The adaptive incorporation of multiple sources of information in Brain Imaging via penalized optimization

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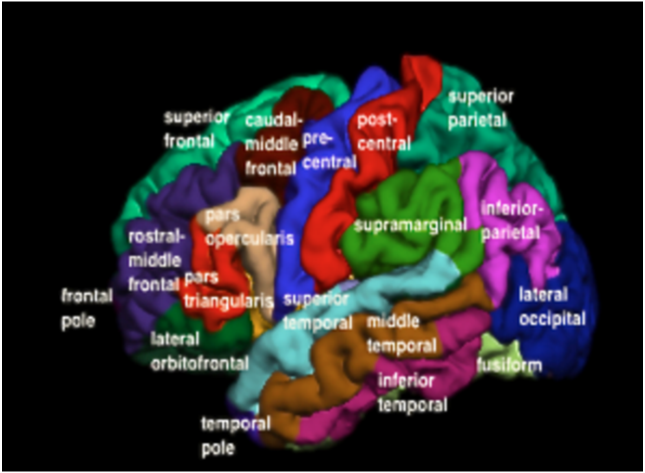
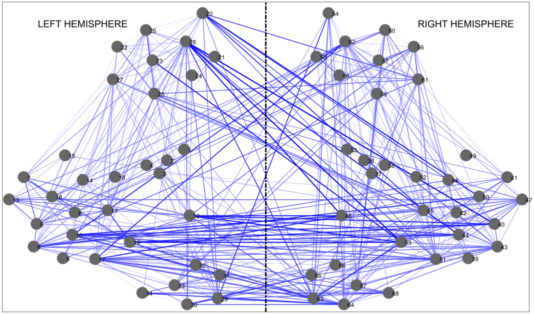
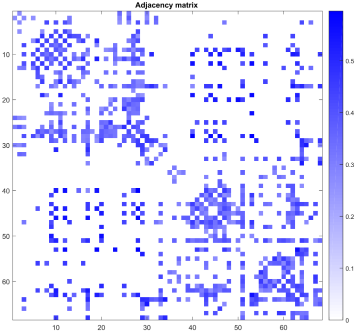
Parcelation of the cortex



