Dynamic brain states sequential modelling based on spontaneous brain activity of resting-state fMRI

Shiyang Chen[1], Jason Langley[1], and Xiaoping Hu[1]

[1]*The Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA, United States*

Introduction: A growing body of literature indicates that human brain function varies across time. Recent studies have demonstrated that the resting state brain is constantly transiting among a small number of states. For example, Allen et al. [1] performed k-means clustering on the temporal covariance matrices of 50 intrinsic connectivity networks in sliding time windows and obtained 7 brain connectivity states. Similarly, Zhang et al. [2] detected the state switching points using a dynamic Bayesian variable partition model and identified 12 states with dictionary learning. Furthermore, these dynamic approaches have been proven to be valuable in detecting neuropsychiatric disorders, such as Schizophrenia [3] and PTSD [4]. These studies all support the hypothesis that dynamic analysis is able to provide more information for identifying disease specific alterations/plasticity than static analysis. In this abstract, we present a dynamic analysis approach based on the Gaussian Hidden Markov Model (GHMM). While a hidden Markov model was previously applied to symbolic labels, determined by hierarchical clustering based on correlation coefficients derived using a sliding window [4], our approach models the raw time series without sliding windows so that spatial activation patterns of states and temporal parameters can be determined directly from the model. We were able to detect 9 reproducible brain states by GHMM on two different datasets.

Methods: The GHMM can be applied on both volumetric data and grayordinate data used in Human Connectome Project (HCP). For the volumetric GHMM, we focused on the resting state fMRI (rfMRI) data of 90 subjects in 1000 Functional Connectomes Project (1000FCP) Beijing_Zang dataset. Standard preprocessing steps were performed as in 1000 FCP preprocessing pipeline [5] sans global signal regression. For each subject, 34745 time courses of fMRI single were extracted from the cortex and then fed into GHMM. For the surface-based GHMM, 38 subjects from HCP S500 release were used and the preprocessing was performed according to the minimal preprocessing pipelines [6]. In particular, we considered the data that had been registered onto 32k Cento69 surface mesh [7] and slightly smoothed with 2 mm FWHM kernel. Two hundred thirty six nodes on the cortical surface were chosen according to [8] and their time courses were used to train GHMM.

In GHMM, each brain state was modeled as a multivariate Gaussian distribution and the transition process among states was modeled as a Markov chain. When training GHMM, we employed an Expectation-Maximization algorithm [9] to solve the following objective function. Our source code was modified based on Scikit Learning [10].

$$\tilde{\lambda} = \arg\max_{\lambda} \sum_{q_0,q_1,\cdots,q_T} P(q_0) \prod_{t=1}^{T} a_{q_{t-1}q_t} \frac{1}{\sqrt{(2\pi)^N |\boldsymbol{\Sigma}_{q_t}|}} exp\left(-\frac{1}{2}(\boldsymbol{O}_t - \boldsymbol{\mu}_{q_t})^T \boldsymbol{\Sigma}_{q_t}^{-1}(\boldsymbol{O}_t - \boldsymbol{\mu}_{q_t})\right),$$

where λ is the parameter set for the Gaussian HMM, $\boldsymbol{O}_t$ and q_t are the observations from fMRI and the hidden state at time t; $a_{ij} = P(q_{t-1} = i | q_t = j)$ denotes the probability of switching from state i to state j; $\boldsymbol{\mu}_i$ and $\boldsymbol{\Sigma}_i$ represent the mean vector and covariance matrix of the multivariate Gaussian distribution under state i; N is the total number of time courses that are fed into the model; and $P(q_0)$ is the initial state probability which is assumed to be uniform distributed. The total state number was determined by maximizing the algorithmic reproducibility. We tried different total state numbers (4, 5, 7, 8, 9, 10, 11, 20 and 30) and repeated the algorithm 30 times for each total state number. When the total state number was less than or equal to 9, all the states were 100% reproducible, but the reproducibility did not hold when state number exceeded 9. Therefore, we set the total state number to 9 and only investigated these reproducible brain states. After training, we used Viterbi algorithm to decode the state transition sequence. Subsequently, the z-scores of the spontaneous activation pattern under each brain state were calculated based on the state sequence.

