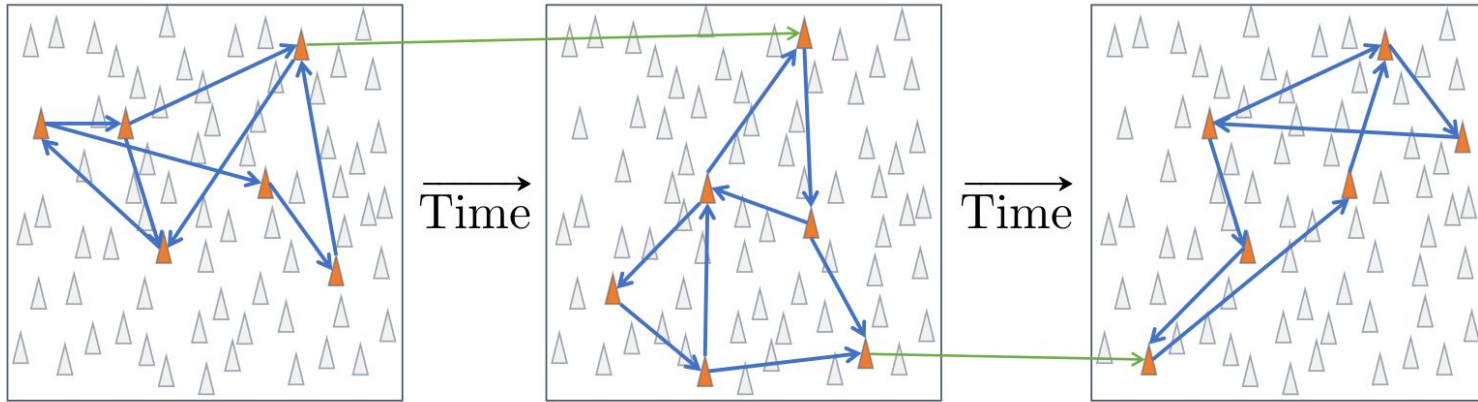


# Significant Spatio-Temporal Spike Patterns in Macaque Monkey Motor Cortex

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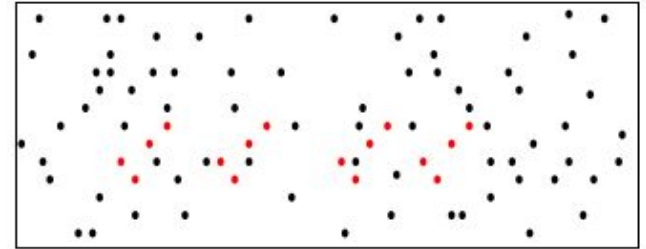
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4. Theoretical Systems Neurobiology, RWTH Aachen University, Germany

# Hebbian assemblies hypothesis



Top: Bous, 2020

Bottom: adapted  
from Quaglio et al.  
2018



- Cell assemblies act as building blocks for information processing
- Assembly membership is expressed by coordinated spiking activity

# Higher order correlation analysis is a statistical challenge

Challenges we have to face:

## 1. Building on pairwise correlation analysis may miss higher-order correlations

- a. HOC analysis, for Spatio-Temporal spike Patterns (STPs)

## 2. Large number of neurons (100 or more)

- a. Combinatorial explosion of patterns for N neurons, duration K:  $2^{(N \cdot K)}$
- b. Massive multiple statistical testing problem

