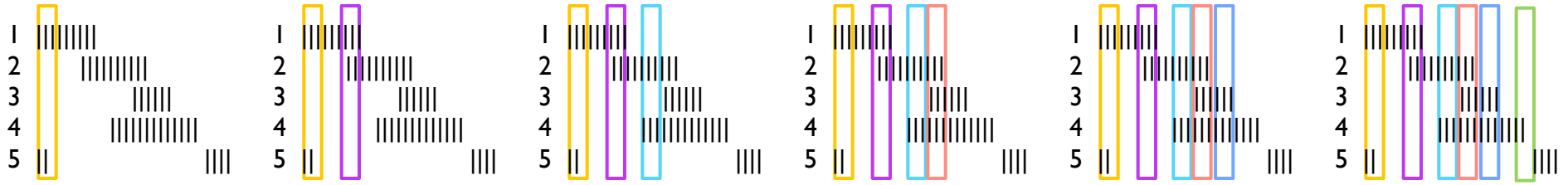


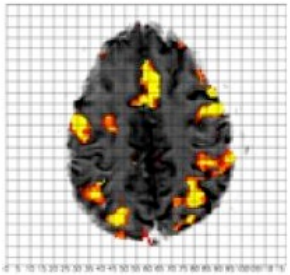
Topological analysis of fMRI brain activity time series data

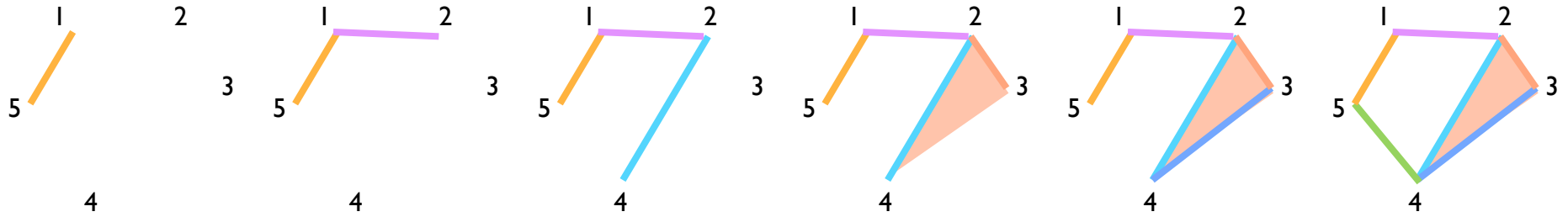
Arno Klein
arno@binarybottle.com

asst. professor of
clinical neurobiology
columbia university

Steve Ellis
spe4@columbia.edu

assoc. professor of
clinical neurobiology
columbia university





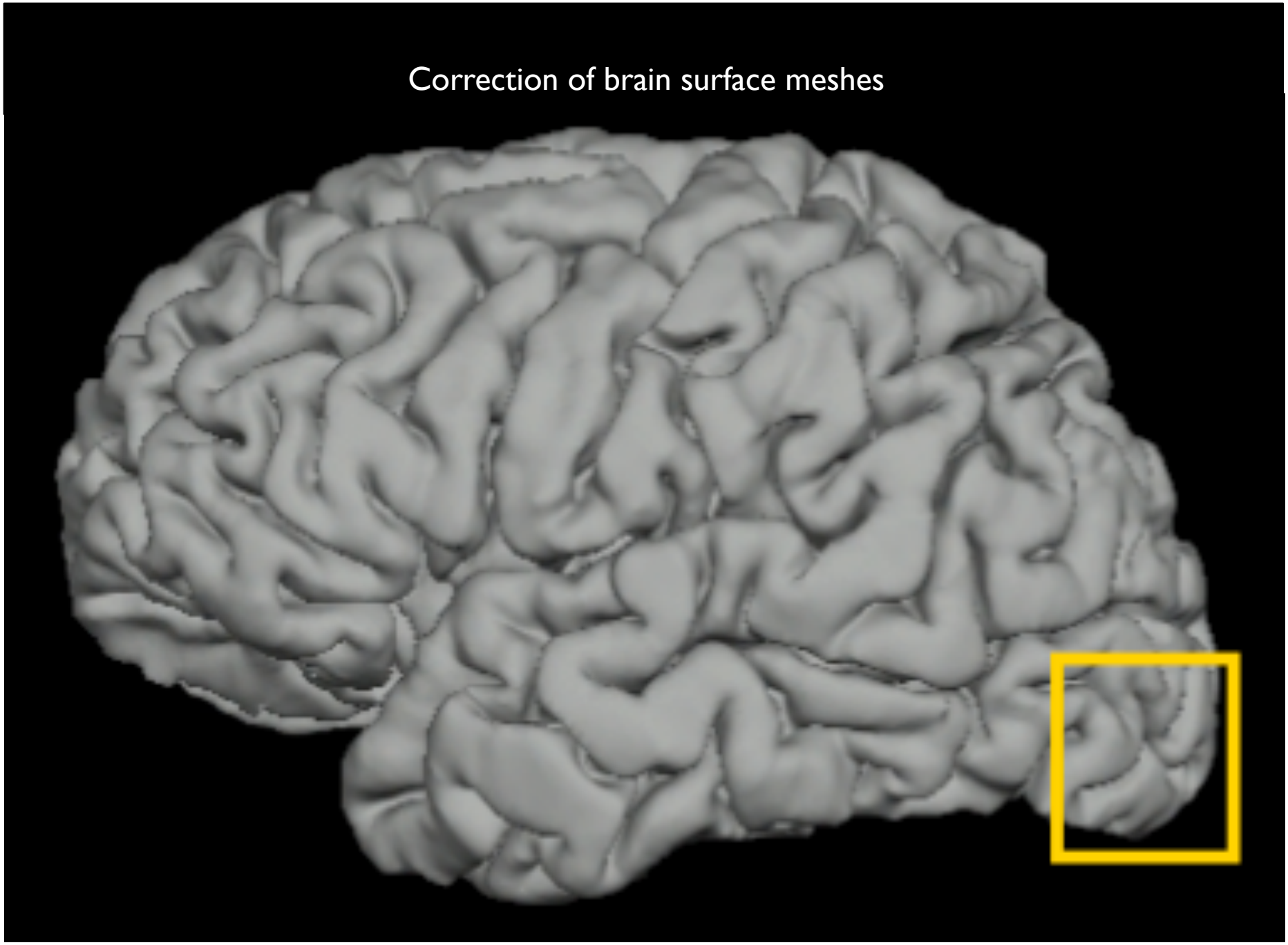
I. Topology and structural brain image data

II. Topology and functional brain activity data

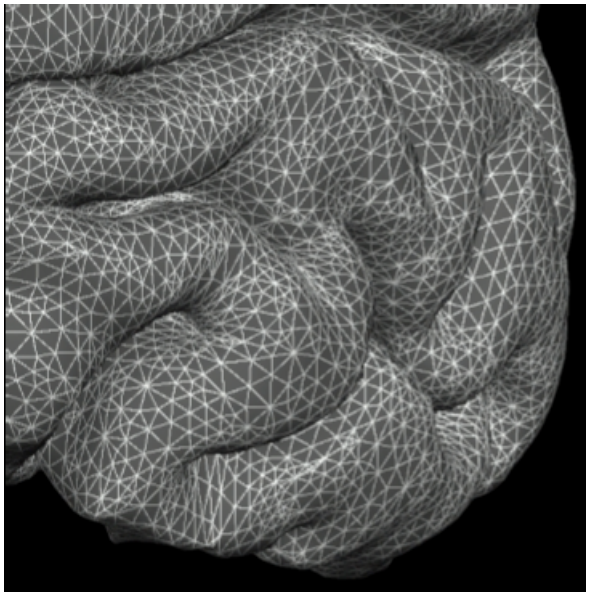
I. Topology and structural brain image data

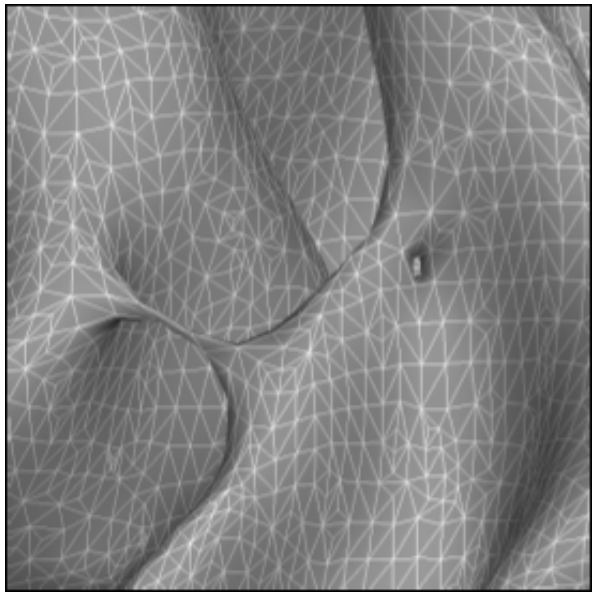
II. Topology and functional brain activity data

