Computational Methods in NeuroImage Analysis

Instructor: Moo K. Chung

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Lecture 7

Topological computation

Brain Network Modeling

October 22, 2010

Everyone submitted research proposal?

Research proposal (10% of the final grade)

What is expected:

Organization (5 points)
Depth & complexity of proposal (5 points)
Methodological Innovation & novelty (5 points)
Sufficient literature review (5 points)

Penalty for late submission (5% / day)

Minimum requirement for A-grad report:
at least 4 page with sufficient number of references excluding references. I don't mind receiving 10 page proposals.

Why do we need topological approaches?

Chung et al. 2009. Information processing in Medical Imaging (IPMI)
Read chung.2009.IPMI.pdf

Usual scientific model: $f = \mu + \epsilon$

Correlated test statistic: $T(x)$

Type-I error computation: $P\left(\sup_{x \in \mathbb{M}} T(x) > h\right)$

Euler characteristic based random field theory
Worsley et al., Human Brain Mapping, 1996

Uses Morse Theory to link analytical & geometric problem to topology

Multiple Comparisons

Read Chapter 1.5

$$X(t) = \mu(t) + e(t), t \in \Omega$$

Search region
Whole brain or ROI

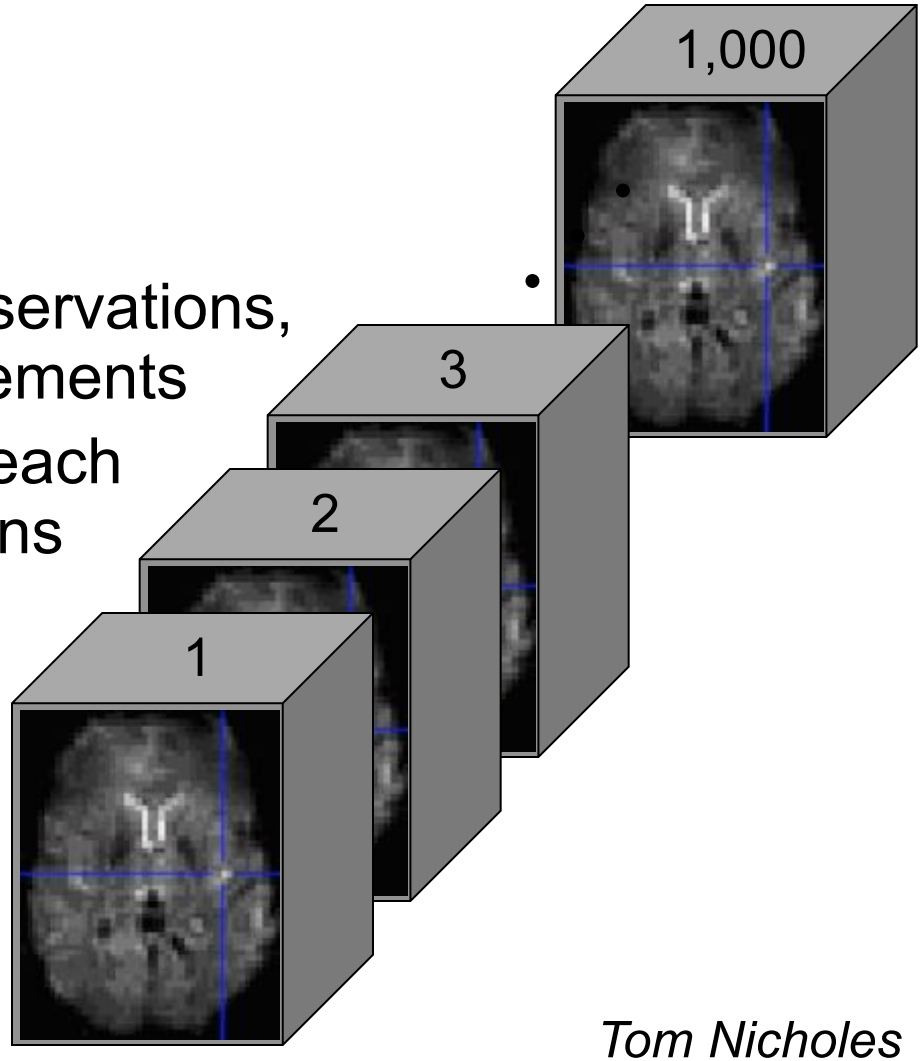
$$H_0 : \mu(t) = 0 \text{ for all } t \in \Omega \text{ vs. } H_1 : \mu(t) > 0 \text{ for some } t \in \Omega.$$

If there is a point t_0 such that $\mu(t_0) > 0$,
reject the null hypothesis.

For smoothed images, clustered voxels around t_0 will satisfy $\mu(t) > 0$.

Ex. fMRI Multiple Comparisons

- 4-Dimensional Data
  - 1,000 multivariate observations, each with 100,000 elements
  - 100,000 time series, each with 1,000 observations
- Massively Univariate Approach
  - 100,000 hypothesis tests



Tom Nicholes

Point-wise inference

$$H_0 : \mu(t) = 0 \text{ for all } t \in \Omega \text{ vs. } H_1 : \mu(t) > 0 \text{ for some } t \in \Omega$$

At each fixed *t*,

$$J_0(t) : \mu(t) = 0. \text{ vs. } J_1(t) : \mu(t) > 0.$$

H_0 is true iff. $J_0(t)$ is true for all *t*: $H_0 = \bigcap_{t \in \Omega} J_0(t)$.

H_1 is true iff $J_1(t)$ is true for some *t*: $H_0^C = \bigcup_{t \in \Omega} J_0^C(t)$.

Test statistic and rejection rule

- Hypothesis testing requires a test statistic and the corresponding rejection rule.

- For one sample test, we can use Z-stat or T-stat. In many applications, Z-stat is sufficient since T-stat is approximately Z-stat for large degrees of freedom.

- Then we construct a rejection rule:

Large T-stat value --> reject the null hypothesis

Small T-stat value --> accept the null hypothesis

Type-I error (alpha-level)

- The type-I error is the probability of rejecting the null hypothesis (there is signal) when the null hypothesis (there is no signal) is true.
- The type-I error is the probability of detecting **false positives**.
- The type-I error computation requires a statistic (Z-stat. t-stat, F-stat, Chi-square stat. etc).
- **Example:** Z-stat. If the Z-statistic value obtained from measurments is 1.65, alpha=0.05=P(Z>1.65).

Alpha-level for multiple comparisons
Family-wise error rate (FER)

$$\begin{aligned}\alpha &= P(\text{ reject } H_0 | H_0 \text{ is true}) \\ &= P\Big(\bigcup_{t\in\Omega} J_0^C(t) \Big| H_0 \text{ is true } \Big)\end{aligned}$$

$$\begin{aligned}\alpha &= P\Big(\bigcup_{t\in\Omega} \{T(t) > h\} \Big) \\ &= 1 - P\Big(\bigcap_{t\in\Omega} \{T(t) \le h\} \Big) \\ &= 1 - P\Big(\sup_{t\in\Omega} T(t) \le h \Big) \\ &= P\Big(\sup_{t\in\Omega} T(t) > h \Big).\end{aligned}$$

Corrected P-value

- P-value: the smallest alpha-level at which the null hypothesis is rejected.

Example: P(Z > observed z-stat. value).

- *Corrected P-value* is the P-value corrected for multiple comparisons.

$$P(\sup T(t) > \text{ observed max T-stat })$$

Determining the distribution of sup *T(t)* is very hard

Bonferroni correction

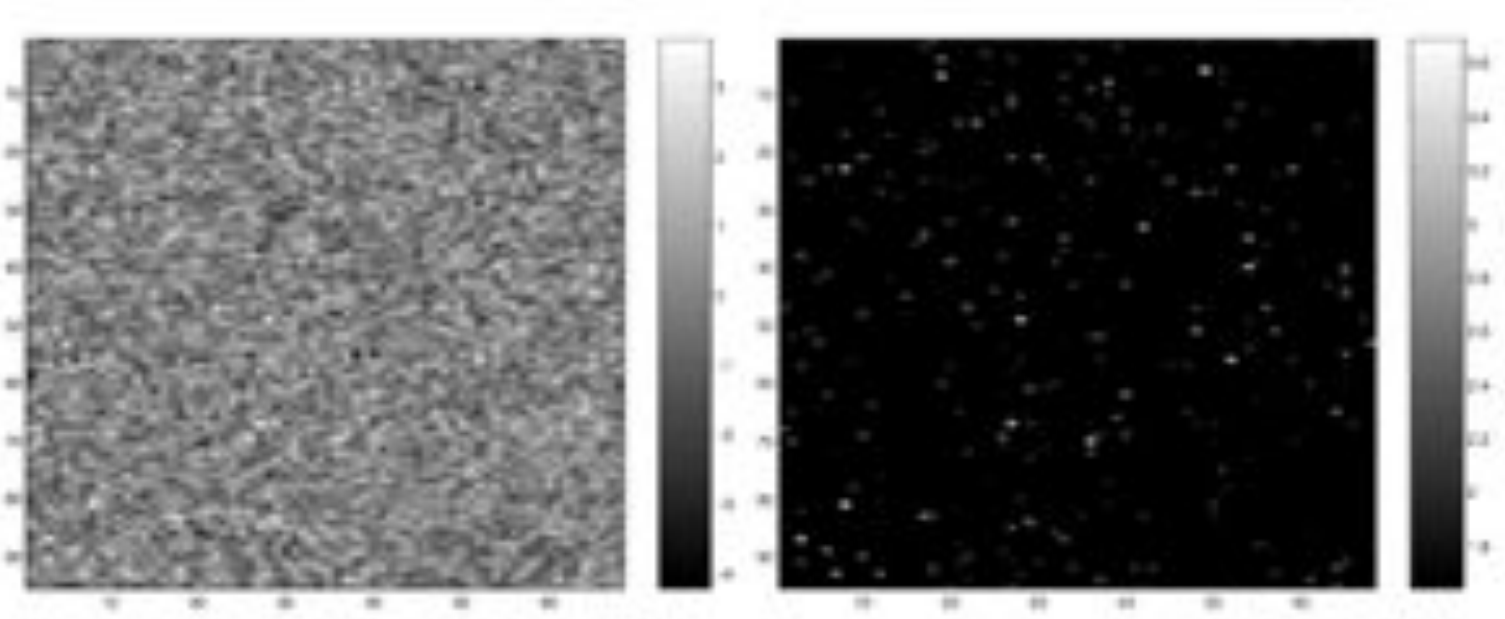
- Assume there are *m*-voxels in the search region: $t_1, \cdots, t_m$

$$\begin{aligned} \alpha &= P\Big(\bigcup_{j=1}^{m}\{T(t_j) > h\}\Big) \\ &\leq \sum_{j=1}^{m} P\big(T(t_j) > h\big). \end{aligned}$$

This becomes exact if *T* statistics are not correlated. We control each T statistic separately.

