Multi-view Brain Network Prediction from a Source View Using Sample Selection via CCA-Based Multi-kernel Connectomic Manifold Learning

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Multi-View Brain Network Prediction From a Source View Using Sample Selection via CCA-based Multi-Kernel Connectomic Manifold Learning

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Abstract. Several challenges emerged from the dataclysm of neuroimaging datasets spanning both healthy and disordered brain spectrum. In particular, samples with missing data views (e.g., functional imaging modality) constitute a hurdle to conventional big data learning techniques which ideally would be trained using a maximum number of samples across all views. Existing works on predicting target data views from a source data view mainly used brain images such as predicting PET image from MRI image. However, to the best of our knowledge, predicting a set of target brain networks from a source network remains unexplored. To fill this gap, a multi-kernel manifold learning (MKML) framework is proposed to learn how to predict multi-view brain networks from a source network to impute missing views in a connectomic dataset. Prior to performing multiple kernel learning of multi-view data, it is typically assumed that the source and target data come from the same distribution. However, multi-view connectomic data can be drawn from different distributions. In order to build robust predictors for predicting target multi-view networks from a source network view, it is necessary to take into account the shift between the source and target domains. Hence, we first estimate a mapping function that transforms the source and the target domains into a shared space where their correlation is maximized using canonical correlation analysis (CCA). Next, we nest the projected training and testing source samples into a connectomic manifold using multiple kernel learning, where we identify the most similar training samples to the testing source network. Given a testing subject, we introduce a cross-domain trust score to assess the reliability of each selected training sample for the target prediction task. Our model outperformed both conventional MKML technique and the proposed CCA-based MKML technique without enhancement by trust scores.

1 Introduction

Neurological disorders, such as Alzheimer's disease and Schizophrenia, alter brain connections in various ways across different brain views. Leveraging multi-view connectomic data can provide complementary information on a disorder

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mechanism. These connectomic multi-view data can be derived from functional magnetic resonance imaging (fMRI) or diffusion tensor imaging (DTI). Recent works introduced multi-view morphological brain networks which quantify changes in brain morphology using various morphological metrics across pairs of anatomical brain regions. These showed promise in diagnosis and brain connectional fingerprint identification [1,2,3] using multi-view brain network data compared to single network views.

However, due to various reasons including high clinical costs, it is common that in real medical practices, a subject does not complete all the scans and thus have missing data points or missing modalities or brain views. For many existing models, these incomplete subjects will have to be discarded. Moreover, it can be difficult to handle cross-domain prediction, since all views come from different distributions. To address this issue, several works focused on designing methods for data imputation. For instance, the Cascaded Residual Autoencoder (CRA) algorithm developed by [4] stacks autoencoders and grows iteratively to model the residual between prediction and original data. Another study on fMRI imputation is based on available case analysis, neighbor replacement and regression [5]. However, all these papers were not applied to connectomic data, i.e., brain networks.

To fill this gap, we design a prediction framework that maps a source brain network into a target brain network. We base our method on a simple hypothesis: if one can identify *the best* neighbors to a given testing subject in the source domain, one can use a weighted average of their corresponding views in the target domain to predict the missing target network. To account for the domain shift between the source and target domains, we use canonical correlation analysis to find a *coupled source-target subspace* where one assumes the existence of a performing linear classifier on the two domains [6]. We bridge the distribution shift by looking for the best coupled space that would nest projected source and target data samples. Next, we learn a subject-to-subject similarity matrix using multi-kernel connectomic manifold learning which models the relationships between all training and testing samples in the coupled space. We then identify the most similar training samples to the testing subject in the source domain for prediction in the target domain. We further prune the selected closest training samples by introducing a trust score which quantifies the cross-domain consistency of selected samples. In essence, the trust score decides if a neighbor is 'trustworthy' by examining whether the nearest neighbors of a training subject in source and target views highly overlap. To the best of our knowledge, this is the first work to predict multiple brain views from a single source view using connectomic data.