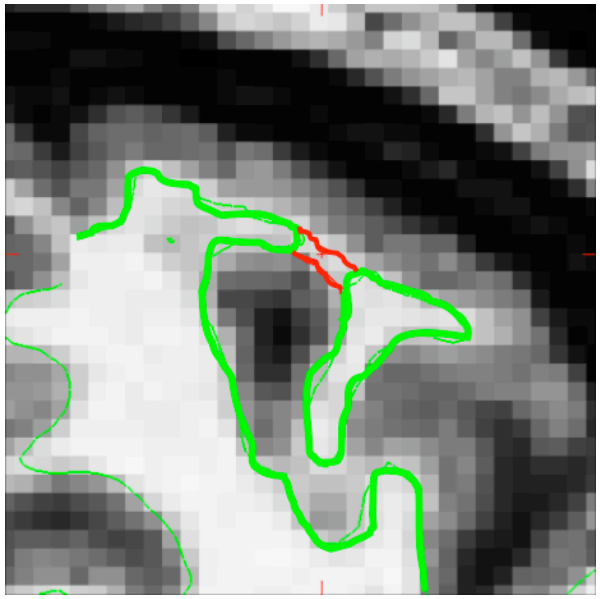
Correction of brain surface meshes



Correction of brain surface meshes

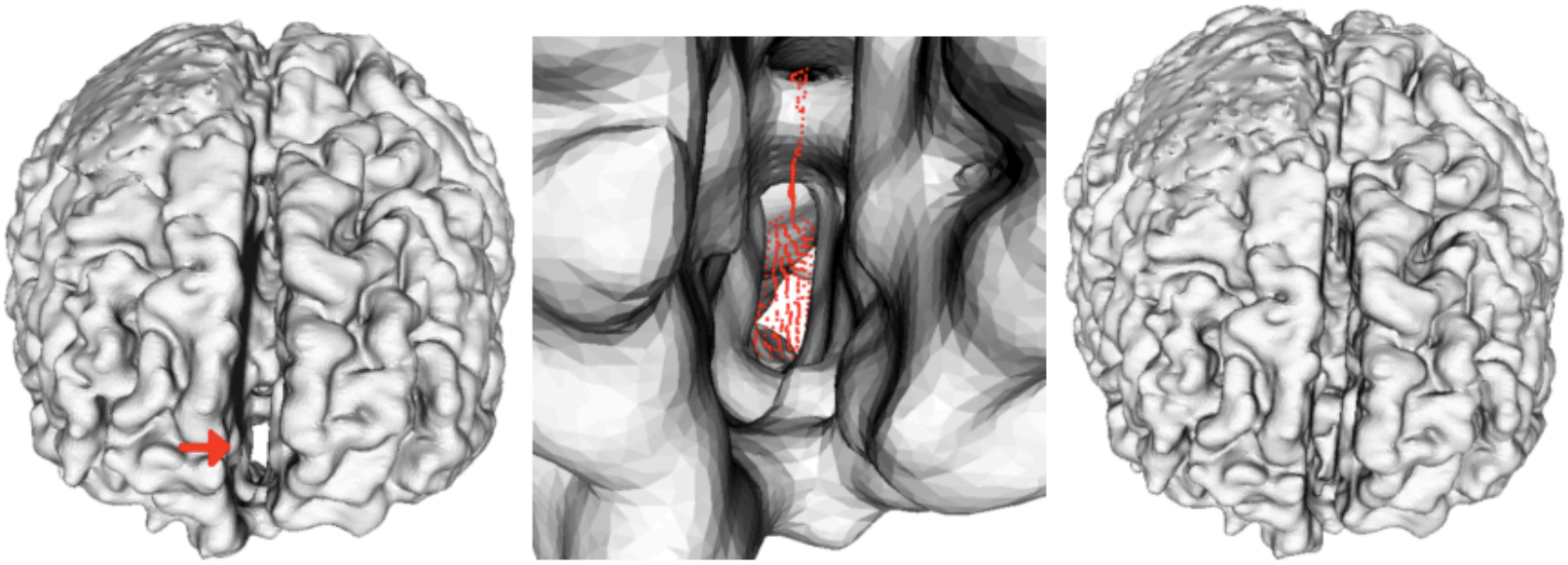






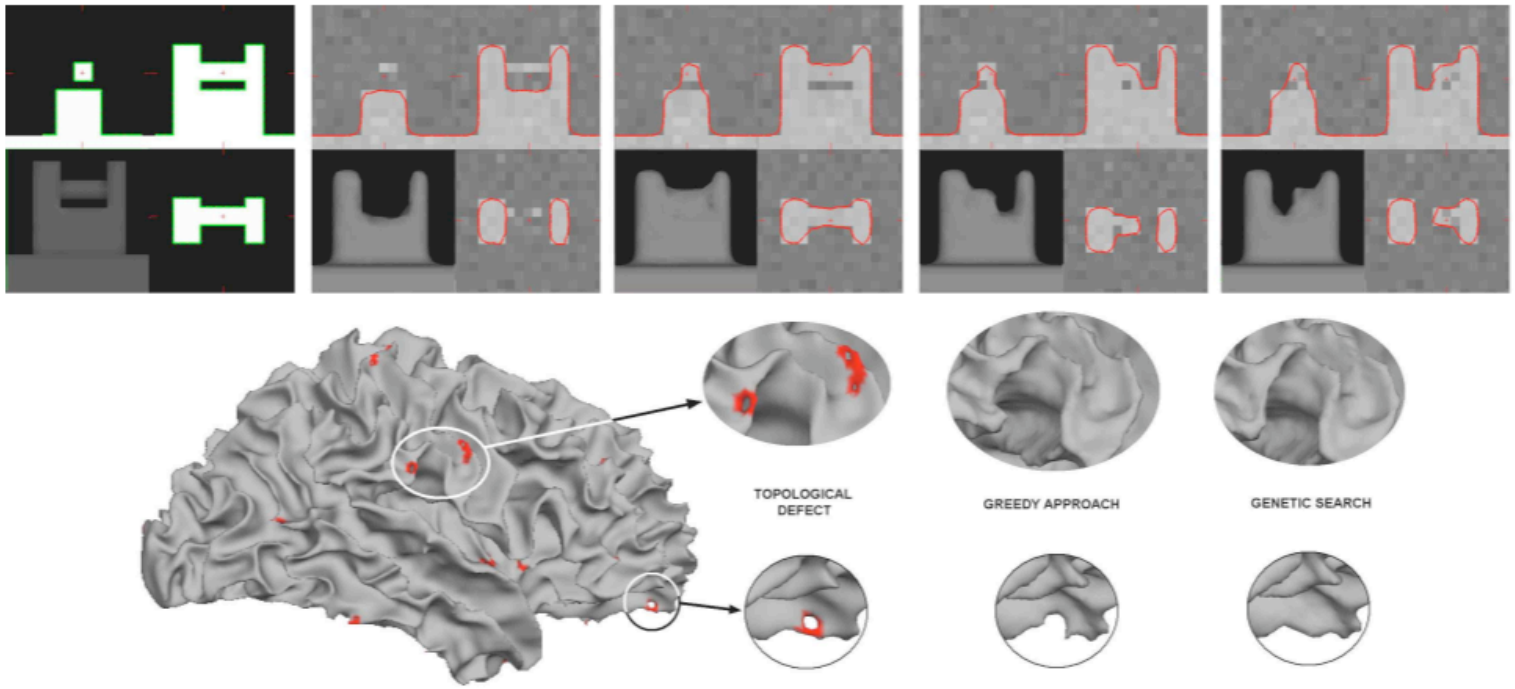
FreeSurfer

Correction of brain surface meshes



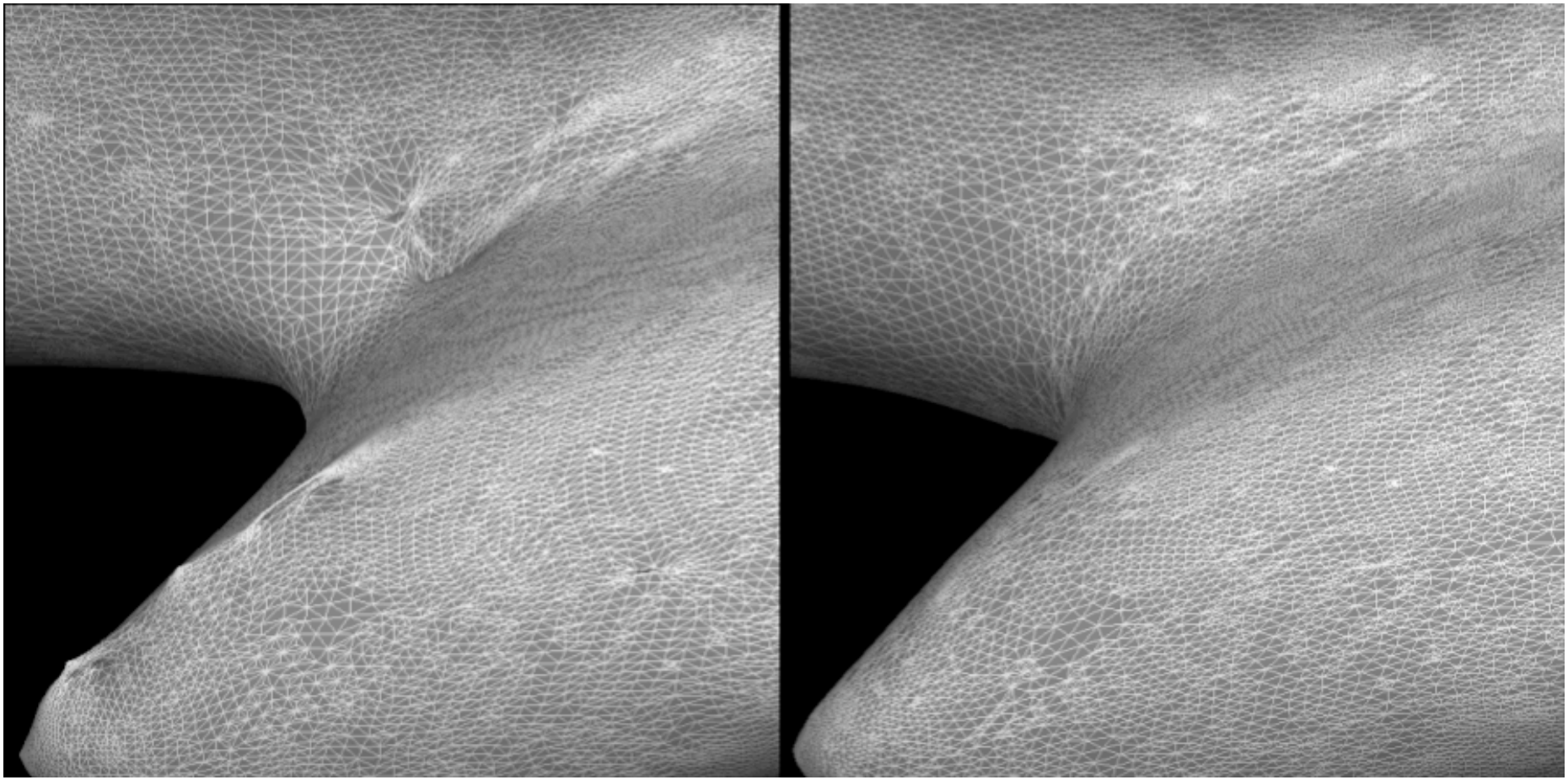
"Open Topology: A Toolkit for Brain Isosurface Correction" (Jaume, et al., 2005)

Correction of brain surface meshes



Ségonne et al. 2005

Correction of brain surface meshes



Freesurfer

Topological classification and topology-preserving deformations

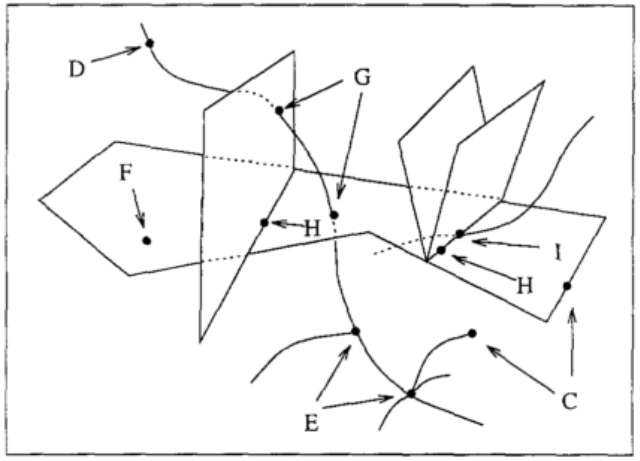
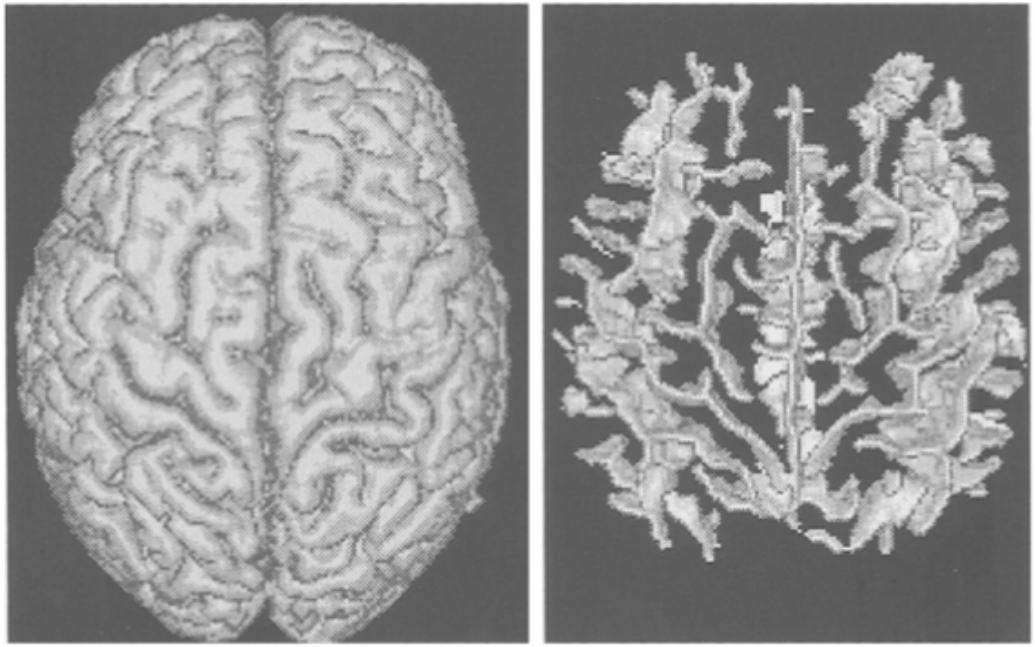
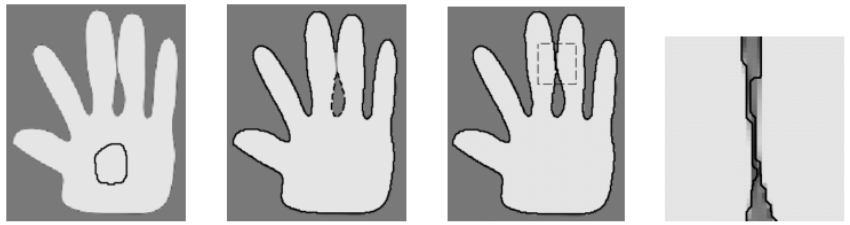


Fig. 12. Exhaustive topological classification of points for a 3D object considered in 26-connectivity [29]. Border points are equivalent to simple points [35].

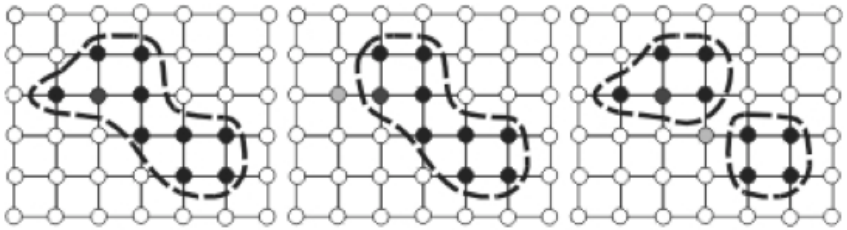


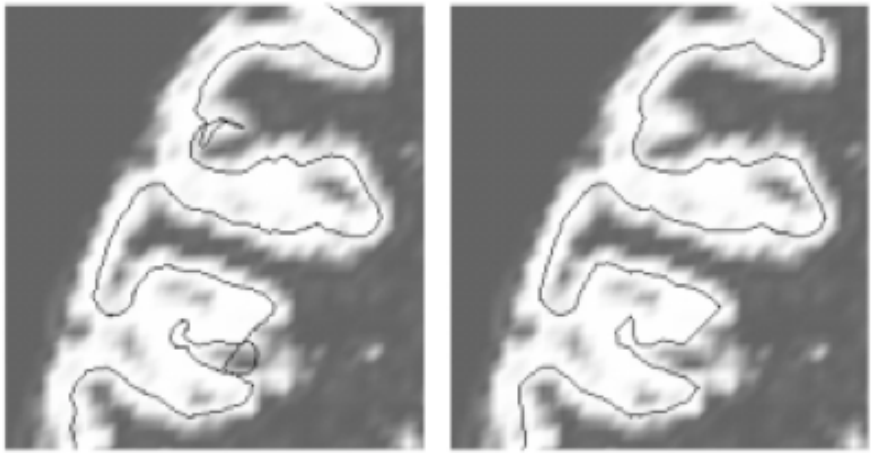
"From 3D Magnetic Resonance Images to Structural Representations of the Cortex Topography using Topology Preserving Deformations"
(Mangin, et al., 1995)

