Independent Vector Analysis Based Subgroup Identification from Multisubject fMRI data

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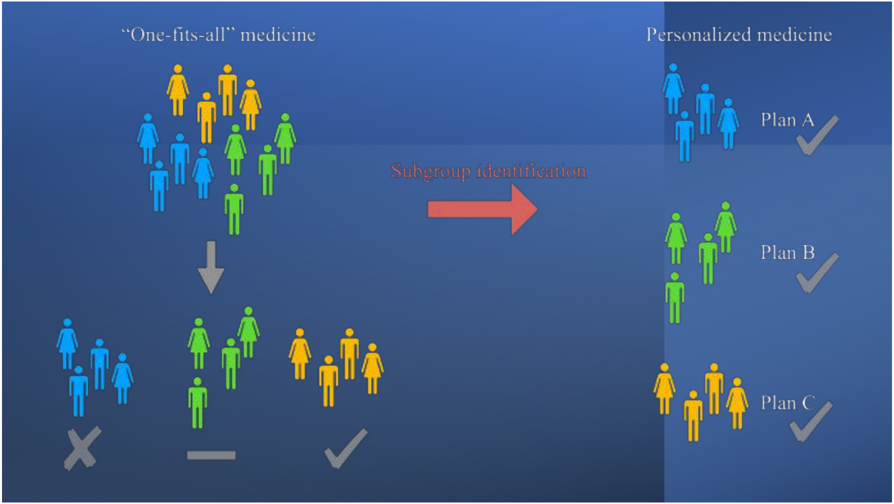
Subgroup identification is the key for personalized medicine



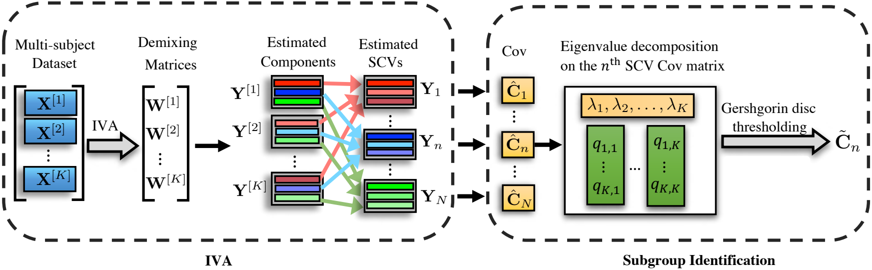
Subgroup identification is the key for personalized medicine

- Individual variability in brain functional networks are fingerprints of identifying subjects [*Finn et al., 2015*]
- Subgroup shows homogeneity

Current methods are limited by multiple factors

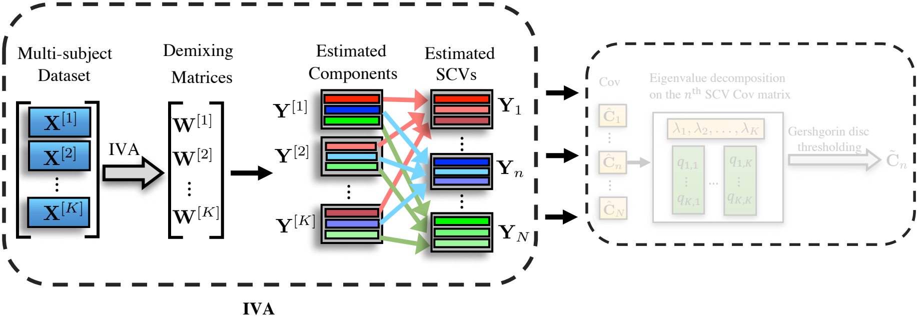
- Identify subgroups with behavioral variables, clinical, cognitive or other related scores [*Bitsika et al., 2008*], [*Veatch et al., 2014*]
- Apply independent component analysis (ICA) on individual subject fMRI data – missing multivariate information across subjects [*Durieux et al., 2019*]
- Apply independent vector analysis (IVA) to multisubject fMRI data – relying on user-defined parameters [*Long et al., 2020*]

Proposed method: subgroup identification using independent vector analysis (SI-IVA)



- SI-IVA:
  - ✓ captures subgroup structures
  - ✓ estimates the number of subgroups in each SCV
  - ✓ identifies the corresponding subjects in each subgroup

