Latent Factor Gaussian Process Model for Dynamic Functional Connectivity

Dustin Pluta, Lingge Li, Norbert Fortin,
Hernando Ombao, Pierre Baldi, Babak Shahbaba

Department of Statistics
University of California, Irvine

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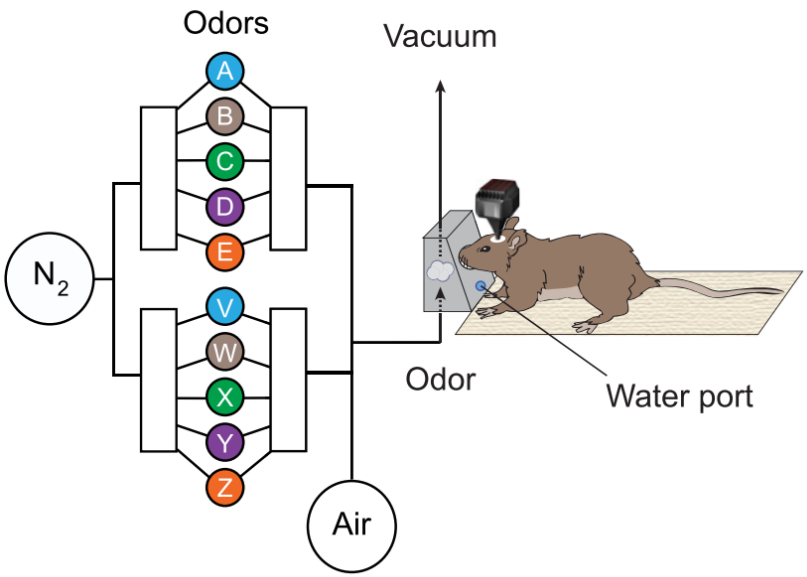
Overview

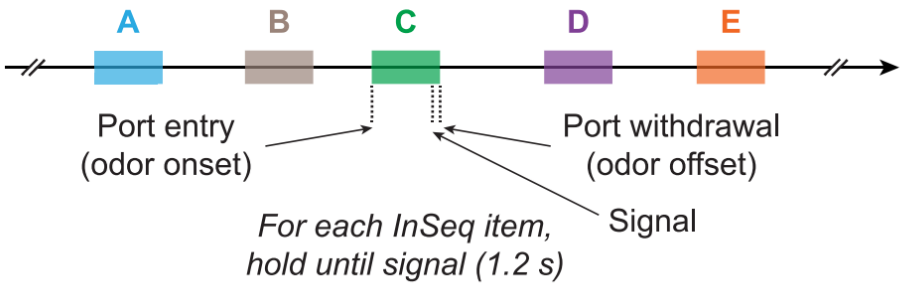
Scientific Background

- We consider a data set of rat *local field potentials* measured from tetrodes implanted in the hippocampus [1].
- LFP was recorded during repeated trials of an odor-based memory experiment.
- There has been substantial study of neural activity associated with spatial memory tasks, but much less is known about non-spatial memories.

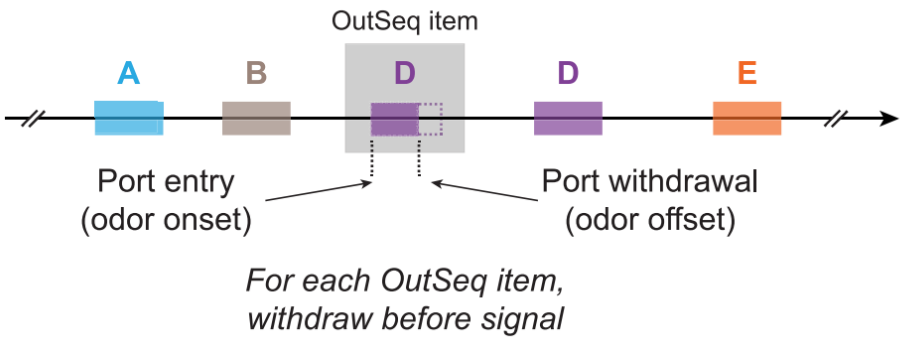
Scientific Background



Example with all odors presented "in sequence" (InSeq)



Example with one odor presented "out of sequence" (OutSeq)



Scientific Background

- There have been extensive results on neural characteristics of *spatial* memories (e.g. place cells, grid cells, memory replay during spatial navigation).
- Much less is known about non-spatial memory.
- Previous work has found that neuronal spike trains can significantly discriminate odor stimuli, but the LFP signals are poor discriminators.