Topology-preserving deformations



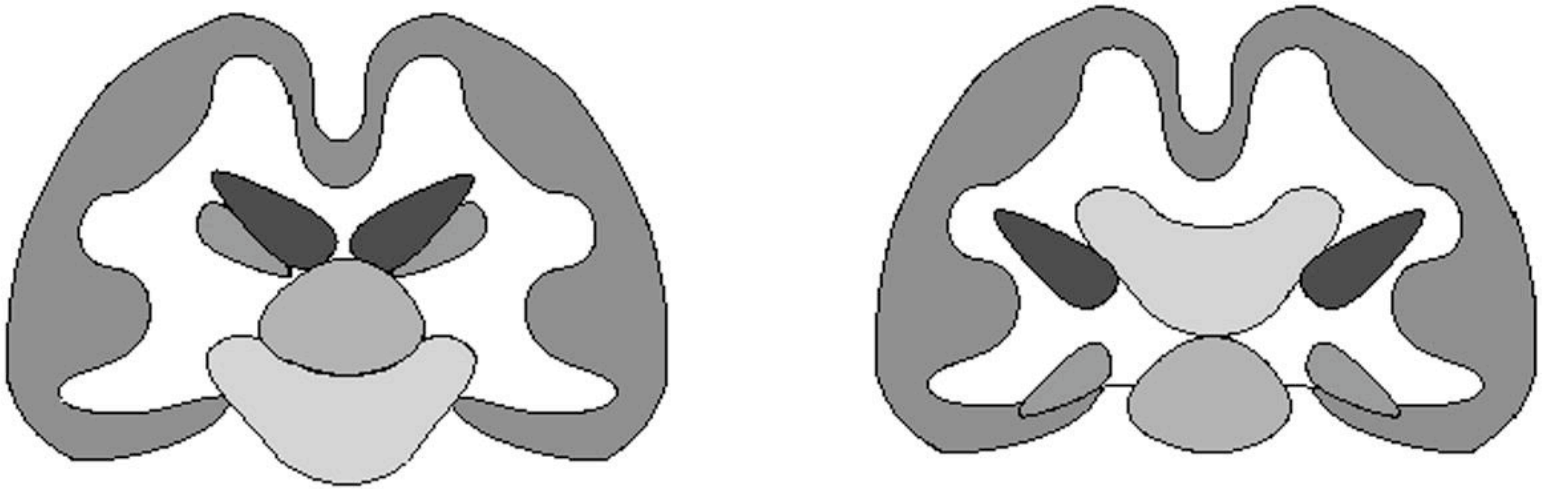
Han et al. (2001)





level set implementation by Xan et al. (2003)

Topology-preserving deformations

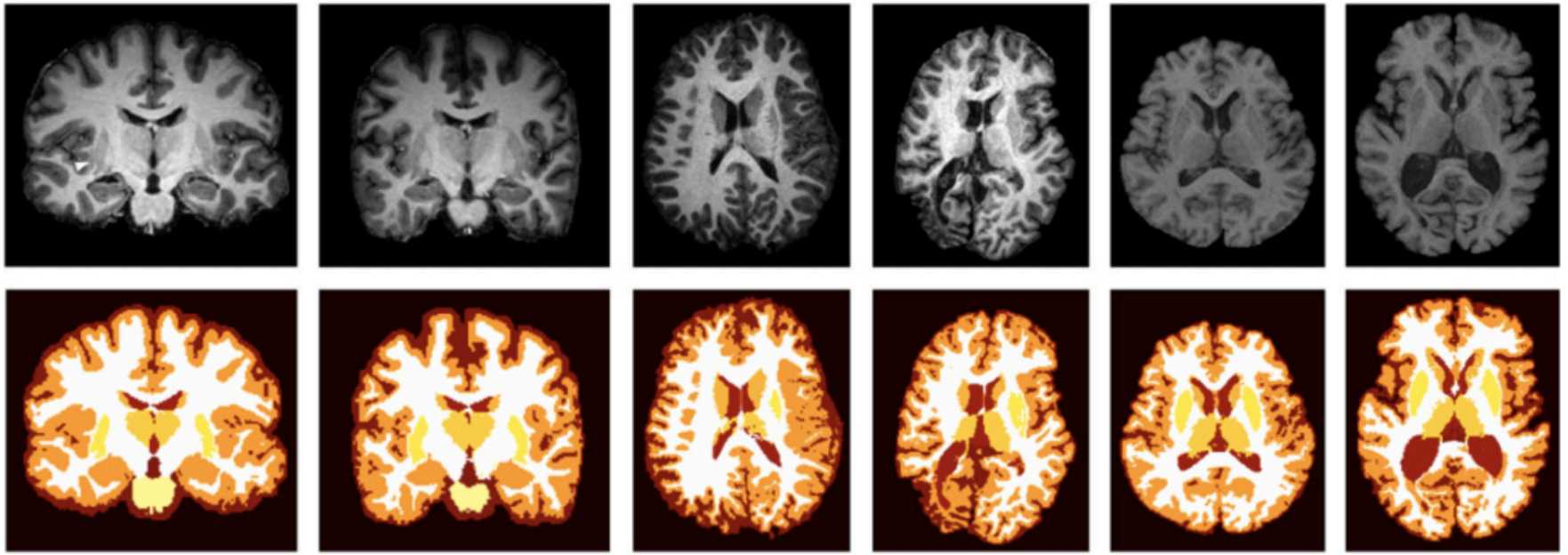


"Homeomorphic brain image segmentation with topological and statistical atlases" (Bazin and Pham, 2008)

Importance of the topology of groups:

The individual structures above have the same topology, but the relationships between them are different, corresponding to changes in the topology of groups (unions) of structures.

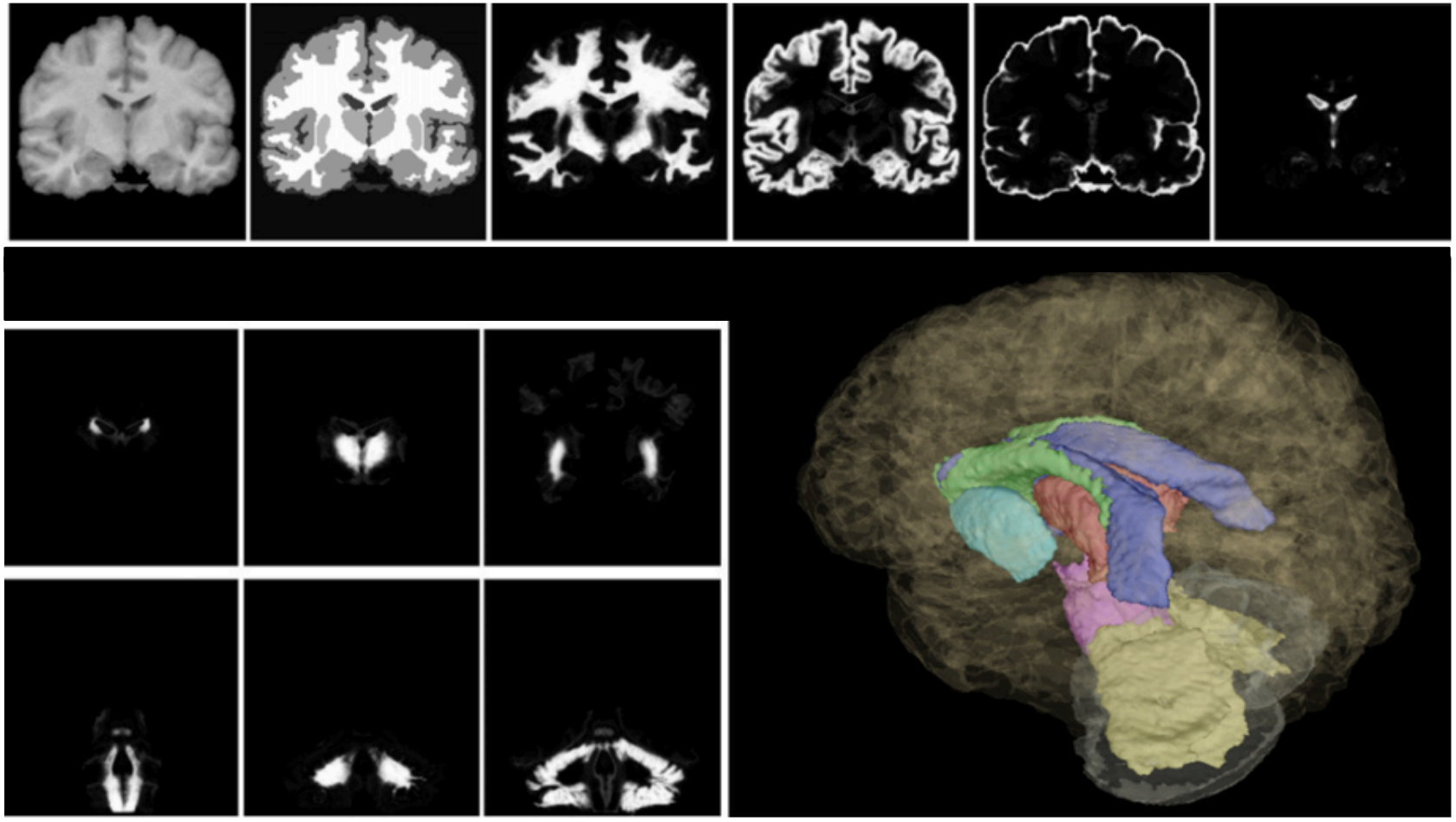
Topology-preserving deformations



Bazin and Pham (2008)

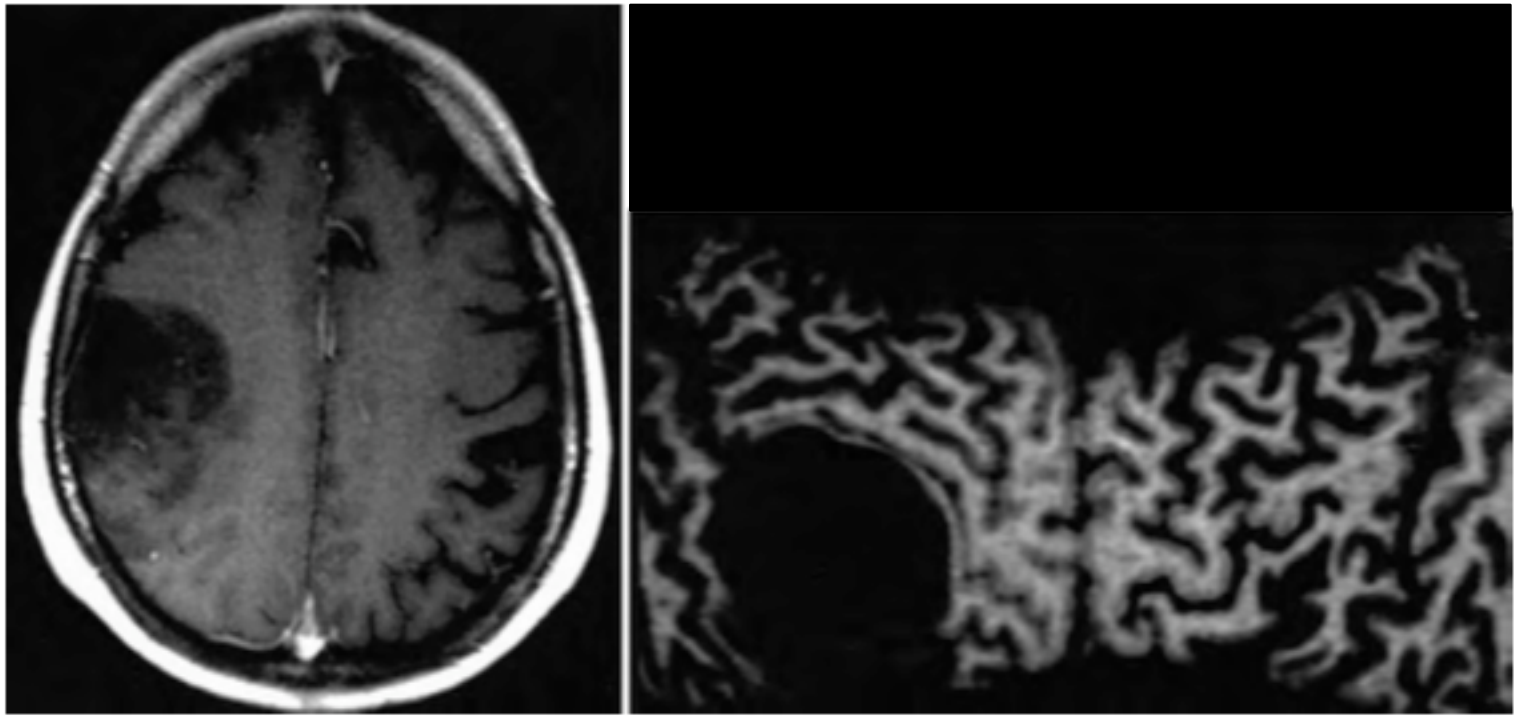
Topological properties of brain tissues encode their continuity and relationships, independently of their shape, and can be used to constrain segmentation.