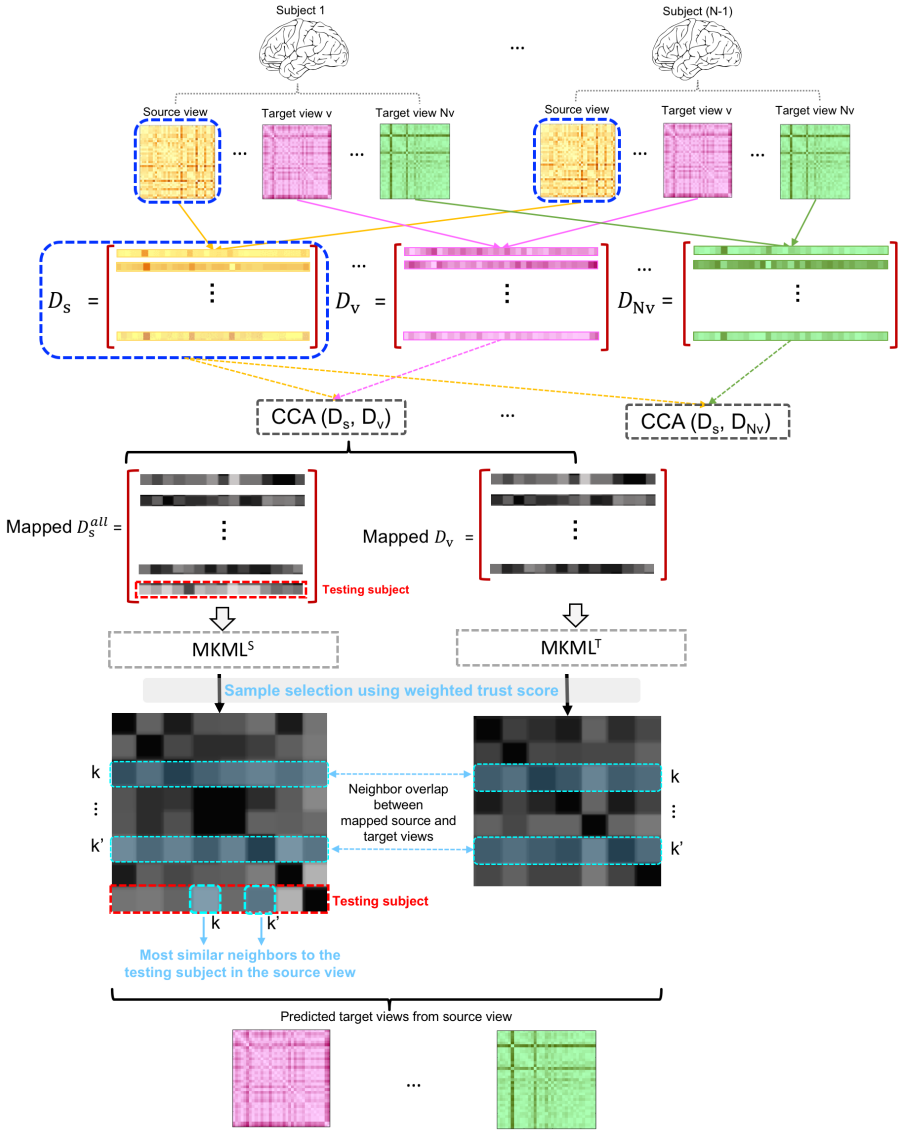

Fig. 1: *Pipeline of the proposed multi-view network predicting from input source network view.* Each training subject has a source network view (outlined in dashed view) and target network views. We represent each view by a feature vector extracted by vectorizing the off-diagonal upper triangular part of each network matrix. We stack training source feature vectors in a training source matrix $\mathbf{D}_s$ and target feature vectors in different training target matrices. Next, by fixing the training source matrix $\mathbf{D}_s$ and pairing it with a particular training target matrix $\mathbf{D}_v$, we learn a coupled source-target subspace using Canonical Correlation Analysis (CCA), where the correlation between both domains is maximized. For a given testing subject, we used the trained CCA model to map its source view onto the shared subspace. We then use multiple kernel manifold learning (MKML) to learn a similarity matrix that models the relationship between all *mapped* training and testing subjects in the shared subspace. For a specific target domain, we also learn a target manifold that nests only *mapped* training subjects. To assess the reliability of the identified most similar training samples in the shared domain, we introduce a trust score which quantifies the cross-domain consistency of selected samples, thereby filtering out 'untrustworthy' samples. Ultimately, we used weighted averaging of the corresponding target networks of the selected source training networks to predict the missing target views for a new testing subject.

2 CCA-based Multi-kernel Manifold Learning for Predicting Multi-View Brain Networks from a Source View

In this section, we present the key components of our proposed target multi-view brain network prediction from a single network view using a multi-kernel connectomic manifold learning in a learned coupled source-target subspace. We denote matrices by boldface capital letters, e.g., $\mathbf{X}$, and scalars by lowercase letters, e.g., x. We denote the transpose operator and the trace operator as $\mathbf{X}^T$ and $tr(\mathbf{X})$, respectively. We illustrate in **Fig.** 1 the key components of the proposed pipeline, and which we detail below.

