New Interpretable Patterns and Discriminative Features from Brain Functional Network Connectivity Using Dictionary Learning

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The increasing importance of data-driven techniques in fMRI

Traditional neuroscience approaches

- Region of interest (ROI) analysis: Selecting specific brain regions involved in a process or behavior
- Forming hypotheses based on prior knowledge or assumptions about the brain
- Valuable in advancing our understanding of the brain
- Limited by the assumptions and biases

Data-driven techniques

- Machine Learning and ICA
- Without being constrained by pre-existing hypotheses or assumptions
- Identifying complex patterns that might be unexpected or unknown
- Analysing large amounts of data

Leveraging ICA and DL jointly being learned with a classifier for identifying interpretable patterns in fMRI

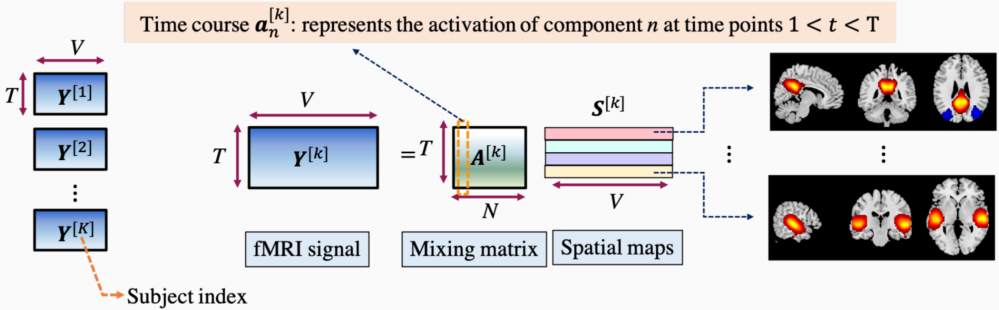
Motivation

- Developing methods for identifying interpretable patterns that can distinguish between HCs and patients
- Aim to improve understanding and diagnosis of these disorders.

Methodology

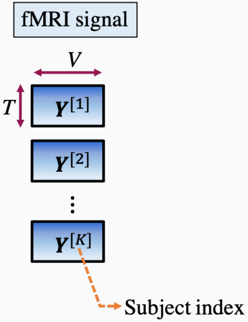
- Leveraging the advantages of ICA and DL to:
  - Extract powerful features from resting-state fMRI data
  - Identify novel, interpretable biomarkers.

Uncovering brain networks: ICA analysis of fMRI data for spatial maps and time courses



Group ICA and back-reconstruction for multi-subject brain network analysis

Group ICA + Back-reconstruction



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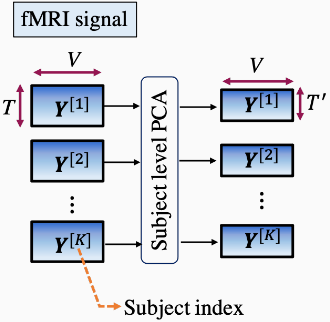

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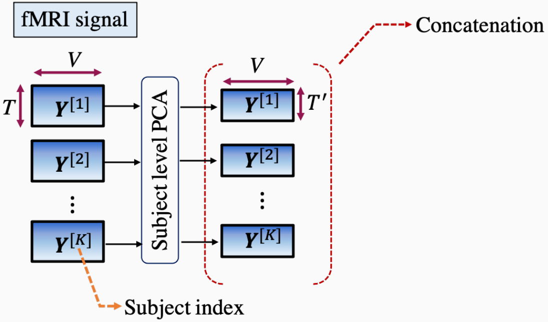

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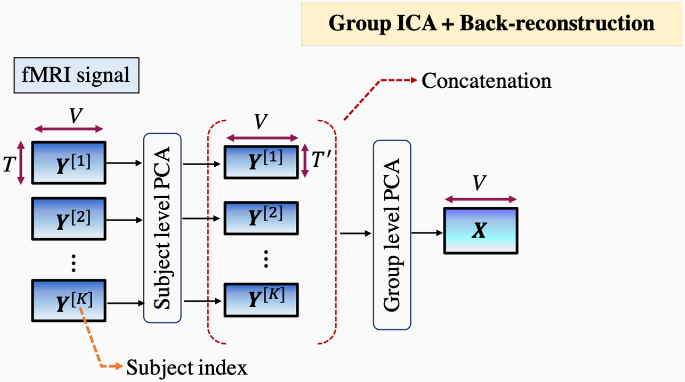