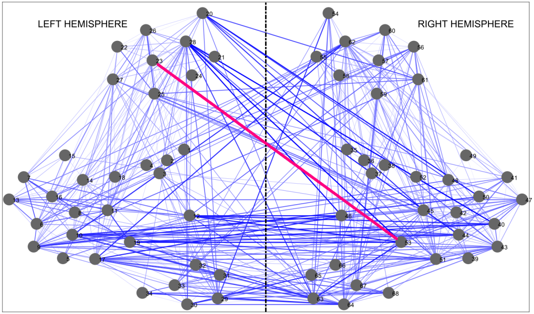


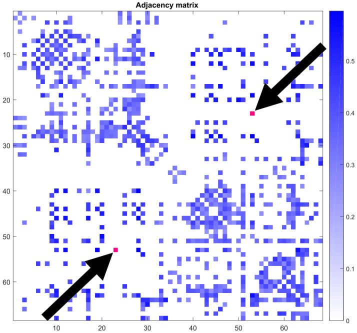
LEFT HEMISPHERE
RIGHT HEMISPHERE



Adjacency matrix

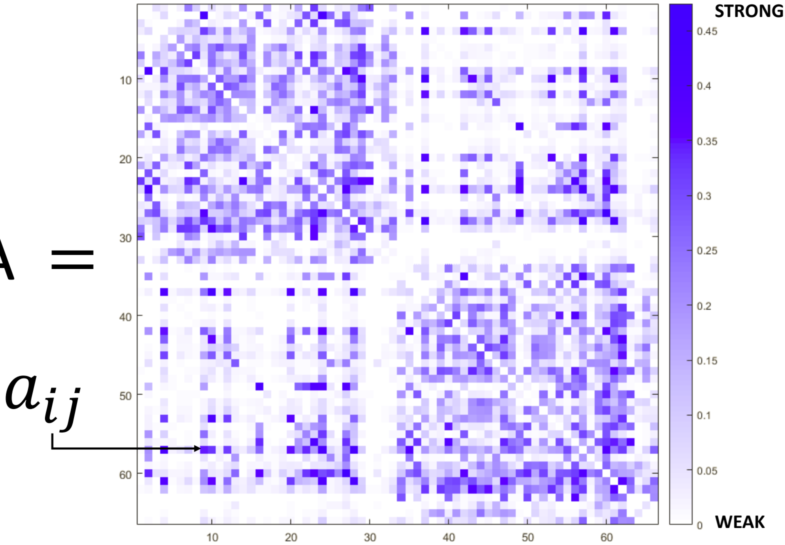
Connectivities in the brain





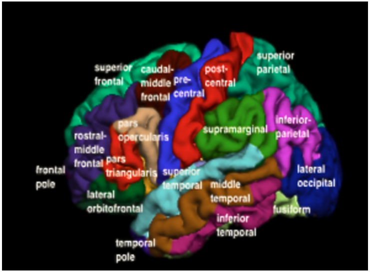
Connectivity information for population

$$A = $$

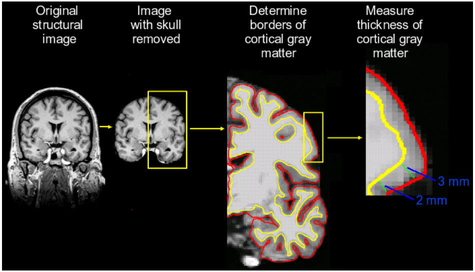


MRI-derived data: cortical thickness

1. We model the association between given response variable and average cortical thickness
2. We consider the parcellation of the brain into 66 regions

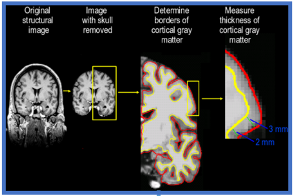


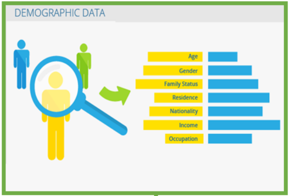
(a) Parcellation of the brain



(b) Cortical thickness

Statistical model





$$y = Zb + X\beta + \varepsilon$$

1. y is n-dimensional vector of considered responses
2. $Z \in \mathbb{R}^{n\times 66}$ and $X \in \mathbb{R}^{n\times m}$
3. $\varepsilon \sim \mathcal{N}\left(0, \sigma^2 I_n\right)$ for some unknown $\sigma^2 > 0$

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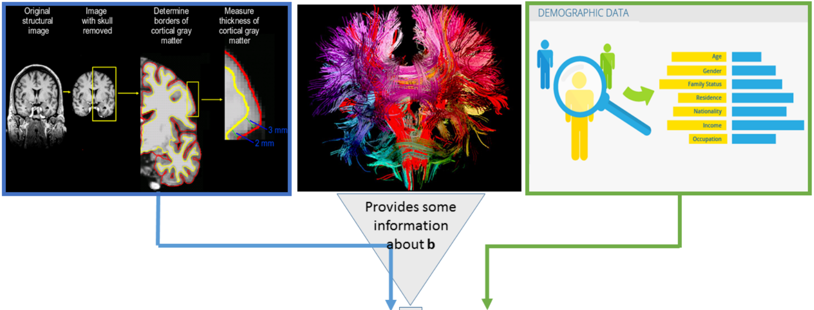

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Penalized estimation

To find estimates of b and β we consider the optimization problem of the form

$$\operatorname*{argmin}_{b,\beta} \Big\{ \underbrace{\|y - Zb - X\beta\|_2^2}_{\textbf{model fit term}} + \lambda \underbrace{g(b)}_{\textbf{penalty on } b} \Big\}.$$

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1. How to select the penalty term g?
2. How to select an optimal regularization parameter λ ?

Penalty selection

We want to get the property

"The stronger brain's regions i and j are connected based on the connectivity matrix entry a_{ij}, the closer coefficients $\hat{b}_i$ and $\hat{b}_j$ are to each other."

