Workshop on Geometry and Shape Analysis in Biological Science

Institute for Mathematical Sciences

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Applications of Conformal Geometry in Brain Mapping & Computational Anatomy

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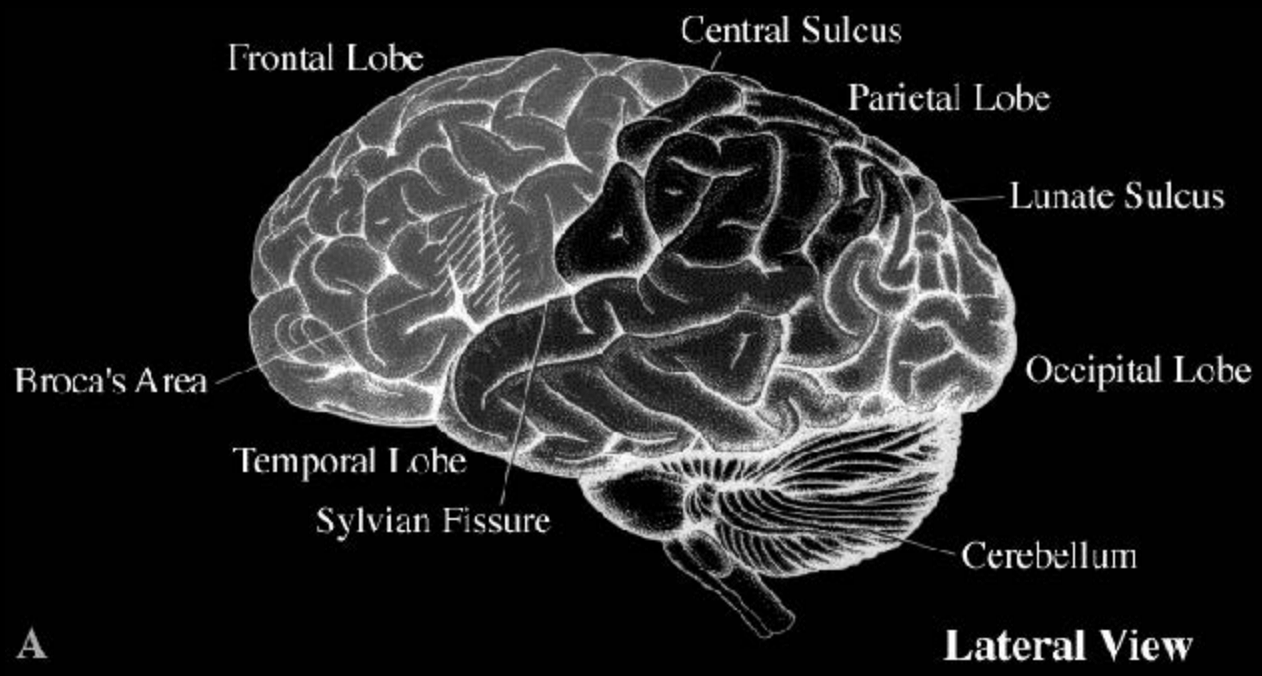
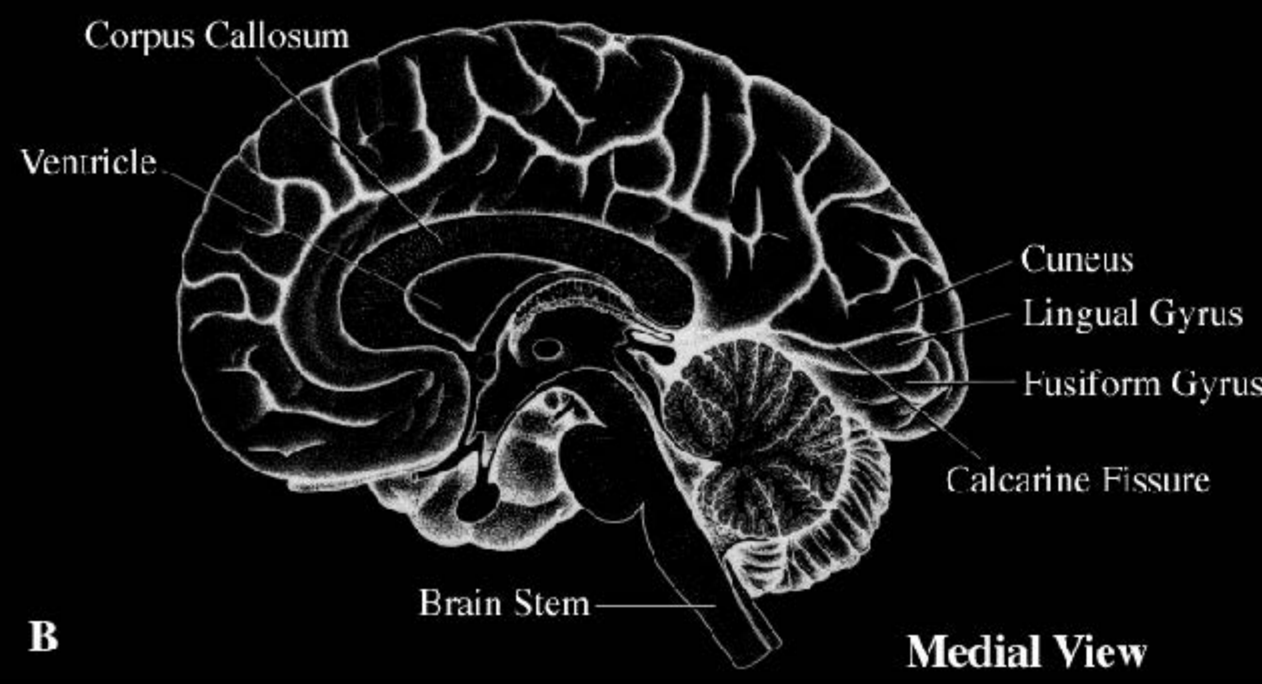
The Human Brain





Cortical Flat Maps of the Brain

- Functional processing mainly on cortical surface
- 2D analysis methods desired: **Cortical Flat Maps**
- Metric-based approaches (i.e. area or length preserving maps) will always have distortion
- Conformal maps offer a number of useful properties including:
  - mathematically unique
  - different geometries available
  - canonical coordinate system

Potential Advantages of Brain Flat Maps

- Cortical flat maps facilitate the determination and analysis of spatial relationships between different cortical regions
- Definition of coordinate system on cortical surface
- Comparison of individual differences in cortical organization or in functional foci
  - identify/quantify specific regions where diseases occur
  - analysis of regions buried within sulci
- Visualization of cortical folding patterns

“Flattening” Surfaces and Conformal Mapping

- By a “flat” surface, we mean a surface of constant curvature:
  - Euclidean plane (identified with the complex plane), $R^2 = C = \{z = x + iy: x, y \in R\}$
  - the unit disc in $C = D = \{(x,y): x^2 + y^2 < 1\}$
  - the unit sphere $S = \{(x,y,z): x^2 + y^2 + z^2 = 1\} \subset R^3$
- Why Conformal? Impossible to flatten a surface with intrinsic curvature without introducing metric or areal distortions: “Map Maker’s Problem” BUT we can preserve angles => ***Conformal Maps***

Uniformization Theorem (1880s)

- Generalization of the Riemann Mapping Theorem (1851)

There exists a unique conformal mapping (up to conformal automorphisms) from a Riemann surface to the Euclidean plane, hyperbolic disc or sphere.

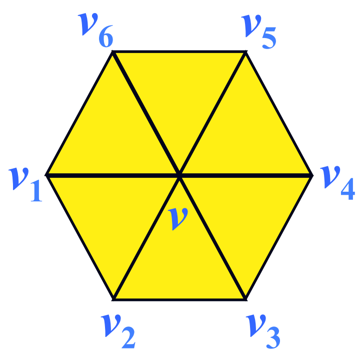
Conformal Maps Exist

and are

Mathematically Unique!

Discrete Conformal Mapping

Given a triangulated mesh: angle sum Θ at a vertex v is sum of angles from triangles emanating out of v.



$$\Theta = \sum_{i=1}^{n} \theta_i$$

The angle at a vertex in original surface maps such that it is the Euclidean measure rescaled so the total angle sum measure is 2π.

In the discrete setting, this corresponds to preserving angle proportion: an angle θ_i at a vertex v in original surface has angle $2\pi\theta_i / \Theta$ in mapping to the Euclidean plane.

Conformal Mapping Methods

Numerical Methods

- PDE methods for solving Cauchy-Riemann equations
- Harmonic energy minimization for solving Laplace-Beltrami equation
- Differential geometric methods based on approximation of holomorphic differentials

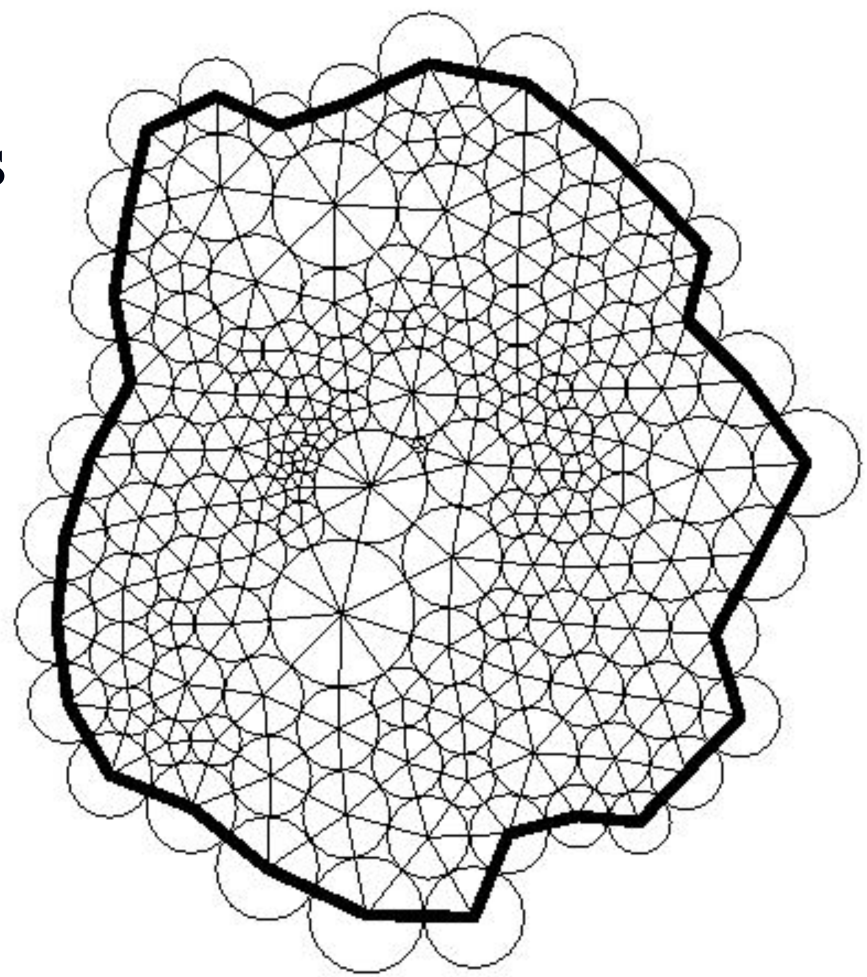
Circle Packing Method

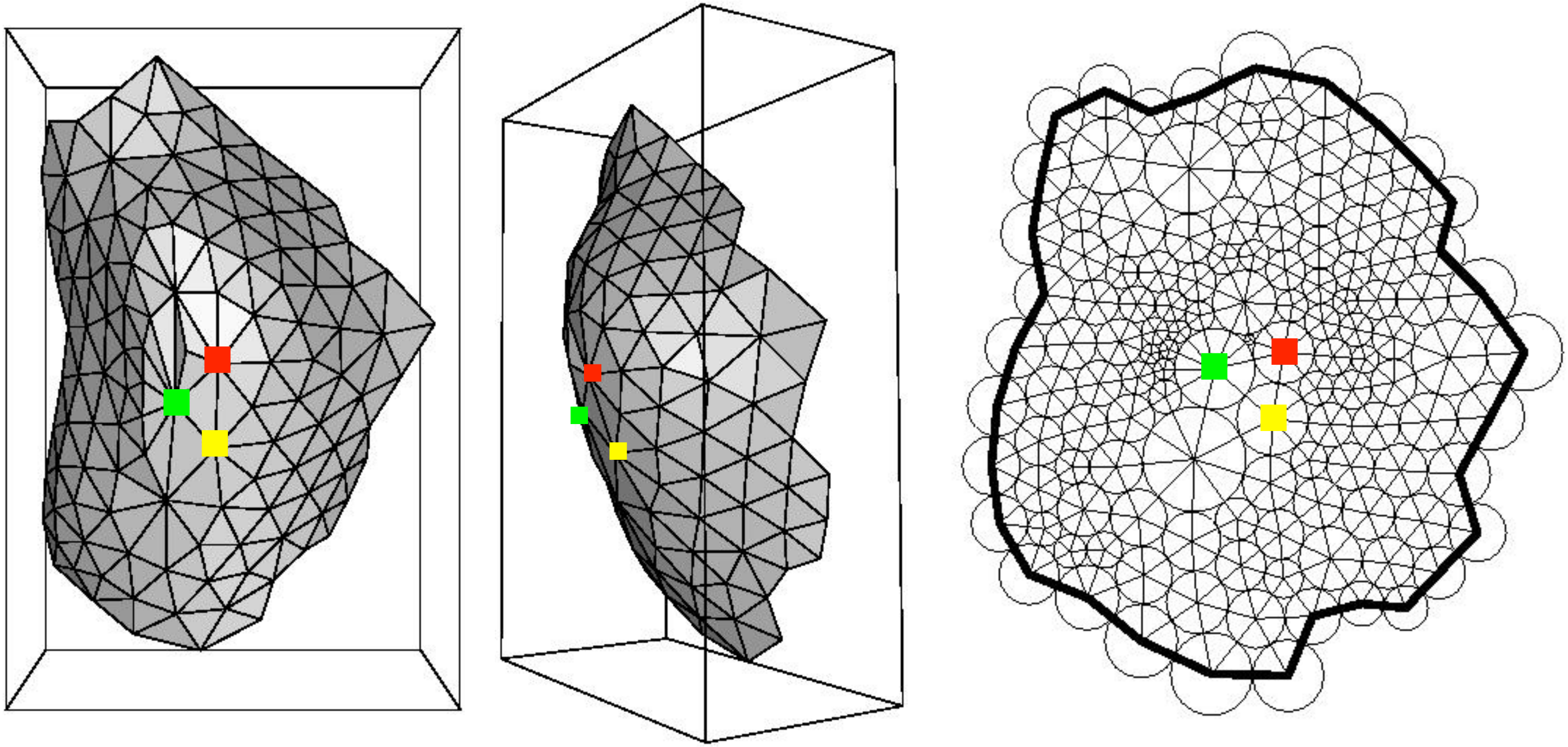
- Circle packing computed to find conformal map

Discrete Conformal Mapping with Circle Packings

Collaboration with Ken Stephenson, Mathematics, U. Tennessee, Knoxville

- A circle packing is a configuration of circles with a specified pattern of tangencies
- Theoretical, computational developments use circle packings to approximate a conformal mapping
- Circle Packing Theorem & Ring Lemma guarantee **this circle packing is unique and quasi-conformal**





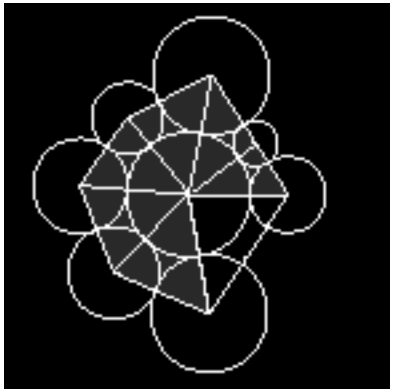
Given a simply-connected triangulated surface:

- represent each vertex by a circle such that each vertex is located at the center of its circle
- if two vertices form an edge in the triangulation, then require their corresponding circles must be tangent in the final packing
- assign a positive number to each boundary vertex

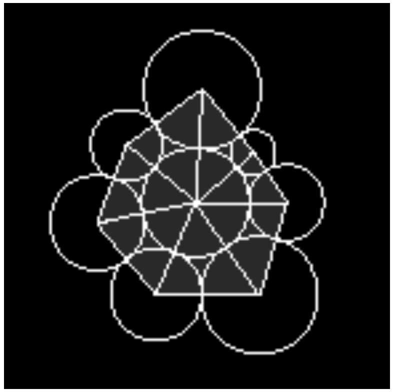
The (Euclidean) Algorithm

- Iterative algorithm has been proven to converge
- Surface curvature is concentrated at the vertices
- A set of circles can be "flattened" in the plane if the angle sum around a vertex is 2π
- To "flatten" a surface at the interior vertices:

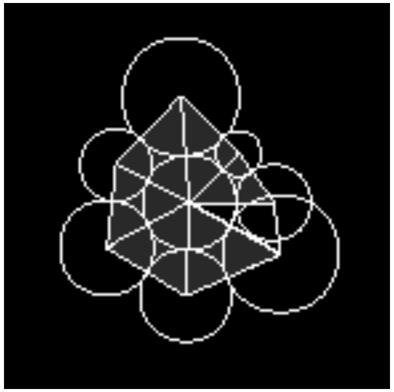
Positive curvature or cone point (angle sum $< 2\pi$)



Zero curvature (angle sum $= 2\pi$)

