

Methods for analysis of parallel spike trains with Elephant

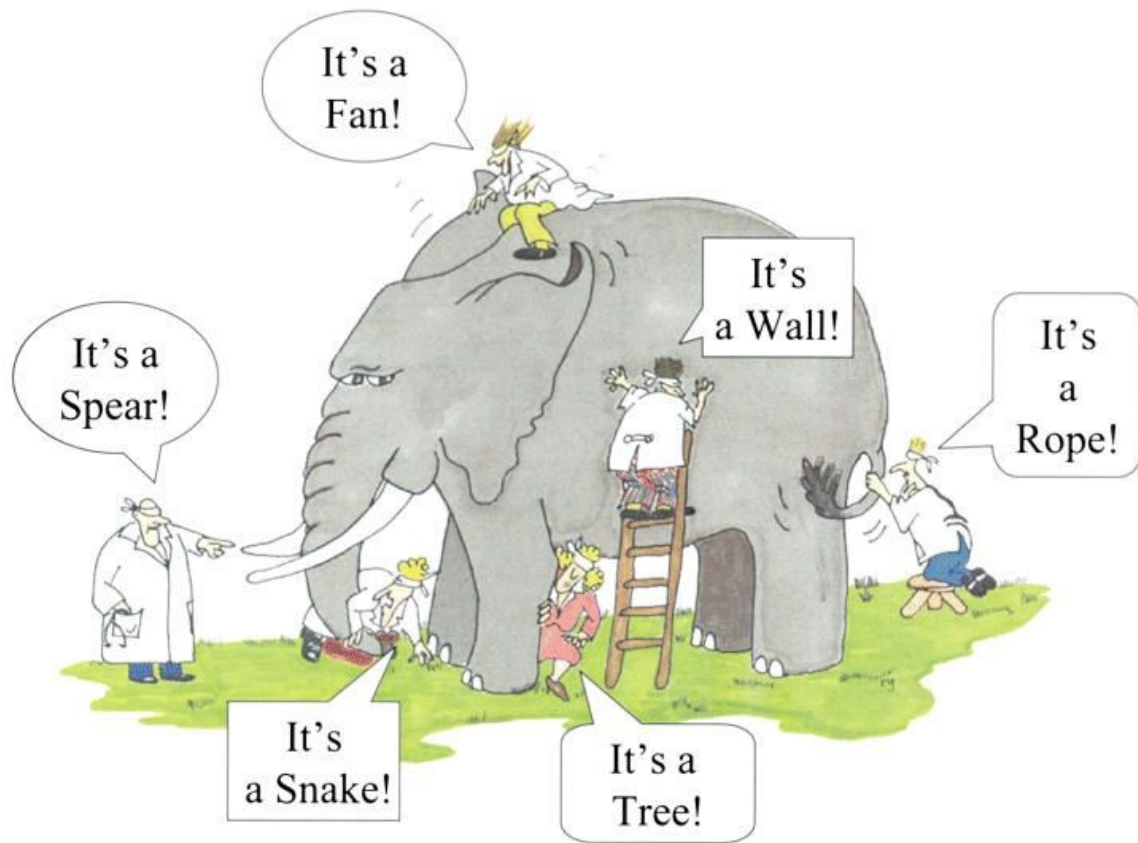
Alessandra Stella
Jülich Research Centre

In2PrimateBrains Thematic Workshop - 7.5.22 Rome



Co-funded by
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Methods for analysis of electrophysiological data

- Spike trains
 - Statistics of spike trains
 - Rate estimation
 - Spike interval statistics
 - Statistics across spike trains
 - Correlative measures on spike trains
 - Spike train correlation
 - Spike train dissimilarity
 - Spike train synchrony
 - Detection of spike patterns
 - Cell assembly detection (CAD)
 - Unitary Event analysis (UE) ←
 - Analysis of sequences of synchronous events (ASSET)
 - Spike pattern detection and evaluation (SPADE) ←
 - Cumulant based inference of higher-order correlations (CUBIC)
 - Detection of non-stationary processes
 - Gaussian Process Factor Analysis (GPFA) ←

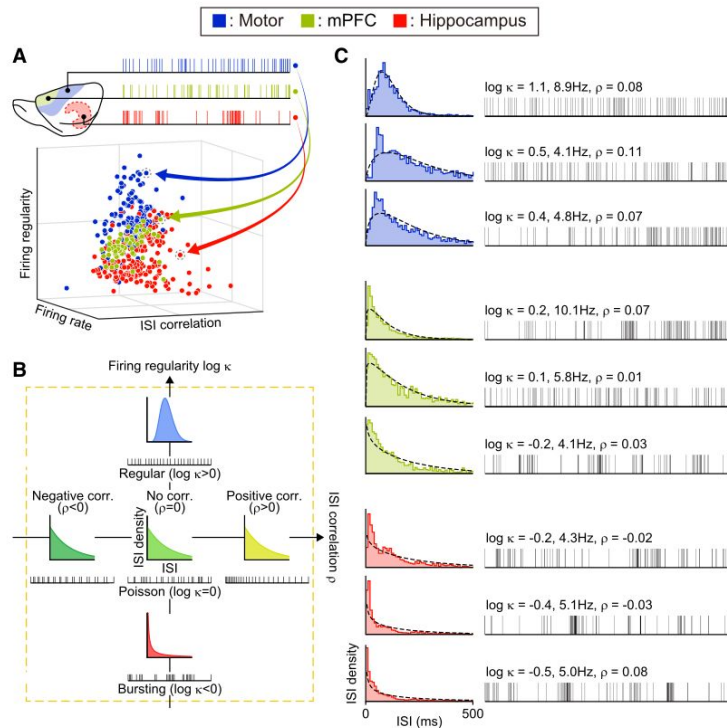


Methods for analysis of electrophysiological data

- Spike trains
 - Spike train surrogates
 - Spike train generation
- LFP and population signals
 - Signal processing
 - Spectral analysis
 - Causality measures
 - Current source density analysis
- LFP and spike trains
 - Spike-triggered average
 - Spike triggered LFP phase
- Kernels
- Waveforms
- Alternative data representations
- Utility functions