Motivation

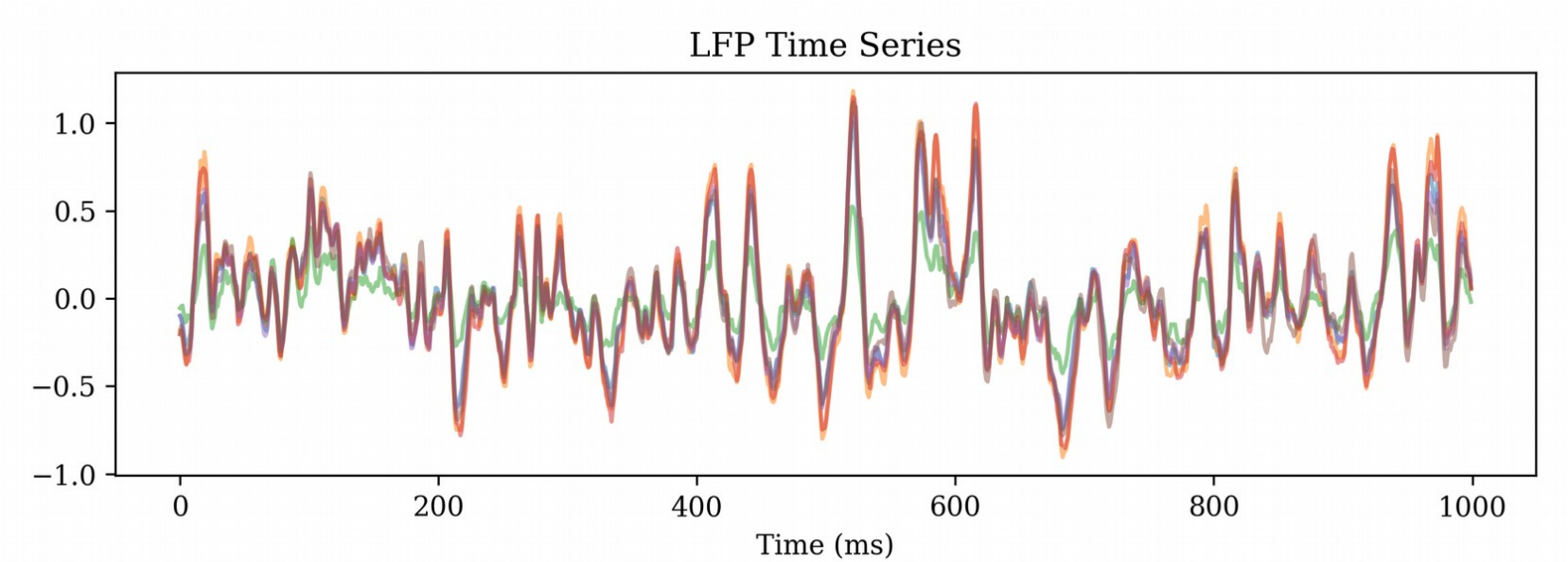
The overall goal of this study is to determine if dynamics in the LFP covariance process are significantly associated with the different odor stimuli.

Scientific Background

Questions of Interest

1. Are there significant changes in brain connectivity in the rat hippocampus during an odor-based memory task?
2. Are there differences in connectivity dynamics across the different experimental conditions?

Statistical Setup



- Let $X_i(t)$ be a p-variate time series for observations $i = 1, \ldots, n$ (the observed LFP signals).
- Let $K_i(t)$ be the $p \times p$ covariance matrix of $X_i(t)$ for observation i at time t.

The questions of interest can be stated as

- Does $K_i(t)$ differ significantly across t?
- Are $K_i(t)$ and $K_j(t)$ differ significantly when i and j are association with different experimental conditions?