$$P\big(Y(t_j) > h\big) < \frac{\alpha}{m}$$

Bonferroni Correction Simulation



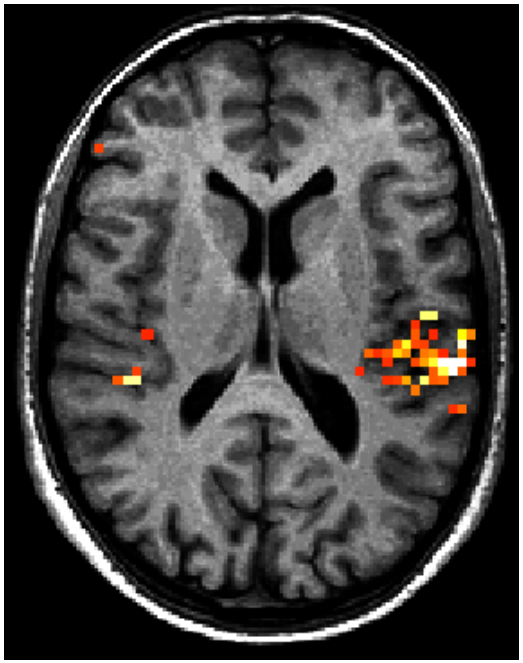
Z ~ N(0,1) noise

P(Z>1.65)=0.05

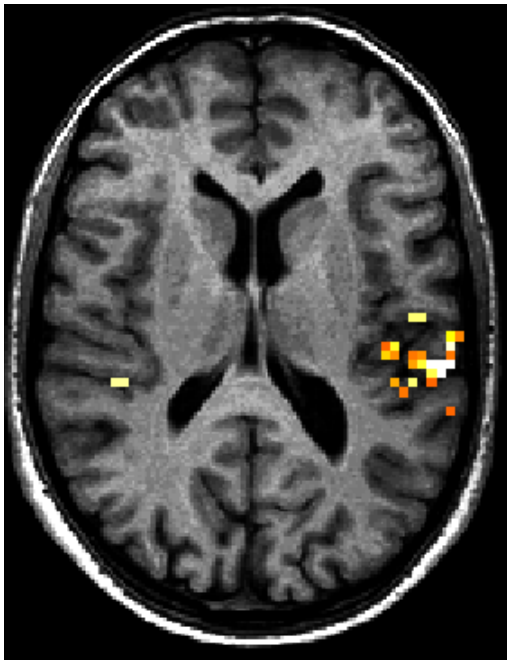
Bonfenoni correction
thresholding at 1.65
5% false positives

For 1 million voxels, 50000 voxels will be found to be signal (false positives)
→ Need multiple comparison correction

fMRI verbal fluency block design example



FDR ≤ 0.05
$t_0 = 3.8119$



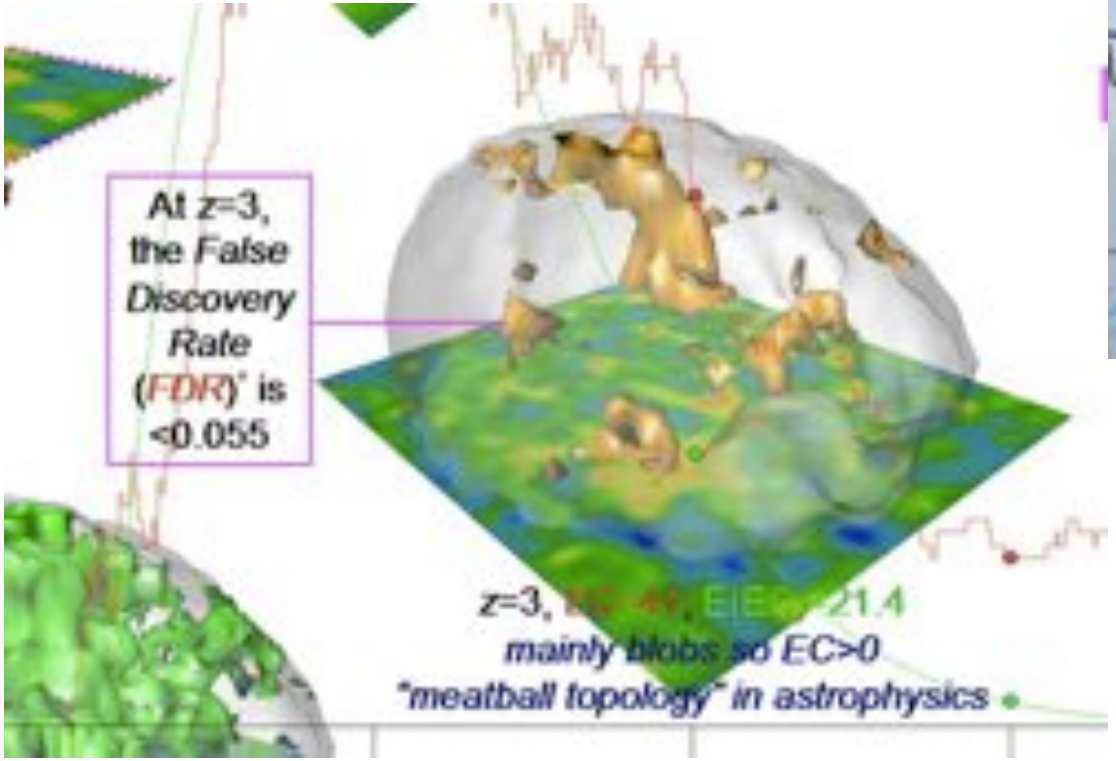
FWER ≤ 0.05
Bonferroni
$t_0 = 5.485$

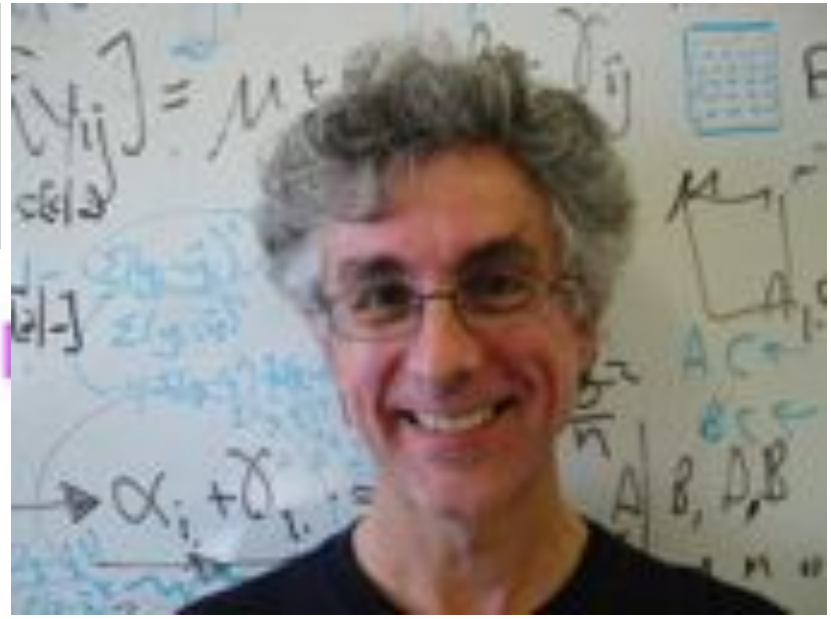
Statistical Methods in NeuroImaging
Attend next year's class

Tom Nicholes

MATLAB demonstration

Random Field Theory
Keith Worsley (1951-2009)





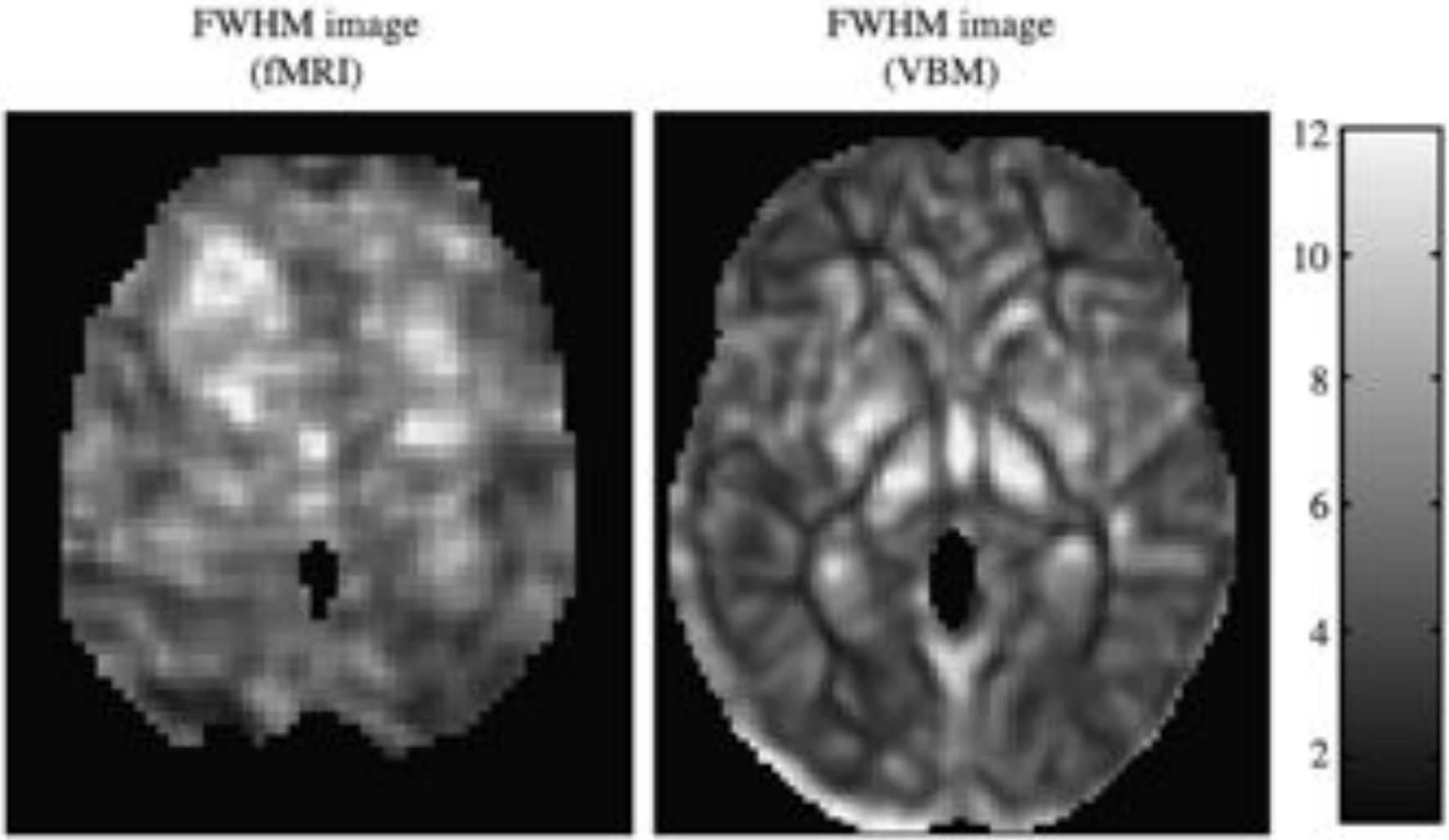
Brain imaging research done for 21 years between 1987-2008. The first major publication in 1992.

See Chapter 1.2 for basics on random fields

Random Field Theory Assumptions

- Images need to follow Gaussian.
- Constructed statistics need to be sufficiently smooth. If underlying images are smooth, constructed statistics are smooth.
- The data need to be stationary (uniform FWHM within a search region). If not, we average FWHM across voxels. This requirement can be relaxed.