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$$g(b) = \sum_{i,j} a_{ij}\left(b_i - b_j\right)^2$$

2. Note $\sum_{i,j} a_{ij}\left(b_i - b_j\right)^2 = b^T Q b$, where Q is the Laplacian of A defined as $Q := D - A$, for $D := diag\left(\sum_j a_{1j}, \ldots, \sum_j a_{pj}\right)$

Connection with linear mixed models (LMM)

Consequently, we get the following form of the objective function

$$\underset{b,\beta}{\operatorname{argmin}} \ \Big\{ \|y - Zb - X\beta\|_2^2 \ + \ \lambda b^T Q b \Big\},$$

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This problem is "equivalent" with LMM formulation

1. $y = Zb + X\beta + \varepsilon$, where β is a vector of fixed effects and b a vector of random effects,
2. $\varepsilon \sim \mathcal{N}\left(0, \sigma^2 I\right)$,
3. $b \sim \mathcal{N}\left(0, \sigma_b^2 Q^{-1}\right)$,
4. λ, σ and σ_b are tied via $\lambda = \sigma^2/\sigma_b^2$.

Selection of regularization parameter

IDEA: define $\hat{\lambda}$ as $\hat{\lambda} = \frac{\hat{\sigma}^2}{\hat{\sigma}_b^2}$ where $\hat{\sigma}^2$ and $\hat{\sigma}_b^2$ are maximum likelihood estimates from the corresponding linear mixed model

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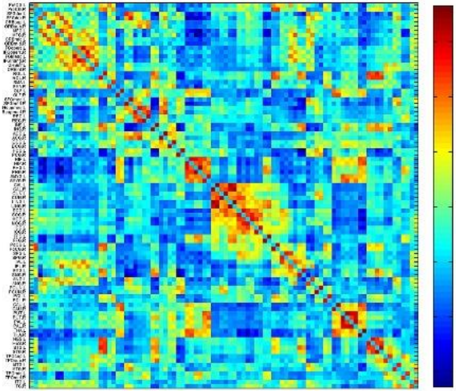
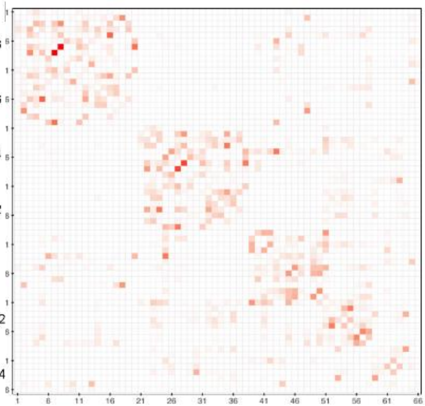
PROBLEM: Neither Laplacian nor normalized Laplacian is an invertible matrix, which is required in computation