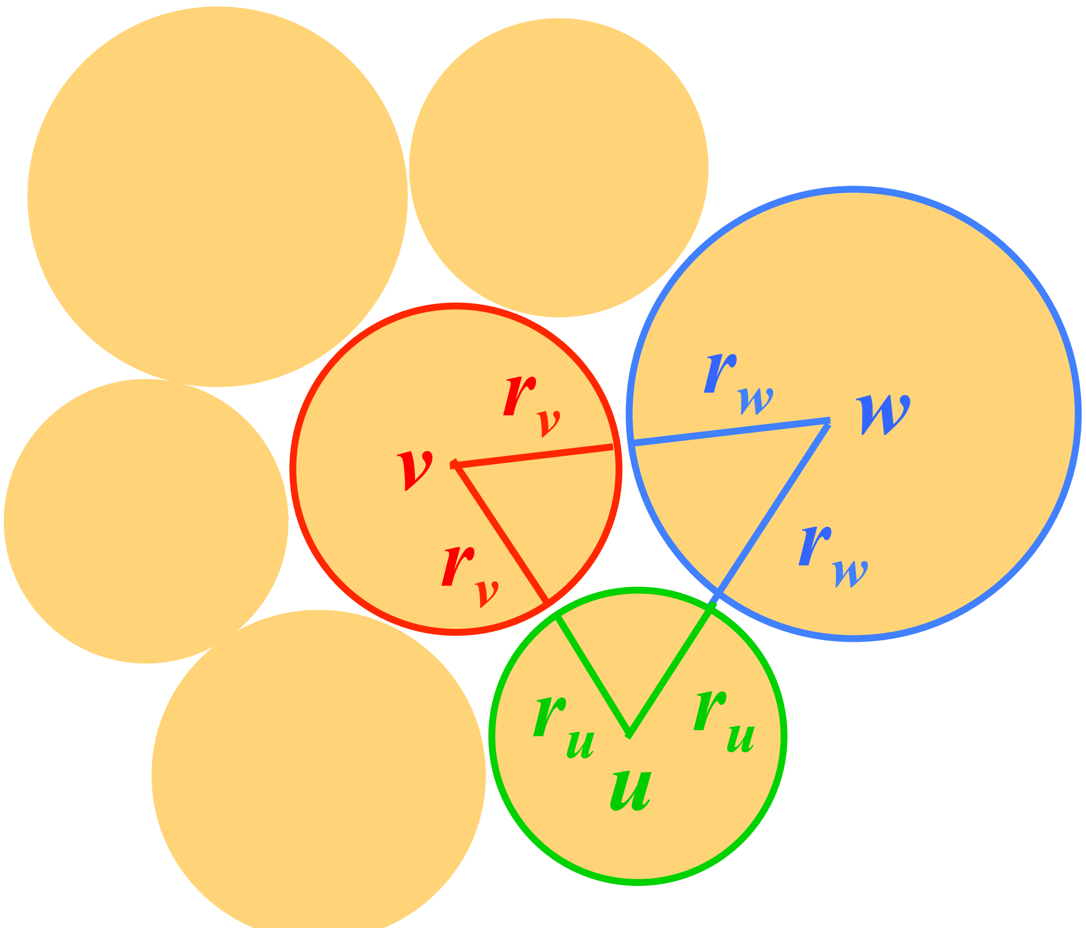


Negative curvature or saddle point (angle sum $> 2\pi$)



For all faces $\langle v,u,w \rangle$ containing vertex v:

$$\sum_{\langle v,u,w \rangle} \arccos\left\{\frac{(r_v+r_u)^2+(r_v+r_w)^2-(r_u+r_w)^2}{2(r_v+r_u)(r_v+r_w)}\right\}=2\pi$$



The Algorithm (Continued)

- This collection of tangent circles is a circle packing and gives a new surface in $\mathbb{R}^2$ which is our quasi-conformal flat mapping
- Easy to compute the location of the circle centers in $\mathbb{R}^2$ once the first 2 tangent circles are laid out
- Each circle in the flat map corresponds to a vertex in the original 3D surface
- Similar algorithm exists for hyperbolic geometry
- No known spherical algorithm: use stereographic projection to generate spherical map
- **NOTE:** A packing only exists once all the radii have been computed!
- Theorem (Bowers-Stephenson): This scheme converges to a conformal picture of the triangulation with repeated hexagonal refinement of the triangulation and repacking

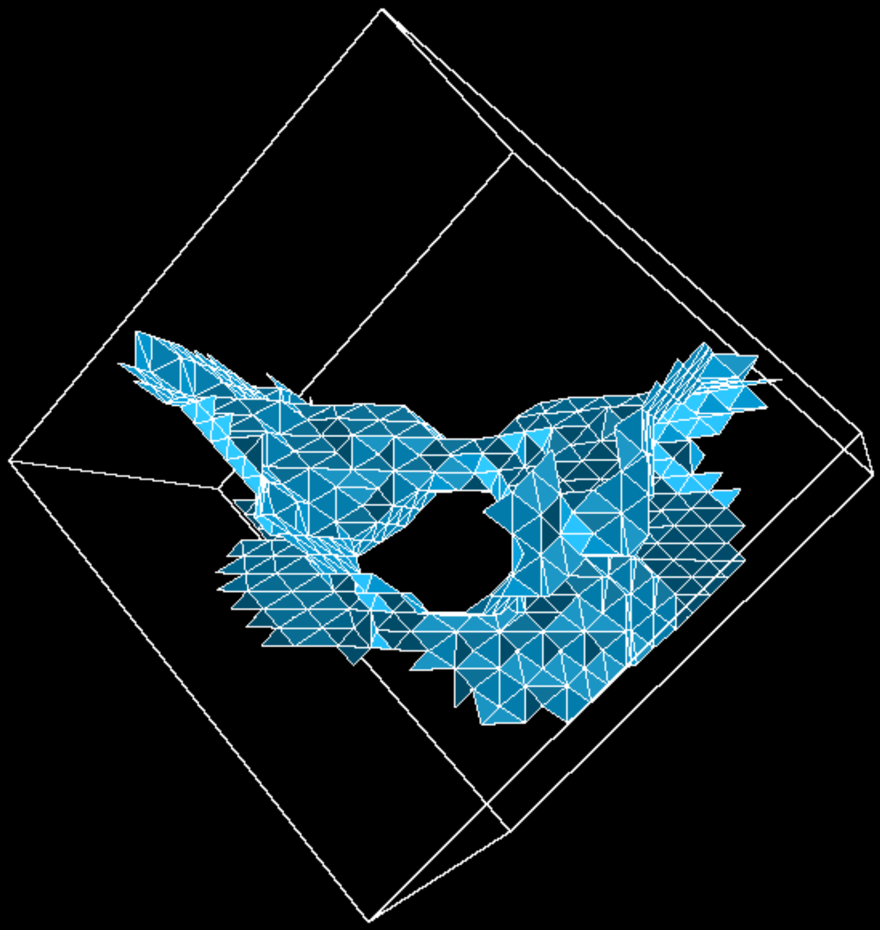
Creating a Cortical Surface

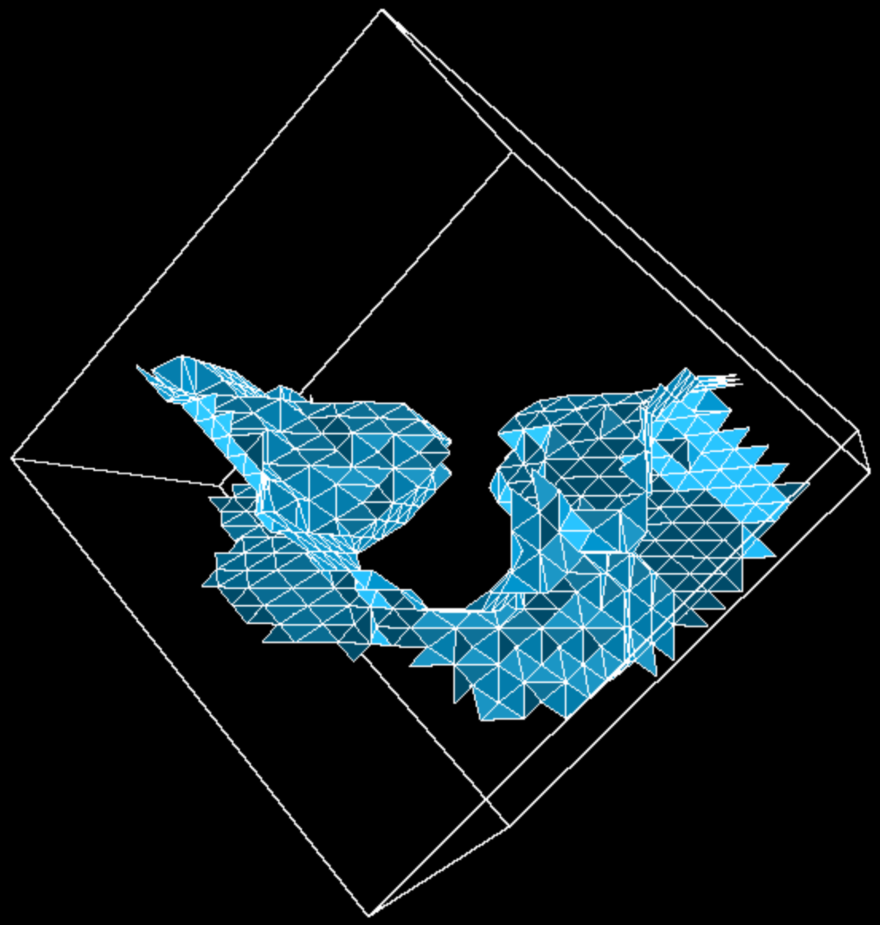
- MRI volume stripped of extraneous regions (i.e. scalp, skull, csf) to leave the region of interest (ROI)
- Resulting volume smoothed and a surface reconstruction algorithm, such as marching cubes applied to produce a triangulated mesh representing the surface of the brain
- The human brain is topologically equivalent to an orientable, 2-manifold (ie. a sphere)
- A boundary may be introduced by introducing cuts to make the brain topologically equivalent to a closed disc
- **Problem:** Many surface reconstruction algorithms produce a surface with topological problems - these must be fixed
- If a surface is topologically correct, then it is a topological sphere if and only if Euler characteristic $= v - e + f = 2$

Topological Surface Problems

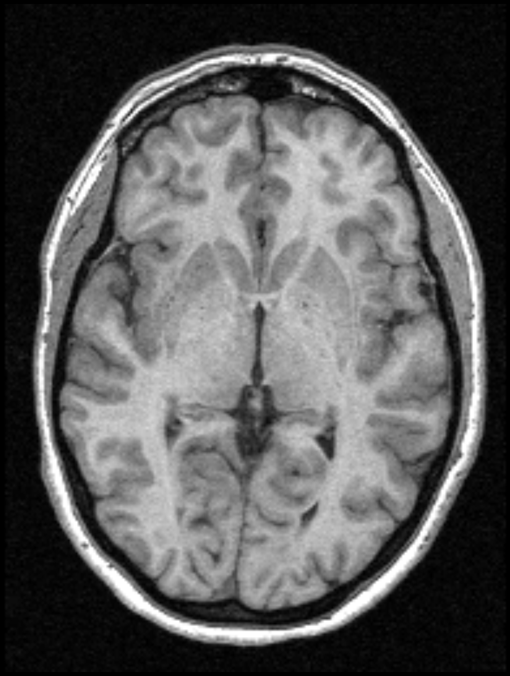
- **Unused vertices:** vertices not forming a triangle
- **Duplicate triangles:** repeated triangles
- **Edge problems:** walls, ridges, bubbles, holes
- **Surface connectedness:** only one surface
- **Triangle orientation:** all counter clockwise
- **Vertex singularity:** pinched surface
- **Handles**
  - very difficult problem
  - each handle contributes -2 to the Euler characteristic
  - need to find handle: cut and cap ends or fill

Fixing Handles

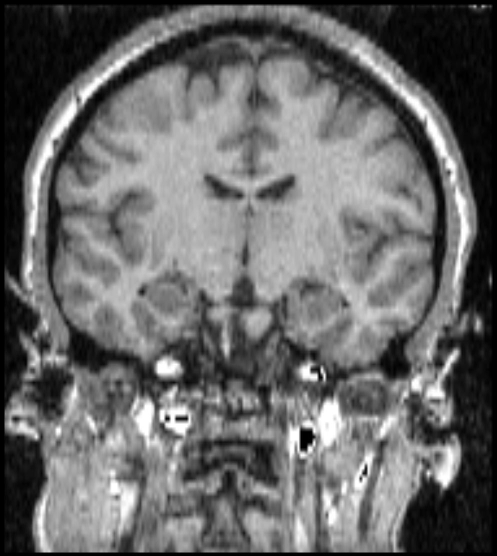




Magnetic Resonance Imaging (MRI)



