A Graph Signal Processing Perspective on Brain Imaging

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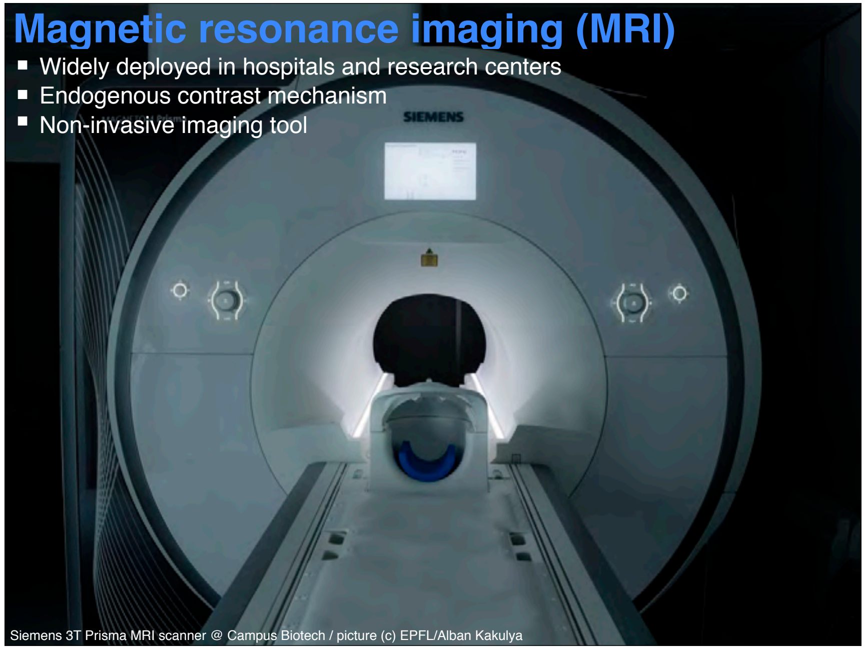
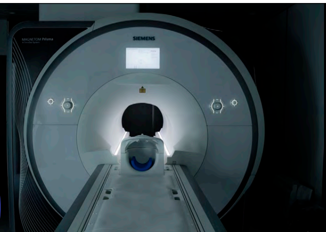
Magnetic resonance imaging (MRI)

- Widely deployed in hospitals and research centers
- Endogenous contrast mechanism
- Non-invasive imaging tool



Siemens 3T Prisma MRI scanner @ Campus Biotech / picture (c) EPFL/Alban Kakulya

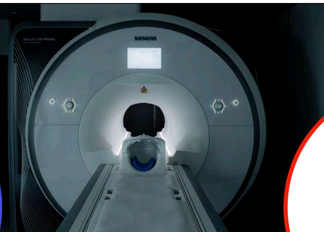


structural information

Brain anatomy

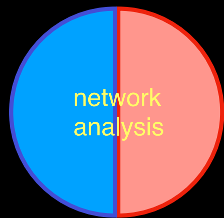
Tissue type, gyrification

White-matter bundles

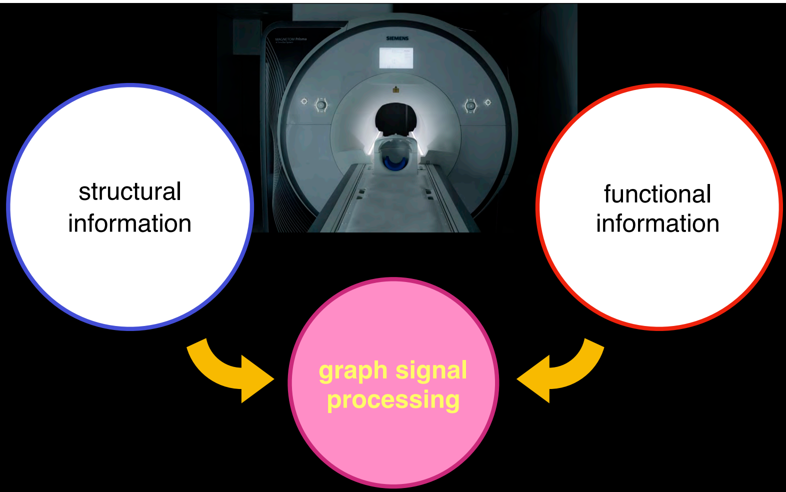


structural information

functional information



Brain anatomy	*Brain function*
Tissue type, gyrification	*Activation levels*
White-matter bundles	*Information flow*
How brain regions are connected	*How brain regions communicate*

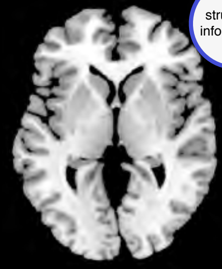


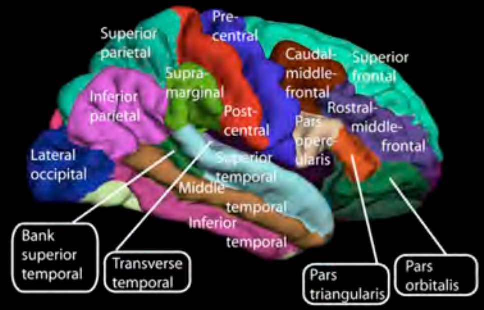
New framework for integrated analysis of brain structure & function

T1-weighted structural MRI provides high-resolution tissue contrast

structural information

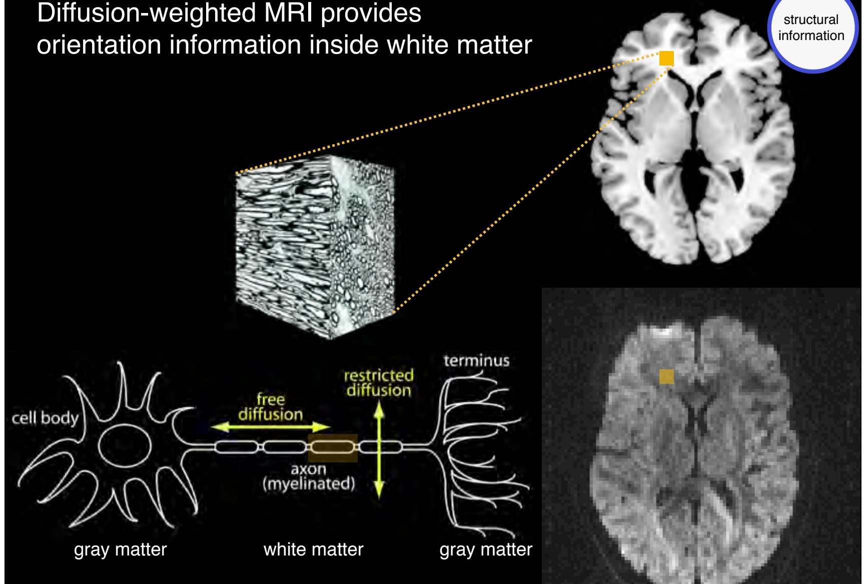
- Gray matter, white matter, cerebrospinal fluid
  - High-spatial resolution volumetric information
  - Gray matter contains cell bodies, dendrites, axon terminals
  - White matter contains bundles of axons
- Gray-matter segmentation provides parcellation of the brain in major cortical regions





