Decoding fMRI functional connectivity

Pattern recognition on a restricted class of graphs

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Agenda for this talk

- From fMRI time-series to functional connectivity graphs
- Classification of functional connectivity graphs using embedding

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- Functional connectivity: "*statistical dependence between time series in distinct brain locations*"

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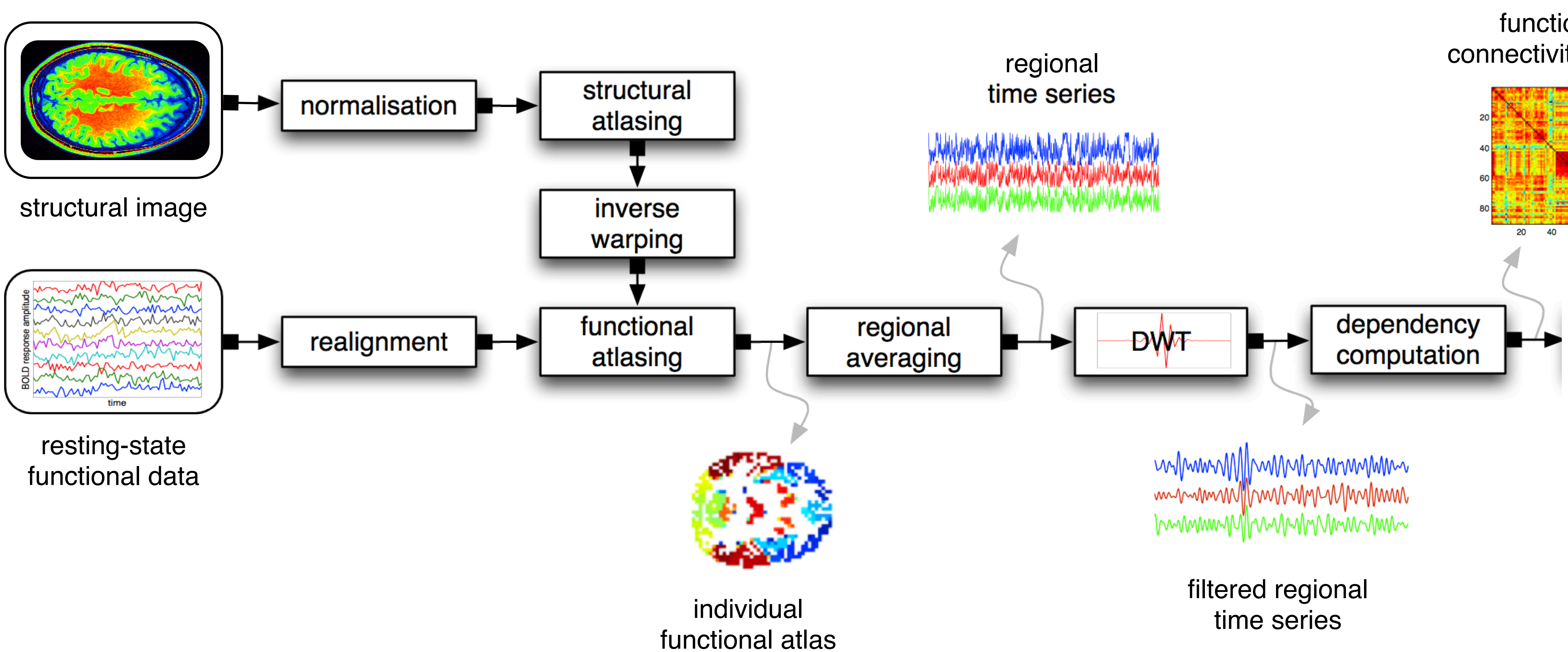

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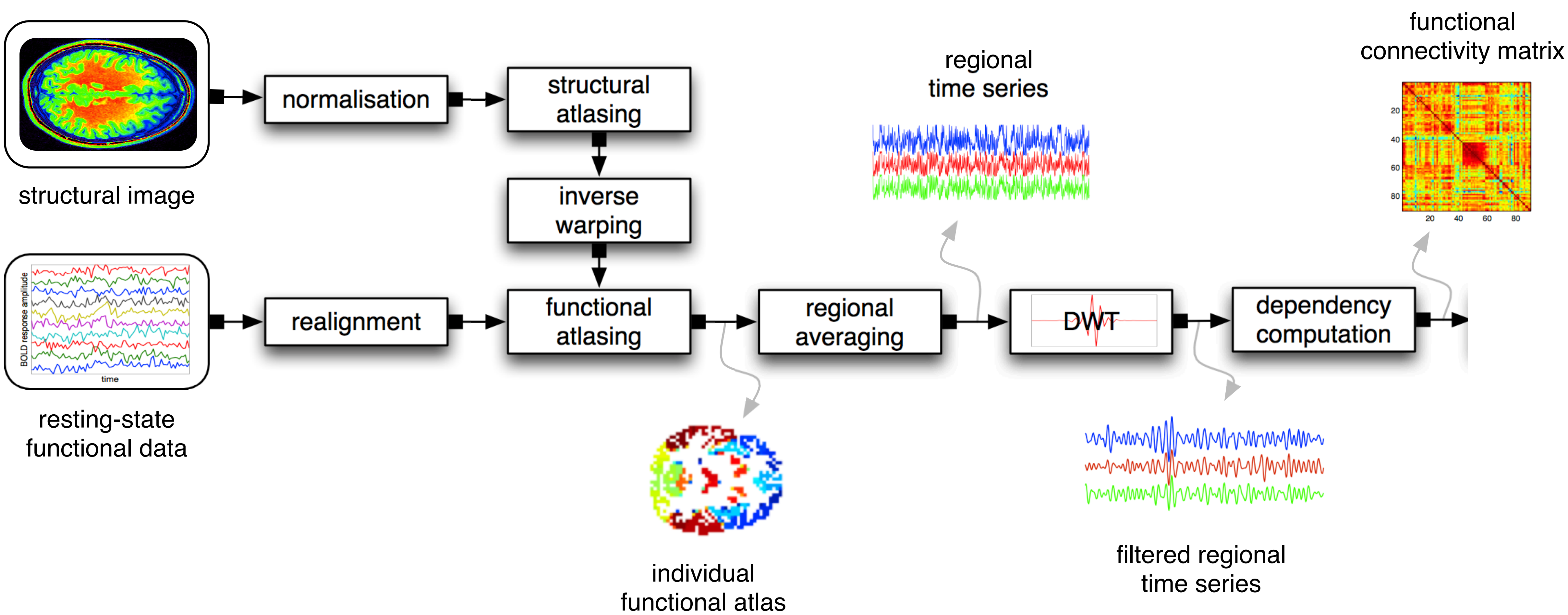

- Important point for interpretation: ROIs as nodes.

