Dynamic dictionary entries are rank-1 functional connectivity networks associated with maturation

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Introduction: challenges and goals

Challenges

- fMRI data usually has very high feature dimension but small sample size
- For instance, using a 264-region template, a subject's functional connectivity (FC) contains 34,716 unique entries; in contrast, most fMRI studies recruit fewer than 30 subjects
- FC captures pairwise relationships between two regions, and not network-level relationships
- FC captures the average connectivity over time and does not reveal brain state dynamics

Goals

1. **Network-Level Differences** Identify differences at the level of networks and not individual FCs
2. **Dynamic States** Find representative states that make up the dynamic chronnectome and correlate with age, sex, ethnicity, and general intelligence
3. **Better Performance** Perform as well as or better at phenotype prediction than traditional decompositions such as PCA and kSVD

Background on fMRI and functional connectivity

- fMRI is an endophenotype that has been used to predict age, sex, intelligence, and disease status
- The most common way to interpret fMRI for prediction is through functional connectivity (FC)
- FC is the Pearson correlation between the BOLD signal of different brain regions

Dynamic dictionary formulation

The problem is formulated as estimating the instantaneous rank-1 FC of a subject at each time point:

$$\mathbf{S}^{(t)} = \mathbf{X}_{:,t}\mathbf{X}_{:,t}^{\top}, \tag{1}$$

where $\mathbf{X} \in \mathbb{R}^{N_d \times N_t}$ is a data matrix of N_d ROIs by N_t time points, and $\mathbf{S}^{(t)}$ is the true instantaneous FC at time t. A dictionary is constructed as:

$$\mathcal{D} = \{\mathbf{a}\mathbf{a}^{\top} \mid \mathbf{a} \in \mathbb{R}^{N_d \times 1}\}, \qquad \hat{\mathbf{S}}^{(s,t)} = \sum_{i=0}^{N_c} w_i^{(s,t)} \mathcal{D}_i, \tag{2}$$

where $\mathcal{D}$ is the FC dictionary, $N_c = |\mathcal{D}|$ is the number of dictionary components, $\mathcal{D}_i = \mathbf{a}\mathbf{a}^{\top}$ is the i^{th} rank-1 connectivity component, $w_i^{(s,t)}$ is a learned weight, and $\hat{\mathbf{S}}^{(s,t)}$ is the estimated FC for subject s at time t.

We perform training on a subset of subjects. Reconstruction loss is minimized along with a smoothness-promoting regularizer α inspired by time-varying graphical Lasso. Weights are constrained to be non-negative.

$$\min_{\mathcal{D}, w_i^{(s,t)}} \Big(\sum_{s,t} ||\mathbf{S}^{(s,t)} - \hat{\mathbf{S}}^{(s,t)}||_F^2 + \alpha \sum_{s,t} ||\hat{\mathbf{S}}^{(s,t)} - \hat{\mathbf{S}}^{(s,t-1)}||_F^2 \Big) \quad \text{s.t.} \quad w_i^{(s,t)} \geq 0, \tag{3}$$

Finally, we estimate component weights $w_i^{(s,t)}$ for all subjects using L2 penalized least squares. The resulting estimated dynamic FC is averaged for predictive tasks.

Dataset

Philadelphia Neurodevelopmental Cohort (PNC)

- fMRI scans for 1,529 healthy adolescents, three scanner tasks: rest, nback, and emoid (4,343 total scans)
- 8-23 years old, 725 males, 804 females
- Dataset enriched for European (EA) and African (AA) ancestry
- fMRI bandpass filtered and **timeseries normalized to L2 norm of 1**

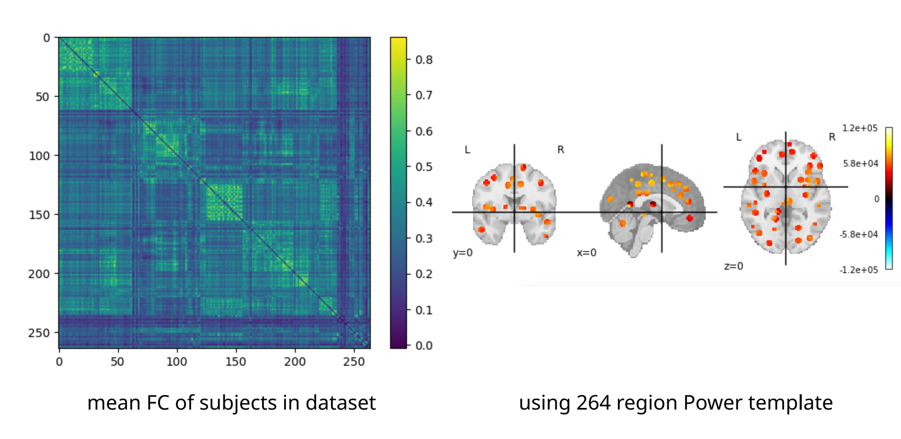

Figure 1. Mean FC of subjects in the PNC cohort, alongside the 264-region Power template used to parcellate normalized subject brain volumes.

