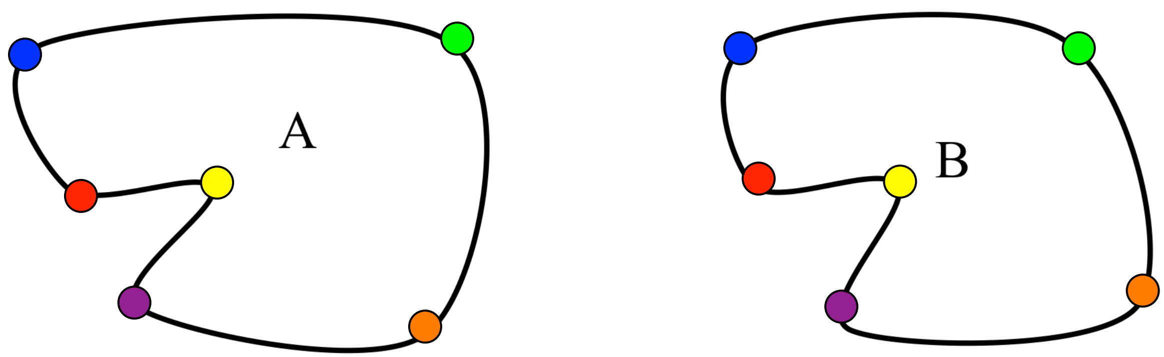
Group-wise Correspondence

- Template free
- Correspondence over all surfaces
- Minimum Description Length
  - Davies et al
  - Parametric framework
- Entropy: Oguz & Cates
  - UNC & Utah



Particle Approach (Cates)

- Point-based sampling of the surface
  - Same number of particles per shape
  - Very different from all other parametric approaches
- Particles are ordered
  - Ordering implies correspondence



Entropy Tradeoff

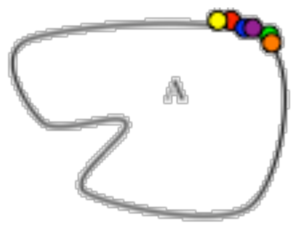
- Simultaneously maximize both the geometric accuracy and the statistical simplicity of the model

$$Q = \underbrace{H(Z)}_{\substack{\text{Ensemble entropy} \\ \text{(small = simple)}}} - \sum_k \underbrace{H(P^k)}_{\substack{\text{Surface entropy} \\ \text{(large = accurate)}}}$$

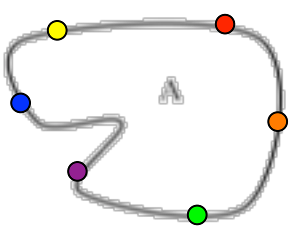
k: shape id
P: particle locations
Z: ensemble distribution

Surface Entropy

- High surface entropy
  - ⇔ uniform sampling of the surface
  - ⇔ high geometric accuracy



Low surface entropy

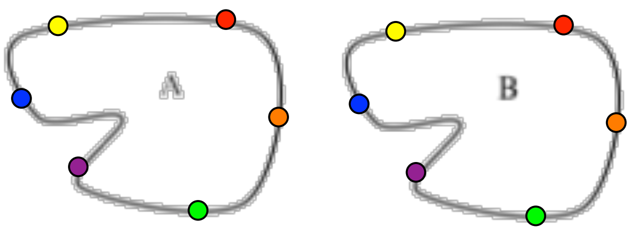


High surface entropy

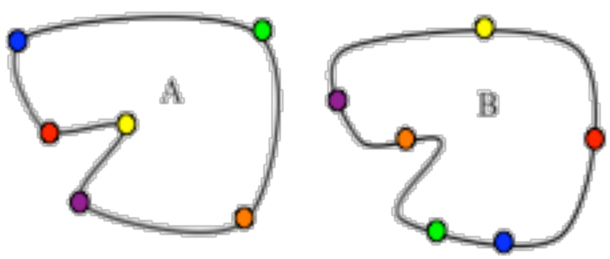
$$Q = H(Z) - \underbrace{\sum_k H(P^k)}_{\text{Surface entropy}}$$

Ensemble Entropy

- Low ensemble entropy
  - ⇔ high similarity of corresponding points
  - ⇔ statistically compact model



Low ensemble entropy



High ensemble entropy

$$Q = H(Z) - \sum_k H(P^k)$$

Ensemble entropy

Generic Local Model (Oguz)

- Allowing correspondence to depend on more than just position

$$\tilde{P} = f(x_j^k)$$

- Examples of "attributes" f(x)
  - Local curvature
  - Sulcal depth
  - DTI - probabilistic connectivity
  - MRA - distance to vessel

Incorporating attributes

$$Q = \boxed{H(Z)} - \boxed{\sum_k H(P^k)}$$

remains the same

- Corresponding particles across surfaces should have similar attribute values f(x)
- Particles should be evenly distributed on each surface