*[Achard et al., J. Neurosci 2006]

Functional connectivity as a graph

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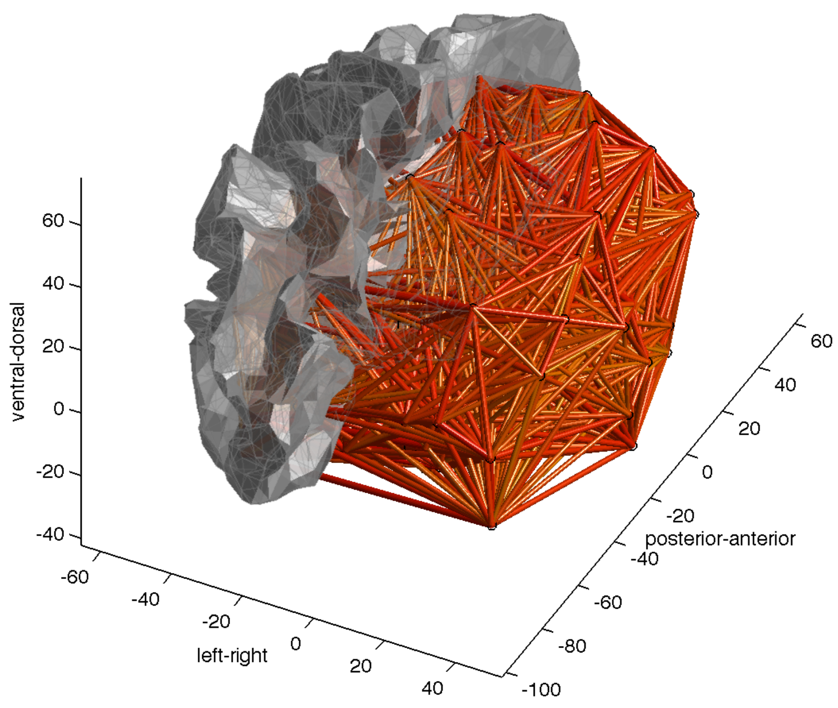
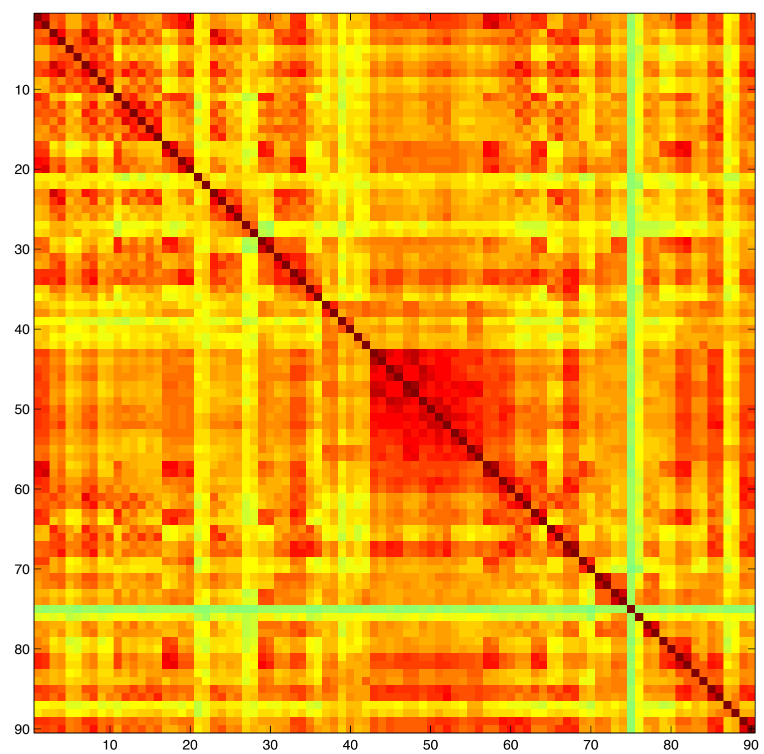
- The correlation matrix (minus the diagonal) can be seen as the adjacency matrix **A** of a “functional connectivity graph”:
  - **Vertices** correspond to voxels or regions
  - **Edge labels** encode pairwise strength of temporal dependence





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- Principle: adopt a "brain decoding" (pattern recognition / predictive modelling / classification) approach for connectivity. This equips us with interesting tools:
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  - Enables single-subject inference
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  - Useful where an analytical model is intractable ("How does connectivity change between state A and state B?")
- We'll need:
  - A clear **definition of brain connectivity graphs**
  - Effective **methods to classify these graphs**

Connectivity graphs as labelled graphs

- Weighted "brain connectivity graphs" can be expressed formally as labelled graphs.
- Labelled graphs are written: $g = (V, E, \alpha, \beta)$
  - V: the *set of vertices* (nodes, brain regions, ICA components)
  - E: the *set of edges* (connections between nodes)
  - α: *vertex labelling function* (returns a name or number for each node, for example the anatomical label of the region)
  - β: *edge labelling function* (returns a name or number for each edge, for example the temporal correlation strength)
  - A square *adjacency matrix* **A** can encode the presence/absence of connections, and their strengths.

Connectivity graphs as restricted labelled graphs

- Functional brain networks obtained by atlasing can adequately be modelled by a restricted class of labelled graphs we call **graphs with fixed-cardinality vertex sequences**, a subclass of Dickinson et al.'s *graphs with unique node labels*:
    - Fixed number of vertices for all graph instances: $\forall i \; |V_i| = M$
    - Fixed ordering of the set (sequence) V: $V = (v_1, v_2, \ldots, v_M)$
    - Scalar edge labelling functions: $\beta : (v_i, v_j) \mapsto \mathbb{R}$
    - Undirected: $\mathbf{A}^T = \mathbf{A}$
- This is a very restricted (but still expressive) class of graphs
- This limits the effectiveness of many classical methods for classifying general graphs (based on *graph matching*).