• ***Step 1: Feature extraction.*** Each brain is represented by a set of connectivity matrices defined in the source and target domains (**Fig.** 1). Each element in a single matrix captures the relationship between two anatomical regions of interest (ROIs) using a specific metric (e.g., correlation between neural activity or similarity in brain morphology). We then vectorize each connectivity matrix i to define a feature vector $\mathbf{f}_s^i$ (resp. $\mathbf{f}_t^i$) for a particular source (resp. target) brain network view by concatenating the the off-diagonal elements in the upper triangular part of the input matrix. Hence, each brain network view of size $n \times n$ is represented by a feature vector of size $(n \times (n-1)/2)$.

• ***Step 2: Source to multi-target CCA mappings.*** Given a set of target brain network views, each capturing a unique and complex relationship between different brain network regions, we aim to learn how to predict these networks from a source brain network view (outlined in dashed blue in **Fig.** 1). Since multi-view brain connectomic data might be drawn from different distributions, investigating associations between these data samples without mapping them onto a space where their distributions are 'aligned' and where they become comparable might mislead any learning method trained in original source and target spaces. To solve this issue and motivated by the fact that canonical correlation analysis is efficient in analyzing and mapping two sets of variables onto a shared space [7,8], we fix the training source network data and pair it with a particular training target network data. By multiple source-target pairings, we generate multiple CCA mappings that align the source data with target multi-view data, respectively. Given a training source matrix $\mathbf{D}_s \in \mathbb{R}^{(N-1)\times d}$ comprising $N-1$ training feature vectors, each of size d, and a training target matrix $\mathbf{D}_k \in \mathbb{R}^{(N-1)\times d}$, we estimate a source transformation $\mathbf{W}_s$ and a target transformation $\mathbf{W}_k$ that map both onto the couple source-target subspace. In the testing stage, we use the learned canonical transformation matrices to map the source feature vector of a testing subject onto the shared space, where we learn how to identify the most similar training source feature vectors to the testing subject using multi-kernel manifold learning (MKML).

• ***Step 3: Multi kernel learning of source and target manifolds.*** Following the CCA-based mapping of both *source* training and testing samples, we learn how to nest all N samples into a manifold using the recent work of [9] where multiple kernels are learned to handle different data sample distributions.