Diffusion-weighted MRI provides orientation information inside white matter

structural information

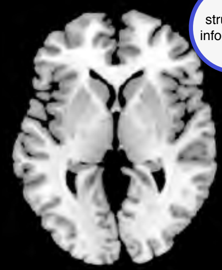


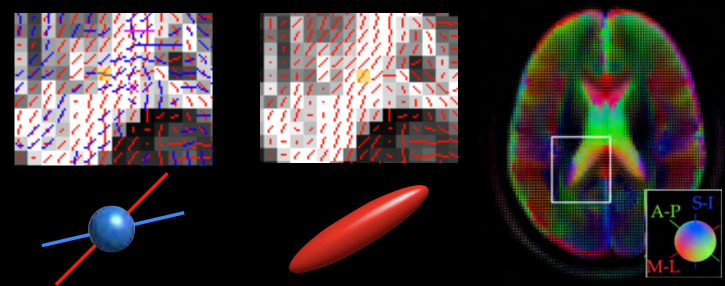
[Beaulieu, 2002; Ohno et al, 2013]

White-matter orientations can be captured using tensors or more complex models

structural information

- Tensor models summarize dominant local orientation of nerve fiber bundles
  - Limited flexibility; e.g., crossings, fanning,…
- More complex models for orientation distribution functions to fit multiple orientations per voxel

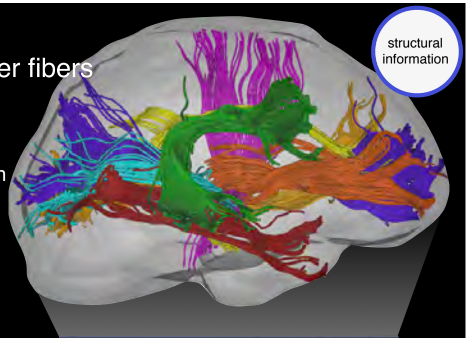


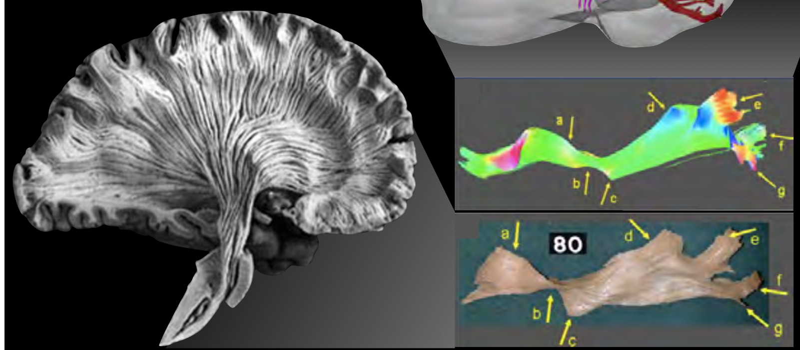


Tractography can perform virtual dissection of white-matter fibers

structural information

- Deterministic and probabilistic methods reconstruct streamlines
  - Non-invasive, in-vivo, whole brain
- Groupings can be matched to neuroanatomical tracts

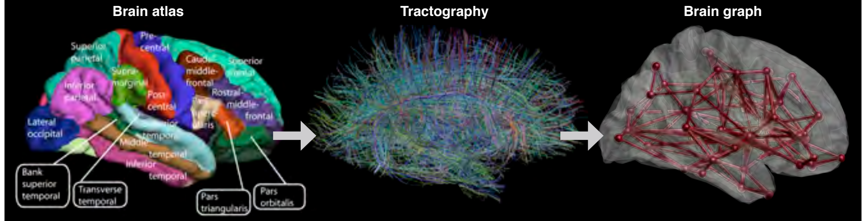


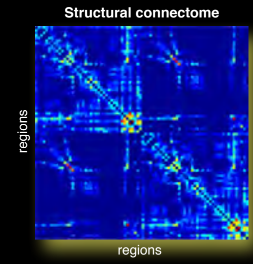


[Lawes et al, 2008]

Structural connectome summarizes wiring of the brain

structural information





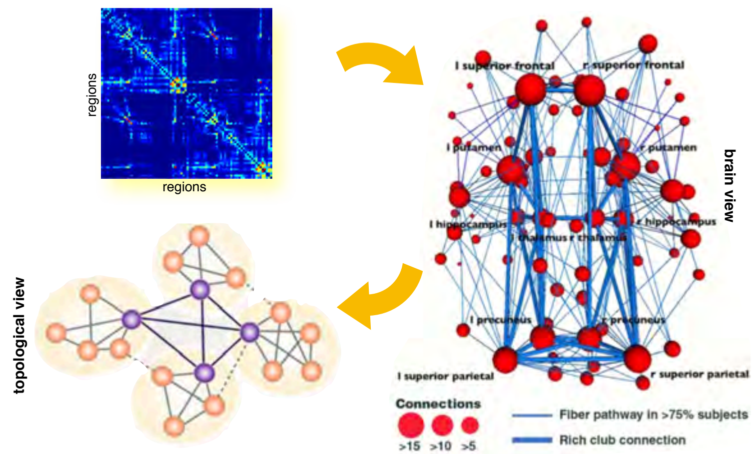
- Comprehensive map of neural connections in the brain
  — the "*wiring* diagram"

[Sporns et al, 2005; Hagmann et al, 2005]

Structural network analysis

structural network analysis

- Nodes, edges, and organization of the brain



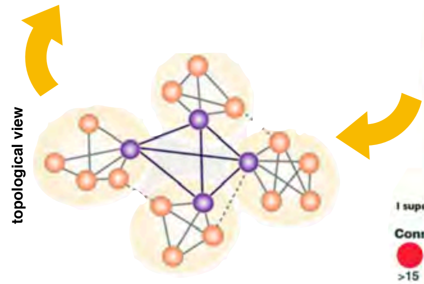
[Park, Friston, *Science*, 2013]

