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Quantifying Temporal States in rs-fMRI Data using Bayesian Nonparametrics

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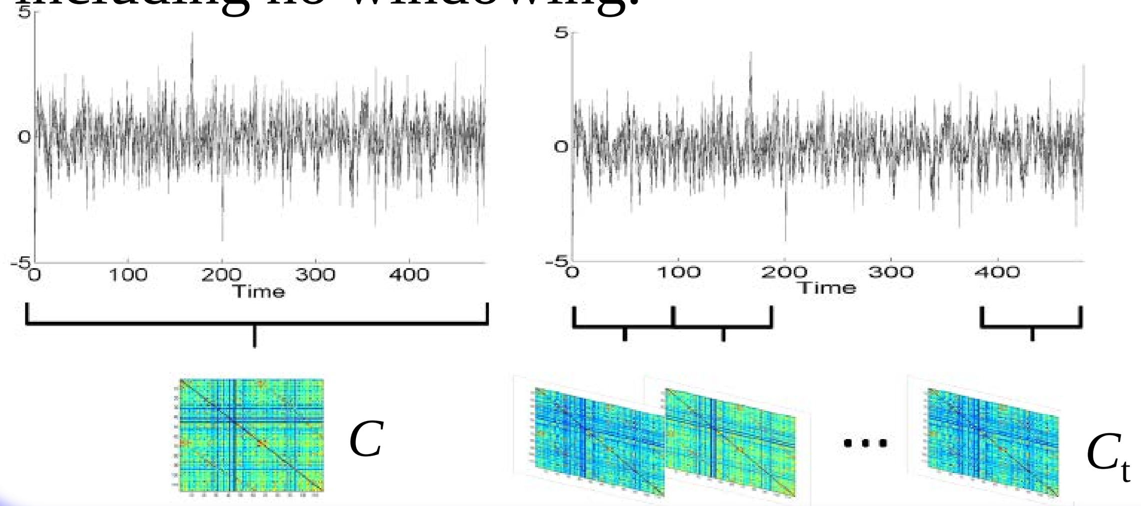
Recently, it has been observed that resting state fMRI (rs-fMRI) exhibits time-evolving dynamics using time-windowed covariance matrices (Allen et al. 2012; Hutchison et al. 2013). We presently aim at quantifying the number of dynamic states in rs-fMRI using an infinite Wishart mixture model. The model automatically quantifies the number of states and handles arbitrary window sizes including no windowing.



Stationary FC between components (left) is estimated as the covariance of the time series visualized above. Dynamic FC (right) is estimated as series of covariance matrices from windowed portions of the above time series.

In this paper we address the following three important research questions:
Can we quantify the number of temporal states in resting fMRI?
To what extend are these states driven by subject variability and temporal dynamics?
How are the quantified states influenced by window length?

The Infinite Wishart Mixture Model

The generative model for the Infinite Wishart Mixture Model is given by:

$$z \sim \mathrm{CRP}(\alpha)$$
$$\Sigma_k \sim \mathrm{invWishart}(\Sigma_0, n_0)$$
$$C_t \sim \mathrm{Wishart}(\Sigma_{z_t}, n_t)$$

$$z \sim \mathrm{CRP}(\alpha)$$
$$\Sigma_k \sim \mathrm{invWishart}(\Sigma_0, n_0)$$
$$\boldsymbol{x}_t \sim \mathrm{N}(0, \Sigma_{z_t})$$

Where the Chinese Restaurant Process (CRP) is used as a non-parametric prior on partitions (Aldous, 1985, Pitman 2006).. By exploiting the conjugacy of the Inverse Wishart prior to the Wishart likelihood, we can analytically marginalize (i.e., collapse) Σ_k to obtain:

$$p(\{C_1,\ldots,C_T\},\mathbf{z}|\mathbf{n},\alpha,\Sigma^{(0)},n_0)=$$
$$\int\prod_k p(\{C_t:z_t=k\}|\{n_t:z_t=k\},\Sigma_k)p(\Sigma_k|\Sigma^{(0)},n_0))d\Sigma_k p(\mathbf{z}|\alpha)$$
$$=\left[\prod_k \frac{|\Sigma_0|^{n_0/2}2^{(N_k+n_0)p/2}\Gamma_p((n_0+N_k)/2)}{|\Sigma_0+\sum_t C_t\delta(z_t=k)|^{(n_0+N_k)/2}2^{n_0p/2}\Gamma_p(n_0/2)}\prod_t \frac{|C_t|^{(n_t-p-1)/2}}{2^{n_tp/2}\Gamma_p(n_t/2)}\right]$$
$$\frac{\Gamma(\alpha)\alpha^K}{\Gamma(\alpha+I)}\prod_k\Gamma(m_k)$$