Connectivity information types

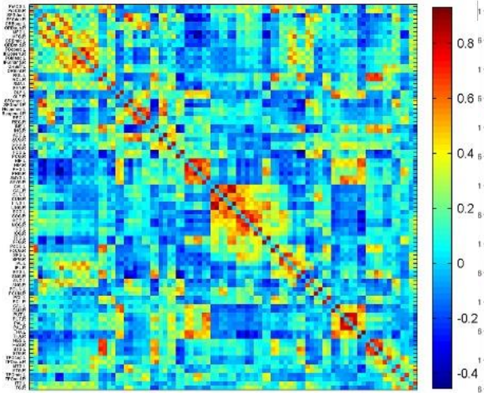


Functional Connectivity



Structural Connectivity

Connectivity information types



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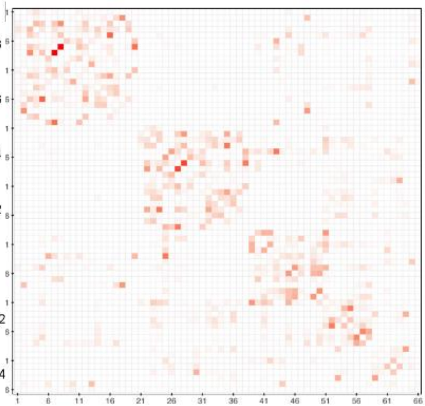
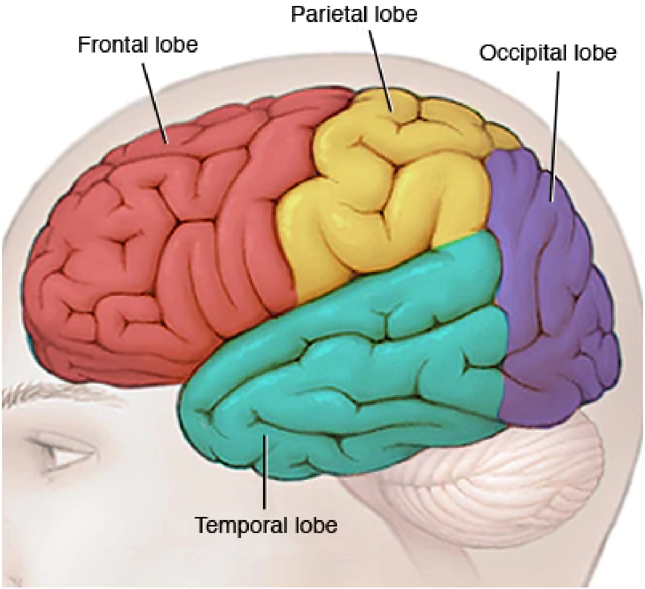


Structural Connectivity

Which connectivity matrix should we use to define Q?

Brain lobes



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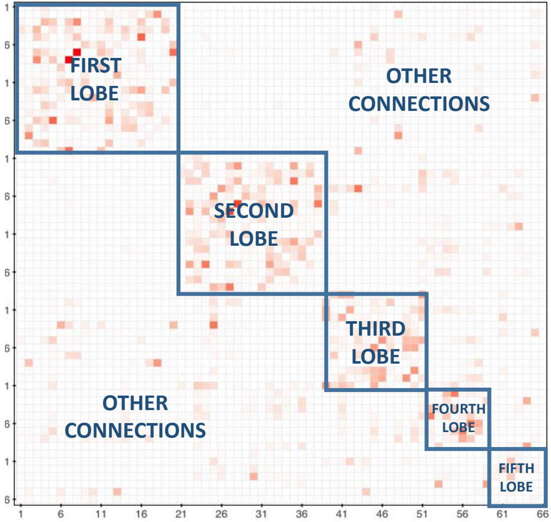
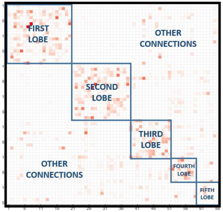

FIRST LOBE
SECOND LOBE
THIRD LOBE
FOURTH LOBE
FIFTH LOBE
OTHER CONNECTIONS
OTHER CONNECTIONS
1
6
11
16
21
26
31
36
41
46
51
56
61
66

Brain Lobes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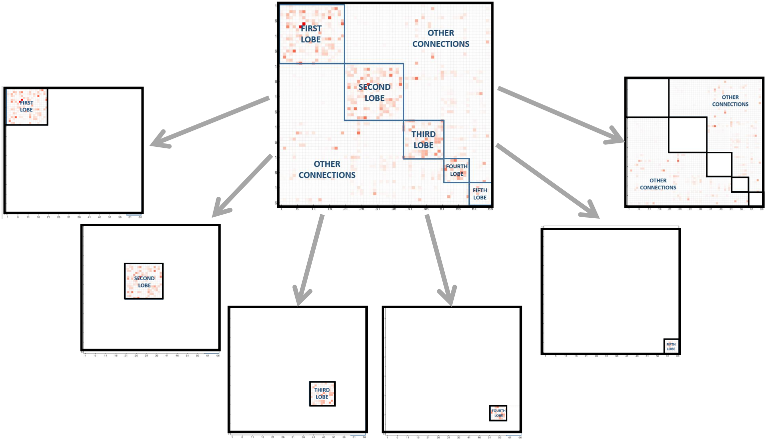
Brain Lobes