Topology-preserving deformations



Bazin and Pham (2008)

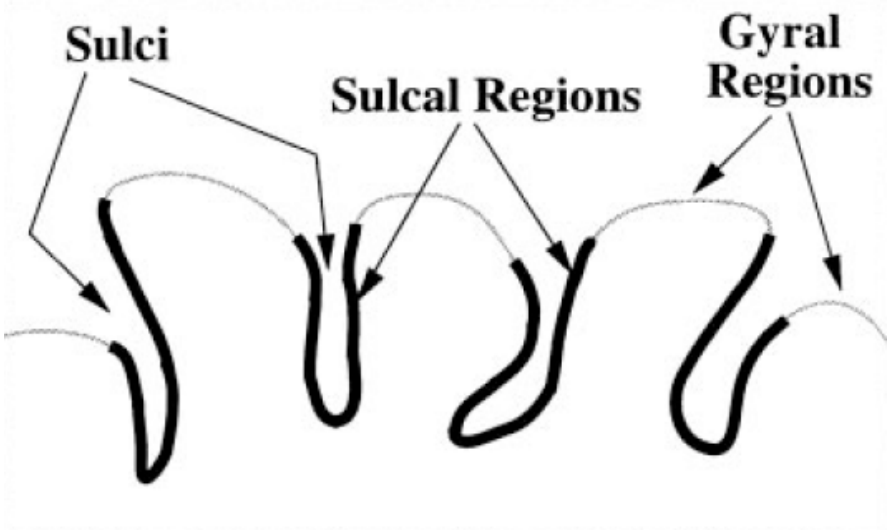
Topology of lesions, plaques, etc.

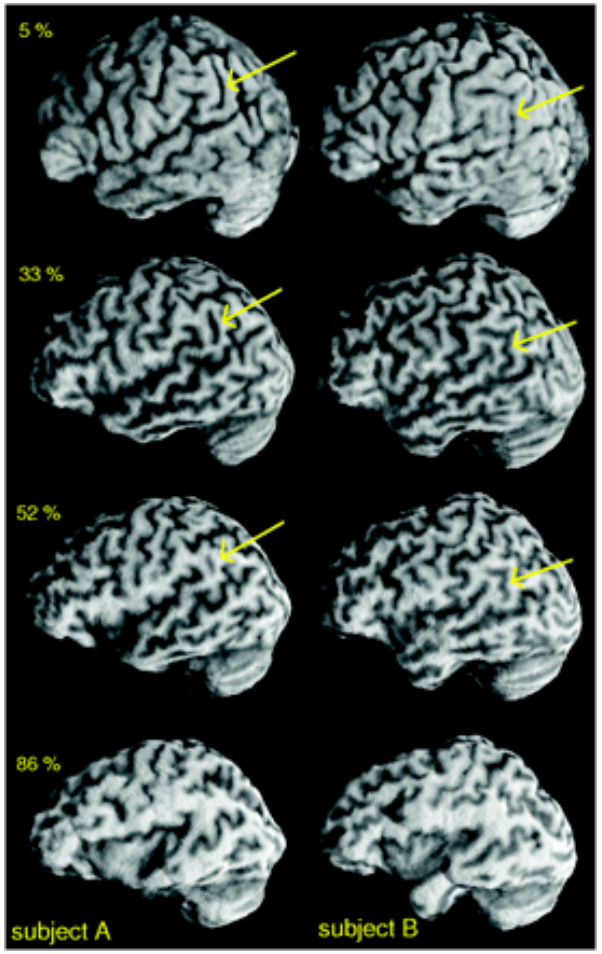


Brain Surface Reformatting for lesion localization

Hattingen et al. 2005

Topology of elevation map of brain folds

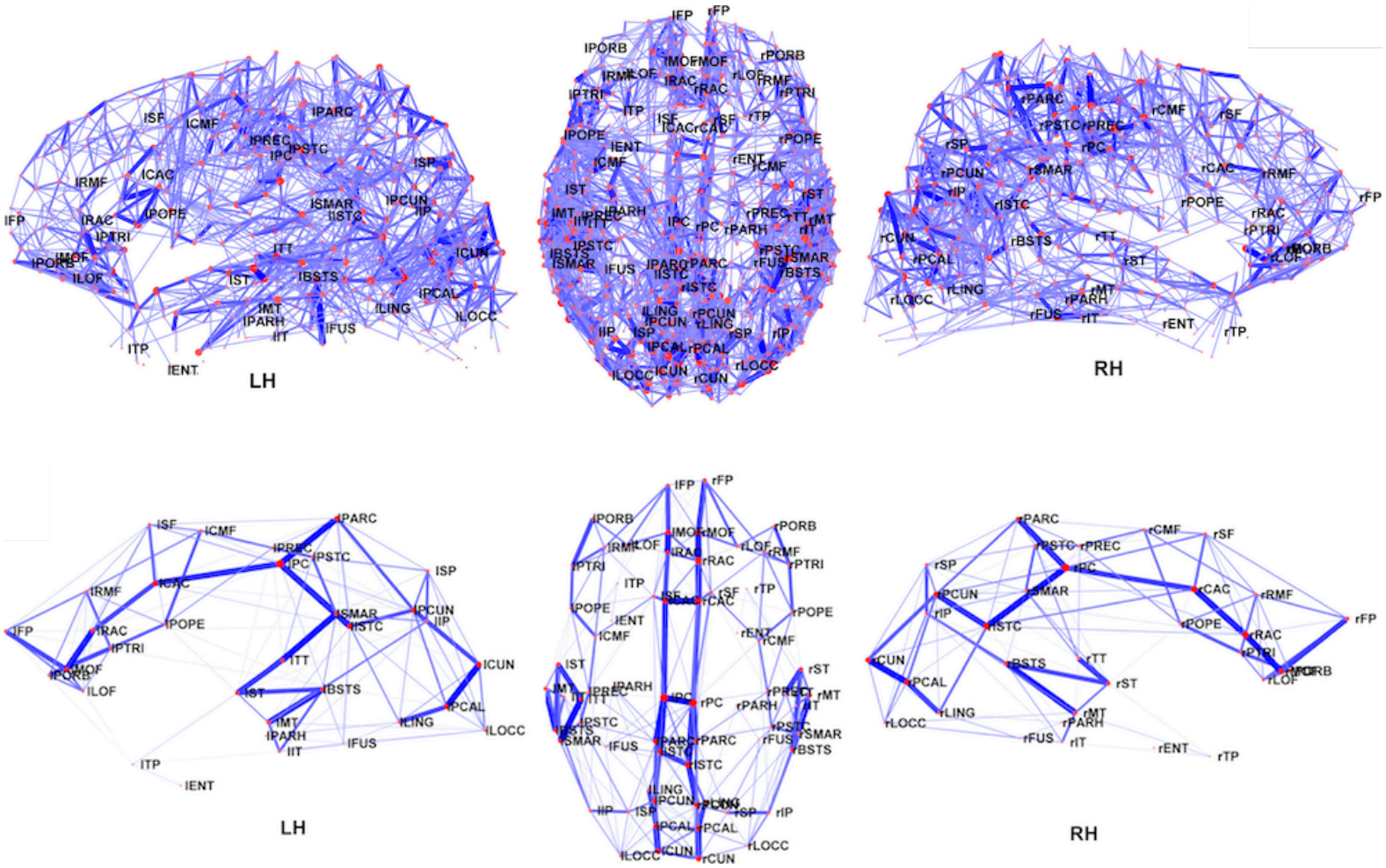




sulcal pattern complexity decreases with depth

Lohmann et al. 2008

Topology of networks



Hagmann et al. (2008)

I. Topology and structural brain image data

II. Topology and functional brain activity data

Topology and brain activity

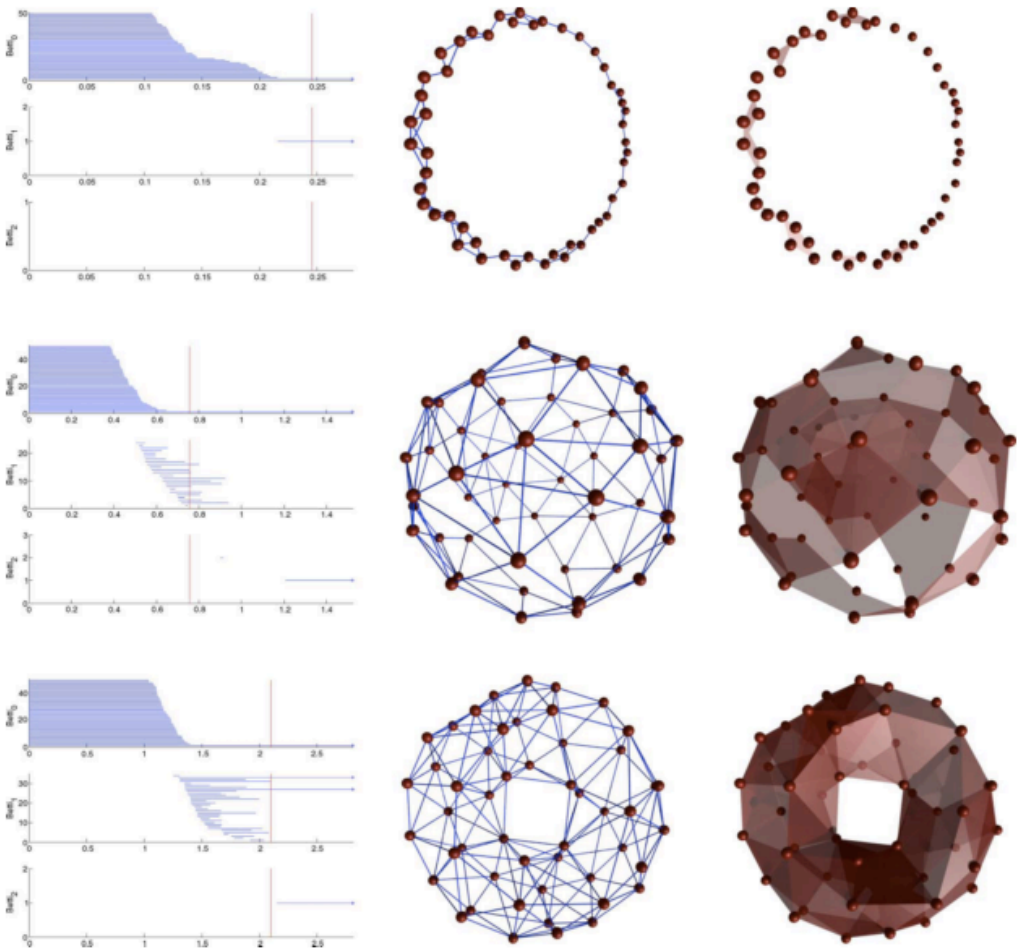
Two studies have used computational topology to analyze patterns of simultaneously firing ("concurrently active") neurons:

– multielectrode data in anesthetized macaque monkey primary visual cortex (Singh et al., 2008)

– simulated rat hippocampal place cells (Curto and Itskov, 2008)

“Topological analysis of population activity in visual cortex”

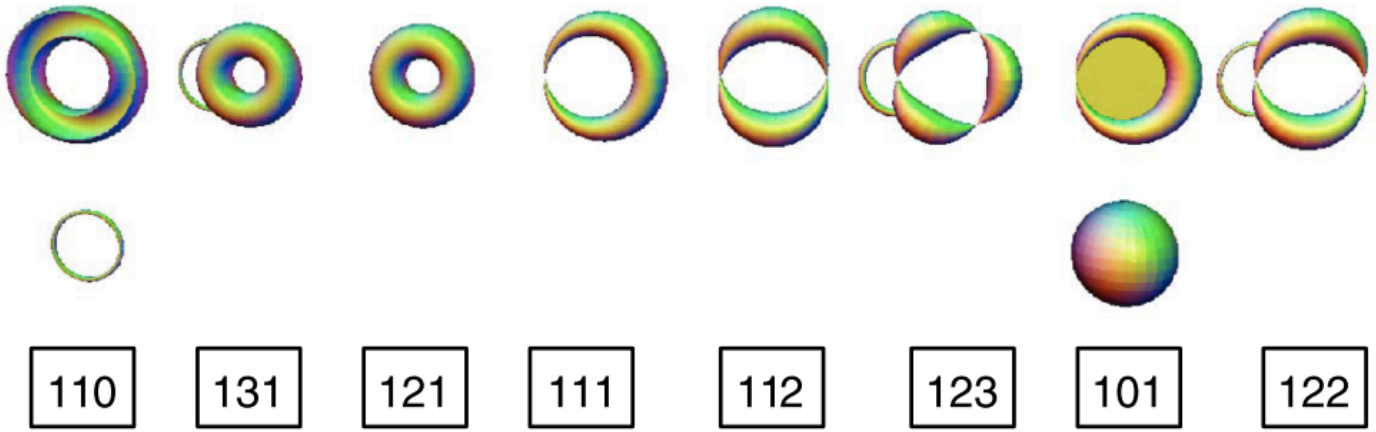
Singh & colleagues analyzed the persistence of spike train data represented as a Rips complex.



Example persistence bar codes and Rips complexes for a circle, sphere, and torus (Singh et al., 2008).

“Topological analysis of population activity in visual cortex”

They showed that both the data for spontaneous and visually stimulated neural activity have similar topological structures, with the circle (Betti numbers 1, 1, 0,...)
and the sphere (Betti numbers 1, 0, 1,...) dominating the results:



Singh et al. (2008)

“Cell Groups Reveal Structure of Stimulus Space”

Curto and Itskov (2008) demonstrated a relationship between

the topology of an internal representation

- patterns of neural activity -

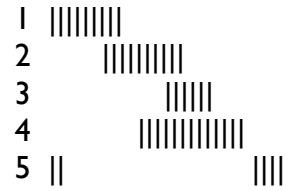
and the topology of external stimuli

- a maze -

We have modeled our “concurrence-based” approach
after their work, substituting *fMRI* for *multielectrode* data.