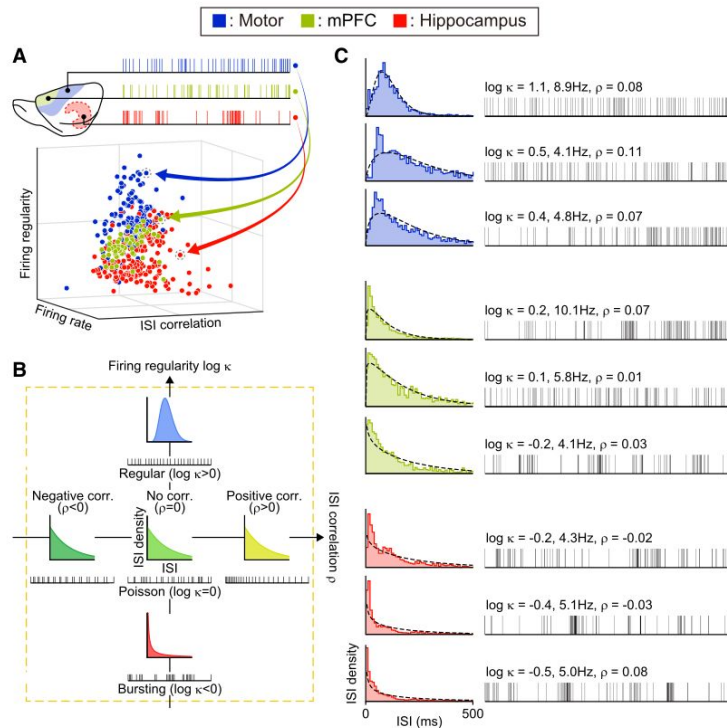
Intro - The stochastic nature of spiking



Mochizuki et al. 2016

- Spike train responses (to repetition of the same stimulus) often highly variable with respect to
 - Spike times
 - Spike count in $[0, T]$
 → may be reflected by
 - Noise, varying initial conditions, varying stimuli
- Intervals between consecutive spikes of one neuron (inter-event intervals or inter spike intervals) are highly variable
 - spike train irregularity

Intro - Variability of neural data



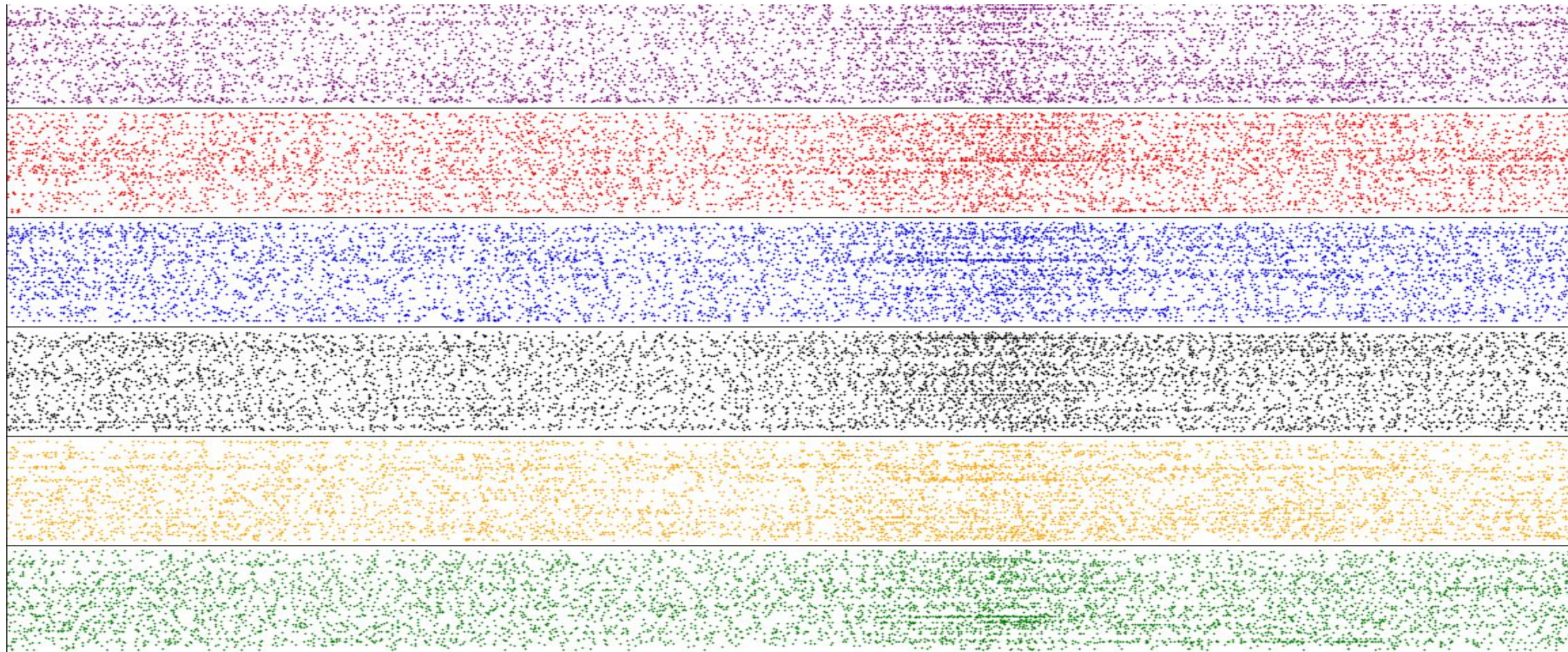
Mochizuki et al. 2016

- Data have complex features, analytical description not possible
- Firing rates change in time (**non-stationarity**), in various ways
- Firing rates change across trials (**inhomogeneity**)
- Spike trains deviate from Poisson (**bursty or regular; serial correlation**)
- Firing onset or offset vary across trials (**latency variability**)

→ Modeling spike trains through Point processes is a hard problem

→ Analyzing highly variable data is too

Intro - Variability of neural data



Intro - Neural coding

There are many different neural coding hypotheses:

- Rate coding
- Temporal coding
- Population coding

But also:

- Sparse coding
- Dense coding
- Phase coding
- etc..