SI-IVA estimates correlated components across subjects



- Generative model: $\mathbf{X}^{[k]} = \mathbf{A}^{[k]}\mathbf{S}^{[k]}$
- Demixing matrices $\mathbf{W}^{[k]}$, and estimated signals $\mathbf{Y}^{[k]} = \mathbf{W}^{[k]}\mathbf{X}^{[k]}$
- source component vectors (SCV), $\mathbf{Y}_n = [\mathbf{y}_n^{[1]}, \mathbf{y}_n^{[2]}, \ldots, \mathbf{y}_n^{[K]}]^\top \in \mathbb{R}^{K\times V}$

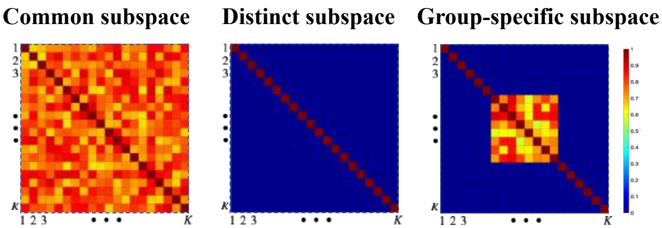
[Kim *et al.*, 2006], [Anderson *et al.*, 2012]

Individual SCV preserves the correlation structure of a component across subjects

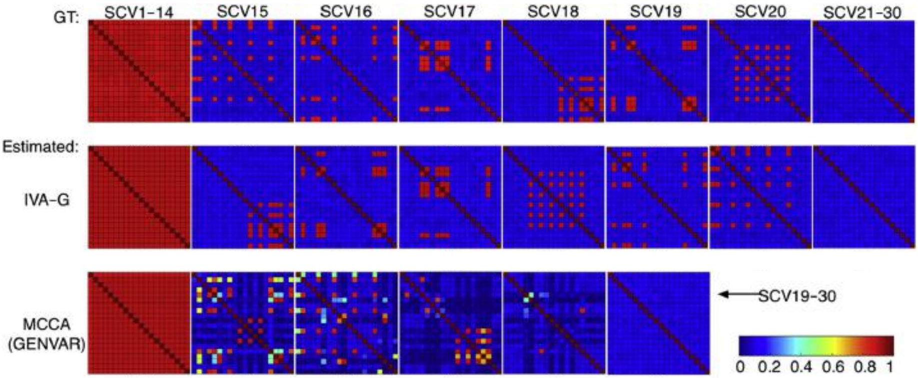
- Sample covariance matrix of n^{th} SCV: $\hat{\mathbf{C}}_n = \begin{bmatrix} 1 & \rho_n^{[1,2]} & \cdots & \rho_n^{[1,K]} \\ \rho_n^{[2,1]} & 1 & \cdots & \rho_n^{[2,K]} \\ \vdots & \vdots & \ddots & \vdots \\ \rho_n^{[K,1]} & \rho_n^{[K,2]} & \cdots & 1 \end{bmatrix} \in \mathbb{R}^{K \times K}$

  $\rho_n^{[k_1,k_2]}$ is the correlation between k_1^{th} and k_2^{th} subjects of n^{th} component

- SCVs construct three subspaces:

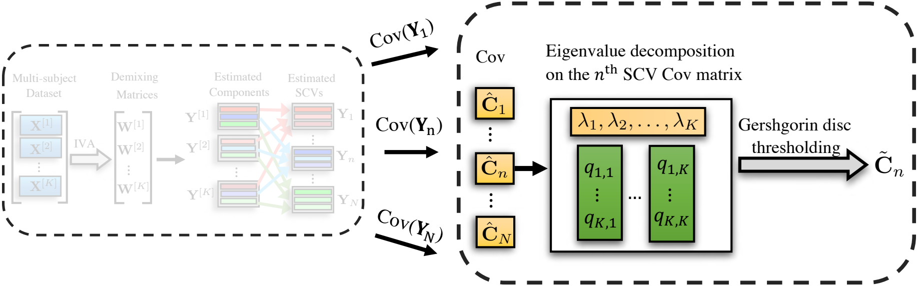


IVA-G preserves correlation structures effectively



[Long *et al.*, 2020], [Anderson *et al.*, 2012]