Each kernel $\mathbf{K}$ is Gaussian defined as The Gaussian kernel is expressed as follows: $\mathbf{K}(\mathbf{f}^i, \mathbf{f}^j) = \frac{1}{\epsilon_{ij}\sqrt{2\pi}} e^{(-\frac{|\mathbf{f}^i - \mathbf{f}^j|^2}{2\epsilon_{ij}^2})}$, where $\mathbf{f}^i$ and $\mathbf{f}^j$ denote the feature vectors of the i-th and j-th subjects respectively and ϵ_{ij} is defined as: $\epsilon_{ij} = \sigma(\mu_i + \mu_j)/2$, where σ is a tuning parameter and $\mu_i = \frac{\sum_{l \in KNN(\mathbf{f}^i)} |\mathbf{f}^i - \mathbf{f}^j|}{k}$, where $KNN(\mathbf{f}^i)$ represents the top k neighboring subjects of subject i. The learned similarity matrix $\mathbf{S_s}$ is estimated by optimizing the following energy functional:

$\min_{\mathbf{S},\mathbf{L},\mathbf{w}} \sum_{i,j} -w_l \mathbf{K}_l(\mathbf{f}^i, \mathbf{f}^j)\mathbf{S}_{ij} + \beta||\mathbf{S}||_F^2 + \gamma \mathbf{tr}(\mathbf{L}^T(\mathbf{I}_n - \mathbf{S})\mathbf{L}) + \rho \sum_l w_l log w_l$

Subject to: $\sum_l w_l = 1$, $w_l \geq 0$, $\mathbf{L}^T\mathbf{L} = \mathbf{I}_c$, $\sum_j \mathbf{S}_{ij} = 1$, and $\mathbf{S}_{ij} \geq 0$ for all (i, j), where:

1. $\sum_{i,j} -w_l \mathbf{K}_l(\mathbf{f}^i, \mathbf{f}^j)\mathbf{S}_{ij}$ refers to the relation between the similarity and the kernel distance with weights w_l between two subjects. The learned similarity should be small if the distance between a pair of subjects is large.
2. $\beta||\mathbf{S}||_F^2$ denotes a regularization term that avoids over-fitting the model to the data.
3. $\gamma \mathbf{tr}(\mathbf{L}^T(\mathbf{I}_n - \mathbf{S})\mathbf{L})$: $\mathbf{L}$ is the latent matrix of size $n \times c$ where n is the number of subjects and c is the number of clusters. The matrix $(\mathbf{I}_n - \mathbf{S})$ denotes the graph Laplacian.
4. $\rho \sum_l w_l log w_l$ imposes constraints on the kernel weights to avoid selection of a single kernel.

To solve this problem, we adopt alternating convex optimization where each variable is optimized while fixing the other variables until convergence [9].

• ***Step 4: Predicting multi-target views using trust score weighting (TSW) strategy for training samples.*** In our designed prediction pipeline, once the the most similar source training samples to the testing sample of the source view are identified, we identify their corresponding views in the target domain, then use weighted average to predict the missing target views. However, relying on the learned similarity matrix based on the mapped source network data is disentangled from the target domain where most similar training subjects to the 'ground truth' missing target view might be different from those identified using the source MKML. Hence, we define a 'trust score' for each training sample i similar to the testing subject j based on the overlap of their local neighborhoods in mapped source and target domains, respectively. Following the learning of $\mathbf{S}_s$ using all samples in the mapped source domain using Step **3**, we identify the top K-closest training subjects to a given testing subject. Next, for each training sample, we find its nearest neighbors using $\mathbf{S}_s$ and $\mathbf{S}_t$, learned in the mapped target domain using only training subjects (**Fig.** 1).

The intuition behind this is that for a training subject k, the more shared neighbors k has across views, the more reliable it is in predicting the target view from the source view, and thus k is considered as 'trustworthy'. We compute a normalized trust score (TS) for each closest training subject k by (i) first identifying the list of its top m closest neighbors $\mathcal{N}_s$ in $\mathbf{S}_s$ and $\mathcal{N}_t$ in $\mathbf{S}_t$, then (ii) computing the normalized overlap between both lists as $TS(k) = \frac{\mathcal{N}_s \bigcap \mathcal{N}_t}{m}$.