Previous Work

Dynamic functional connectivity is an active area of research in the neuroscience community.
Previous modelling approaches include:

- Sliding window (SW) methods, often with PCA, [2, 3]
- Variants of the Hidden Markov Model (HMM), [4]
- Latent factor models, such as Latent Factor Stochastic Volatility (LFSV).[5, 6]

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- Latent factor models, such as Latent Factor Stochastic Volatility (LFSV).
  Scalable, good for modeling volatility and smooth dynamics.
  Imposes a specific structure on the covariance that depends on the factor loadings on the observed signals.

LFGP Model

Idea

Instead of placing a factor structure on the observed time series (as in the LFSV model), we can represent the covariance process itself as a linear combination of factors.

1. Estimate the covariance process via sliding windows, which gives a time series of symmetric positive definite matrices.
2. Apply the matrix logarithm to the estimated covariance process, giving a time series of real symmetric matrices.
3. Fit a multivariate time series factor model to the vectorized upper triangle of the log-covariance process.

LFGP Model

Let $X_i(t)$ be the p-variate time series for observation $i, i = 1, \cdots, n$, with (unspecified) distribution $\mathcal{D}$ and $p \times p$ covariance $K_i(t)$ at time t.

The LFGP model can be written

$$
\begin{aligned}
X_i(t) &\sim \mathcal{D}(0, K_i(t)) \text{ where } K_i(t) = \exp\left(\vec{\mathbf{u}}^{-1}(Y_i(t))\right) \\
Y_i(t) &= B \cdot F_i(t) + \epsilon_i \text{ where } \epsilon_i \overset{iid}{\sim} \mathcal{N}(0, I\sigma^2) \\
F_i(t) &\sim \mathcal{GP}(0, \kappa(t; \theta)) \\
B &\sim p_1, \sigma^2 \sim p_2, \theta \sim p_3,
\end{aligned}
$$

where $Y_i(t)$ is the vectorized Log-covariance, $F_i(t)$ is the r-length factor vector, B is $p(p+1)/2 \times r$ loading matrix, and p_1, p_2, p_3 are priors.

LFGP Model

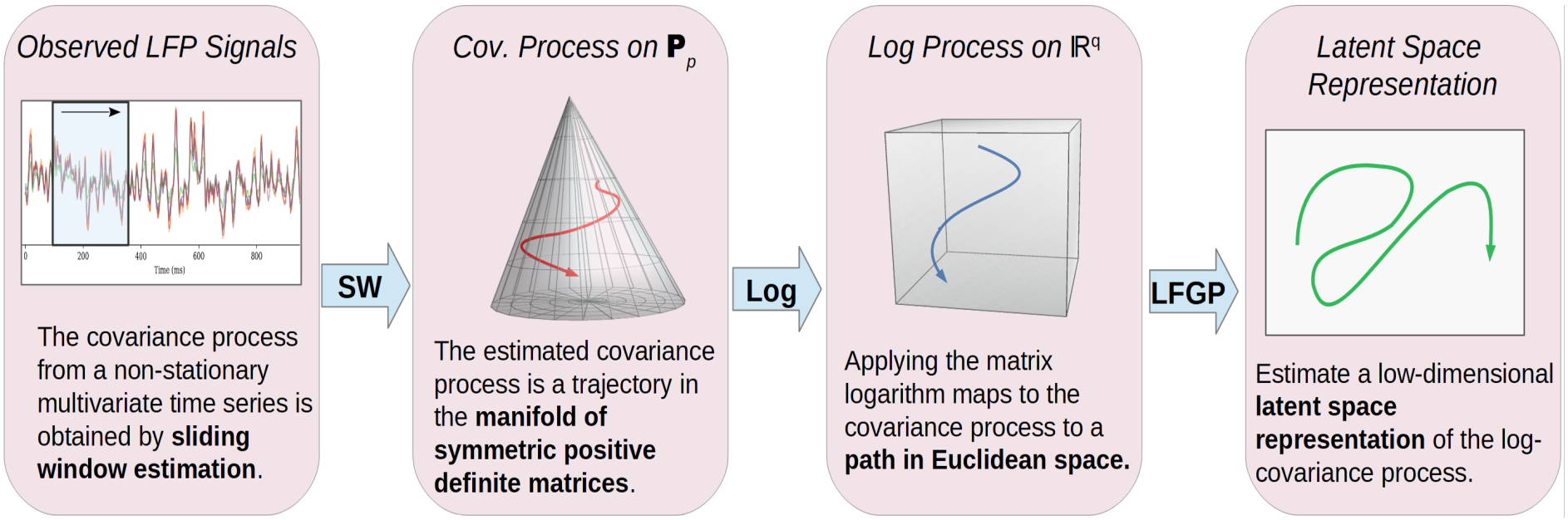


Figure: Overview of LFGP model.