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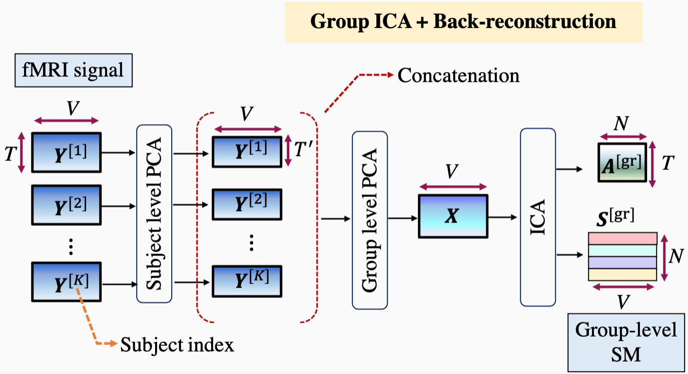

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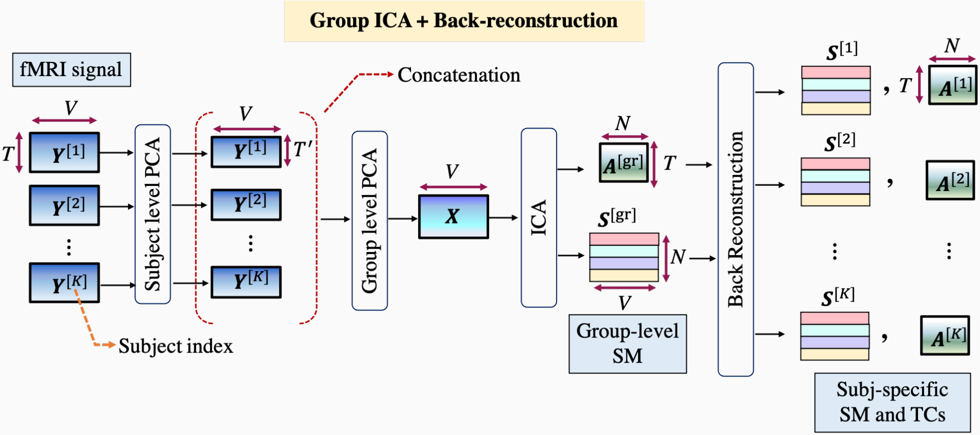

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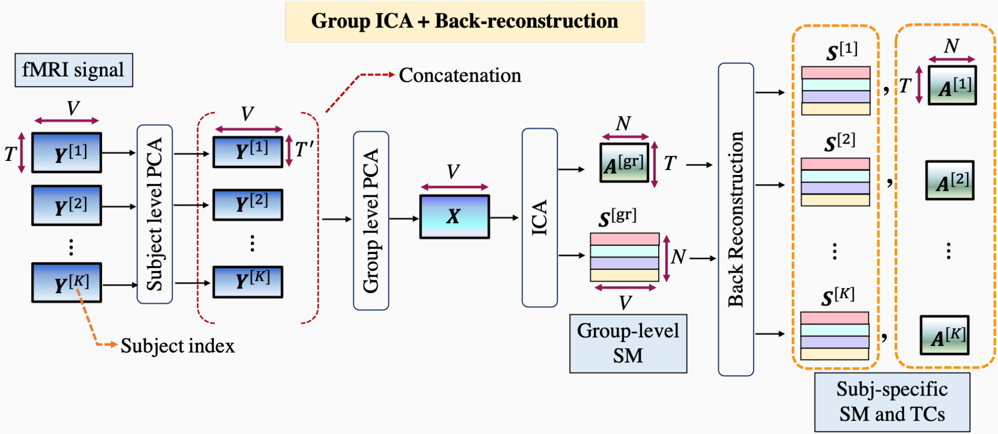
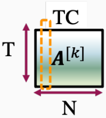


Inter-network relationships are studied through temporal functional network connectivity (tFNC)



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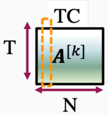

tFNC: Pearson correlations between pairs of time courses (TCs)

tFNC: $(\boldsymbol{A}^{[k]})^T \boldsymbol{A}^{[k]} =$

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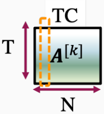

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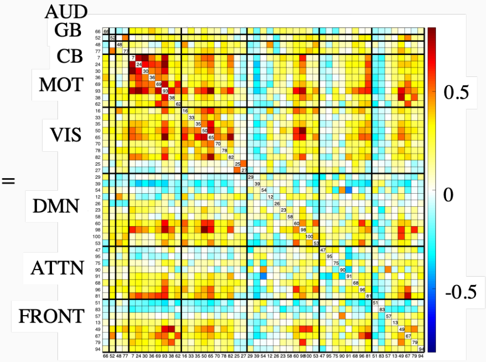

