Shagun Ajmera[1], Shreya Rajagopal[1], Razi Ur Rehman[2], Devarajan Sridharan ✉[1,2]

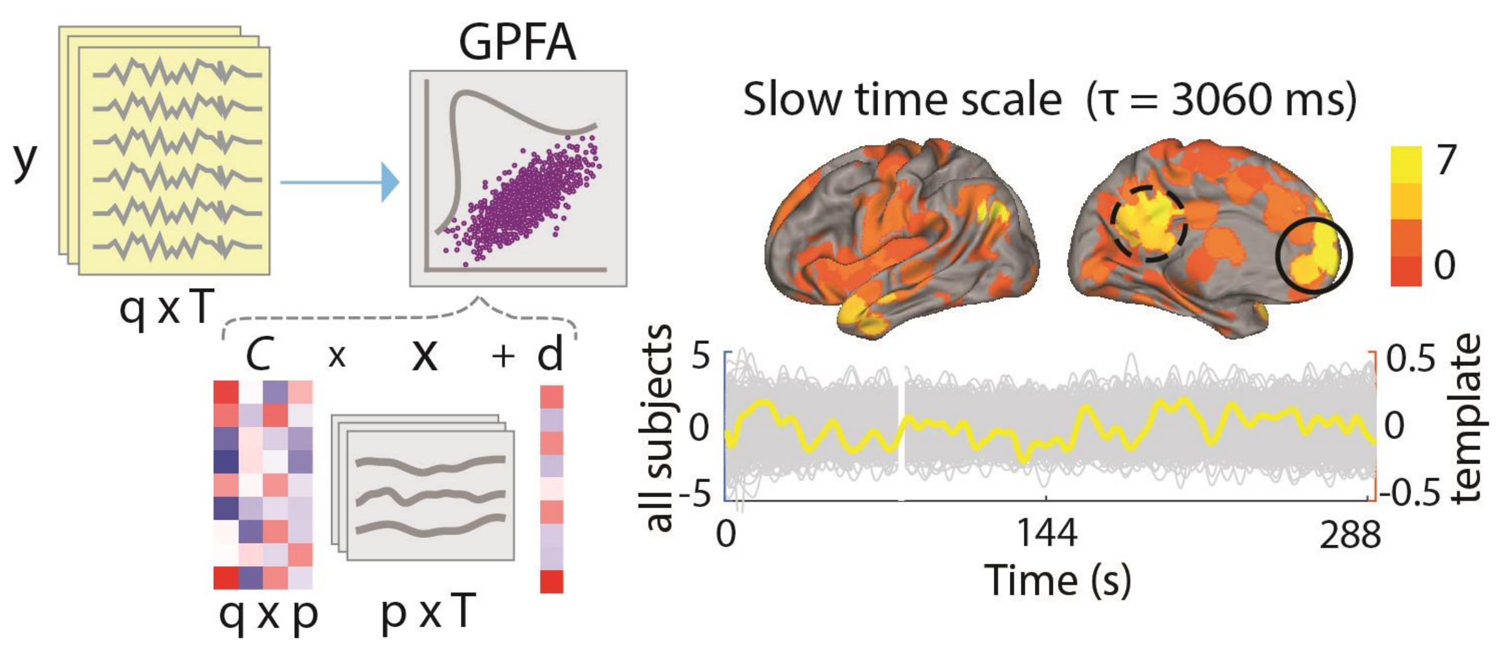
✉ sridhar@iisc.ac.in
[1]Center for Neuroscience, and
[2]Department of Computer Science and Automation
Indian Institute of Science, Bangalore