Axial Slice

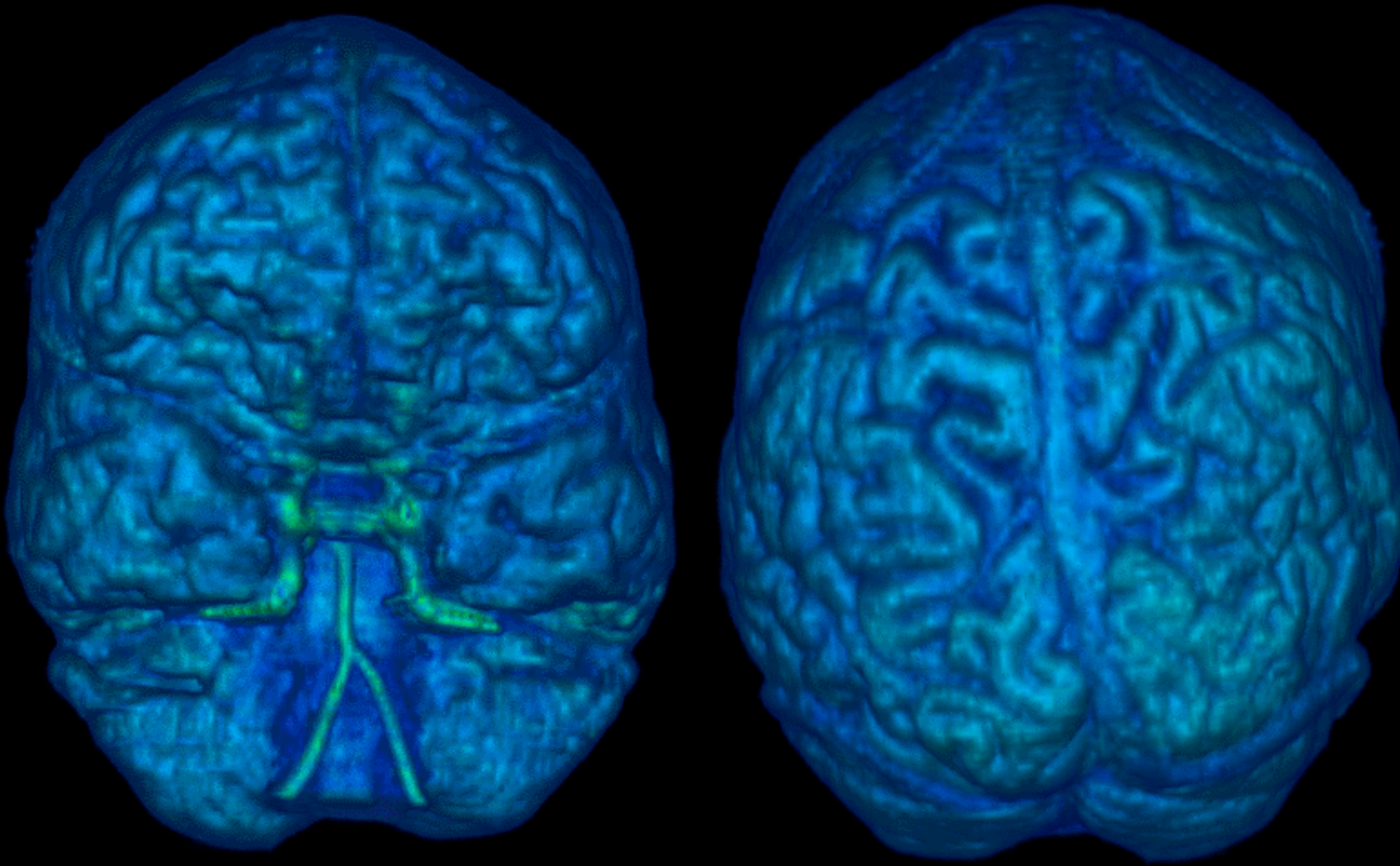


Coronal Slice

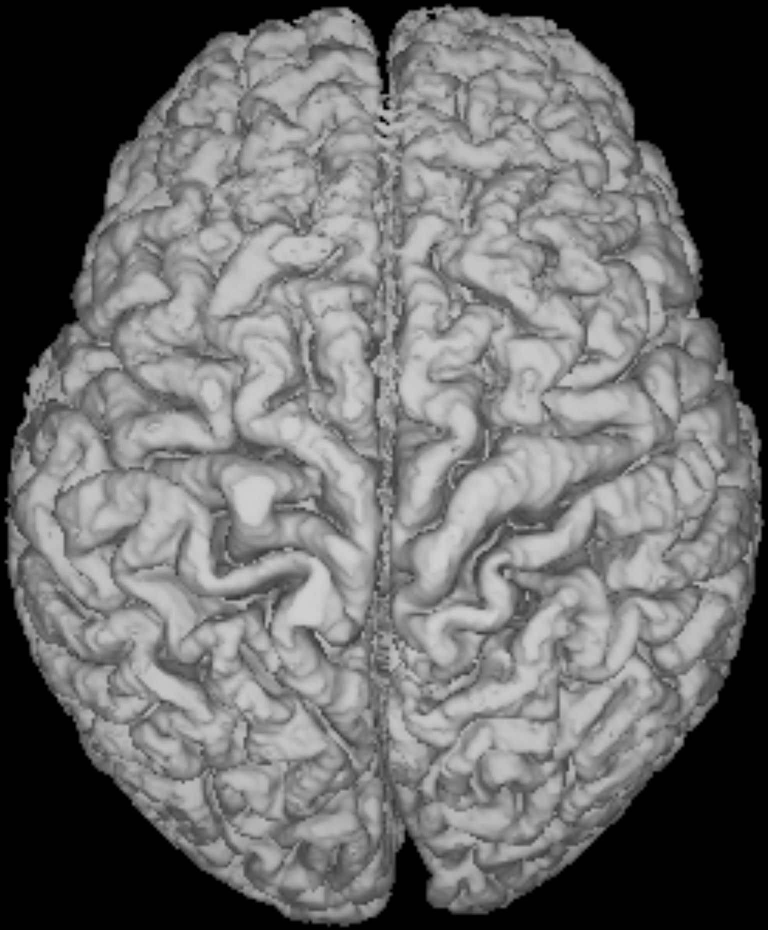
Sagittal Slice

Reconstruction of MR Images

Neural Tissue Reconstruction

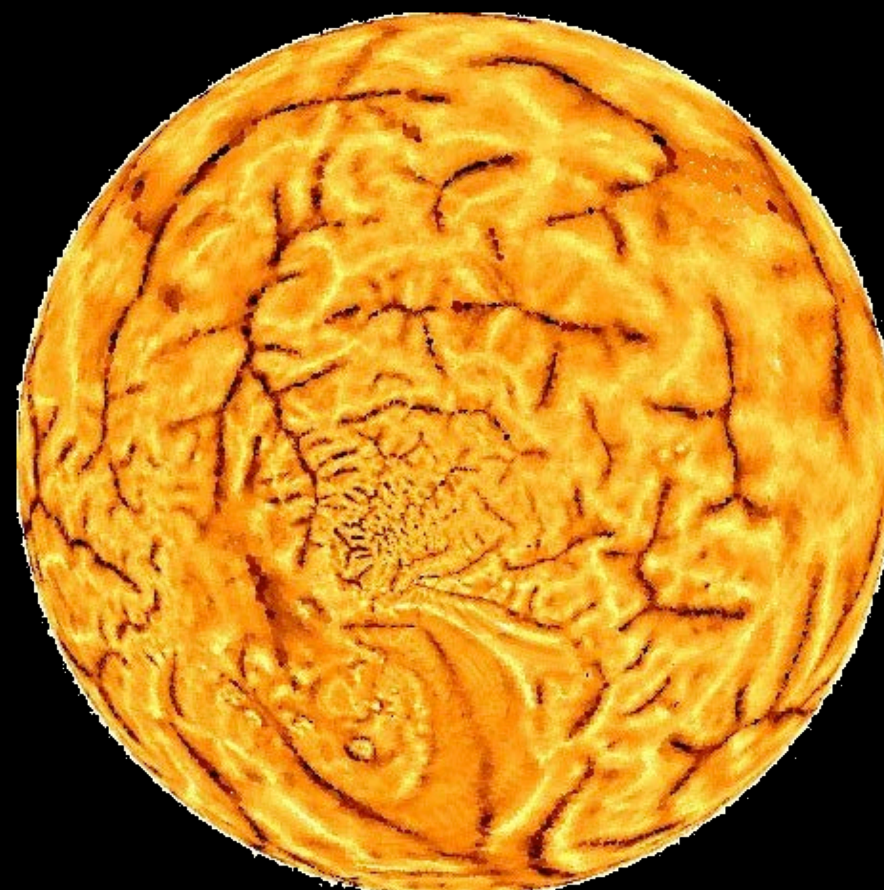


Individual Variability

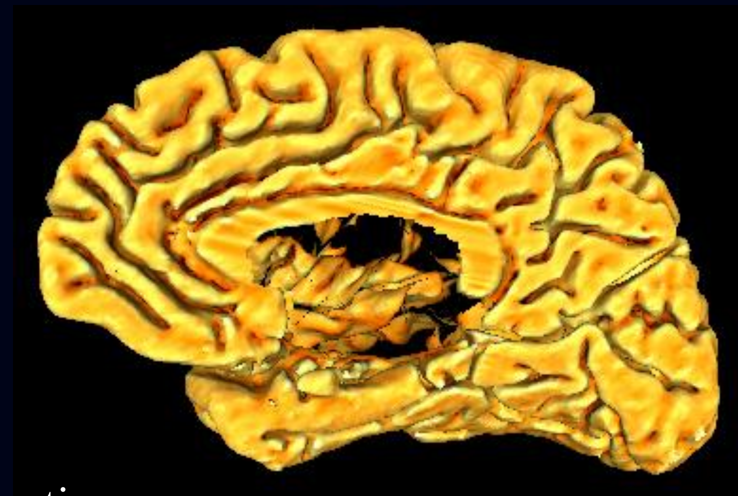


Mapping a Cortical Hemisphere

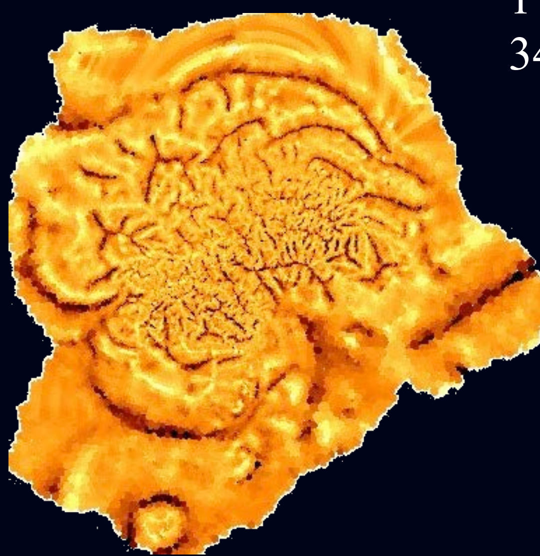
181,154 vertices
362,304 triangles



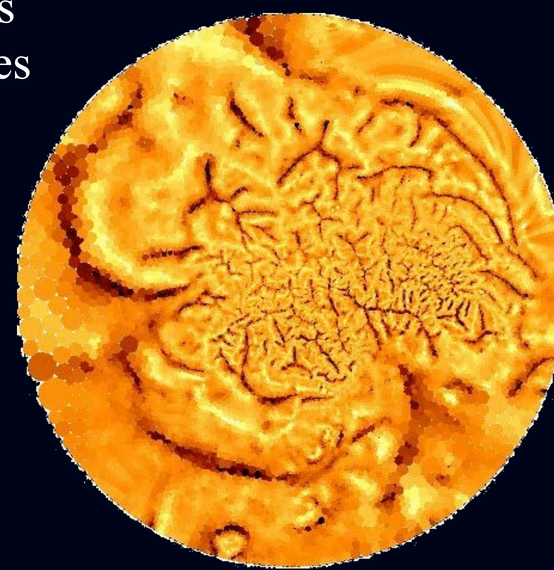
Mapping to the Plane



170,909 vertices
341,463 triangles



Euclidean Map

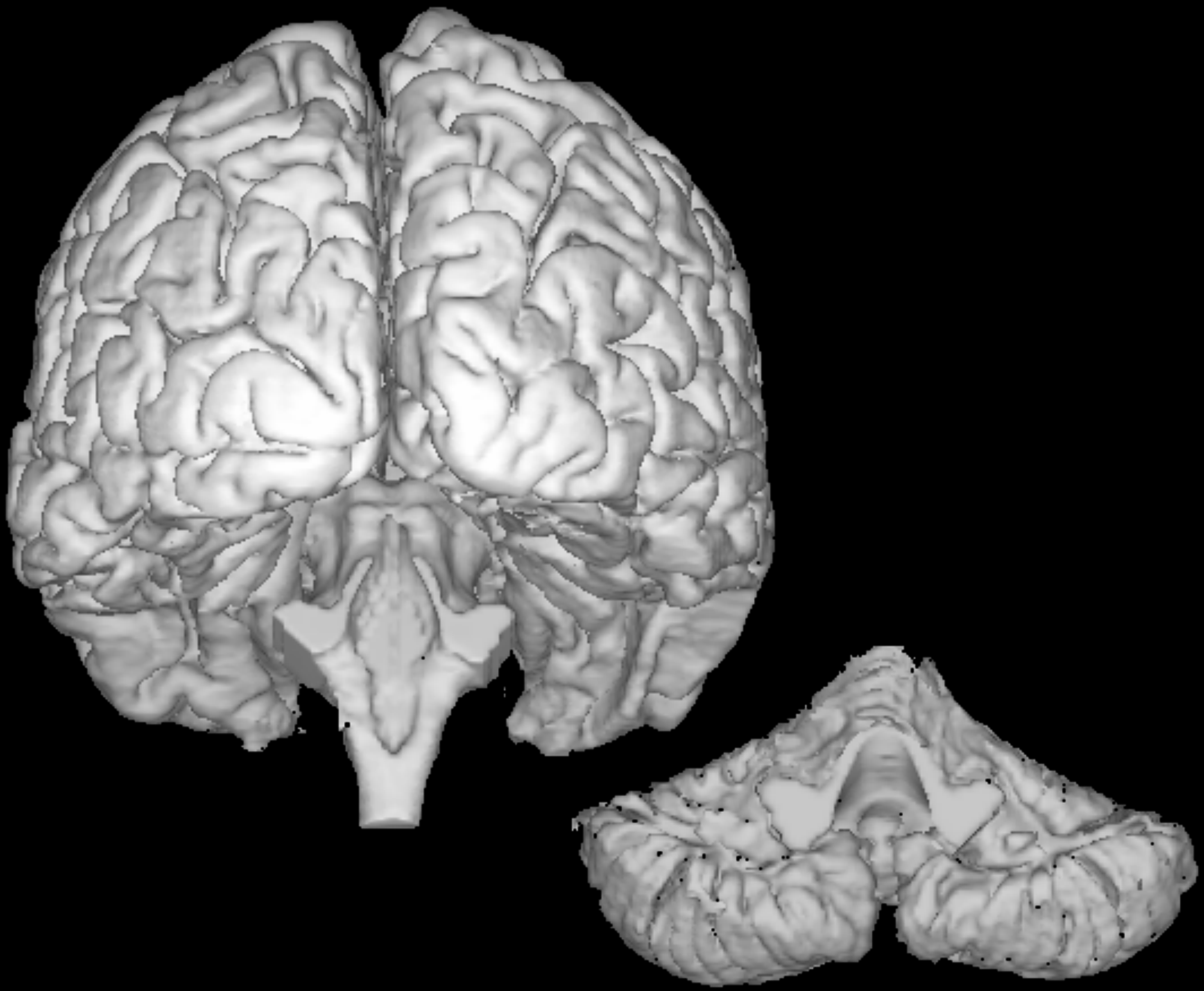


Hyperbolic Map

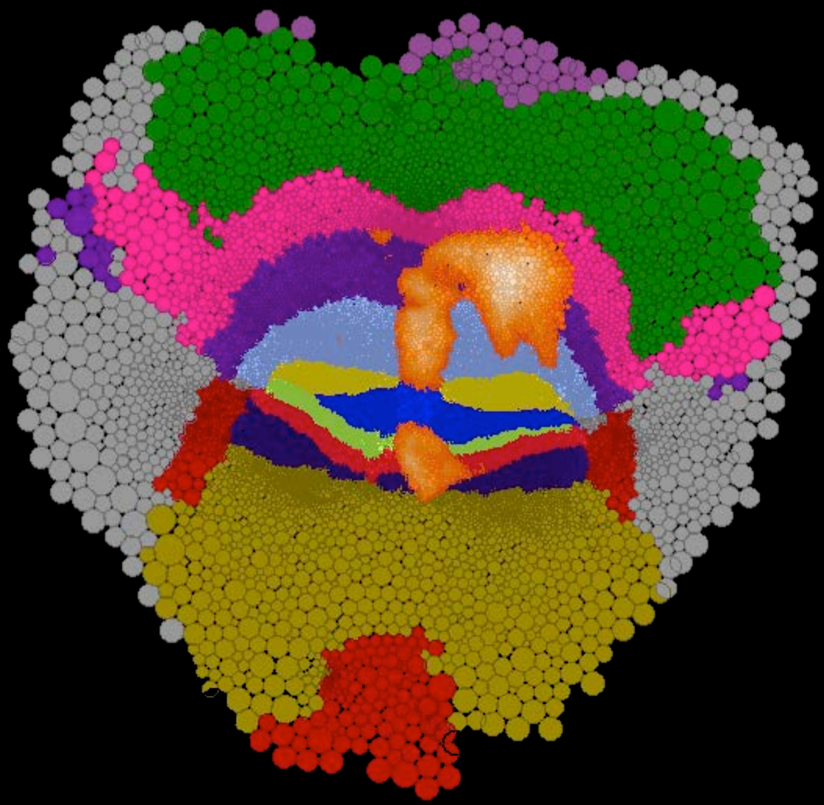
Visualizing Flat Maps

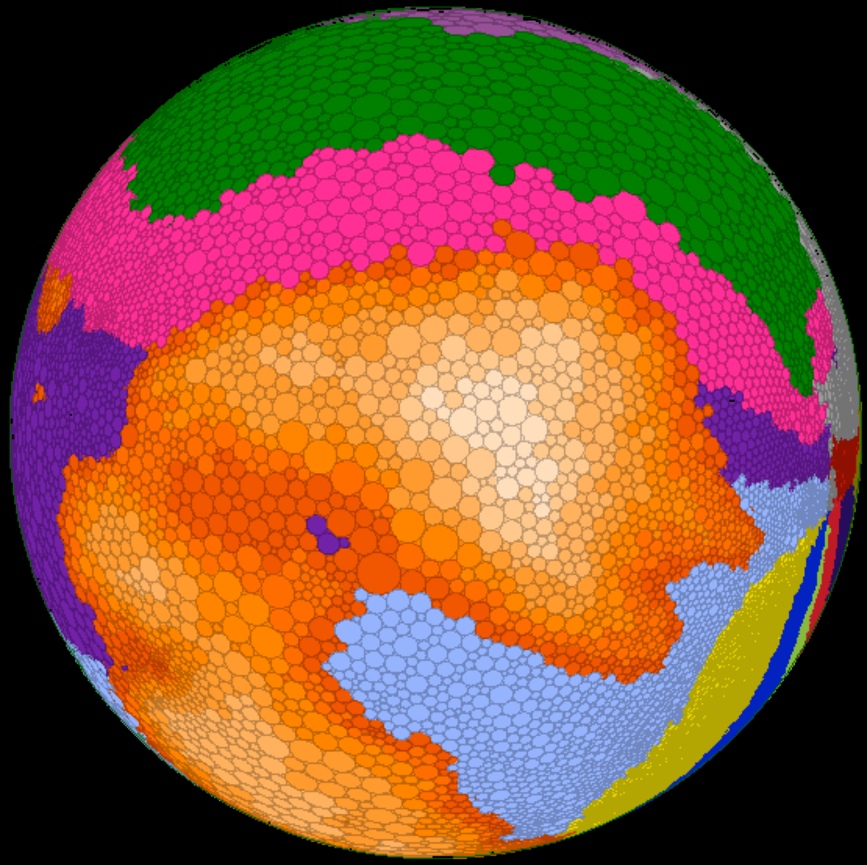
Mapping a Cerebellum

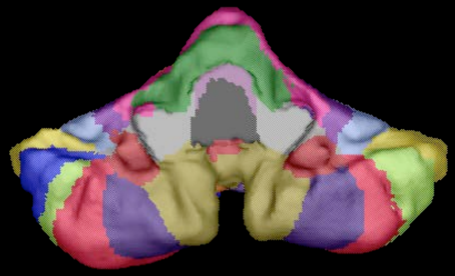
Data courtesy of D. Rottenberg, U. Minnesota



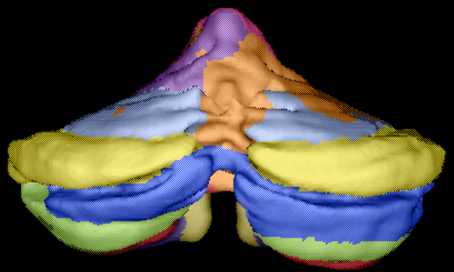
Euclidean & Spherical Maps



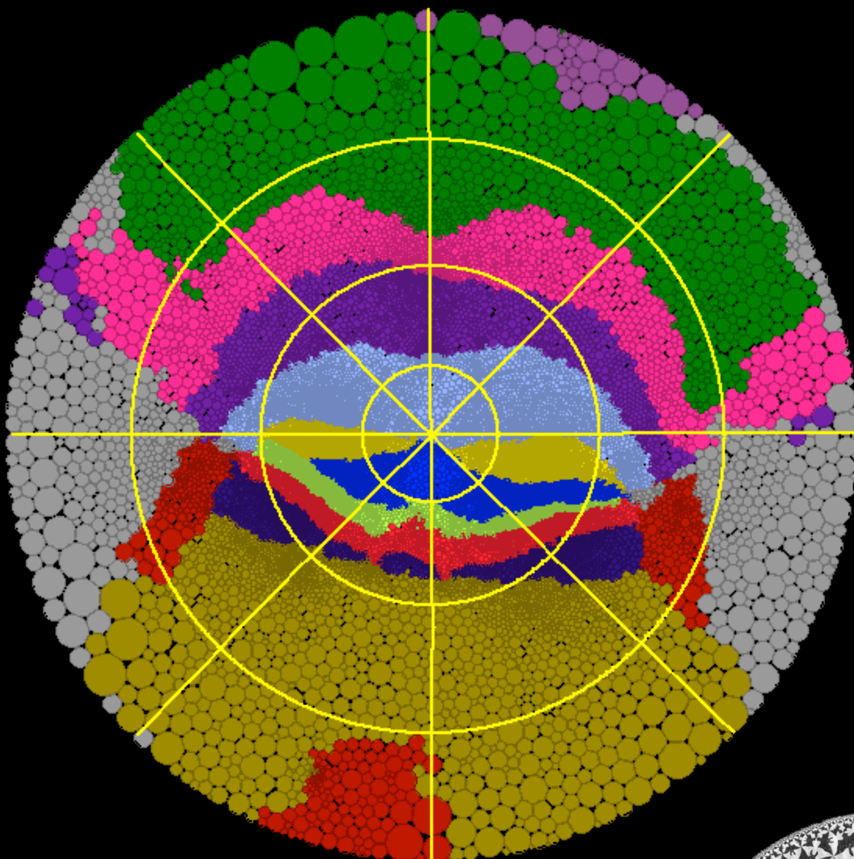


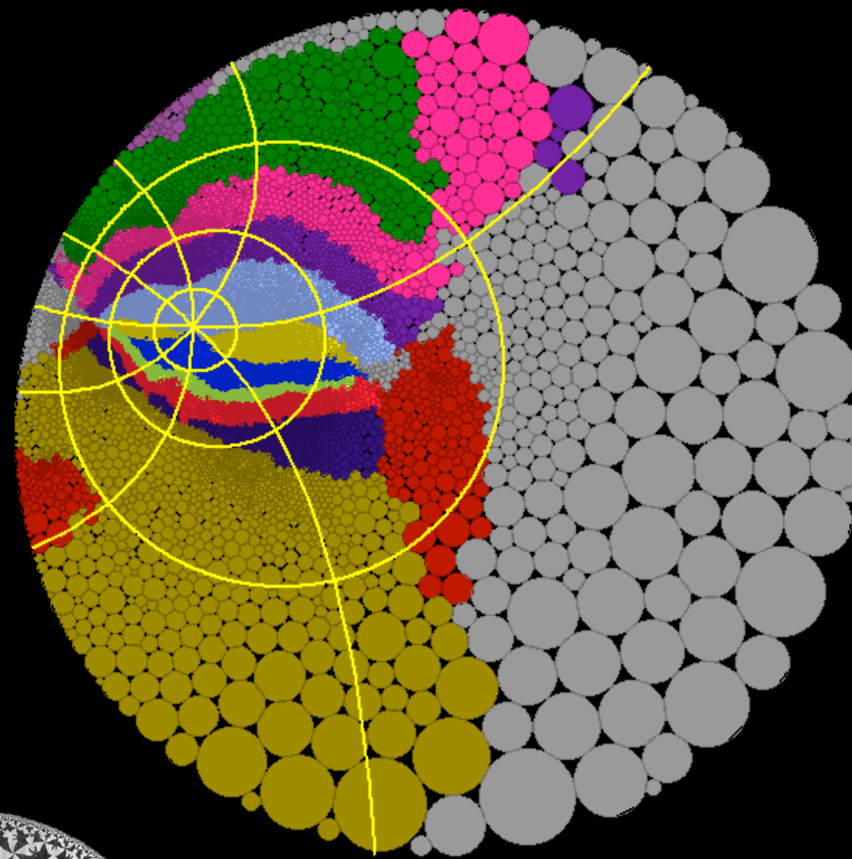


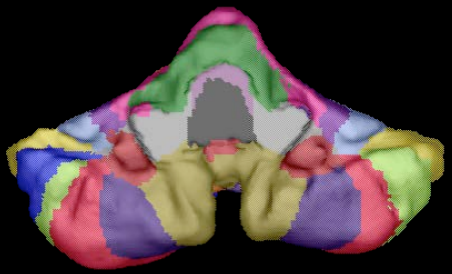
Surface:
28,340 vertices
56,676 triangles

