Coupled Harmonic Bases for Longitudinal Characterization of Brain Networks

Seong Jae Hwang   Nagesh Adluru   Maxwell D. Collins   Sathya N. Ravi   Barbara B. Bendlin   Sterling C. Johnson   Vikas Singh

http://pages.cs.wisc.edu/~sjh

THE UNIVERSITY of WISCONSIN MADISON

Objective

Characterize evolution of brain networks over ordinal cognitive scores via harmonic bases coupling.

Motivation: Longitudinal + Cross-sectional Evolutions

- Increasing interest in **characterizing disease progressions** in 2 directions:
  1. **Longitudinal:** individual brain network evolves/ages over **multiple time points/visits**, potentially by disease progression.
  2. **Cross-sectional:** set of brain networks shows progressive patterns over **disease-related covariates** (i.e., cognitive test scores).
- **Need: Characterize individual brain connectivity evolutions while preserving variances (i.e., cognitive healths) among subjects.**

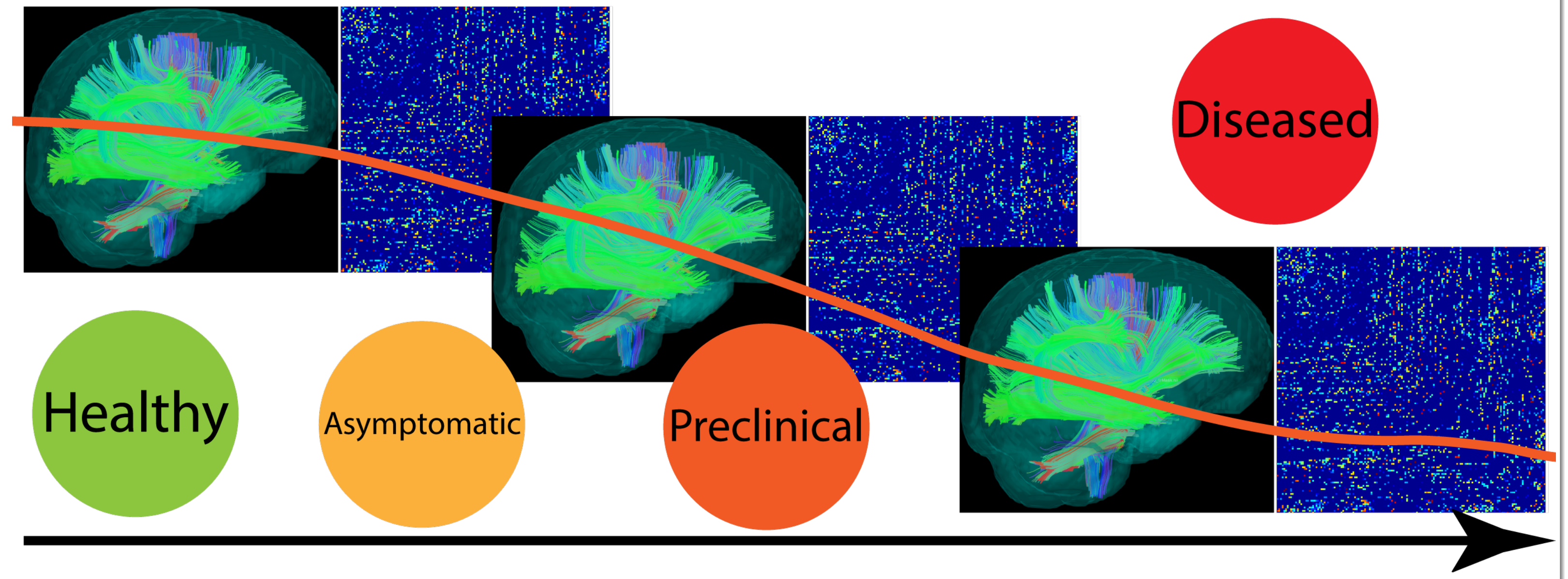

Figure: Brain connectivity evolves as the cognitive stage changes from healthy to diseased.