Age prediction results

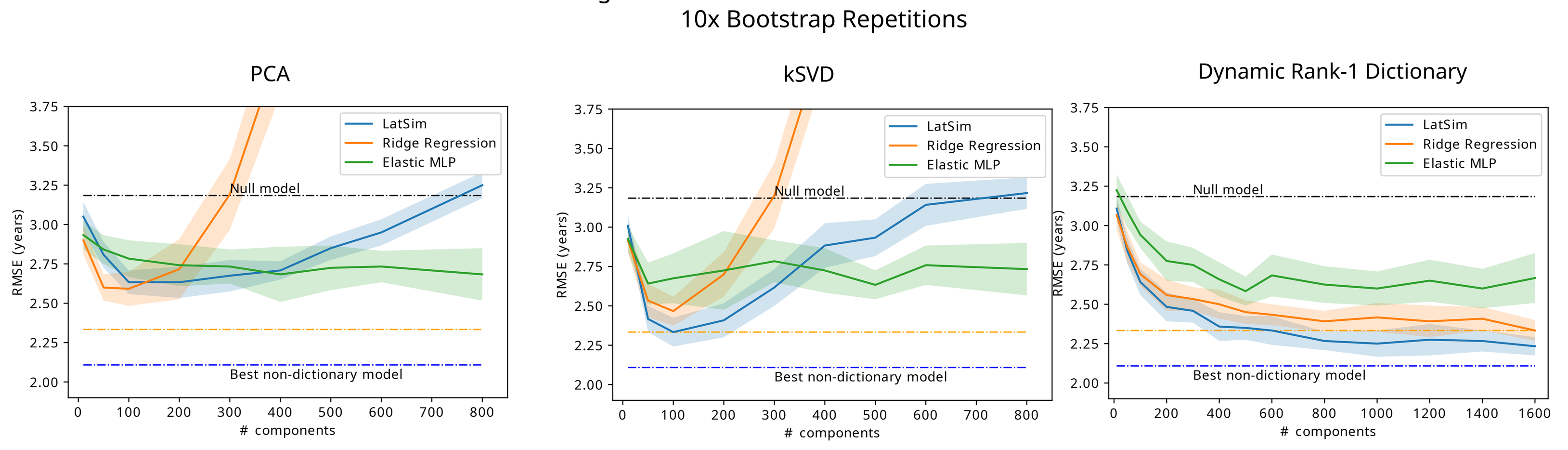

Figure 2. Comparison of age prediction error after dimensionality reduction by PCA, kSVD, and our dynamic rank-1 dictionary. Prediction was carried out using ridge regression, elastic MLP, and our Latent Similarity model.

Connectivity in children vs young adults

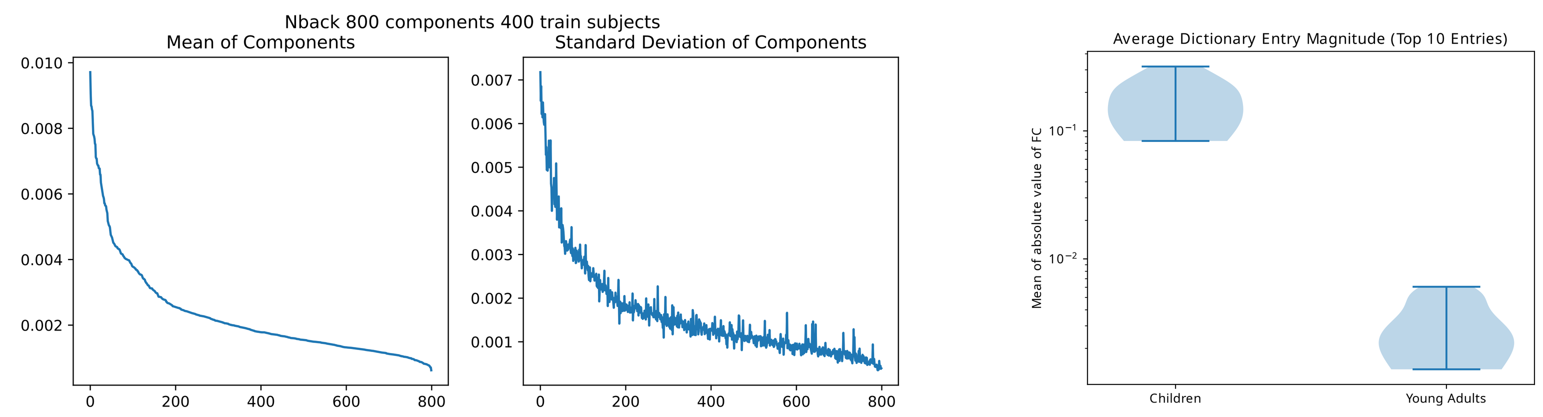

Figure 3. Weight magnitude distribution for each component (left) and within-component average FC for top components associated with children vs. young adults (right). We see that children have much higher average connectivity than young adults; see also Figure 4.

