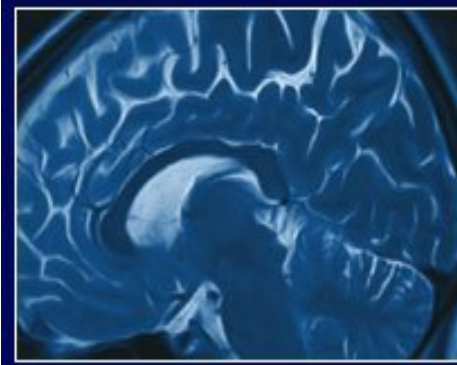




University of Wisconsin
**SCHOOL OF MEDICINE
AND PUBLIC HEALTH**



*The Waisman Laboratory
for Brain Imaging and Behavior*

August 10, 2015

Large-scale Brain Network Construction and Its Application to Twin fMRI Study

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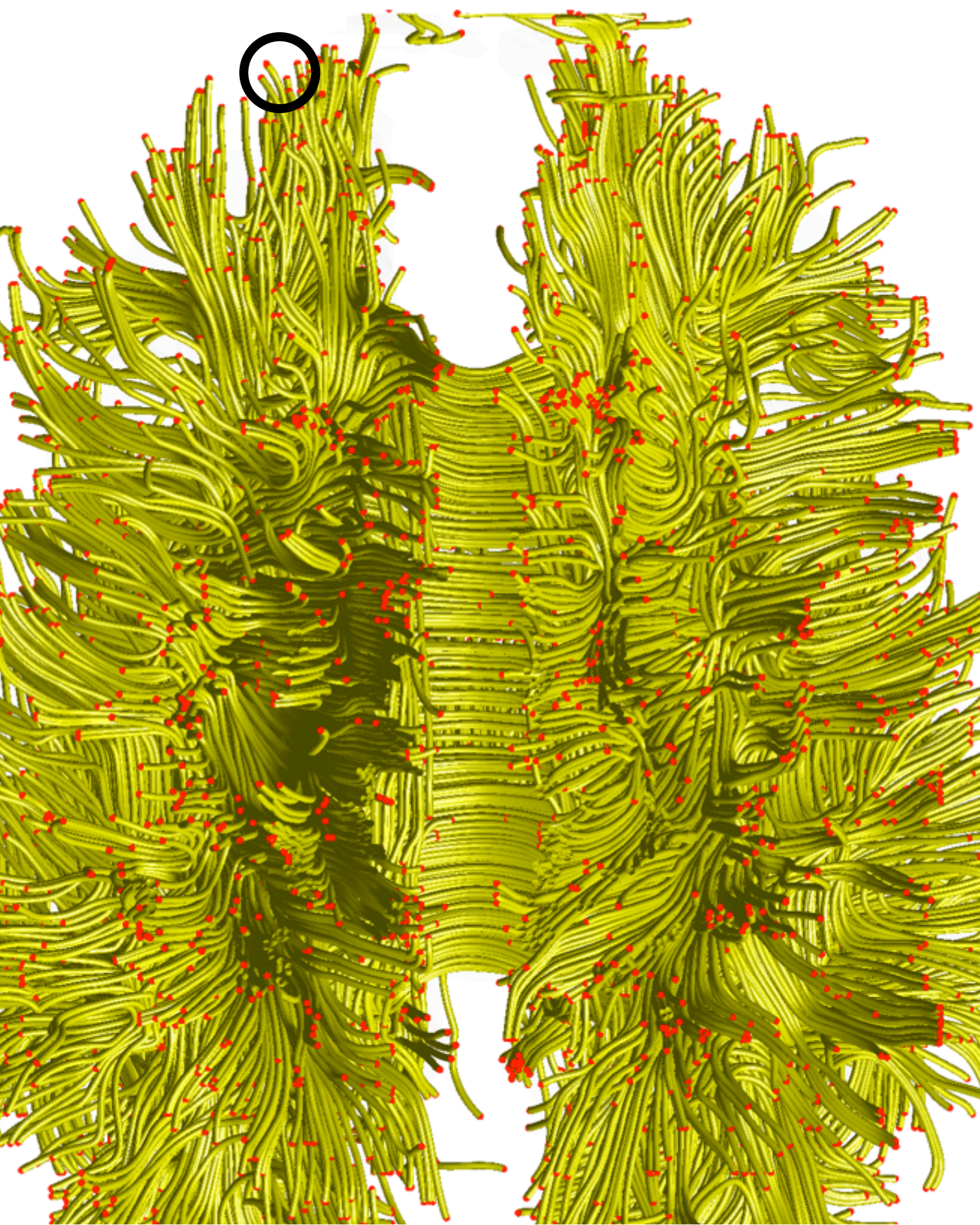
Victoria G. Vilalta, David H. Zald

Department of Psychology
Vanderbilt University

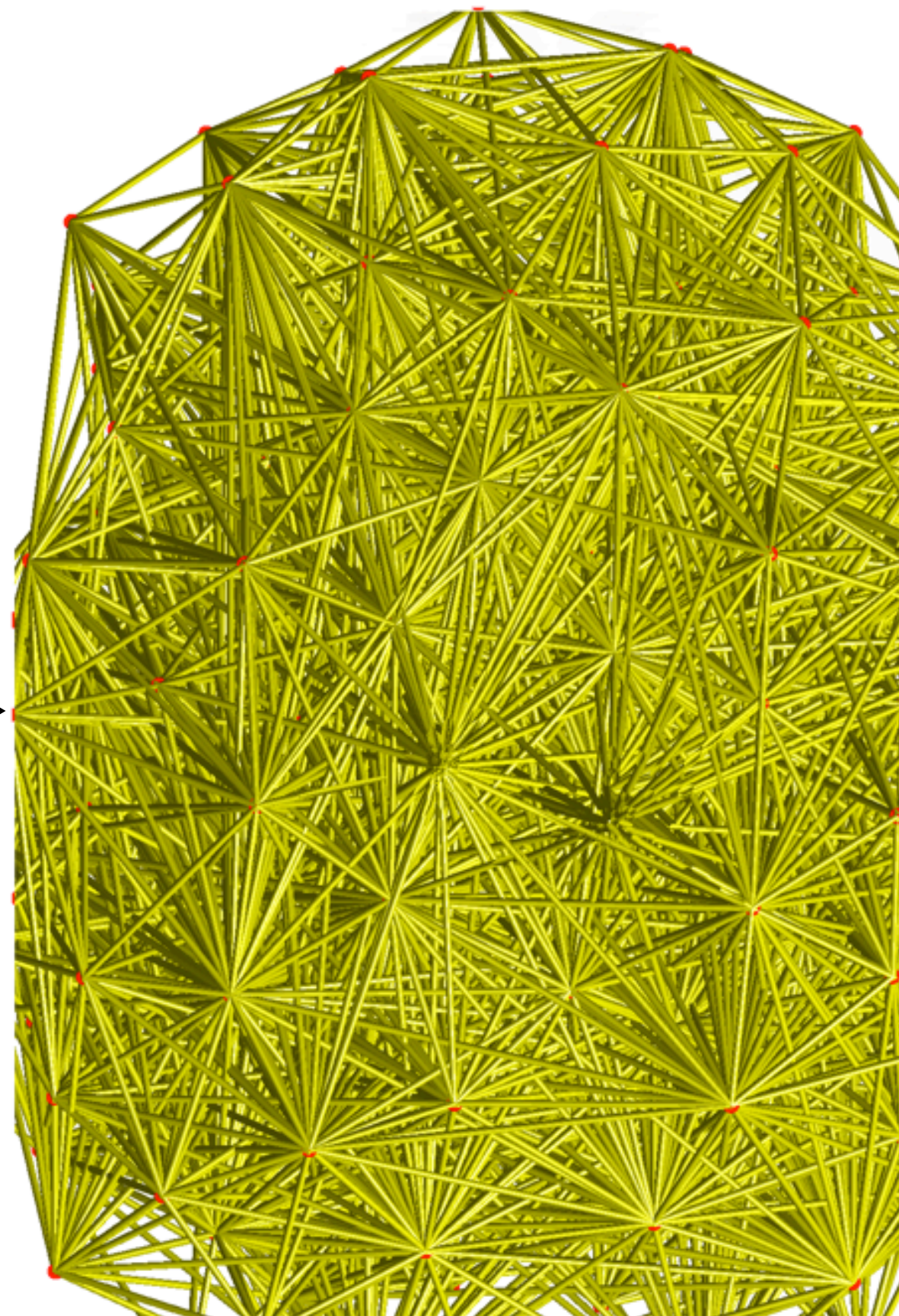
Benjamin B. Lahey

Department of Public Health Sciences
University of Chicago

Motivation 1: Dense structural network



White matter fiber tracts



Motivation 2: Dense functional network

11 monozygotic (MZ) pairs

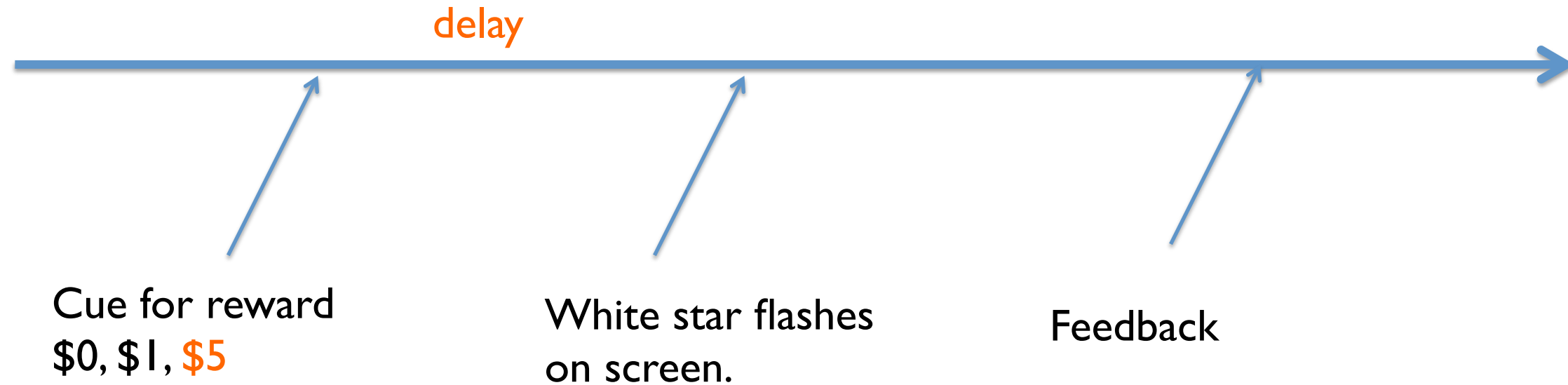
14 dizygotic (DZ) pairs

9 same-sex DZ pairs (5 male, 4 female)

5 different-sex DZ pairs

fMRI resolution 53x63x46

Reward experiment



Win if the response
button is pushed in time

3 runs of 40 randomized trials.