The ultimate $TSW(k)$ score is thus calculated as a soft overlap between $\mathcal{N}_t$ and $\mathbf{S}_t$ weighted by $\mathbf{S}_s$.

3 Results and Discussion

Multi-view connectomic dataset and method parameters. We used leave-one-out cross-validation to evaluate the proposed prediction framework on 186 normal controls (NC) from Autism Brain Imaging Data Exchange (ABIDE I)[1] public dataset, each with structural T1w MR image. We used FreeSurfer [10] to reconstruct both right and left cortical hemispheres for each subject from T1-w MRI, and then parcellated each cortical hemisphere into 35 cortical regions using Desikan-Killiany Atlas. For each subject, we generated $N_v = 3$ cortical morphological brain networks using the technique proposed in [2]: $\mathbf{D}_1$ denotes the maximum principal curvature brain view, $\mathbf{D}_2$ denotes the mean sulcal depth brain view, and $\mathbf{D}_3$ denotes the mean of average curvature. For MKML, we used a nested grid search on all views respectfully, fixing the number of clusters c ($1 \leq c \leq 5$) and the number of top neighbors n_b ($3 \leq n_b \leq 50$). We used 10 kernels. For prediction, we set the number of training source neighbors to select to $m = 5$.

Evaluation and comparison methods. To compare the performance of our multi-target view prediction framework, we benchmark our framework against the baseline multi-kernel similarity learning method [9] using leave-one-out cross-validation. We further evaluated the contribution of the proposed trust score weighting strategy by comparing our results with those generated using TS with no additional weight derived from the learned source similarity learning. Our CCA-based MKML integrating TSW strategy significantly outperformed both conventional MKML and CCA-based MKML using TS for training sample selection ($p - value < 0.001$ using two tailed sample t-test) in left and right hemispheres (LH and RH). (**Fig.** 2) shows the mean absolute error (MAE) for all methods. **Fig.** 3 displays the predicted target views from a source view along with the residuals in both left and the right hemispheres for a representative testing subject using the proposed method. Best result is given when predicting LH View 2 (mean sulcal depth) from LH View 1 (the maximum principal curvature) prediction, achieving the lowest MAE.

4 Conclusion

This paper presents a multi-view brain network prediction framework from a source framework, which first bridges the gap between source and target domains, then learns how to select the best training samples using a cross-domain trust score weighting strategy. Specifically, for handling differences across brain views, we performed canonical correlation analysis to map the data onto coupled source-target correlated subspace. We then applied multi-kernel manifold

[1] `http://fcon_1000.projects.nitrc.org/indi/abide/`

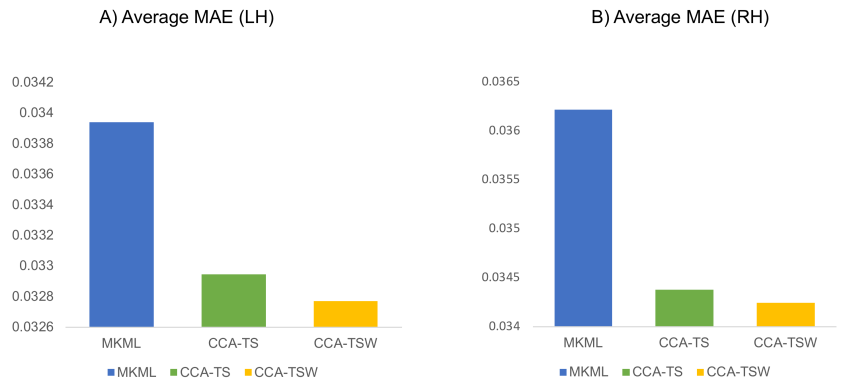

Fig. 2: *Evaluating the prediction performance of our proposed CCA-based multi-kernel manifold learning framework among all brain views applied on left and right hemisphere respectively using Mean absolute error (MAE).* MKML: multi-kernel manifold learning. CCA-TS: CCA-based MKML using only Trust Score (TS) for training sample selections. CCA-TSW: CCA-based MKML combining our Trust Score Weighting strategy.

learning combined with the trust score weighting for prediction. Our method achieved the best prediction performance in comparison with the baseline methods. In our future work, we will learn how to *jointly* map all target views into a shared space using tensor CCA [11]. We will also evaluate our seminal pipeline on larger datasets to predict other types of brain networks (e.g., functional brain connectivity from structural connectivity).