Nonuniformity of FWHM

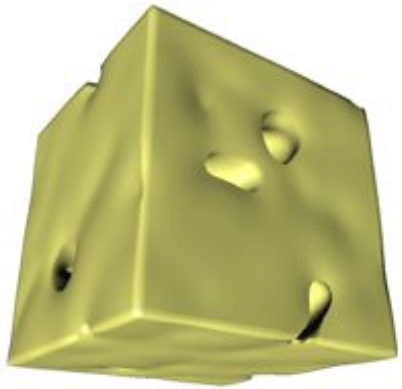


Excursion Probability

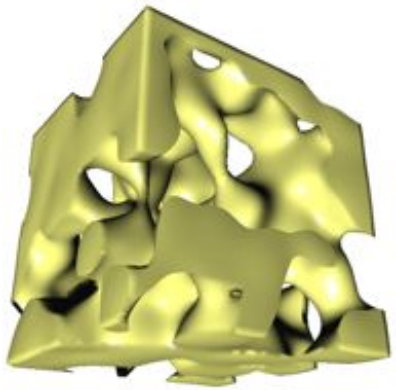
$Z(x)$: Stationary isotropic random field in $x \in \Omega \subset \mathbb{R}^N$

$A_z = \{x : Z(x) > z\}$ excursion set

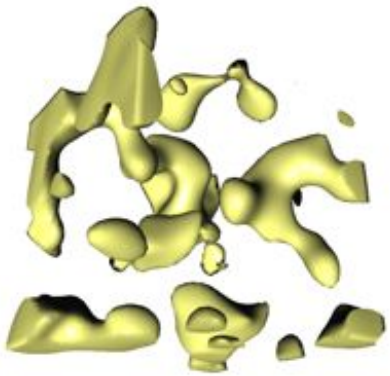
$\chi(A_z)$: Euler characteristic



***z* = -10**



***z* = 0**

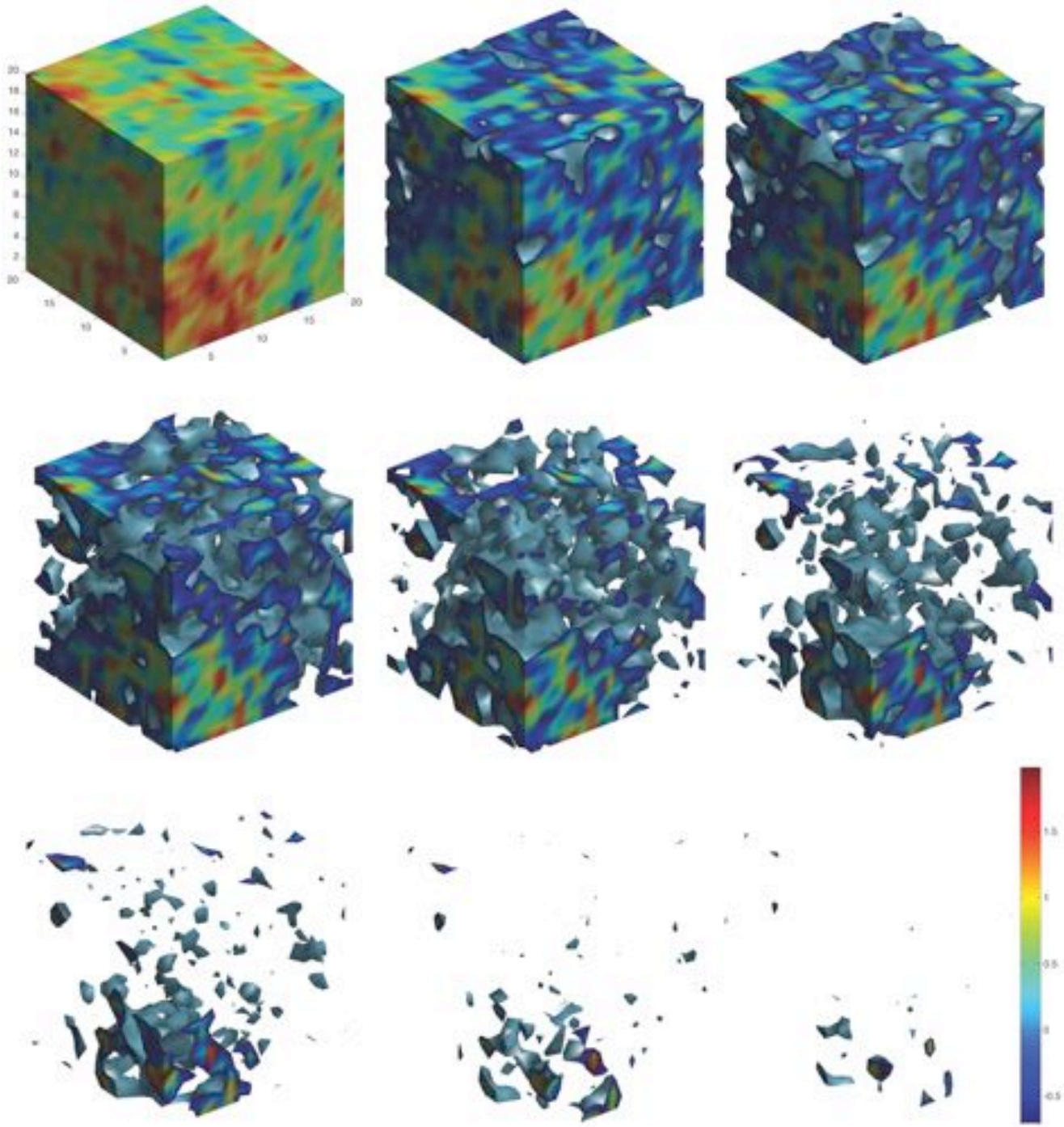


***z* = 10**

$$P\left(\max_{x\in\Omega} Z(x) > z\right) \approx \mathbb{E}\left(\chi(A_z)\right)$$

(Adler, 1984)

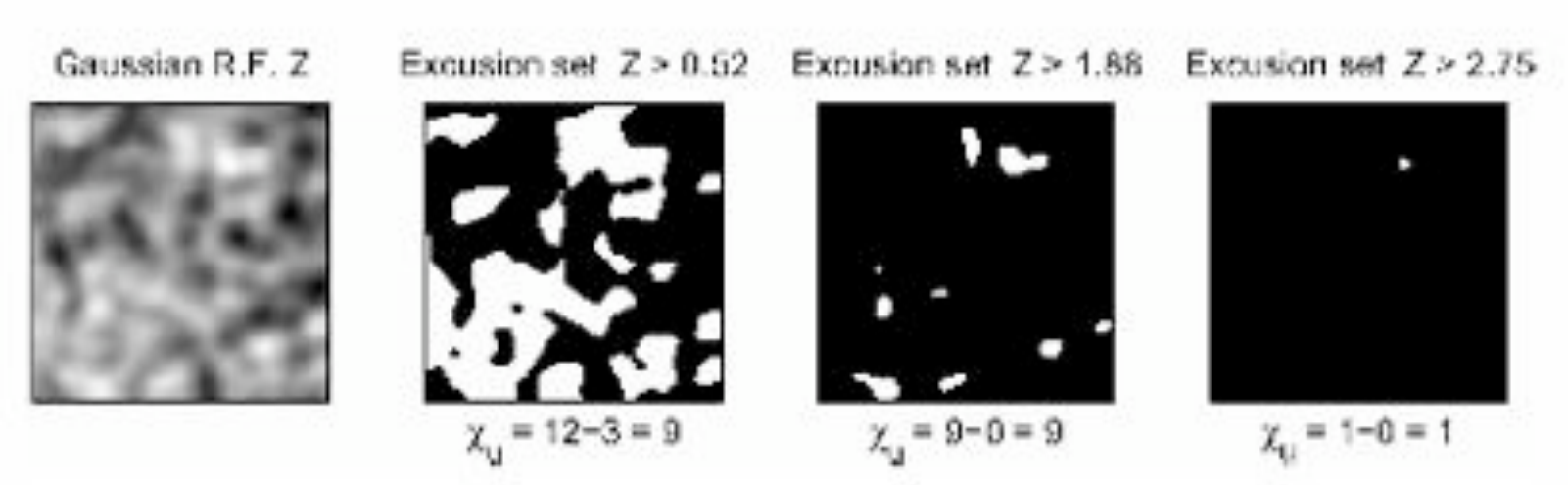
Change of excursion set

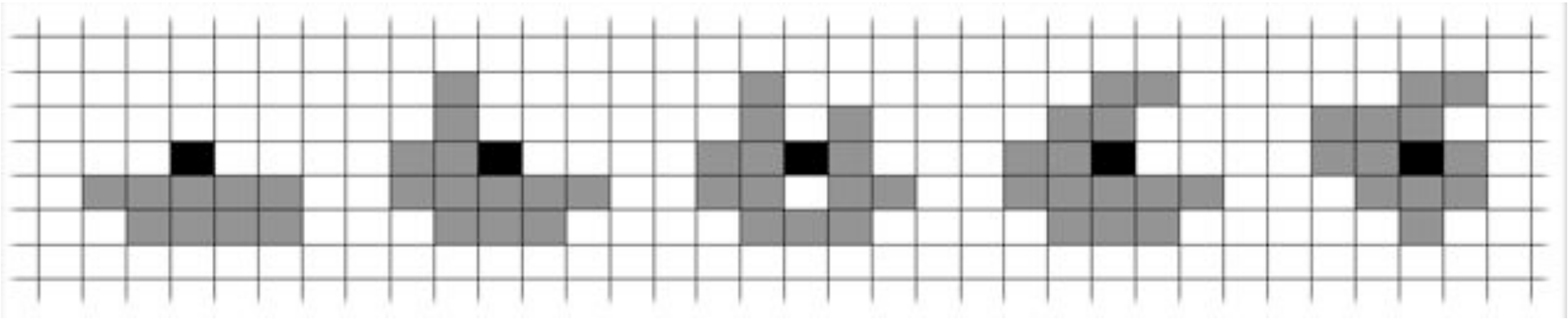


Heuristic Argument for Adler's formula

$$P\left(\sup_{t\in\Omega} T(t) > h\right) \approx P(\chi(A_h) > 0) \approx E(\chi(A_h))$$

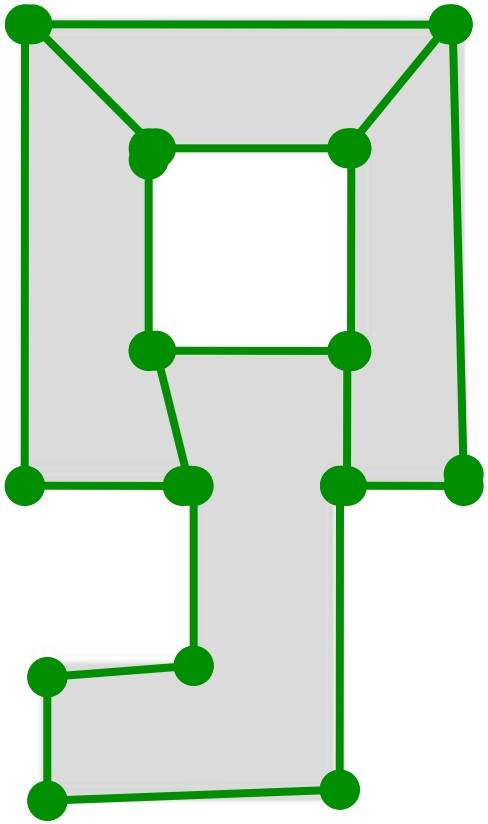
For very high *h* value, the Euler characteristic counts the number of clusters, which is one.