Correlation of dictionary entries with phenotype

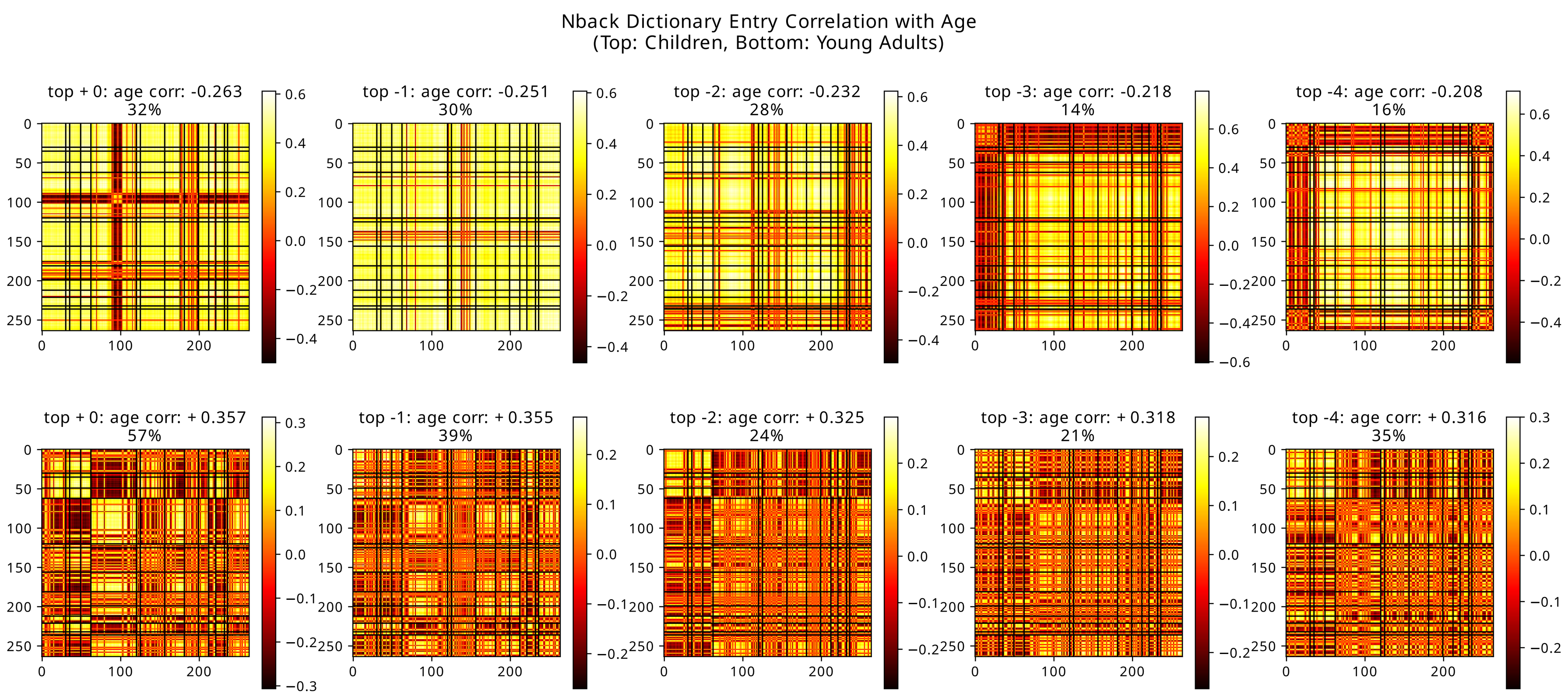

Figure 4. Correlation of dictionary entries with age. Working memory (nback) task. Note the scale of the colorbars: components correlated with young age have much higher average connectivity.