$$p(\boldsymbol{X},\mathbf{z}|\alpha,\Sigma^{(0)},n_0)=$$
$$\int\prod_k p(\{x_t:z_t=k\}|\Sigma_k)p(\Sigma_k|\Sigma^{(0)},n_0))d\Sigma_k p(\mathbf{z}|\alpha)$$
$$=\left[\prod_k \frac{|\Sigma_0|^{n_0/2}2^{(N_k+n_0)p/2}\Gamma_p((n_0+N_k)/2)}{|\Sigma_0+\sum_t C_t\delta(z_t=k)|^{(n_0+N_k)/2}2^{n_0p/2}\Gamma_p(n_0/2)}\right](2\pi)^{-Tp/2}$$
$$\frac{\Gamma(\alpha)\alpha^K}{\Gamma(\alpha+I)}\prod_k\Gamma(m_k)$$

where m_k is the number of observations assigned to cluster k and N_k is the total number of time points for the covariance matrices of cluster k. We note that finite Wishart mixture models have been considered previously where the inference was based on the EM-algorithm (Hidot et al., 2010). A drawback of the EM procedure being that the procedure potentially requires explicit evaluation of $|C_t|$ which is not feasible when n_t<p. By imposing an inverse Wishart prior on the covariance centers of each cluster Σ_k it is feasible to infer the parameters of the models despite that $|C_t|$ can not be explicitly evaluated. We use Gibbs sampling in combination with split-merge Metropolis-Hastings moves as proposed in (Jain and Neal, 2004). for inferring **z**. We further parameterize $\Sigma^{(0)}=\gamma I$ and infer γ and α using Metropolis-Hastings random walk by imposing uniform priors and transforming the parameters to the log-domain using a normal distribution with standard deviation 0.1 as proposal distribution. In our analysis we set n_0=p which is the smallest admissible integer value for evaluating $\Gamma_p(n_0/2)$.

References

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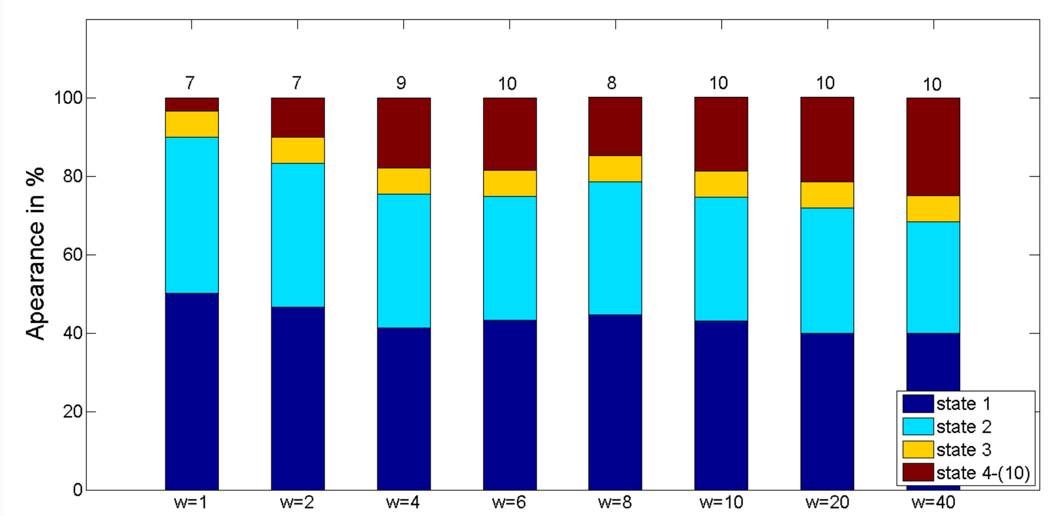
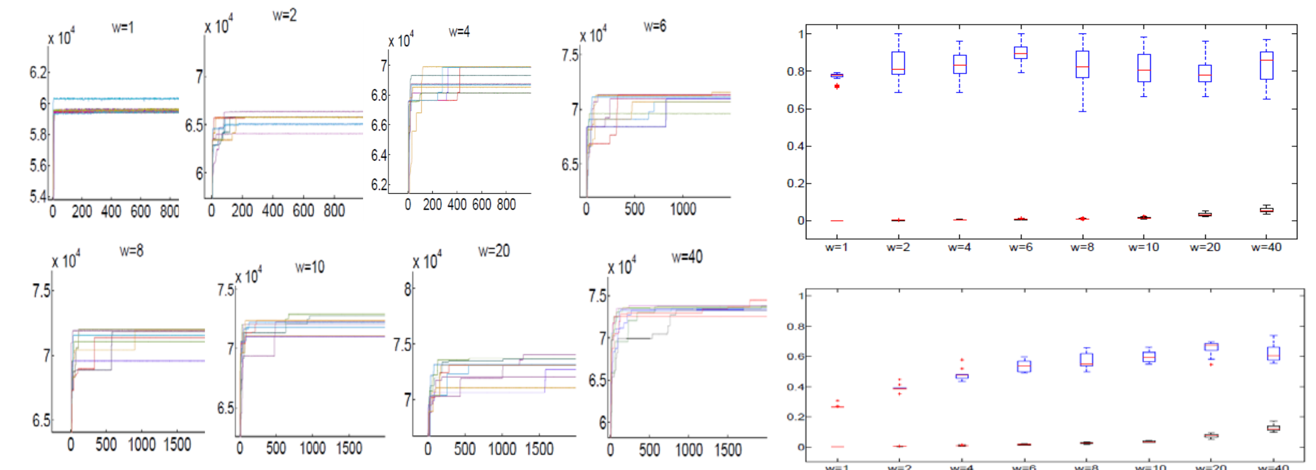
Analysis of RS-fMRI