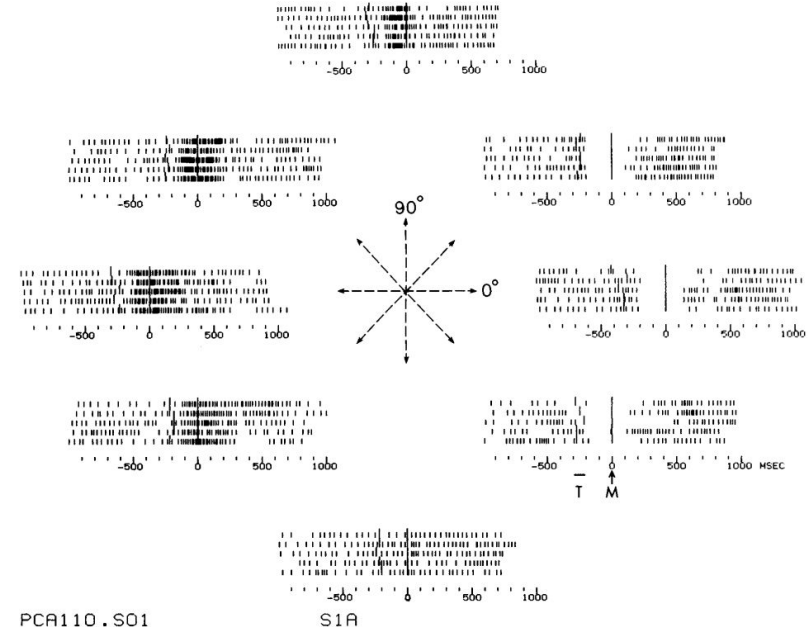
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Dayan and Abbott (2005), reprinted from Georgopoulos et al. (1984)

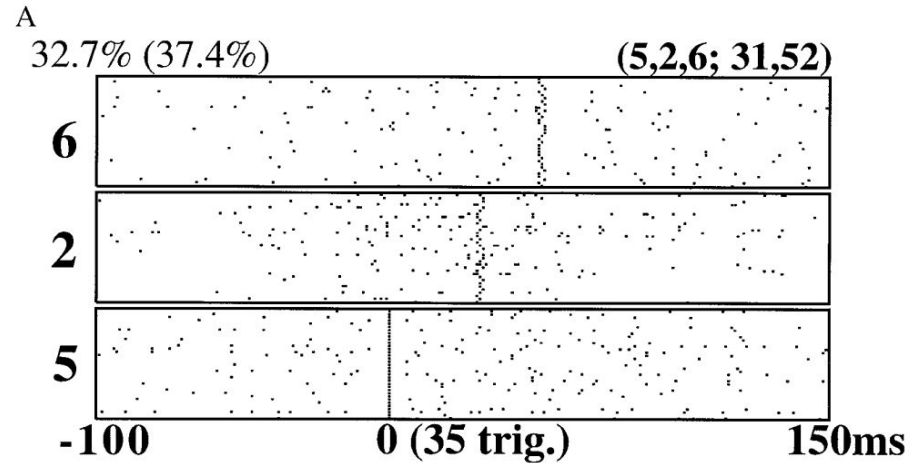
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Adapted from Prut et al. 1998, J. Neurophys

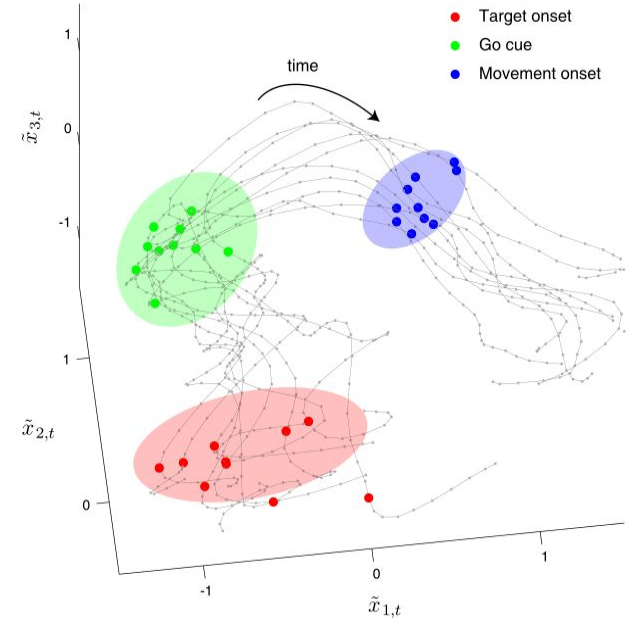
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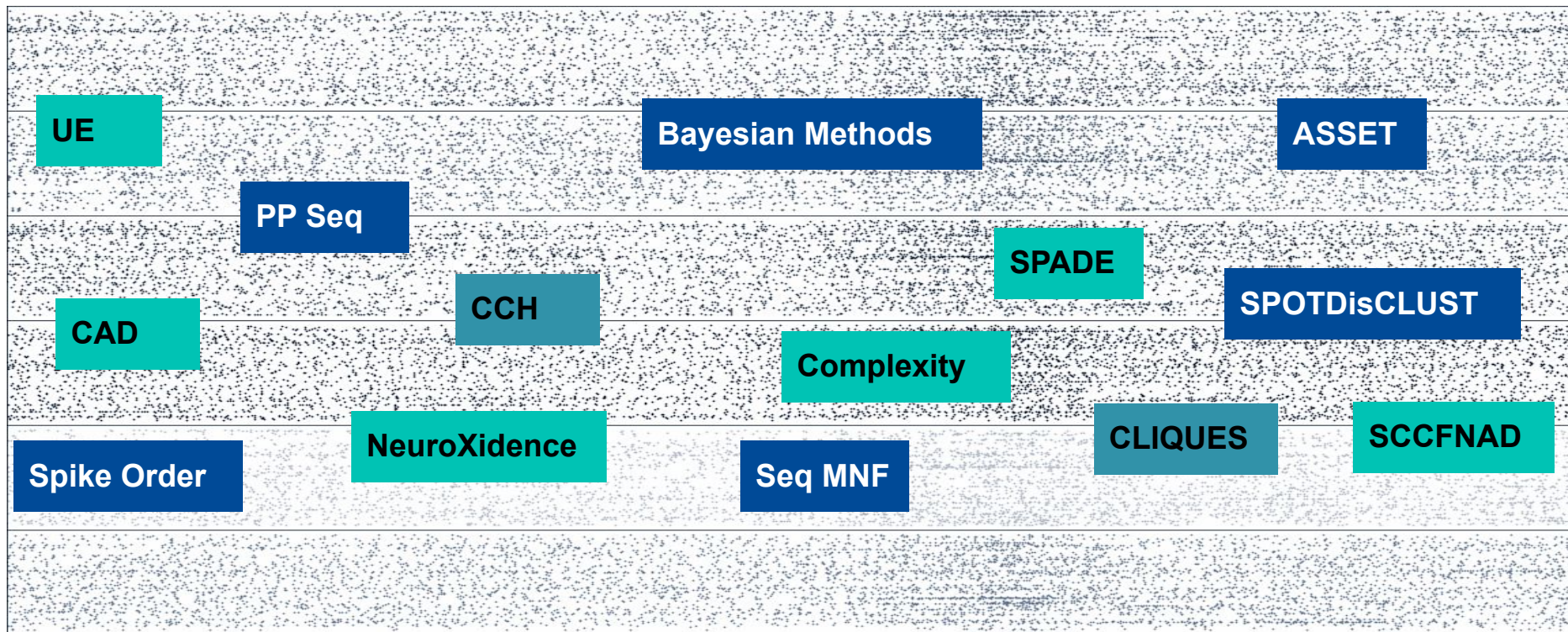