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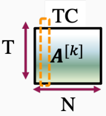

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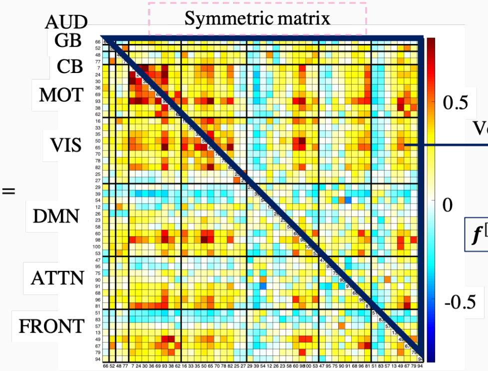

Vectorized upper triangular

$f^{[k]}$: tFNC-feature vector of subject k

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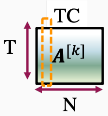

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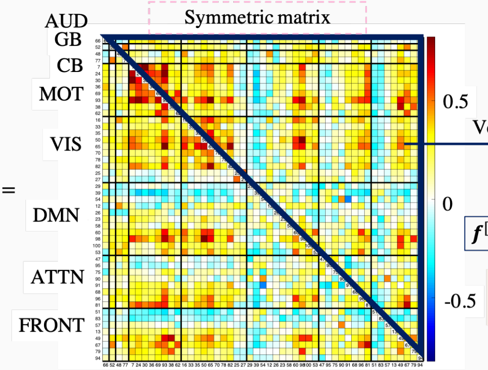

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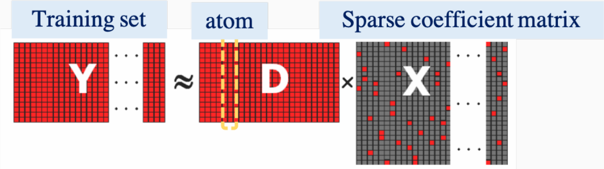
Strength and directionality of inter-network relationships

Sparse dictionary learning for FNC feature extraction



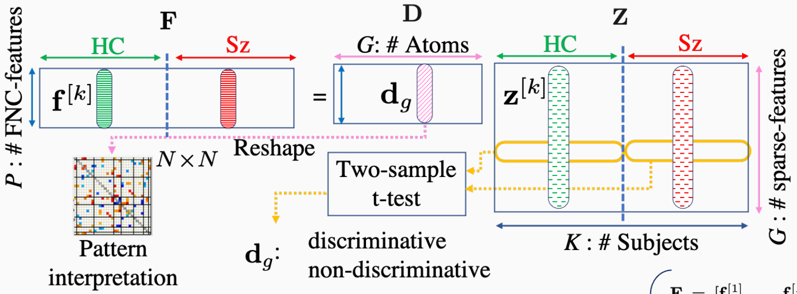
Dictionary learning problem: $\min_{\mathbf{D},\mathbf{X}} \sum_{i=1}^{L} \frac{1}{2}||\mathbf{y}_i - \mathbf{D}\mathbf{x}_i||_2 = \frac{1}{2}||\mathbf{Y}-\mathbf{D}\mathbf{X}||_F^2$ s.t. $\mathbf{D} \in \mathcal{D}$, $\boxed{\mathbf{X} \in \mathcal{X}}$

Alternating Minimization

Start with $(\mathbf{D}^{(0)}, \mathbf{X}^{(0)})$. Alternate between two steps:

1. Sparse representation: $\mathbf{X}^{(k+1)} = \text{argmin}_{\mathbf{X}\in\mathcal{X}} \frac{1}{2}||\mathbf{Y} - \mathbf{D}^{(k)}\mathbf{X}||_F^2$
   - OMP, IST, SL0
2. Dictionary update: $\mathbf{D}^{(k+1)} = \text{argmin}_{\mathbf{D}\in\mathcal{D}} \frac{1}{2}||\mathbf{Y} - \mathbf{D}\mathbf{X}^{(k+1)}||_F^2$
   - MOD, KSVD

Sparse representation of tFNCs can reveal new interpretable patterns and discriminant features



$$
\begin{cases}
\mathbf{F} = [\mathbf{f}^{[1]}, \ldots, \mathbf{f}^{[K]}] \in \mathbb{R}^{P \times K} \\
\mathbf{D} = [\mathbf{d}_1, \ldots, \mathbf{d}_G] \in \mathbb{R}^{P \times G} \\
\mathbf{Z} = [\mathbf{z}^{[1]}, \ldots, \mathbf{z}^{[K]}] \in \mathbb{R}^{G \times K} \\
\mathbf{f}^{[k]} = \sum_{i=1}^{G} z_g \mathbf{d}_g
\end{cases}
$$