Ensemble entropy with attributes

- P = x
- Y is the matrix of particle **locations** minus the ensemble's sample mean

$$G(P) = \log \left| \frac{1}{M-1} Y^T Y \right|$$

$$-\frac{\partial G}{\partial P} = Y(Y^T Y + \alpha I)^{-1}$$

becomes

P = f(x)

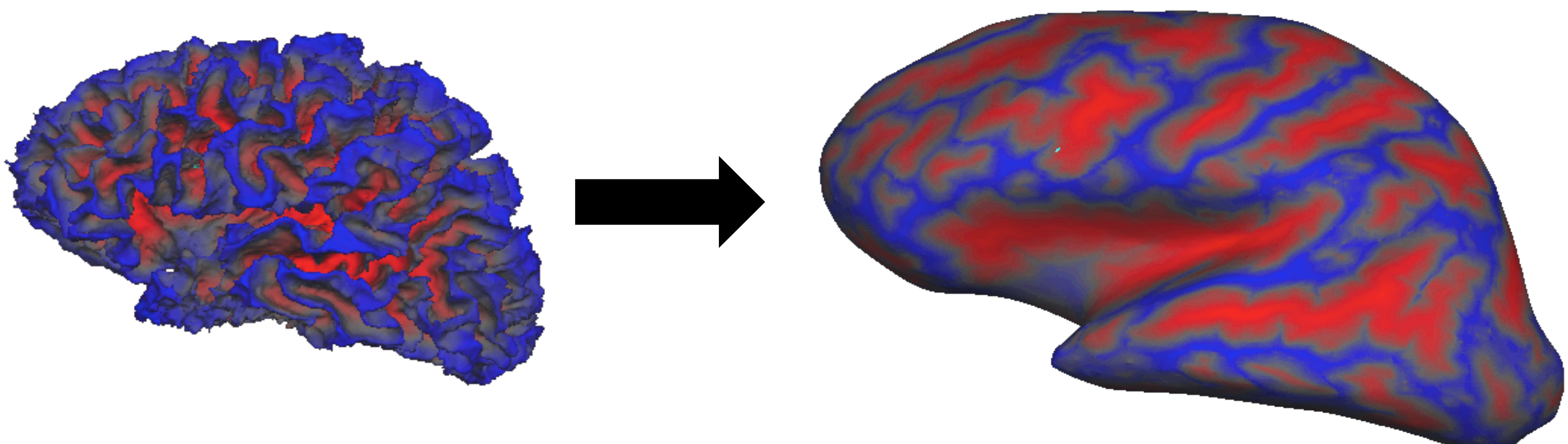
Y is the matrix of the function values at the particle points minus the means of those functions at the points

$$G(P) = \log \left| \frac{1}{M-1} Y^T Y \right|$$

$$-\frac{\partial G}{\partial P} = J^T (Y^T Y + \alpha I)^{-1}$$

Dealing with Cortical Geometry

- Highly convoluted surface is a problem
- Solution: Inflate the brain
  - Convex move inwards, concave move outwards
  - Minimizes metric distortion



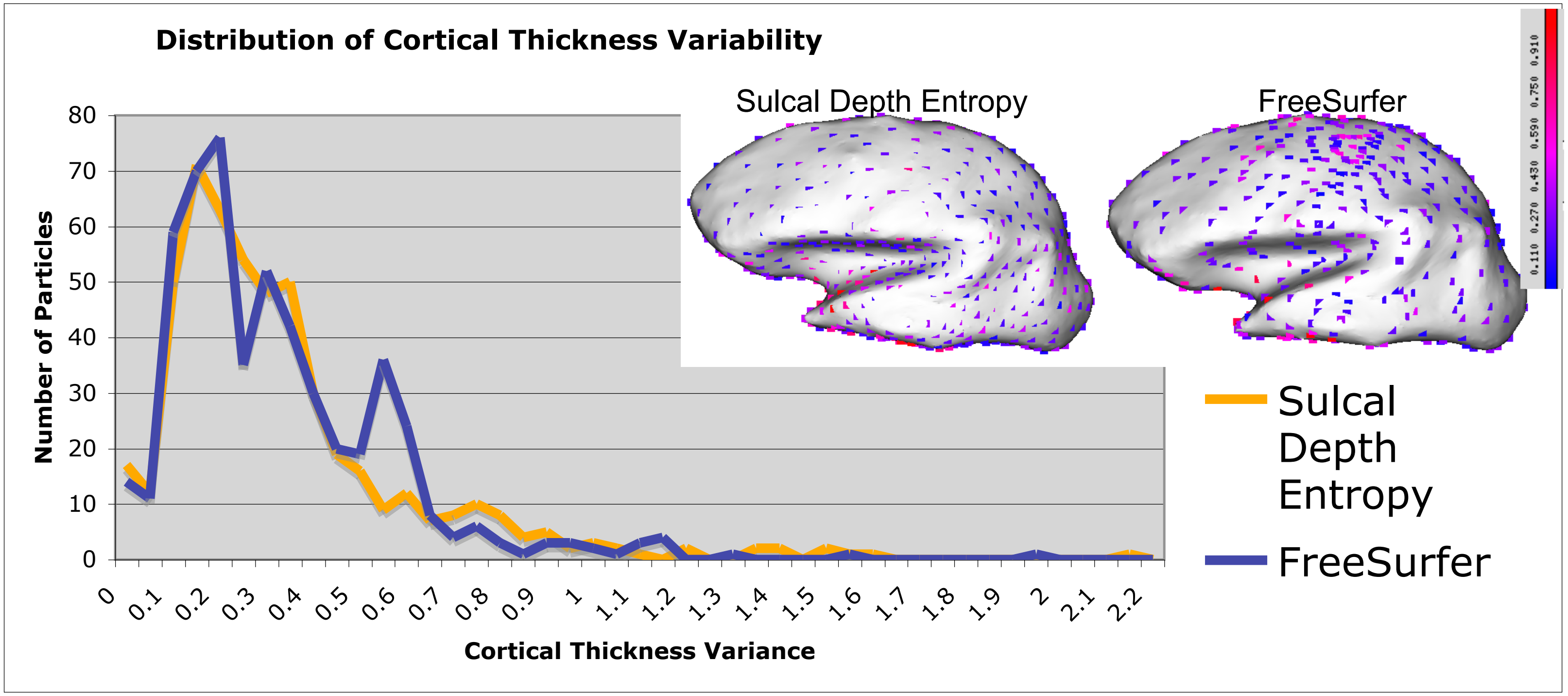
Color map: sulcal depth (integral of the motion along the normal)