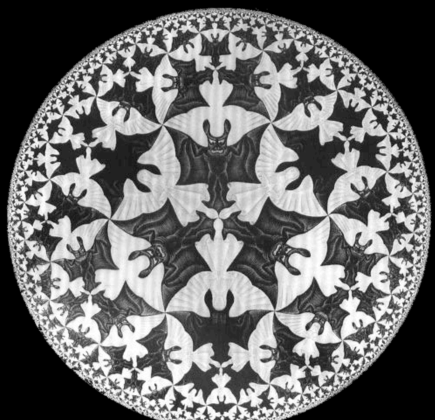


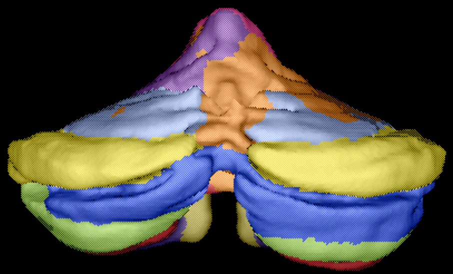
Hyperbolic Maps



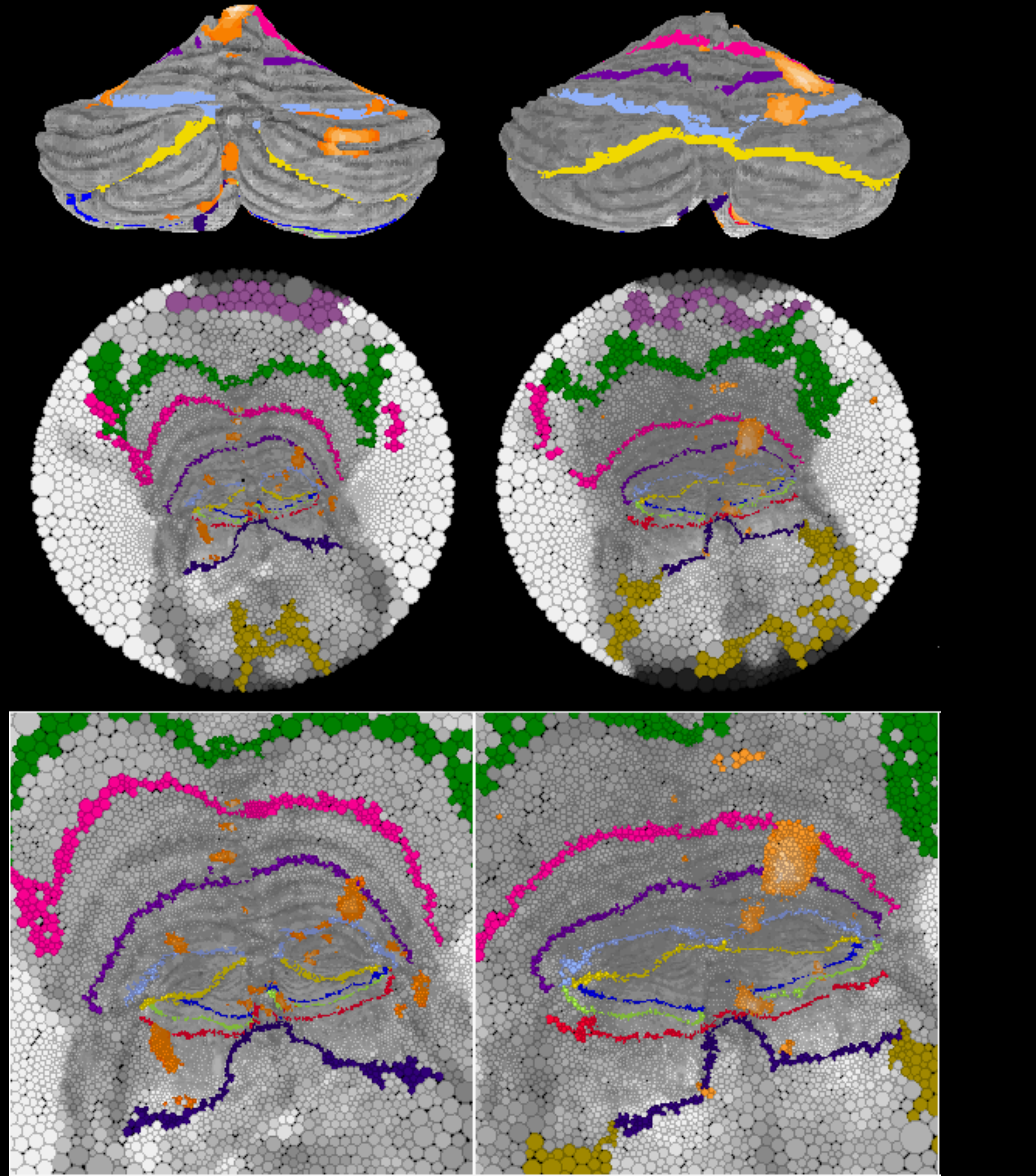








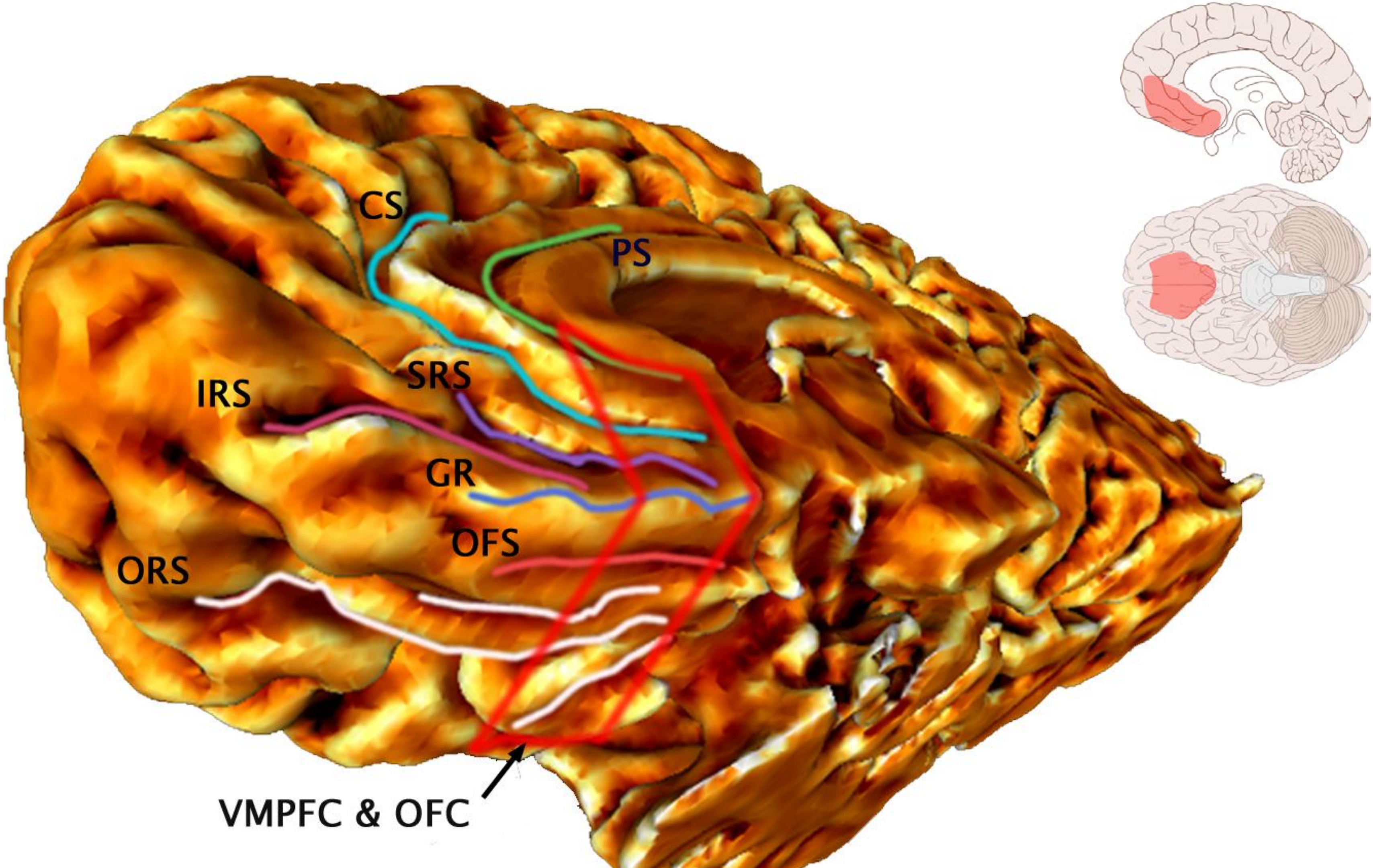
Flat Maps of Different Subjects



Twin Study

Collaboration with Center for Imaging Science (Biomed. Eng.), Johns Hopkins U. & Psychiatry and Radiology Departments, Washington U. School of Medicine

- As with non-twin brains, identical twin brains have individual variability i.e. brains are **NOT** identical in the location, size and extent of folds
- Aim: determine if twin brains more similar than non-twin brains
  - if so, this can be used to help identify where a disease manifests itself if one twin has a disease/condition that the other does not
- Flat maps can help identify similarities and differences in the curvature and folding patterns
- Examining ventral medial prefrontal cortex (VMPFC)



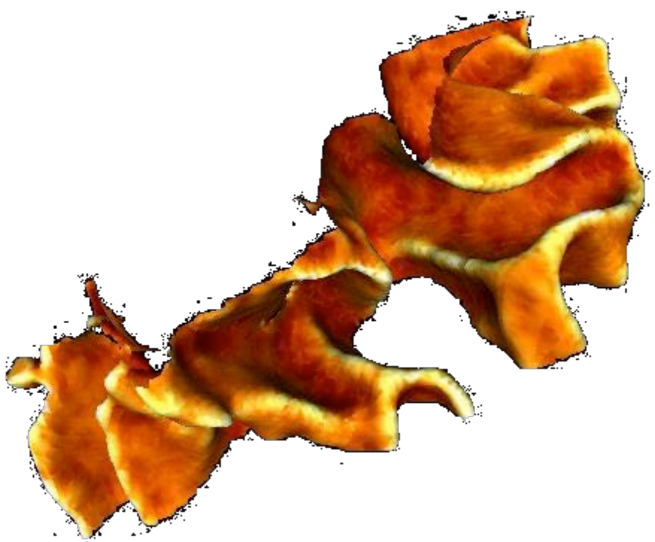
CS: Cingulate Sulcus
GR: Gyrus Rectus
IRS: Inferior Rostral Sulcus
OFC: Olfactory Cortex

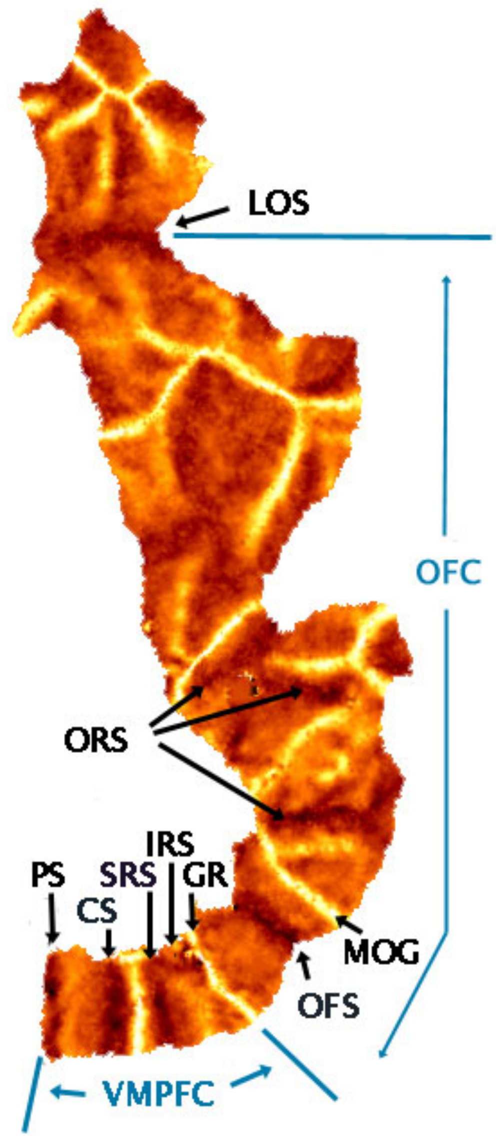
OFS: Olfactory Sulcus
ORS: Orbital Sulcus
PS: Pericallosal Sulcus
SRS: Superior Rostral Sulcus

VMPFC: Ventral Medial Prefrontal Cortex

Mapping a Cortical Region

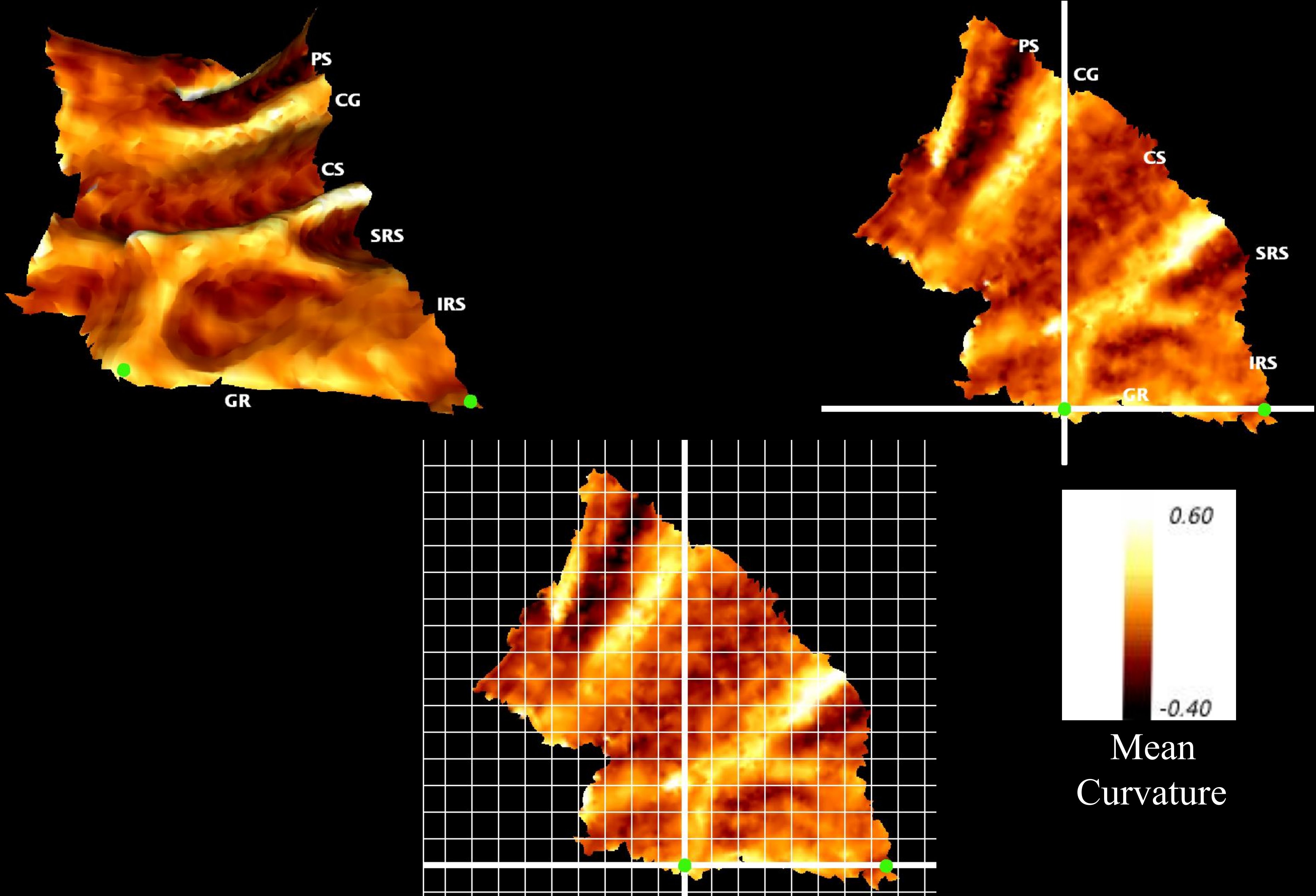
Data courtesy of K. Botteron, Washington U. School of Medicine





CG = cingulate gyrus
CS = cingulate sulcus
GR = gyrus rectus
IRS = inferior rostral sulcus
LOS = lateral orbital sulcus
MOG = medial orbital gyrus
OFC = orbital frontal cortex
OFS = olfactory sulcus
ORS = orbital sulci
PS = pericallosal sulcus
SRS = superior rostral sulcus