FIRST
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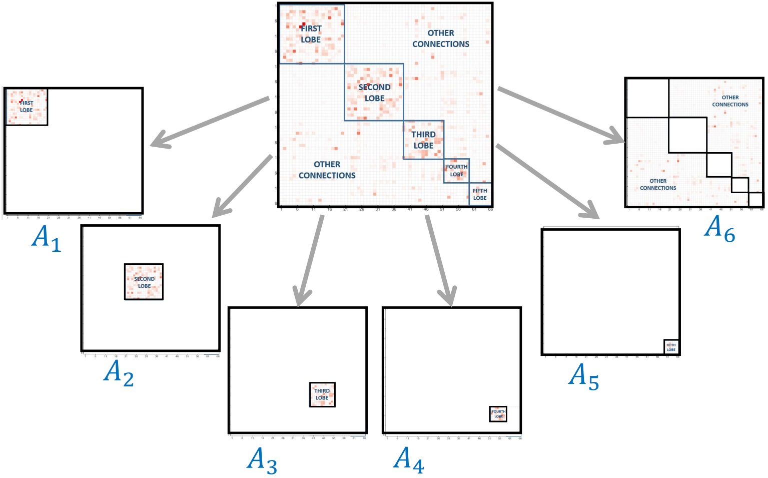
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A_2
A_3
A_4
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A_6

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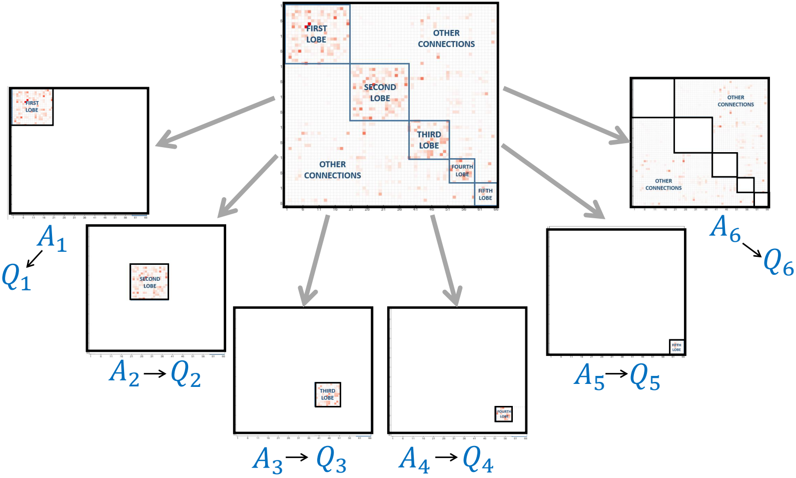
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A_1
Q_1
$A_2 \rightarrow Q_2$
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A_6
Q_6

Merging a few sources of information

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where $\lambda_1, \dots \lambda_n$ are tuning parameters.

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Noninvertability problem is also addressed!

The example

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- Method reduces to *riPEER*

Simulation scheme

Two methods compared:

1. ridge: $\lambda_Q := 0$ (connectivity information is not used)
2. riPEER (both lambdas are selected in an adaptive way)

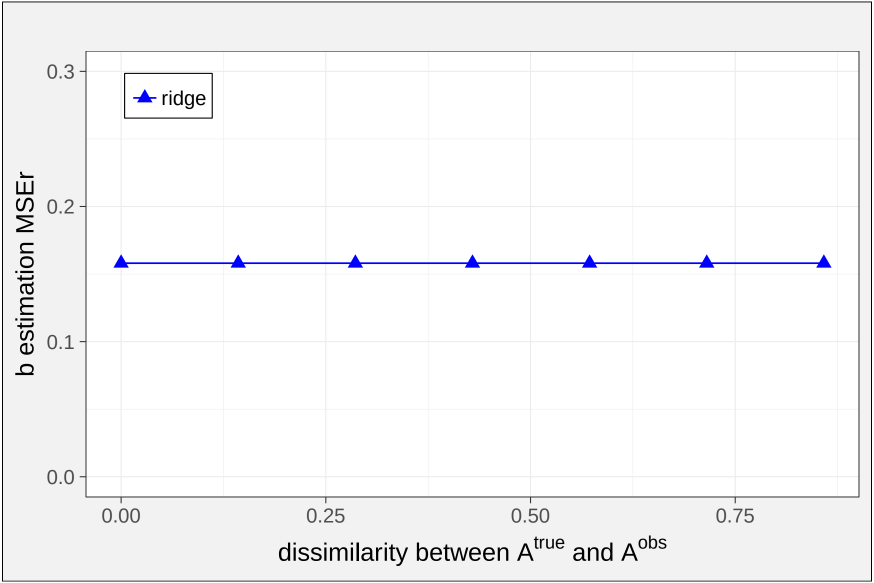
Axis of the plot

1. X axis:

$$diss(A^{true}, A^{obs}) := \frac{\text{number of removed/added connections}}{\text{number of all nonzero connections in } A^{true}}$$