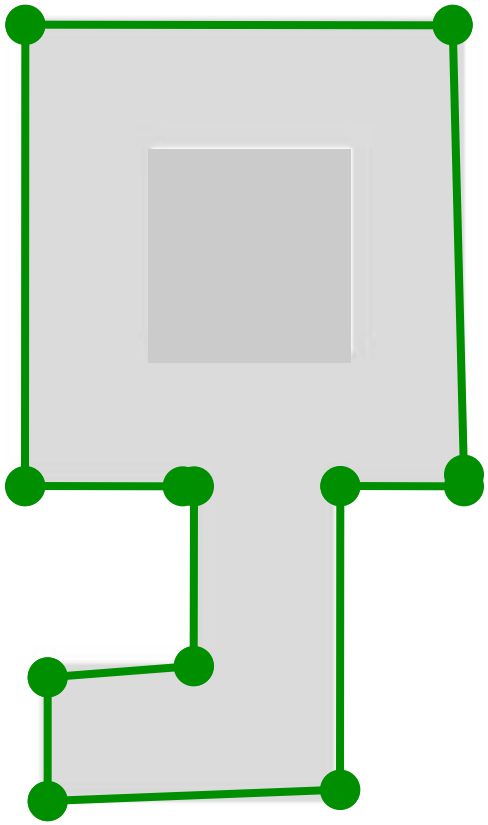


# neighbors	1	2	2	3	4
# Vertex	2	1	0	0	0
# Edge	3	2	2	1	0
# Face	1	1	1	1	1
EC change	0	0	-1	0	1

Computing Euler characteristic (2D)



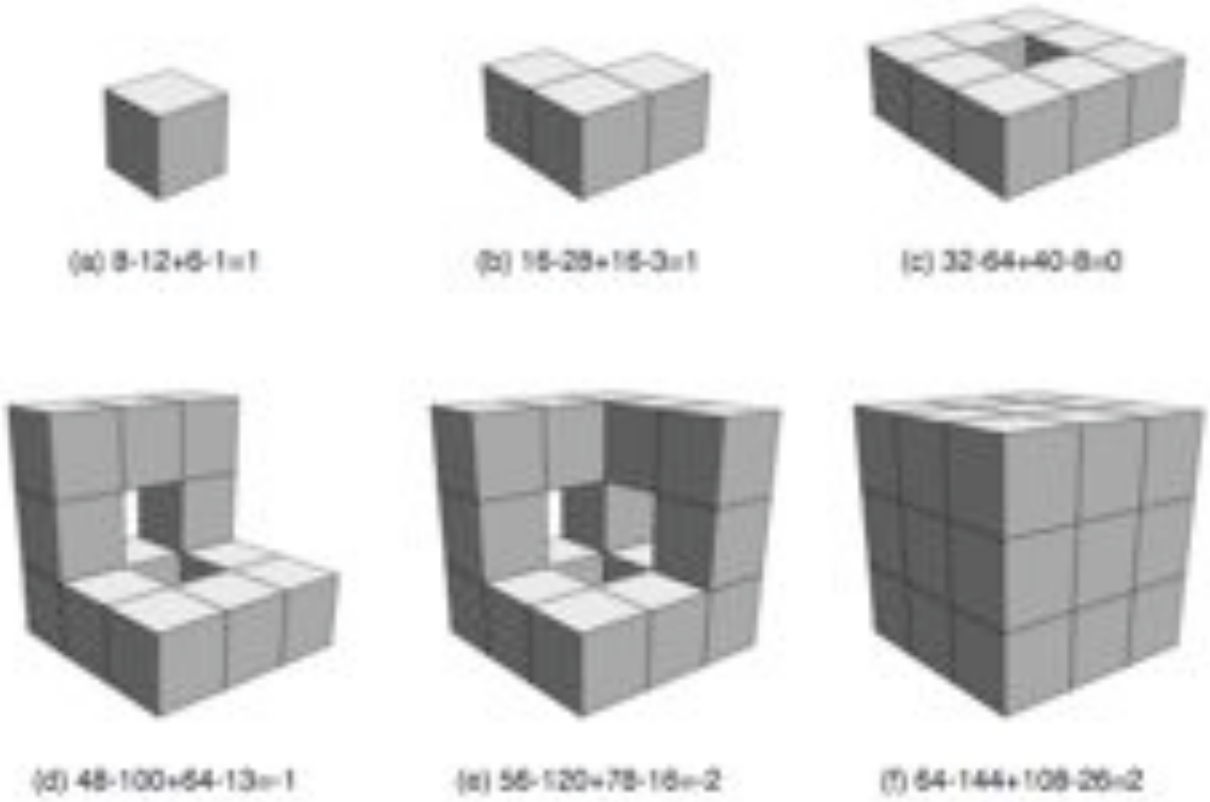
Filling hole
increase EC by 1



EC = N – E + F
=14 – 18 + 4
= 0

EC = N – E + F
=10 – 10 + 1
= 1

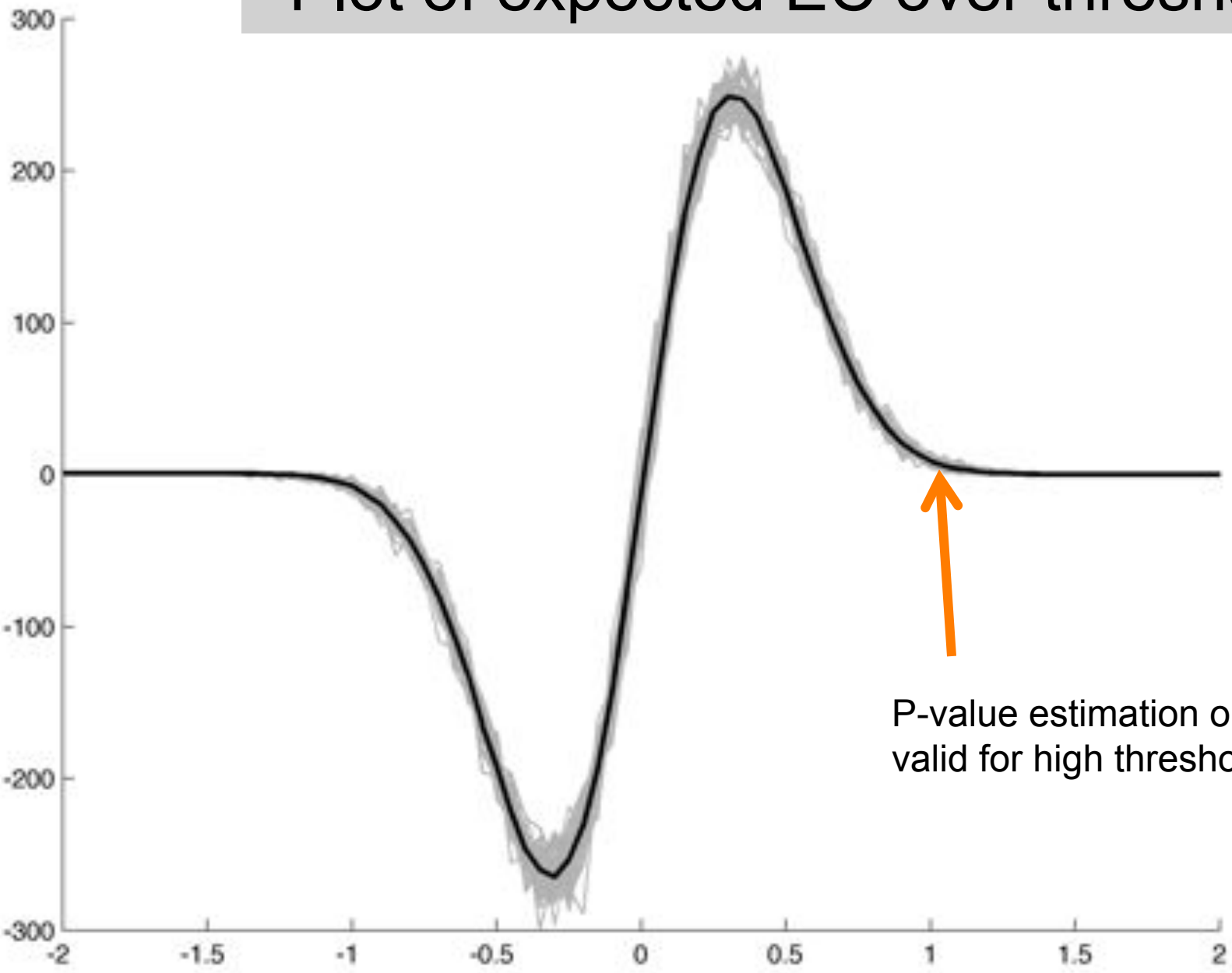
Computing Euler characteristic (3D)



Partition search region into voxels.

EC = # volume - # faces + # edges - # vertices

Plot of expected EC over threshold



MATLAB demonstration

Expected Euler Characteristic

$$\mathbb{E}\chi(A_z) = P\Big(Z(x) > z\Big) + \sum_{i=1}^{N} \phi_i(\Omega)\rho_i(z)$$

ρ_i i-dimensional EC density

$$\rho_i(z) = \mathbb{E}\Big[(Z-z)^+ \det(-\ddot{Z}_i) | \dot{Z}_i = 0\Big] f_{\dot{Z}_i}(0)$$

$\phi_i(\Omega)$ Minkowski functional of Ω

$$\phi_i(\Omega) = \frac{1}{2\pi^{\frac{N-i}{2}}\Gamma(\frac{N-i}{2})} \int_{\partial\Omega} \mathrm{detr}_{N-1-i}(K_{\partial\Omega})\, dA$$

$K_{\partial\Omega}$ curvature matrix of $\partial\Omega$

$\mathrm{detr}_i(K_{\partial\Omega})$ sum of $i \times i$ principal minors of $K_{\partial\Omega}$

Expected EC for a stationary Gaussian field

Smoothness of random field.
Proportional to 1/FWHM

$$
\begin{aligned}
E(\mathrm{EC}) &= \frac{\mathrm{Volume}\,\lambda^3}{(2\pi)^2}(t^2-1)e^{-t^2/2} \\
&+ \frac{(1/2)\ \mathrm{Area}\ \lambda^2}{(2\pi)^{3/2}}te^{-t^2/2} \\
&+ \frac{2\ \mathrm{Diameter}\ \lambda}{(2\pi)}e^{-t^2/2} \\
&+ \frac{\mathrm{EC}}{(2\pi)^{1/2}}\int_t^\infty e^{-z^2/2}dz.
\end{aligned}
$$

MATLAB demonstration

Application to autism

Autistic children (n=17)

Control subjects (n=14)

Matched for age, handedness, IQ and head size

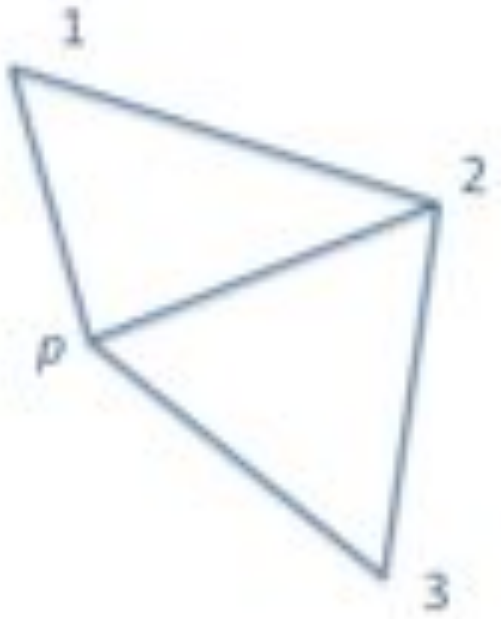
Abnormal connectivity hypothesis in autism:
local over-connectivity
long-range under-connectivity

Clustering coefficient

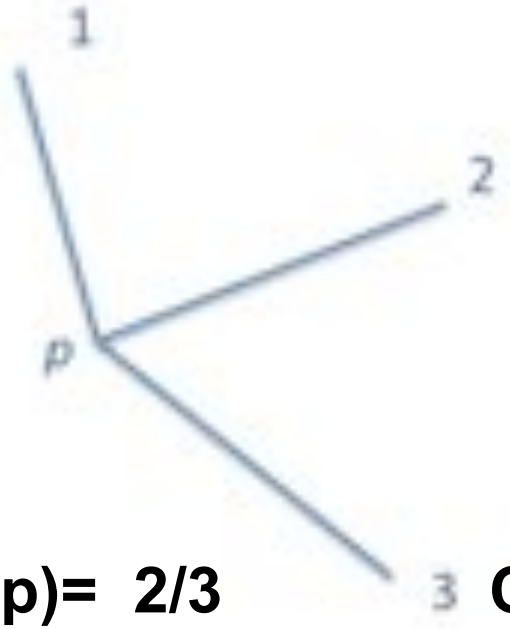
Newman et al., (2001)