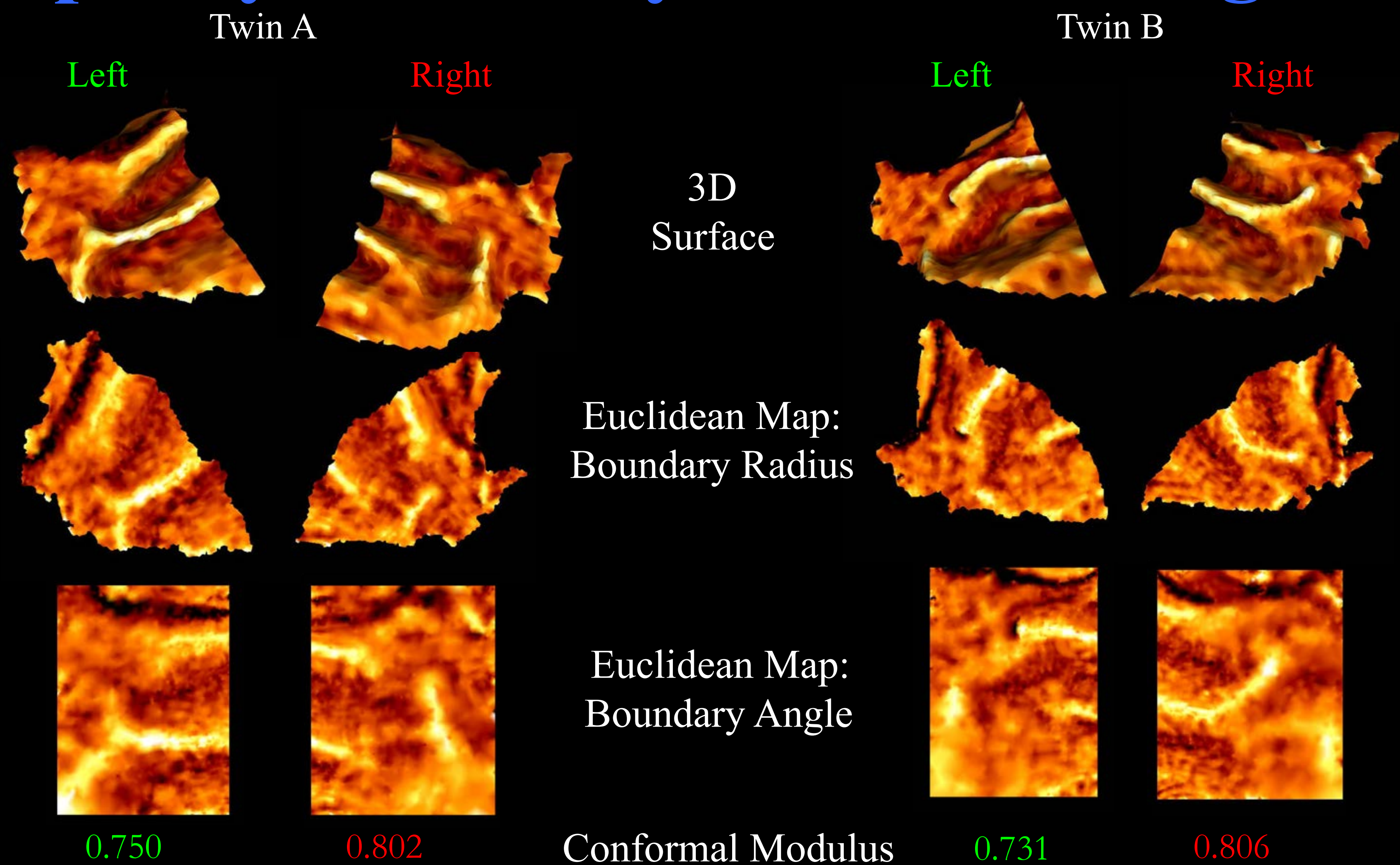
VMPFC Coordinate System



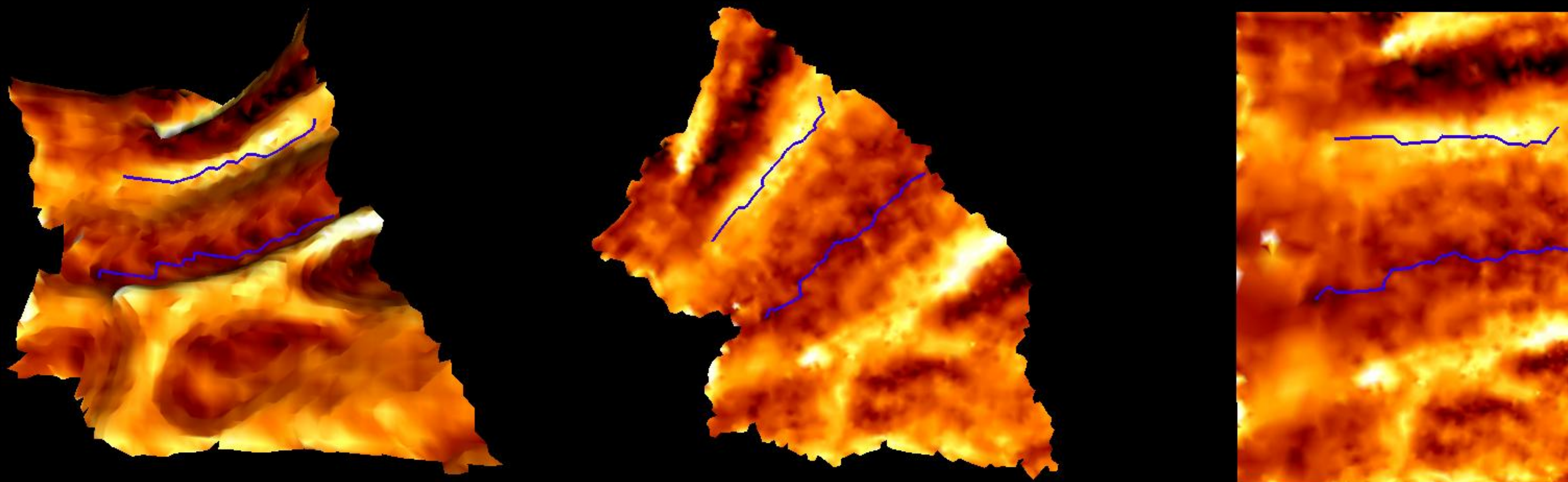
Circle Packing Flexibility: Rectangular Discrete Conformal Maps

- An advantage of conformal mapping via circle packing is the flexibility to map a region to a desired shape
- Boundary angles, rather than boundary radii are preserved
- For a rectangle: 4 boundary vertices are nominated to act as the corners of the rectangle
- Aspect ratio (width/height) is a ***conformal invariant*** of the surface (relative to the 4 corners) and is called the ***extremal length***
- Conformal extremal length represents one measure of shape
- Two surfaces are conformally equivalent if and only if their conformal modulus is the same

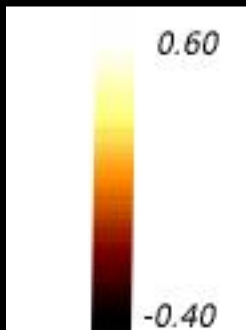
Euclidean Maps: Specify Boundary Radius or Angle



Tracking Lines of Principal Curvature



- Path of maximal curvature tracks along a gyrus / fold (top line).
- Path of minimal curvature tracks along a sulcus / fissure (bottom line).



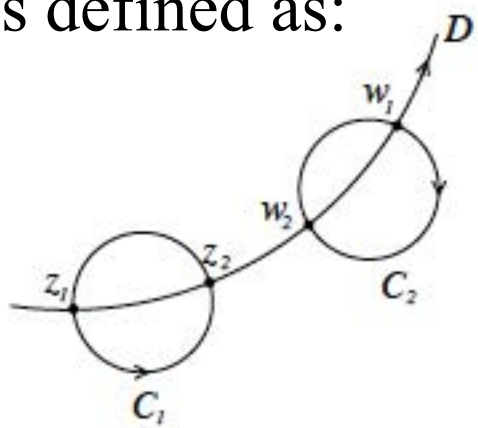
Mean Curvature

Circle Packing Flexibility: Preserve Inversive Distance Rather than Circle Tangency

- Inversive distance between two oriented circles in the Riemann sphere is a conformal invariant of the location of the circles and their relative orientations
- As with tangency packings, inversive distance packings require radii of boundary circles or angle sums at boundary vertices to be specified

Inversive Distance

Let oriented circle D be mutually orthogonal to oriented circles C_1 and C_2. Denote z_1, z_2 as the points of intersection of D with C_1 and w_1, w_2 as the points of intersection of D with C_2. The inversive distance between C_1 and C_2 is defined as:



- $\mathrm{InvDist}(C_1, C_2) = 2[\, z_1, z_2\, ;\, w_1, w_2\,] - 1$

$$= 2\frac{(z_1 - w_1)(z_2 - w_2)}{(z_1 - z_2)(w_1 - w_2)} - 1$$

- $\mathrm{InvDist}(C_1, C_2) = 1$ if C_1 and C_2 are tangent
- $\mathrm{InvDist}(C_1, C_2) = \cos\alpha$, if C_1 and C_2 intersect with angle α, $\Rightarrow 0 \le \mathrm{InvDist}(C_1, C_2) < 1$
- $\mathrm{InvDist}(C_1, C_2) = \cosh\delta$, where δ is the hyperbolic distance between the hyperbolic planes bounded by disjoint circles C_1 and $C_2 \Rightarrow 1 < \mathrm{InvDist}(C_1, C_2) < \infty$

Computing Inversive Distance Circle Patterns (Rectangle Maps)

- K = triangulation of a disk with four distinguished boundary vertices with edge set E and vertex set V;

  $\Phi: E \rightarrow [0, \infty)$ an inversive distance edge labeling

Euclidean Formulation

- For oriented circles C_1 and C_2 with radii R_1 and R_2 and centered at a_1 and a_2 respectively:

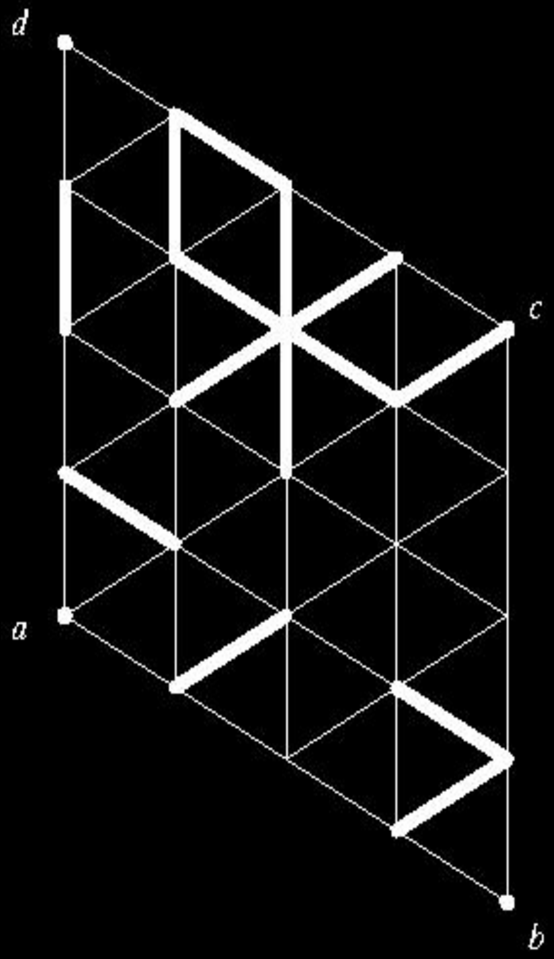
$$\mathrm{InvDist}(C_1, C_2) = (|a_1 - a_2|^2 - R_1{}^2 - R_2{}^2)/2R_1R_2$$

- Observe $|a_1 - a_2|$ = edge length $e_{1,2} = \langle v_1, v_2 \rangle$
- For convergence, require R_i to be a constant function. Thus:

$$\mathrm{InvDist}(C_1, C_2) = \Phi(e_{1,2}, R) = e^2/(2R^2) - 1$$

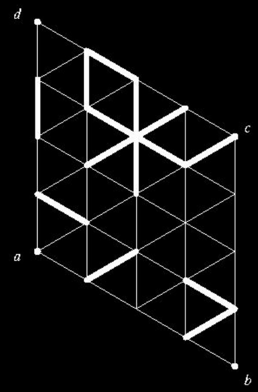
Existence questions??? Uniqueness proved by Luo, 2011

Example: Hexagonal Grid



- Lengths of bold edges are 1.1
- Other edge lengths are 1.4

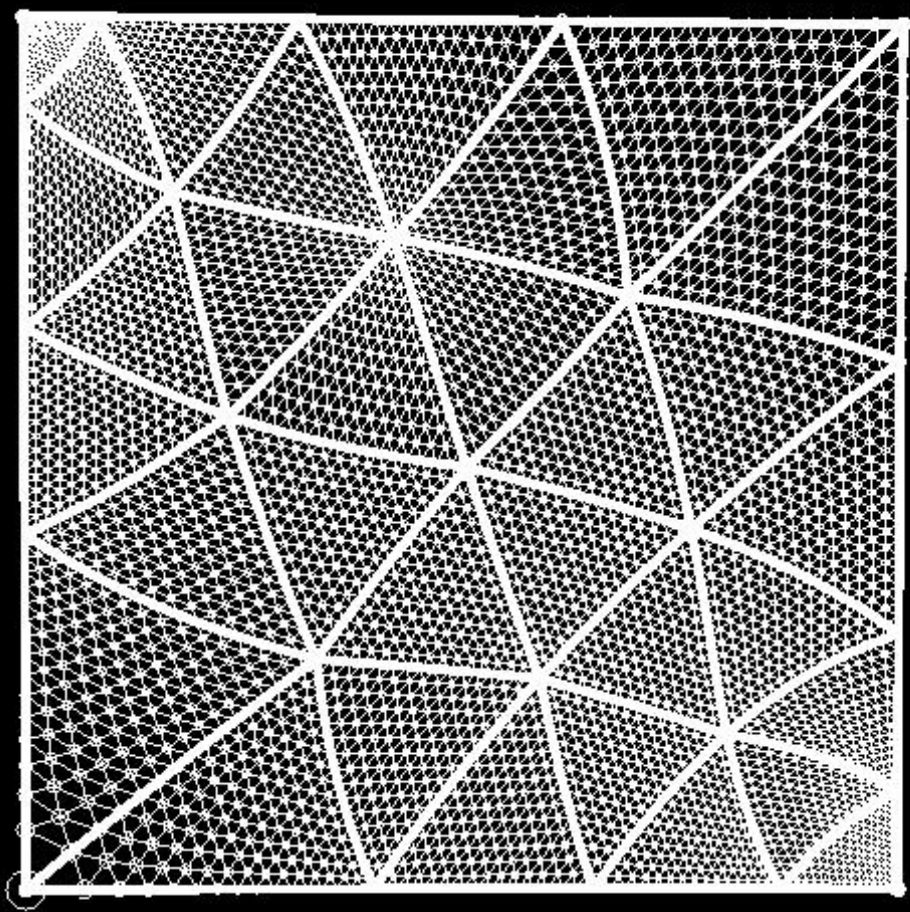
- Now: adjust R to construct a variety of overlapping, tangent, and disjoint circle packings using inversive distance