40 \$0 rewards

40 \$1 rewards

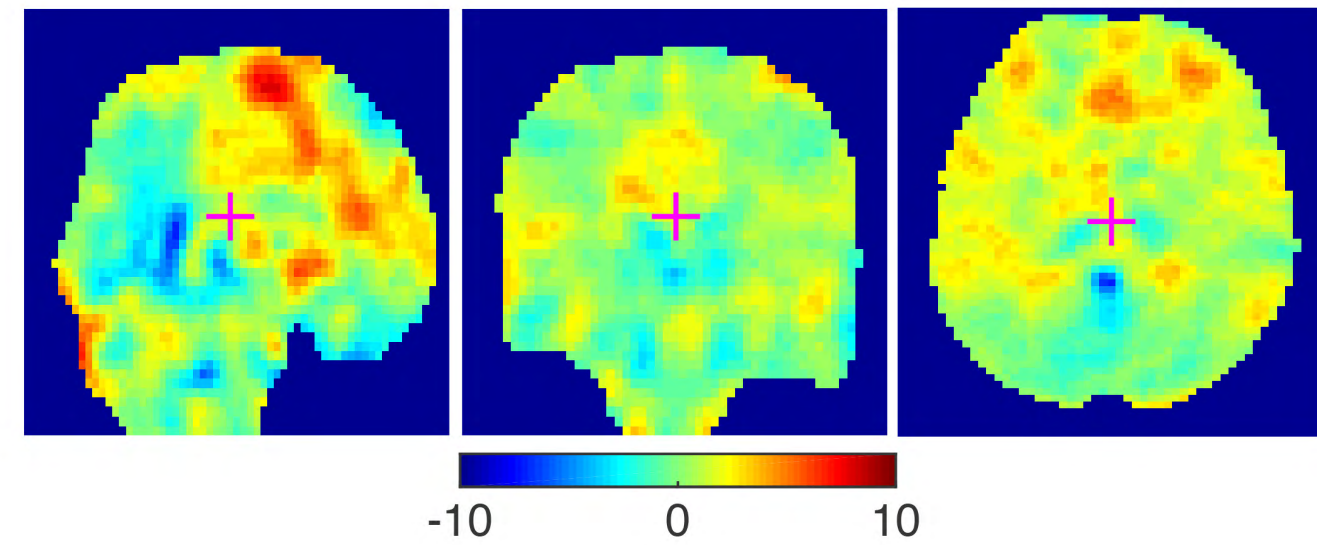
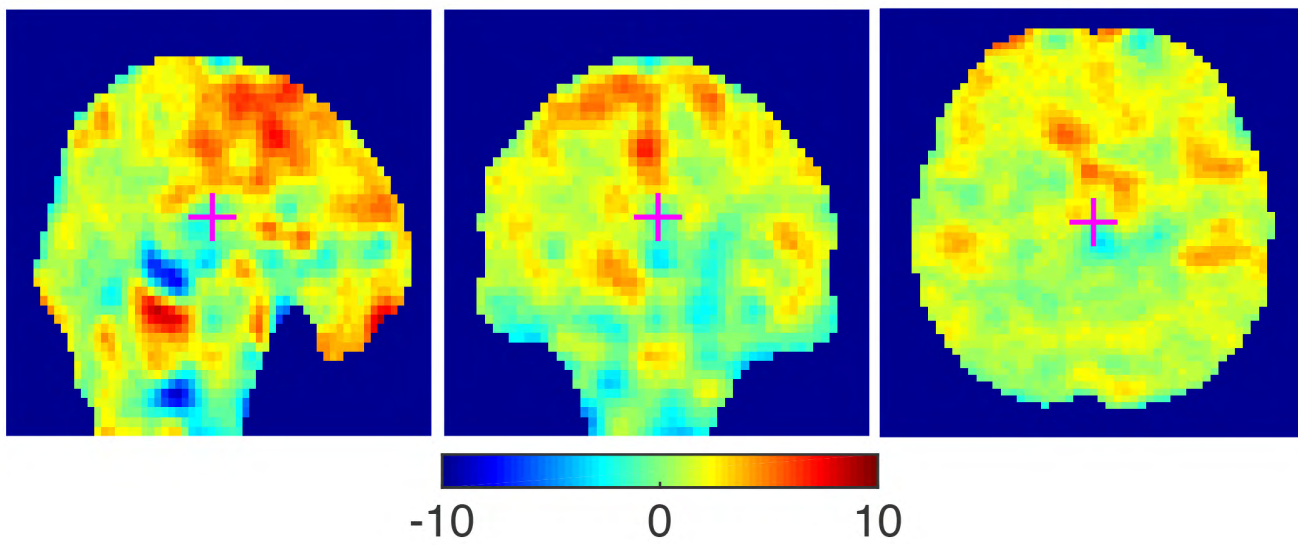
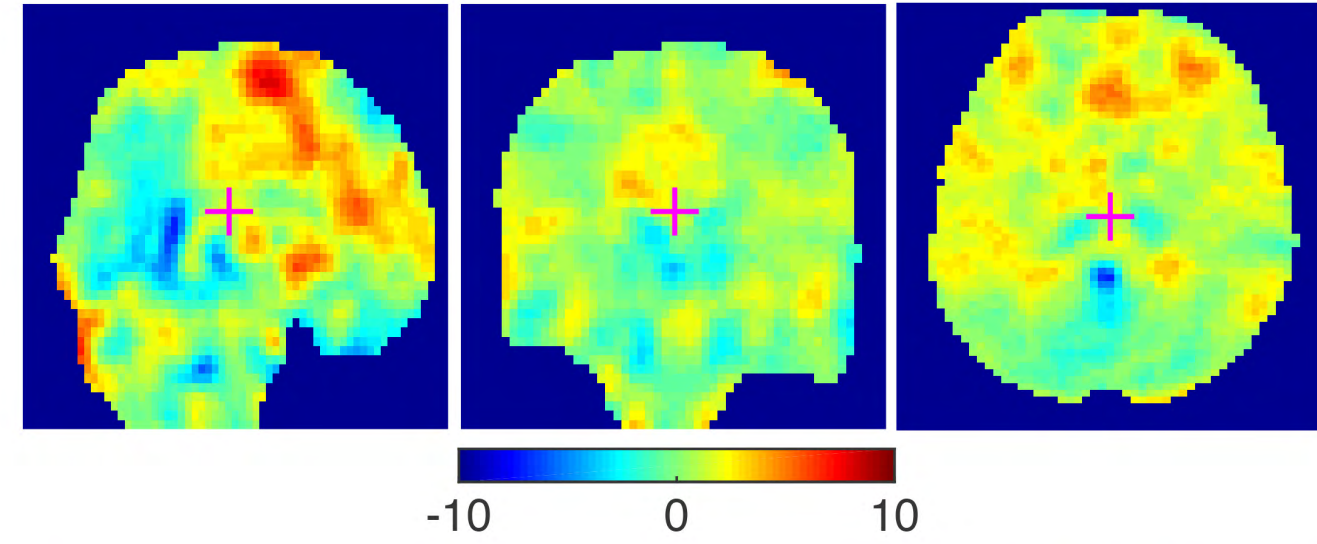
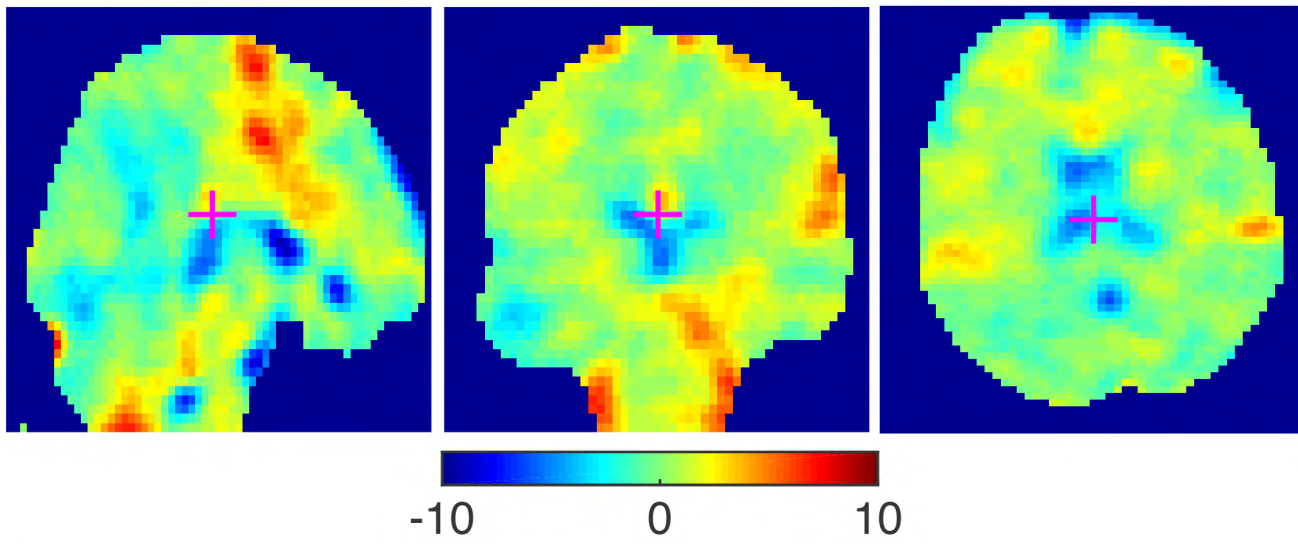
40 \$5 rewards

9 conditions (each condition also includes a time and a dispersion derivative):

- delay for \$0 trials
- delay for \$1 trials
- **delay for \$5 trials**
- reward \$0
- reward \$1
- reward \$5
- miss \$0
- miss \$1
- miss \$5

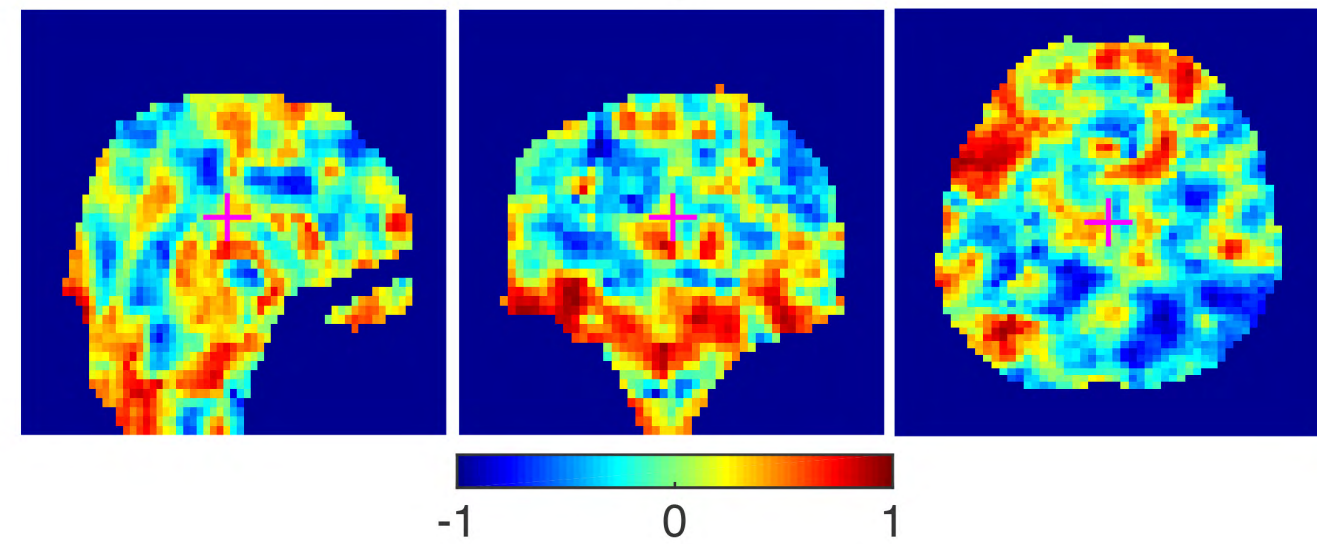
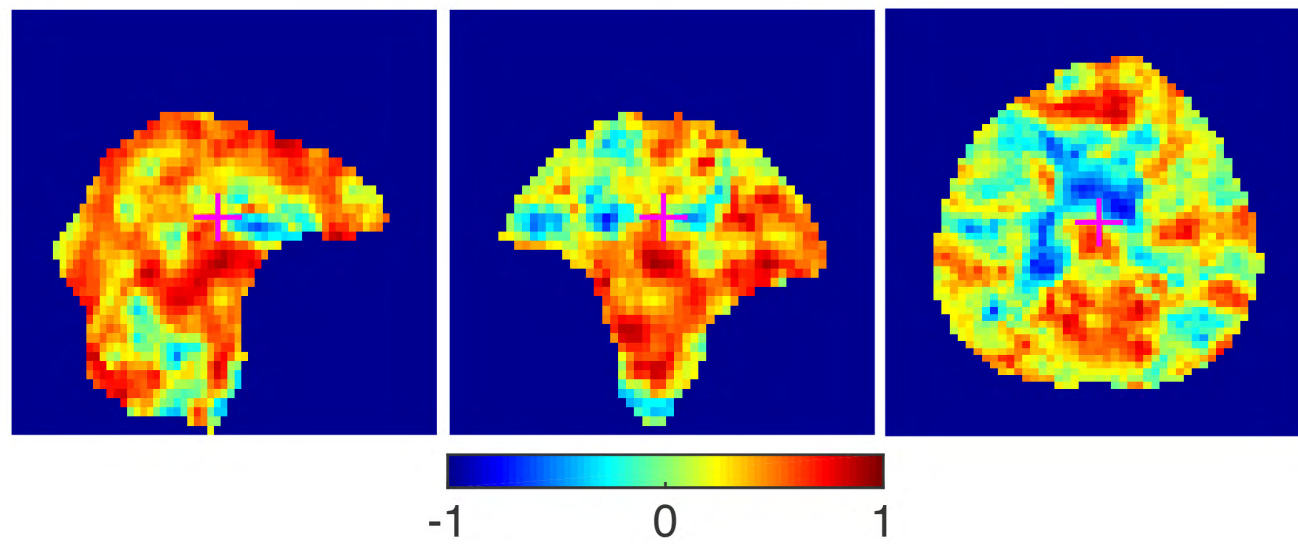
MZ-twins

DZ-twins



ρ_{MZ}

ρ_{DZ}



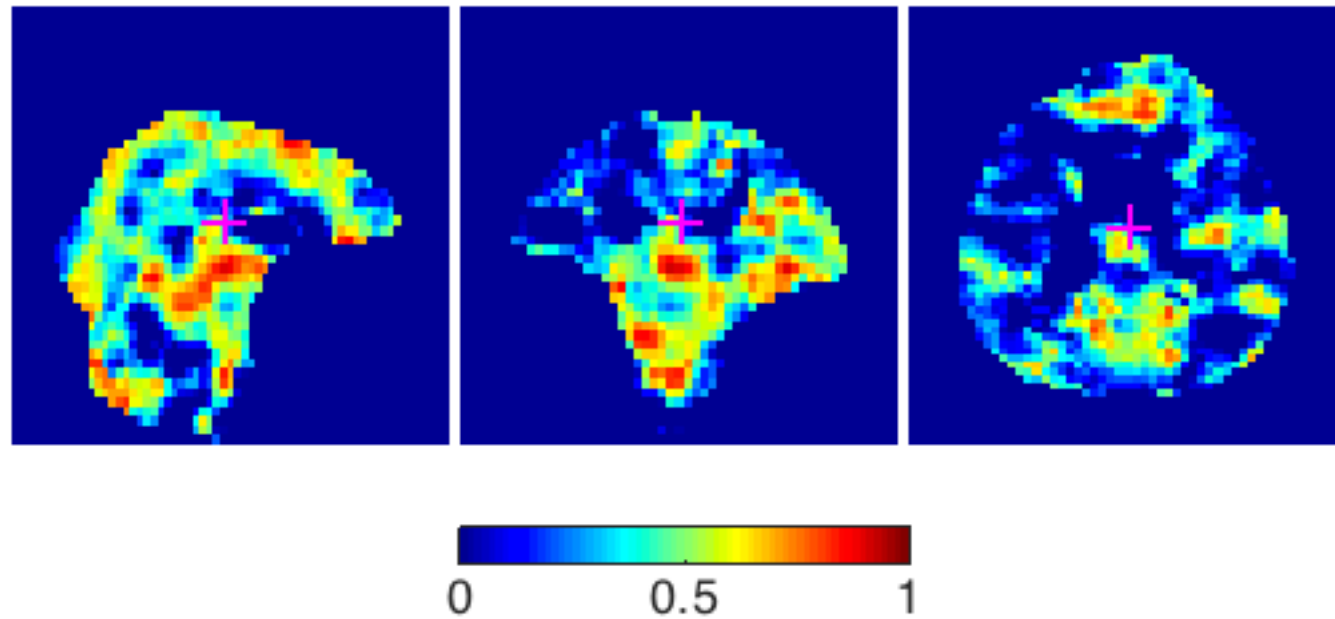
Heritability index

Heritability index (HI) determines the amount of variation due to genetic influence and usually estimated using Falconer's formula:

