Class-Aware Hidden Markov Model for functional connectivity estimation and classification

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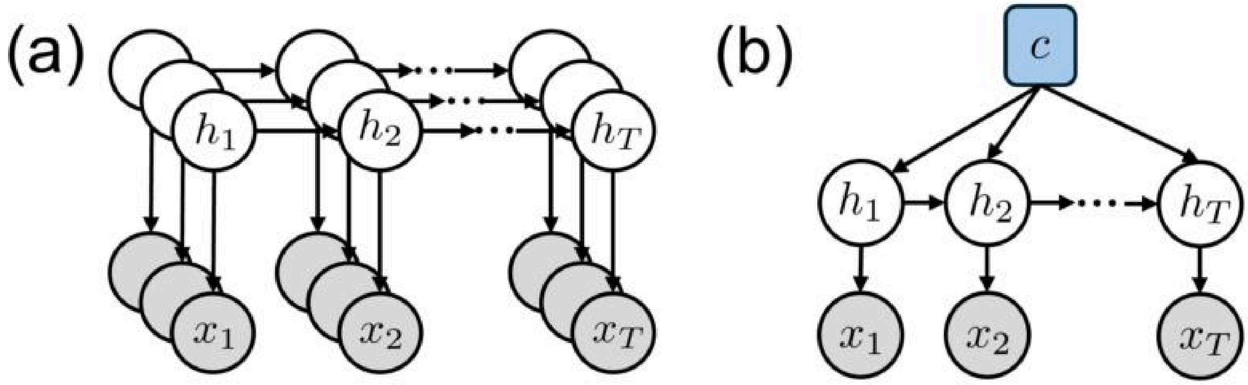
Introduction:

Several approaches have been adopted to characterize the temporal dynamics of resting-state fMRI connectivity. Compared to sliding window methods (Allen, 2014; Cai, 2017), Hidden Markov Models (HMM) are suitable for rapid state transitions, with the covariance matrix directly measuring brain connectivity (Vidaurre, 2017; Zhang, 2019). In this paper, we propose a framework to classify fMRI data based on HMM. Compared with the two-step approach, feature extraction and subsequent classification based on selected features (Ji, 2012; Zhao, 2022; Jin, 2023; Canal-Garcia, 2024), our proposed method using the joint probability directly to computes the posterior probability, which is more efficient and maintain the interpretability (Quattoni, 2007; Sutton, 2012). We evaluate the classification accuracy using real fMRI datasets.

Methods:

Consider fMRI data labeled as $X \in R^{N*p*T}$, indicating N subjects with length T and p components. Each subject has a ground truth class label among C classes. We assume fMRI data in each class follow a time-independent Hidden Markov Model (HMM). Specifically, the model has $K^{(c)}$ hidden states, with transition probability matrix $A^{(c)} \in R^{K^{(c)}*K^{(c)}}$, and the emission probability follows a Gaussian distribution with mean $\mu^{(c)} \in R^{K^{(c)}*p}$ and covariance $\sigma^{(c)} \in R^{K^{(c)}*p*p}$. The covariance matrix is regarded as the dynamic functional connectivity (Vidaurre, 2017; Zhang, 2019). During parameter estimation, we assume that $K^{(c)}=3$ for all classes, while other parameters $\theta=\{A,\mu,\sigma\}$ are treated as optimization parameters. For each class, the Expectation-Maximization (EM) algorithm can be used to maximize the joint probability Ψ, as shown in Figure 1(a). One potential problem is that performing the EM algorithm separately for each class may not generate good class separation. We implement additional gradient descent to minimize the Cross Entropy Loss (CEL) between the posterior probability and the ground truth. This method is also called Hidden Conditional Random Field (HCRF) (Quattoni, 2007; Sutton, 2012), as shown in Figure 1(b). Suppose we have a new time series X_{test} with unknown class labels. To assign these labels, we use an unsupervised classifier based on an HMM and a supervised classifier based on an HCRF.



(c)

Transition probability: $$p^{(c)}(h_t|h_{t-1}) = A^{(c)}_{h_{t-1}h_t}$$

Emission probability: $$p^{(c)}(x_t|h_t) = \mathcal{N}\left[\mu^{(c)}(h_t), \Sigma^{(c)}(h_t)\right]$$

Joint probability: $$\Psi^{(c)}(\theta|X) = \sum_t \sum_{\mathcal{H}} p^{(c)}(h_t|h_{t-1})p^{(c)}(x_t|h_t)$$