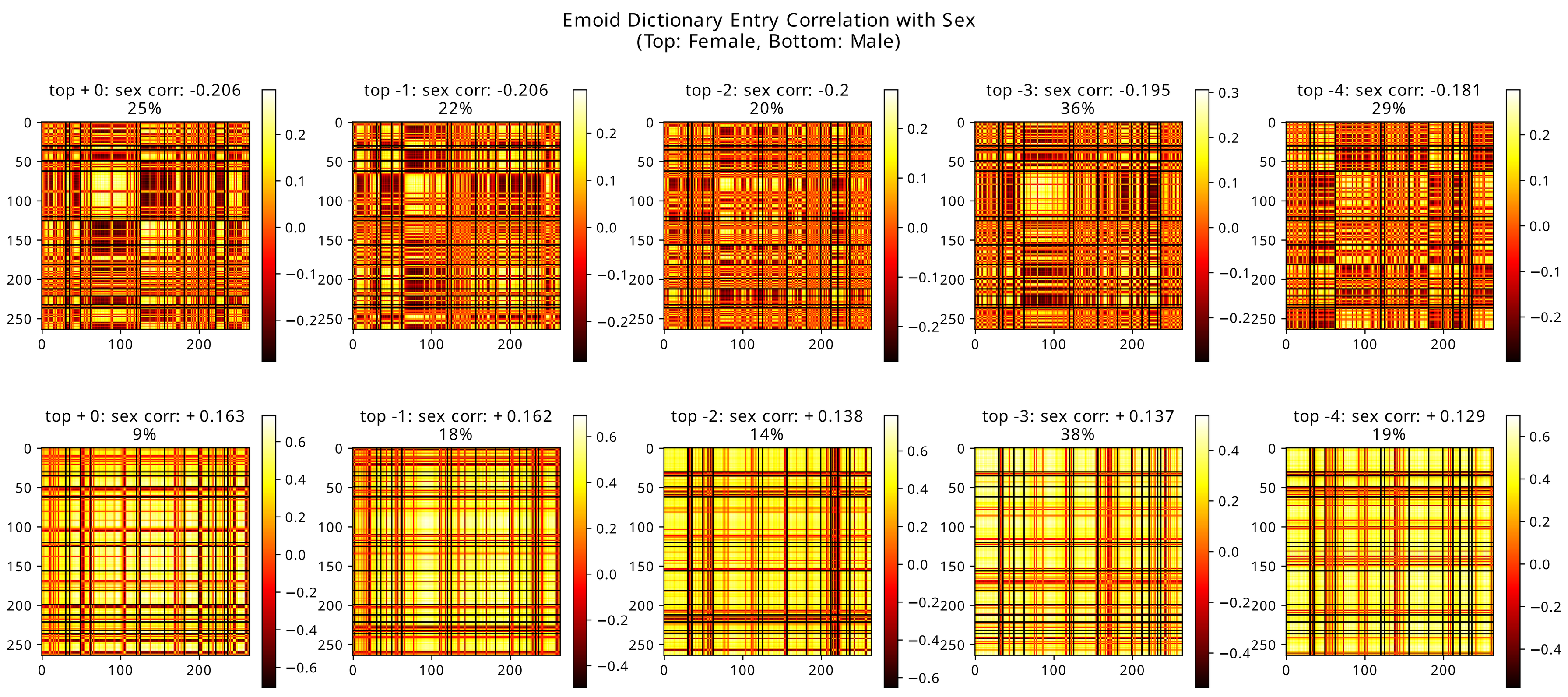

Figure 5. Correlation of dictionary entries with sex. Emotion identification (emoid) task. Note the high intra-DMN connectivity in females and flat, high magnitude connectivity in males.

Functional Networks

ROIs		ROIs	
0-29	Somatomotor Hand	156-180	Frontoparietal
30-34	Somatomotor Mouth	181-198	Salience
35-48	Cinguloopercular	199-211	Subcortical
49-61	Auditory	212-220	Ventral Attention
62-119	Default Mode (DMN)	221-231	Dorsal Attention
120-124	Memory	232-235	Cerebellar
125-155	Visual	236-263	Uncertain

Phenotype Signal in Dynamic Dict

Phenotype	Min Entry Corr	Max Entry Corr	Scanner Task
Age	-0.263	+0.357	nback
Sex	-0.206	+0.163	emoid
Race	-0.246	+0.198	emoid
Intelligence	-0.151	+0.159	nback

Table 1. Power atlas regions (left) and minimum/maximum correlation of components with phenotype (right) - higher absolute values indicate stronger signal.

Summary of findings

- Dynamic dictionary decomposition has somewhat **better prediction** compared to PCA and kSVD
- Our decomposition does not suffer from the **U-shaped error curve**, as seen with PCA and kSVD (see Figure 2).
- Components associated with males and children have **much higher average connectivity** and the connectivity is constant for almost connections
- Young adult and female-associated components display **higher modularity**, in particular **high intra-DMN connectivity**