2. Y axis: $MSEr := \mathbb{E}\left[\frac{\|\hat{b}-b^{true}\|_2^2}{\|b^{true}\|_2^2}\right]$.

Simulation results



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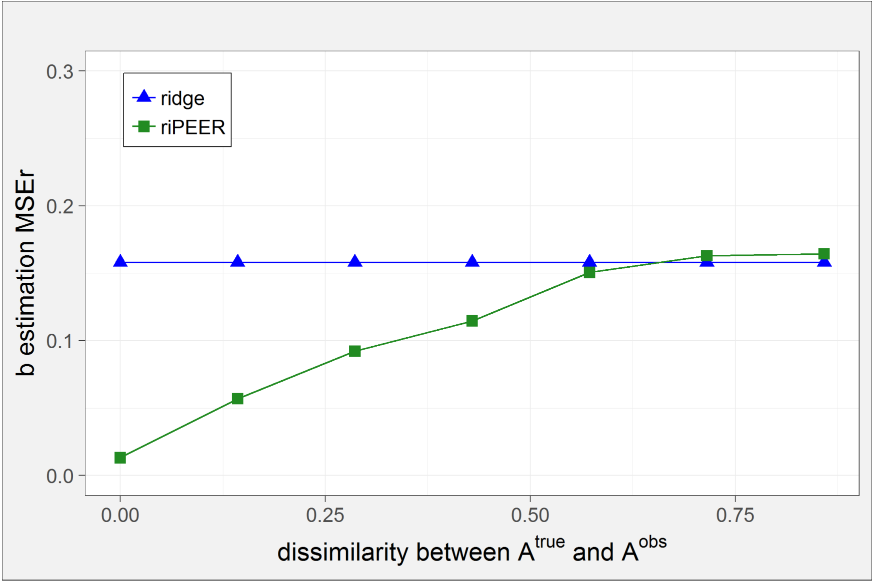
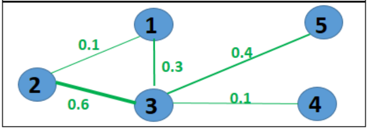


Simulation scheme

SIMULATED SIGNAL

Graph given by adjacency matrix A^{true}



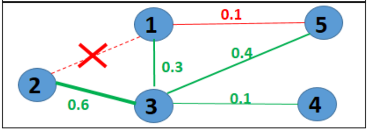
Normalized Laplacian : Q_{true}

„Invertible Normalized Laplacian" :
$\tilde{Q}_{true} := Q_{true} + 0.001 \cdot I$

True signal used in simulation:
$b^{true} \sim N(0,\ \sigma_b^2\, \tilde{Q}_{true}^{-1})$

ESTIMATION

Rewired graph which gives A^{obs}



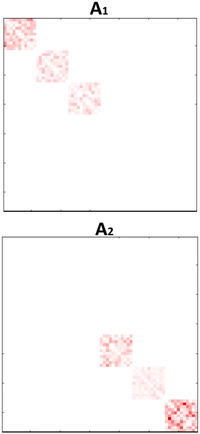
Normalized Laplacian of rewired graph was used to find the estimate, $\hat{b}$

MSEr defined as

$$\text{MSEr:} = \mathbb{E}\left[\frac{\|\hat{b} - b_{true}\|_2^2}{\|b_{true}\|_2^2}\right]$$

as a measure of estimation accuracy

Simulation scheme: multiple sources



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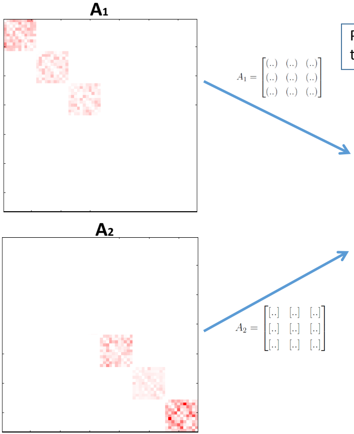