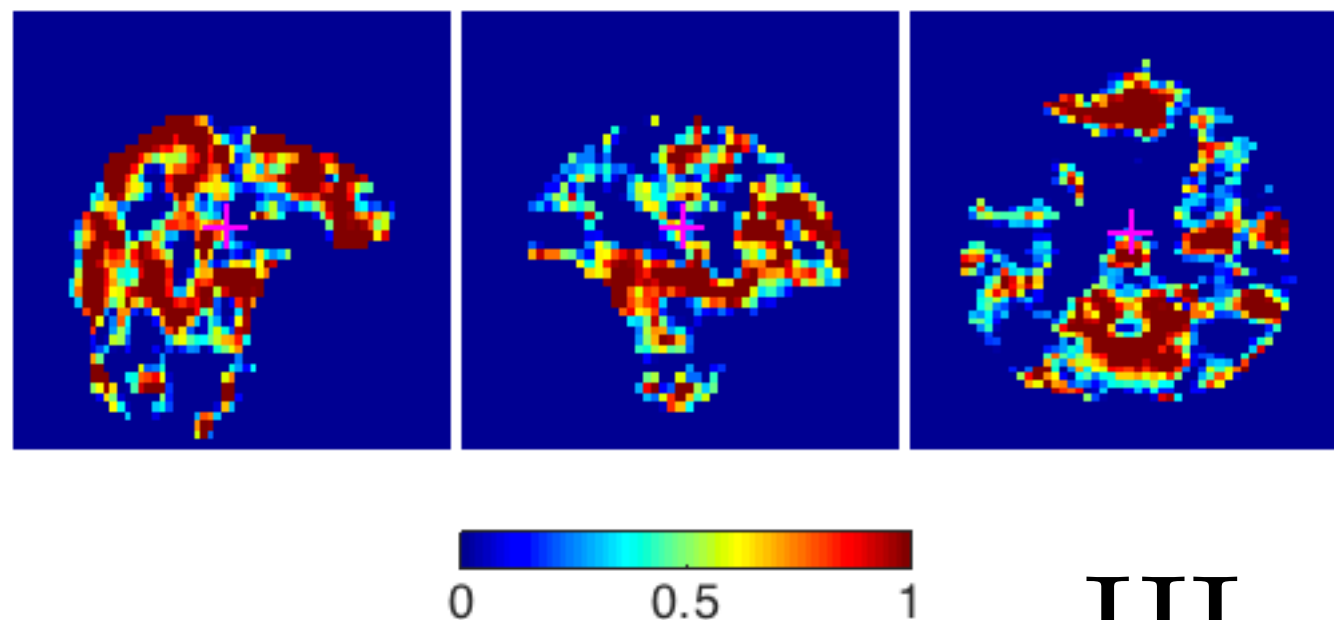
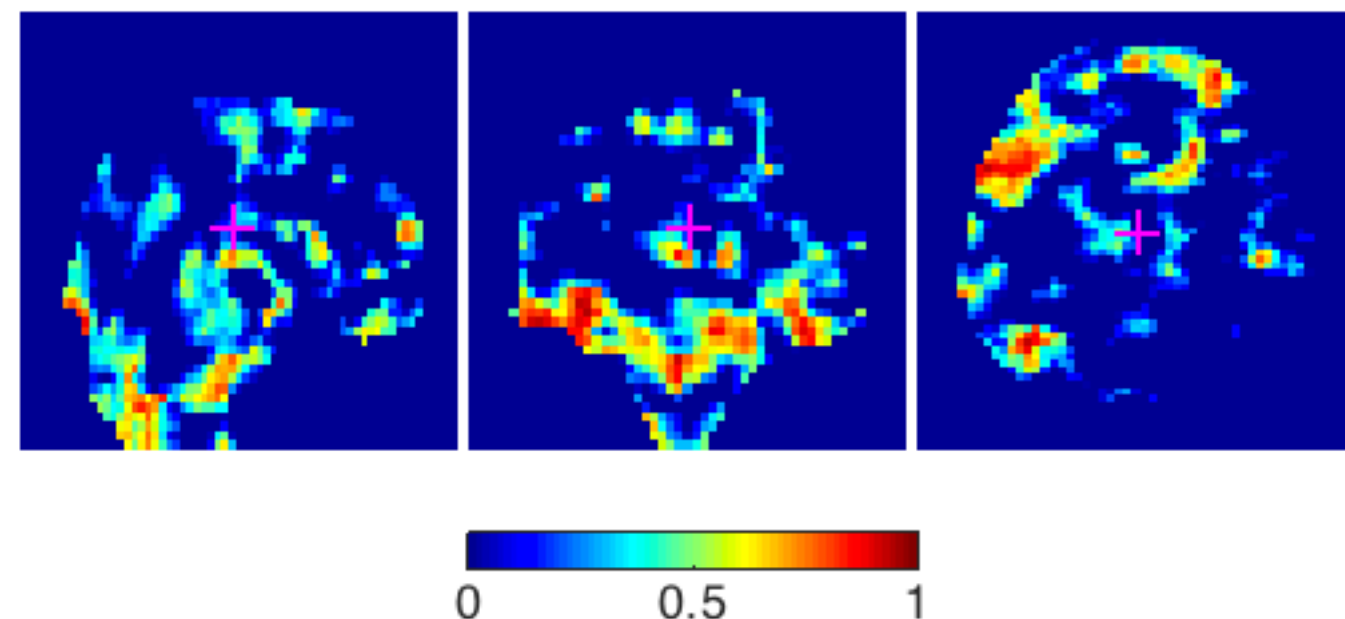
$$HI_i = 2[\rho_{MZ}(v_i) - \rho_{DZ}(v_i)]$$

Heritability Index (HI) map: fMRI

Correlation of MZ-pairs



Correlation of DZ-pairs



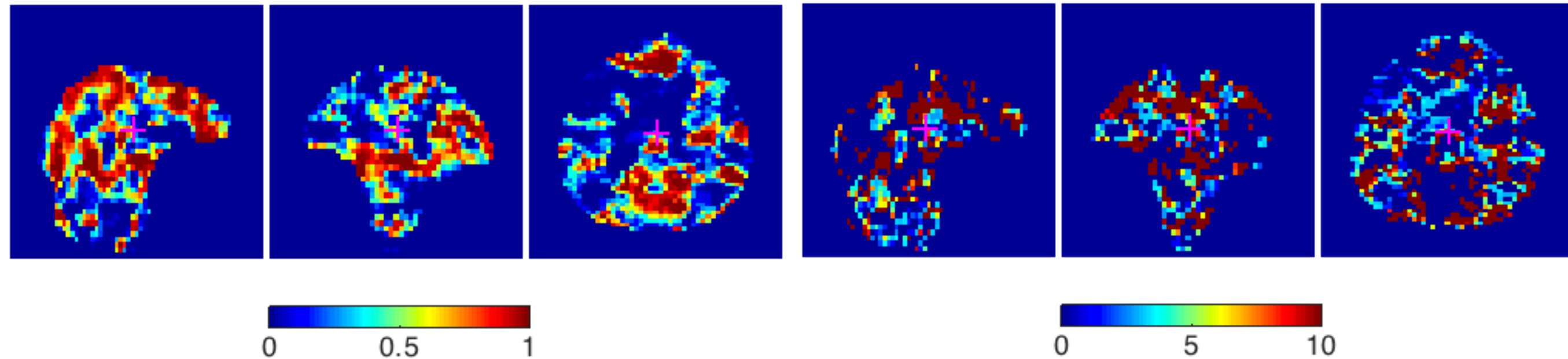
Heritability index

$$HI_i = 2[\rho_{\text{MZ}}(v_i) - \rho_{\text{DZ}}(v_i)]$$

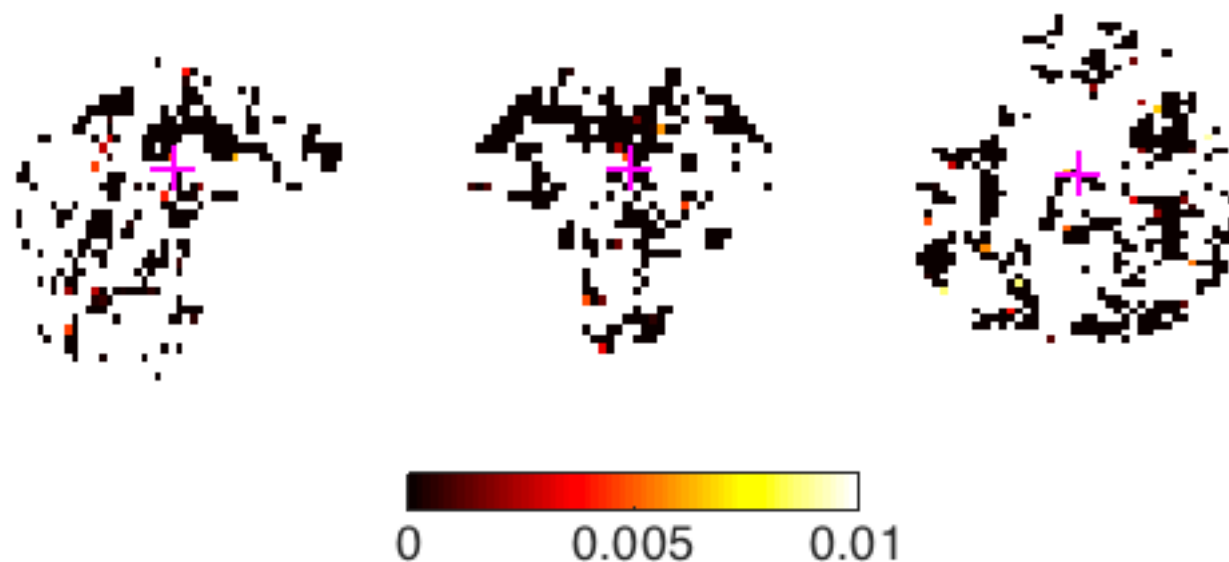
Jackknife on Heritability Index (HI)

Mean of jackknife resampled HI

t-statistic map on jackknife



p-value (corrected)

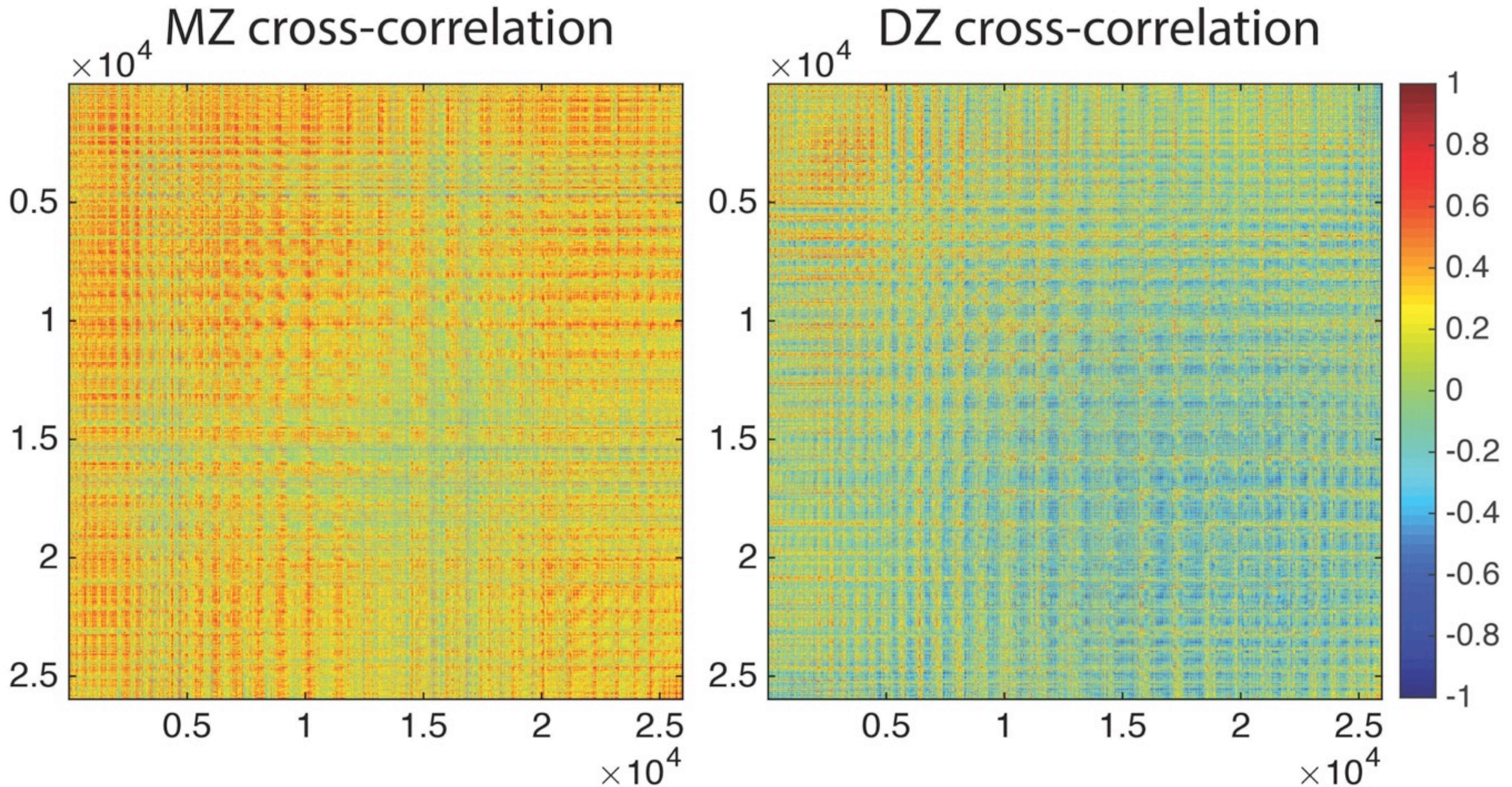


Heritability graph index

Heritability index (HI) does not tell us about the genetic influence on brain networks.