At a given node *p*, there are *k* neighboring nodes.

$$c(p) = \frac{\text{actual number of edges}}{k(k-1)/2}$$

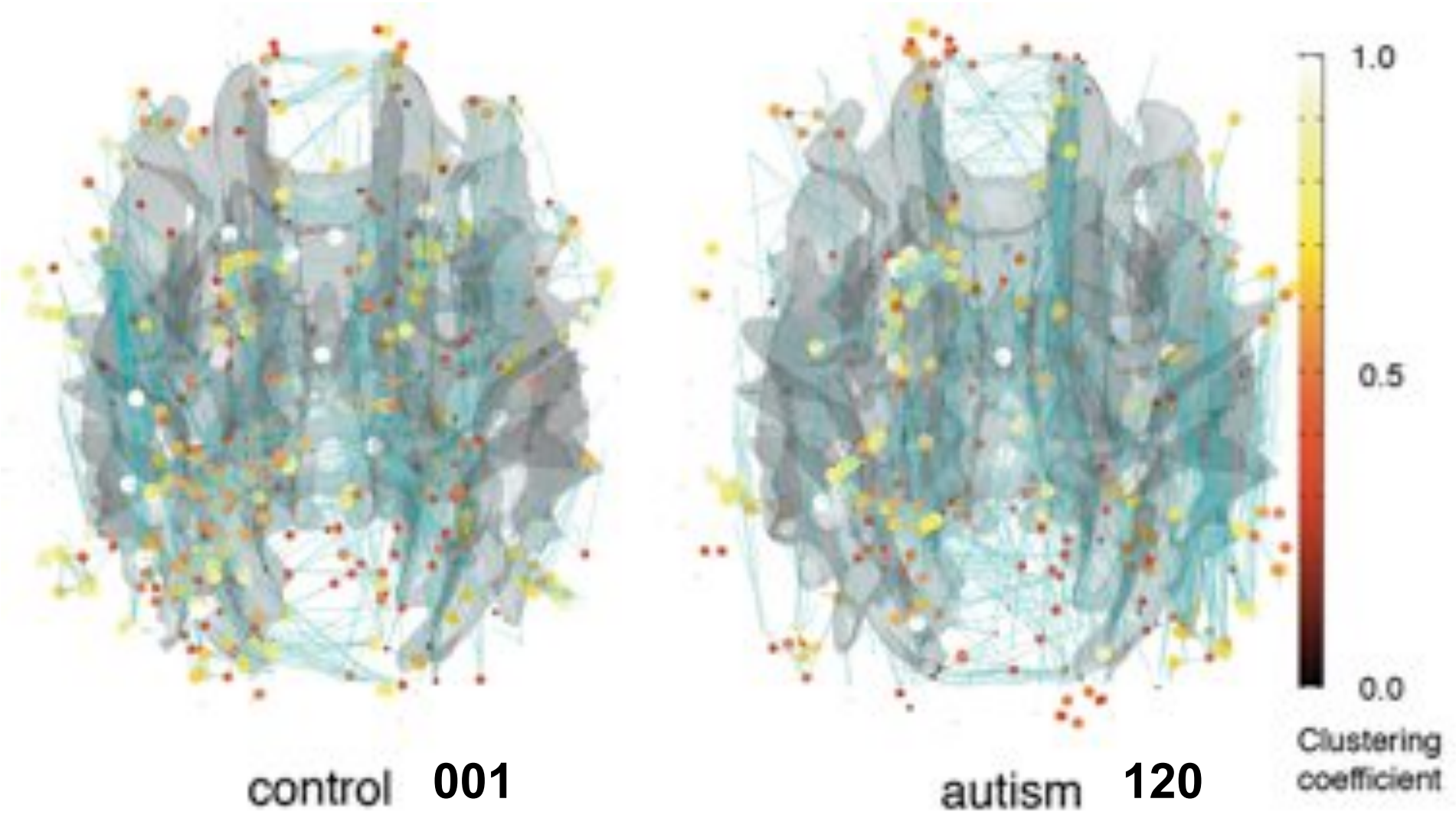


C(p)= 2/3

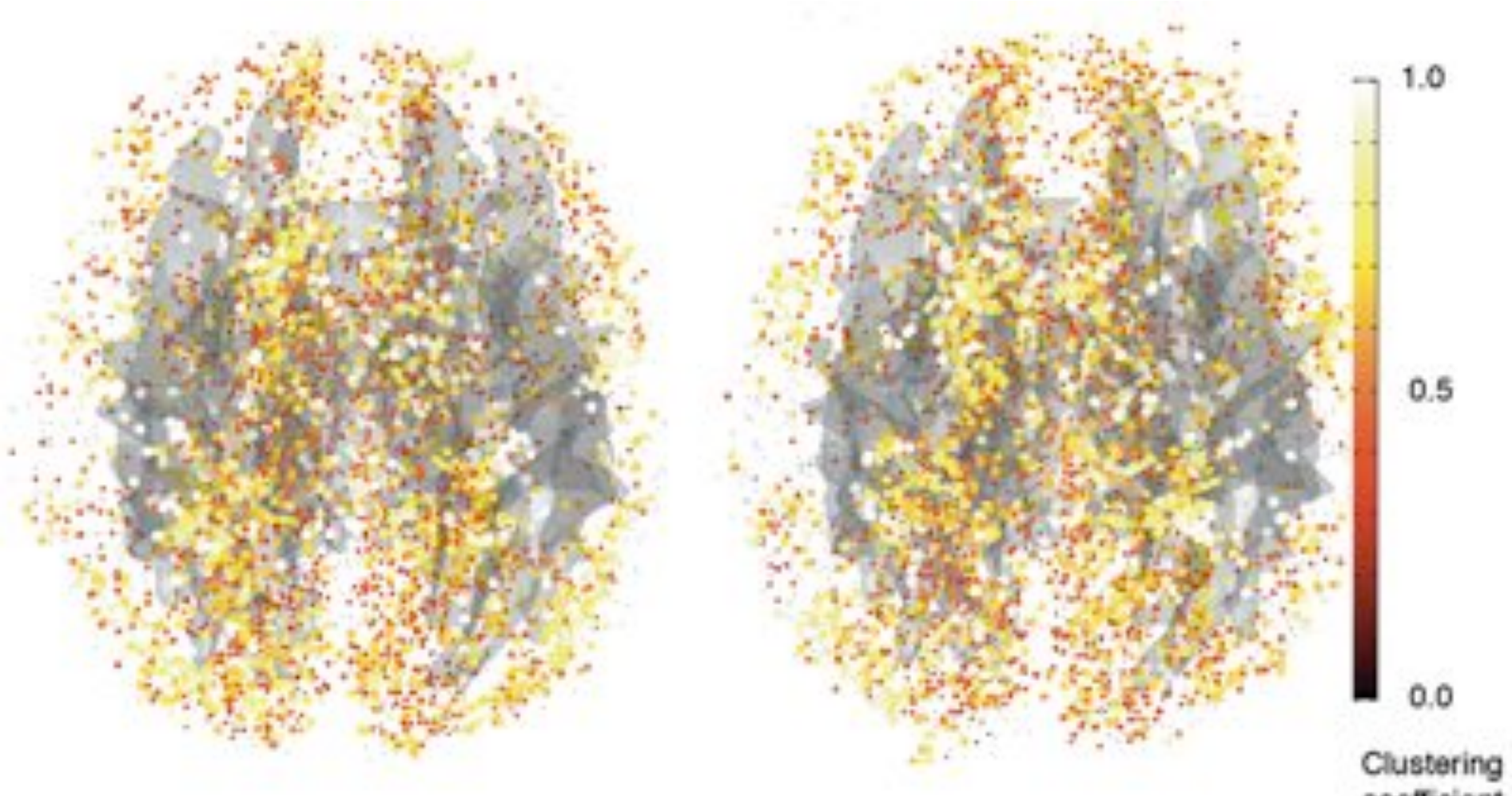


C(p)=0/3

Clustering coefficient for a single subject



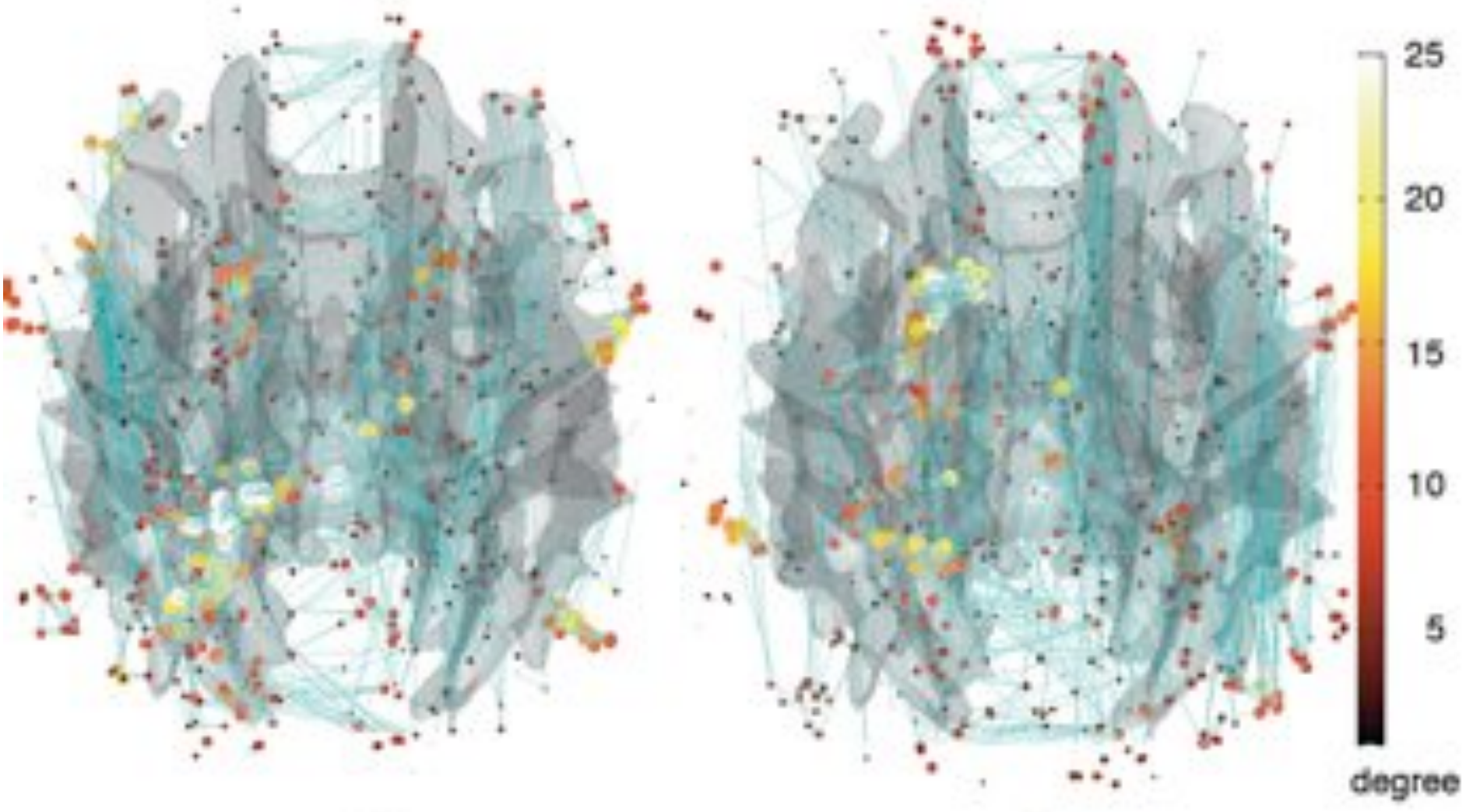
Clustering coefficients for all subjects