Parameter r_t is the probability that the entry of **A** comes from **A1**

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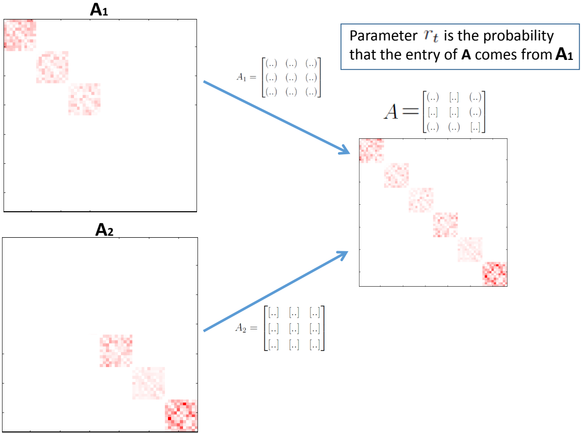

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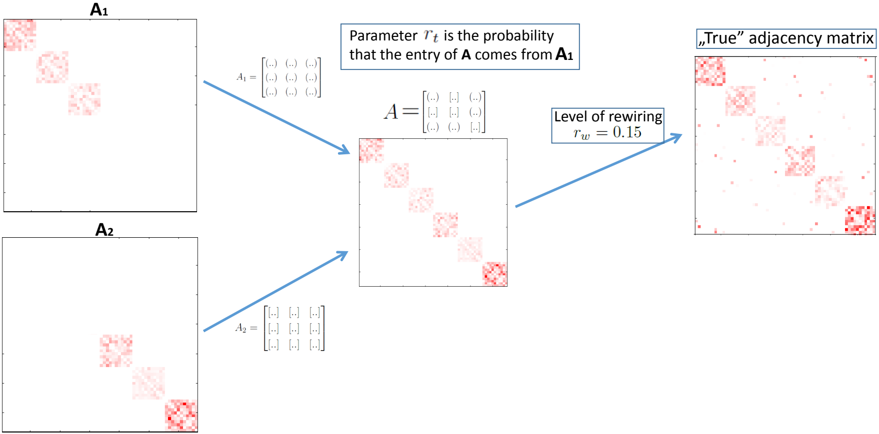

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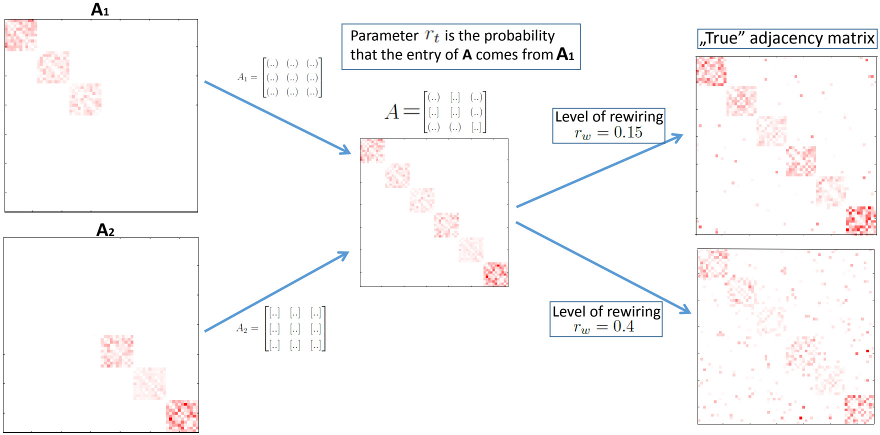