Heritability graph index (HGI):

$$\text{HGI}_{ij} = 2[\varrho_{\text{MZ}}(v_i, v_j) - \varrho_{\text{DZ}}(v_i, v_j)]$$



more than 337 million correlations

more than 3 million connections above
correlation 0.7

Sparse Network Model

Centered and scaled data

n paired images in p voxels ($n < p$)

$x_k(v_i)$ k -th image intensity value at voxel v_i

$y_k(v_i)$ k -th image intensity value at voxel v_i

$$\sum_{k=1}^n x_k = \sum_{k=1}^n y_k = 0$$

$$x = (x_1, \dots, x_n)' \quad y = (y_1, \dots, y_n)'$$

$$\|x\|^2 = x'x = \|y\|^2 = y'y = 1$$

Sparse cross-correlation

Sample correlation at v_i and v_j : $x'(v_i)y(v_j)$

Cross-correlation $x'(v_i)y(v_j)$ minimizes

$$\sum_{i=1}^p \sum_{j=1}^p \|x(v_i) - \beta_{ij} y(v_j)\|^2$$

Sparse cross-correlation: $\beta = (\beta_{ij})$

$$\hat{\beta} = \operatorname{argmin}_{\beta} \frac{1}{2} \sum_{i=1}^p \sum_{j=1}^p \|x(v_i) - \hat{\beta}_{ij} y(v_j)\|^2 + \lambda \sum_{i,j} |\beta_{ij}|$$

Sparse correlations

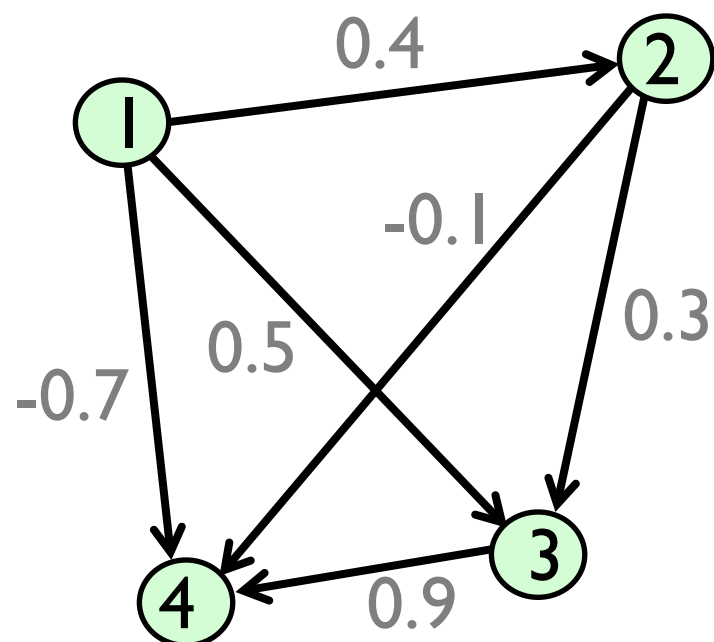
$$\hat{\beta} = \operatorname{argmin}_{\beta} \frac{1}{2} \sum_{i=1}^p \sum_{j=1}^p \|x(v_i) - \beta_{ij} y(v_j)\|^2 + \lambda \sum_{i,j} |\beta_{ij}|$$

Adjacency
matrix

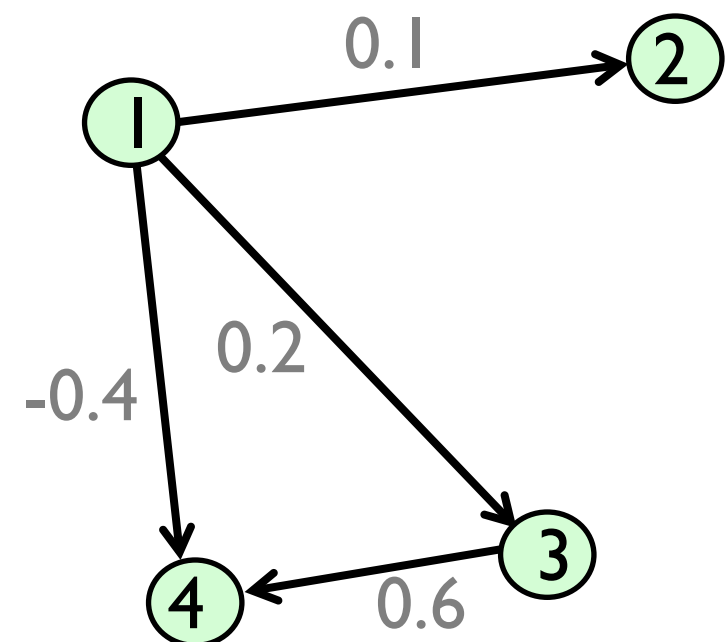
$$b_{ij}(\lambda) = \begin{cases} 1 & \text{if } \hat{\beta}_{ij} \neq 0 \\ 0 & \text{otherwise} \end{cases}$$

Sparse network

$$G(\lambda)$$



$$\lambda=0.3$$



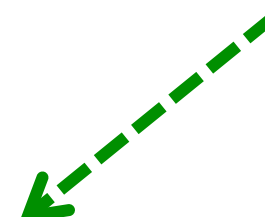
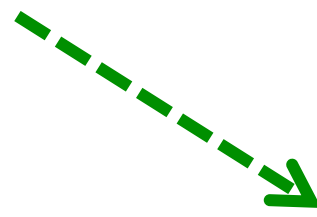
Sparse cross-correlation via soft-thresholding

Sparse optimization

$$a_{ij}(\lambda) = \begin{cases} 1 & \text{if } \hat{\beta}_{ij}(\lambda) \neq 0 \\ 0 & \text{otherwise} \end{cases}$$

Soft-thresholding

$$b_{ij}(\lambda) = \begin{cases} 1 & \text{if } |x'(v_i)y(v_j)| > \lambda \\ 0 & \text{otherwise} \end{cases}$$



$G(\lambda)$

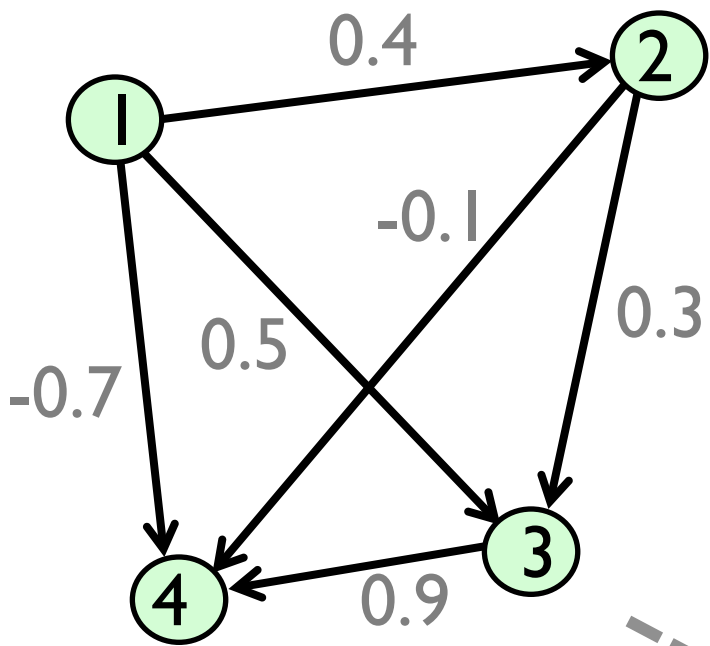


$$G(\lambda_1) \supset G(\lambda_2) \supset G(\lambda_3) \supset \dots$$

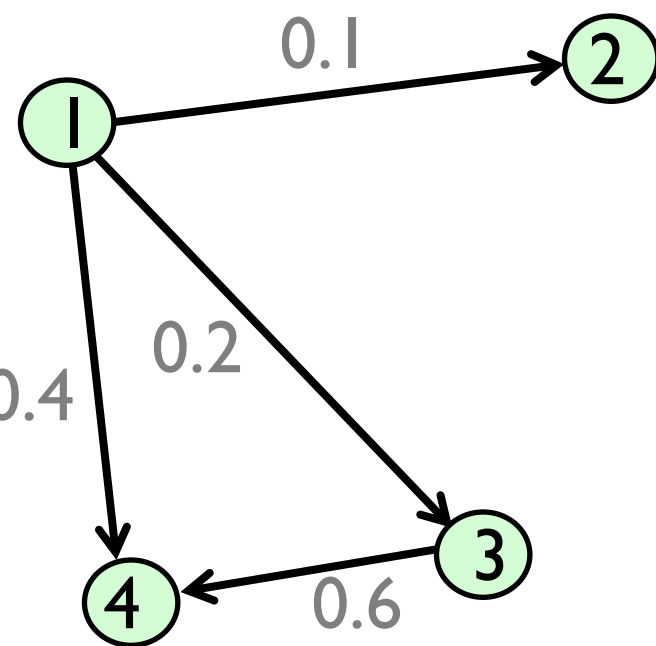
$$\text{for } \lambda_1 \leq \lambda_2 \leq \lambda_3 \leq \dots$$

$$\mathbf{x}'\mathbf{y} = \begin{pmatrix} \times & 0.4 & 0.5 & -0.7 \\ \times & \times & 0.3 & -0.1 \\ \times & \times & \times & 0.9 \end{pmatrix}$$

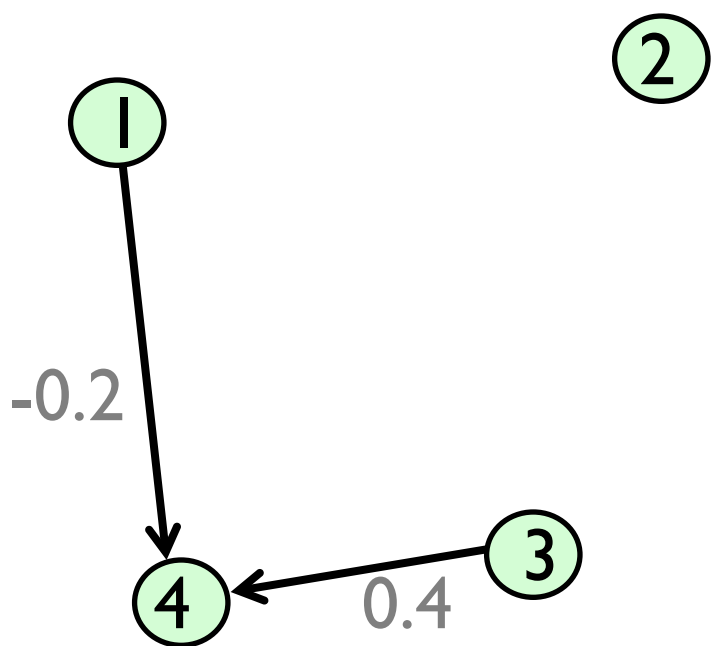
Sparse cross-correlation



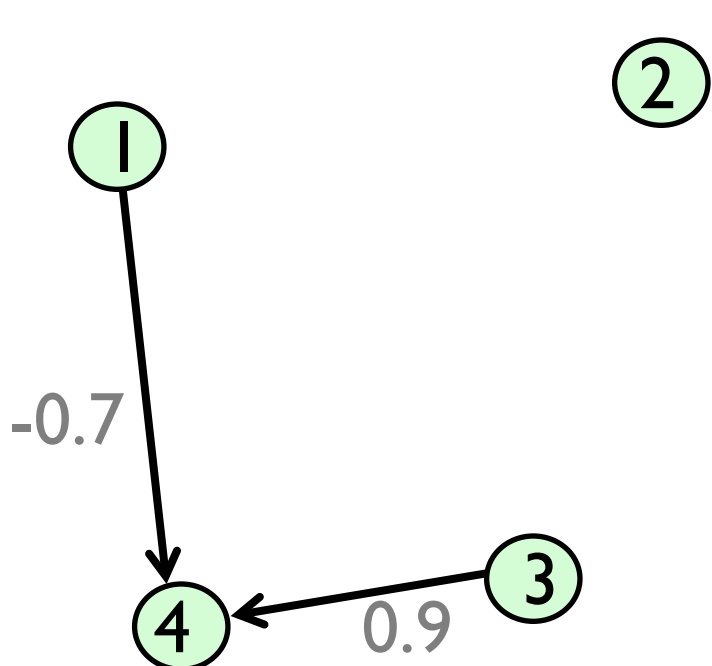
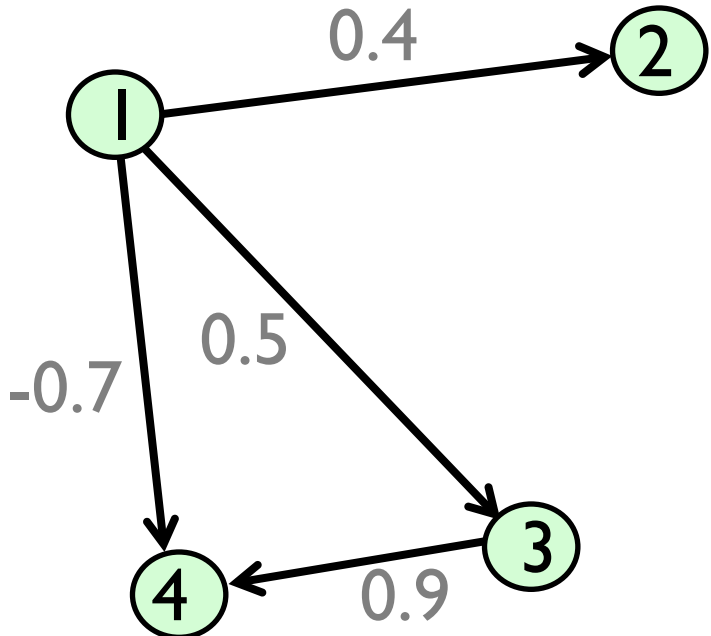
Soft-thresholding