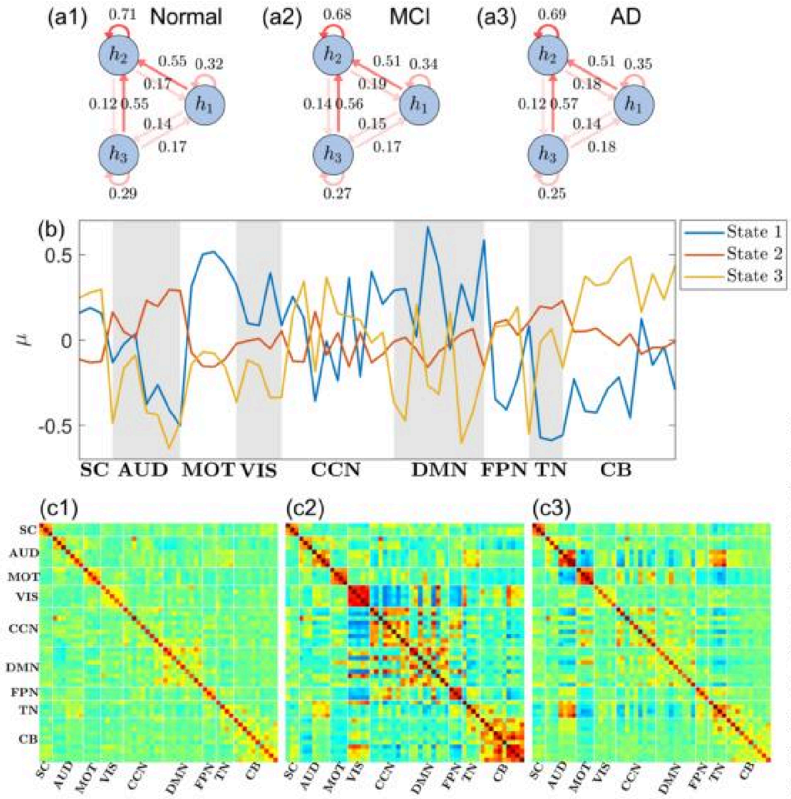
Posterior probability: $$p(c|\theta, X) = \frac{\Psi_c(\theta^{(c)}|X)}{\sum_i \Psi_i(\theta^{(i)}|X)}$$

Objective function: $$\theta_{\mathrm{HCRF}} = \min_\theta \mathrm{CEL}\left[p(c|\theta, X), c\right]$$

Figure 1: (a) Illustration of Hidden Markov Models (HMMs) corresponding to different classes. Each HMM is performed separately, given an unsupervised approach. (b) Illustration of a Hidden Conditional Random Field (HCRF), a supervised approach where the class information is integrated into the loss function. (c) Mathematical expression for the HMM and HCRF. Unsupervised learning (HMM) maximizes the joint probability, while supervised learning (HCRF) minimizes the Cross-Entropy Loss (CEL) between the posterior probability and the ground truth.

Results:

The real fMRI data containing 292 subjects with 74 Cognitively Normal (CN), 119 with Mild Cognitive Impairment (MCI), and 99 with Alzheimer's Disease (AD). Resting-state fMRI data were acquired with 3T, TR=3000 ms, TE=30 ms, flip angle=90°, FoV=220 mm, slice thickness=3.4 mm, EPI factor=64, echo spacing=0.72 ms. After group independent component analysis, the time series per subject has size T=135 and p=54. The data is split into training, evaluation, and testing sets in a 7/2/1 ratio. Figure 2 (a-c) shows the transition probabilities, means, and covariance matrices from class-level EM results. For the supervised training, we find that data augmentation in the time domain and Lasso regularization could help to reduce CEL in the validation dataset (Zhang, 2019). The whole process is repeated 100 times. Figure 2 (d) shows the performance of different methods. Our proposed HCRF shows the highest performance, with classification accuracy close to 50%.



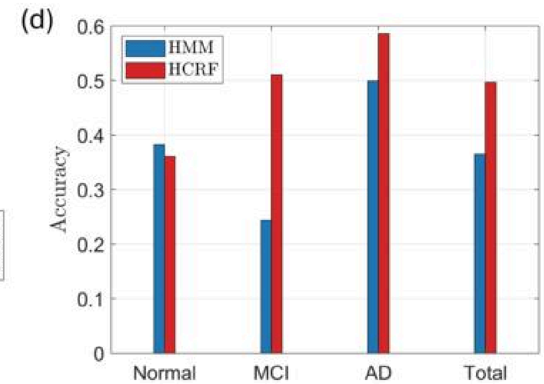


Figure 2: Dynamic functional connectivity analysis for resting-state fMRI data using class-level EM. Different classes share the same mean and covariance. (a1)-(a3) The transition probabilities for CN/MCI/AD. (b) Mean values for each hidden state. (c1)-(c3) Covariance matrices for each hidden state, organized into nine functional groups: subcortical (SC), auditory (AUD), motor (MOT), visual (VIS), cognitive control (CCN), default mode (DMN), frontal (FN), temporal (TN), and cerebellar (CB). (d) Classification accuracy comparison across different methods and classes. On average, supervised training improves classification accuracy. The mean accuracies for HMM and HCRF are 36.50% and 49.67%, respectively.

Conclusions:

The key findings of this study are that one-step posterior probability can be used for disease classification, and that supervised HCRF shows better performance compared with unsupervised HMM.

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Disorders of the Nervous System:

Neurodegenerative/ Late Life (eg. Parkinson’s, Alzheimer’s) [2]

Modeling and Analysis Methods:

Classification and Predictive Modeling
Connectivity (eg. functional, effective, structural)
fMRI Connectivity and Network Modeling [1]

Novel Imaging Acquisition Methods:

BOLD fMRI

Keywords:

Data analysis
FUNCTIONAL MRI
Machine Learning

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Not applicable

Please indicate which methods were used in your research:

Functional MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

SPM

Provide references using APA citation style.

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