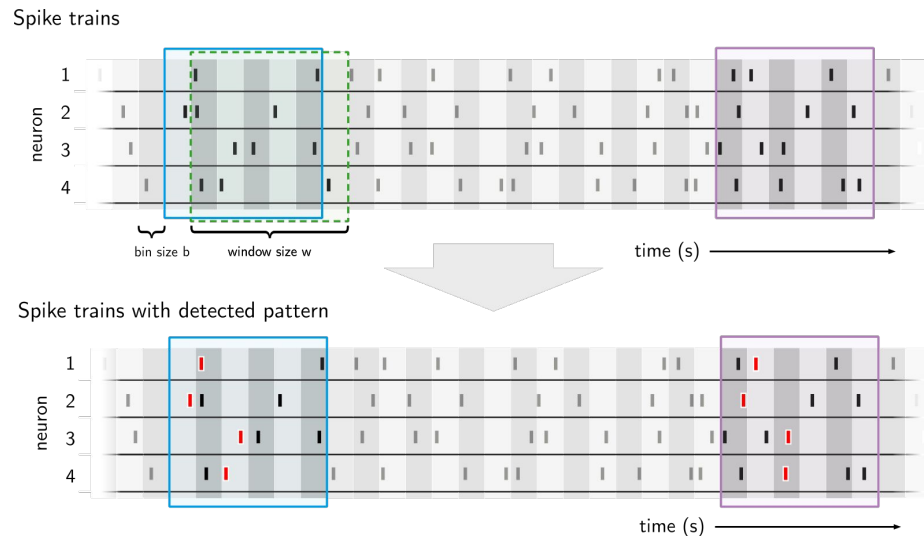
## 3. Development of methods

- a. Detection of STPs
- b. Significance of STP beyond chance based on firing rates
- c. Can cope with non-stationary data

- Torre et al. (2013) Front Comput Neurosci
- Torre et al. (2016) J Neurosci
- Yegenoglu et al. (2016)
- Quaglio et al. (2017) Front Comput Neurosci
- Stella, Quaglio et al. (2019) Biosystems
- Stella, Bouss et al., in preparation

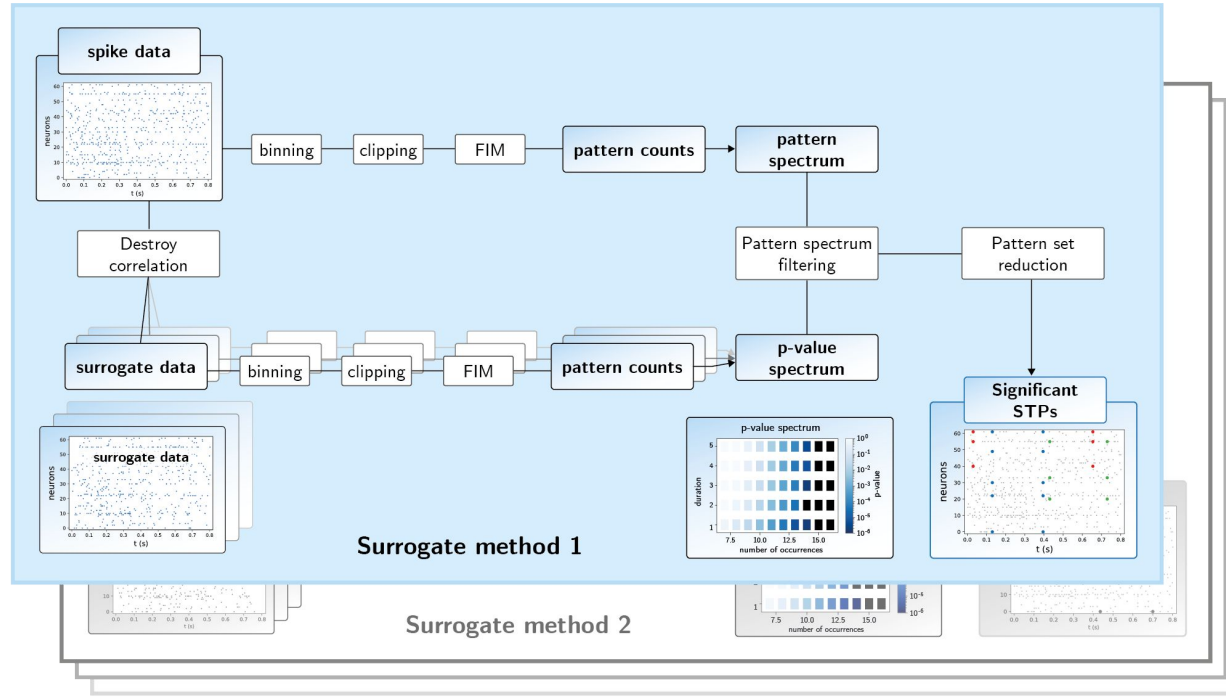
# Detection of spatio-temporal spike patterns with SPADE