$\lambda=0.3$

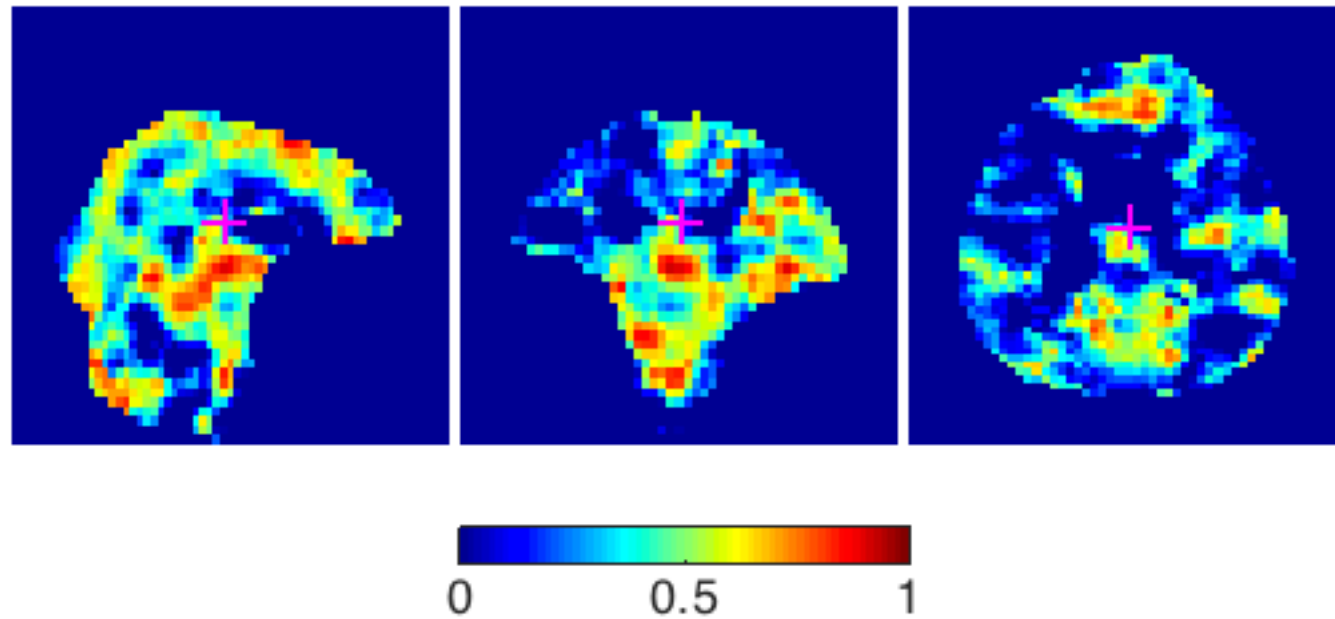


$\lambda=0.5$

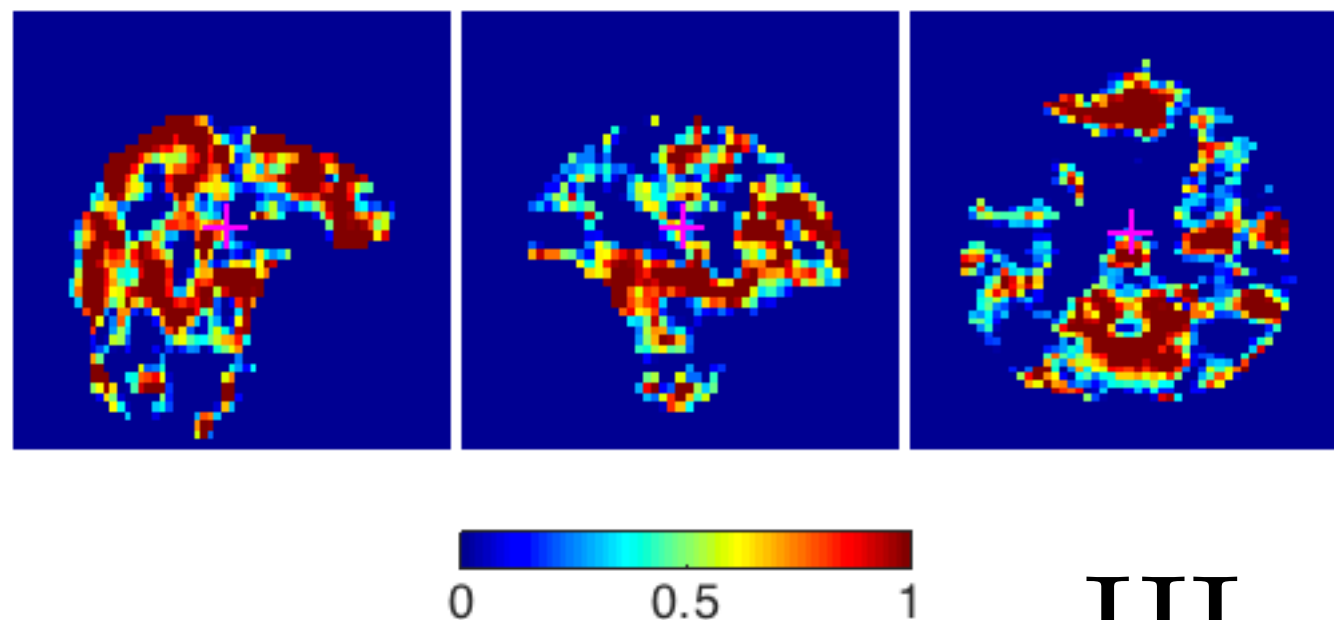
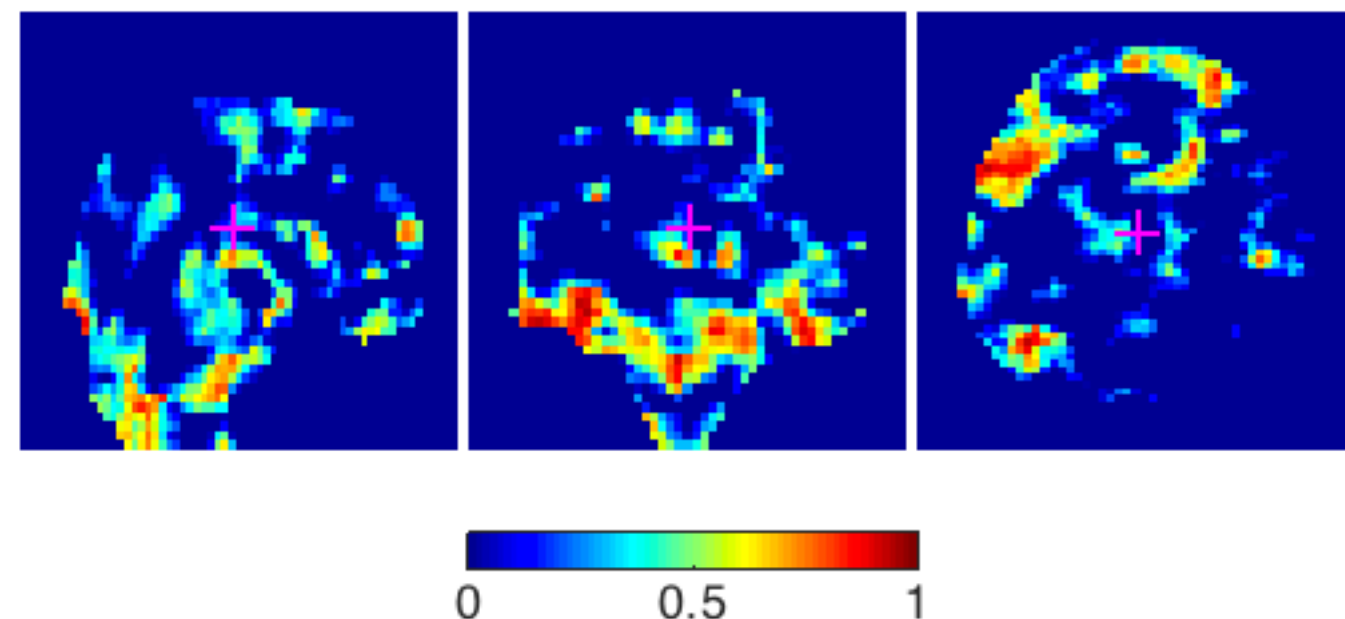