Experiments

- 9 healthy subjects
- Correspondence metric: sulcal depth
- Reduction of sulcal depth variance

	Sulcal Depth	Cortical Thickness
Initial Data	0.227634	0.334858
XYZ-entropy	0.219627	0.341715
SulcalDepth-entropy	0.00346167	0.310751
FreeSurfer	0.075644	0.303376

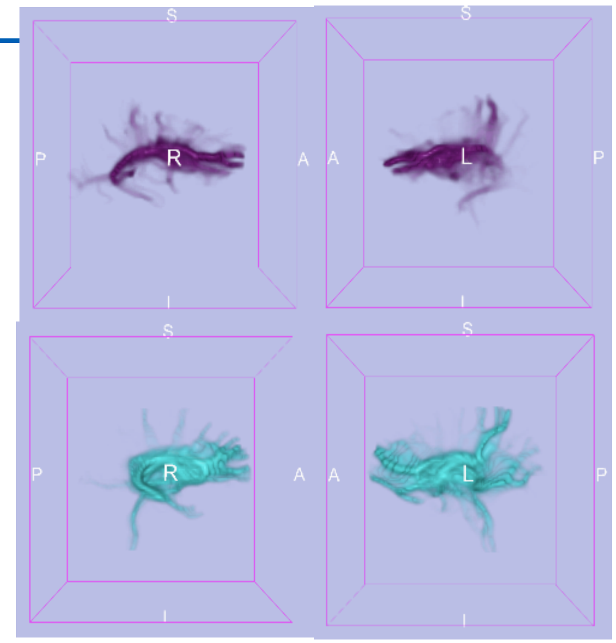
Localization of variance

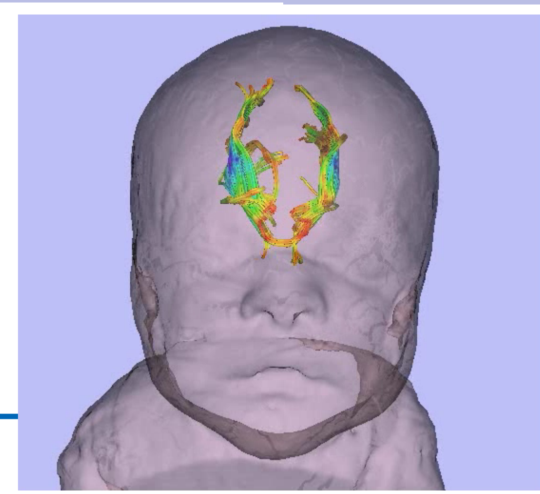


- Color map: Local variance of cortical thickness
- Entropy method has high error only in small patch

DTI Incorporation

- Add probabilistic connectivity to ROI's
  - Incorporating fiber structure from DWI
  - Projecting tractography results to the white matter surface
  - Multiple cortical connectivity maps
    - CC, caudate, brainstem…





Open Source Framework

- All BSD style open source
- Slicer external modules for all individual steps
- Slicer external "super" module
  - Generates and run BatchMake script that calls steps
  - Can be run local or on grid
- Brand-new, methods paper published
- Regional CT: First study papers in review

Discussion & Future Work

- Cortical thickness
  - Important for neuroimaging studies
    - Critical gray matter development
  - Many tools, get better and better
  - NAMIC cortical thickness
- Next steps
  - Full Framework, testing, tutorials
  - Lots of studies
  - Cortical thickness in rodents