[Richiardi et al., ICPR, 2010] [Dickinson et al., IJPRAI, 2004]

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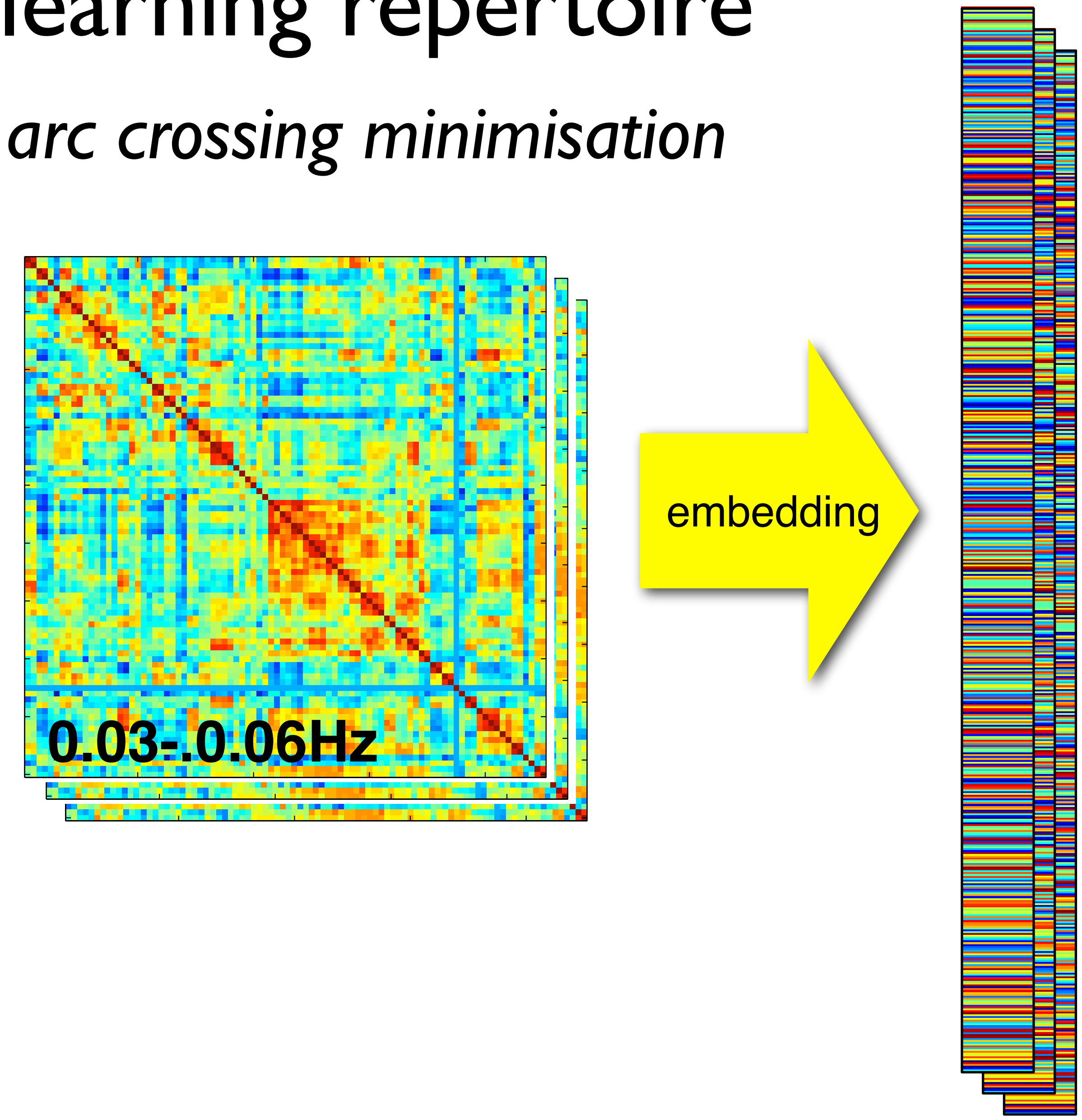
  - Here we're not interested in the *arc crossing minimisation problem* or *planar graphs*



Embedding connectivity graphs

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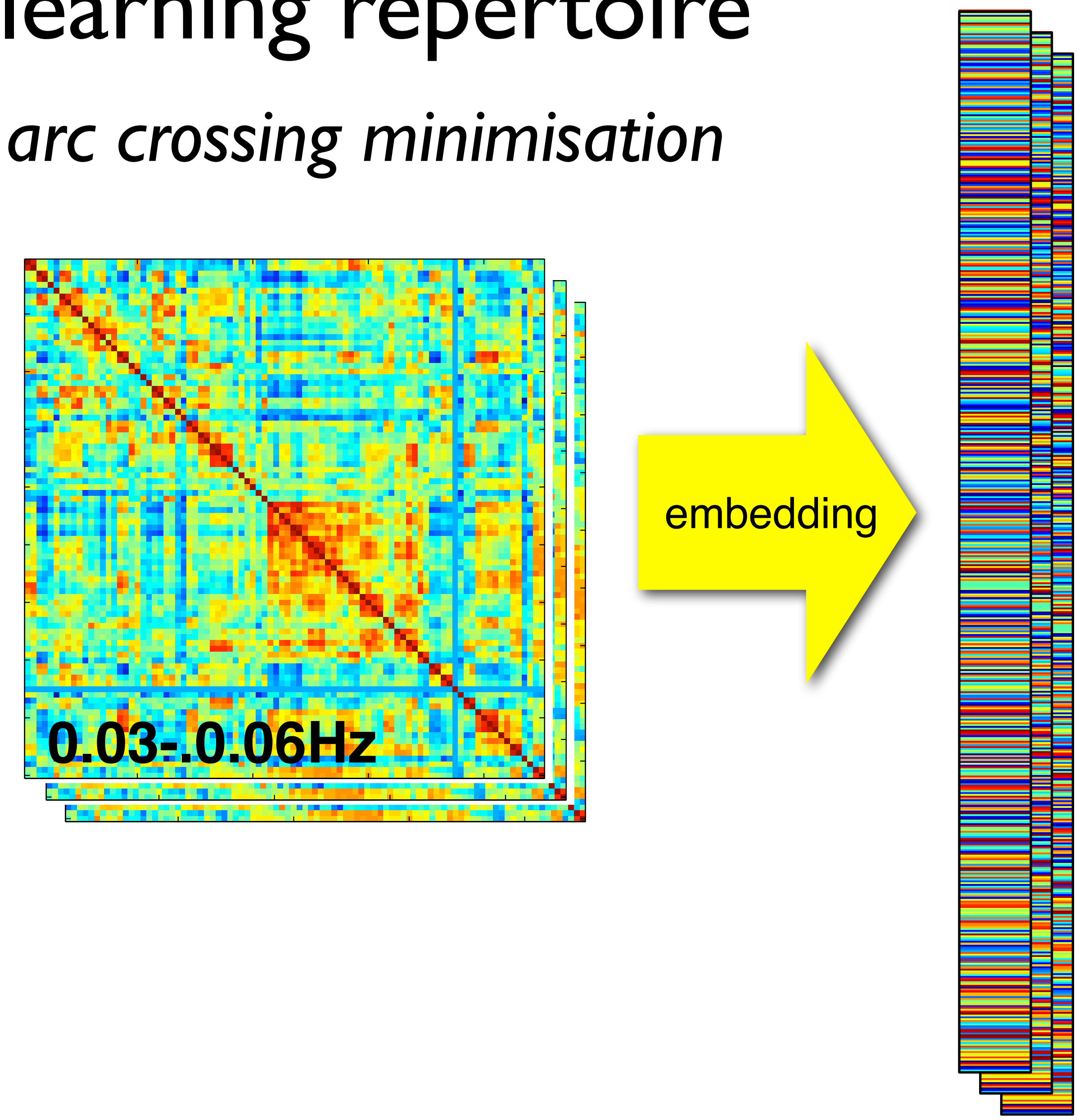
- We proposed several ways of doing this, including:

1. Direct embedding
2. Dissimilarity embedding
3. Graph and vertex attribute embedding



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1: Direct graph embedding

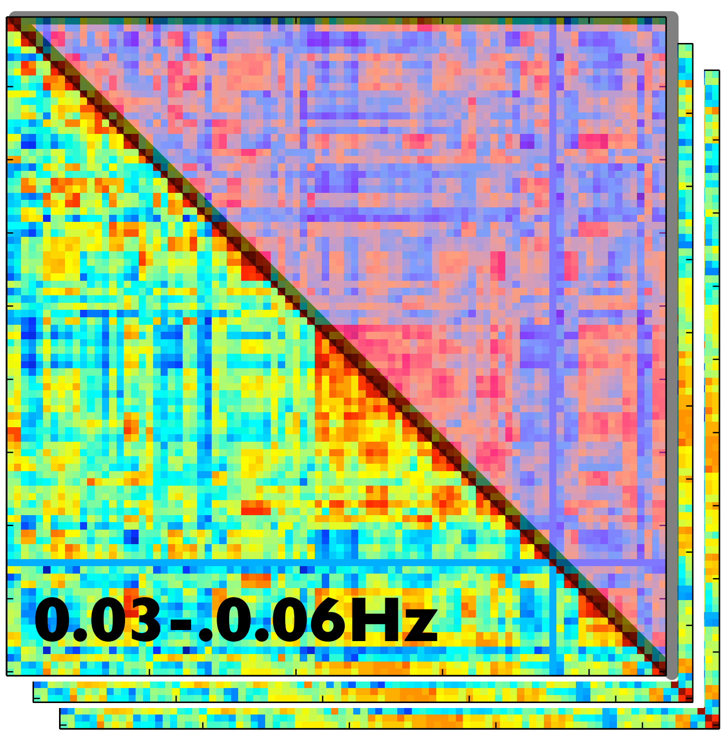
- Direct embedding provides a suitable vector-space representation for the class of graphs of interest

$$\begin{pmatrix} (1,1) & \dots & (1,|V_i|) \\ & \ddots & \\ & & (|V_i|,|V_i|) \end{pmatrix}$$

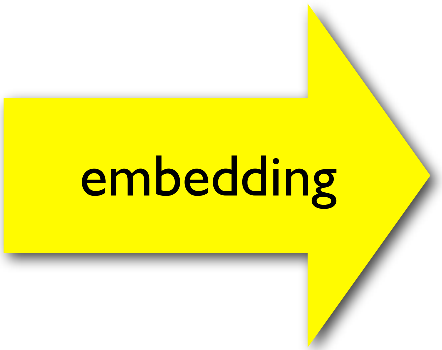
$$\mathbf{A}_i \in \mathbb{R}^{|V_i|\times|V_i|}$$

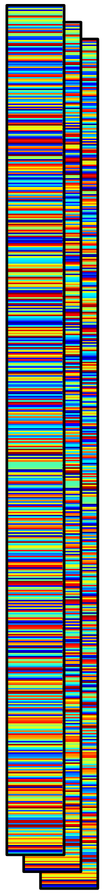
$$\begin{pmatrix} (1,2) \\ \vdots \\ (|V_i|-1,|V_i|) \end{pmatrix}$$