- SPADE **detects Spatio-temporal Spike Patterns** in massively parallel spike trains. (Quaglio et al. 2017)
  - Combines
    - an **optimized pattern mining algorithm** (collaboration with Uni Bielefeld: Pormann et al., subm.)
- together with
- **robust statistical testing** (Stella et al. 2019; Stella et al., in preparation)



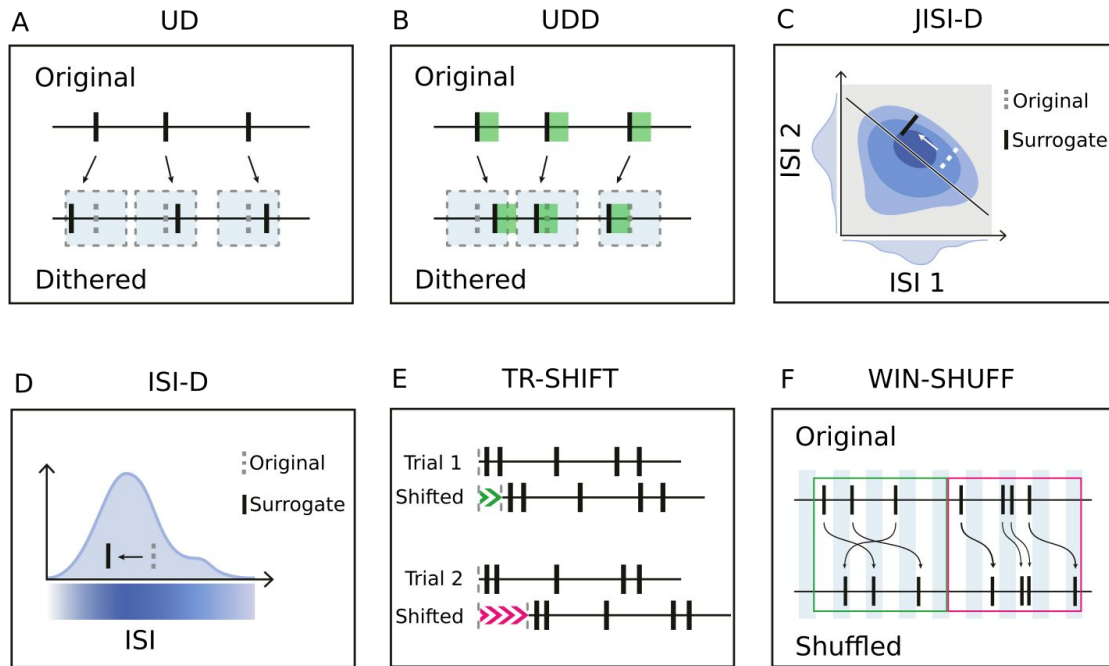
STP detection on parallel spike trains. Adapted from Stella et al. 2019

# Detection of spatio-temporal spike patterns with SPADE



- Mine original data for STPs
- Generate surrogates and analyze them in the same way
- Repeat the procedure for  $N \gg$
- Derive significance
- Significant patterns → STPs