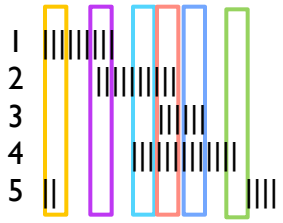
Curto and Itskov

1. Simulated binary (“on” or “off”) times series data of neural activity in the brain of a rat running a maze.



Curto and Itskov

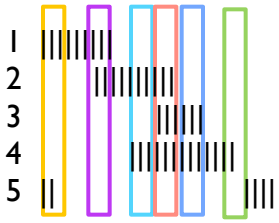
1. Simulated binary (“on” or “off”)
   times series data of neural activity
   in the brain of a rat running a maze.



2. Bin simultaneous activity
   (we’ll call a “concurrence”).

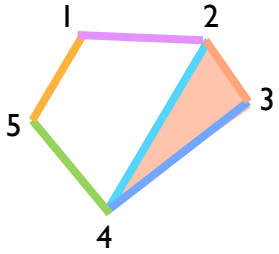
Curto and Itskov

1. Simulated binary (“on” or “off”) times series data of neural activity in the brain of a rat running a maze.



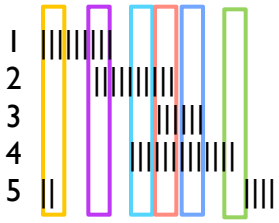
2. Bin simultaneous activity (we’ll call a “concurrence”).

3. Represent the data as a simplicial complex, K.



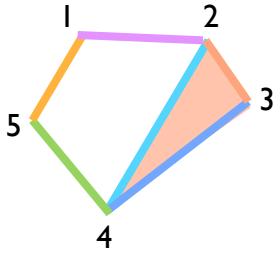
Curto and Itskov

1. Simulated binary (“on” or “off”) times series data of neural activity in the brain of a rat running a maze.



2. Bin simultaneous activity (we’ll call a “concurrence”).

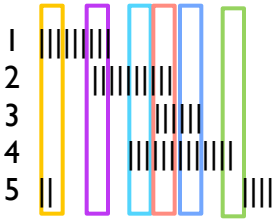
3. Represent the data as a simplicial complex, K.



4. Compute Betti numbers of K.

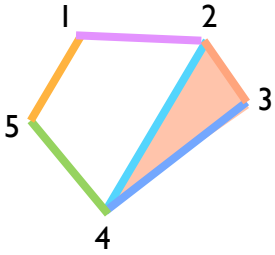
Concurrence

– A concurrence may be thought of as a simplex whose vertices are locations in a brain.

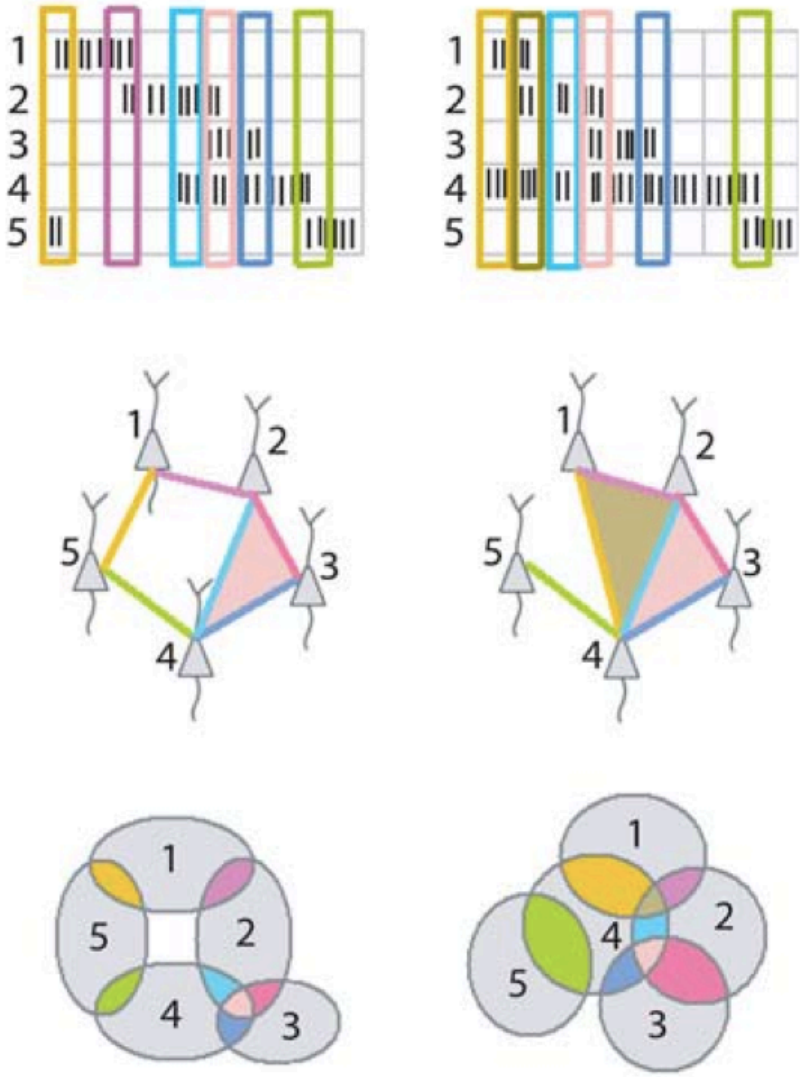


– A collection of concurrences forms a simplicial complex (if one includes all faces of all the simplices).

– Geometrically, the Betti numbers represent gaps, holes, voids, cavities, tunnels in the complex.



– This approach ignores *when* concurrences take place.



Curto & Itskov (2008)

Curto and Itskov results:

After many simulations of a rat wandering around mazes, they found that the Betti numbers of the complex were the same as the Betti numbers of the mazes.

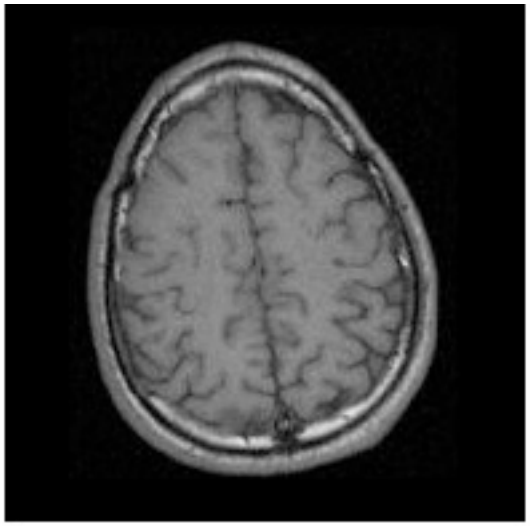
In other words, they used topological methods to test an algorithm whereby the rat might integrate local information to form a global picture of the maze.

fMRI: functional magnetic resonance imaging:

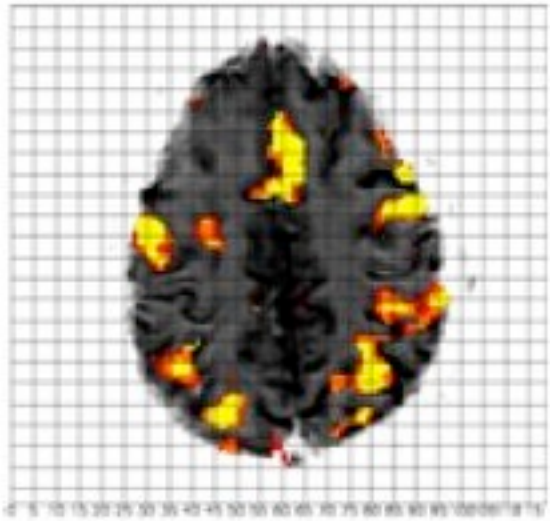
– fMRI images of a human brain are acquired once every few seconds.

– Spatial resolution is a few mm^3.

– In our data set, we have average activity values in 92 brain regions at about 190 time points.



MRI



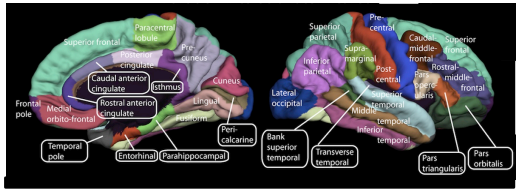
fMRI

Data and preprocessing

Largest publicly available “resting state” fMRI data set containing clinical data (ADHD: N=25; control: N=43).

I. Labeled regions

1. Labeled anatomical regions.
2. Registered regions to fMRI data.
3. Removed intensity outliers.



II. Detrended time series data

1. For each subject, we fitted a (robust) straight line to the activity vs. time data to remove a time trend in the overall *level* of activity.
2. Fitted a (robust) straight line to the logarithms of the absolute values of the above to correct for time trends in the *variability* of activity.

III. Retained only “variable” regions

1. We’re interested in covariation, and not in trivial variations.
2. For each subject, we dropped the 20% least variable regions (74 remained). (Potentially, different regions are dropped in different subjects.)

Correlating activity in different brain regions is a hard statistics problem:

– Each region's activity varies over time, corresponding to a separate variable.

– We are interested in statistical dependence among the variables.

– Hardly any statistical methods exist for studying the dependence among ≈90 variables in an "agnostic" fashion, especially among 3 or more variables.

So we modified Curto & Itskov's method for fMRI:

– Concurrences can be a part of larger concurrences.

– Concurrences can take place multiple times,
and in fMRI, frequency of concurrence is important.

– The more often a concurrence takes place, the stronger
is the correlation among the regions involved.

Frequency of a concurrence

The frequency of a concurrence is the number of times it occurs even as part of another concurrence.

Simplices occurring at least:

Example data:	t1	t2	t3	t4	*twice:* t1	t2	t3	*thrice:* t1	t2	t3	*four times:* t3
r1	X	X	X	X	X	X	X	X	X	X	X
r2				X							
r3	X	X	X	X	X	X	X	X	X	X	X
r4	X	X		X	X	X		X	X		

Frequency of a concurrence

The frequency of a concurrence is the number of times it occurs even as part of another concurrence.

Simplices occurring at least:

Example data:

	t1	t2	t3	t4
r1	X	X	X	X
r2				X
r3	X	X	X	X
r4	X	X		X

twice:

t1	t2	t3
X	X	X
X	X	X
X	X	

thrice:

t1	t2	t3
X	X	X
X	X	X
X	X	

four times:

t3
X
X

Frequency of a concurrence

The frequency of a concurrence is the number of times it occurs even as part of another concurrence.

Simplices occurring at least:

Example data:

	t1	t2	t3	t4
r1	X	X	X	X
r2				X
r3	X	X	X	X
r4	X	X		X

twice:

t1	t2	t3
X	X	X
X	X	X
X	X	

thrice:

t1	t2	t3
X	X	X
X	X	X
X	X	

four times:

t3
X
X

Frequency of a concurrence

The frequency of a concurrence is the number of times it occurs even as part of another concurrence.

Simplices occurring at least:

Example data:

	t1	t2	t3	t4
r1	X	X	X	X
r2				X
r3	X	X	X	X
r4	X	X		X

twice:

t1	t2	t3
X	X	X
X	X	X
X	X	

thrice:

t1	t2	t3
X	X	X
X	X	X

four times:

t3
X
X

Homology to study "positive" occurrences:

"Positive analysis": analyzing concurrences of activity:
If a concurrence a – b – c frequently occurs, then we have evidence of "positive association" among regions a, b, and c.

– It is therefore easy to detect positive associations:
We merely tabulate complete concurrences.

Homology to study “negative” occurrence:

“Negative analysis”: analyzing inactivity (“holes”)

– An astronomical number of concurrences never take place.

– Virtually none are interesting.

– Homology provides a data-driven way of identifying potentially interesting absent concurrences.
Betti numbers count absent concurrences that are surrounded by concurrences that are present.

Persistent homology

We've looked at homology of the simplicial complexes corresponding to each frequency threshold separately.
But each of those complexes are nested in the previous one.
Might there be information in how they fit inside each other?

"Persistent homology" can identify holes in a complex that are still there in the complex at the next frequency cutoff.
Such a persistent structure would probably be more "real" than one with a fleeting existence.

For complex K:

$$K_1 \leftarrow K_2 \leftarrow \cdots \leftarrow K_N$$

subscripts are frequency levels
arrows are inclusion maps
N is the number of frequency levels

Persistent homology

Dmitriy Morozov is assisting us with Dionysus software.