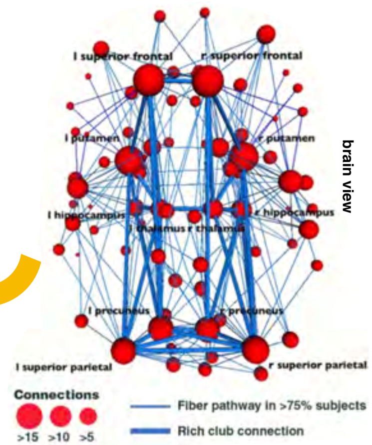
Structural network analysis

structural network analysis

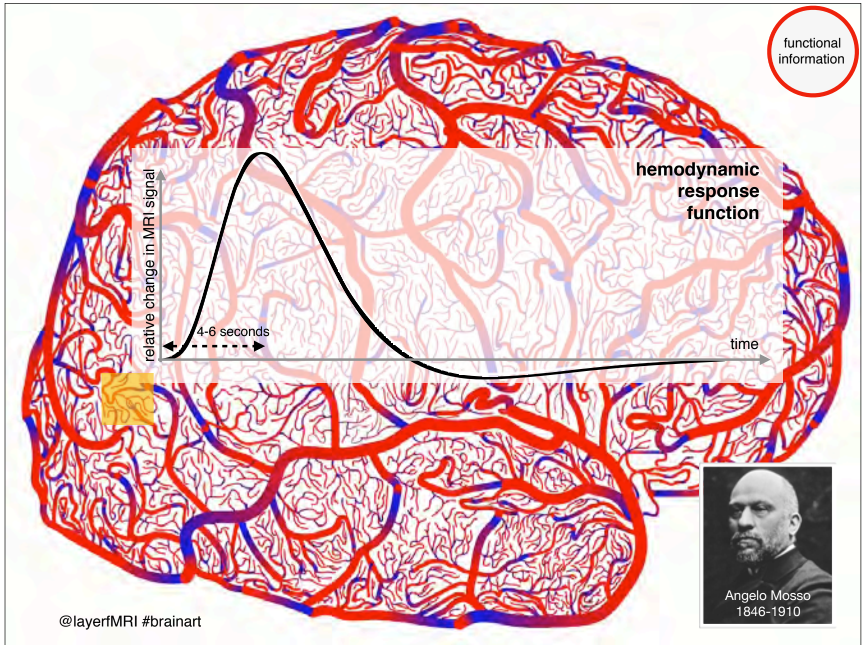
- Nodes, edges, and organization of the brain network

modular organization
- intra-modular connections
  ~ common functionality
- inter-modular connections through hub nodes
  ~ facilitate communication





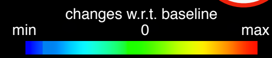
[Park, Friston, *Science*, 2013]

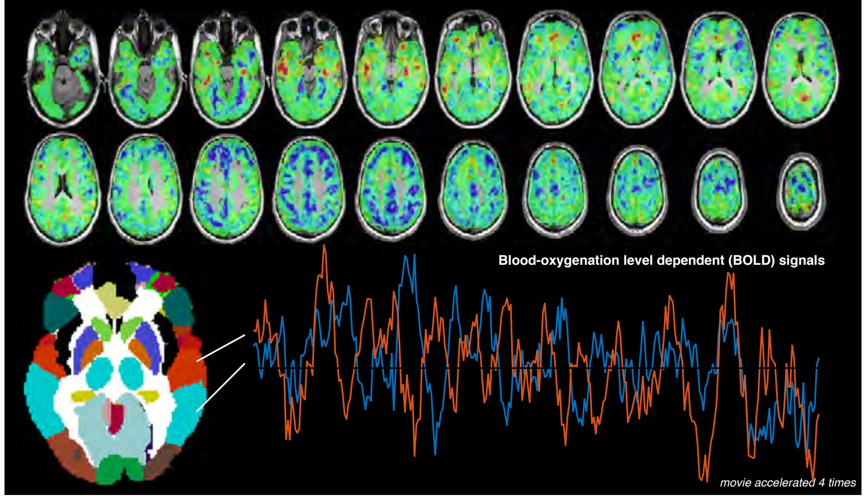


Functional MRI provides information on brain activity based on changes in blood perfusion

functional information

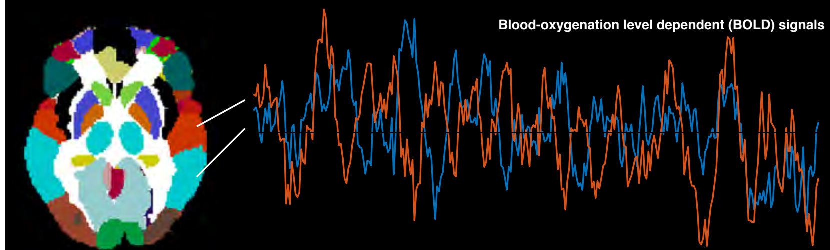
resting-state scan of 8 minutes (minimally preprocessed)



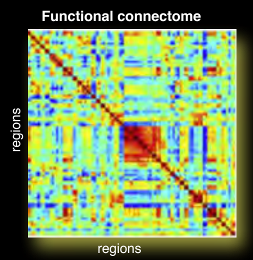


Functional connectivity to quantify statistical interdependencies of activity timecourses

functional information



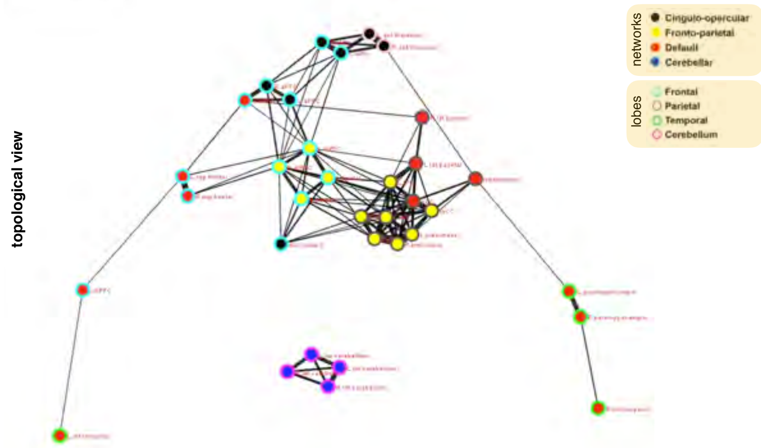
- Comprehensive map of information sharing through activity in the brain
  — the "*communication* diagram"



Functional network analysis

functional network analysis

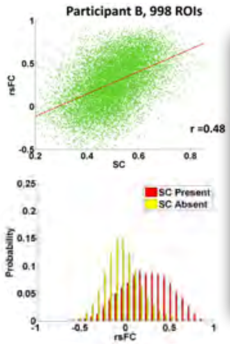
- Neurodevelopment: from local to distributed organization

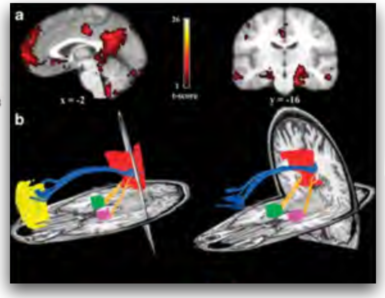


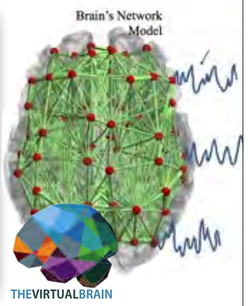
[Fair et al, *PLOS Comp Biol*, 2009]

Different ways to integrate structure-function

- Correlation between structural and functional connectivity
- Functionally-guided structural analysis
- Brain simulation approaches (e.g., The Virtual Brain)