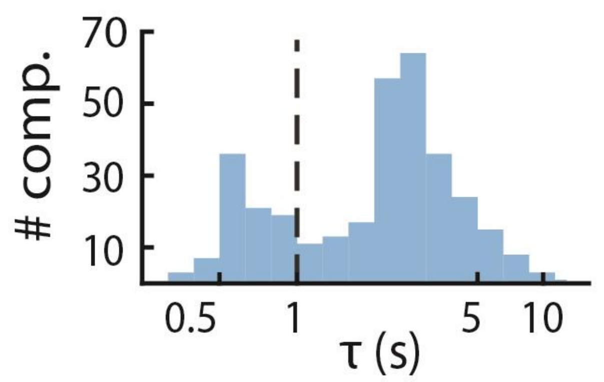
INFRA-SLOW BRAIN DYNAMICS AS A MARKER FOR COGNITIVE FUNCTION AND DECLINE

Summary

- Functional magnetic resonance imaging (fMRI) enables measuring human brain activity, in vivo [1]. Yet, the fMRI response unfolds over very slow timescales (<0.1-1 Hz) compared to neural spiking [2].
- Are slow fMRI dynamics relevant for cognitive function?
- We investigated this by applying Gaussian Process Factor Analysis (GPFA) [3] and machine learning to human fMRI data from 1000 healthy participants (Human Connectome Project database) and 95 patients with mild cognitive impairment (MCI; ADNI database).
- GPFA reduced dimensionality and extracted smooth latent dynamics with slow (<1 Hz) and infra-slow (<0.1 Hz) timescales.
- These dimensions sufficed to accurately classify task-specific cognitive states and to predict cognitive scores in healthy subjects as well as clinical dementia rating (CDR) scores in MCI patients.
- Slow and infra-slow brain dynamics are relevant for understanding the neural basis of cognitive function, in health and disease.

Gaussian Process Factor Analysis (GPFA)



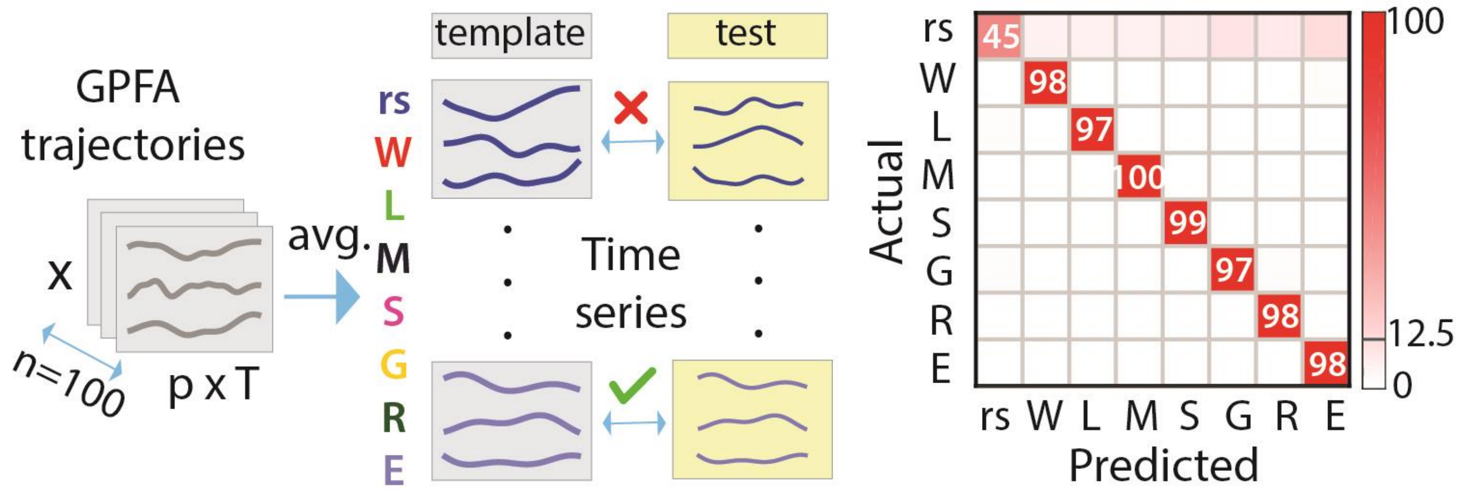


- GPFA extracted latent functional networks with smooth dynamics from slowly sampled fMRI data (1000 subjects from Human Connectome Project HCP database).