$$\mathbf{B}_i \in \mathbb{R}^{\binom{|V_i|}{2}\times 1}$$



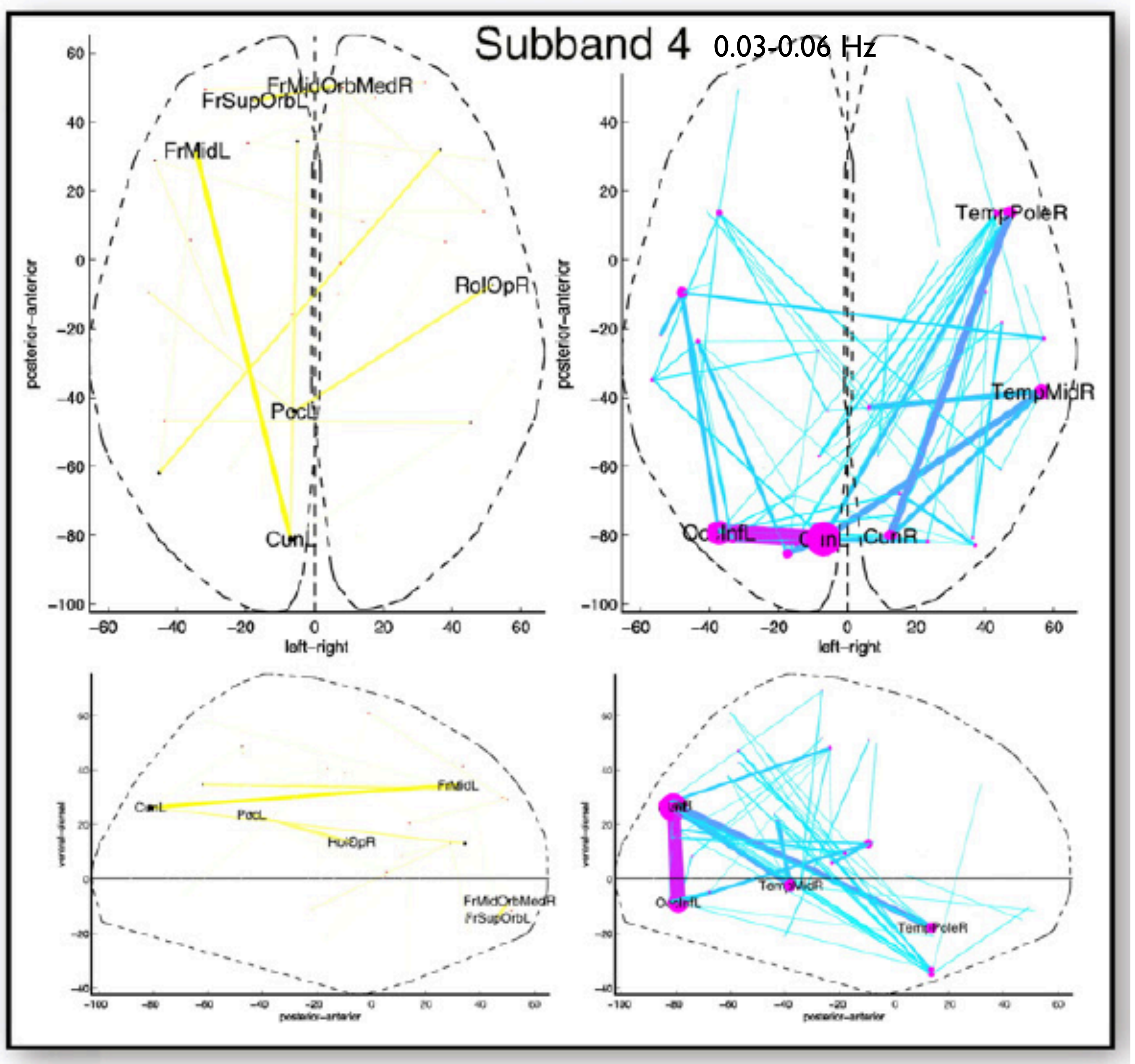
90 regions,
4005 connections

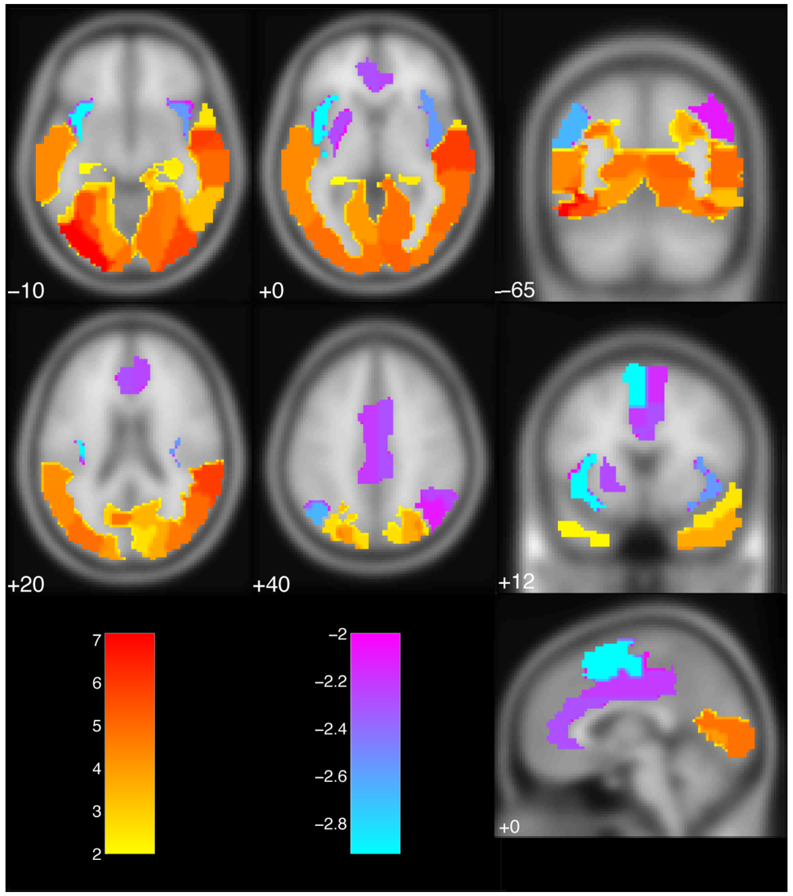




Experimental results: cognitive

- Data: 15 subjects, each in movie watching (14 min) and rest (8 min)
- Question: can we infer "brain state" (rest versus movie) across subjects?
- Results: yes, 80%-97% accuracy in CV in the low subbands





- Regional activity and connectivity have an inverse relationship
- Nir et al.* also report decoherence during stimulus

[Richiardi et al., Neuroimage, 2011]

*[Nir et al., Neuroimage, 2006]

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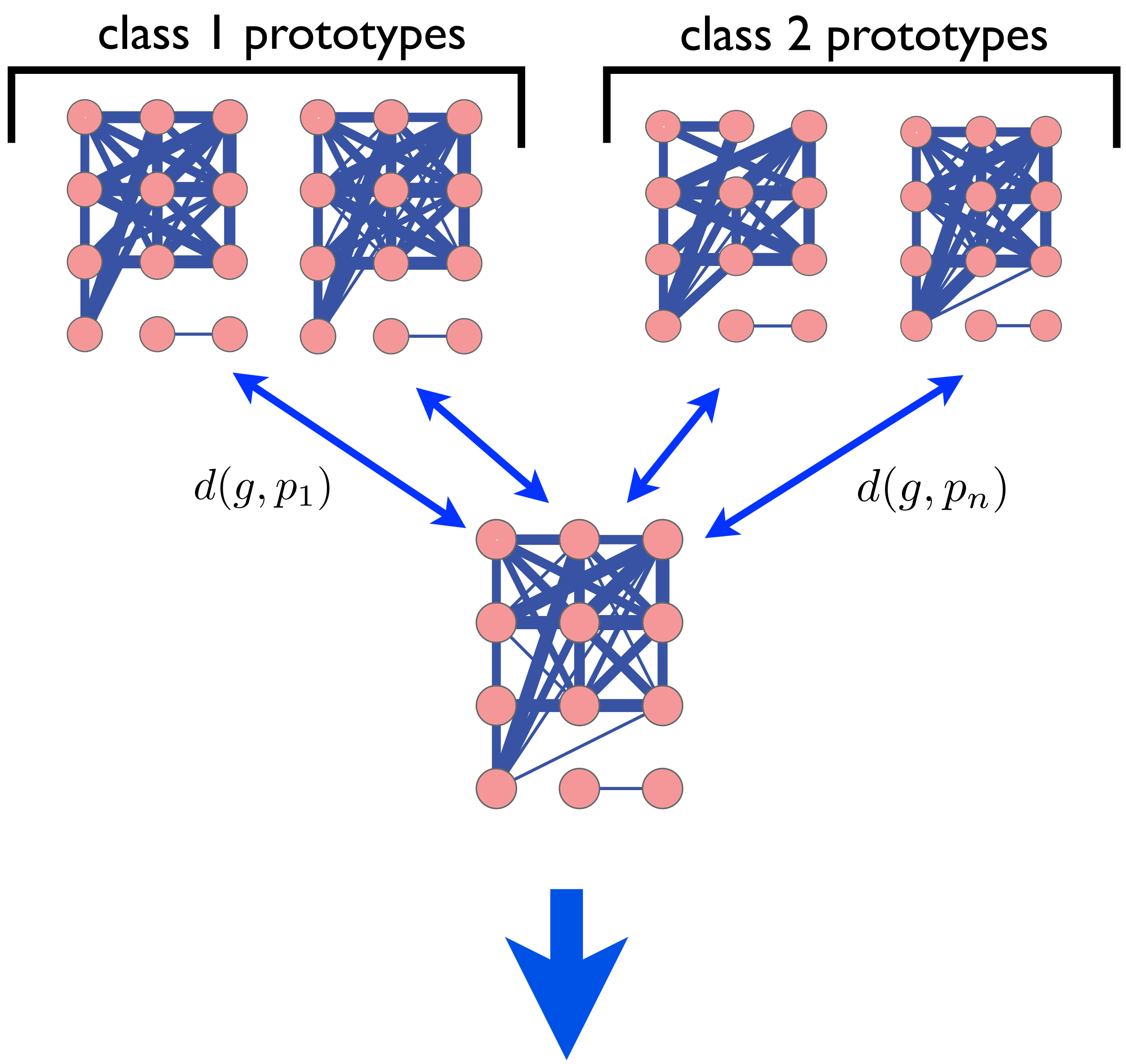
2: dissimilarity embedding