Adapted from Yu et al. 2008, NIPS conference

Spike-time correlation detection methods for parallel spike train data

Unitary events analysis
Spatio-temporal PAttern Detection and Evaluation (SPADE)

Spike time correlation detection methods for parallel spike train data



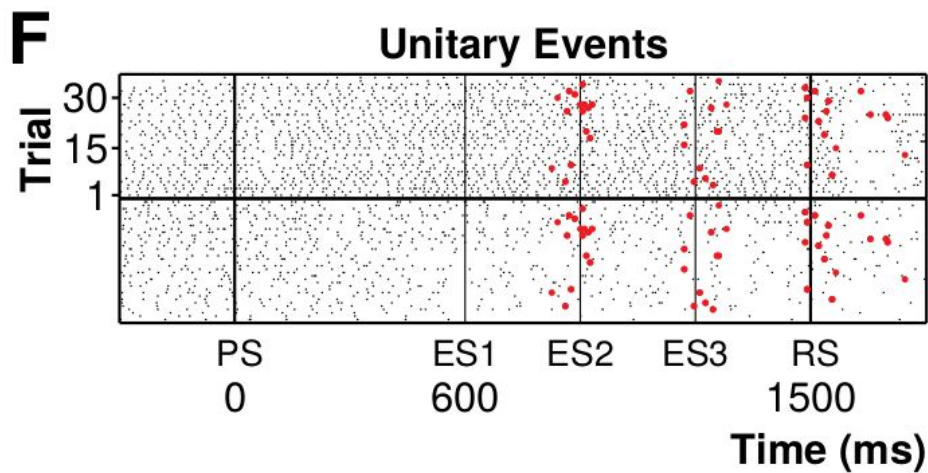
Spike time correlation detection in parallel spike trains

Challenges:

1. Building on pairwise correlation analysis may miss higher-order correlations
 - a. HOC analysis, e.g, for Synchronous or Spatio-Temporal spike Patterns (STPs)
2. Large number of neurons (100 or more)
 - a. Combinatorial explosion of patterns for N neurons
 - b. Massive multiple statistical testing problem
3. Development of methods
 - a. Detection of STPs
 - b. Significance of STP beyond chance based on firing rates
 - c. Can cope with non-stationary data

Gruen, Rotter (2010), Springer
Torre et al. (2013) Front Comput Neurosci
Stella, Quaglio et al. (2019) Biosystems
Stella, Bouss et al., (2021) biorxiv, Accepted

Spike time correlation detection in parallel spike trains



Adapted from Riehle et al. 1997, Science

Unitary events analysis

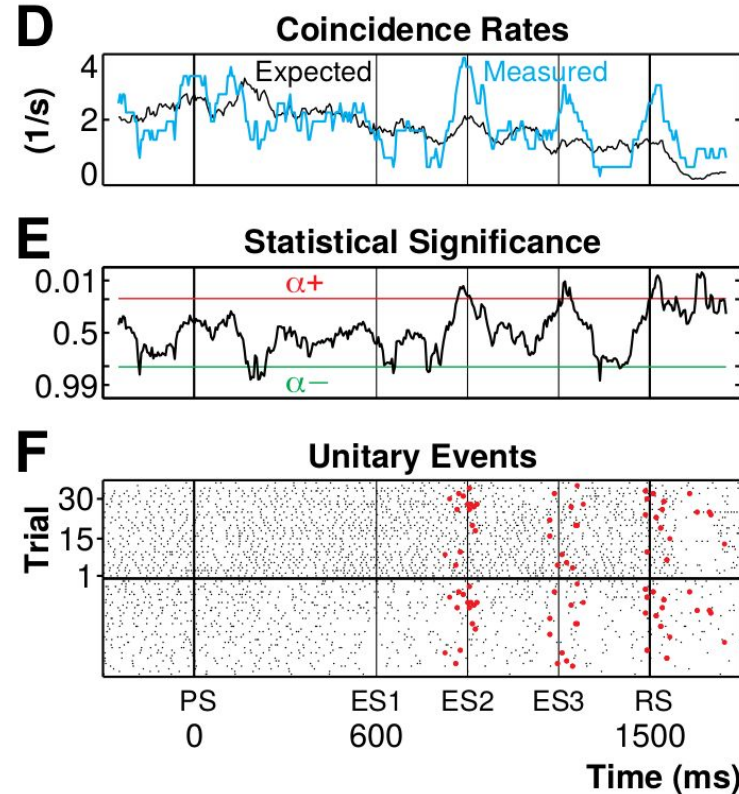
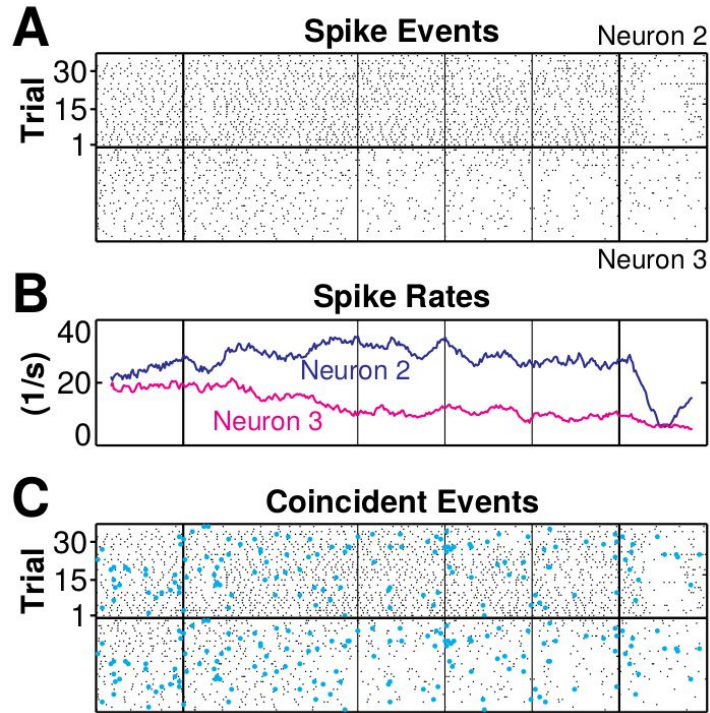
Unitary events (UEs) analysis is a statistical method detecting patterns of **synchronous spiking activity** among simultaneously recorded spike trains.