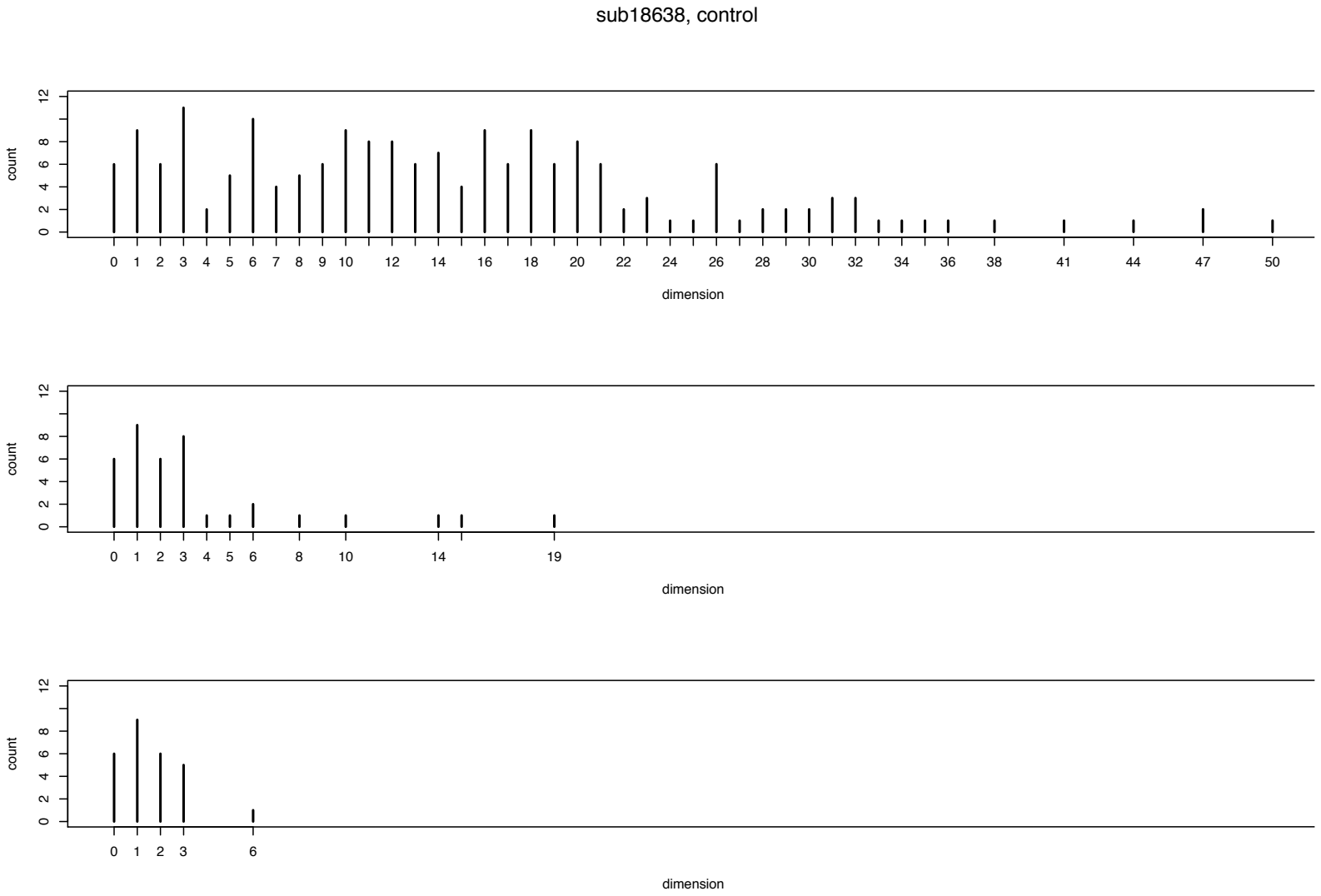
Vidit Nanda and Konstantin Mischaikov are assisting us with their Chomp2 and custom-made software.

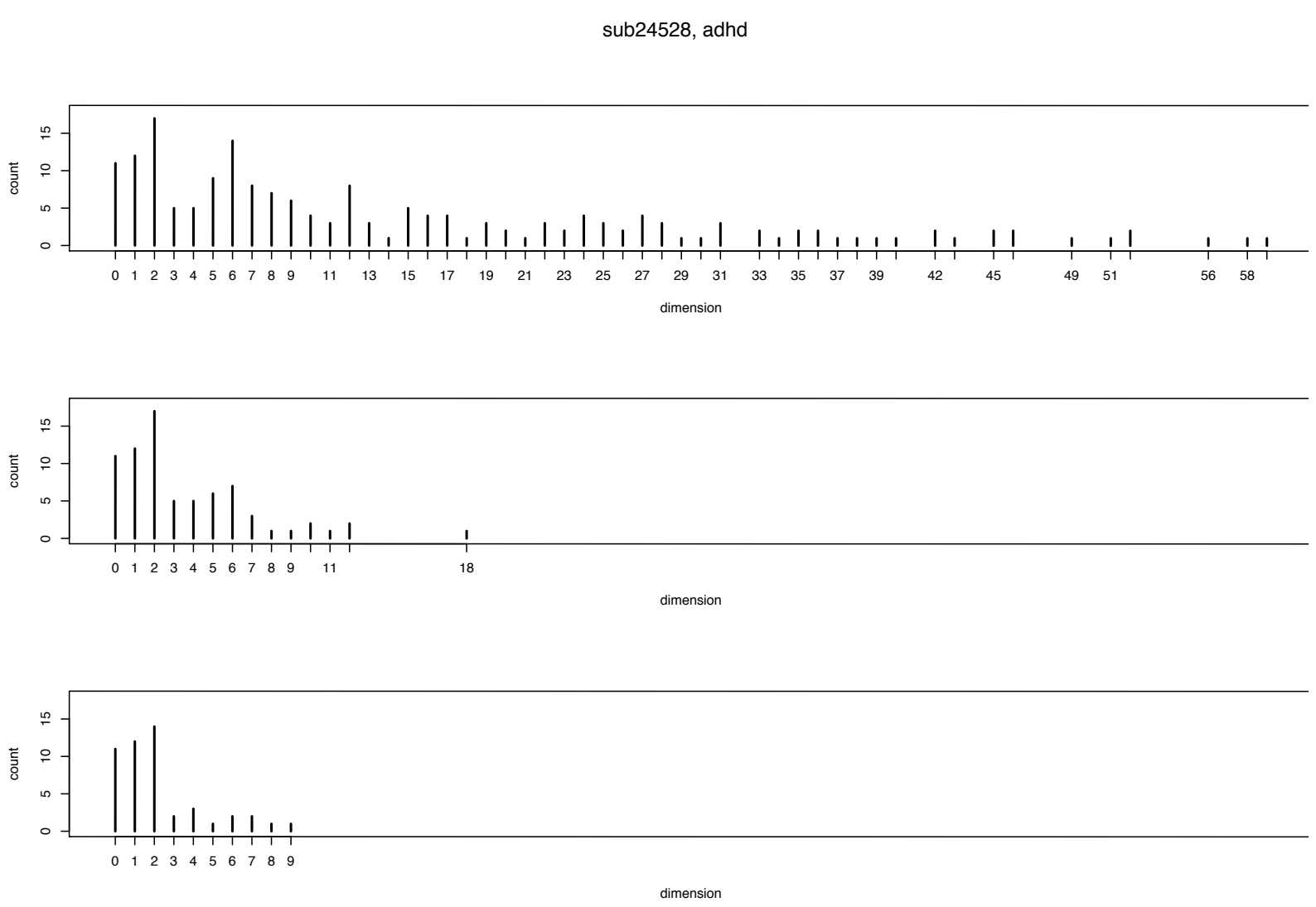
Presently, we are running data from 60+ subjects through Dionysus's dynamic persistence chains code.

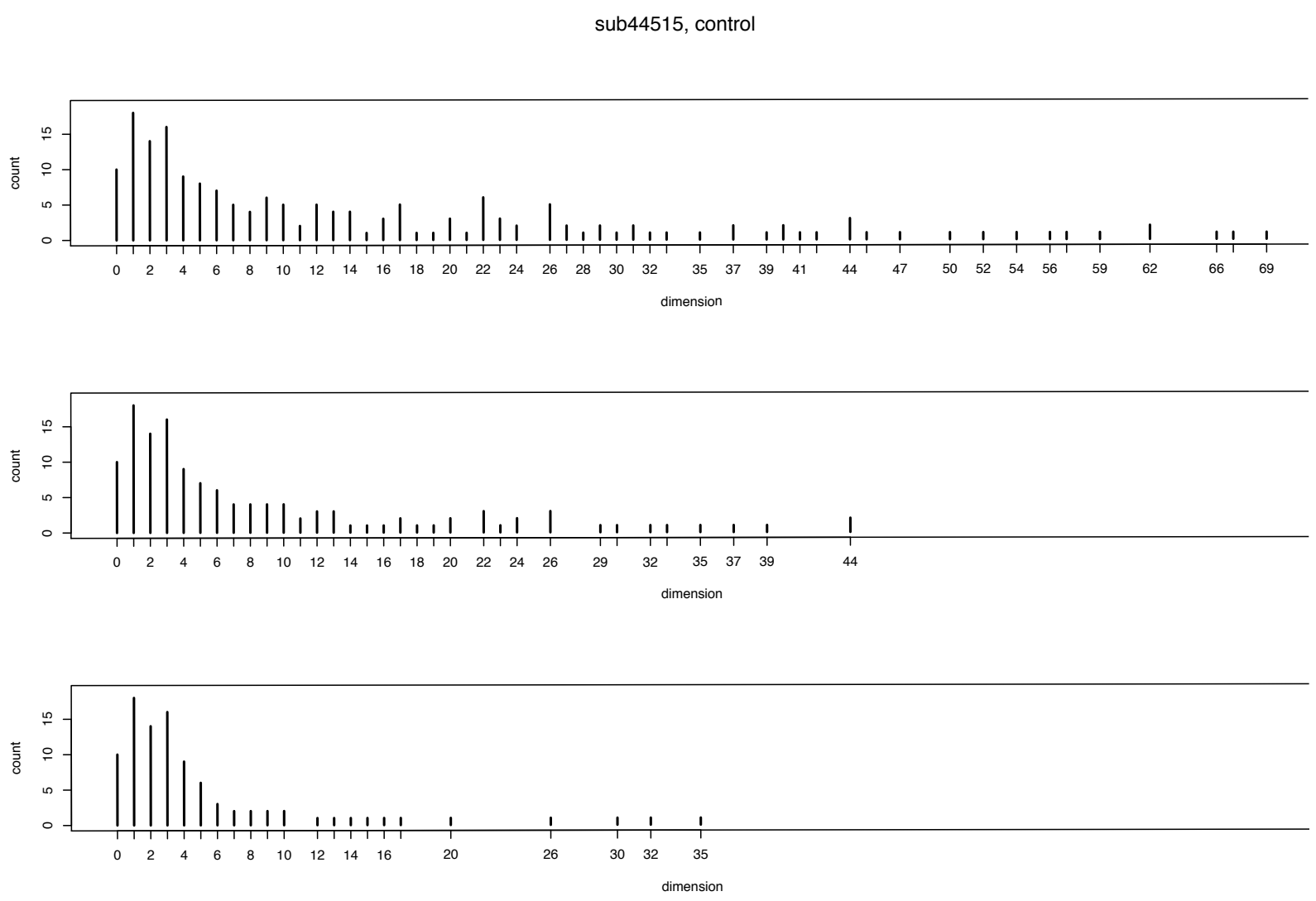
In the meantime, we can compute the Betti numbers for each frequency level separately...