Parameterizing Brain Networks as Harmonic Bases

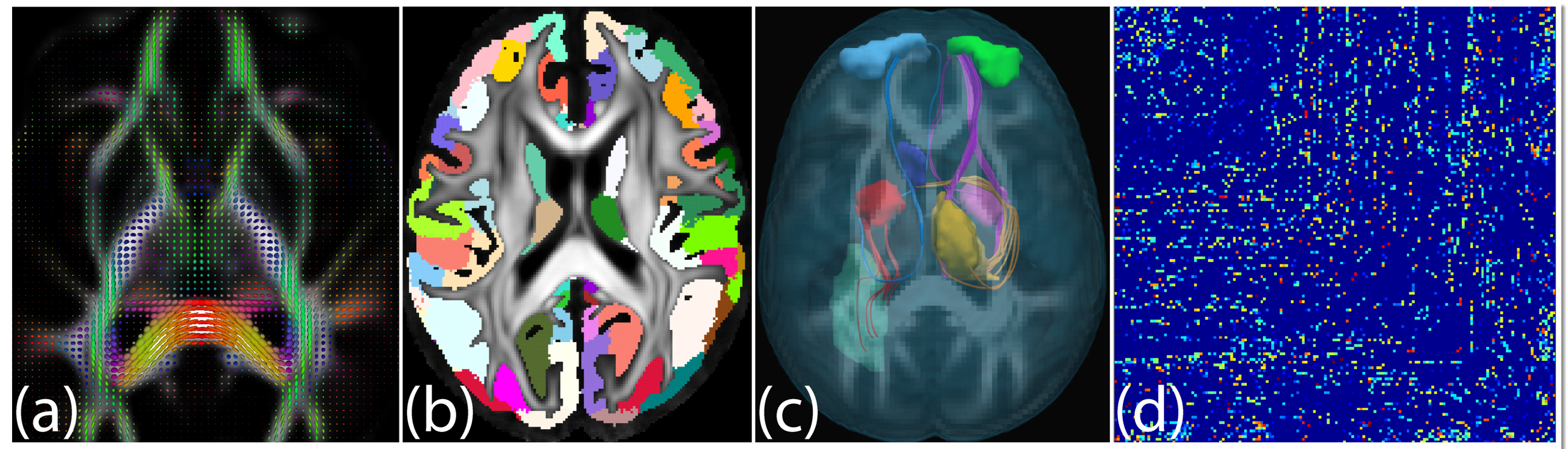

Figure: **From brain image to adjacency matrix:** (a) Diffusion tensor ellipsoids from dMRI. (b) Gray matter regions as meaningful graph nodes. (c) Fiber tracts (axonal pathways between brain regions) estimated via tractography as graph edges between gray matter nodes. (d) Symmetric adjacency matrix representation of the graph.

- Derive adjacency matrix $A_{n\times n}$ from brain image data.
- Construct graph Laplacian $L_{n\times n}$ with degree matrix $D_{n\times n}$:

$$L = D - A, \quad D(i,i) = \sum_{j=1}^{n} A(i,j)$$

- Find p smallest eigenvalues and its set of eigenvectors $V_{n\times p}$ as 'low frequency' bases of L:

$$\min_{V\in\mathbb{R}^{n\times p}} \operatorname{tr}(V^T L V), \quad \text{s.t. } V^T V = I \tag{1}$$

- **Finally, for longitudinal data of N subjects at T time points, find $V_{[i,j]}$ for each $L_{[i,j]}$:**

$$\min_{V_{[i,j]}\in\mathbb{R}^{n\times p}} \sum_{i=1}^{N}\sum_{j=1}^{T} \operatorname{tr}(V_{[i,j]}^T L_{[i,j]} V_{[i,j]}), \quad \text{s.t. } V_{[i,j]}^T V_{[i,j]} = I, \tag{2}$$