It captures:

- Synchronous spiking activity over time across neurons
- With high temporal precision
- Evaluates the probability of such events, given a null-hypothesis of spike train independence given the firing rate modulations

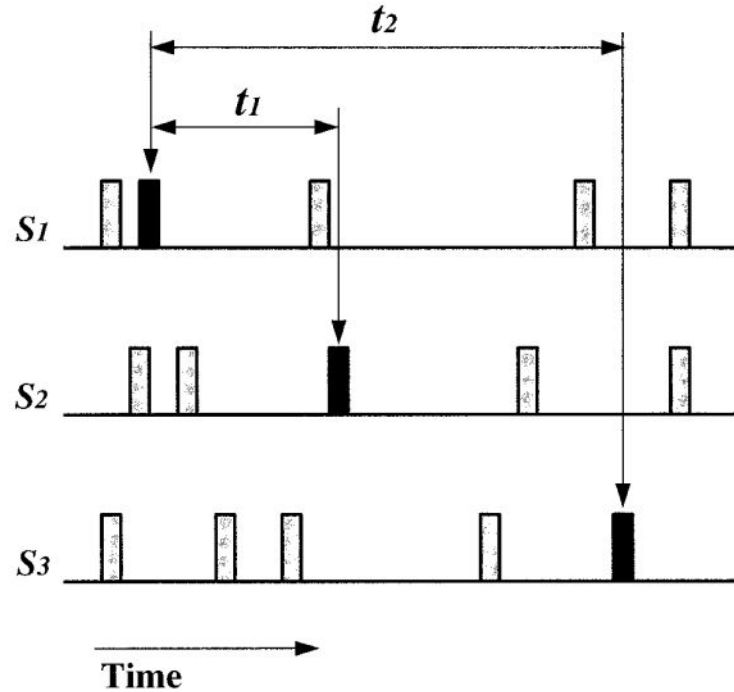
Refs UE: Gruen et al. 2002a; Gruen et al. 2002b;
Riehle et al. 1997; Gruen and Rotter, 2010

Unitary events analysis



Adapted from Riehle et al. 1997, Science

Spike time correlation detection in parallel spike trains



Adapted from Prut et al. 1998, J. Neurophys

SPADE

SPADE detects spatio-temporal spike patterns in parallel spike trains.

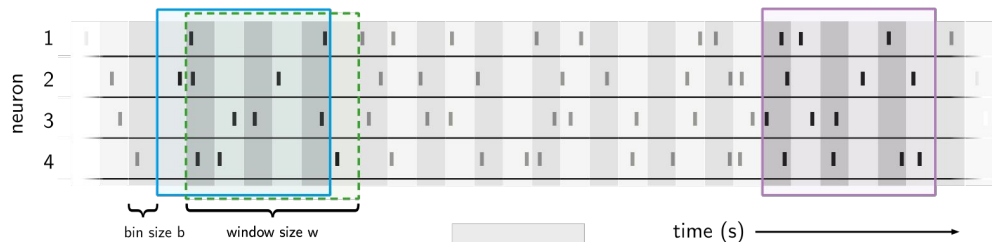
It combines

- An optimized pattern mining algorithm

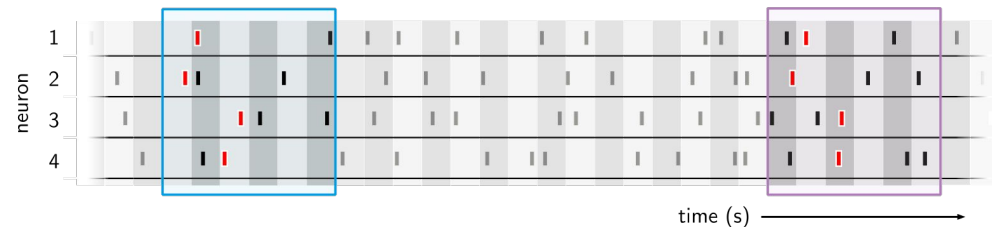
together with

- Robust statistical testing (surrogate generation)

Spike trains



Spike trains with detected pattern



Adapted from Stella et al. 2019, Biosystems
Refs: SPADE (Torre et al. 2013; Quaglio et al. 2017;
Stella et al.. 2019; Stella et al. 2021)