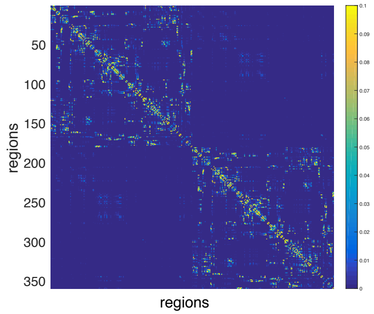




[Honey et al, *PNAS*, 2009; Greicius et al, *Cerebral Cortex*, 2009; Deco, Jirsa, McIntosh, *TiN*, 2013]

Graph signal processing framework

- Consider undirected weighted graph with N nodes
  - Edge weights are in $N \times N$ symmetric adjacency matrix $\boldsymbol{A}$; degree matrix $\boldsymbol{D}$

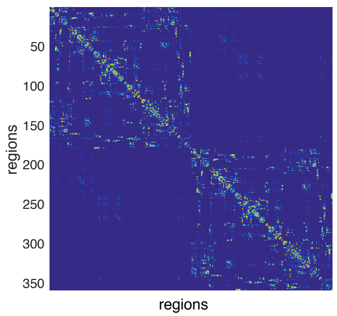


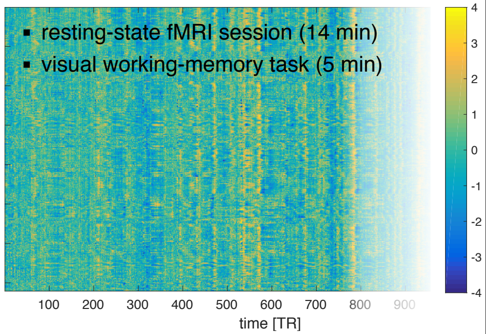
- 21 healthy subjects
- Glasser's multimodal cortical parcellation 360 ROIs, converted to volume mask
- Adjacency matrix derived from tractography
  - Multi-shell multi-tissue response function estimation, spherical deconvolution, tractogram generation with 10^7 output streamlines
  - Normalization of fiber counts by ROIs volumes (sum of connected regions)
  - Symmetric normalization of adjacency matrix

[Glasser et al, *Nature*, 2016]

Graph signal processing framework

- Consider undirected weighted graph with N nodes
  - Edge weights are in $N \times N$ symmetric adjacency matrix $\boldsymbol{A}$; degree matrix $\boldsymbol{D}$
  - Graph signal is length-N vector associating a value with every node





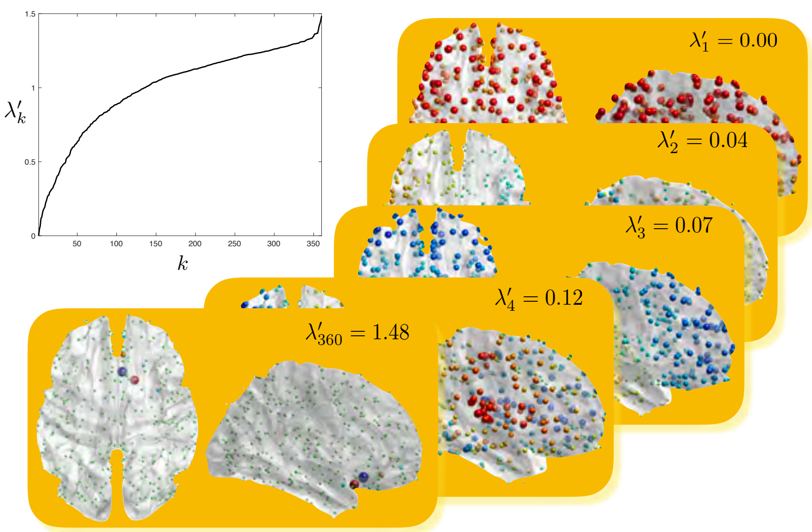
[Shuman et al, *IEEE Signal Processing Magazine*, 2013]

Graph Fourier transform

- Consider undirected weighted graph with N nodes
  - Edge weights are in $N \times N$ symmetric adjacency matrix $\boldsymbol{A}$; degree matrix $\boldsymbol{D}$
  - Graph signal is length-N vector associating a value with every node
- Laplacian $\boldsymbol{L} = \boldsymbol{D} - \boldsymbol{A}$
  - Second-order derivative on graph
  - Eigendecomposition $\boldsymbol{U}\boldsymbol{\Lambda} = \boldsymbol{L}\boldsymbol{U}$
  - Eigenvalues play role of frequencies and eigenvectors of frequency components
  - Order as increasing eigenvalues $\lambda_1 = 0 \leq \lambda_2 \leq \ldots \leq \lambda_N$
- Adjacency matrix $\boldsymbol{A}$
  - Shift operator on graph
  - Eigendecomposition $\boldsymbol{U}\boldsymbol{\Lambda} = \boldsymbol{A}\boldsymbol{U}$
  - Frequencies encoded as $\lambda'_k = \lambda_{\text{max}} - \lambda_k$; order by increasing $\lambda'_1 = 0 \leq \lambda'_2 \leq \ldots \leq \lambda'_N$
  - Can generalize to directed graphs
- Graph Fourier transform (GFT): $\hat{\boldsymbol{s}} = \boldsymbol{U}^T\boldsymbol{s}$, and $\boldsymbol{s} = \boldsymbol{U}\hat{\boldsymbol{s}}$

[Shuman et al, *IEEE Signal Processing Magazine*, 2013; Sandryhaila, Moura, *IEEE TSP*, 2013]

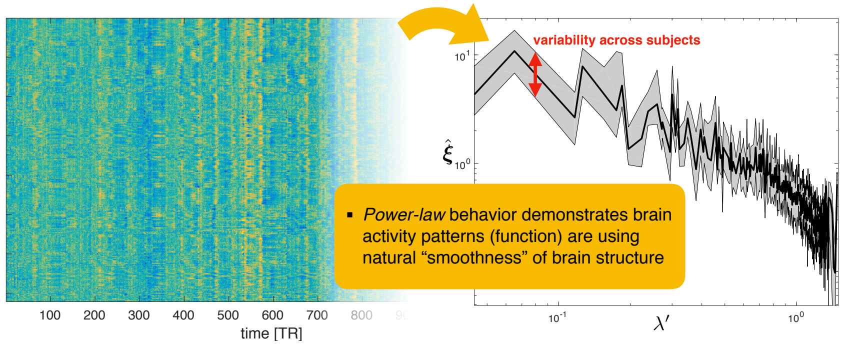
Graph Fourier modes of the brain



Graph energy spectral density

- Graph energy spectral density: $\hat{\boldsymbol{\xi}}_{ss} = |\hat{\boldsymbol{s}}|^2$
  - Average density of resting-state fMRI data with K frames $\{\boldsymbol{s}_k\}_{k=1,\ldots,K}$