Jointly learn a linear classifier and a dictionary for tFNC sparse representation to improve discrimination

Problem formulation

$$\min_{\mathbf{D},\mathbf{Z},\mathbf{W}} \frac{1}{2}\|\mathbf{F}-\mathbf{D}\mathbf{Z}\|_F^2+\lambda\cdot r(\mathbf{Z})+\frac{\beta}{2}\|\mathbf{L}_{\text{tr}}-\mathbf{W}\mathbf{Z}_{\text{tr}}\|_F^2,$$

$$\text{s.t. } \mathbf{D}\in\mathcal{D}:=\{\mathbf{D}:\|\mathbf{d}_g\|_2=1, g=1,2,\dots,G\}.$$

Binary group labels:

$$\begin{cases} \mathbf{L}_{\text{tr}} = [\mathbf{l}_{\text{tr}}^{[1]},\dots,\mathbf{l}_{\text{tr}}^{[K_{\text{tr}}]}] \\ \mathbf{l}^{(\text{HC})} = [0,1]^T \text{ and } \mathbf{l}^{(\text{Sz})} = [1,0]^T \end{cases}$$

Jointly learn a linear classifier and a dictionary for tFNC sparse representation to improve discrimination

Problem formulation

Sparse representation error

$$\min_{\mathbf{D},\mathbf{Z},\mathbf{W}} \frac{1}{2}\overbrace{\|\mathbf{F}-\mathbf{DZ}\|_F^2}+\lambda \cdot r(\mathbf{Z}) + \frac{\beta}{2}\|\mathbf{L}_{\text{tr}} - \mathbf{W}\mathbf{Z}_{\text{tr}}\|_F^2,$$

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Problem formulation

Sparsity promoting function
- convex/non-convex
- Smooth/non-smooth

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Jointly learn a linear classifier and a dictionary for tFNC sparse representation to improve discrimination

Problem formulation

Sparsity promoting function
- convex/non-convex
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Sparse representation error

Linear classifier (only on training set)

$$\min_{\mathbf{D},\mathbf{Z},\mathbf{W}} \frac{1}{2}\overbrace{\|\mathbf{F}-\mathbf{D}\mathbf{Z}\|_F^2}+\lambda\cdot r(\mathbf{Z})+\frac{\beta}{2}\|\mathbf{L}_{\text{tr}}-\mathbf{W}\mathbf{Z}_{\text{tr}}\|_F^2,$$

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Iterative proximal-projection as a flexible approach to a range of sparsity-promoting functions including non-convex and non-smooth

$$
\begin{aligned}
\min_{\mathbf{D},\mathbf{Z},\mathbf{W}} \quad & \frac{1}{2}\|\mathbf{F}-\mathbf{D}\mathbf{Z}\|_F^2 + \lambda \cdot r(\mathbf{Z}) + \frac{\beta}{2}\|\mathbf{L}_{\text{tr}} - \mathbf{W}\mathbf{Z}_{\text{tr}}\|_F^2, \\
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\end{aligned}
$$

1. Perform alternating minimization over $\mathbf{D}$, $\mathbf{Z}$, and $\mathbf{W}$
2. Using iterative proximal-projection approach
   - Flexible to a range of sparsity-promoting functions, including non-convex and non-smooth scenarios

Experimental setup

Data preparation

- Bipolar-schizophrenia network on intermediate phenotypes resting-state fMRI dataset (five sites)
- 179 HC and 179 Sz patients
- To obtain subject-specific tFNC-feature vectors $\mathbf{f}^{[k]}$:
- Group ICA-EBM with order $N = 55$
- Selecting $N = 32$ functionally relevant components

DL setup

- **D** and **W** are initialized with DCT dictionary
- **Z** initialized with a null matrix
- Complete dictionary
- Sparsity level 50%
- Two scenarios:
  - $\beta = 0$: DL without learning a linear classifier
  - $\beta = 0.05$: linear classifier jointly learned with **D**

Jointly learned sparse features improve different classification metrics

- Training SVM classifiers with polynomial kernels of order 3 using tFNC-features and sparse-features
- Repeating the experiment 100 times and reporting the average results

Table 1: Average classification rates [%].