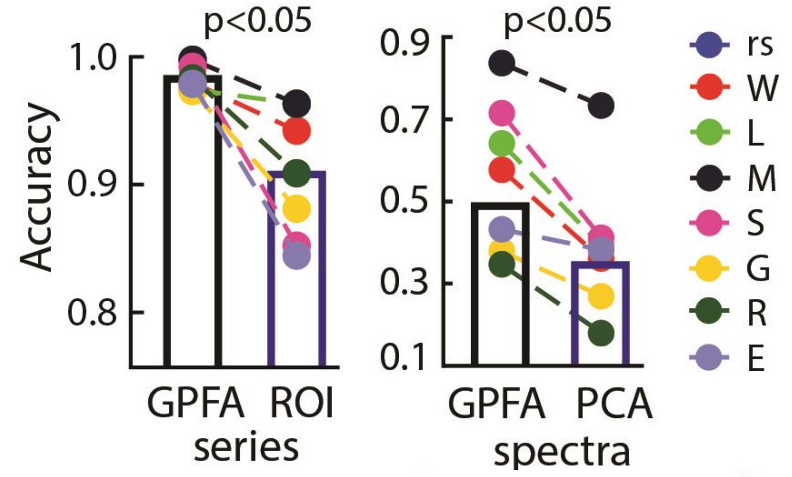
Results

Slow latent dynamics characterize cognitive states

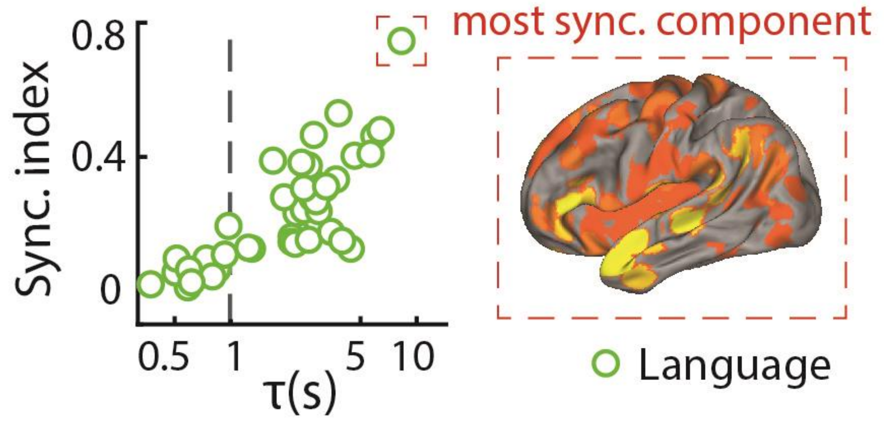
- GPFA latent dynamics yielded superlative accuracies for classifying task-specific cognitive states.



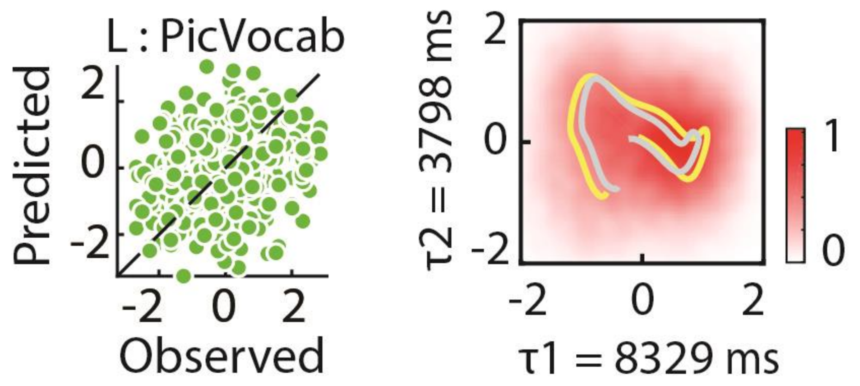
- GPFA outperformed other dimensionality reduction methods