Principle



Embedding vector

$$\varphi_n^{\mathcal{P}}(g) = (d(g, p_1), \ldots, d(g, p_n)) \in \mathbb{R}^n$$

Fixed dissimilarity

Edge label disssimilarity

$$d(c_{ij}, c'_{ij}) = \begin{cases} |\beta(i,j) - \beta'(i,j)| & c_{ij} \in C, c'_{ij} \in C' \\ K & otherwise \end{cases}$$

Graph dissimilarity

$$d(g, p) = \sum_{i=1}^{|E|} \sum_{j=i+1}^{|E|} d(c_{ij}, c'_{ij})$$

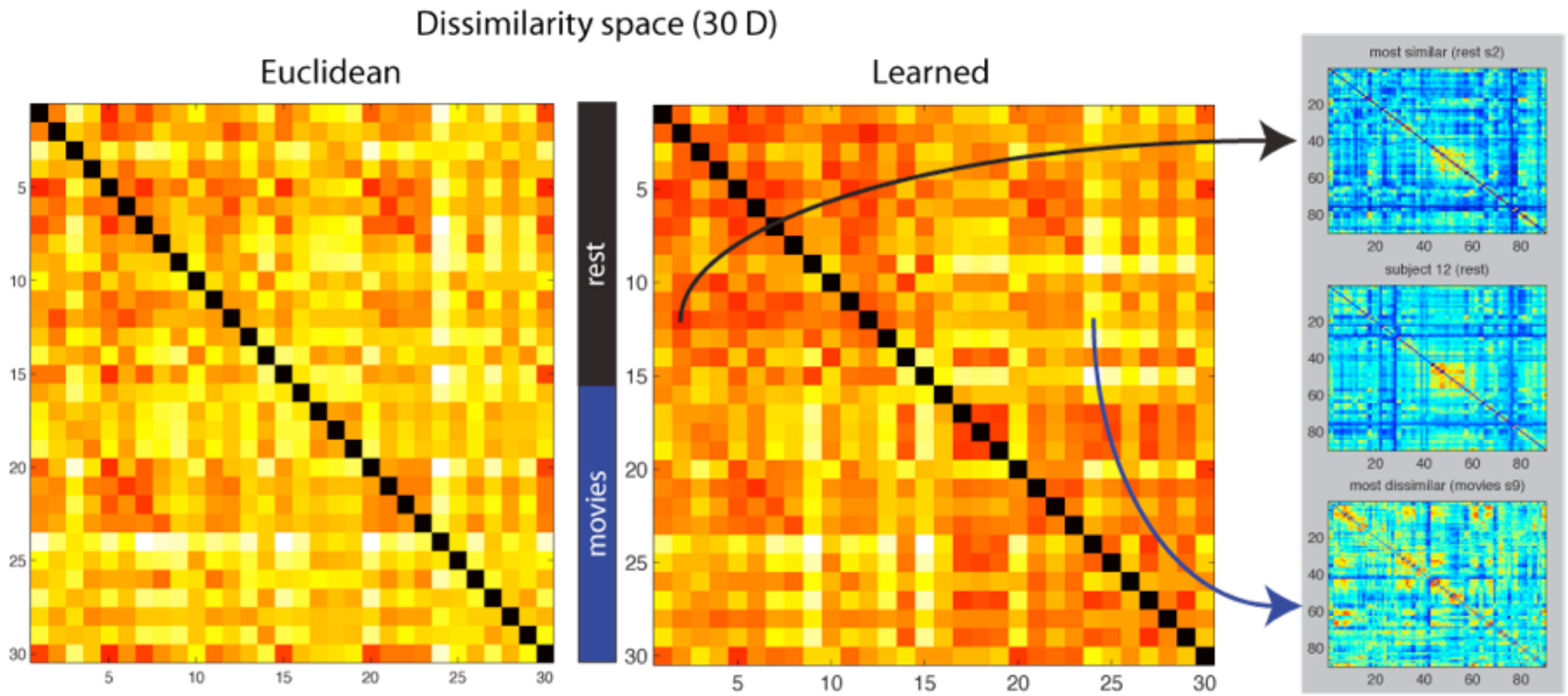
$$d(g, p) = \tfrac{1}{2} ||\mathbf{a}_g - \mathbf{a}_p||_1 \quad \text{(if no missing edges)}$$

Dissimilarity metric learning

$$d(g, p) = ||\mathbf{a}_g - \mathbf{a}_p||_{\mathbf{D}} = \sqrt{(\mathbf{a}_g - \mathbf{a}_p)^T \mathbf{D} (\mathbf{a}_g - \mathbf{a}_p)}$$

[Richiardi et al., ICPR 2010]
based on [Riesen & Bunke, Int. J. Pat. Rec. Artif. Int. 2009]
and [Xing et al. NIPS 2002]

Dissimilarity space



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- Graphs G, H are isomorphic iff there exists a permutation matrix **P** s.t. $\mathbf{P}\mathbf{A}_g\mathbf{P}^T = \mathbf{A}_h$
  - In our case (atlased connectivity graph): $\mathbf{P} \triangleq \mathbf{I}$
  - Hence connectivity graphs are isomorphic iff

$$\begin{aligned} &\mathcal{E}_g = \mathcal{E}_h \quad and \\ &\forall i, j \;\; \beta_g(v_i, v_j) = \beta_h(v_i, v_j) \end{aligned}$$