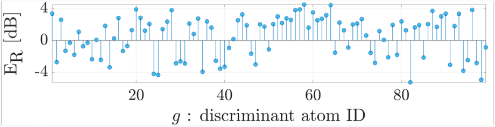
Metric\Feature	tFNC	Sparse ($\beta = 0$)	Sparse ($\beta = 0.05$)
Recall	74.75 ± 0.61	73.56 ± 0.65	**75.19** ± 0.65
Specificity	73.78 ± 0.70	74.14 ± 0.70	**74.47** ± 0.68
Precision	74.35 ± 0.50	74.27 ± 0.53	**74.93** ± 0.51
Accuracy	74.26 ± 0.40	73.85 ± 0.45	**74.83** ± 0.43
F1-score	74.35 ± 0.40	73.72 ± 0.46	**74.87** ± 0.45

- Sparse features outperform tFNC features

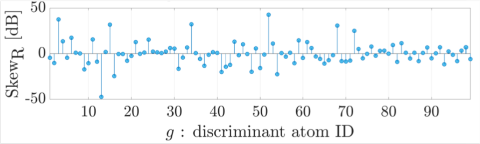
Sparse coefficients give statistics on each atom's contribution

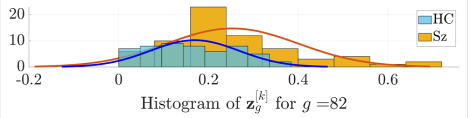
Two-sample t-test on sparse coefficients: 99 atoms discriminate HC and Sz groups

$$E_R = 10\log(||\mathbf{z}_g^{[k_{HC}]}||_2^2/||\mathbf{z}_g^{[k_{Sz}]}||_2^2)$$



$$\text{Skew}_R = 10\log(|\text{skew}(\mathbf{z}_g^{[k_{HC}]})|/|\text{skew}(\mathbf{z}_g^{[k_{Sz}]})|)$$





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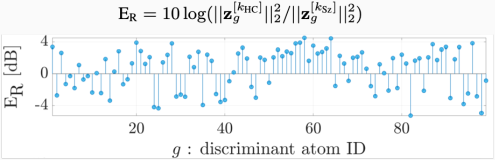
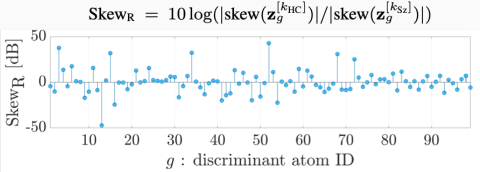
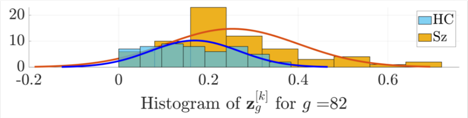


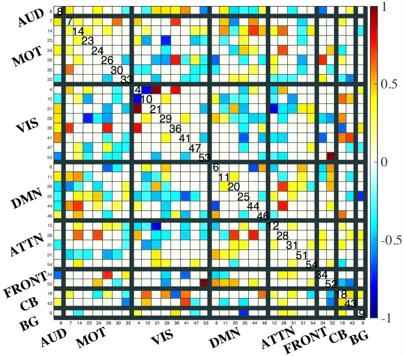




- Atoms with energy ratios $E_R > 0$ are dominant in HC, and atoms with $E_R < 0$ are dominant in Sz
- Skewness differs in one group compared with the other

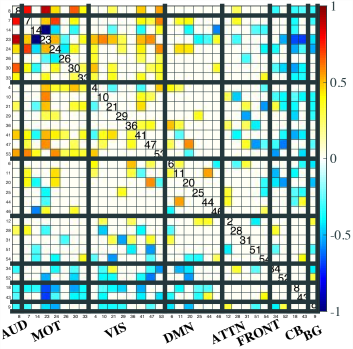
Discriminant atoms are interpretable

- Reshaped discriminant atoms reveal different network interaction patterns in HC and Sz.



$\sum_g \bar{\mathbf{z}}_g^{[\mathrm{Sz}]}$ for g's dominant in Sz

- Less structured
- With extreme values



$\sum_g \bar{\mathbf{z}}_g^{[\mathrm{Sz}]}$ for g's dominant in HC

- More modularity
- More anatomical organization

Conclusion and perspectives

- Sparse representation of brain temporal functional network connectivity (tFNC) is presented
- A dictionary and linear classifier were jointly learned to classify HC and Sz subjects using sparse coefficients
- Sparse features improved classification and identified new discriminative patterns in brain network interaction
- The approach offers new perspectives to study fMRI dynamics and can be extended to multiple fMRI datasets
- A non-linear classifier learned with the dictionary can improve classification rates

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