Heritability Index (HI) map: fMRI

Correlation of MZ-pairs



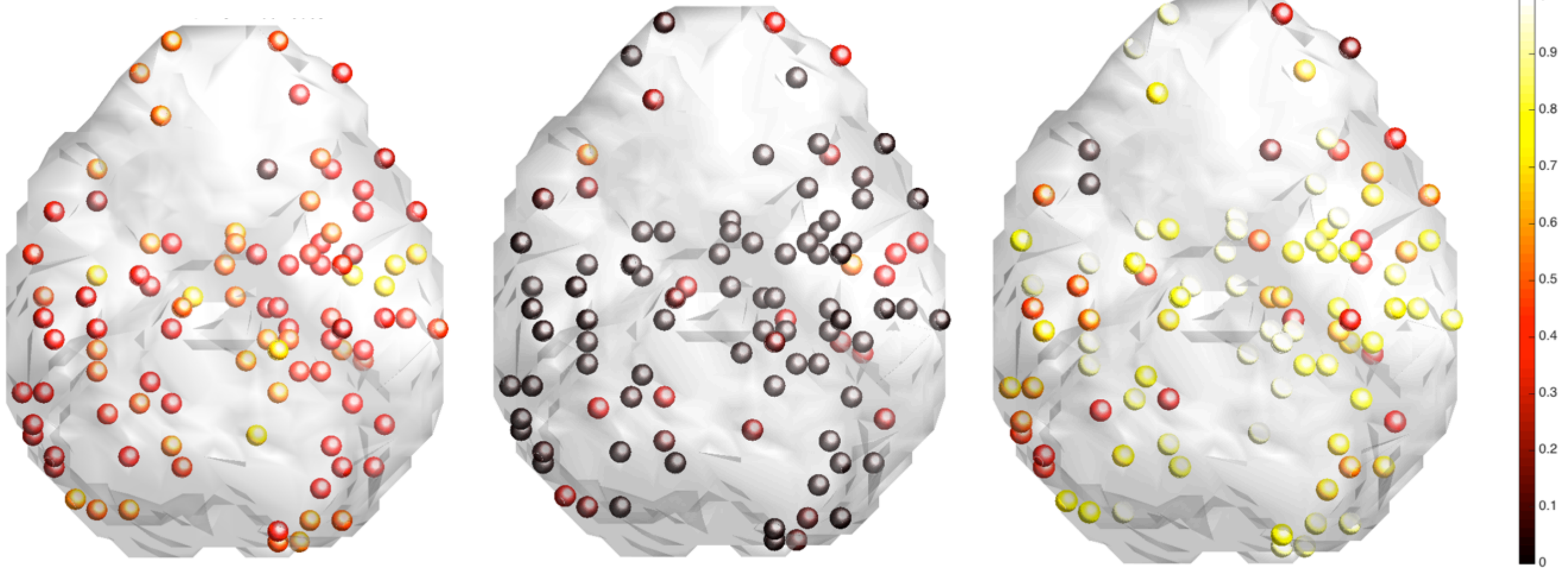
Correlation of DZ-pairs



Heritability index

$$HI_i = 2[\rho_{\text{MZ}}(v_i) - \rho_{\text{DZ}}(v_i)]$$

HI-values at 100 nodes



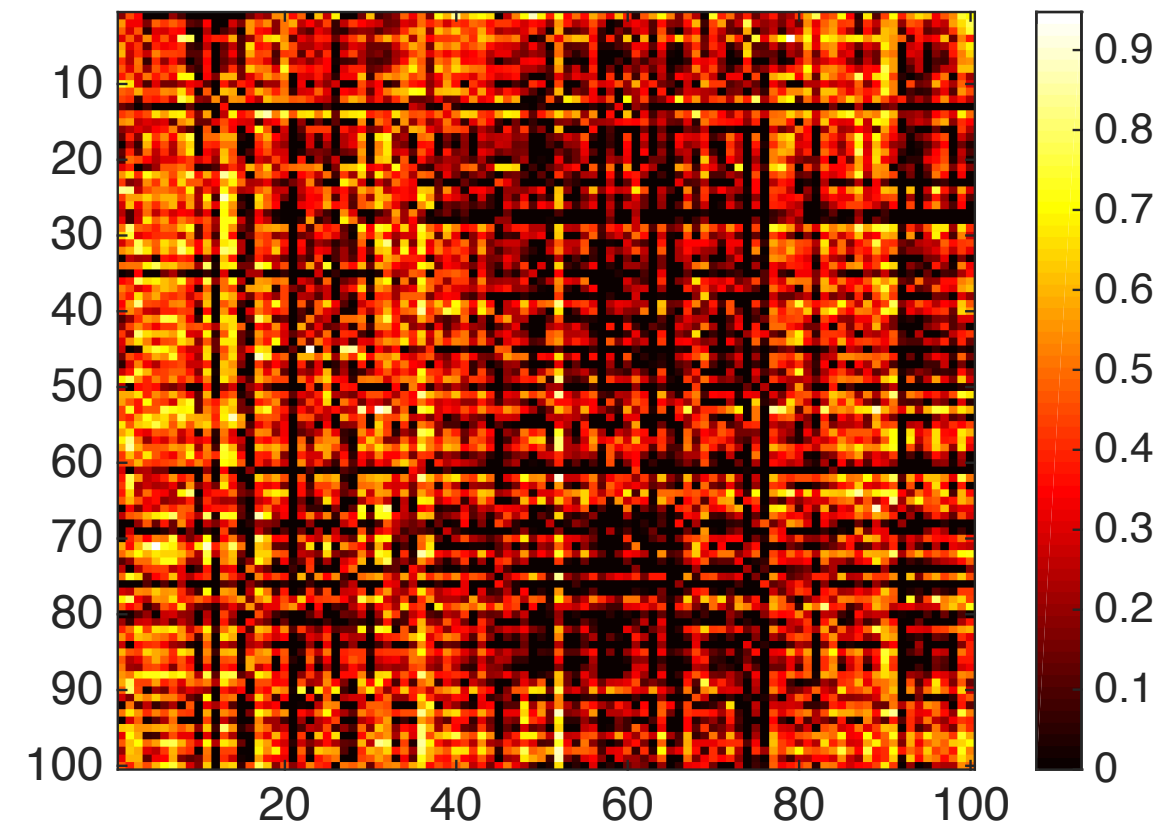
Correlation
in MZ-twins

Correlation
In DZ-twins

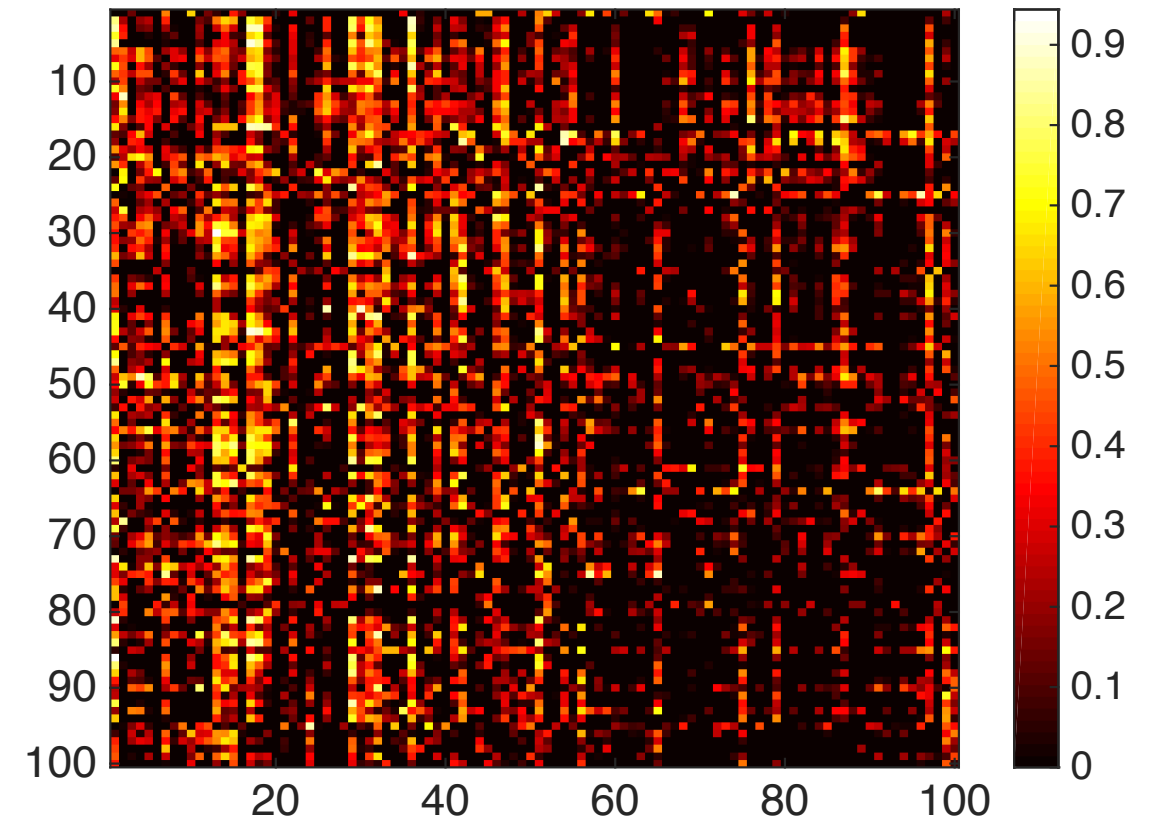
Heritability
Index

Heritability graph index (HGI) in 100 nodes

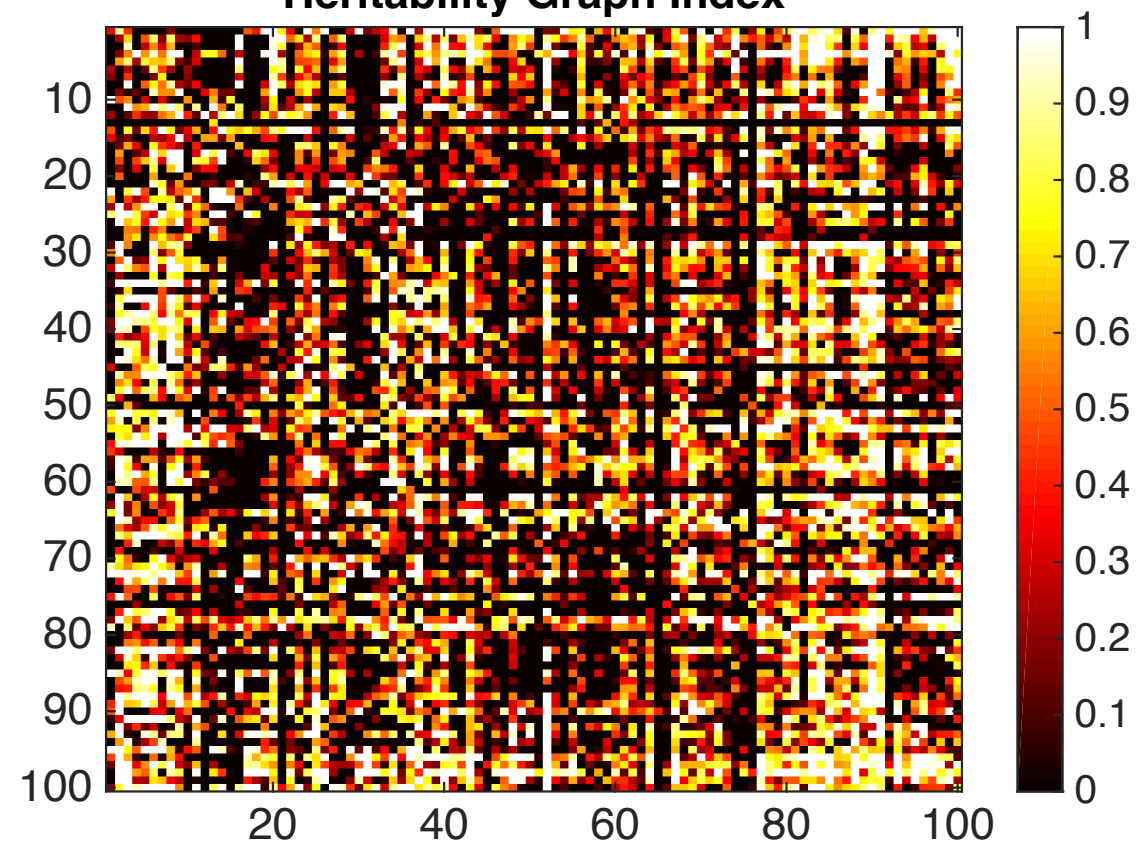
Cross-Correlations in MZ-twins



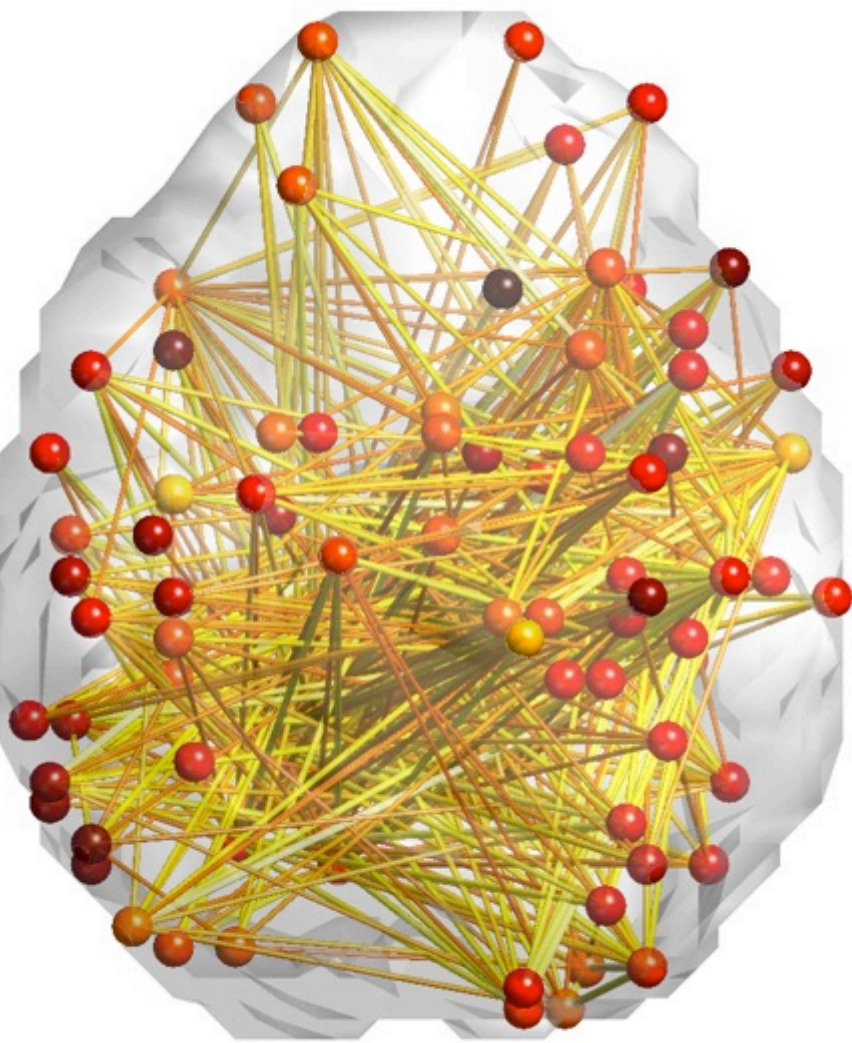
Cross-Correlations in DZ-twins



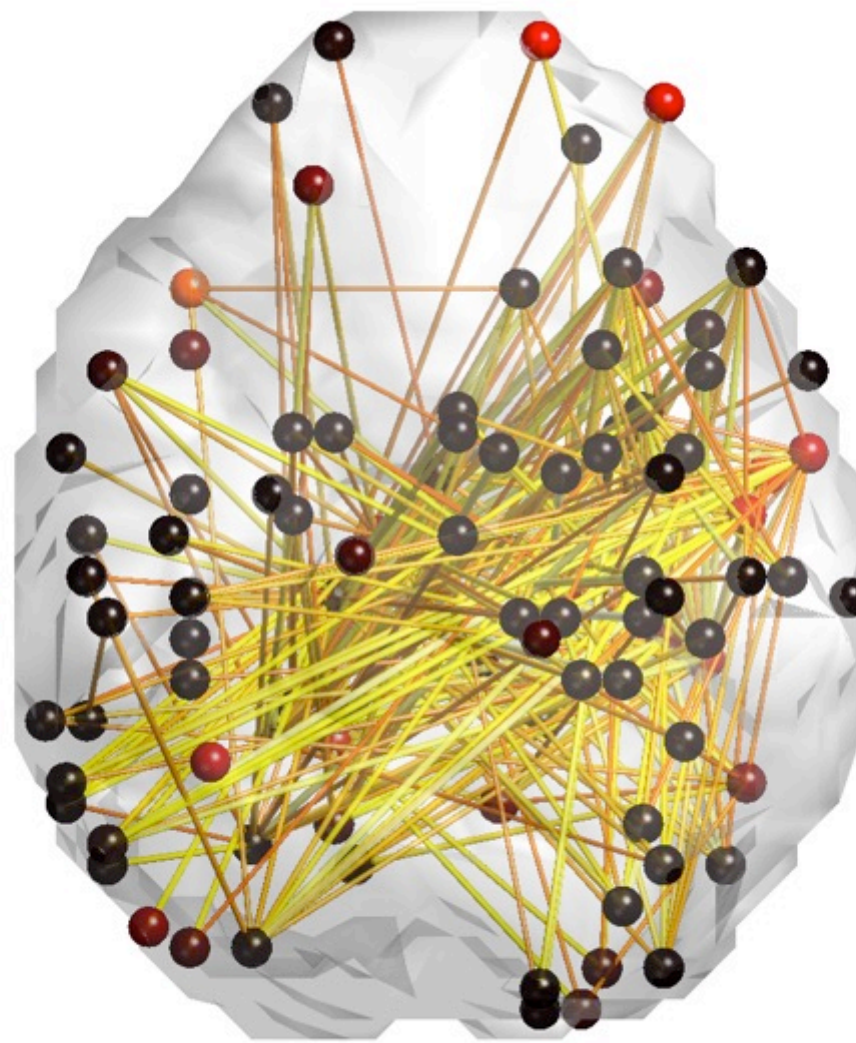
Heritability Graph Index



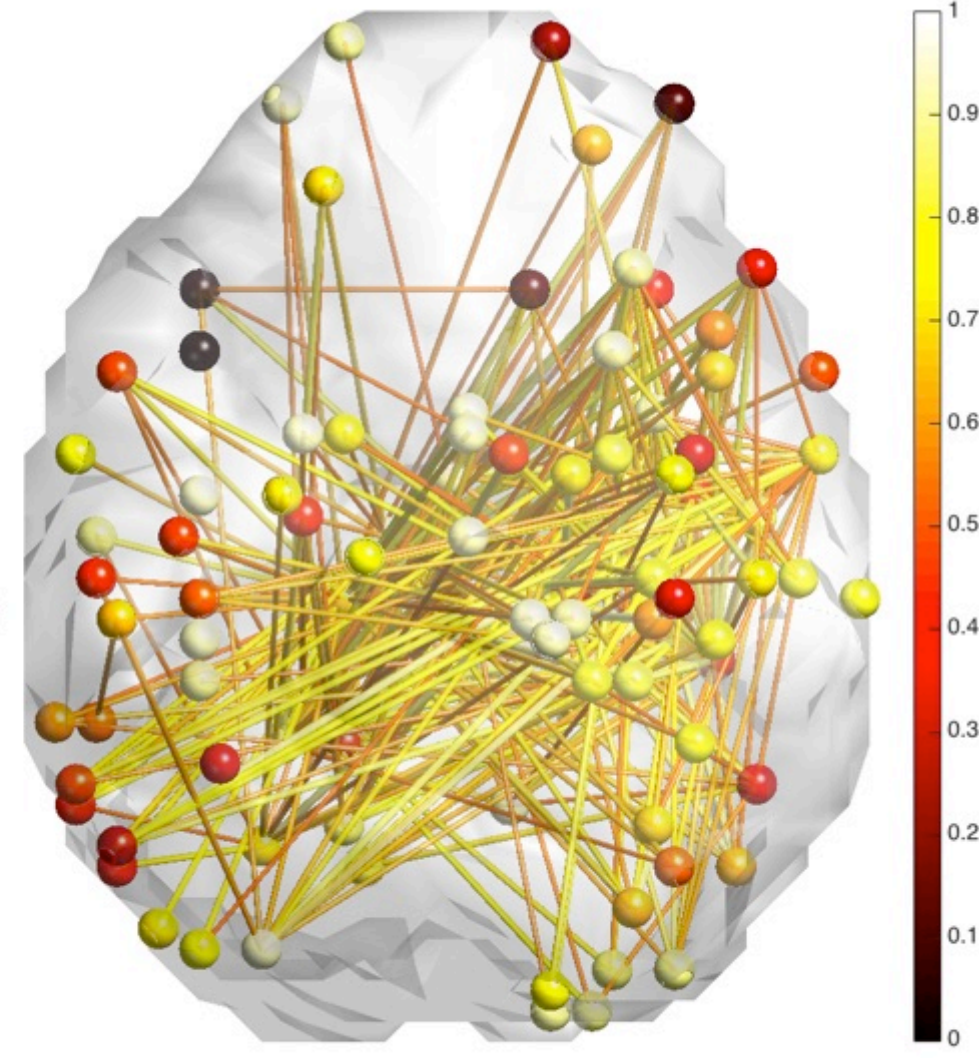
Heritability Graph Index (HGI) thresholded at correlation 0.5
= graphs obtained at sparse parameter 0.5