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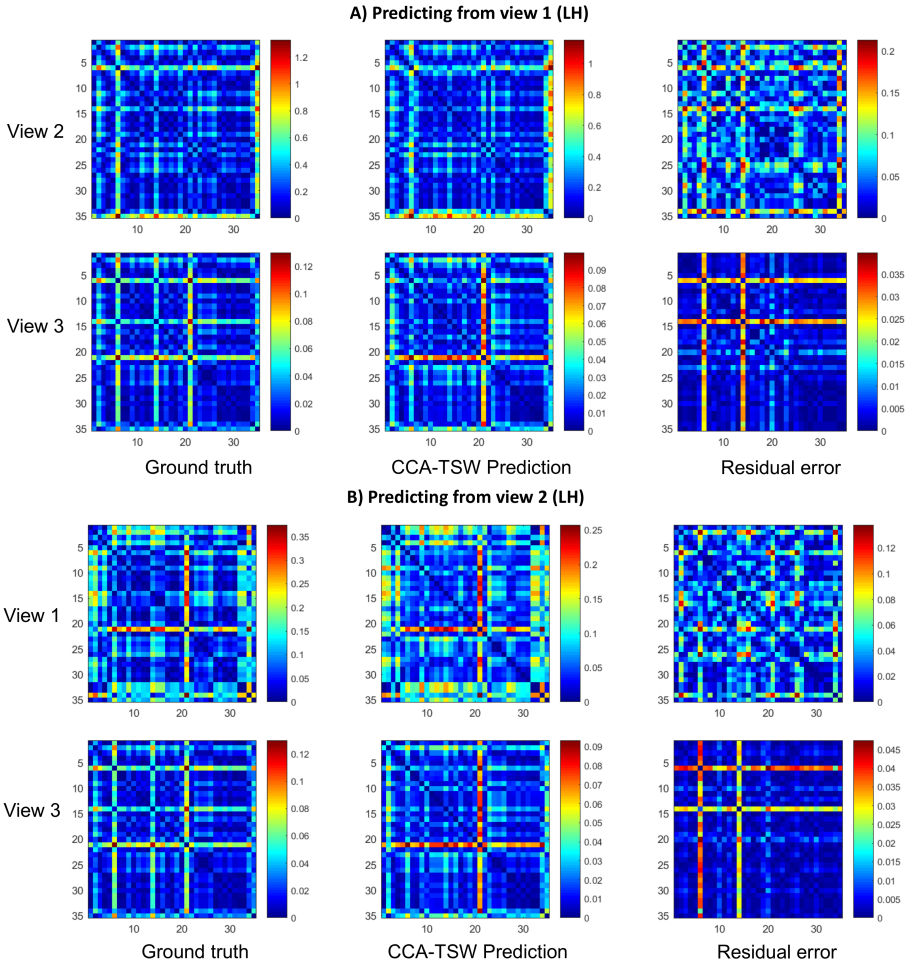

Fig. 3: *Comparison between the ground truth and predicted target networks from respectively source views 1 and 2 of the left hemisphere for a representative testing subject by the proposed CCA-based MKML framework.* We display the residual matrices computed using element-wise absolute difference between ground truth and predicted networks. View 1: the maximum principal curvature. View 2: mean sulcal depth. View 3: average curvature. Ground truth: the ground truth target view of a testing subject. CCA-TSW prediction: prediction of target views using our purposed framework. Note that each graph is scaled differently for the best display effect.

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