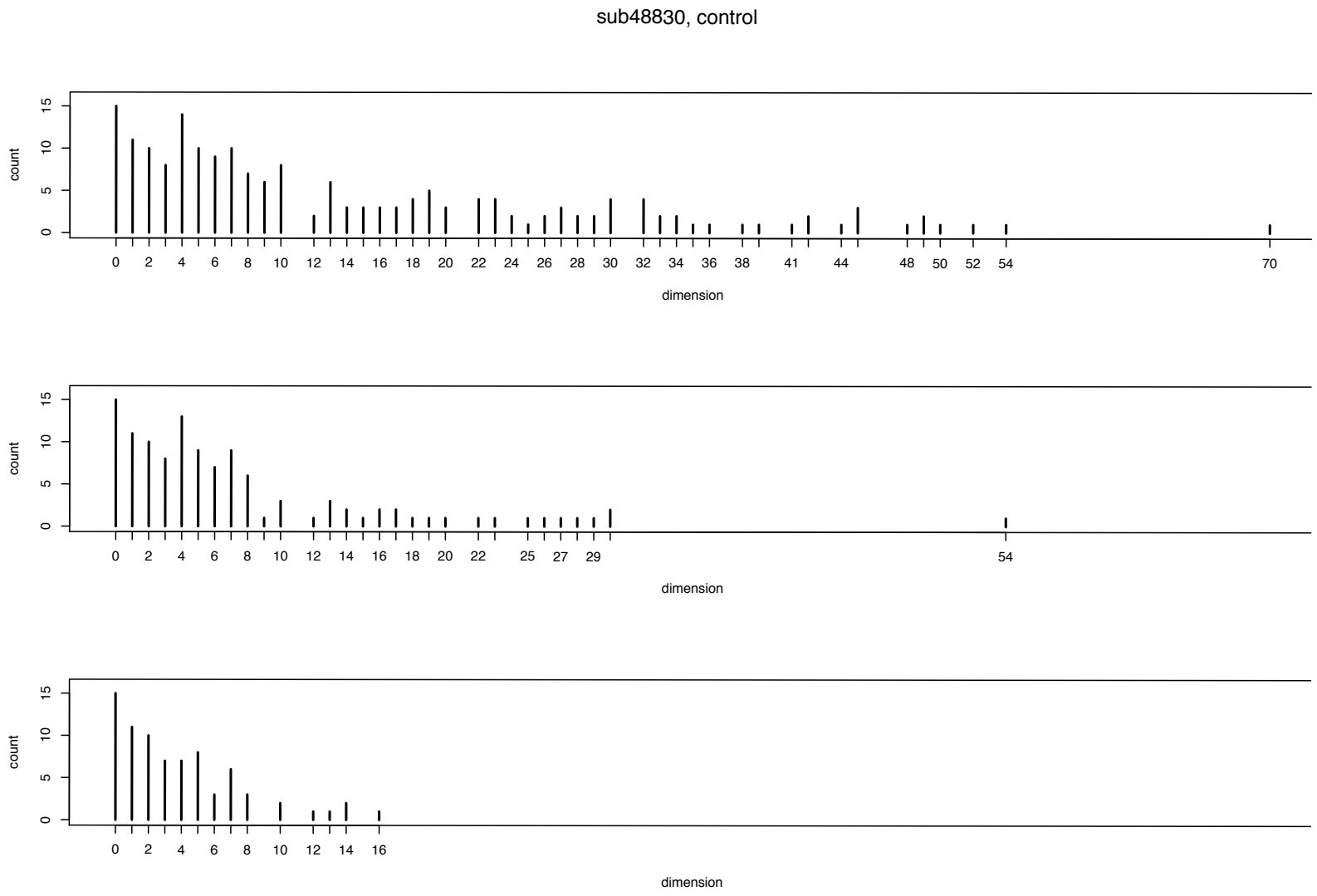
Positive analyses

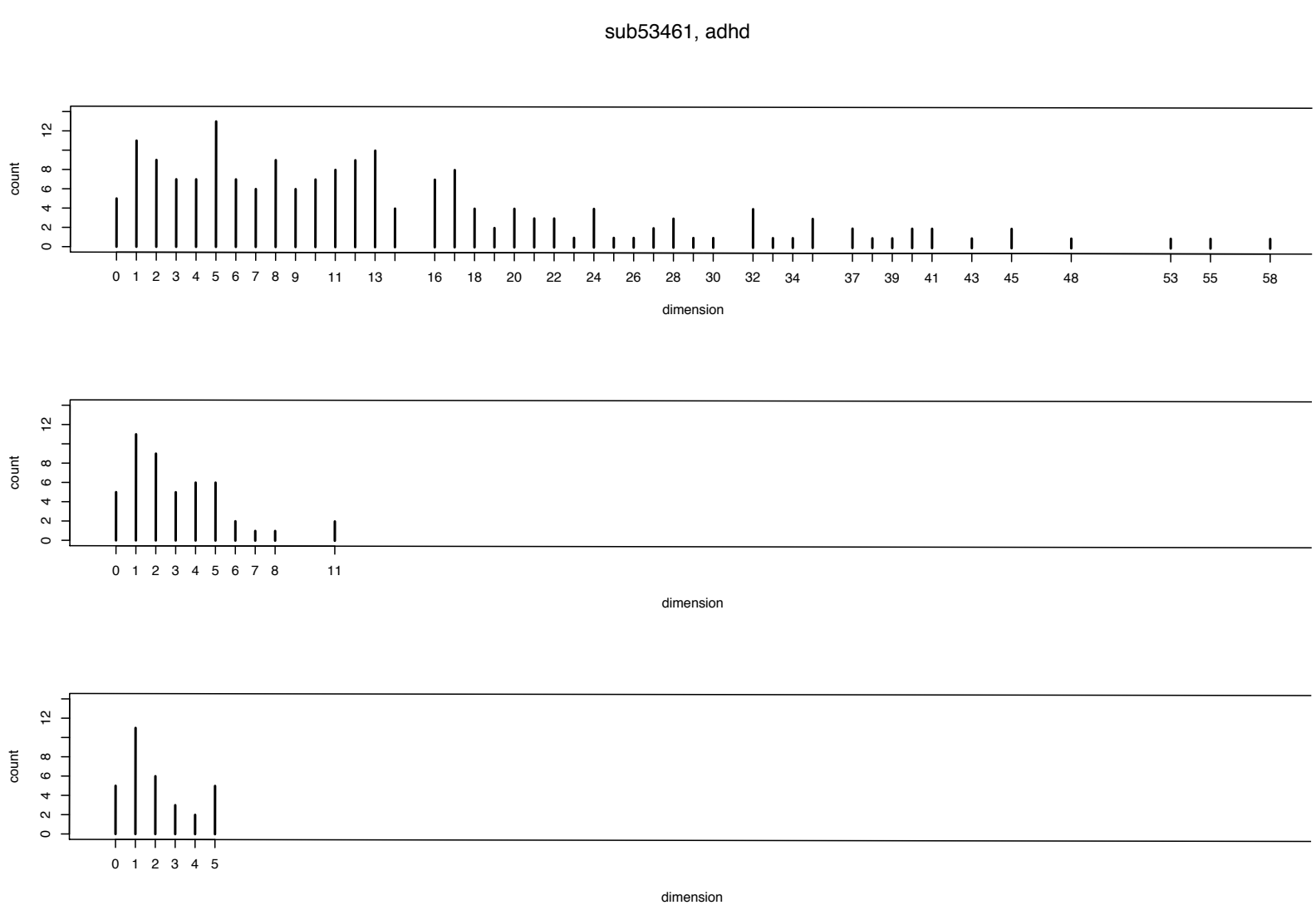
Counts of simplices (concurrences) by dimension
(number of regions per concurrence) for a few subjects...


sub18638, control
count
0 2 4 6 8 12
0 1 2 3 4 5 6 7 8 9 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 41 44 47 50
dimension
count
0 2 4 6 8 12
0 1 2 3 4 5 6 8 10 14 19
dimension
count
0 2 4 6 8 12
0 1 2 3 6
dimension


sub24528, adhd
count
0
5
10
15
0 1 2 3 4 5 6 7 8 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 42 45 49 51 56 58
dimension
count
0
5
10
15
0 1 2 3 4 5 6 7 8 9 11 18
dimension
count
0
5
10
15
0 1 2 3 4 5 6 7 8 9
dimension


sub44515, control
count
0
5
10
15
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 35 37 39 41 44 47 50 52 54 56 59 62 66 69
dimension
count
0
5
10
15
0 2 4 6 8 10 12 14 16 18 20 22 24 26 29 32 35 37 39 44
dimension
count
0
5
10
15
0 2 4 6 8 10 12 14 16 20 26 30 32 35
dimension

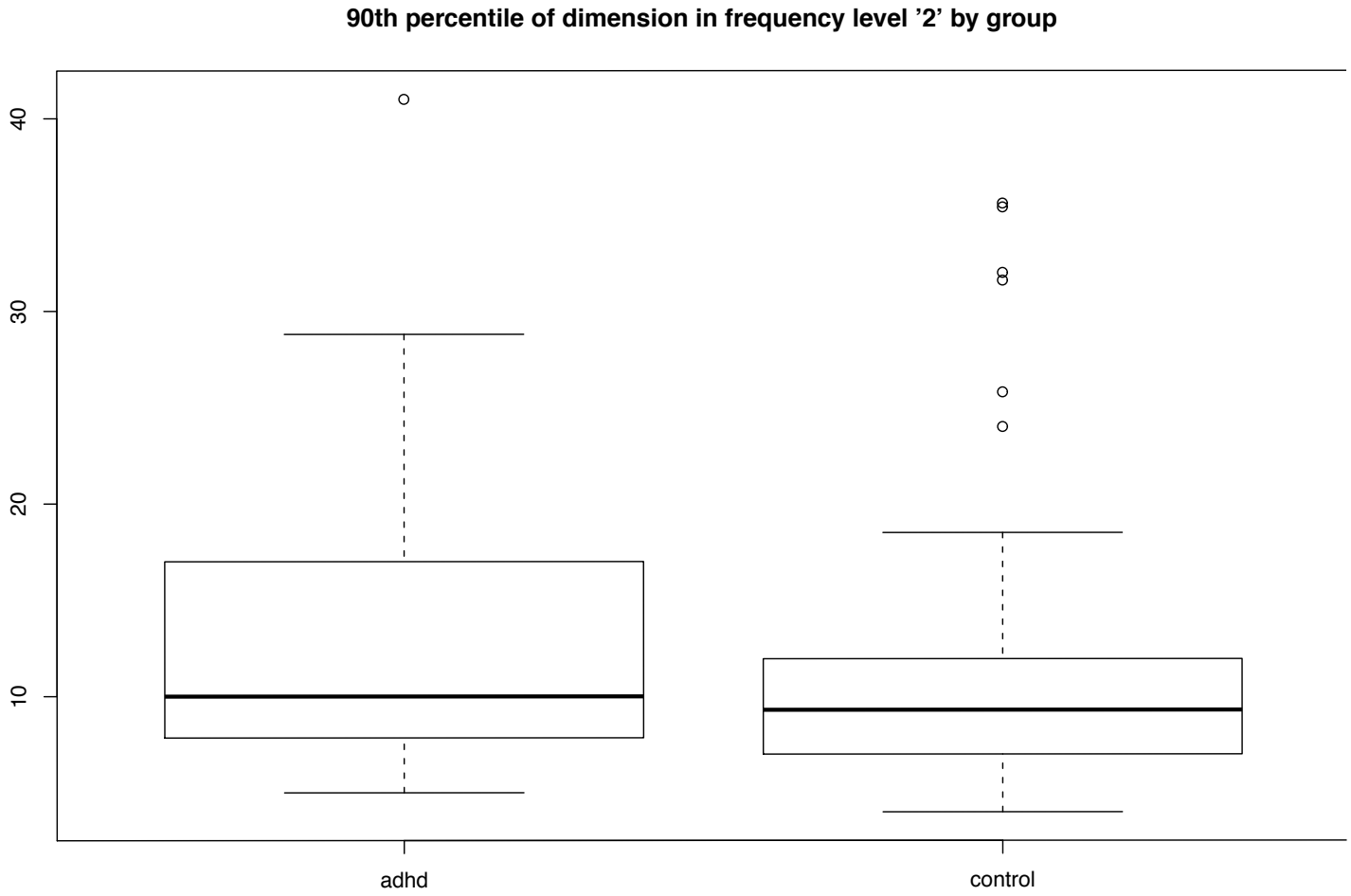

sub48830, control
count
0
5
10
15
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 41 44 48 50 52 54 70
dimension
count
0
5
10
15
0 2 4 6 8 10 12 14 16 18 20 22 25 27 29 54
dimension
count
0
5
10
15
0 2 4 6 8 10 12 14 16
dimension


sub53461, adhd
count
0 2 4 6 8 12
0 1 2 3 4 5 6 7 8 9 11 13 16 18 20 22 24 26 28 30 32 34 37 39 41 43 45 48 53 55 58
dimension
count
0 2 4 6 8 12
0 1 2 3 4 5 6 7 8 11
dimension
count
0 2 4 6 8 12
0 1 2 3 4 5
dimension

Positive analyses

Ignore frequency level 1 and look at simplices
of frequency level 2...