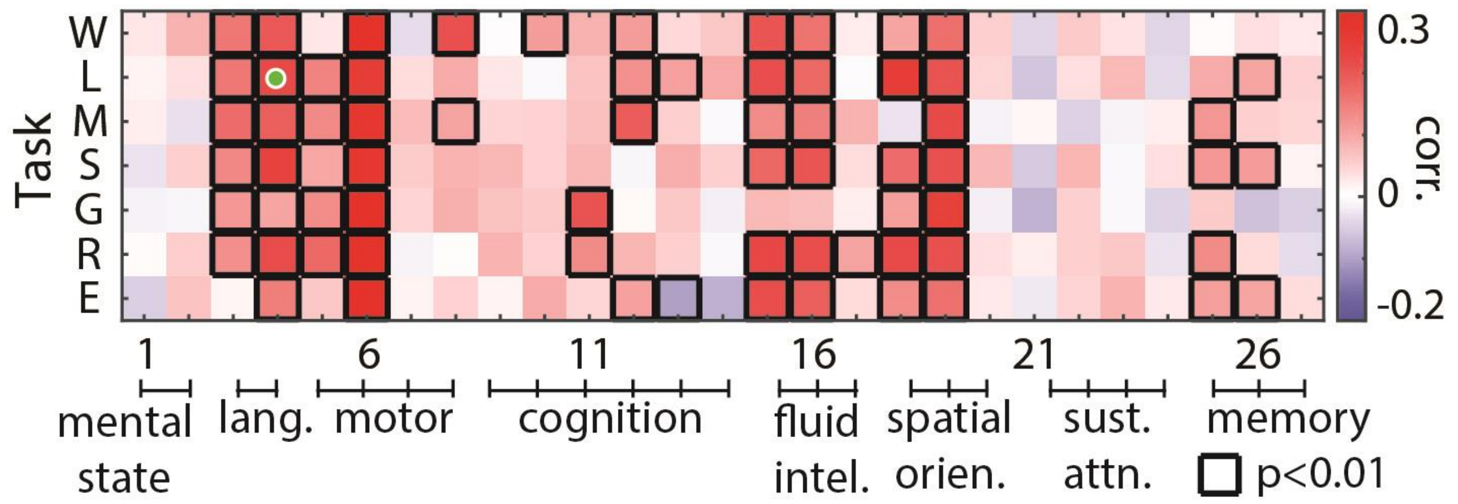


- GPFA latent timeseries with high synchronization (across subjects) corresponded to task-relevant functional networks

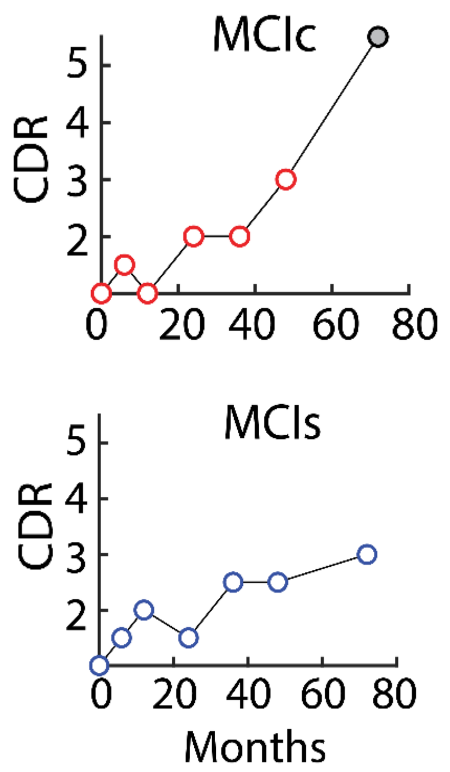


- Functional connectivity in GPFA latents predicted inter-subject variations in cognitive scores