Control ⟷ Autism

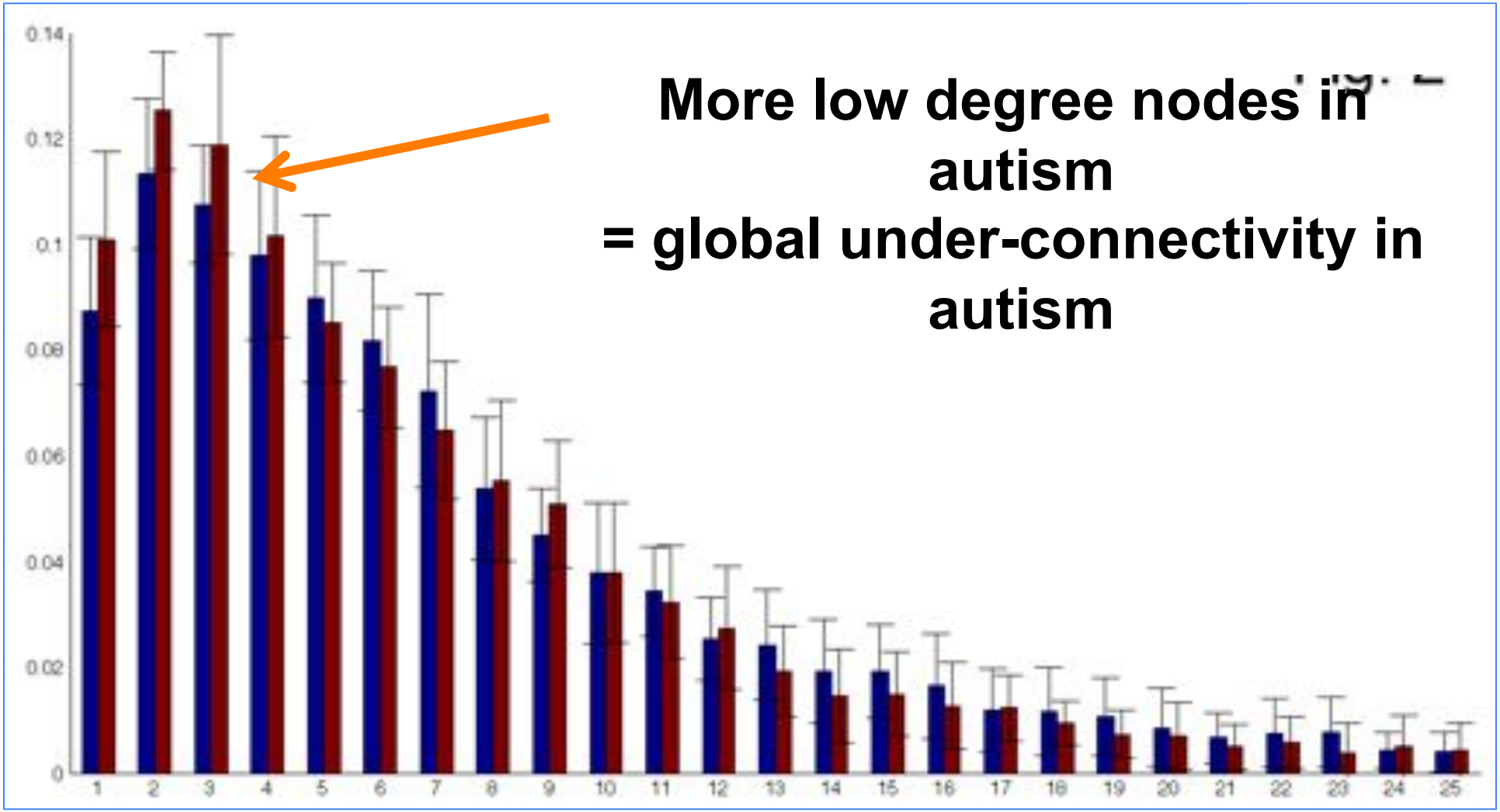
No group differenc

Degree of nodes for a single subject



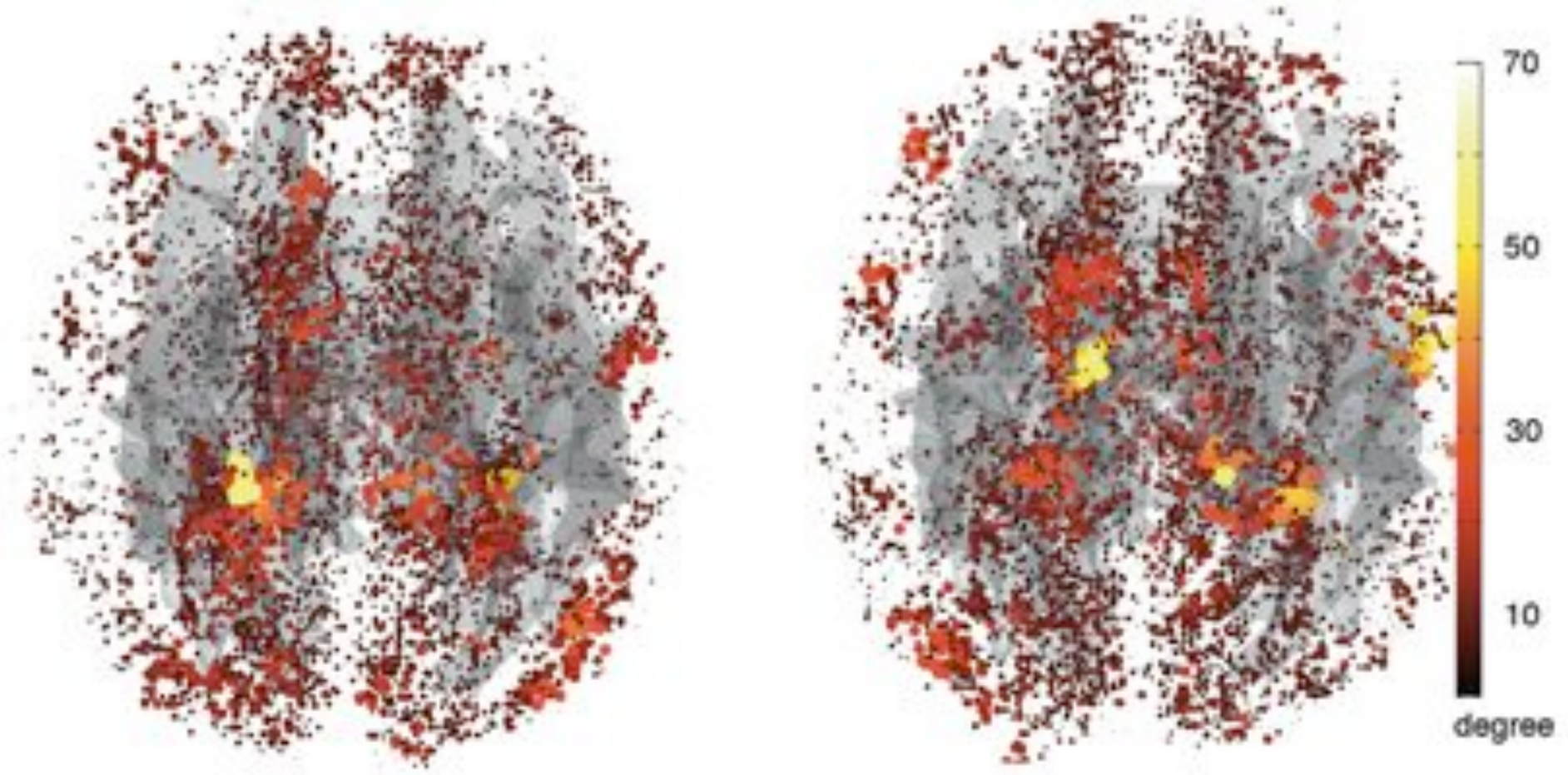
Global degree distribution

red: autism
blue: control



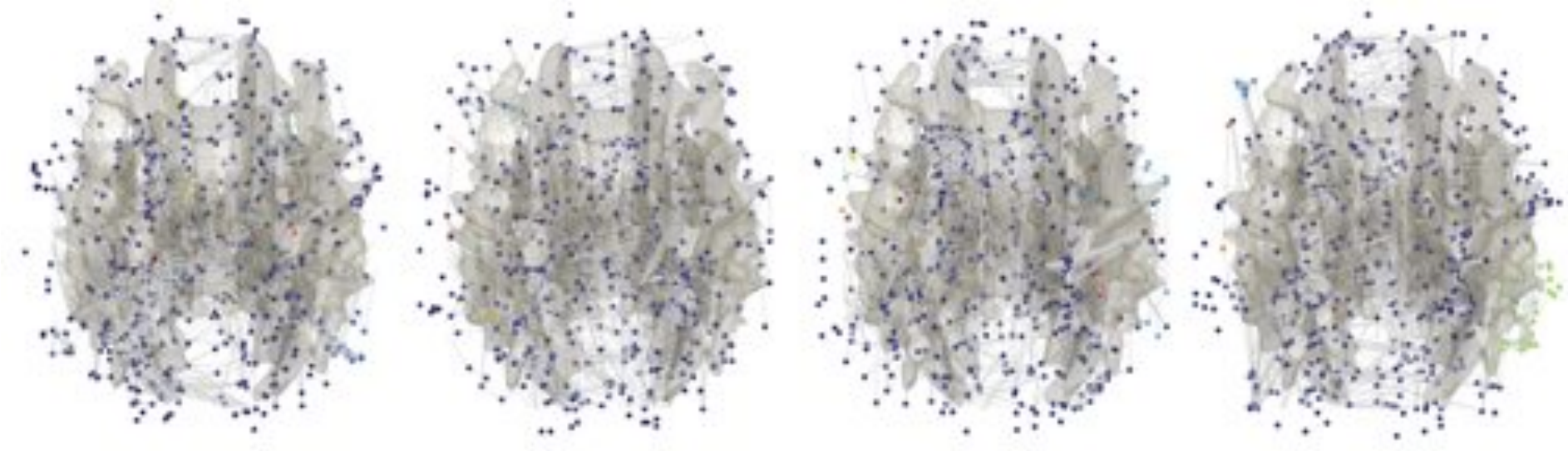
pvalues = 0.024, 0.015 and 0.080 for degrees 1, 2 and 3.