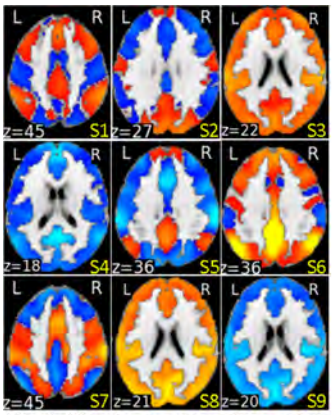

Fig. 1. Nine brain states detected on 1000 FCP volumetric data.

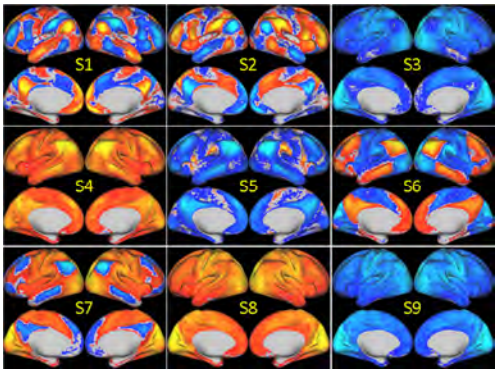

Fig. 2. Nine brain states detected on HCP data.

Results and Discussions: Fig. 1 and Fig. 2 demonstrate the 9 brain activation states (z-scores larger than 1.96 are plotted) derived for 1000FCP volumetric data and HCP cortical surface data, respectively. The states are sorted by their average time occupation during the scan. Conventional Resting States Networks (RSNs) can be found in these states of both datasets. For example, the default mode network (DMN) is activated in S5, S6 of Fig. 1 and S1, S6 of Fig. 2, and deactivated in S4 of Fig.1 and S5 of Fig. 2. The attention network is activated in S7 of Fig. 1 and S2 of Fig. 2. S8 and S9 in both figures show whole brain activation and whole brain deactivation states, in which the visual cortex is the most activated and deactivated region. Other states are different in two datasets (In Fig. 1, S1: activated executive network, S2: activated visual + sensory networks, S3-whole brain activation; in Fig. 2, S3: whole brain deactivation with visual cortex most deactivated, S4: whole brain activation with DMN most activated, S7: deactivated DMN). The difference between the states of two datasets could result from different scan protocol and preprocessing steps. However, these 9 brain states are all combination of conventional RSNs and 6 states are reproducible on both datasets.

Conclusion: We developed a new modeling approach, GHMM, for characterizing the dynamics of rfMRI data. Nine brain states were detected on both volumetric and surface data, partially overlapping with conventional RSNs. Future work will focus on analyzing the temporal characteristics of the states, such as occurrence and duration, as well as investigating and identifying differences between disease and control groups.

References: [1] Allen, E.A., et al., Cerebral cortex, 2012: p. bhs352. [2] Zhang, J., et al., Human brain mapping, 2013. [3] Ma, S., et al., NeuroImage, 2014. 90: p. 196-206. [4] Ou, J., et al., Brain topography, 2014: p. 1-14. [5] Biswal BB, et al. Proc Natl Acad Sci USA. 2010; 107(10):4734-9. [6] Glasser MF, et al. Neuroimage. 2013; 80:105-24.[7] Van Essen DC, et al. Cereb Cortex. 2012. [8] Power, Jonathan D., et al., Neuron 72.4 (2011): 665-678. [9] Rabiner, L. et al., Proceedings of the IEEE, 1989. 77(2): p. 257-286. [10] Pedregosa, F., et al., The Journal of Machine Learning Research, 2011. 12: p. 2825-2830.