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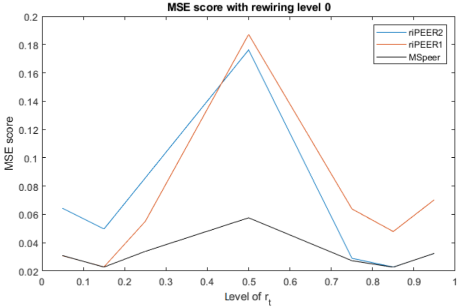
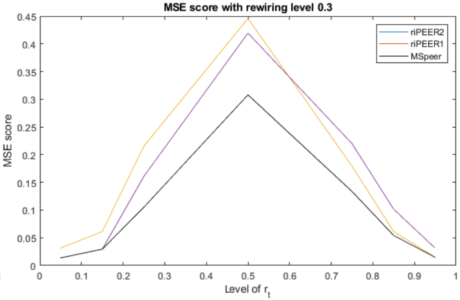
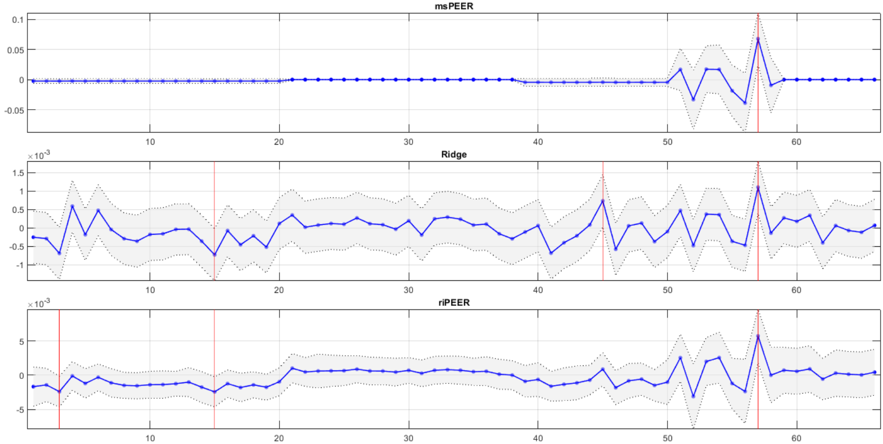




Real data analysis: some examples of estimates



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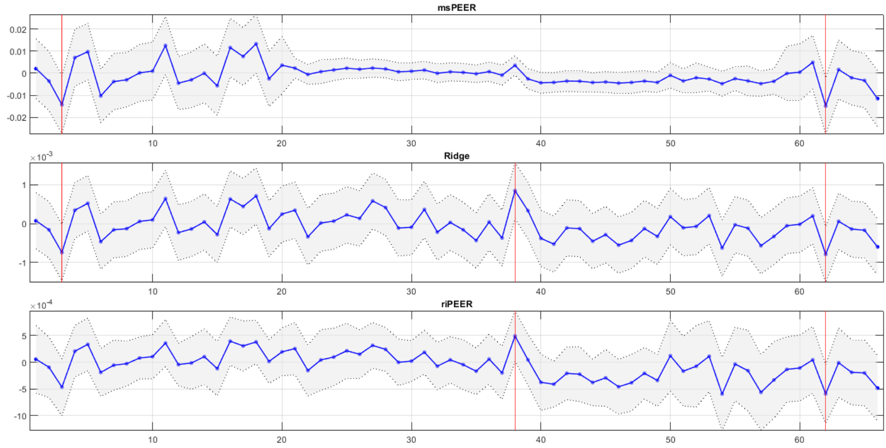

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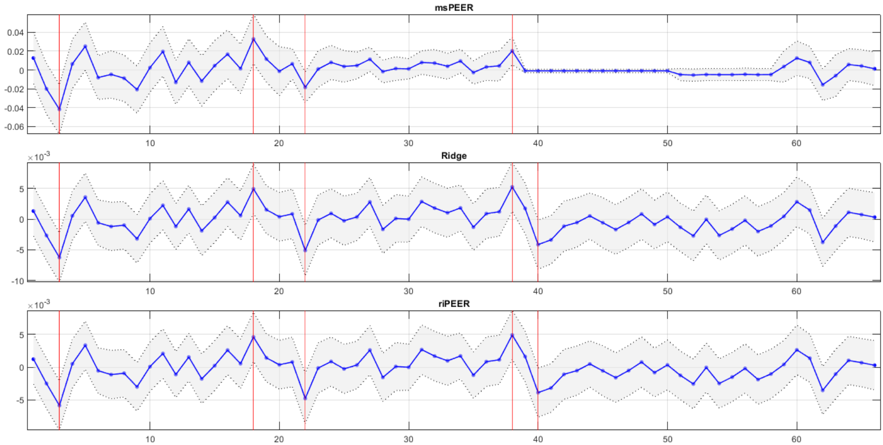

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