

EVALUATING MODELS OF DYNAMIC FUNCTIONAL CONNECTIVITY USING PREDICTIVE CLASSIFICATION ACCURACY



Søren Føns Vind Nielsen¹, Yuri Levin-Schwartz², Diego Vidaurre³, Tulay Adali²,
Vince D. Calhoun^{5,6}, Kristoffer H. Madsen^{1,4}, Lars Kai Hansen¹ and Morten Mørup¹

¹ DTU Compute, Technical University of Denmark, ² CSSE, University of Maryland, Baltimore County, USA, ³ OHBA, University of Oxford, UK
⁴ DRCMR, Copenhagen University Hospital Hvidovre, Denmark, ⁵ The Mind Research Network, Albuquerque, USA, ⁶ ECE, University of New Mexico, Albuquerque, USA

INTRODUCTION

In the study of how the brain integrates information, communication between disjoint regions is often described using *functional connectivity* (FC). Over the last two decades, FC analysis has relied on a stationary assumption, i.e. that the statistical dependencies between regions do not change over time. This assumption has been shown to disregard a potential wealth of information in the changes in between-region connectivity, especially in resting-state functional magnetic resonance imaging (rs-fMRI) where this analysis approach has been coined dynamic functional connectivity (dFC) [1].

In this paper, we investigate how different modeling assumptions on the dynamics in resting state fMRI translate into classification accuracy using a cohort of patients diagnosed with schizophrenia (SZ) and healthy controls (HC). We accomplish this using the Bayesian hidden Markov model framework [4] with different emission models and investigate their ability to discriminate between SZ and HC. The different emission models, that each encode different assumptions on dynamics, will be compared using classification accuracy on held-out data.

Research Questions:

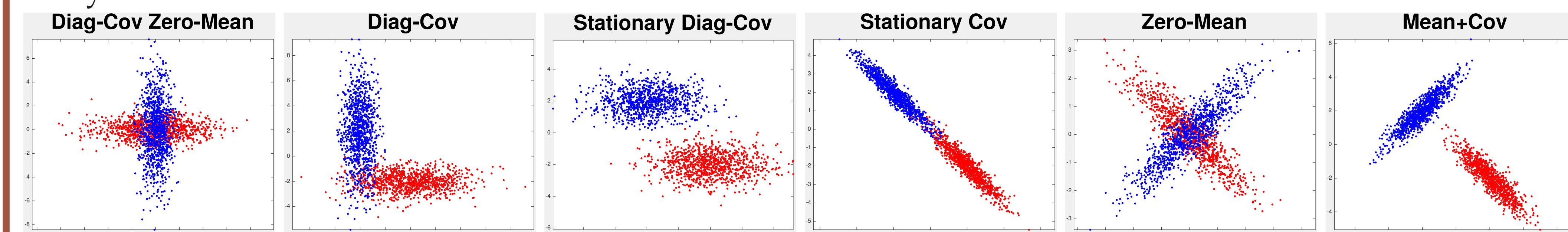
- How do different assumptions on dynamic functional connectivity models influence classification performance?
- To what extent does modeling dynamic (as opposed to static) functional connectivity influence classification performance?

HIDDEN MARKOV MODEL

Let $\mathbf{x}_t \in \mathbb{R}^p$ be a Gaussian distributed signal at time point t . The VB-HMM with K states has the generative model for the observations \mathbf{x}_t for $t = 1 \dots T$,

$$\begin{aligned} \boldsymbol{\pi}_0 &\sim \text{Dir}(\boldsymbol{\kappa}_0) & \boldsymbol{\pi}^{(k)} &\sim \text{Dir}(\boldsymbol{\kappa}^{(k)}) & z_t | z_{t-1} &\sim \text{Multinomial}(\boldsymbol{\pi}^{(z_{t-1})}), \\ \boldsymbol{\Sigma}^{(k)-1} &\sim \mathcal{W}(\boldsymbol{\Sigma}_0, \nu_0), & \boldsymbol{\mu}^{(k)} &\sim \mathcal{N}(\boldsymbol{\mu}_0, \lambda^{-1} \boldsymbol{\Sigma}^{(k)}) & \mathbf{x}_t &\sim \mathcal{N}(\boldsymbol{\mu}^{(z_t)}, \boldsymbol{\Sigma}^{(z_t)}), \end{aligned}$$