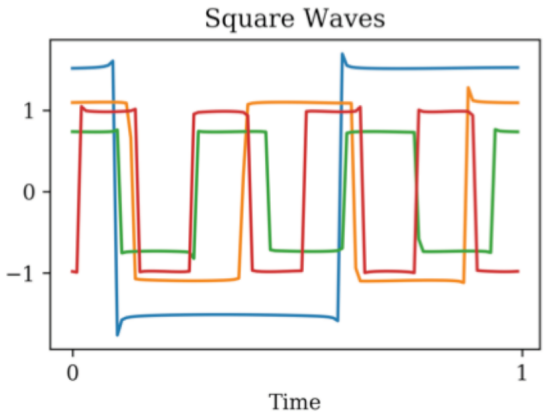
Sketch of Sampling Algorithm

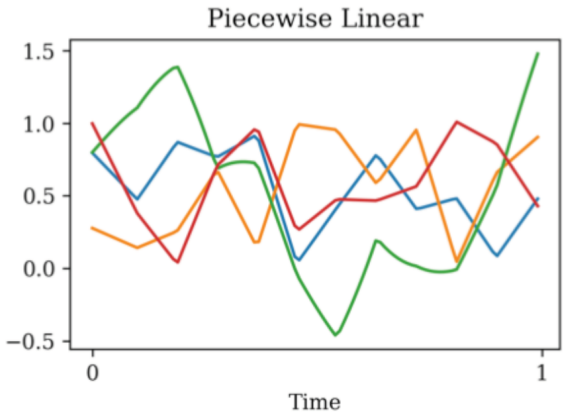
To generate posterior draws from the model, we can apply a combination of Gibbs sampling and Metropolis or slice sampling.

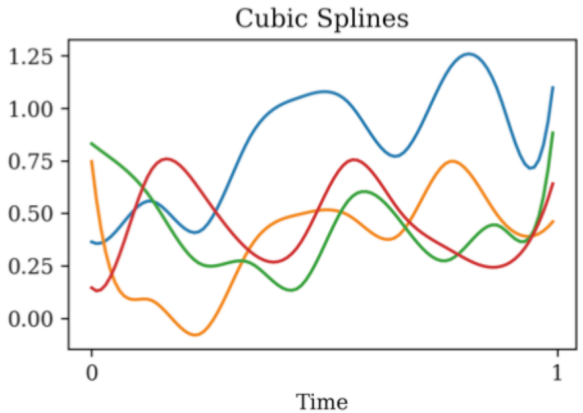
Input: Vectorized log-covariance $Y_i(t), i = 1, \ldots, n$.
Input: GP kernel κ and priors p_1, p_2, p_3.
Output: Posterior samples of factors F and factor loadings B.

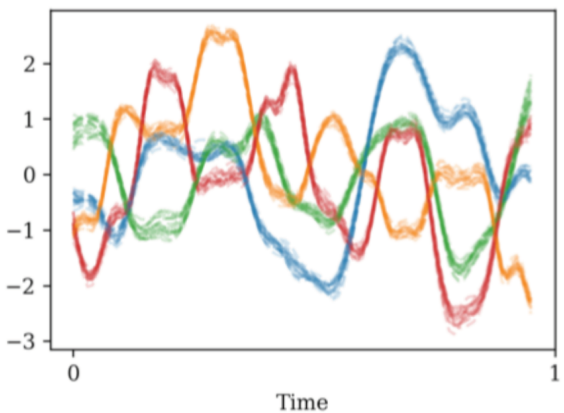
Initialize values for $B_0, \sigma_0^2, \theta_0$.
for $s = 1, ..., S$ **do**
  Sample $F_s | B_{s-1}, \sigma_{s-1}^2, \theta_{s-1}$ from $p(F|Y)$.
  Sample $B_s, \sigma_s^2, \theta_s$ conditional on F_s
end