SPADE

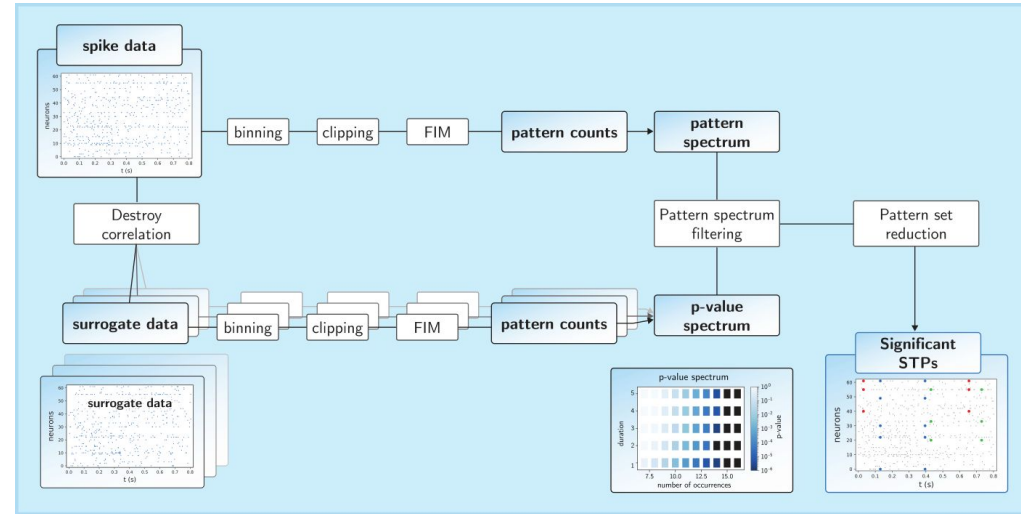
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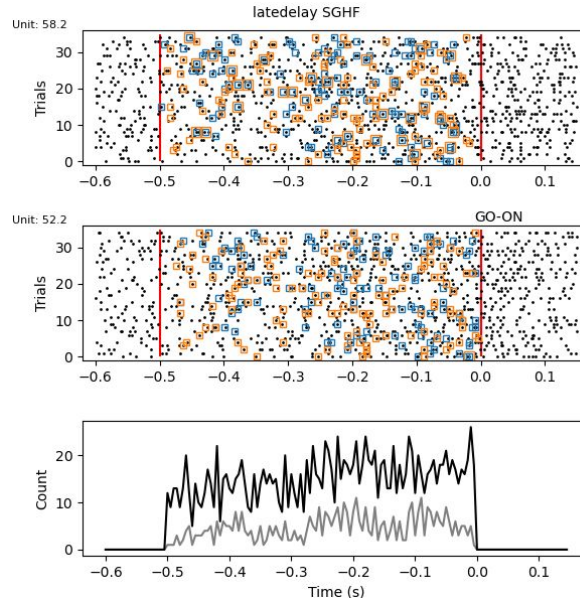
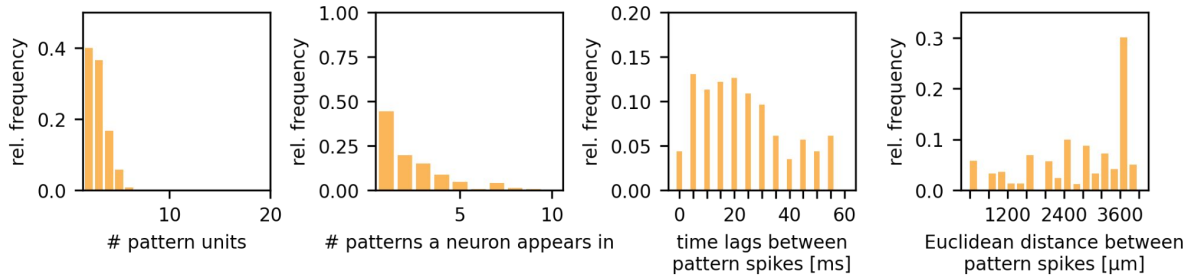
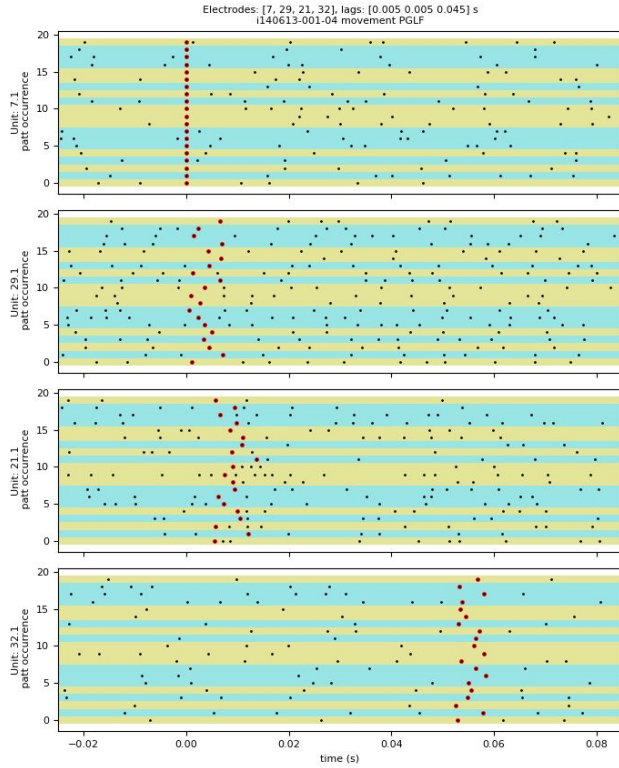
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Adapted from Stella et al. 2022, biorxiv, Accepted