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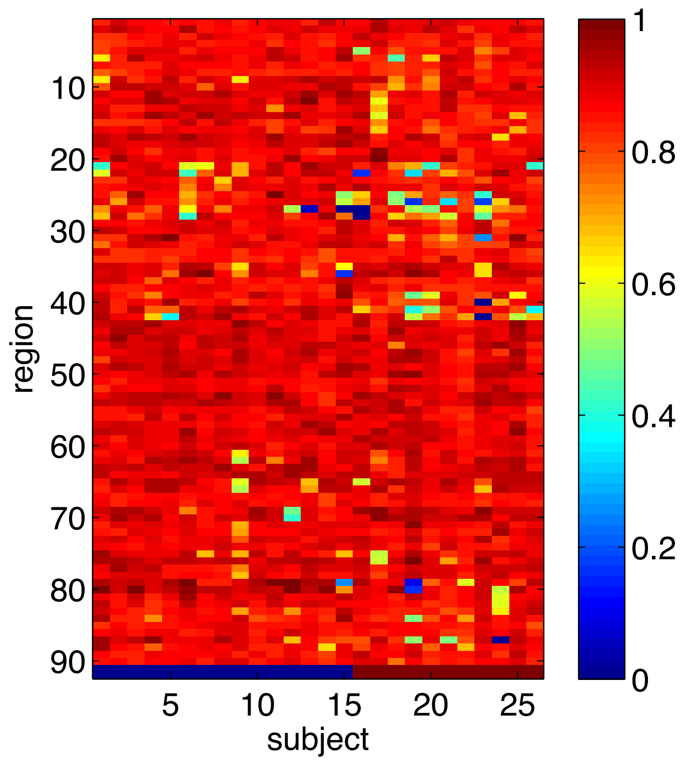
- Graph invariant: *(set of) parameter(s) yielding the same value for isomorphic graphs*
  - To compare noisy connectivity graphs we are more interested in ε-isomorphism, and ε-invariants*
  - Some invariants may degenerate depending on $|\mathcal{V}|$: non-isomorphic graphs may have the same value
  - We use several invariants to mitigate degeneracy**

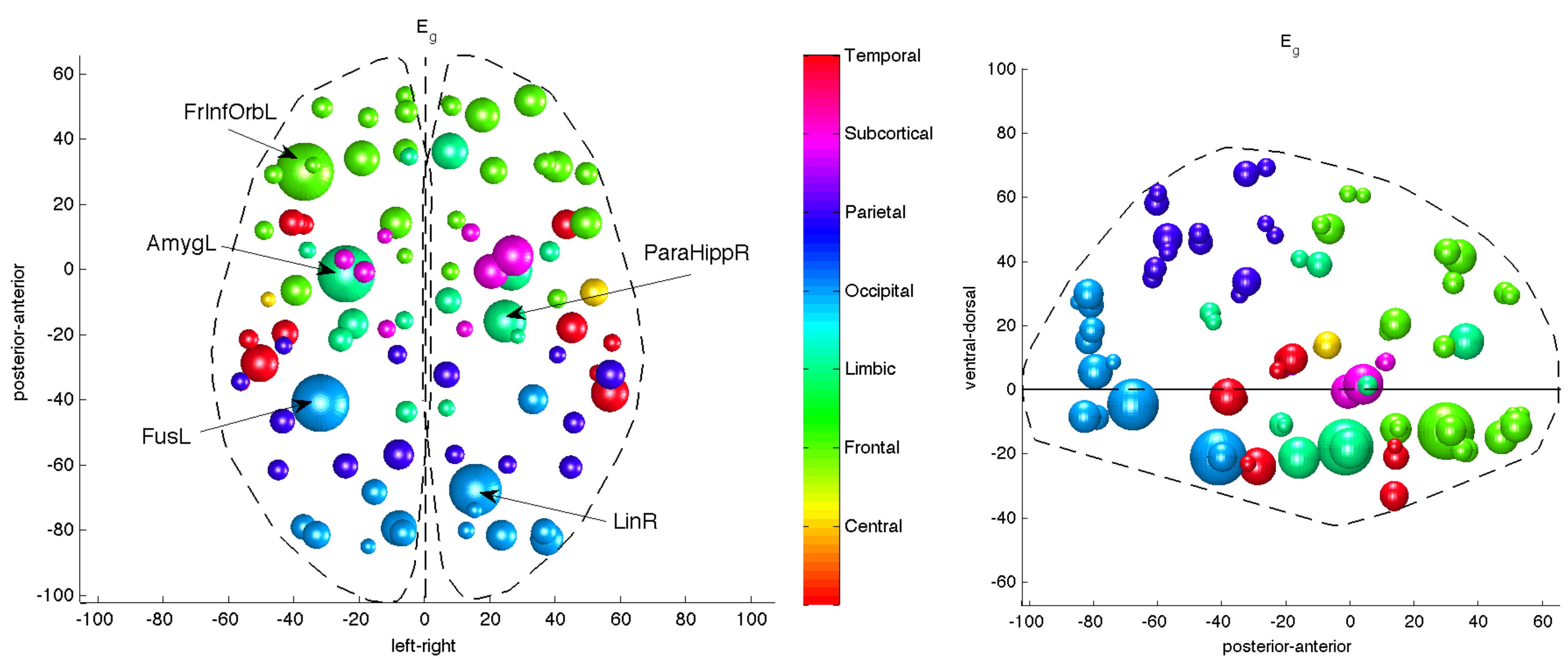
*[Jain & Wysotzki, Neurocomputing, 2005]

 ** as in chemometrics: [Bonchev et al, J Comput Chemistry 1981]

Experiments

- Data: 26 subjects: 15 young (18-33, mean 24), 11 old (62-76, mean 67). 9.5 minutes resting-state, TR 1.1s.
- Question: Can we predict the age group of an unseen subject from graph/vertex properties of resting-state connectivity graphs?
- Results: only global and local efficiency are convincing (up to 89% accuracy). But on this dataset this works better than direct embedding.