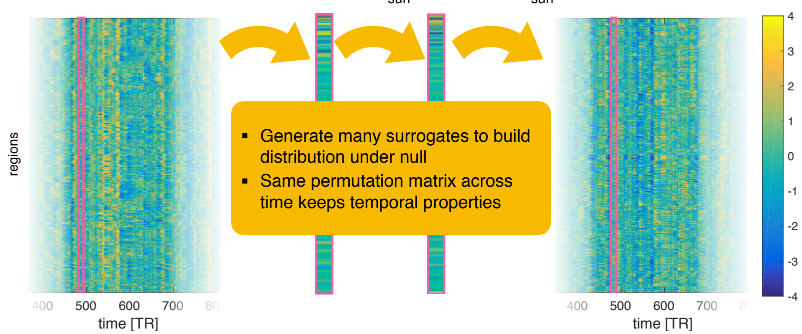
$$\boldsymbol{s}_k \longrightarrow \hat{\boldsymbol{s}}_k \longrightarrow \hat{\boldsymbol{\xi}}_{\boldsymbol{s}_k \boldsymbol{s}_k} = |\hat{\boldsymbol{s}}_k|^2 \longrightarrow \hat{\boldsymbol{\xi}}_{\bar{\boldsymbol{s}}\bar{\boldsymbol{s}}} = \frac{1}{K} \sum_{k=1}^{K} \hat{\boldsymbol{\xi}}_{\boldsymbol{s}_k \boldsymbol{s}_k}$$



Graph surrogates — randomization

- Generate graph signals with same spectral density as empirical
  - Powerful surrogate data with same "graph correlation" to build null-hypothesis distributions
  - Permute signs: diagonal sign permutation matrix $\boldsymbol{P}$

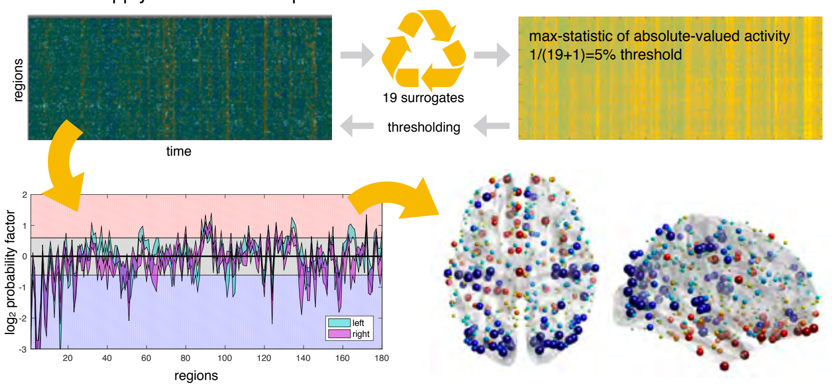
$$\boldsymbol{s} \longrightarrow \hat{\boldsymbol{s}} \longrightarrow \hat{\boldsymbol{s}}_{\text{surr}} = \boldsymbol{P}\hat{\boldsymbol{s}} \longrightarrow \boldsymbol{s}_{\text{surr}}$$



[Theiler et al, *Physica D*, 1992; Pirondini, Vybornova, Coscia, VDV, *IEEE SPL*, 2016]

Which brain regions get wild (or tame)?

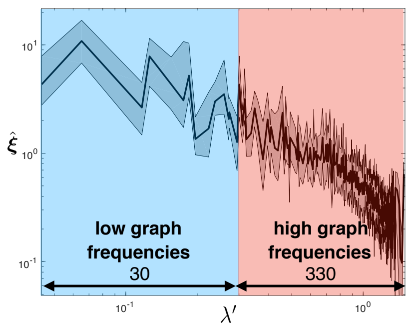
- Detect spatial "non-stationarities"
  - For resting-state, determine 5% threshold on absolute-valued activity based on surrogates
  - Apply threshold to empirical data



[Huang, Bolton et al, *Proceedings of the IEEE*, 2018]

Graph filtering by spectral windowing

- Define ideal low- and high-pass spectral windows
  - Equal energy based on average spectral densities
  - Low graph frequencies are aligned w.r.t. brain structure
  - High graph frequencies are liberal w.r.t. brain structure

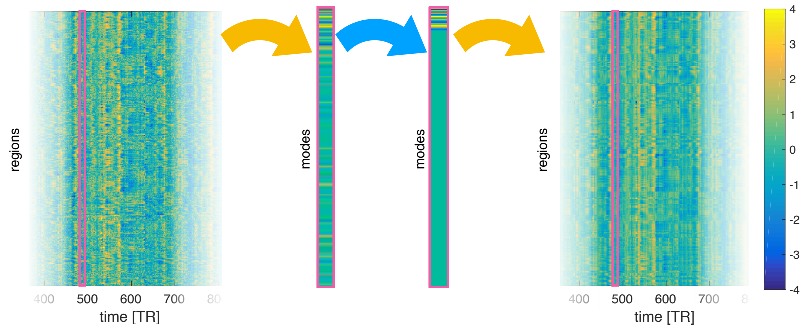


[Huang et al, *IEEE JSTSP*, 2016; Huang, Bolton et al, *Proceedings of the IEEE*, 2018]

Graph signal filtering

- Processing graph signals by filters that are spectrally defined
  - Convolution is not shift-invariant due to irregularity of graph
  - Spectral filtering: diagonal matrix $\boldsymbol{F}$ contains spectral window

$$\boldsymbol{s} \longrightarrow \hat{\boldsymbol{s}} = \boldsymbol{U}^T\boldsymbol{s} \longrightarrow \hat{\boldsymbol{s}}_{\text{filt}} = \boldsymbol{F}\hat{\boldsymbol{s}} \longrightarrow \boldsymbol{s}_{\text{filt}} = \boldsymbol{U}\hat{\boldsymbol{s}}_{\text{filt}}$$



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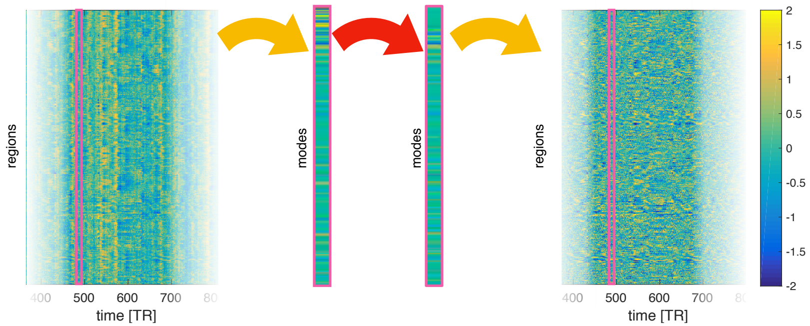
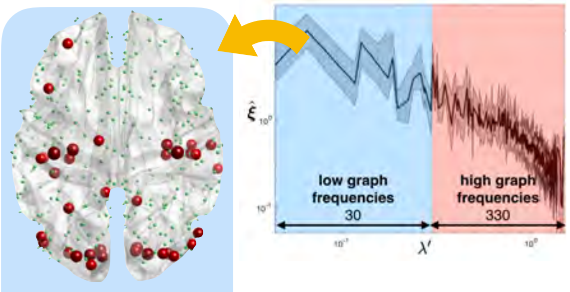
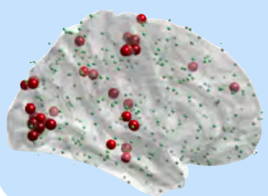