Cross-correlation of MZ-twins

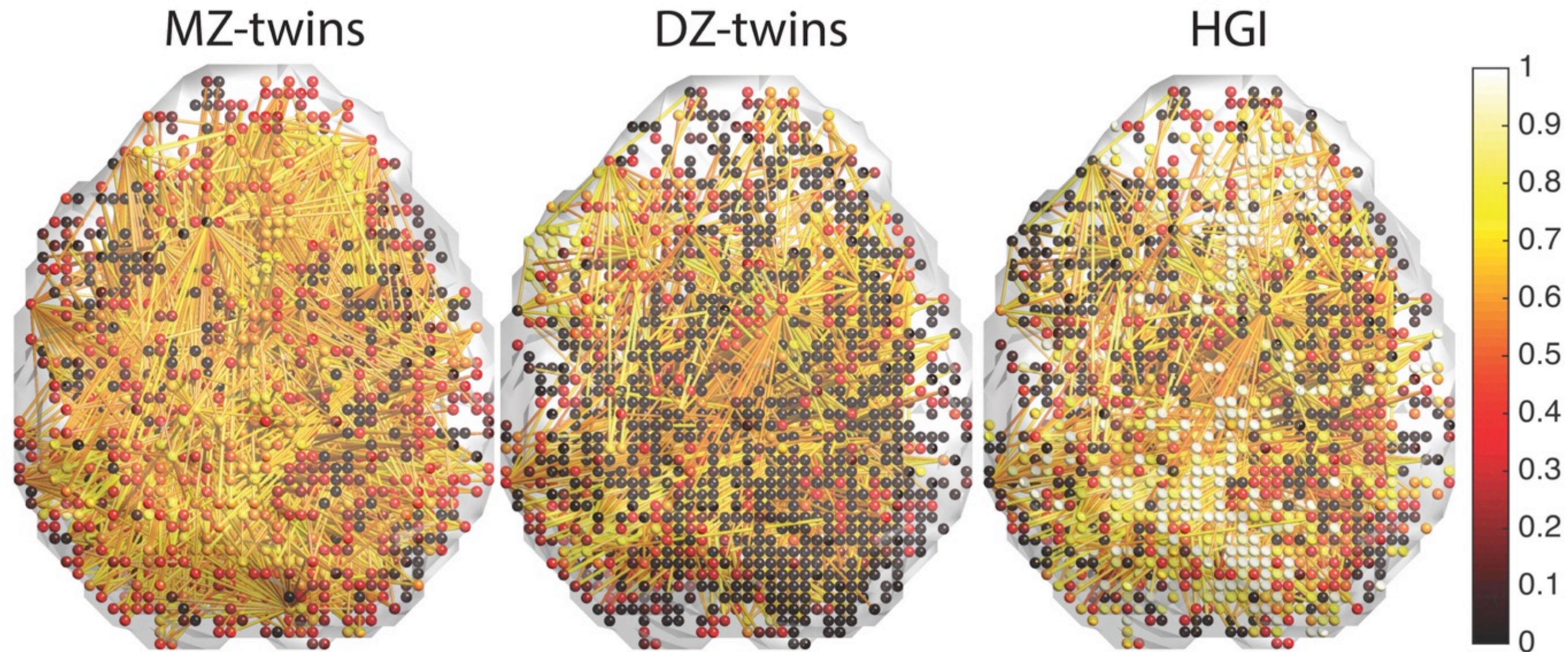


Cross-correlation of DZ-twins

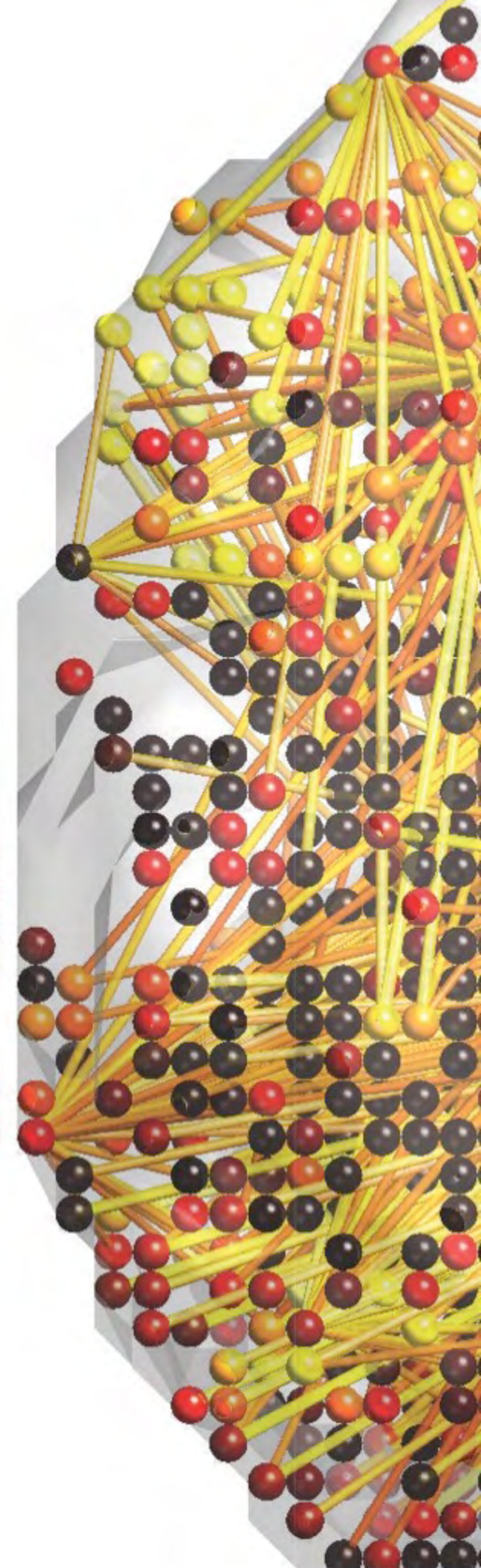
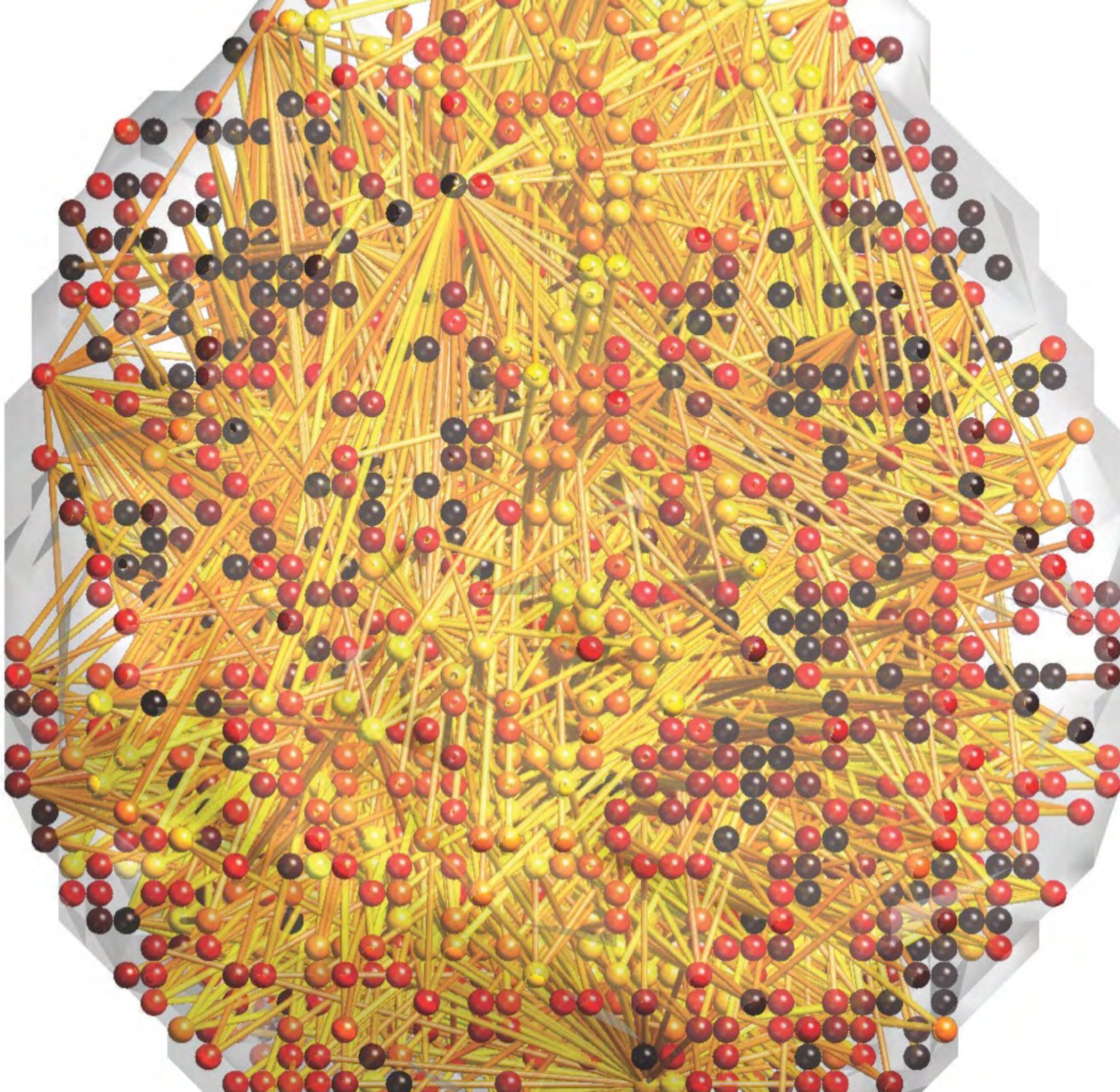


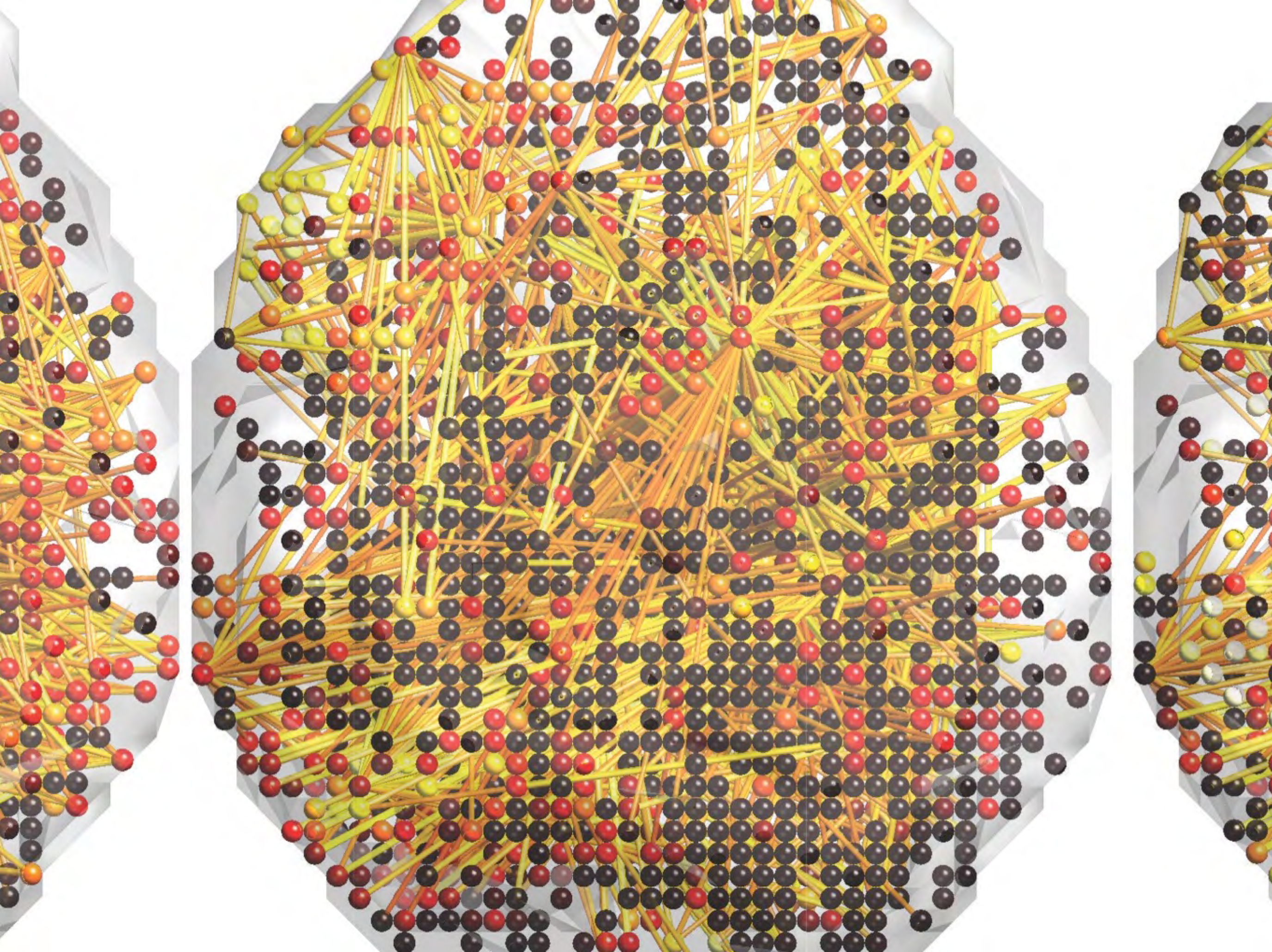
Heritability graph index (HGI)