- Orbito-frontal cortex, amygdala, and parahippocampal formation are the most predictive regions (broadly agrees with previous studies*)
- In addition, the lingual gyrus shows age-related activation changes during memory tasks**

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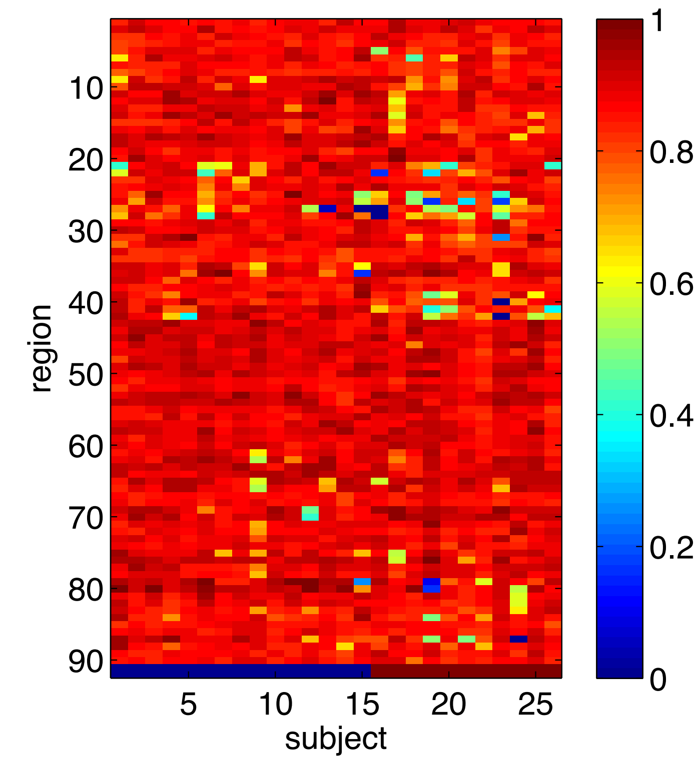

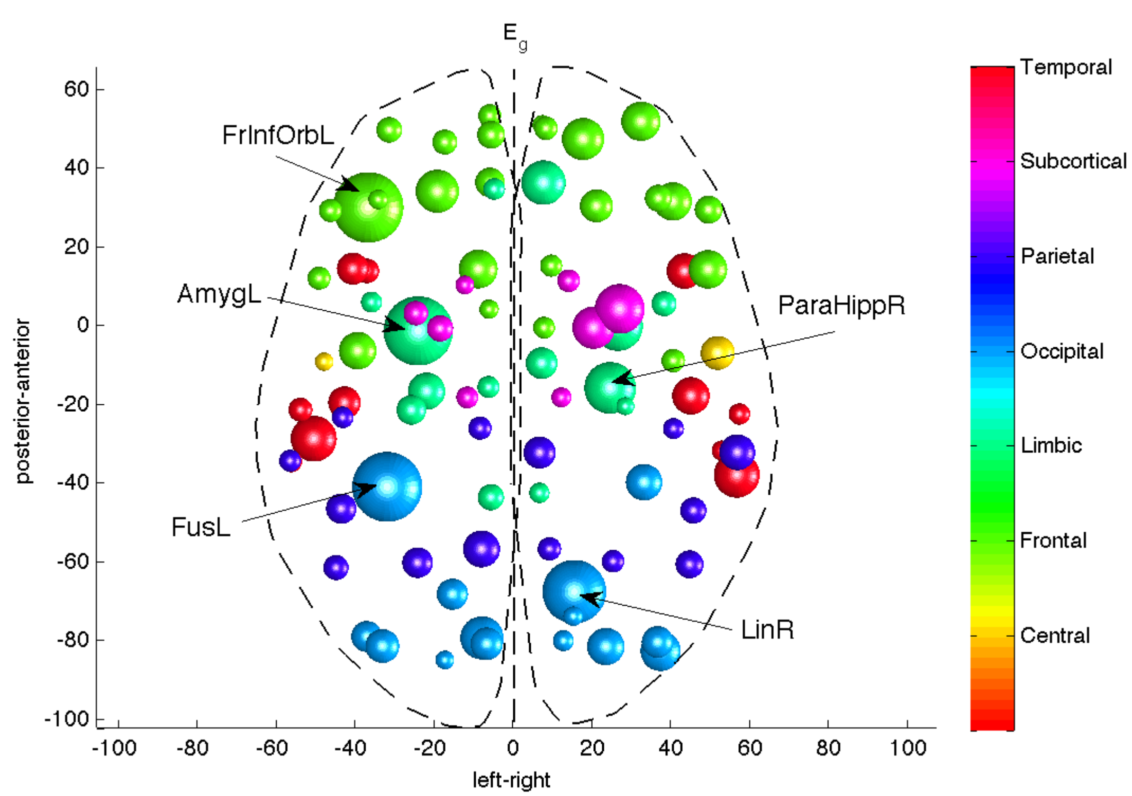

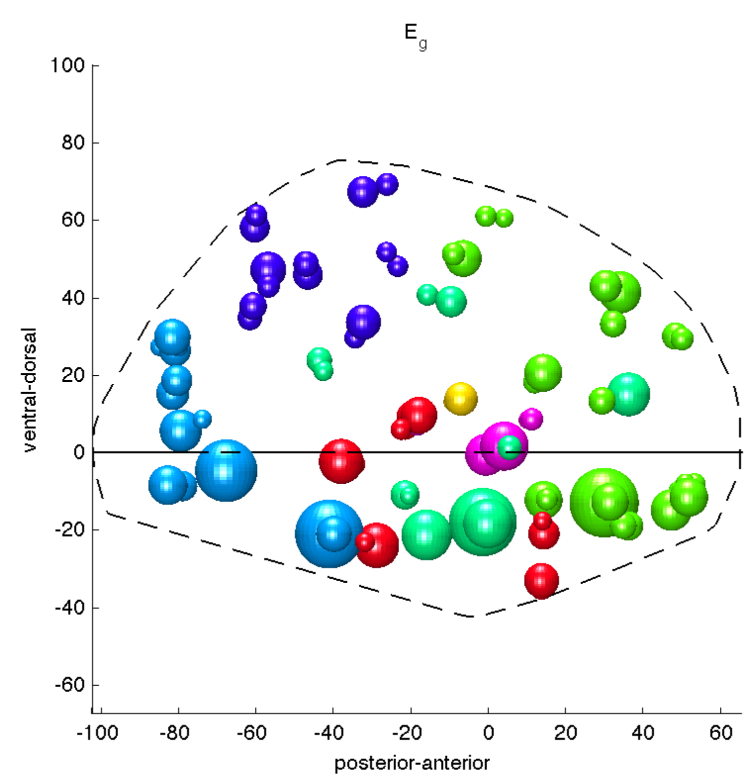

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*[Achard & Bullmore, PLoS CompBiol, 2007]
**[Mencl et al., Micros Res. Tech., 2000]

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  - It can be used in a predictive setting
  - We can trivially restrict analysis to small subnetworks (e.g. speech processing areas)
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- Of course there is still much work to do: physiological noise, modelling, and interpretation (where do LF oscillations come from, what are they useful for?) are currently weak points.

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