Aligned versus liberal — in resting state

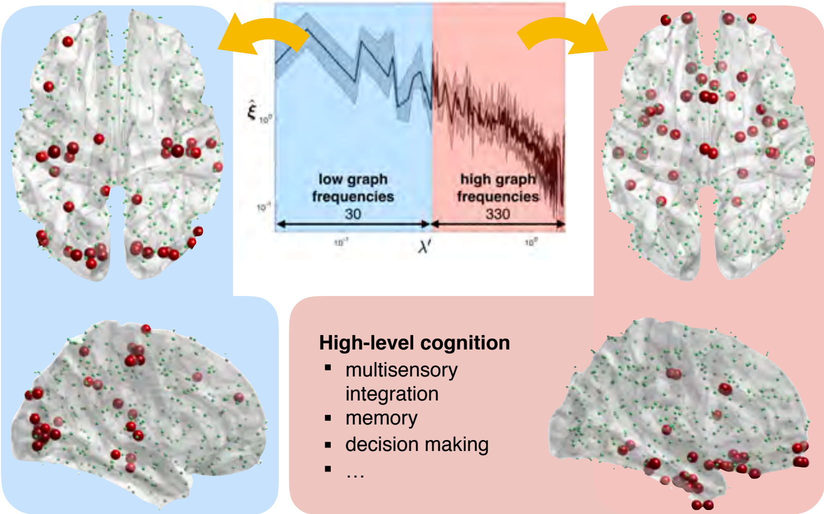




Sensory regions

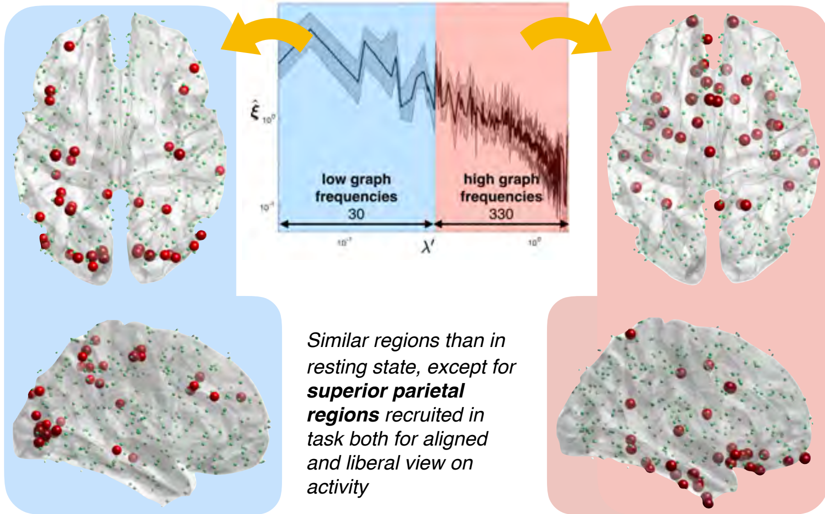
- occipital (visual)
- pre- and post-central (somatomotor)
- temporal (auditory)

Aligned versus liberal — in resting state



High-level cognition
- multisensory integration
- memory
- decision making
- …

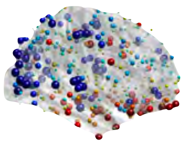
Aligned versus liberal — in task



Similar regions than in resting state, except for ***superior parietal regions*** *recruited in task both for aligned and liberal view on activity*

Function-structure relationships

- New way to investigate function-structure integration
  - For different regions, significantly more/less activity than expected by signals with equal "spatial graph smoothness"
  - Alignment with structure differs as well

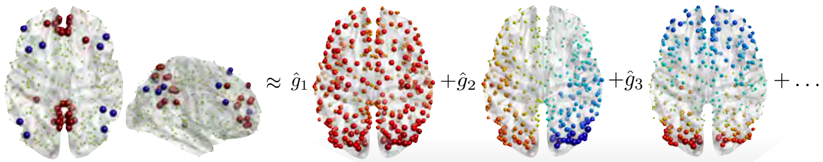


high-level regions	more active than expected	activity is more liberal
sensory regions	less active than expected	activity is more aligned

- In line with other studies
  - Medaglia *et al.* show relationship between liberal activity and perceptual switching task **(see talk Alejandro Ribeiro)**
  - Sensory regions are less information for fMRI-fingerprinting
- Graph spectral windows are still "easy"
  - Other designs (e.g., graph wavelets) could refine results

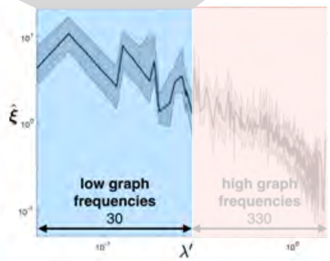
[Medaglia et al., *Nat Hum Beh*, 2018; Finn et al, *Nat Neuro*, 2017; Hammond et al, *ACHA*, 2011]

Investigating major functional networks



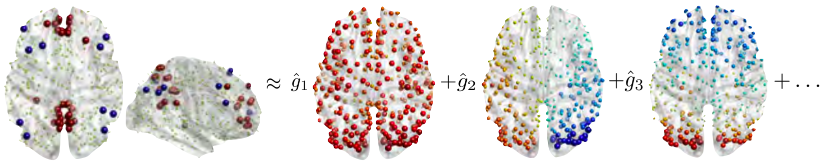
task-positive/fronto-parietal network (10 nodes)
task-negative/default-mode network (30 nodes)

- Brain regions highly studied for task-positive vs -negative involvement
  - Selection of subgraphs according to two sets of regions
- Explain pattern by low graph-frequency components
  - Aligned with structure



[Christoff et al., *Nat Rev Neurosci*, 2016; relates also to Atasoy et al., *Nat Comm*, 2016]

Graph Slepians



task-positive/fronto-parietal network (10 nodes)
task-negative/default-mode network (30 nodes)

- Slepian design problem transposed to graphs:

David S. Slepian
1923-2007

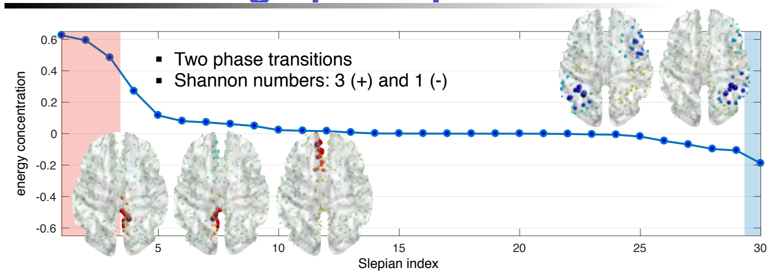
Find band-limited graph signals with maximal energy concentration in selected subgraph $\mathcal{S}$ (indicated by $\boldsymbol{S}$)

$$\mu = \frac{\hat{\boldsymbol{g}}^T \boldsymbol{U}_W^T \boldsymbol{S} \boldsymbol{U}_W \hat{\boldsymbol{g}}}{\hat{\boldsymbol{g}}^T \hat{\boldsymbol{g}}}, \quad \text{(Rayleigh quotient)}$$

where $\boldsymbol{U}_W$ only contains first N_W GFT basis vectors, and $\boldsymbol{C} = \boldsymbol{U}_W^T \boldsymbol{S} \boldsymbol{U}_W$ is the concentration matrix. Graph Slepians are then given by $\boldsymbol{g} = \boldsymbol{U}_W \hat{\boldsymbol{g}}$.