Evolution of Real Fiber Tracts derived from Coupled Harmonic Bases

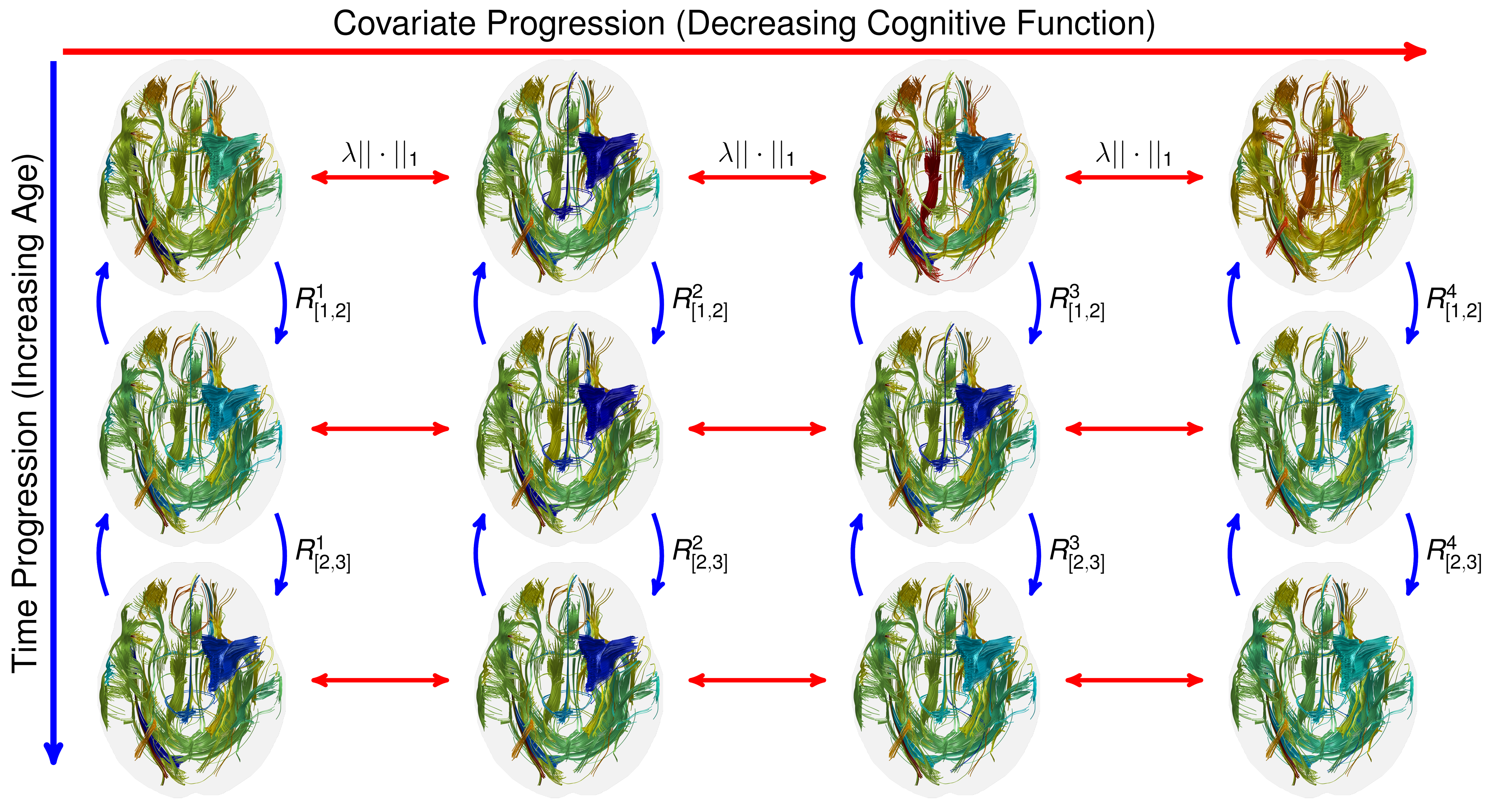

Figure: **The evolution of top 50 most changing fiber tracts of the real data derived from the coupled harmonic bases.** The tract colors represent their strong (blue) and weak (red) connectivity strengths. Cross-sectional coupling (red arrows) via ℓ_1-norm in each row. Longitudinal coupling (blue arrows) via rotation constraints in each column.