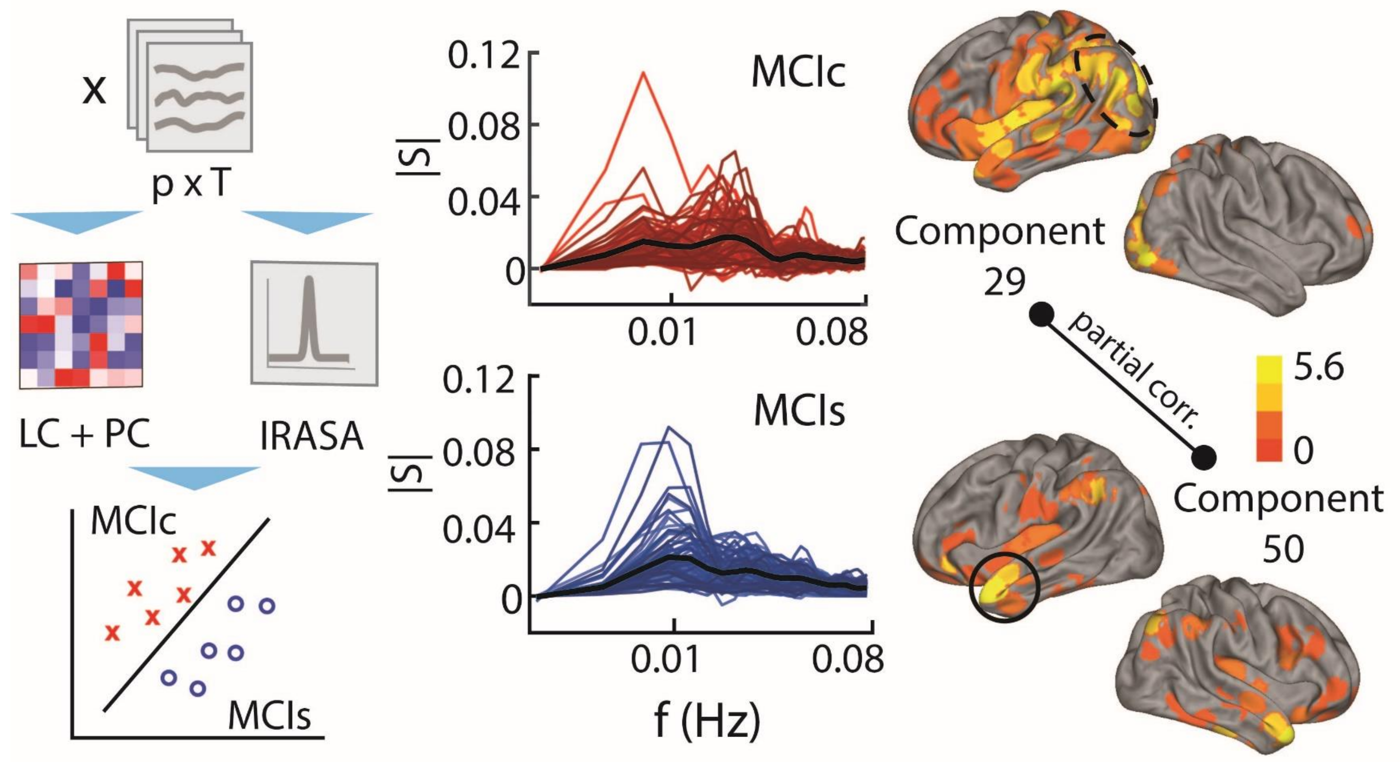




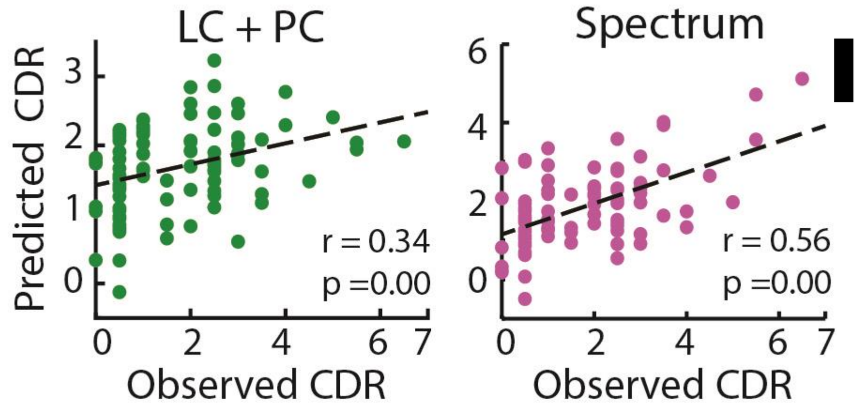
Infra-slow dynamics characterize cognitive decline



- Clinical Dementia Rating (CDR) score measures cognitive decline, and is used in the clinical diagnosis of Alzheimer's Dementia (AD; grey dot)
- Patients with Mild Cognitive Impairment (MCI) who progressed to develop AD are MCI-Converters (MCIc). Those who remained stably diagnosed as MCI for 24 months (or more) are MCI-Stable (MCIs).



- An SVM-RFE [4] classifier, trained with functional connectivity among GPFA latents (lagged covariance, LC and partial correlation, PC), distinguished MCIc from MCIs with a high cross-validation accuracy (73.6%).
- Infra-slow (<0.1 Hz) spectral features (IRASA) [5] of GPFA latents also yielded above-chance accuracy (67.2%).



- Regression analysis with either connectivity or spectral features of GPFA latents accurately predicted individual MCI patients' CDR scores.

Glossary

- Gaussian Process Factor Analysis (GPFA):

$y_{:,t} \in \mathbb{R}^{q\times1}$	high-dimensional fMRI data
$x_{:,t} \in \mathbb{R}^{p\times1}$	low-dimensional GPFA latent components (p < q)
$y_{:,t} \mid x_{:,t} \sim \mathcal{N}(Cx_{:,t} + d, R)$	linear-Gaussian model
where $C \in \mathbb{R}^{q\times p}$,	weight matrix
$d \in \mathbb{R}^{q\times1}$,	mean of each fMRI series
and $R \in \mathbb{R}^{q\times q}$	independent noise variances