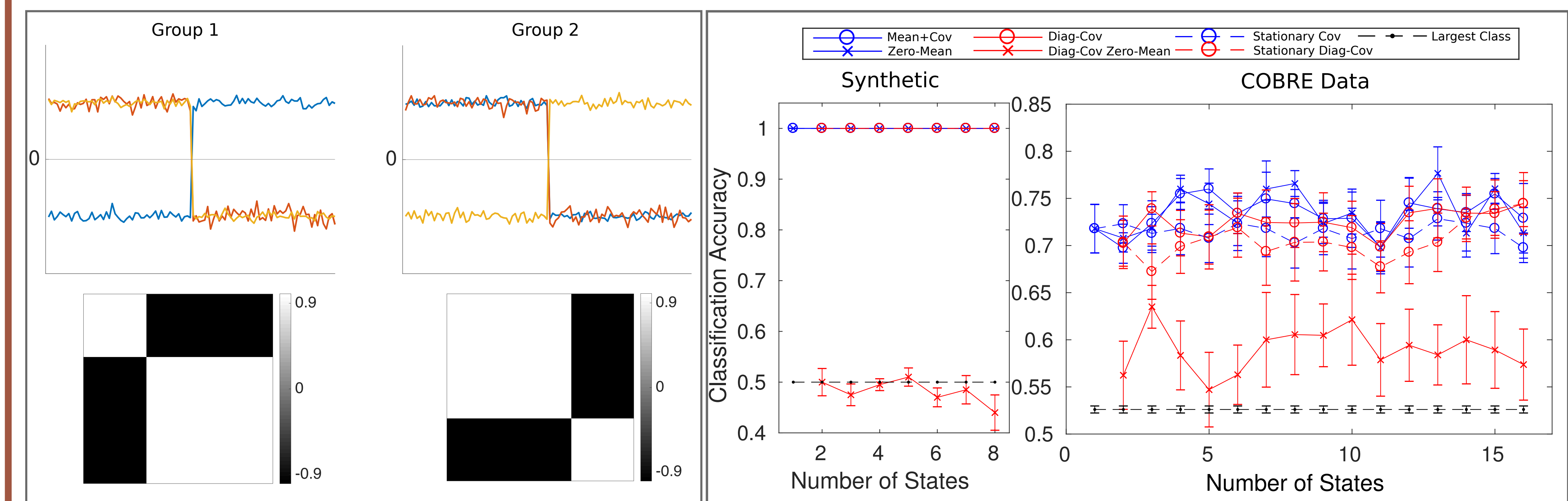
How we parameterize the states, i.e. $\boldsymbol{\mu}^{(k)}$ and $\boldsymbol{\Sigma}^{(k)}$, encodes our assumptions on the brain's dynamics. A zero mean model with full covariance for instance comes conceptually close to the sliding-window k-means approach from [1]. We highlight different ways of parameterizing dynamic functional connectivity



To create a classifier from an HMM-model we use a density-based approach. For that we use the predictive likelihood [3], $p(X^* | \mathcal{M})$, on held out subjects, yielding the Bayes classifier,

$$p(\mathcal{M}_{SZ} | X^*) = \frac{p(X^* | \mathcal{M}_{SZ}) p(\mathcal{M}_{SZ})}{\sum_{c \in \{HC, SZ\}} p(X^* | \mathcal{M}_c) p(\mathcal{M}_c)}$$

RESULTS



Left panel:

In the six emission models we have chosen there are some equivalences in the representations which we have to take into consideration when interpreting the results. To illustrate this we have generated two data sets (mimicking two groups for classification) from two "Stationary Diag-Cov". In the bottom of the figure we show the static covariance matrix for each group, i.e., equivalent to fitting the "Zero-Mean" model with one state.

Right panel:

We ran our analysis on a cohort consisting of 192 subjects' resting-state fMRI data (COBRE) [2]. Of those, 101 subjects were diagnosed as schizophrenic or schizoaffective (SZ) and 91 subjects were healthy controls (HC). We ran a group ICA using the GIFT toolbox with 85 components and after removal of components (fALLF and spatial overlap with known noise sources) we ended up with 44 components. We estimate the accuracy of the classifiers by stratified 10-fold cross-validation.

Conclusions:

- The discriminative signal is most simply characterized by within component differences, and not in their coupling.
- We saw that the performance of the different models was not highly influenced by the number of states chosen in the model, i.e. static FC suffices in the discriminative task.

ACKNOWLEDGEMENTS

This work was supported by the Lundbeckfonden grant no. R105-9813, the Novo Nordisk Foundation Interdisciplinary Synergy Program 2014 (BASICS) grant no. NNF14OC0011413 and by the NIH grant R01-EB-020407. We thank Qunfang Long for assistance with the group ICA.

References

- [1] E. A. Allen, E. Damaraju, S. M. Plis, E. B. Erhardt, T. Eichele, and V. D. Calhoun. Tracking whole-brain connectivity dynamics in the resting state. *Cereb. Cortex*, 24(3):663–676, Mar. 2014.
- [2] S. Ma, V. D. Calhoun, R. Phlypo, and T. Adali. Dynamic changes of spatial functional network connectivity in healthy individuals and schizophrenia patients using independent vector analysis. *Neuroimage*, 90:196–206, Apr. 2014.
- [3] S. F. V. Nielsen, M. N. Schmidt, K. H. Madsen, and M. Mørup. Predictive assessment of models for dynamic functional connectivity. *Neuroimage*, 171:116–134, Dec. 2017.
- [4] D. Vidaurre, A. J. Quinn, A. P. Baker, D. Dupret, A. Tejero-Cantero, and M. W. Woolrich. Spectrally resolved fast transient brain states in electrophysiological data. *Neuroimage*, 126:81–95, Feb. 2016.