Longitudinal Coupling via Mass Matrix

- Temporally consecutive bases differ only by a small degree of *rotation*.
- Align $V_{[\bullet,j]}$ at time j and $V_{[\bullet,j+1]}$ at time $j+1$ using $R^{\bullet}_{[j,j+1]} \in \mathbb{SO}(n)$:

$$V_{[\bullet,j+1]} = R^{\bullet}_{[j,j+1]} V_{[\bullet,j]}. \tag{3}$$

- Forward and backward relationship between $V_{[\bullet,j]}$ and $V_{[\bullet,j+1]}$ allows:

$$V_{[\bullet,j]}^T V_{[\bullet,j]} = V_{[\bullet,j]}^T R^{\bullet}_{[j+1,j]} V_{[\bullet,j+1]} = I, \qquad V_{[\bullet,j+1]}^T V_{[\bullet,j+1]} = V_{[\bullet,j+1]}^T R^{\bullet}_{[j,j+1]} V_{[\bullet,j]} = I. \tag{4}$$

- Multiplying the above two equations we have

$$\left(V_{[\bullet,j]}^T R^{\bullet}_{[j+1,j]} V_{[\bullet,j+1]}\right)\left(V_{[\bullet,j+1]}^T R^{\bullet}_{[j,j+1]} V_{[\bullet,j]}\right) = I$$
$$\implies V_{[\bullet,j]}^T \underbrace{\left(R^{\bullet}_{[j+1,j]} V_{[\bullet,j+1]} V_{[\bullet,j+1]}^T R^{\bullet T}_{[j+1,j]}\right)}_{M'_{[j+1,j]}} V_{[\bullet,j]} = I.$$

- Accounting for both $j-1$ and $j+1$ relations, compute the *mass matrix* for $V_{[\bullet,j]}$ as

$$M_{[\bullet,j]} = \frac{M'_{[j-1,j]} + M'_{[j+1,j]}}{2}. \tag{5}$$

- Enforce the **longitudinal coupling** as a new constraint on $V_{[\bullet,j]}$ using (5) for the initial problem formulation (2):

$$V_{[\bullet,j]}^T M_{[\bullet,j]} V_{[\bullet,j]} = I. \tag{6}$$

Cross-sectional Coupling via Sparsity Constraint

- Partition N subjects into K distinct groups (columns in above figure) based on their covariates (i.e., cognitive scores).
- i.e., average Laplacians of three consecutive groups: $X_{[i-1,\bullet]}$, $X_{[i,\bullet]}$ and $X_{[i+1,\bullet]}$.
- Their corresponding eigenvectors are $V_{[i-1,\bullet]}$, $V_{[i,\bullet]}$ and $V_{[i+1,\bullet]}$.
- The partitions consist of disjoint/distinct groups of subjects, so we *cannot* assume a homological relationship (i.e., rotation) between them.
- **Cross-sectional coupling** via ℓ_1-norm constraint on the difference of the bases into the initial problem formulation (2):

$$g(V_{[i,\bullet]}) = \lambda\left(||V_{[i-1,\bullet]} - V_{[i,\bullet]}||_1 + ||V_{[i,\bullet]} - V_{[i+1,\bullet]}||_1\right) \tag{7}$$

Combining Longitudinal + Cross-sectional Coupling

- **Extending the initial formulation (2) to enforce both longitudinal (5) and cross-sectional (7) coupling to obtain the final formulation:**

$$\min_{V_{[i,j]}} \sum_{i=1}^{K}\sum_{j=1}^{T} \operatorname{tr}(V_{[i,j]}^T X_{[i,j]} V_{[i,j]}) + \lambda \sum_{i=1}^{K-1}\sum_{j=1}^{T} ||V_{[i+1,j]} - V_{[i,j]}||_1$$
$$\text{s.t.} \quad V_{[i,j]}^T M_{[i,j]} V_{[i,j]} = I; \quad V_{[i,j]} \in \mathbb{R}^{n\times p}.$$

Algorithms

- **For each time point i and partition j:** Stochastic block coordinate descent algorithm to solve for each basis $V_{[i,j]\in\mathbb{R}^{n\times p}} \in \mathrm{GF}_{n,p}(M)$.