[Tsitsvero et al, *IEEE TSP*, 2016; Van De Ville et al, *IEEE Signal Processing Letters*, 2017]

Generalized graph Slepians



- Criterion with positive and negative subgraph:

We introduce two types of nodal selection, which lead to a new criterion:

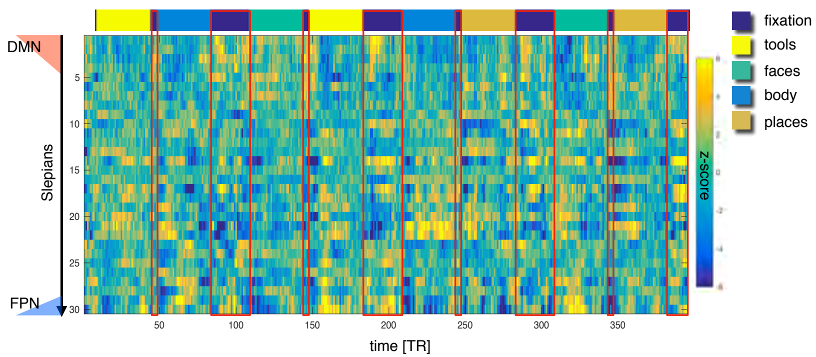
$$\mu = \frac{\hat{\boldsymbol{g}}^T \boldsymbol{U}_W^T (\boldsymbol{S}^+ - \boldsymbol{S}^-) \boldsymbol{U}_W \hat{\boldsymbol{g}}}{\hat{\boldsymbol{g}}^T \hat{\boldsymbol{g}}}$$

- We order the Graph Slepians according to decreasing energy concentration: $1 > \mu_1 \geq \mu_2 \geq \ldots > -1$

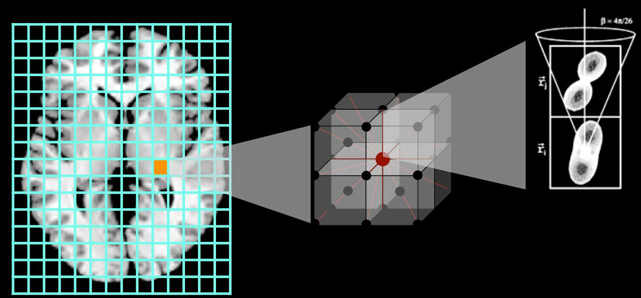
[Demesmaeker, Preti, Van De Ville, *IEEE Transactions on Signal Processing*, in press; see arXiv]

Projecting on the Slepian basis

- Task data
  - Slepian basis, using main structural backbone, captures nicely *switches* of task-positive vs -negative patterns



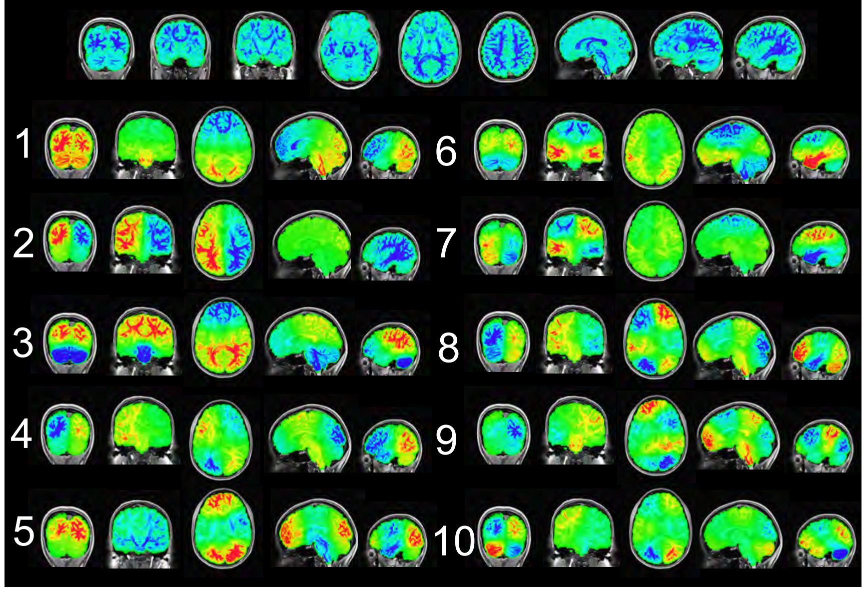
Brain graph revisited



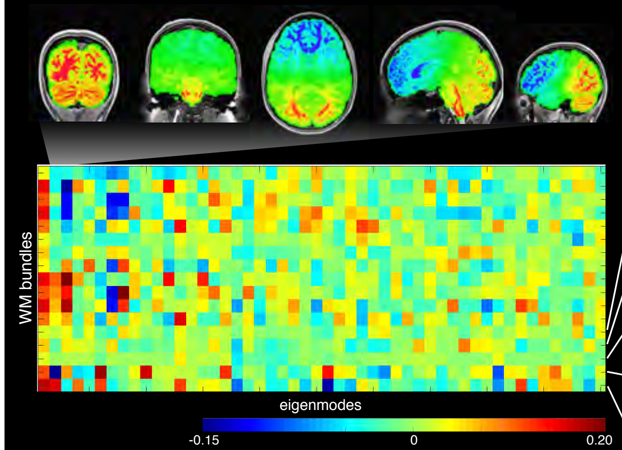
- Build large voxel-level brain graph (in subject space)
  - Single node represent 1.25x1.25x1.25 mm^3
  - Total of about 850K nodes
  - Local connectivity extracted from diffusion-weighted information
    - diffusion shape from orientation distribution function
    - strength from quantitative anisotropy
  - Huge, but sparse adjacency matrix
- Computing leading eigenvectors using large-scale numerical eigensolvers