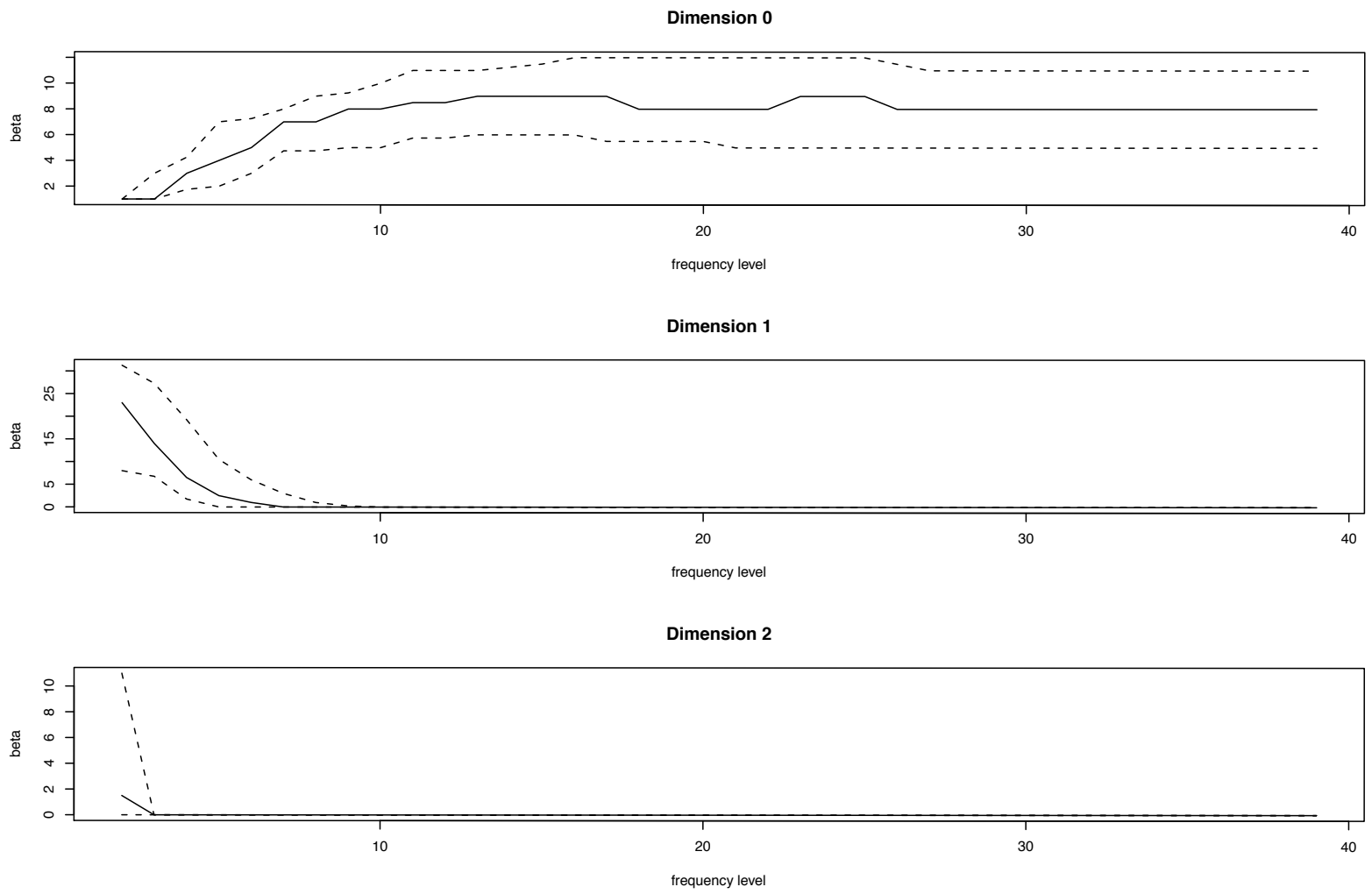
Positive analyses

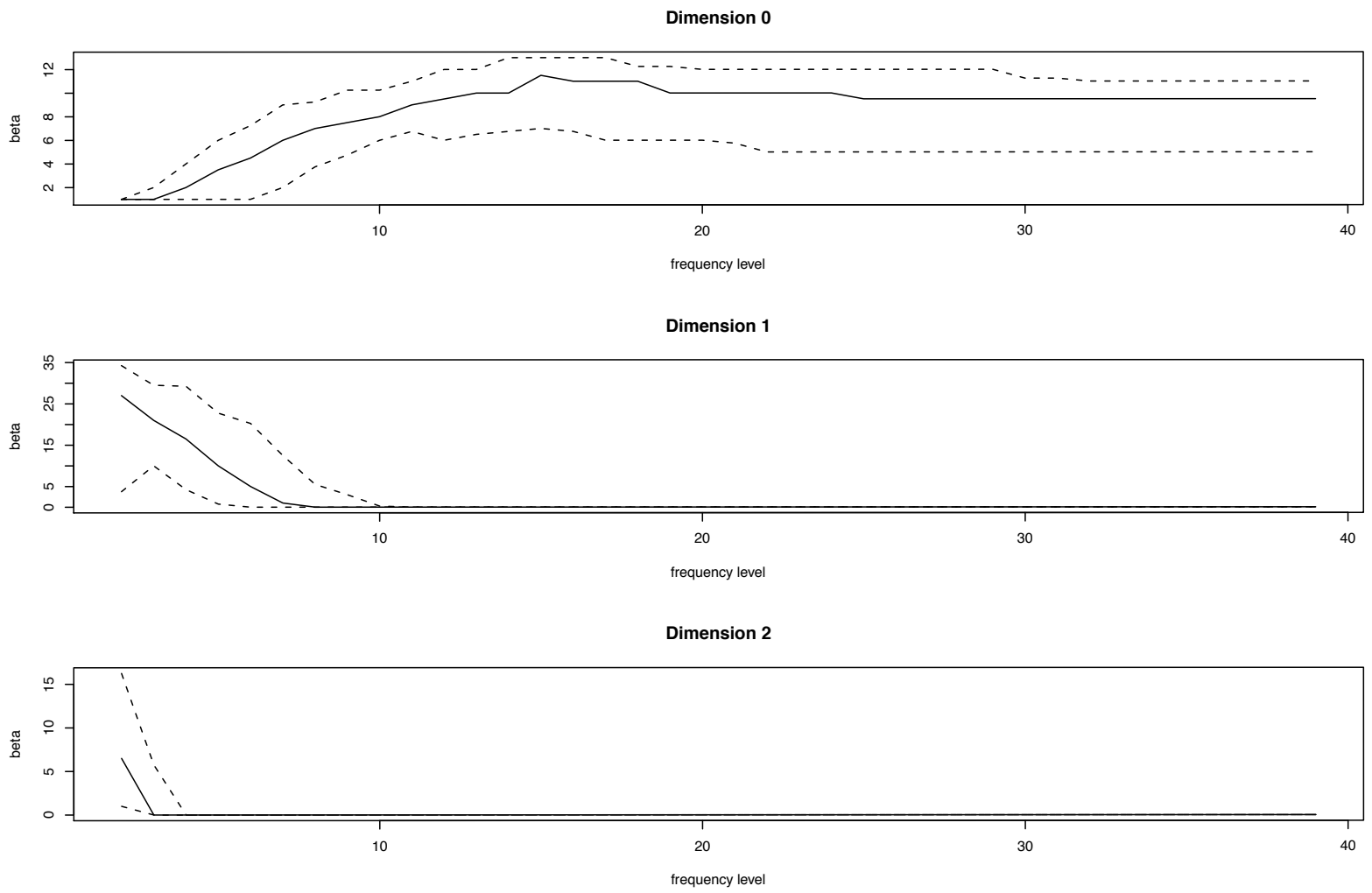


Mon Feb 7 15:51:20 2011

Negative analyses

Compute Betti numbers in dimensions 0 – 2
for frequency levels 2 and above...


25th, 50th, 75th percentiles of beta vs. freq. level by dimension in control group
Dimension 0
beta
2
4
6
8
10
10
20
30
40
frequency level
Dimension 1
beta
0
5
15
25
10
20
30
40
frequency level
Dimension 2
beta
0
2
4
6
8
10
10
20
30
40
frequency level
Freq. levels 2––39; Tue Feb 8 10:17:02 2011

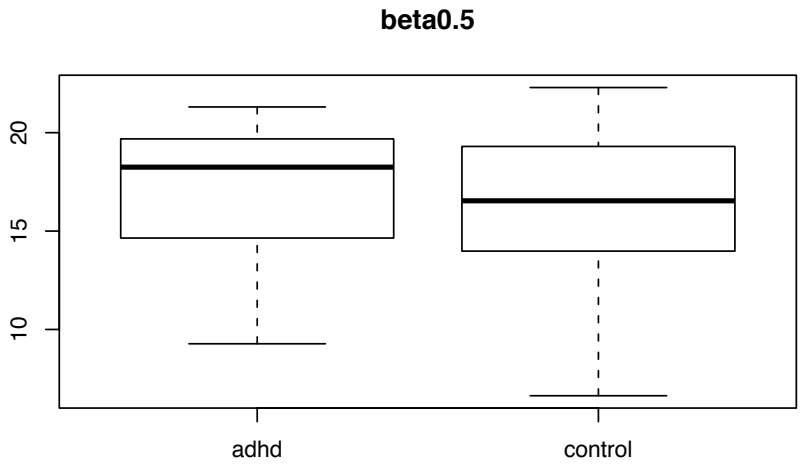

25th, 50th, 75th percentiles of beta vs. freq. level by dimension in ADHD group
Dimension 0
beta
2
4
6
8
10
12
10
20
30
40
frequency level
Dimension 1
beta
0
5
15
25
35
10
20
30
40
frequency level
Dimension 2
beta
0
5
10
15
10
20
30
40
frequency level
Freq. levels 2––39; Tue Feb 8 10:17:32 2011

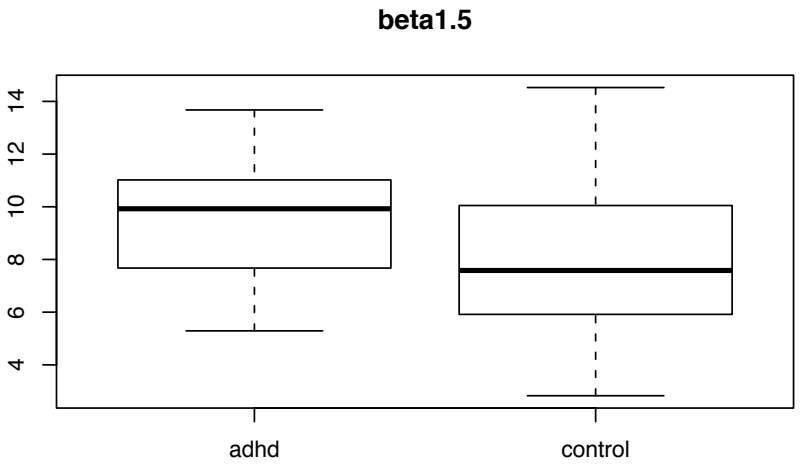
“Poor man’s persistent homology”

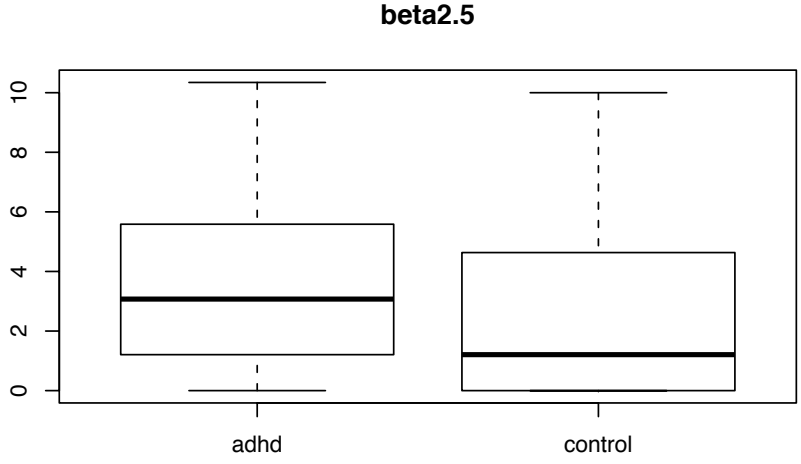
Sum up Betti numbers across frequency levels,
for each subject, in each dimension...

(Take square root to condense distribution.)

Square root of sums of Betti numbers by group and dimension







Future work

→ Make time important: durations, order, pattern:

Idea 1: Use coherence measure on a “sliding window” to determine functionally connected concurrences within the window.

Idea 2: Compute the Fourier transform and treat the moduli of the Fourier coefficients as we did the activity levels.

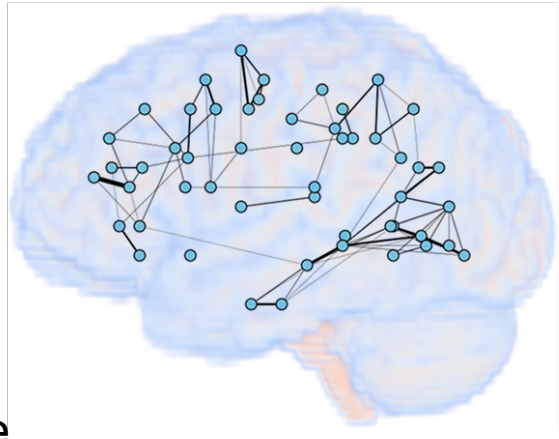
– If a group of regions all have power at a number of frequencies, that’s evidence that they are causally related.

– They can have power at the same frequency, but be out of phase (active at different times).

Future work

→ Use non-binary data (do not threshold).

Would it be possible to create “soft simplices” by a probabilistic vertex assignment?

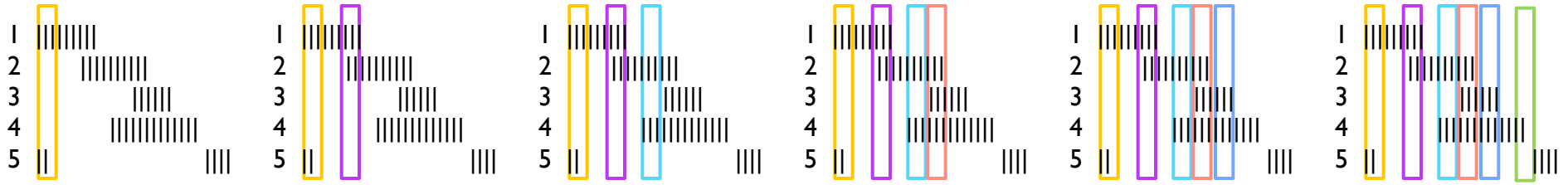


Future work

→ Learn something about the brain!

Localizing homology:
Neuroscientists will want to know where in the brain the activity “holes” are found, and there may be many “cycles” representing the same homology class. Topological cycles may reflect brain network architectural elements such as feedback loops.

Topological diagnosis:
We will try to relate topological indicators of neuropsychiatric disease to underlying anatomy to create a richer understanding of how the brain functions and how it fails.

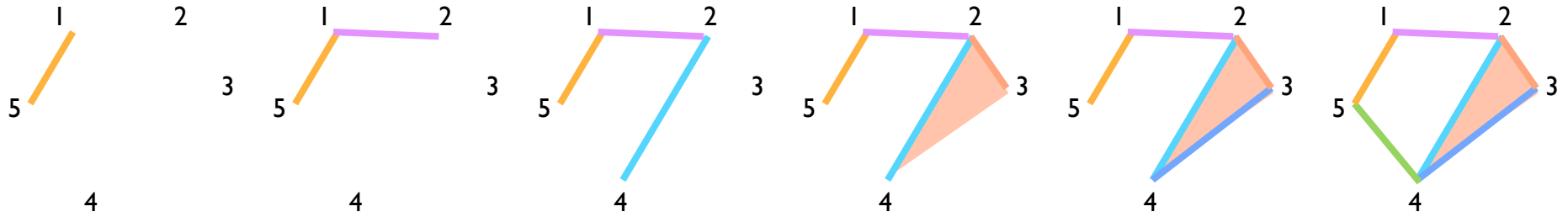


Acknowledgments

This work was done in collaboration with **Steve Ellis** at Columbia University.

Dmitriy Morozov (LBNL)
is working with us on persistence using Dionysus software.

Vidit Nanda (Rutgers)
has just joined us on persistence atop Chomp2 software.

Questions?

Arno Klein
arno@binarybottle.com