SI-IVA identifies subgroup structures

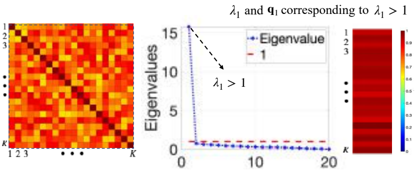


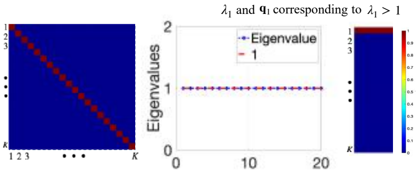
Subgroup Identification

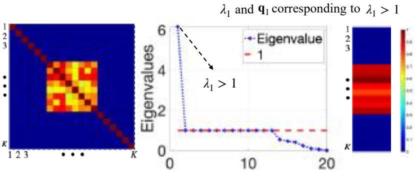
- Decompose each $\hat{\mathbf{C}}_n = \mathbf{Q}\mathbf{D}\mathbf{Q}^{\mathsf{T}}$
- Estimates the number of subgroups from SCVs, $\mathbf{Y}_1 \ldots \mathbf{Y}_N$
- Identify subjects that are correlated within a SCV, $\rho_n^{[k_1,k_2]} \neq 0$

Eigenvalues and eigenvectors of $\hat{c}_n$ reveal subgroups

- $\#(\lambda > 1) \rightarrow \#$ subgroups
- $q_{k,1} \neq 0 \in \mathbf{q}_1 \rightarrow$ subject index







The variation in eigenvalues can lead to overestimation of subgroups

[Hasija *et al.*, 2020], [Akhonda *et al.*, 2021]

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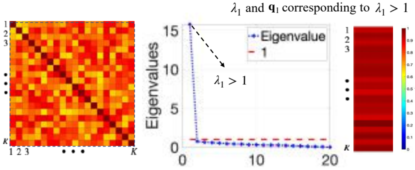

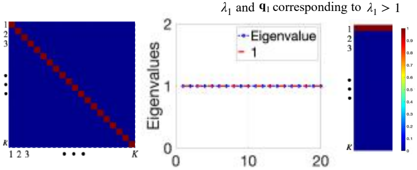

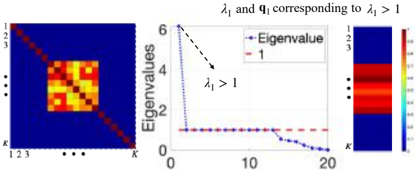

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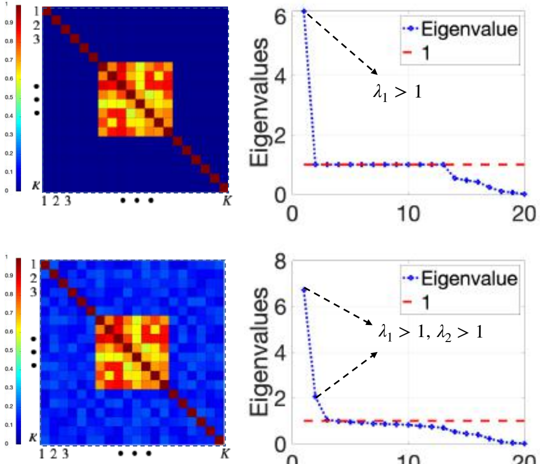
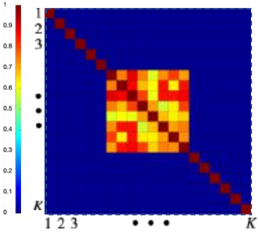
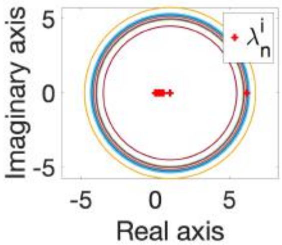


Gershgorin disc transforms eigenvalues' variation

- Gershgorin disc: $\left\{z \in \mathbb{R} : \left|z - \rho_n^{[i,i]}\right| \leq R_i\right\}$, where $R_i = \sum_{j \neq i} \left|\rho_n^{[i,j]}\right|$
- $\text{eig}(\hat{\mathbf{C}}_n) \in \bigcup_{i=1}^{K} \left\{z \in \mathbb{R} : \left|z - \rho_n^{[i,i]}\right| \leq R_i\right\}$
- Gershgorin discs of $\hat{\mathbf{C}}_n$ are located at (1,0)





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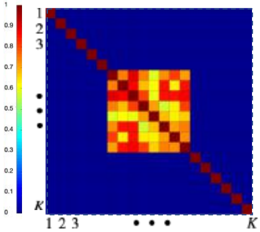