Degree of nodes for all subjects



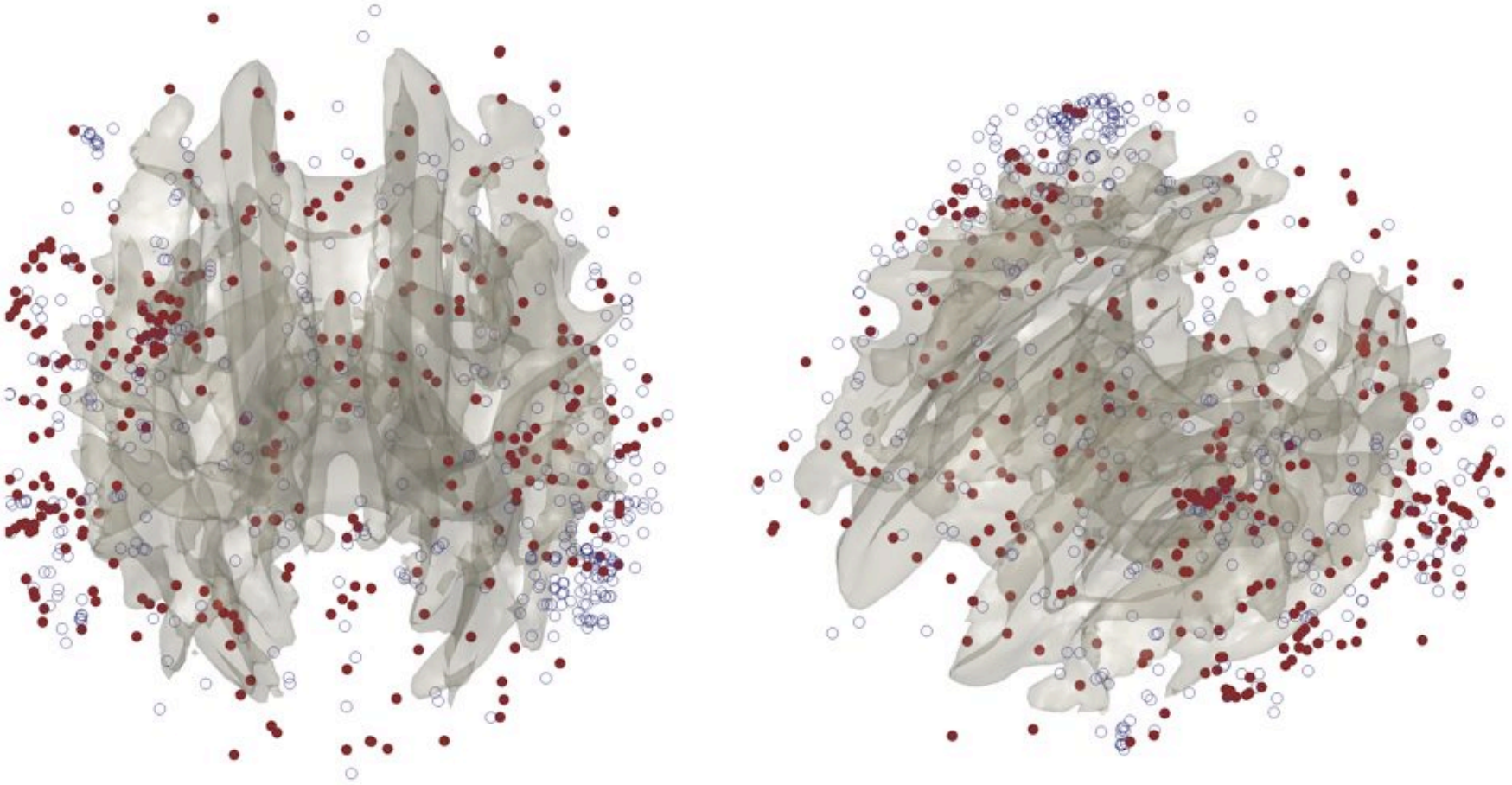
Control **Autism**

Largest connected component for 4 subjects



In average 96% of all nodes are connected to each other. We believe 100% of all nodes are supposed to be connected. 4% is a processing noise caused by weak connections.

Group difference in disconnected components



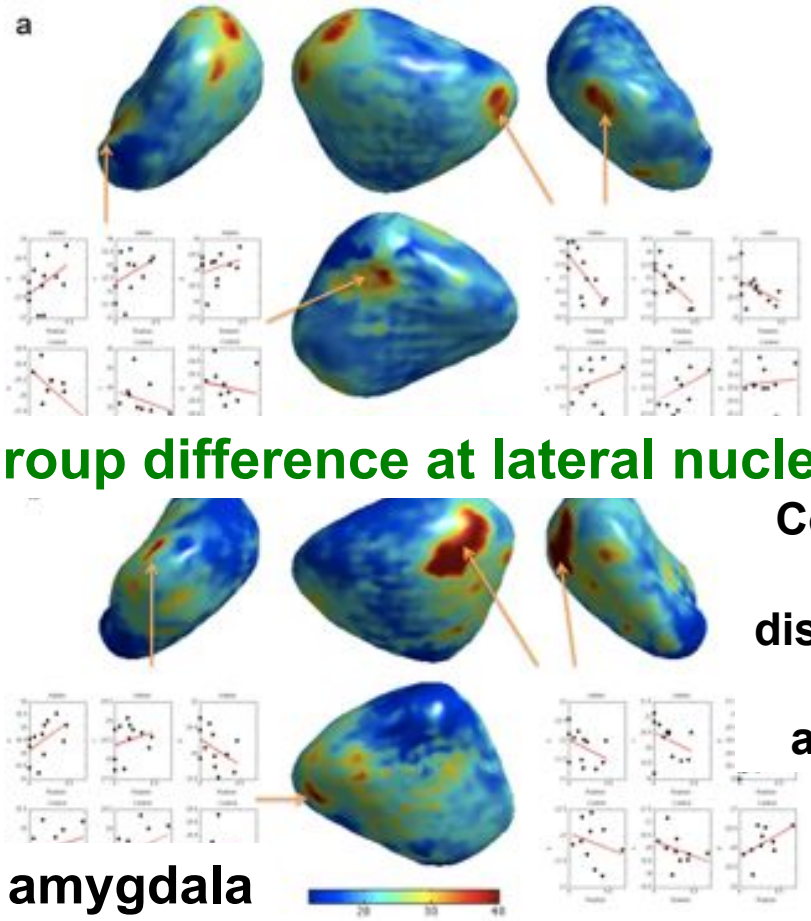
Control=blue
Autism=red

high clustering on the right parietal lobe
(pvalue = 0.01)