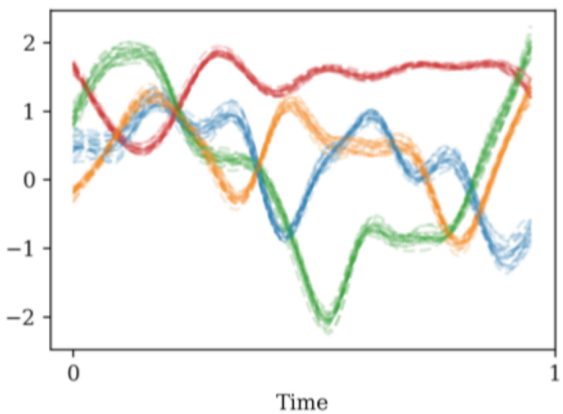
Simulations

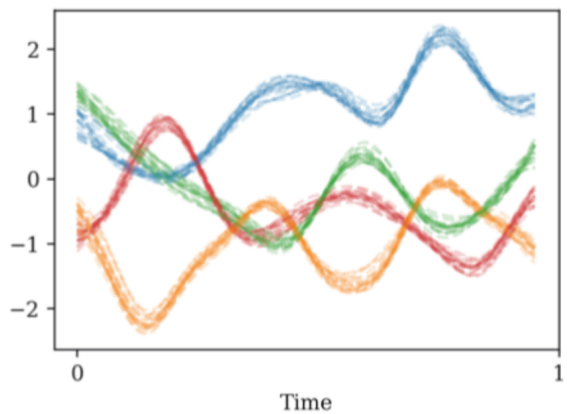












Simulations

Table: Median reconstruction loss (standard deviation) across 100 data sets.

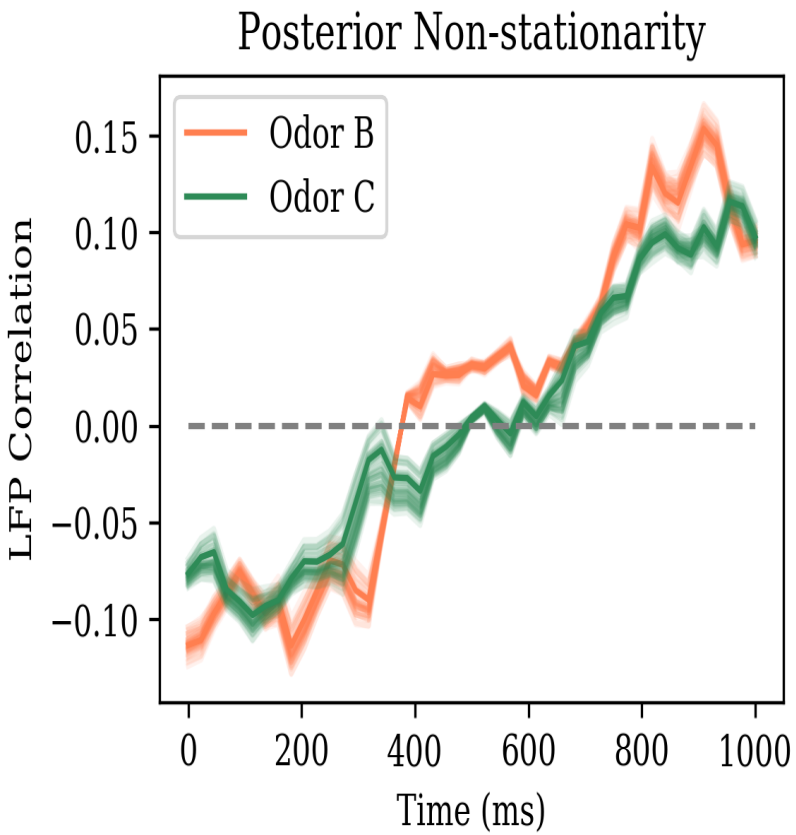
	SW-PCA	HMM	LFSV	LFGP
Square save	0.69 (0.50)	1.00 (1.30)	4.46 (2.42)	0.38 (0.42)
Piece-wise	0.03 (0.09)	0.13 (0.12)	0.66 (0.89)	0.03 (0.09)
Smooth spline	0.04 (0.02)	0.13 (0.11)	0.53 (0.40)	0.03 (0.12)