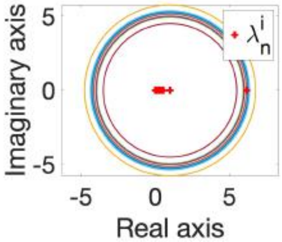

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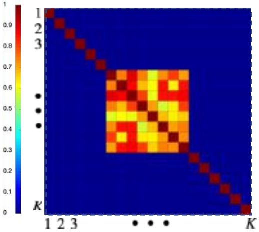
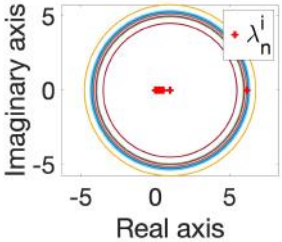
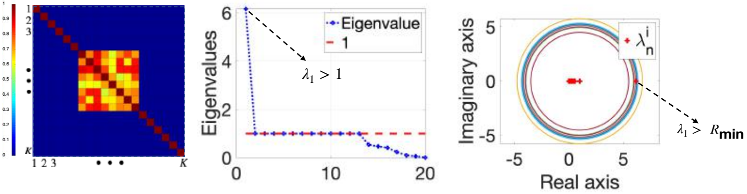




Gershgorin disc solves the overestimating issue

- Instead of looking for eigenvalues $\lambda > 1$, SI-IVA looks for $\lambda > (R_{\min} + 1)$

- Eigenvalue decomposition with Gershgorin disc (EGD) incorporates eigenvalue decomposition with hard thresholding (EHT)



- EGD solves the overestimating issue that is caused by hard thresholding

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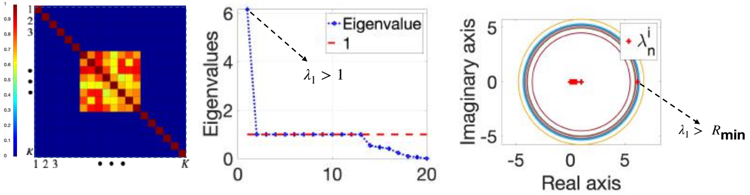

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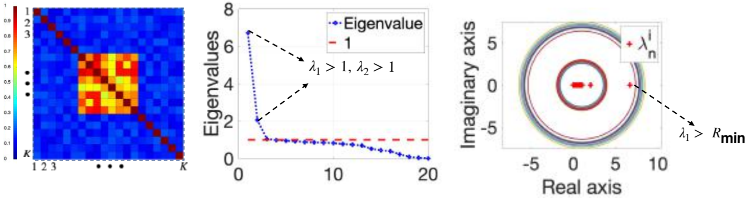
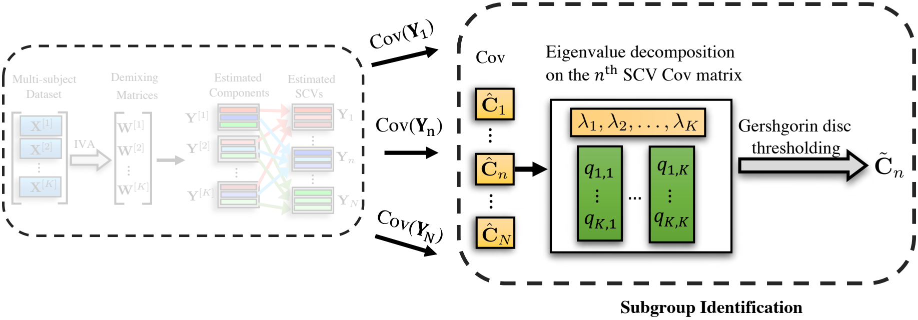
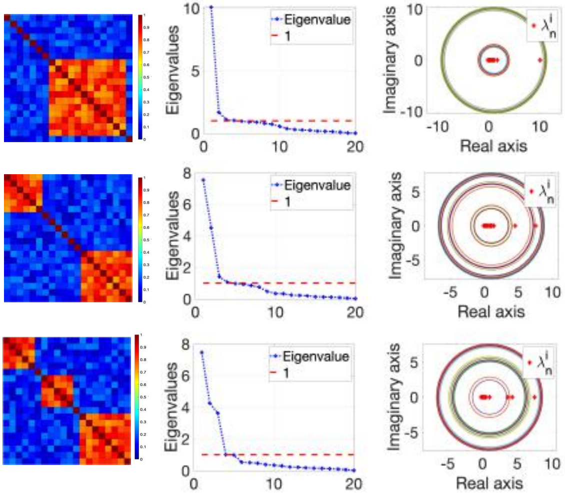