Chung et al., Neuroimage 2010

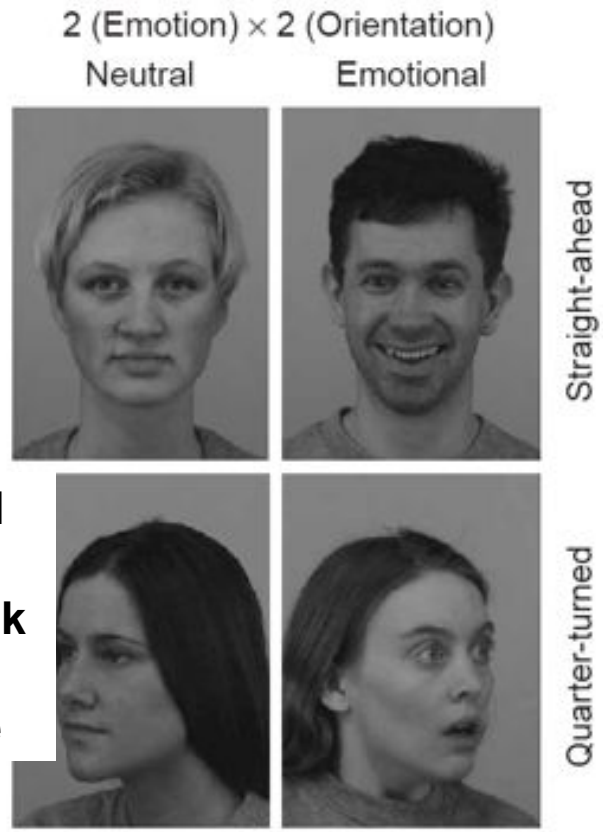
Discussion

Left amygdala



group difference at lateral nuclei

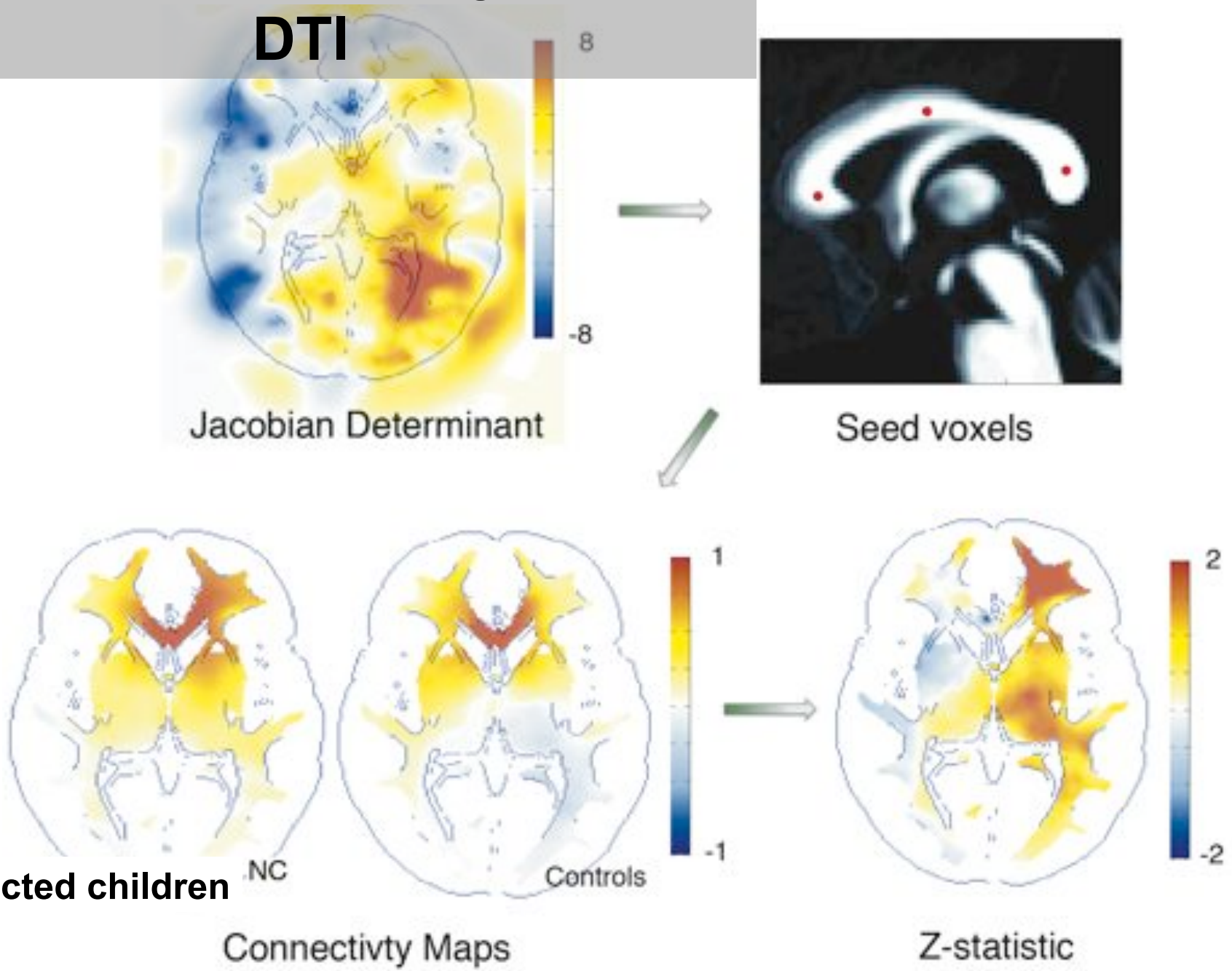
Right amygdala



Correlating facial emotion discrimination task response and amygdala shape

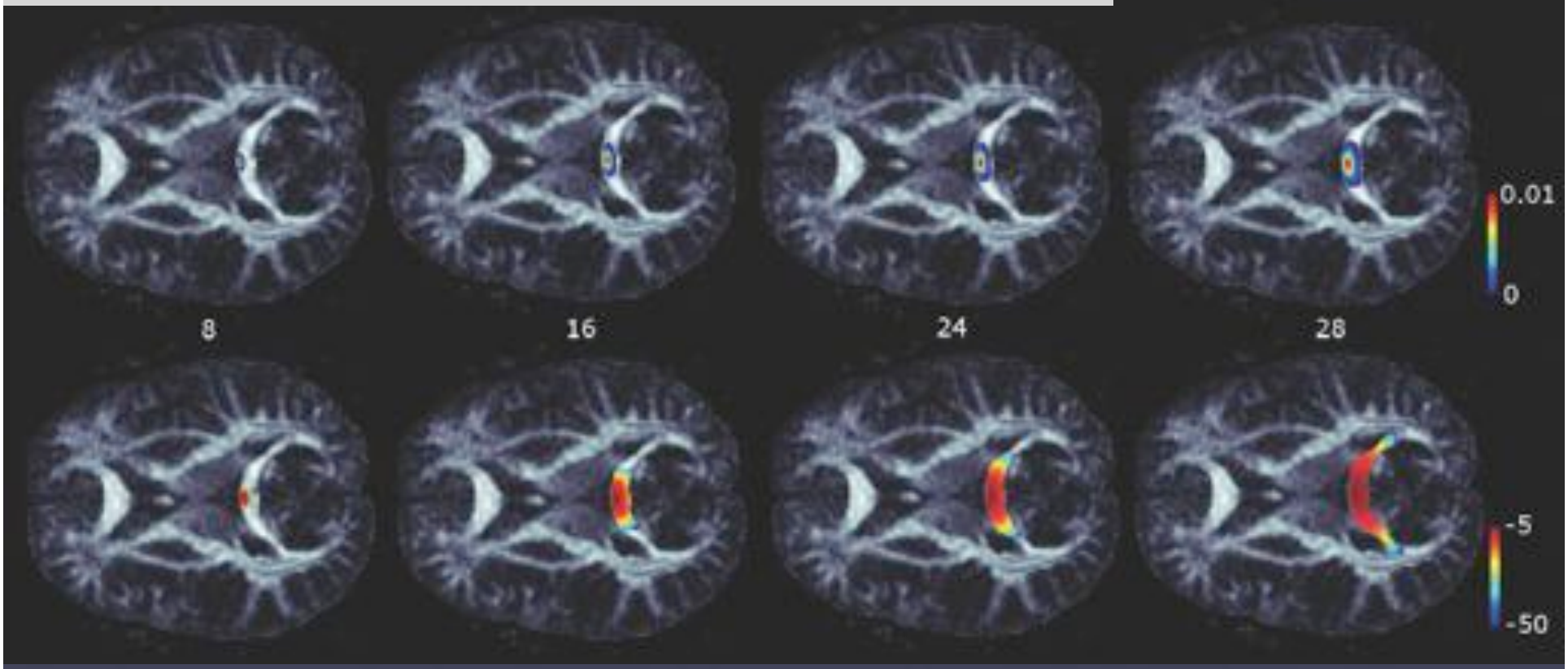
Amygdala network correlated with behavioral measures

Structural connectivity without DTI



NC=neglected children

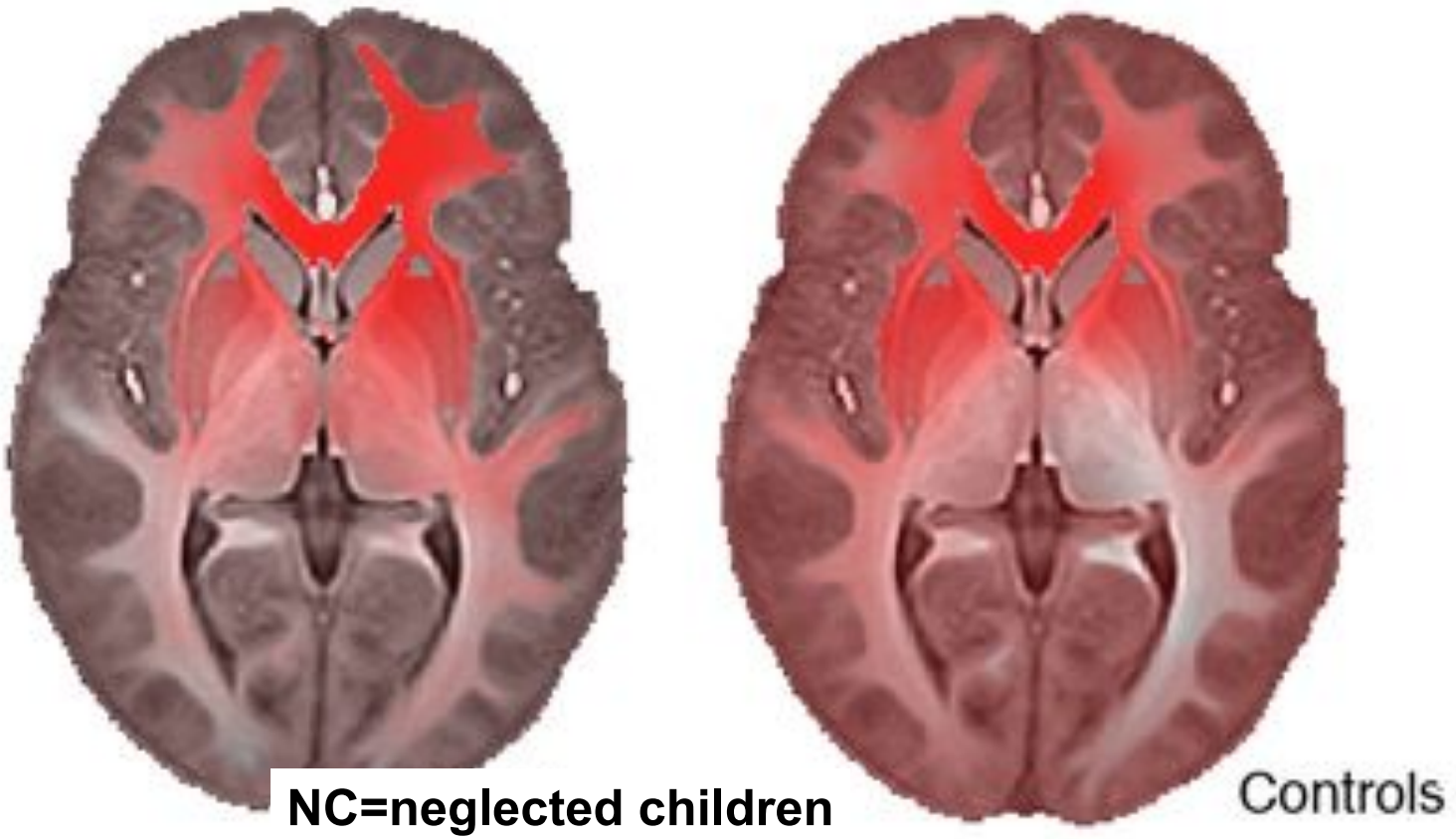
Probabilistic connectivity map using DTI



ransition probability of random walk is iteratively computed from the seed voxel

Compare this with our Jacobian determinant-based connectivity map.

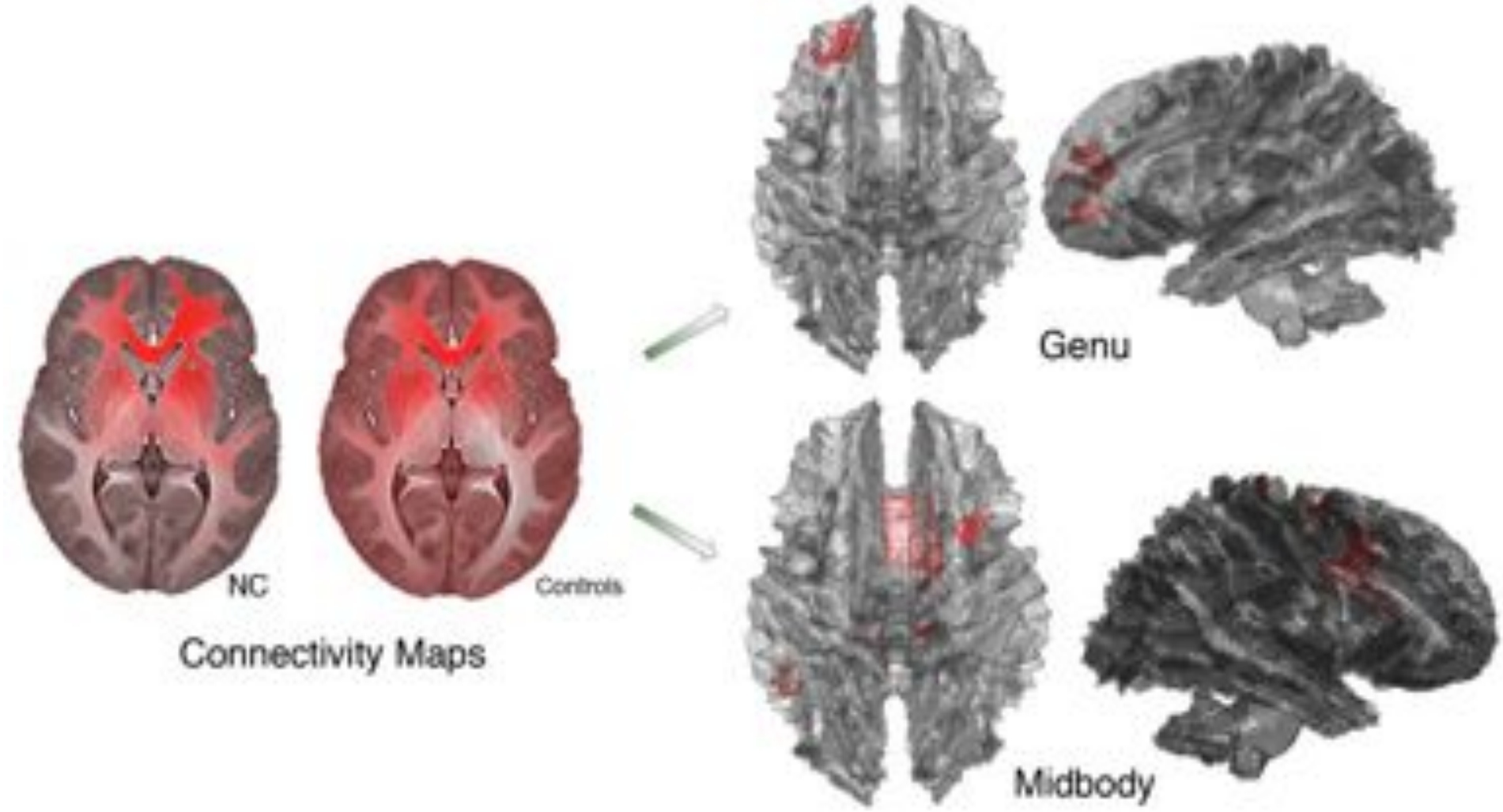
White matter connectivity based on correlating Jacobian determinant



NC=neglected children

Controls

No need for DTI doing structural connectivity analysis



Speaker:
Jee Eun Lee, PhD.
Waisman Laboratory for Brain Imaging and Behavior
University of Wisconsin-Madison

Time: October 22 Friday 11:00-11:50am
Place: SNUH Bldg 001 (의대 본관) Rm. 308

Title: Diffusion tensor imaging and its applications in autism

Abstract: Diffusion tensor imaging (DTI) is a non-invasive imaging method for assessing the characteristic and organization of tissue microstructures. Since DTI is sensitive to abnormal tissues, this fact has been exploited in characterizing various clinical populations. In this talk we first discuss the basic tensor model in DTI and a method for acquiring less noisy DTI data by applying anisotropic diffusion weighting schemes. Secondly we present our new method “tissue-specific smoothing-compensated voxel based analysis” and results from applying the method to DTI of autistic children.

KAIST-SNU JOINT WORKSHOP ON SPARSE DATA RECOVERY AND ITS APPLICATION TO MEDICAL IMAGING

Time: November 9 Tuesday 10:00am-5:00pm
Place: SNUH 연건캠퍼스

Lecture 8

Geometric Computation

Read

seo.2010.pdf
chung.2004.ISBI.pdf

Lecture 9-10 More on network modeling

(not going to teach about network complexity measures)