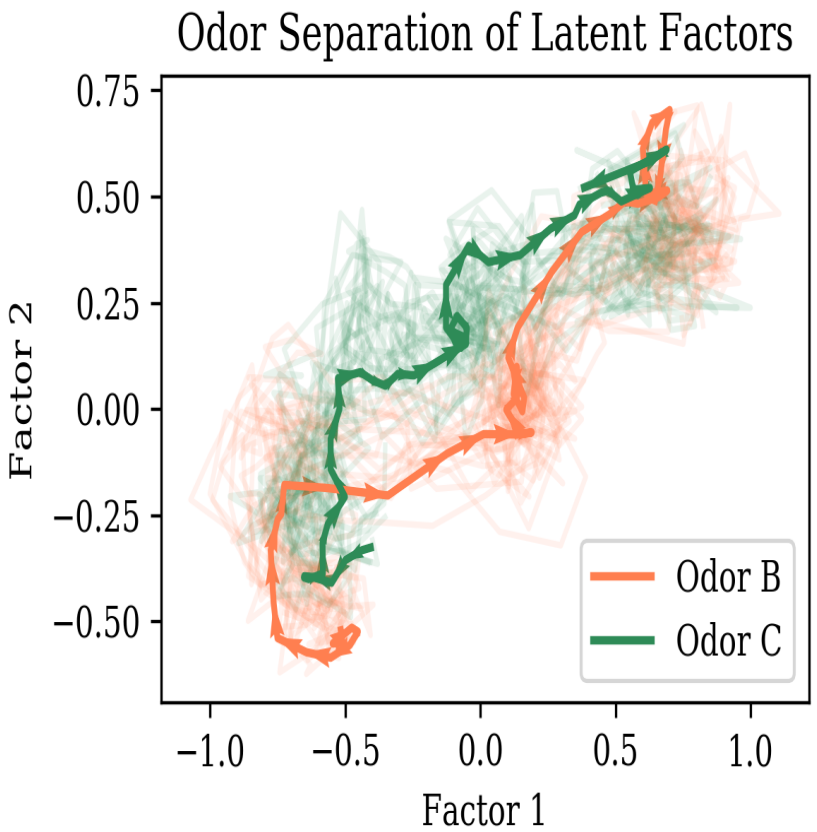
Application to LFP Data

Data Description

- For this work, we consider LFP data from *correctly identified, in-sequence* trials of odors **B** and **C** for a single rat.
  1. 41 trials for odor B
  2. 37 trials for odor C
- LFP data was recorded from 21 tetrodes implanted in the rat hippocampus, targeted at CA1.
- For analysis, we selected 6 tetrodes that contain the majority of the recorded neurons.