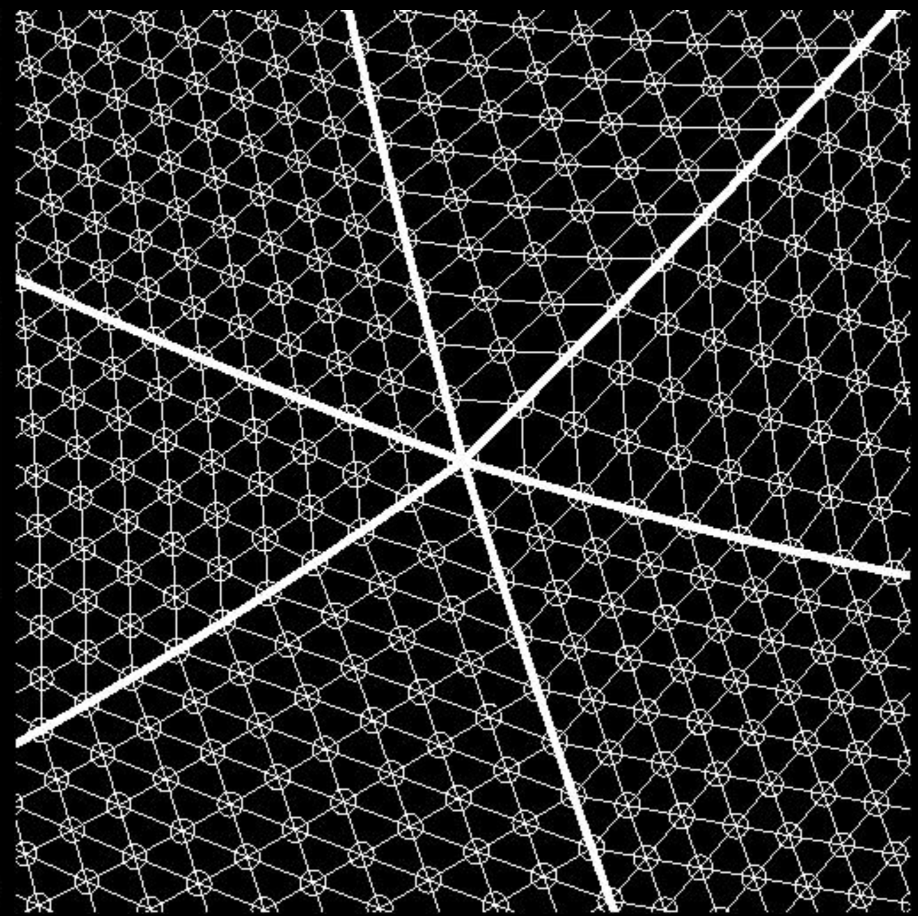


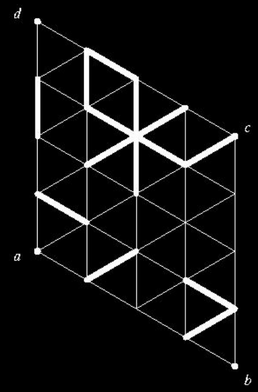
Disjoint Circles: $R = 1/4$

$\Phi(e\_bold = 1.1, R = 1/4) = 8.6800$

$\Phi(e\_other = 1.4, R = 1/4) = 14.6800$



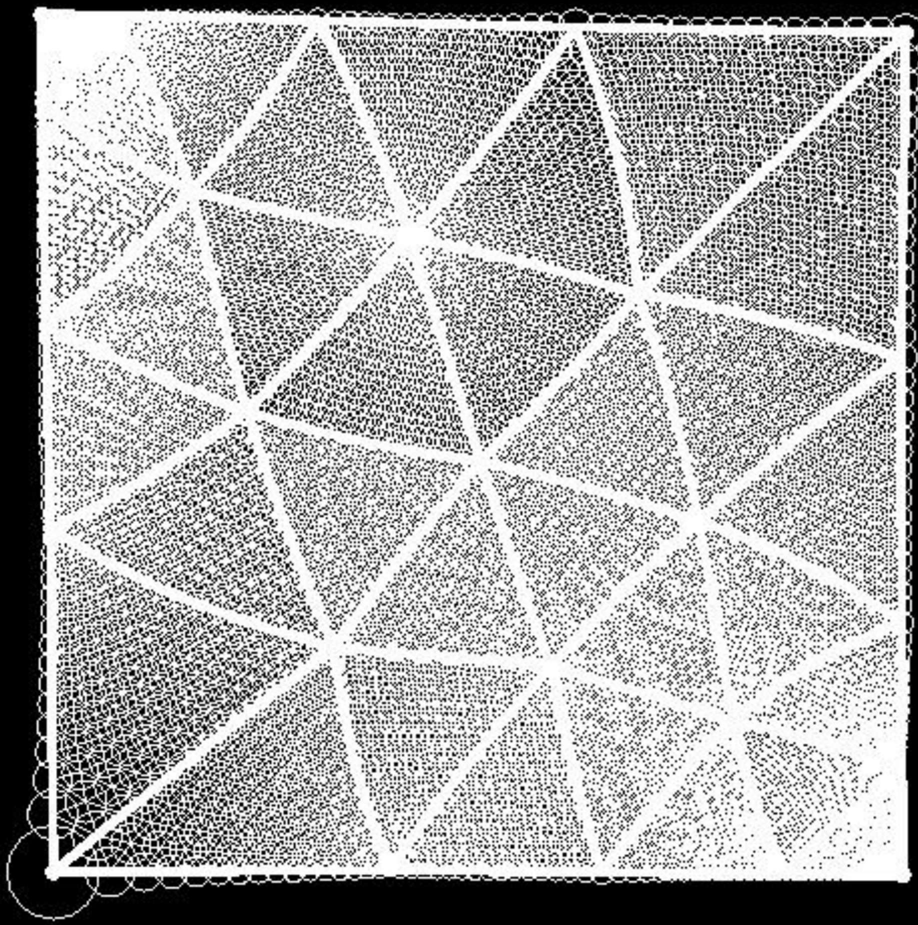


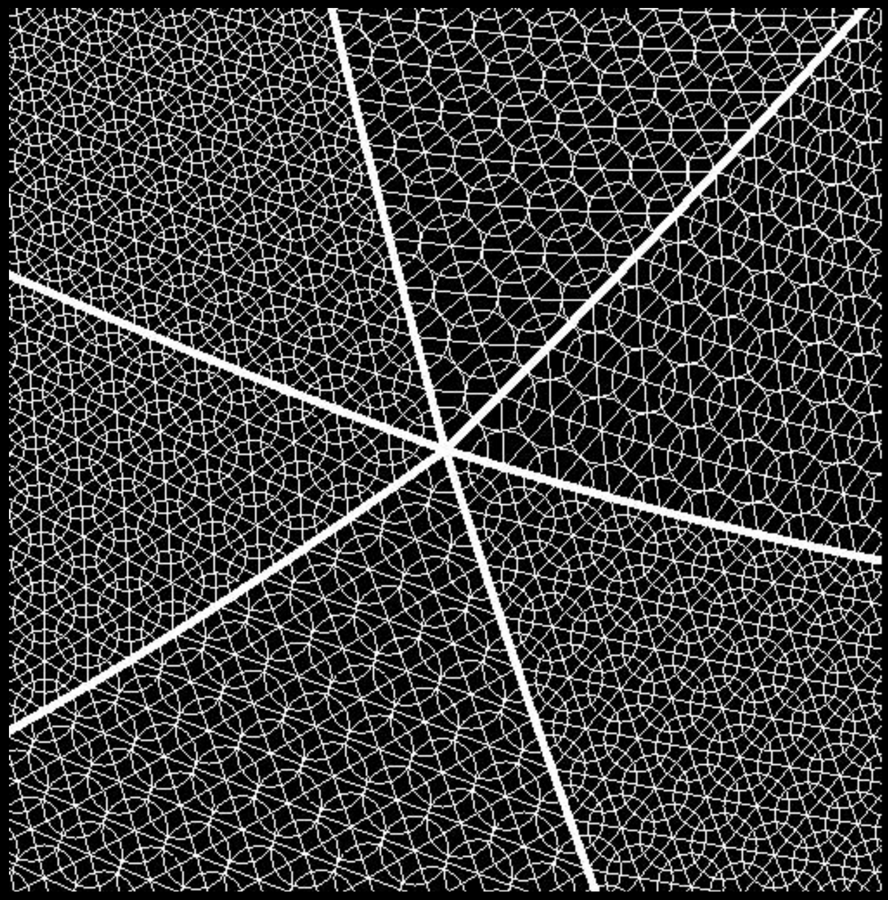


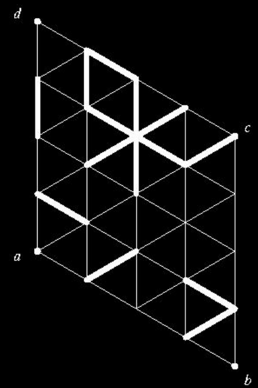
Overlapping Circles: R = 1/sqrt(2)

$\Phi(e\_bold = 1.1, R = 1/\mathrm{sqrt}(2)) = 0.2100$

$\Phi(e\_other = 1.4, R = 1/\mathrm{sqrt}(2)) = 0.9600$



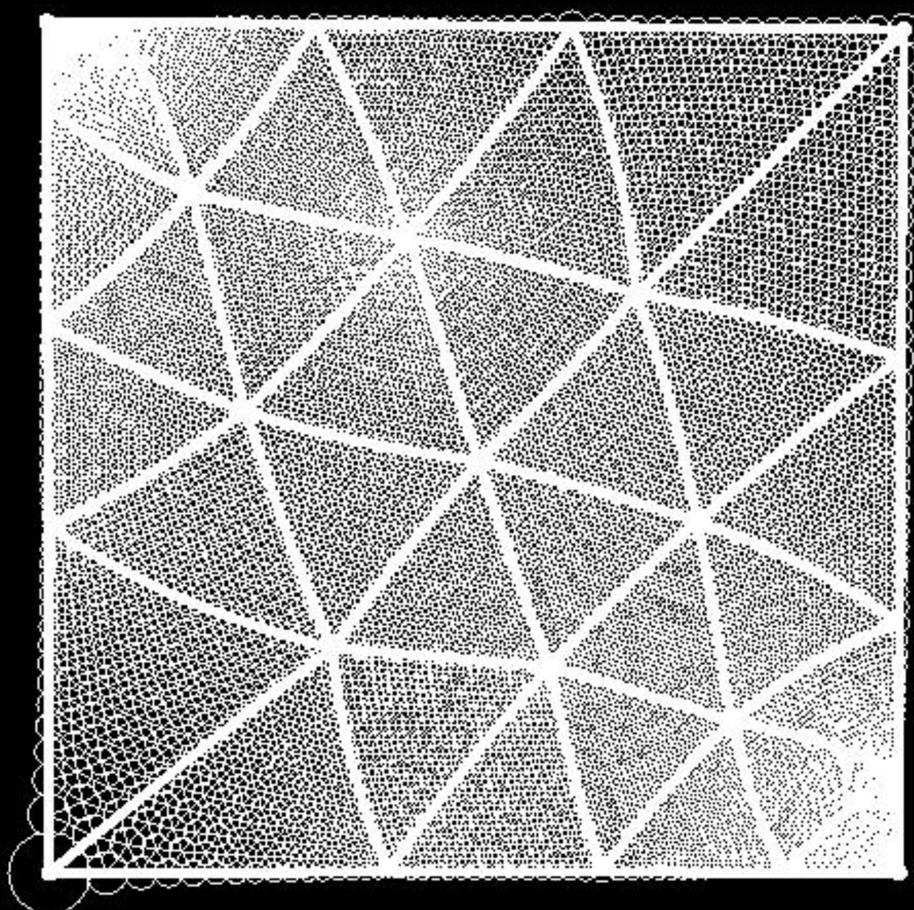


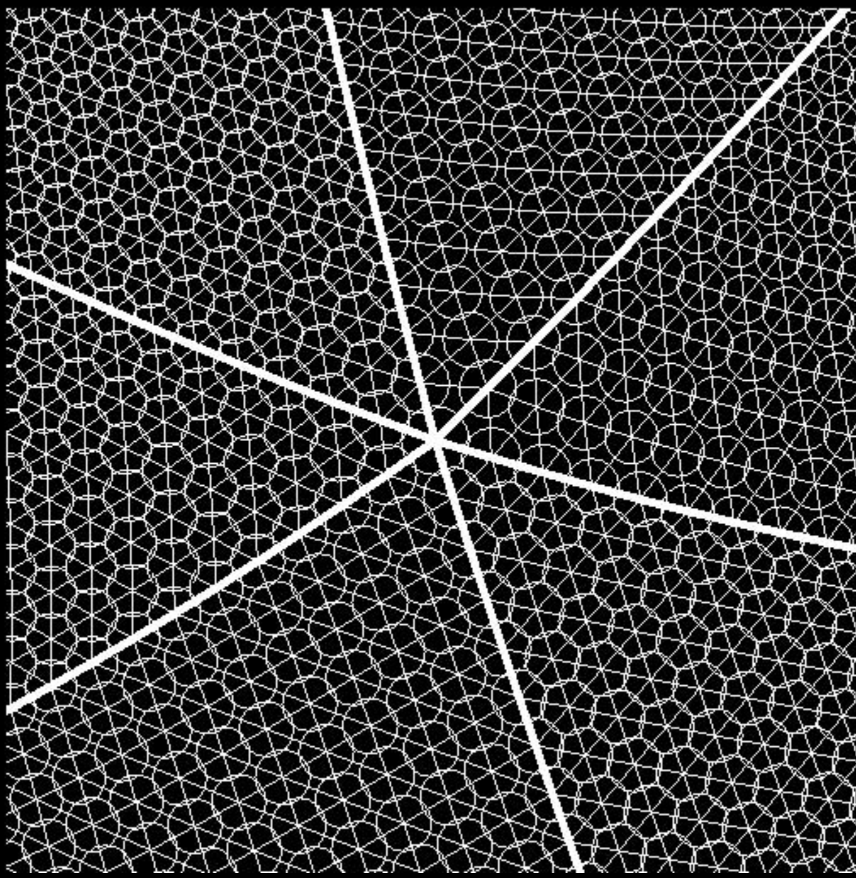


Overlapping and Disjoint Circles: R = 3/5

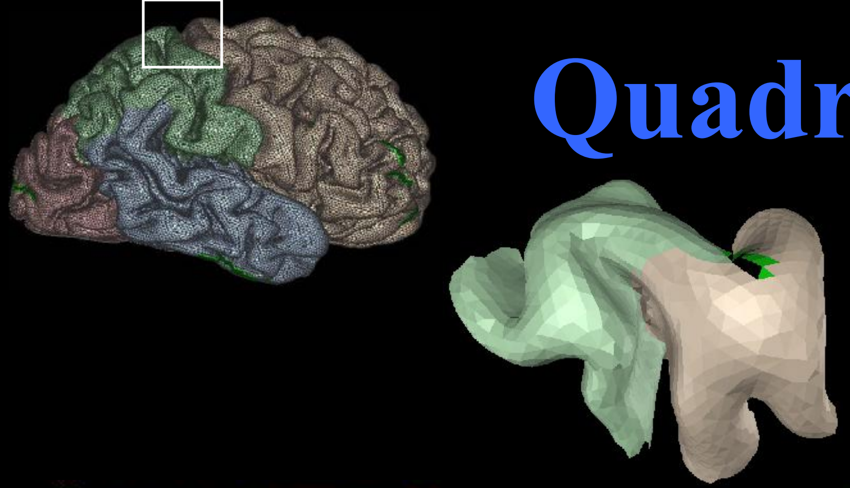
$\Phi(e\_bold = 1.1,\ R = 3/5) = 0.6806$

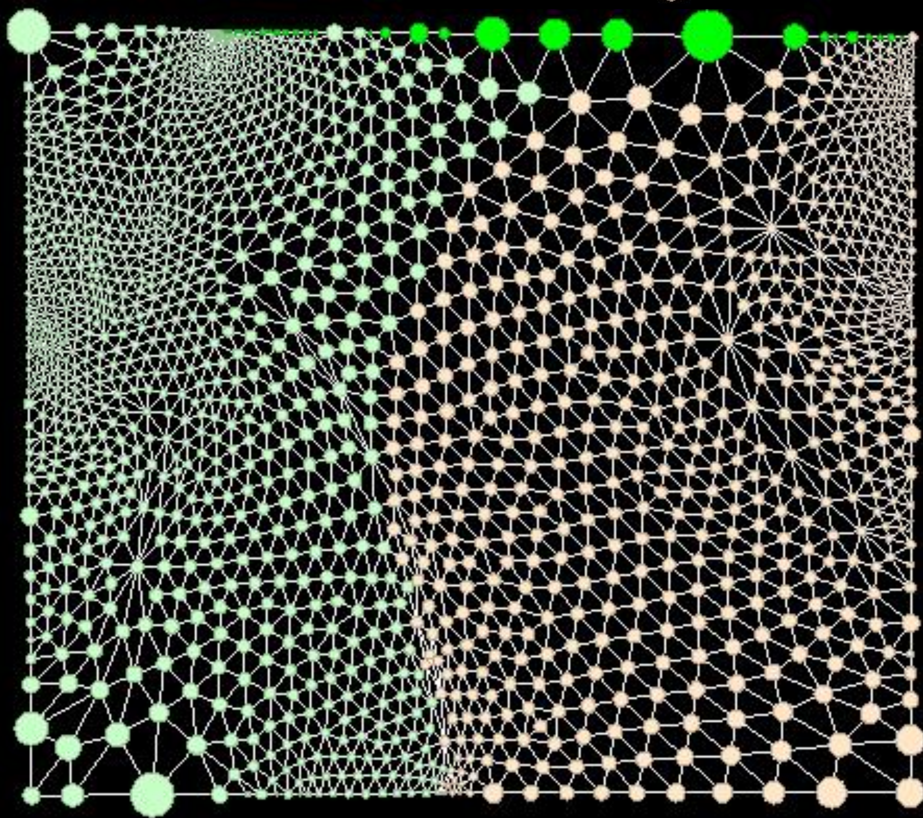
$\Phi(e\_other = 1.4,\ R = 3/5) = 1.7222$

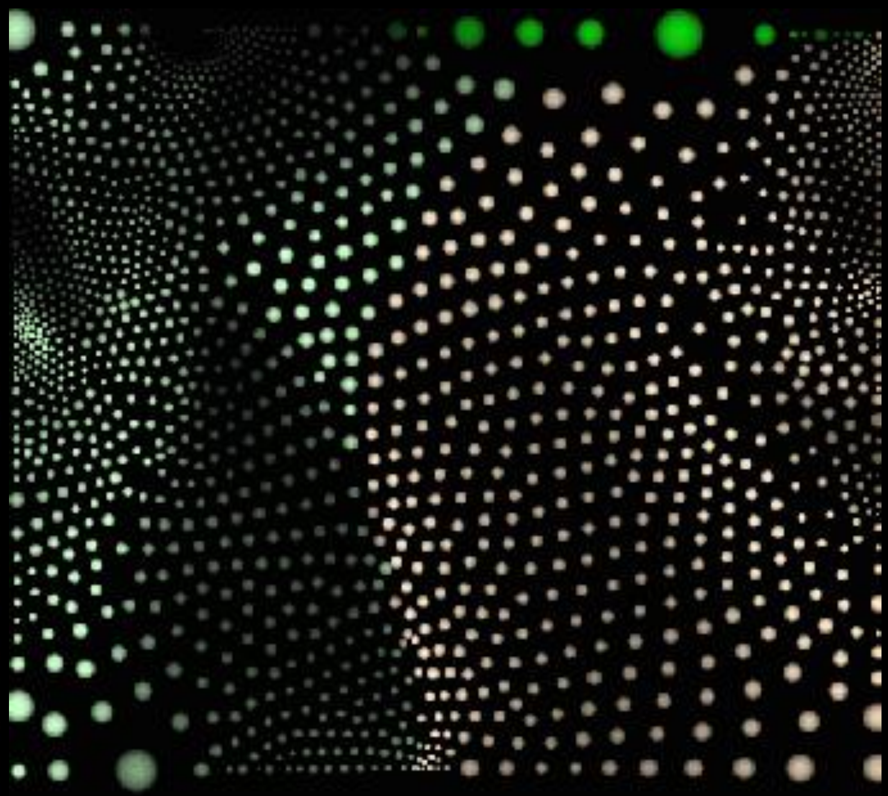




Quadrilateral Subsurface: Inversive Distance Packings

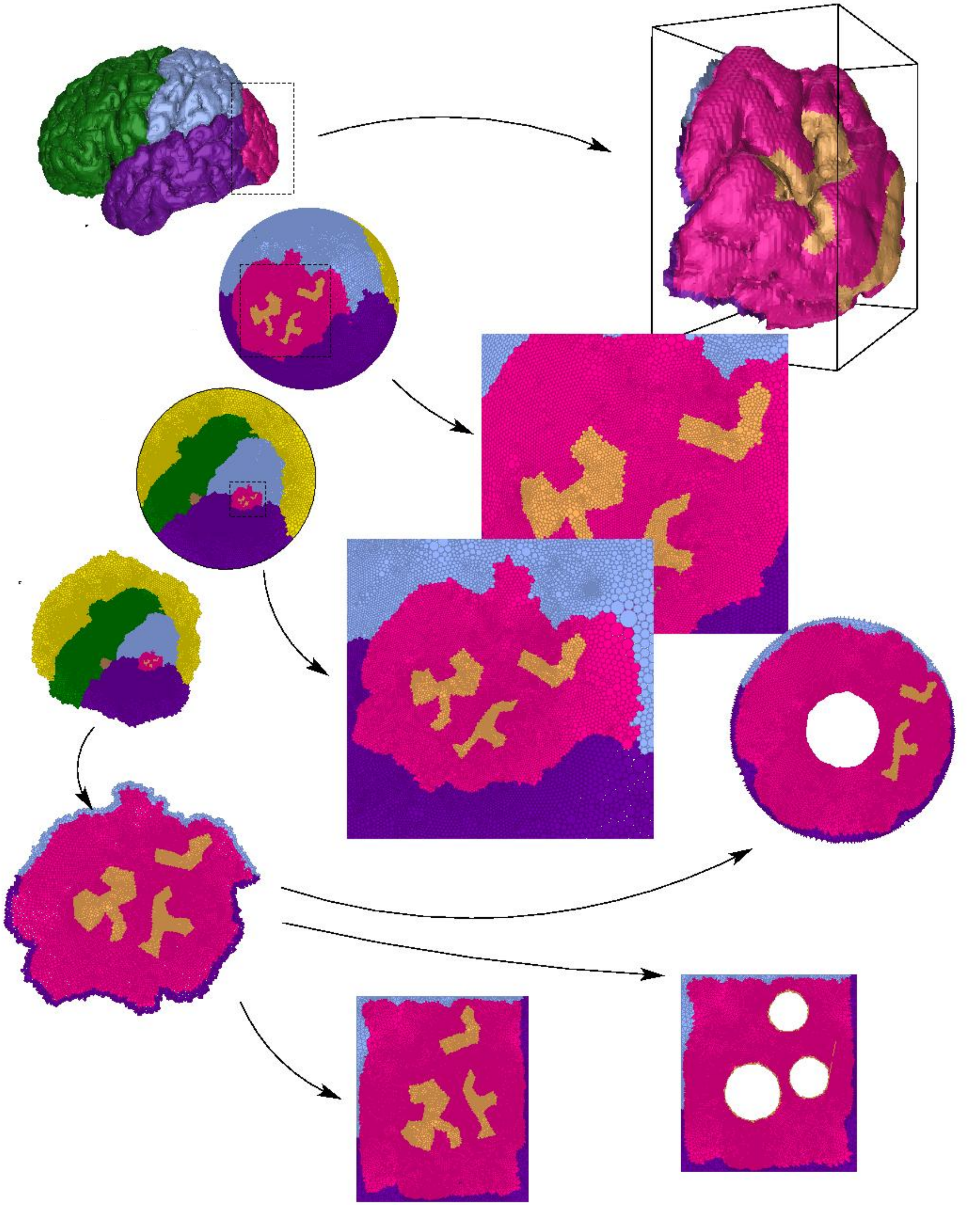






Bump Map Texture

More Examples of Conformal Maps & Conformal Invariants



Conformal Maps in Neuroscience

Used in neuroimaging studies of

- Hippocampus
- Alzheimer's disease
- Schizophrenia
- Cerebellum
- Cortical shape matching
- Hemispheric assymetry