SPADE



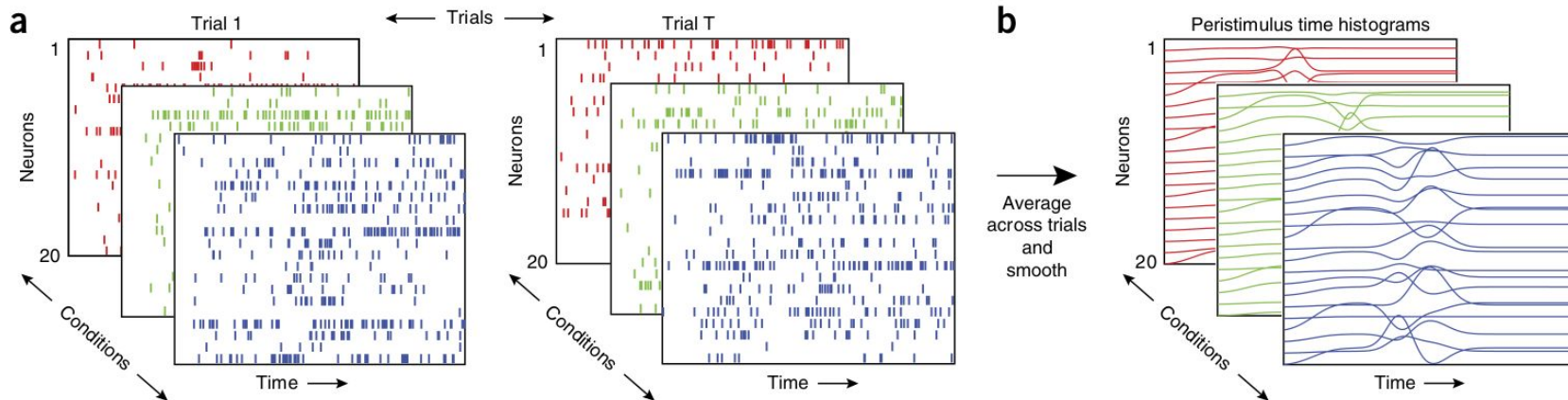
Kleinjohann et al. (2022), in prep.

Stella, Bouss, Palm, Riehle, Brochier, Gruen (2022), in prep.

Dimensionality reduction methods for parallel spike trains

Gaussian Process Factor Analysis (GPFA)

Dimensionality reduction methods for parallel spike trains



PCA

LFADS

ICA

TCA

dPCA

FA

ISOMAP

CCA

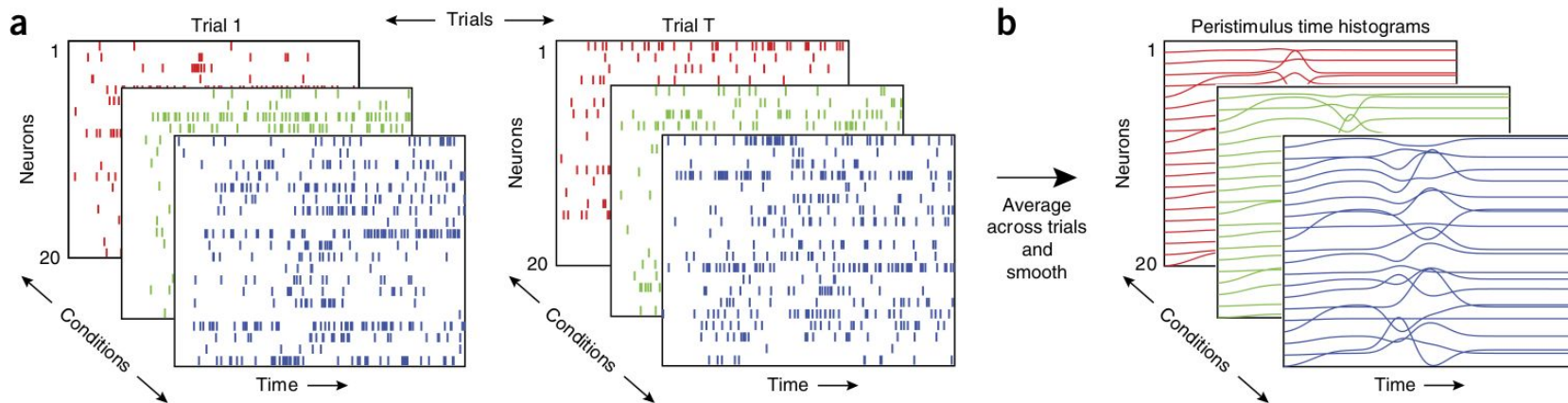
LLE

LDS

GPFA

Adapted from Cunningham and Yu. 2014, Nat. Review

Dimensionality reduction methods for parallel spike trains



Reasons to use dimensionality reduction methods:

1. Single trial analyses of neural population activity
2. Hypotheses about population activity structure
3. Exploratory analyses of large datasets

Adapted from Cunningham and Yu. 2014, Nat. Review
Byron Yu lectures at Champalimaud summer school 2017, Lisbon

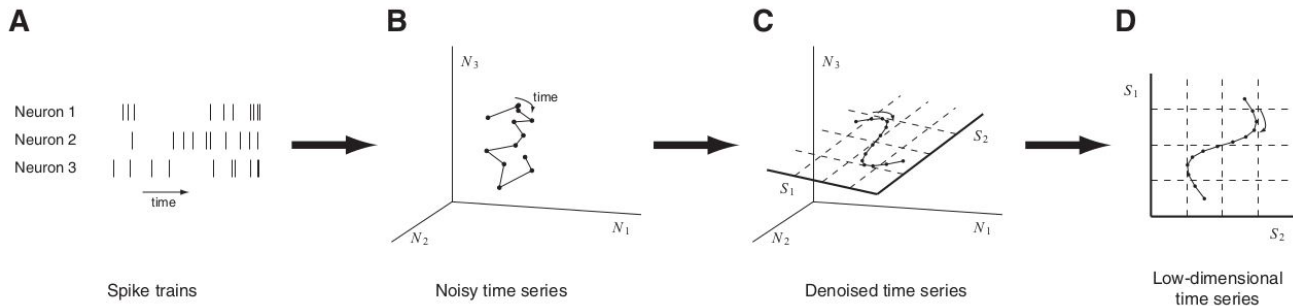
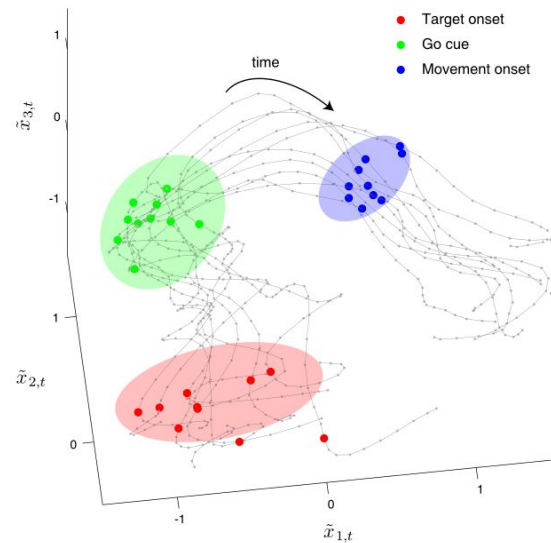
For more ref to: https://www.youtube.com/watch?v=KaTnWP1SVpk&ab_channel=FENS

GPFA

Gaussian Process Factor Analysis (GPFA) is a dimensionality reduction technique for parallel spike train data.