Application to LFP Data





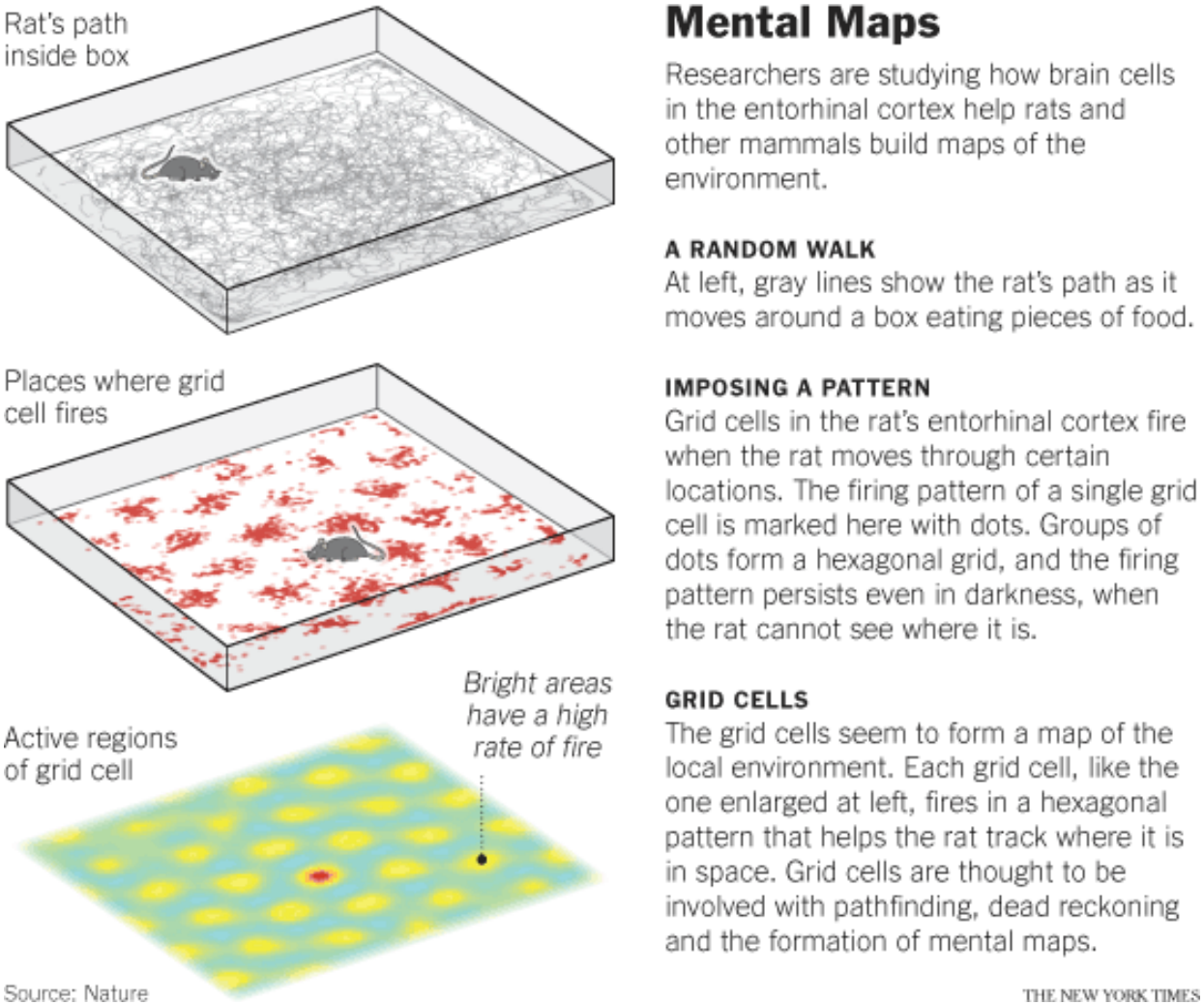
Discussion

- The LFGP model is a novel method for the analysis of DFC.
- By placing the factor structure on the covariance process itself, rather than the observed time series, the LFGP provides a flexible alternative to other factor models, such as LFSV.
- As a fully Bayesian model, LFGP can incorporate prior scientific knowledge and adjust hyperparameters to target specific questions.
- The LFGP model is competitive with existing DFC methods in simulation studies.
- Application to real LFP data provide evidence for significant differences in covariance dynamics between odor stimuli.

Future Work

- Further assess robustness and performance of the model. In particular, how serious are the known issues with sliding window estimates for the LFGP model?
- Develop a full likelihood approach, incorporating a distribution on the observed signals.
- Improve scalability of algorithm.
- Develop interpretations of the factor loading matrix to better understand which LFP tetrodes are most discriminative of stimuli.
- Apply the LFGP model to human fMRI and EEG studies.

Future Work



Mental Maps

Researchers are studying how brain cells in the entorhinal cortex help rats and other mammals build maps of the environment.

A RANDOM WALK
At left, gray lines show the rat's path as it moves around a box eating pieces of food.

IMPOSING A PATTERN
Grid cells in the rat's entorhinal cortex fire when the rat moves through certain locations. The firing pattern of a single grid cell is marked here with dots. Groups of dots form a hexagonal grid, and the firing pattern persists even in darkness, when the rat cannot see where it is.

GRID CELLS
The grid cells seem to form a map of the local environment. Each grid cell, like the one enlarged at left, fires in a hexagonal pattern that helps the rat track where it is in space. Grid cells are thought to be involved with pathfinding, dead reckoning and the formation of mental maps.

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- Slides: `github.com/dspluta/Presentations/JSM2019.pdf`

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