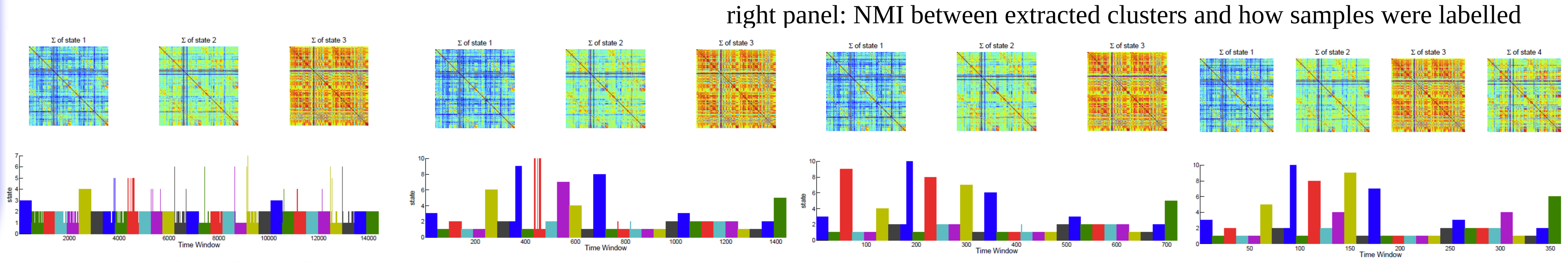
Data: After informed consent functional MRI was acquired from 30 healthy control subjects. The data consisted of 480 T2* weighted EPI volumes recorded over 20 min in a closed eyes resting state session (42 interleaved slices, 192 mm FOV, 3mm isotropic resolution, TR=2.49s, TE=30ms). Preprocessing was performed in SPM8 and included realignment, normalization to MNI space, temporal filtering (highpass, cardiac and respiratory cycles, timeseries from CSF and white matter) (Lund et al. 2006) and mean time-series from each of the 116 ROIs defined in the AAL atlas (TzourioMazoyer et al., 2002) extracted. We used the following window lengths: *w* = {1, 2,4,6,8,10,20, 40} with no overlap.



Size of components as function of window length displaying two prominent states.



Left panel: log[P(**X**, **z**|α ,$\Sigma^{(0)}$,n_0)] (disregarding constant terms) as a function of sampling iterations displaying some mixing issues. Top right panel: Normalized mutual information (NMI) between the samples with highest value of P(**X**, **z**|α $\Sigma^{(0)}$,n_0) in each of the 10 random initialized chains. Bottom right panel: NMI between extracted clusters and how samples were labelled



(a) Window length 1 (b) Window length 10 (c) Window length 20 (d) Window length 40

The final 116x116 covariance matrices of the most dominating states with a 5% frequency threshold. The ROIs are sorted such that the frontal lobe of the right brain is seen in the upper left side of the covariance matrices and the Occipital lobe and Cerebellum are placed in the lower right corner. The bottom plots show the assignments of the windowed time series to the states identified by the model. The coloring indicates the 30 subjects.

Conclusion: Our modeling identified multiple states in rs-fMRI. These states were mainly subject specific, however, prominent temporal dynamics within subjects were observed when no time-windowing was applied. The results support, that temporal dynamics should be taken into account when modeling rs-fMRI. The results also suggest that it is important to efficiently handle between subject variation when identifying temporal dynamics in rs-fMRI. Thus, future work will focus on improved preprocessing and ROI estimation as well as improving the inference procedure.

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