Used to model retinotopic mapping of visual cortex

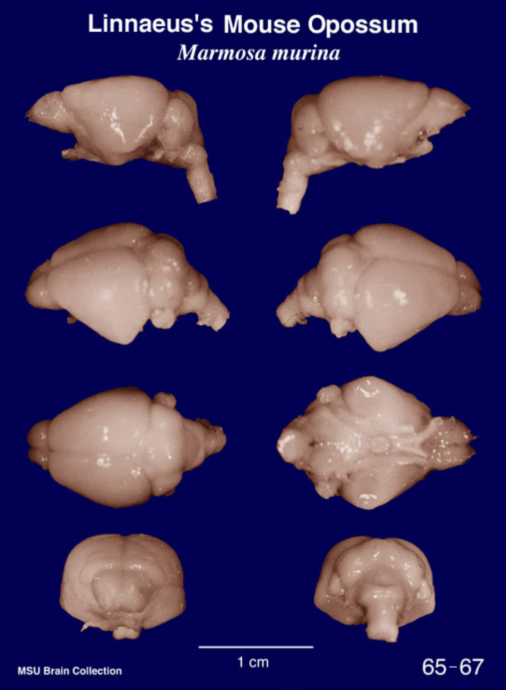
Summary

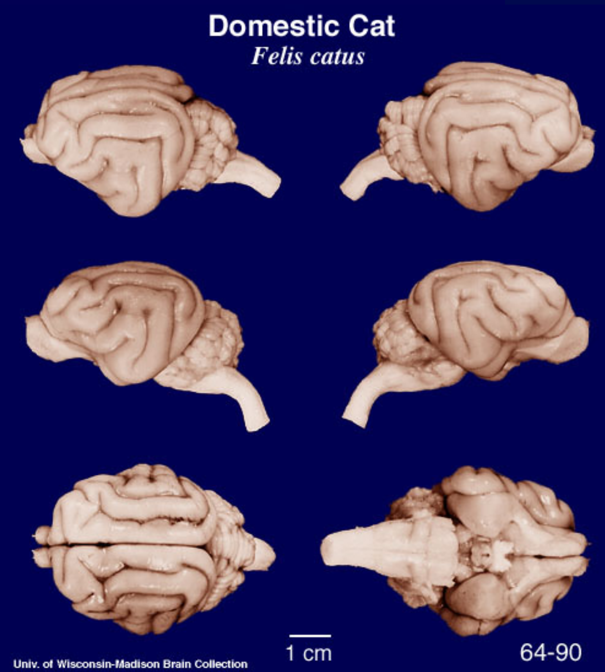
- Circle packings are mathematically unique and converge to the discrete conformal map of a surface in the limit (i.e. through hex refinement) if triangulation is equilateral; otherwise yields an approximation to a discrete conformal map
- Euclidean, hyperbolic, spherical geometries available
- Flexible in terms of conformal mappings to shapes, circle tangency, inversive distance packings
- Inversive distance data allows more geometric information to be encoded
- Some known applications: brain mapping, tilings, Dessins
- Open questions remain regarding existence for inversive distance packings; theory proved for tangency & overlap packings with prescribed angles of overlap

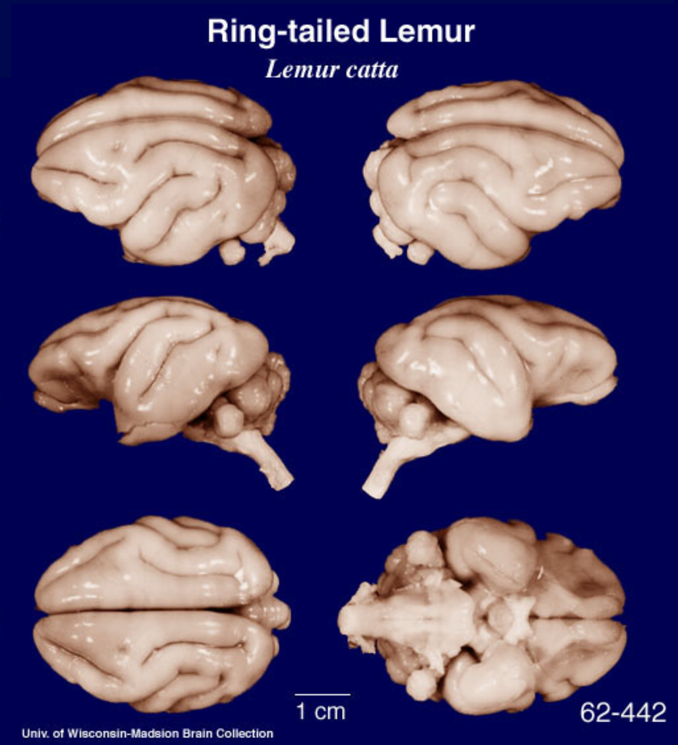
Future Issues: Conformal Mapping in Neuroscience

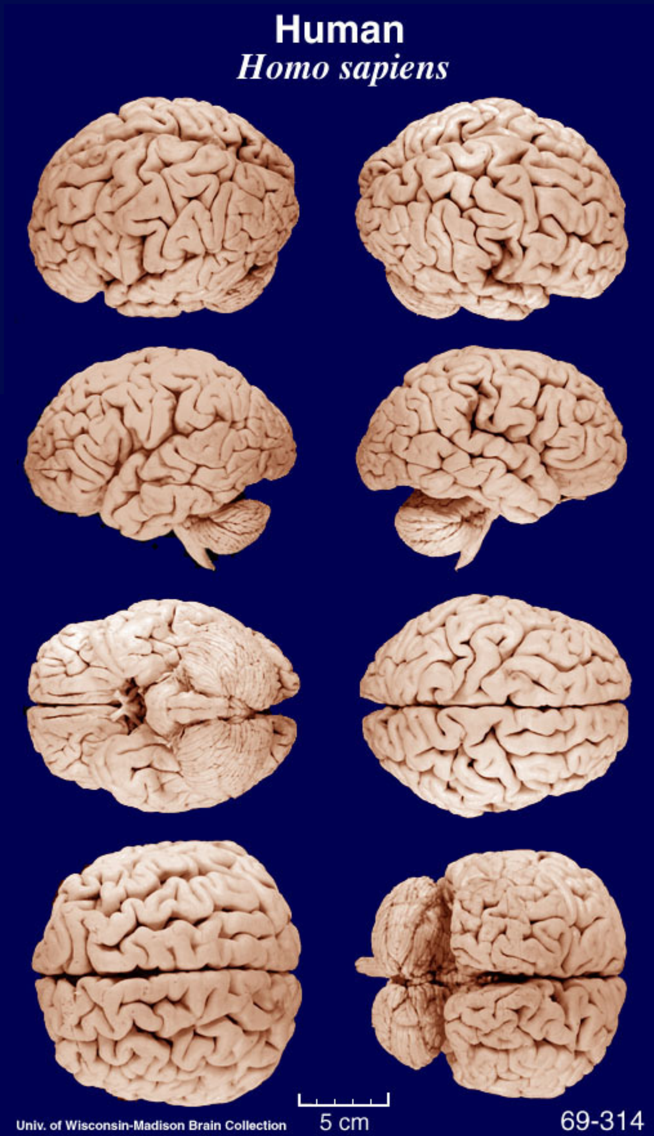
- Compare maps between subjects: metrics
- Alignment of different regions
  - align one volume or surface in 3-space to another and then conformally flat map
  - conformally flat map 2 different surfaces and then align/morph one to the other (in 2D)
- Analysis of similarities, differences between different map regions
- Experiment with rectangular tangency versus inversive distance maps
- Other conformal invariants? Other applications?

Development of Cortical Folding Patterns Across Species



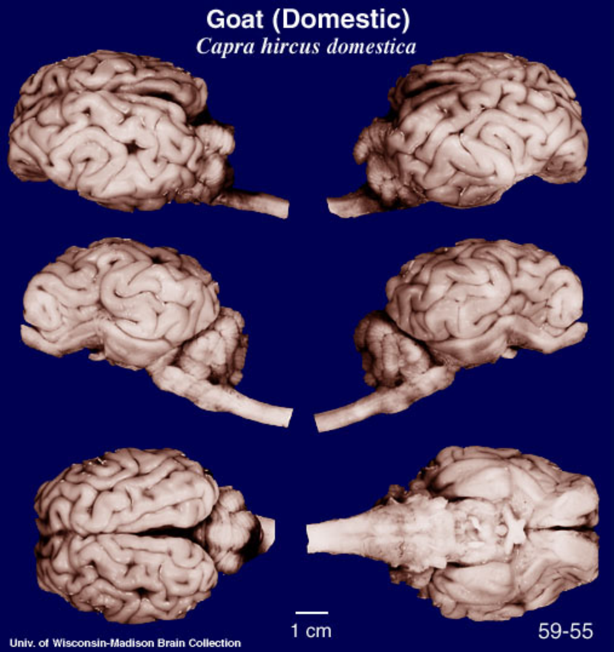


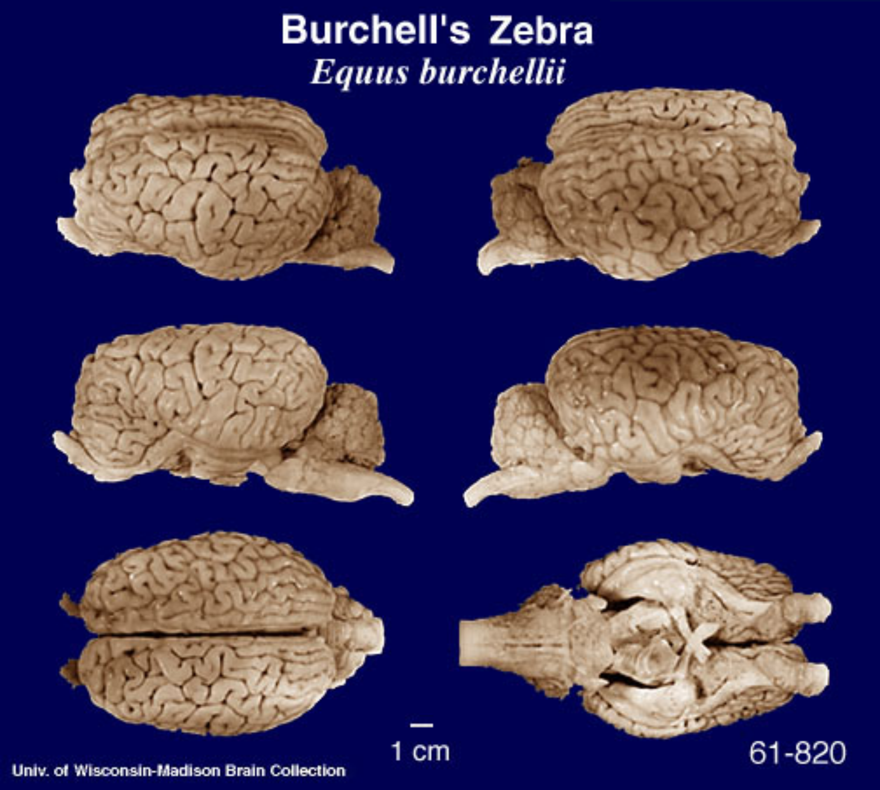


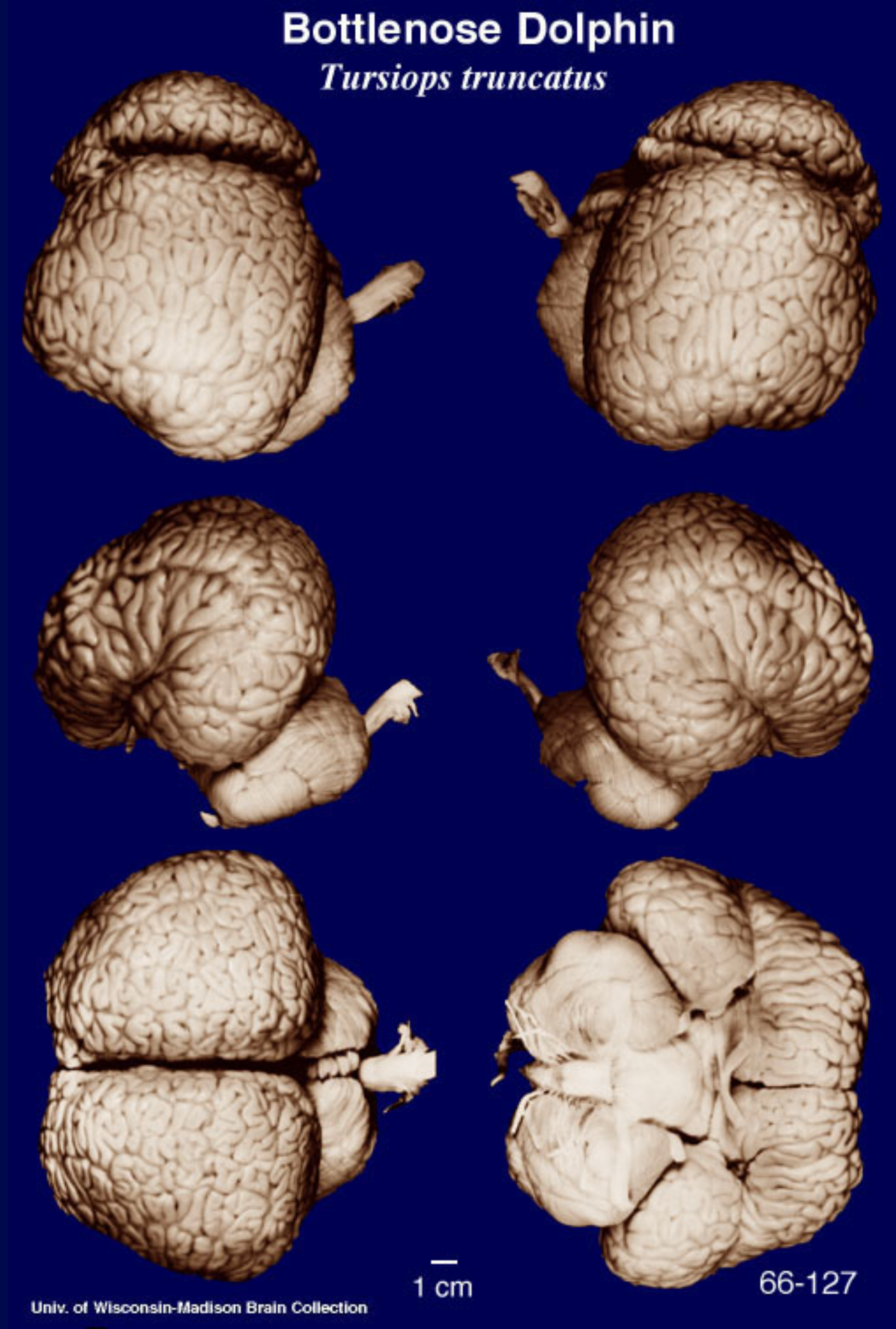


www.brainmuseum.org

Large Species



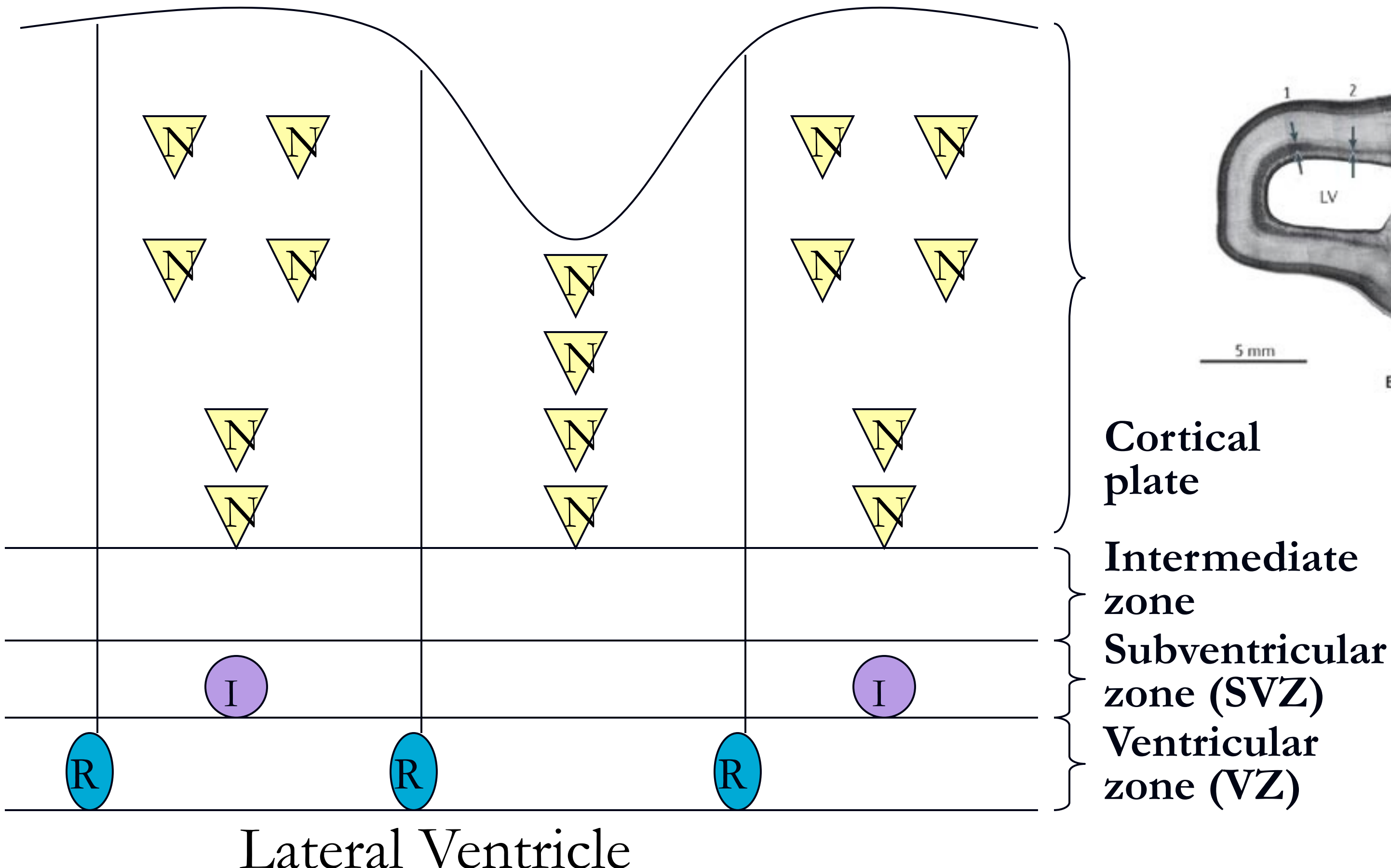


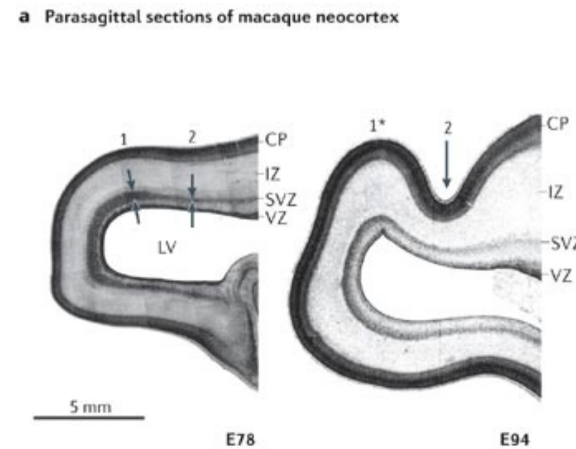


Development of Sulcal Pattern

Upper Layers: Intermediate Progenitor Model (Kriegstein, 2006)