Algorithm 1 Stochastic block coordinate descent in $\mathrm{GF}_{n,p}$

```
Given: f : GF_{n,p} → ℝ, V ∈ GF_{n,p}(M), M ∈ ℝ^{n×n}
while Convergence criteria not met do
    S := Subproblem row indices
    P_0 := Initial feasible submatrix
    G := Subdifferential of f w.r.t. P_0
    W := Descent curve in the direction of −G on GF_{s,p}(M_SS) at P_0
    τ := Step size under strong Wolfe conditions
    P := Feasible point W(τ) of subproblem with sufficient decrease in f
    V′(P) := Update new feasible point
end while
```

- **For all T time points and K partitions:** Alternating SBCD (**Algorithm 1**) framework to iteratively find all coupled bases.

Algorithm 2 Coupled bases framework using SBCD

```
Given: f : GF_{n,p} → ℝ, V_[:,:] ∈ GF_{n,p}(M_[:,:]), M_[:,:] ∈ ℝ^{n×n}
while Convergence criteria not met do
    for i = 1, ..., K do
        for j = 1, ..., T do
            V_[i,j] := Free variable
            V_[i,j] := SBCD(V_[i,j]) (Alg. 1)
        end for
        for j = 1, ..., T do
            R_[i,j] := Rotation matrix (3)
        end for
        for j = 1, ..., T do
            M_[i,j] := Mass matrix (6)(5)
        end for
    end for
end while
```

Experiments and Results

- **Data: Preclinical Alzheimer's Disease (AD) Dataset**
  - 89 middle-aged subjects at risk for Alzheimer's disease with ***very subtle*** AD related brain changes.
  - **Three time points** $T = 3$ with **two cognitive test scores**: Rey Auditory Verbal Learning Test (RAVLT) and Mini Mental State Exam (MMSE).
- **Experiment setup: cognitive progression prediction**
  - Coupled bases modeling **(training)**: 68 subjects
    1. Group the subjects into $P \in \{2,3,4\}$ partitions and find average graph Laplacians $X_{[i,j]}$ for each partition i and time point j.
    2. Compute coupled harmonic bases $V_{[i,j]}$ for each $X_{[i,j]}$ using **Algorithm 1**.
  - Cognitive progression prediction **(testing)**: 21 subjects (separate from training subjects)
    1. For each subject, compute its non-coupled bases $V'_{n\times p}$.
    2. Find the closest (ℓ_1 distance) **training** coupled bases $V_{[i,j]}$.
    3. Predicted partition (cognitive progression) $j' \leftarrow$ partition j of $V_{[i,j]}$
- **Partition (Cognitive Progression) Prediction Results:**

K	Non-coupled		Longitudinal		Cross-section		Coupled	
	j=1	{1,2,3}	1	{1,2,3}	1	{1,2,3}	1	{1,2,3}
R:2	33.33	34.92	42.86	42.86	66.67	60.32	**71.43**	**71.43**
R:3	38.10	33.33	52.38	36.51	57.14	44.44	**57.14**	**55.56**
R:4	28.57	28.57	23.81	30.16	30.16	23.81	**47.62**	**34.92**
M:2	42.86	41.27	28.57	30.16	57.14	39.68	**76.19**	**71.43**
M:3	42.86	38.10	47.62	49.21	47.62	46.03	**47.62**	**50.79**
M:4	34.92	28.57	23.81	14.29	19.05	12.70	**47.62**	**28.57**

Table: Prediction accuracy (%) of RAVLT (R:$K \in \{2,3,4\}$ quantiles) and MMSE (M:$K \in \{2,3,4\}$ quantiles) on $j = 1$ time point and $j = \{1,2,3\}$. Best results are in red.

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