$x_{i,:} \sim \mathcal{N}(0, K_i)$	GPFA latent dimensions, with
$K_i \in \mathbb{R}^{T\times T}$	temporal covariance being
$K_i(t_1,t_2) \propto \exp(-\frac{(t_1-t_2)^2}{2\tau_i^2})$	a squared exponential function
$\theta = \{C, d, R, \tau_1, \ldots, \tau_p\}$	GPFA parameters learnt via Expectation Maximization [3]

- Task abbreviations: *rs*: resting state, *W*: working memory, *L*: language processing, *M*: motor, *S*: social cognition, *G*: gambling, *R*: relational processing, *E*: emotion processing
- MCI: Mild Cognitive Impairment, a state of cognitive decline, which could be a precursor to dementia. Diagnosed using a battery of cognitive tests, and physician's evaluation.
- IRASA: Irregular Resampling Auto-Spectral Analysis, a procedure for extracting oscillatory components from the power spectrum after removing the 1/f component [5]
- SVM-RFE: Support Vector Machine classification, with Recursive Feature Elimination [4]

References

[1] Glover, G. H., 2011
[2] Mitra, A. et. al, 2018
[3] Yu et. al, 2009
[4] Sundaresan, M et. al, 2017
[5] Wen, H., Liu, Z., 2016

Acknowledgements: Wellcome Trust DBT-India Alliance, SERB Early Career Research Award, Pratiksha Trust Young Investigator Award, DBT-IISc Partnership Program Grant, Sonata Software Grant, Human Connectome Project, Alzheimers Disease Neuroimaging Initiative.

33rd Conference on Neural Information Processing Systems (NeurIPS). Vancouver, Canada. 08-14 Dec, 2019