→ Particularly indicated for single-trial population activity

→ GPFA captures shared variance in data and incorporates it in time-varying latent variables



Adapted from Yu et al. 2019, J Neurophys

Exercises

Over these 1.5hrs, you will be presented with two jupyter notebooks:

- UE and SPADE
- GPFA

You can divide in groups and concentrate in either one of the two notebooks.
In the last minutes, we'll go through the results and comment them.

Elephant team & INM-6



Around 45 contributors from 13 institutions!

<https://elephant.readthedocs.io/en/latest/index.html>

Thank you!

www.humanbrainproject.eu

www.ebrains.eu



Co-funded by
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References

- Mochizuki, Yasuhiro, et al. "Similarity in neuronal firing regimes across mammalian species." *Journal of Neuroscience* 36.21 (2016): 5736-5747.
- Dayan, Peter, and Laurence F. Abbott. *Theoretical neuroscience: computational and mathematical modeling of neural systems*. MIT press, 2005.
- Prut, Yifat, et al. "Spatiotemporal structure of cortical activity: properties and behavioral relevance." *Journal of neurophysiology* 79.6 (1998): 2857-2874.
- Yu, Byron M., et al. "Gaussian-process factor analysis for low-dimensional single-trial analysis of neural population activity." *Advances in neural information processing systems* 21 (2008).
- Grün, Sonja, Markus Diesmann, and Ad Aertsen. "Unitary events in multiple single-neuron spiking activity: I. Detection and significance." *Neural computation* 14.1 (2002): 43-80.
- Williams, Alex, et al. "Point process models for sequence detection in high-dimensional neural spike trains." *Advances in neural information processing systems* 33 (2020): 14350-14361.
- Russo, Eleonora, and Daniel Durstewitz. "Cell assemblies at multiple time scales with arbitrary lag constellations." *Elife* 6 (2017): e19428.
- Stella, Alessandra, et al. "3d-SPADE: Significance evaluation of spatio-temporal patterns of various temporal extents." *Biosystems* 185 (2019): 104022.
- Watanabe, Keita, et al. "Unsupervised detection of cell-assembly sequences by similarity-based clustering." *Frontiers in Grossberger*, Lukas, Francesco P. Battaglia, and Martin Vinck. "Unsupervised clustering of temporal patterns in high-dimensional neuronal ensembles using a novel dissimilarity measure." *PLoS computational biology* 14.7 (2018): e1006283.
- Neuroinformatics* 13 (2019): 39.
- Peter, Sven, et al. "Sparse convolutional coding for neuronal assembly detection." *Advances in Neural Information Processing Systems* 30 (2017).

References

- Mackevicius, Emily L., et al. "Unsupervised discovery of temporal sequences in high-dimensional datasets, with applications to neuroscience." *Elife* 8 (2019): e38471.
- Williams, Alex H., et al. "Unsupervised discovery of demixed, low-dimensional neural dynamics across multiple timescales through tensor component analysis." *Neuron* 98.6 (2018): 1099-1115.
- Diana, Giovanni, Thomas TJ Sainsbury, and Martin P. Meyer. "Bayesian inference of neuronal assemblies." *PLoS computational biology* 15.10 (2019): e1007481.
- Torre, Emiliano, et al. "ASSET: analysis of sequences of synchronous events in massively parallel spike trains." *PLoS computational biology* 12.7 (2016): e1004939.
- Kreuz, Thomas, et al. "Leaders and followers: Quantifying consistency in spatio-temporal propagation patterns." *New Journal of Physics* 19.4 (2017): 043028.
- Grün, Sonja, and Stefan Rotter, eds. *Analysis of parallel spike trains*. Vol. 7. Springer Science & Business Media, 2010.
- Torre, Emiliano, et al. "Statistical evaluation of synchronous spike patterns extracted by frequent item set mining." *Frontiers in computational neuroscience* 7 (2013): 132.
- Stella, Alessandra, et al. "Generating surrogates for significance estimation of spatio-temporal spike patterns." *bioRxiv* (2021).
- Riehle, Alexa, et al. "Spike synchronization and rate modulation differentially involved in motor cortical function." *Science* 278.5345 (1997): 1950-1953.
- Quaglio, Pietro, et al. "Detection and evaluation of spatio-temporal spike patterns in massively parallel spike train data with spade." *Frontiers in computational neuroscience* 11 (2017): 41.
- Anowar, Farzana, Samira Sadaoui, and Bassant Selim. "Conceptual and empirical comparison of dimensionality reduction algorithms (pca, kpca, lda, mds, svd, lle, isomap, le, ica, t-sne)." *Computer Science Review* 40 (2021): 100378.
- Cunningham, John P., and M. Yu Byron. "Dimensionality reduction for large-scale neural recordings." *Nature neuroscience* 17.11 (2014): 1500-1509.

References

- Kobak, Dmitry, et al. "Demixed principal component analysis of neural population data." *Elife* 5 (2016): e10989.
- Takahashi, Kazutaka, et al. "Encoding of both reaching and grasping kinematics in dorsal and ventral premotor cortices." *Journal of Neuroscience* 37.7 (2017): 1733-1746.
- Groppe, David M., et al. "Independent component analysis of event-related potentials." *Cognitive science online* 6.1 (2008): 1-44.
- Williams, Alex H., et al. "Unsupervised discovery of demixed, low-dimensional neural dynamics across multiple timescales through tensor component analysis." *Neuron* 98.6 (2018): 1099-1115.
- Zhuang, Xiaowei, Zhengshi Yang, and Dietmar Cordes. "A technical review of canonical correlation analysis for neuroscience applications." *Human Brain Mapping* 41.13 (2020): 3807-3833.