- only subsets of RGCs are activated to create IPCs
- result is non-uniform distribution of IPCs, which create local amplication of neuroblasts surrounded by areas of non-amplification



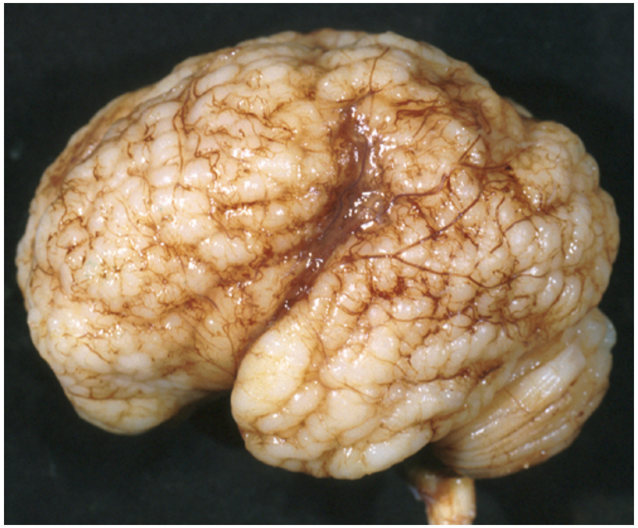


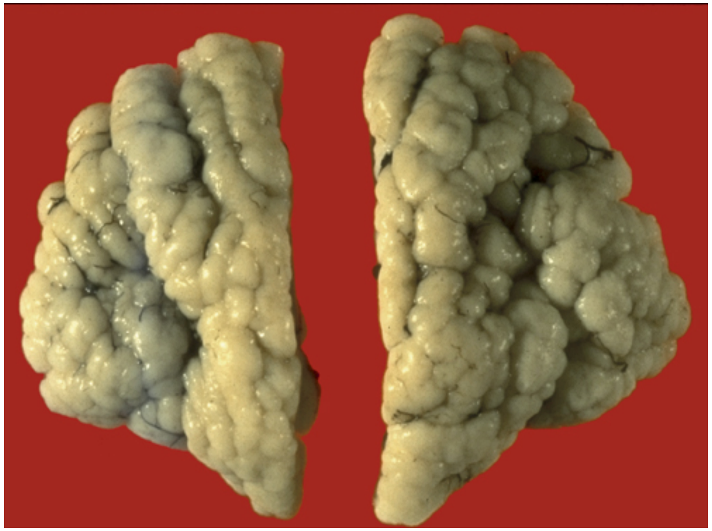
R - Radial glial cell   N - Neuron   I - Intermediate progenitor cell

A. Kriegstein, S. Noctor, V. Martinez-Cerdeno, *Nature Reviews Neuroscience*, **7(11)**, 883-890 (2006).

Application: Human Malformations: Polymicrogyria ("many small gyri")

- A neural migration disorder
- Characterized by an excessive number of small prominent convolutions spaced out be shallow and enlarged sulci.
- Many different types of polymicrogyria
    - Focal / Diffuse
    - Bilateral / Unilateral
    - Alone / Associated with other diseases
- "About 65% of patients [with polymicrogyria] have severe epilepsy" (Guerrini, 2006)
- Focal polymicrogyrias are often associated with malformations in **GPR56** (regulates regional cortical patterning). (Rakic, 2004)





http://www.neuropathologyweb.org/chapter11/chapter11dNMD.html

P. Rakic, *Science*, **303**, 1983-84 (2004).
R. Guerrini, *Exp Brain Res*, **173**, 322-333 (2006).

Math Model: Turing Systems

- Modeling the development and growth of brain folding with a Turing reaction-diffusion system using dynamic growth
- Turing System: stability in the absence of diffusion and diffusion driven instability.

Reaction Diffusion System – BVM (Barrio, Varea, and Maini)

$$u_t = \frac{D}{\rho^2}\nabla_+^2 u - 2Ru + \omega F(u,v)$$
$$v_t = \frac{1}{\rho^2}\nabla_+^2 v - 2Rv + \omega G(u,v)$$

where

$$F(u,v) = \alpha u(1 - r_3 v^2) + v(1 - r_2 u)$$
$$G(u,v) = \beta v\left(1 + \frac{\alpha r_3}{\beta}uv\right) + u(\gamma + r_2 v)$$

and u is an activator and v is an inhibitor

$d = \frac{D_u}{D_v} << 1$ ratio of diffusion terms — ***Constant***

ω = domain scaling — ***Vary*** ω

$\rho(t) = e^{Rt}$ = growth rate function — ***Vary R***

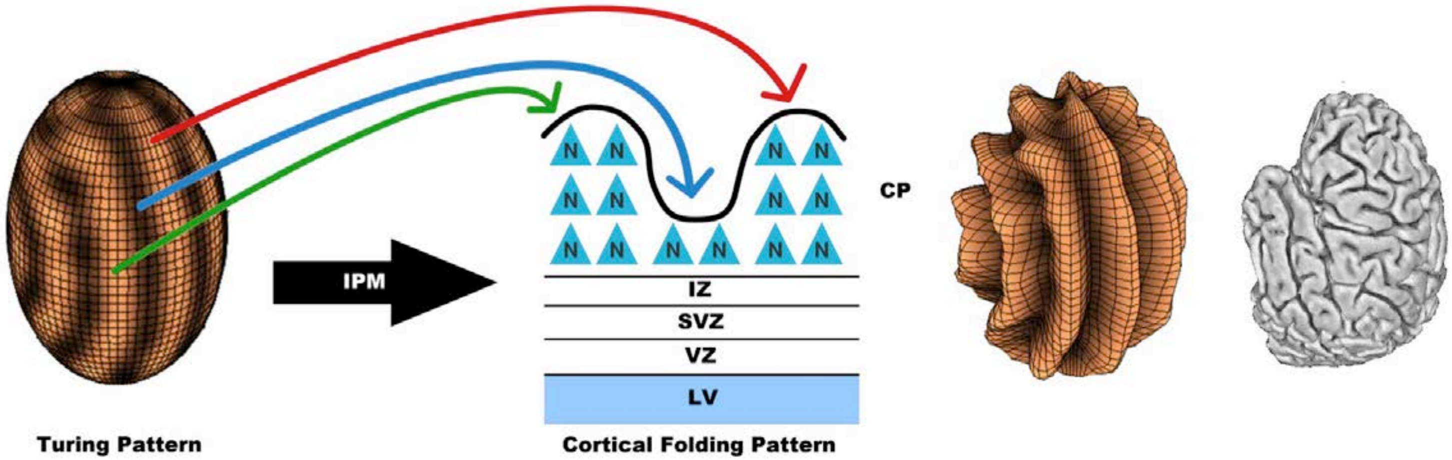
α, β = linear interactions — ***Constant***

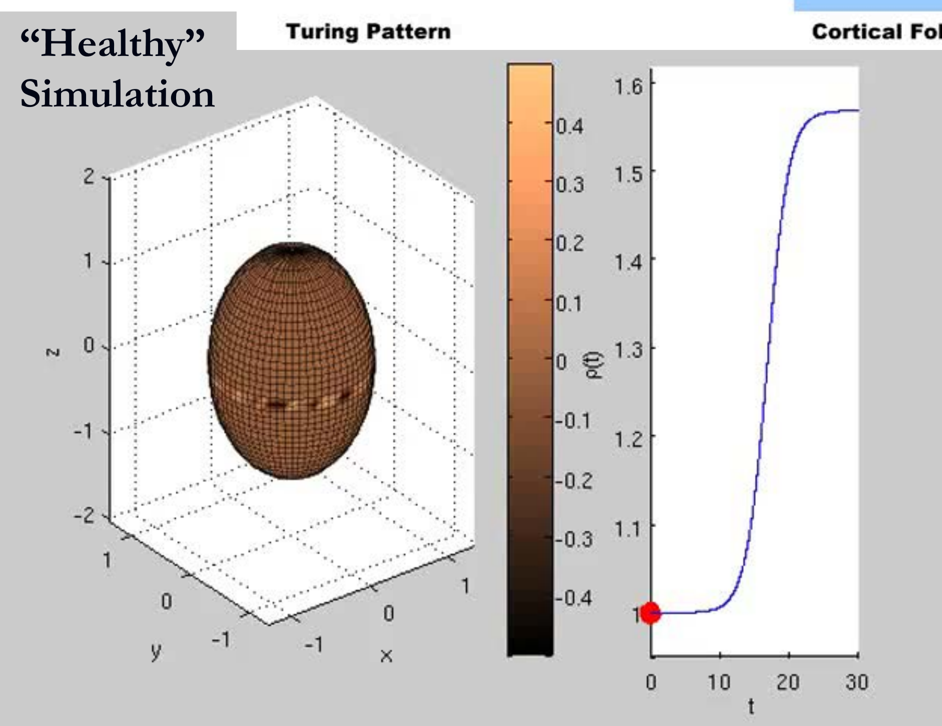
r_2, r_3 = quadratic, cubic interactions — ***Constant***

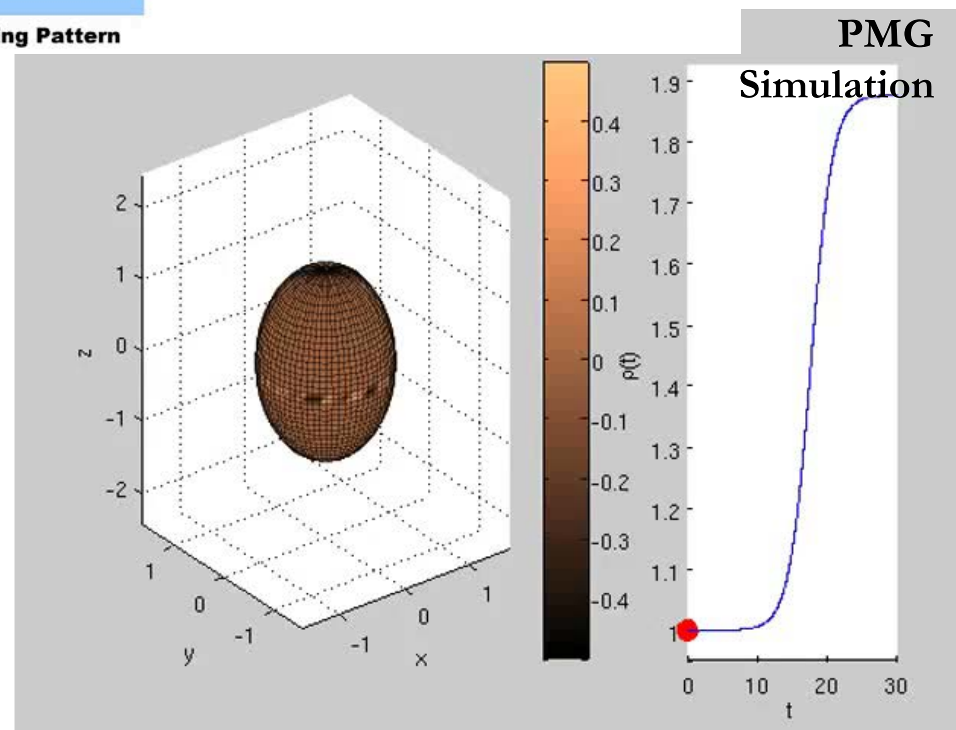
A.M. Turing, *Phil. Trans. Roy. Soc. of Lon. B*, **237**, 37-72 (1952).
R.A. Barrio, C. Varea, J. L. Aragon, P. K. Maini, *Bull Math Bio*, **61**(**3**), 483-505 (1999).

Pattern Formation

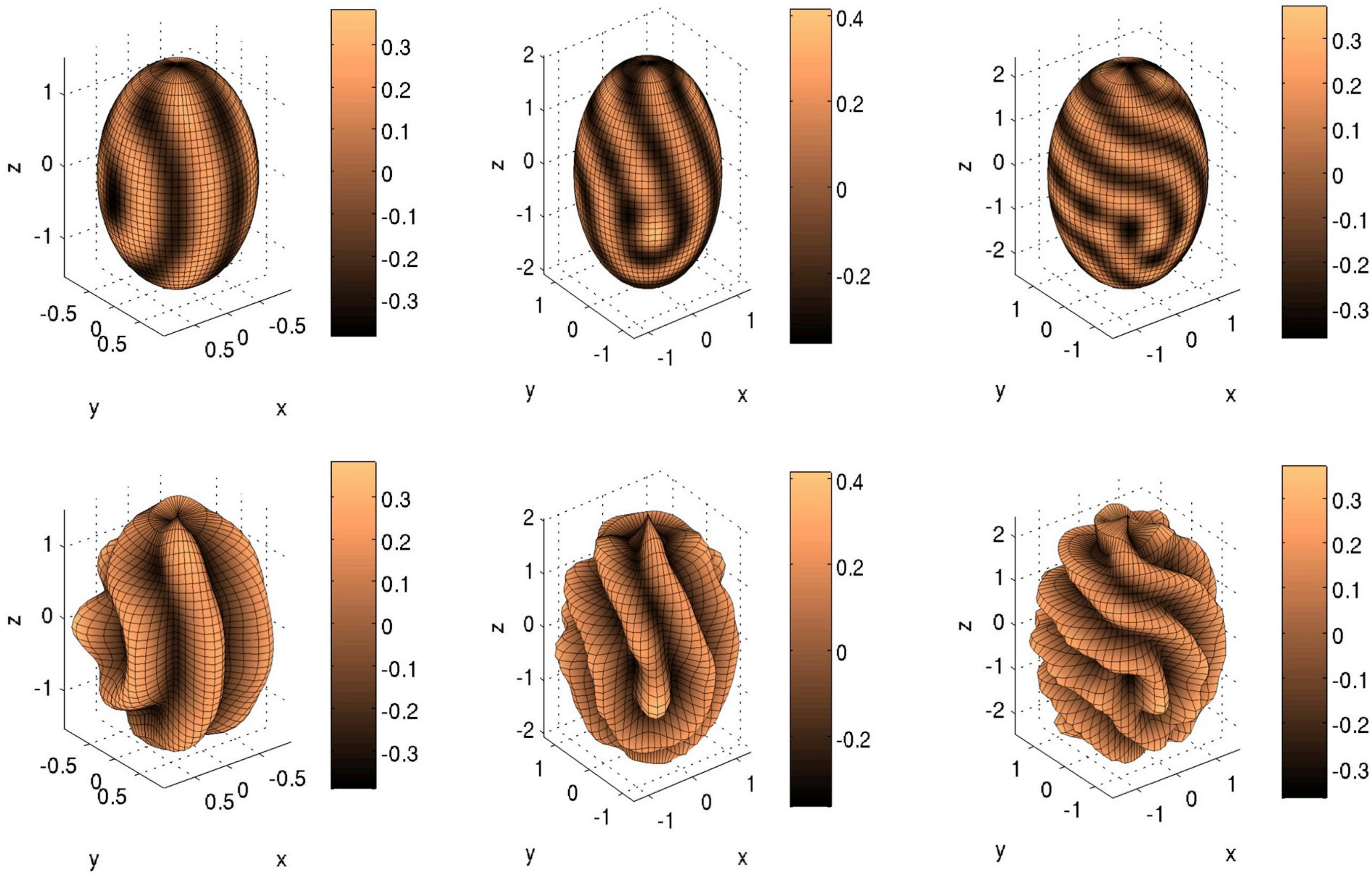
Modeling and understanding cortical folding pattern formation is important for quantifying cortical development







Modeling Cortical Diseases



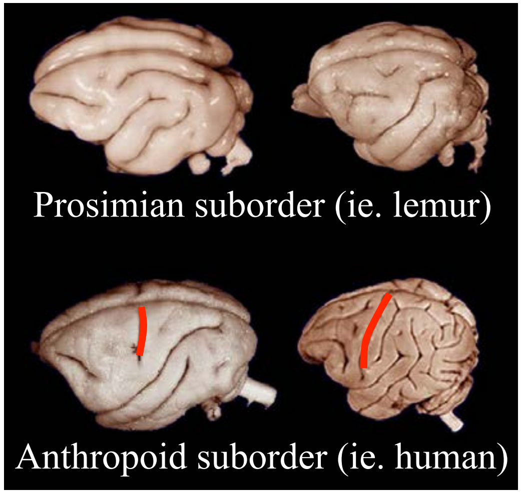
NRS: R=0.005, ω=115
Smaller ventricles

Normal: R=0.015, ω=115

PMG: R=0.021, ω=115
Enlarged ventricles

Model Results

- Our model is able to elucidate which parameters can lead to excessive cortical folding in disease
- Domain (focal distance) seems to play a role in sulcal pattern formation across species of increasing evolutionary complexity:
  - Earlier in evolutionary timelines when LV focal distances are smaller, our model shows sectorial sulci appear before transverse sulci (ie. domesticated cat, lemur, human)
  - Later, when LV focal distances are larger, a first transverse sulcus appears, corresponding to calcarine sulcus (ie. lemur, human)
  - Later, when LV focal distances are even larger, a 2nd transverse sulcus appears, corresponding central sulcus (ie. human)



- Modeling and understanding cortical folding pattern formation is important for quantifying cortical development

Can applying conformal mapping to these simulated folding patterns contribute anything???

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More Information on Brain Mapping:

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- Email: mhurdal@math.fsu.edu