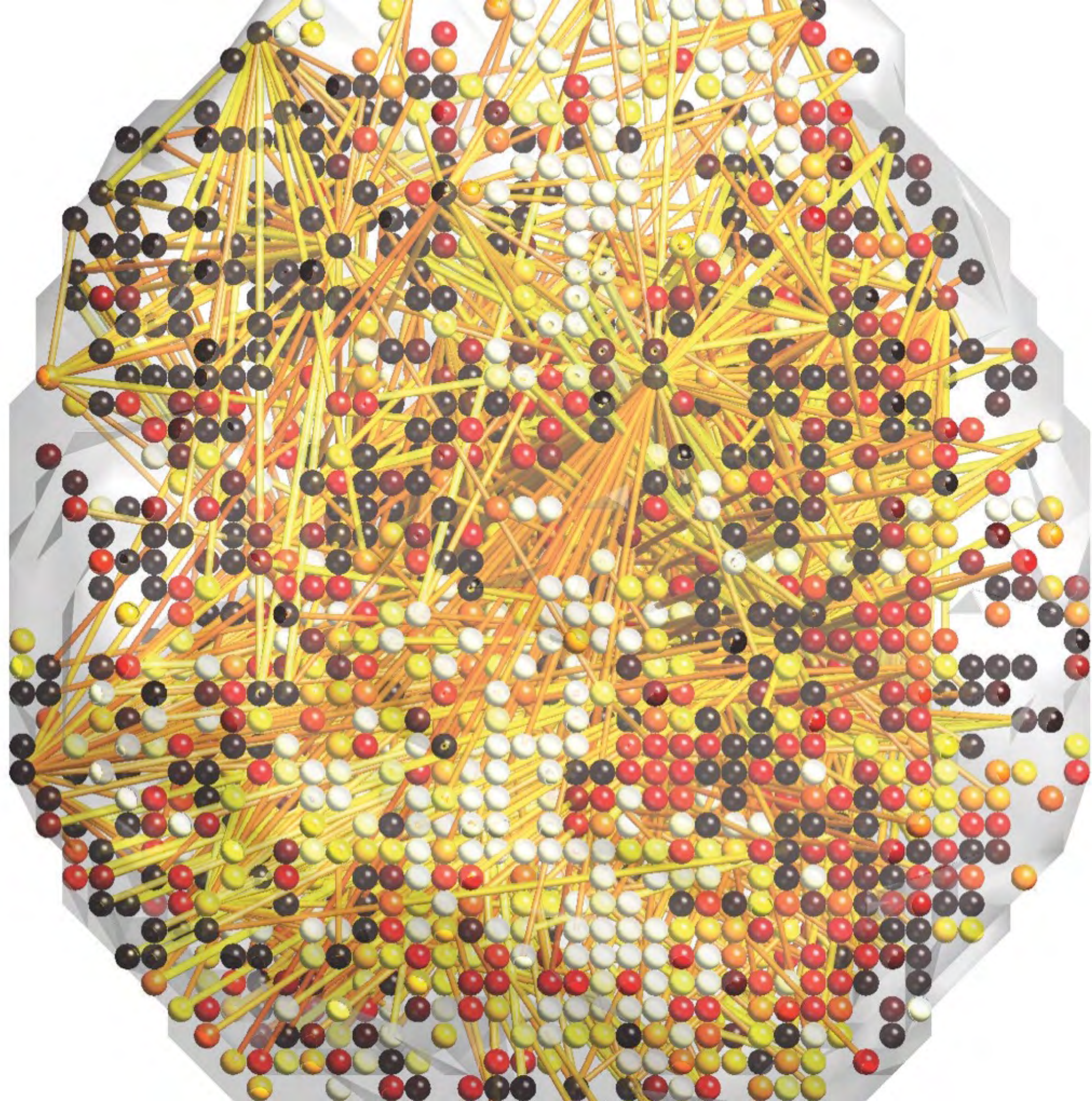
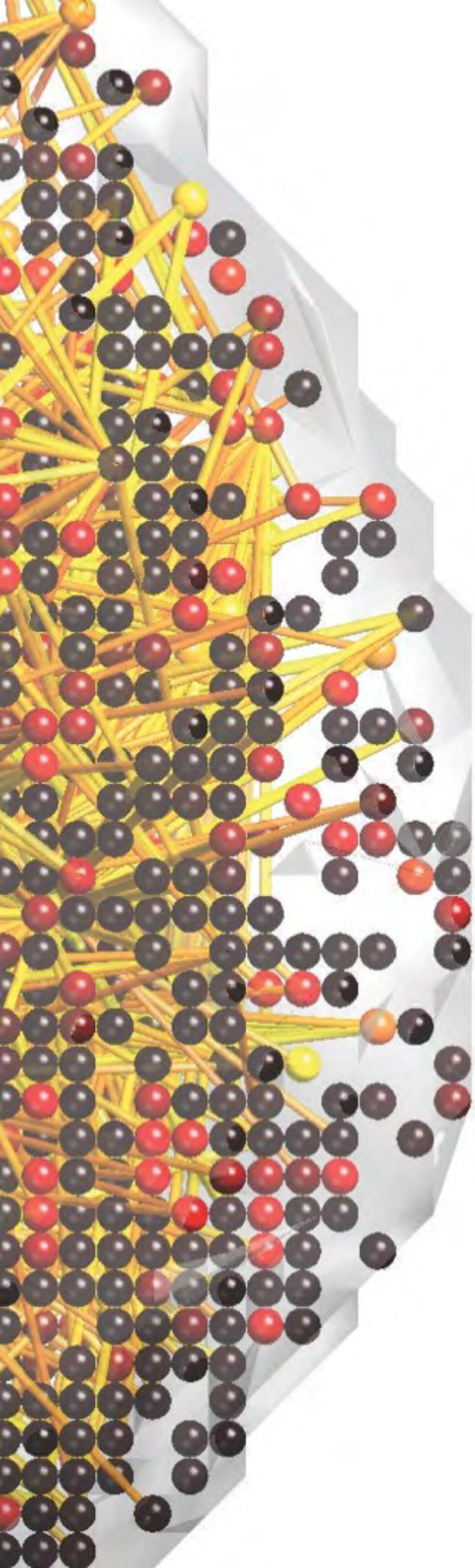
Heritability Graph Index (HGI) thresholded at correlation 0.5
= graphs obtained at sparse parameter 0.5



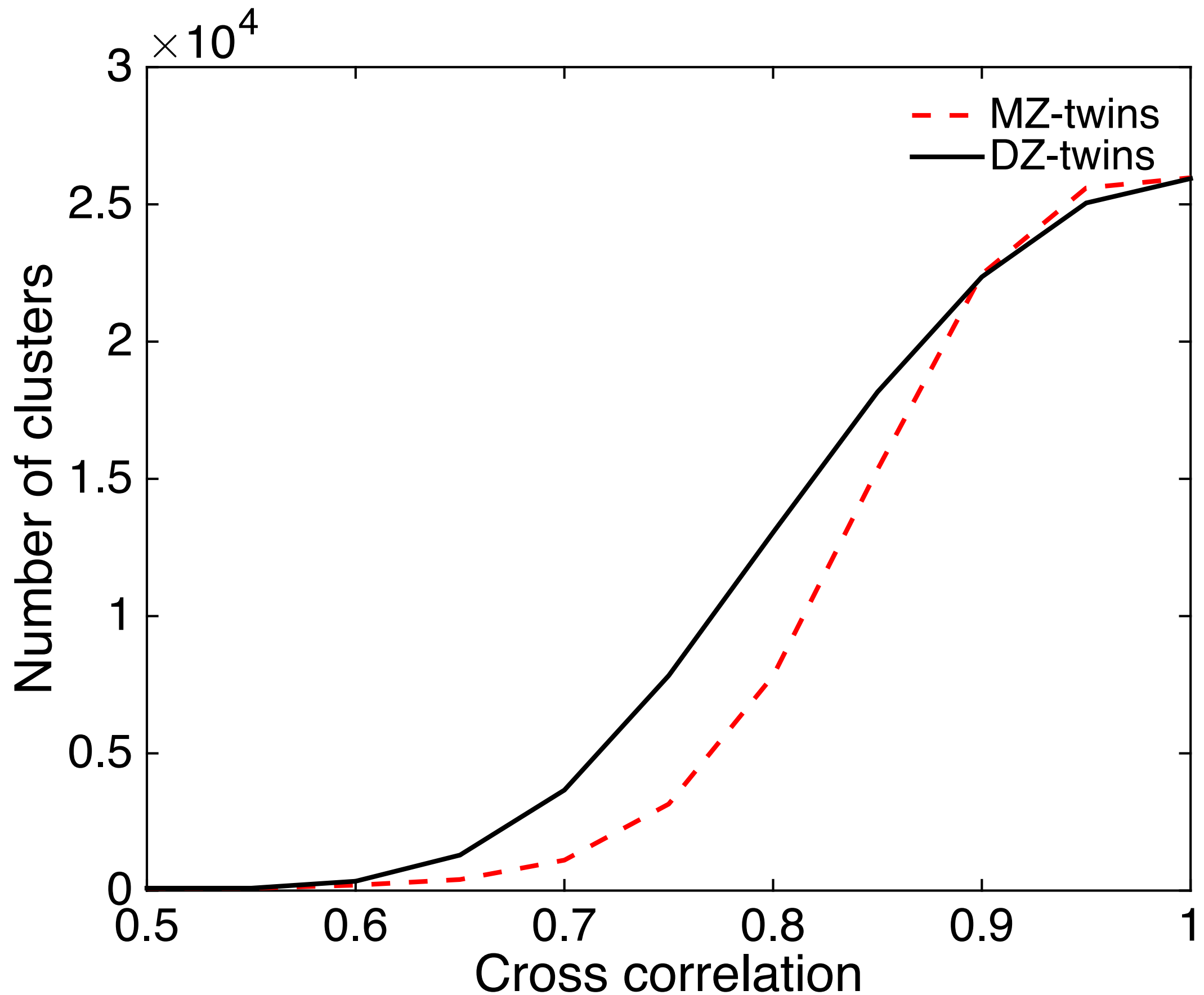
3000 nodes visualization



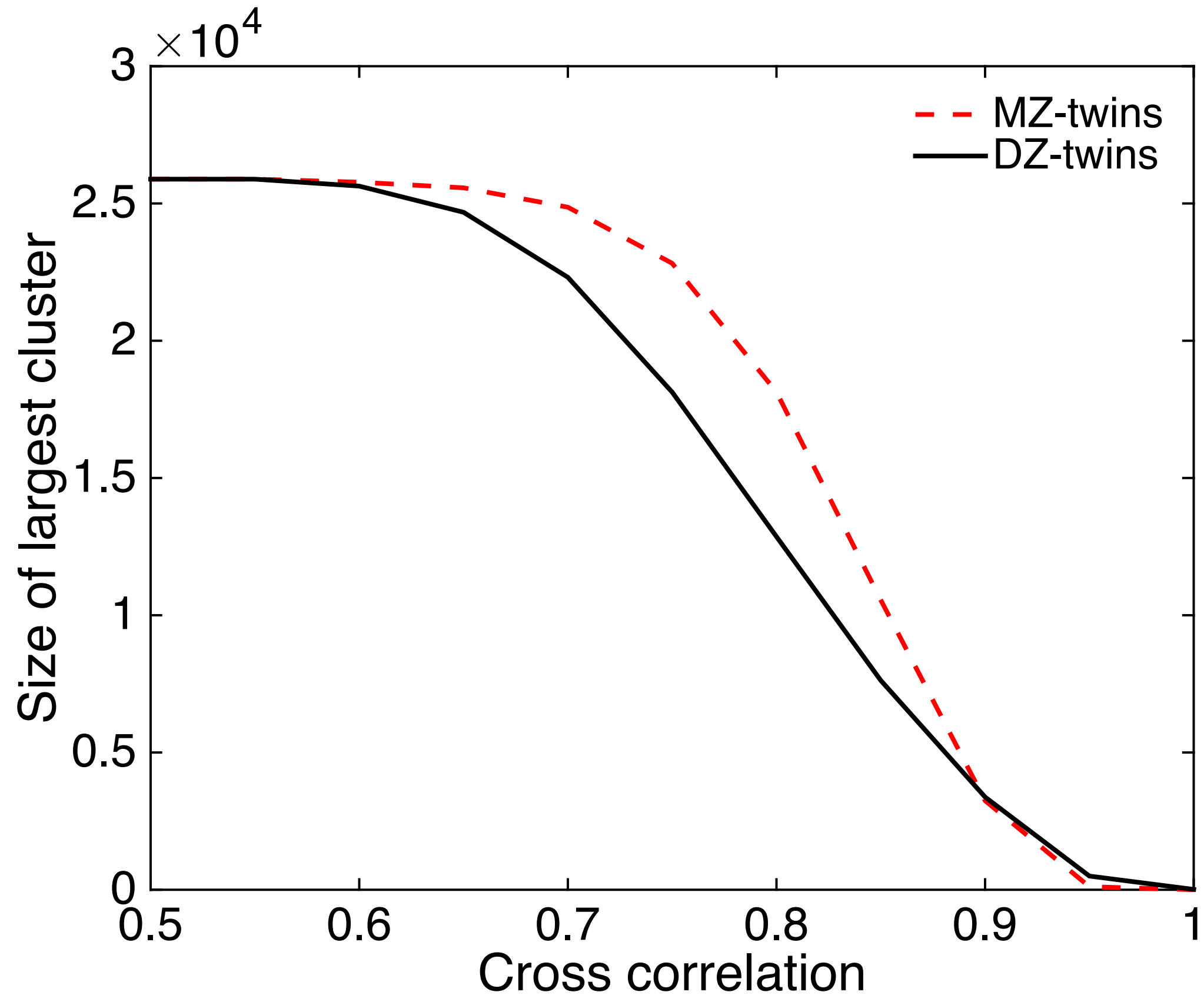




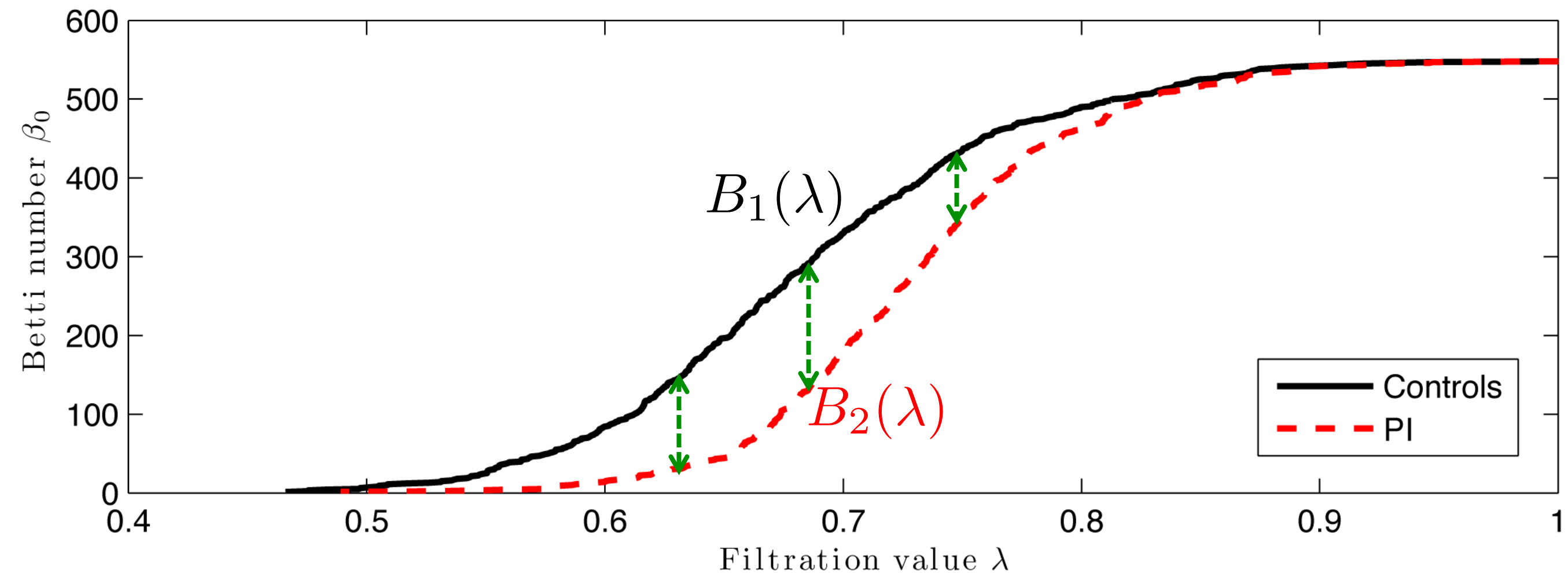
MZ-twins have more clusters of higher correlations



MZ-twins have more clusters of higher correlations



Inference on Barcodes



KS-like Statistic: $\max_{\lambda} |B_1(\lambda) - B_2(\lambda)|$

Inference by Jackknife resampling

pvalue = 0.001