SI-IVA: Identification of subgroup structure



- # $(\lambda_n^1 \ldots \lambda_n^M) > (R_{min} + 1) \rightarrow$ # subgroups
- $\mathbf{q}_n^1 \ldots \mathbf{q}_n^M \rightarrow$ subject index

Simulation: EGD predicts correct number of subgroups



- $\rho_c \sim \mathcal{U}[0.7, 0.9]$, $\rho_d \sim \mathcal{U}[0.05, 0.25]$
- SCVs: MGGD, $\beta \sim \mathcal{U}[0.1, 0.8]$

SI-IVA identifies subgroup structures with multisubject resting-state fMRI data

- 50 schizophrenia patients' resting-state fMRI data were collected from the Center of Biomedical Research Excellence (COBRE) (https://coins.trendscenter.org)
- IVA-G was implemented with order number as 85
- Cross intersymbol interference (Cross-ISI) was used to select the most consistent run for 10 runs with random initialization [Long and Jia et al., 2018]

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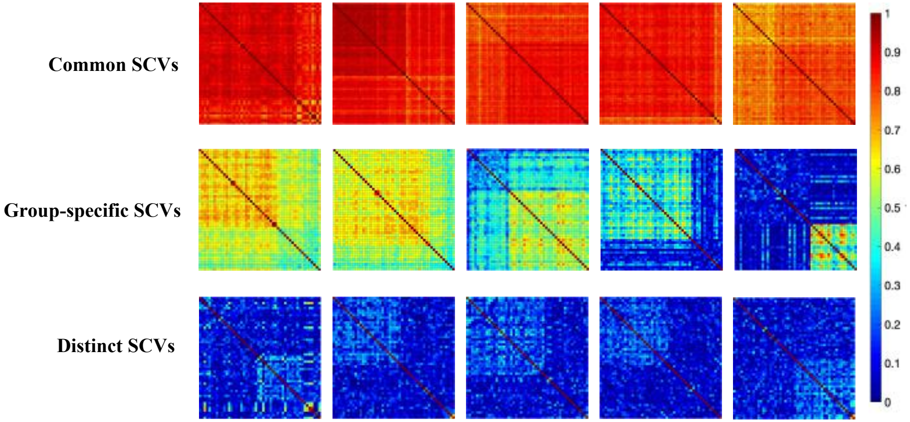
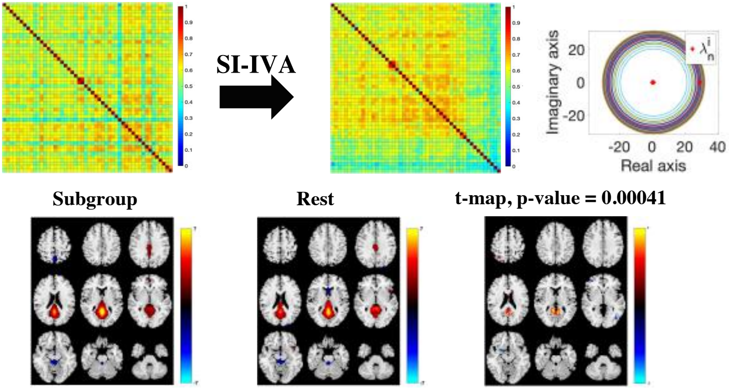


SI-IVA identifies subgroup structures with multisubject resting-state fMRI data

- Mean components are thresholded at $Z = 2$
- Two-sample t-test used to identify the discriminative components ($p < 0.05$)



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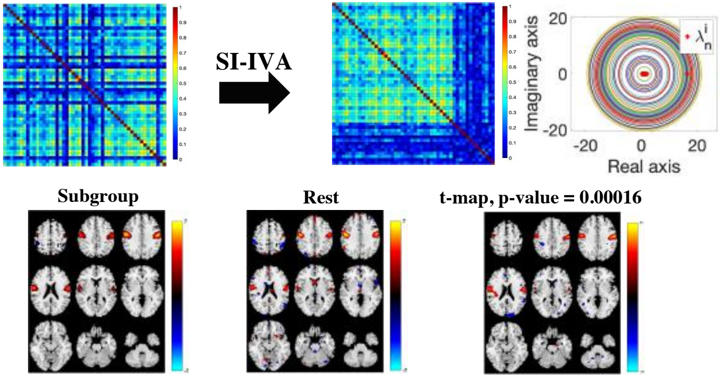

Summary

SI-IVA

- identifies subgroup structures
- yields meaningful components and subgroups
- requires no user-defined parameters
- can be adopted to other multi-set data

Acknowledgements

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