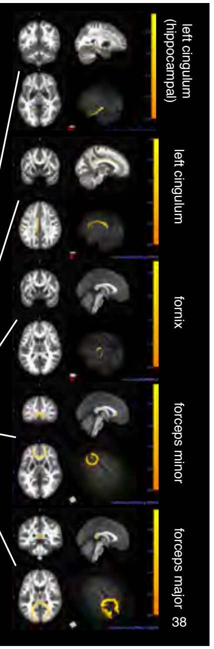
[Itturia-Medina et al, *NeuroImage*, 2007; Yet et al, *IEEE TMI*, 2010]

Graph Fourier modes revisited



Graph Fourier modes revisited

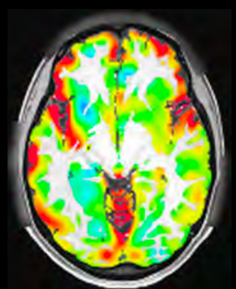




- Procrustes transform between subject-specific eigenmodes shows consistency up to approx. 300

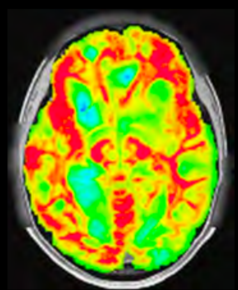
[Zhang, Arfanakis, *NeuroImage*, 2018; O'Muircheartaigh, Jbabdi, *NeuroImage*, 2017]

Brain graph “inpainting”



$$\frac{\partial s}{\partial t} = -\beta L s$$

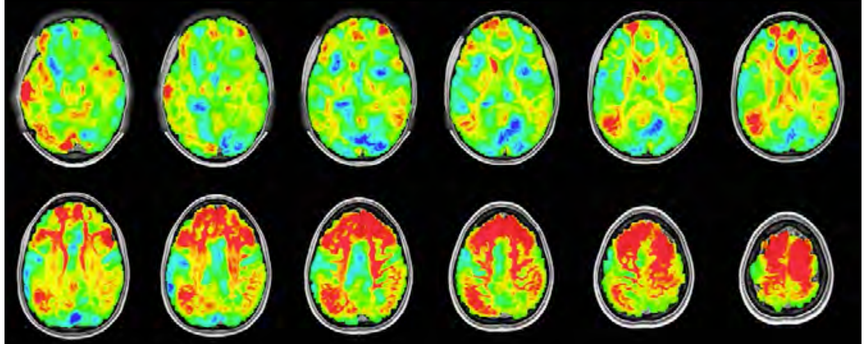
$$s\big|_{\text{GM}} = \text{BOLD}$$



- fMRI BOLD signals are only meaningful on the gray matter
- Graph signal recovery problem on the complete brain graph
  - Fill in plausible activity signals on white matter
  - Using measured gray-matter fMRI activity as *boundary condition*
  - Diffusion of activity into white matter using brain graph

[Tarun et al, *OHBM*, 2018]

Brain graph “inpainting”



- Shows how gray-matter activity “exploits” the white-matter wiring
- Different from tractography due to boundary conditions
- Recovered graph signals have a direct physical embedding as brain volume, which allows for further processing steps

[Tarun et al, *OHBM*, 2018]

Conclusion

- Systems-level neuroscience today
  - Integration
    - Brain structure, (dys)function, and (ultimately) behavior
  - Understand organizational principles of the brain
    - Network organization
    - Dynamics and interactions
  - Large amounts of data become available

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Conclusion

- Systems-level neuroscience today
  - Integration
    - Brain structure, (dys)function, and (ultimately) behavior
  - Understand organizational principles of the brain
    - Network organization
    - Dynamics and interactions
  - Large amounts of data become available
- Graph signal processing, a new and elegant framework for computational neuroimaging
  - Natural way to incorporate brain structure
    - Connectome provides "backbone" graph
  - Investigate brain function frame-by-frame
    - Functional information can be analyzed dynamically
- Challenges
  - Give precise interpretation to GSP operations such as filtering,…
    - Normalization, spectral windowing, stability of eigenvectors, implementations,…
  - Joint modeling of space and time
  - Integrate different types information (i.e., multiplex graphs) at multiples scales (i.e., multilevel graphs)

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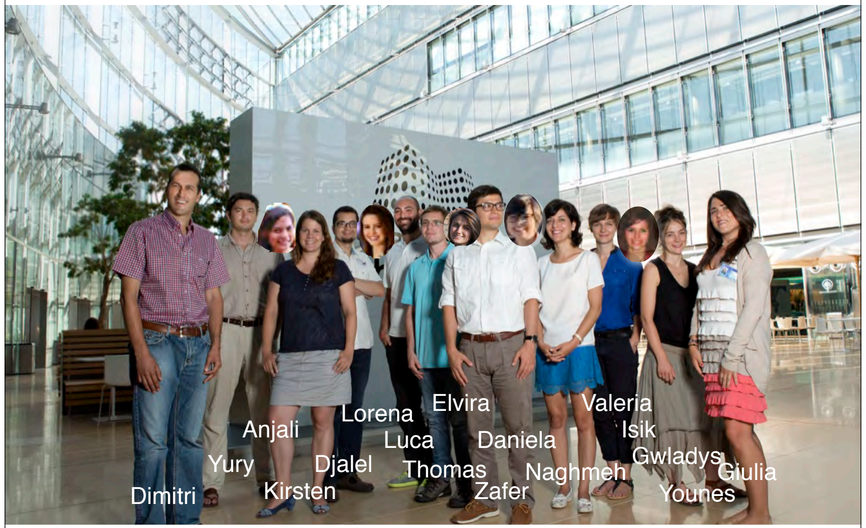

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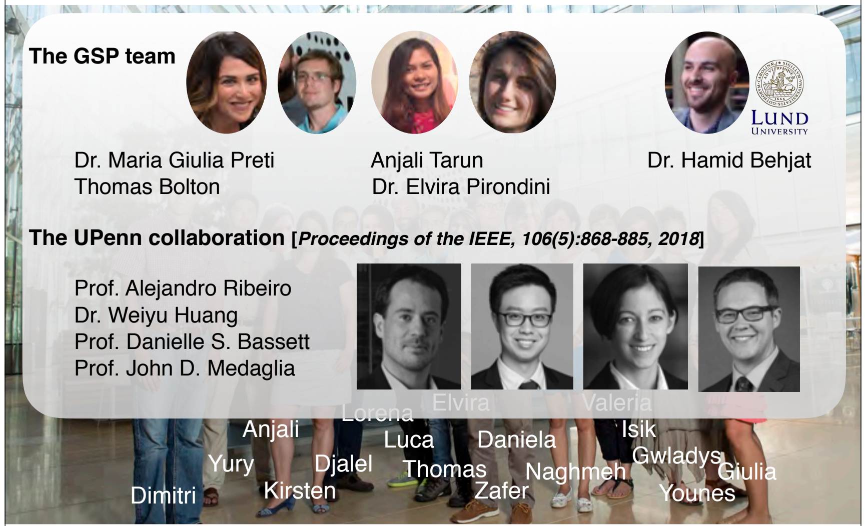

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The UPenn collaboration [*Proceedings of the IEEE, 106(5):868-885, 2018*]

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