# Comparison and evaluation of Surrogate techniques



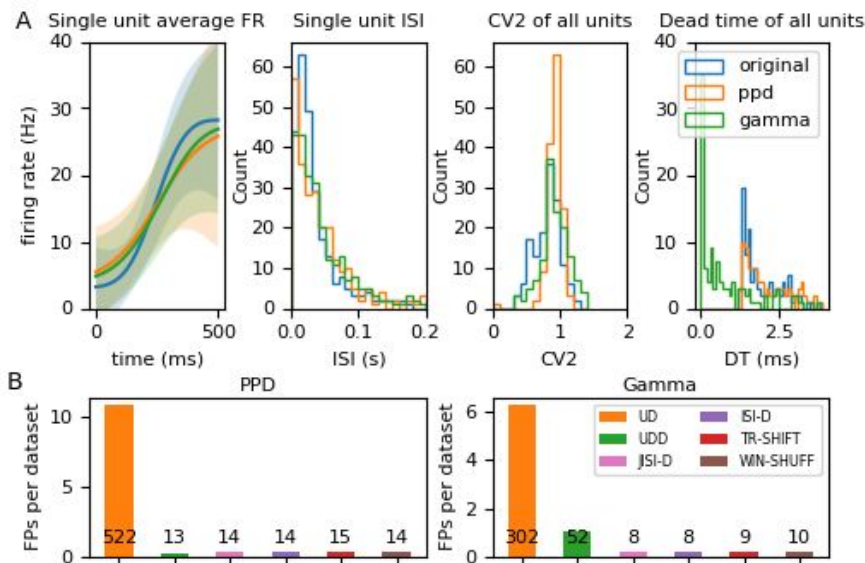
- A. Uniform Dithering (UD) (Date et al. 1998; Grün and Rotter 2010)
- B. Uniform dithering with Dead Time (UDD) (Bouss 2020 - Master Thesis)
- C. Joint ISI-Dithering (JISI-D) (Gerstein 2004)
- D. ISI-Dithering (ISI-D)
- E. Trial Shifting (TR-Shift) (Pipa et al. 2008; Louis et al. 2010a Grün and Rotter (2010))
- F. Window Shuffling (Win-Shuff)

# Which surrogate technique to choose?

Feature/ Method	Uniform Dithering	Uniform Dithering with Dead Time	ISI Dithering	Joint-ISI Dithering	Trial Shifting	Window Shuffling
<b>Spike count</b>	no	approx	approx	approx	yes	yes
<b>ISI</b>	no	no	approx	approx	yes	approx
<b>Dead time</b>	no	yes	yes	yes	yes	no
<b>Auto-correlation</b>	no	no	no	no	yes	approx
<b>Rate modulation</b>	approx	approx	approx	approx	approx	approx
<b>CV &gt; 1 (regular neurons)</b>	no	no	approx	approx	yes	no
<b>CV &lt; 1 (bursty neurons)</b>	no	no	approx	approx	yes	approx

# Comparison of surrogate techniques on non-stationary artificial data

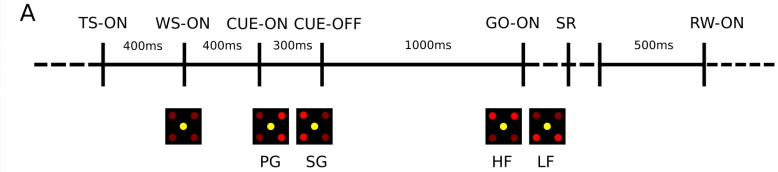
Artificial data modeled on two sessions of experimental data (Brochier et al. 2018) by Poisson process with dead time (PPD; Deger et al. 2012) and Gamma process.



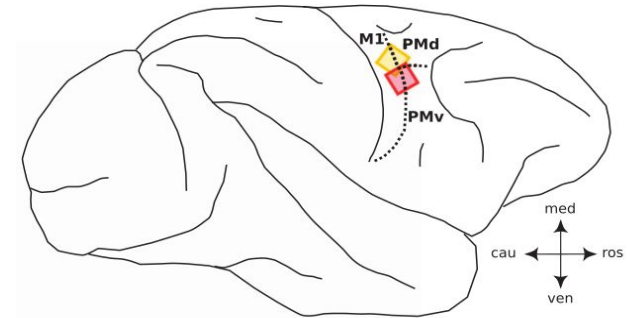
## In artificial data:

- In case of non-Poisson data, **UD leads to a strong reduction in spike count** after clipping, causing a large number of false positives (FPs)
- The other methods show a small number of FPs

# SPADE analysis of experimental data



- **Instructed delay reaching and grasping experiment**
- One 10x10 Utah electrode array is inserted in pre-/motor cortex of two macaque monkeys
- Two grip types, two force types
- Simultaneous recordings from ~100 neurons
- References: Riehle et al. 2013, Brochier et al. 2018



Figures adapted from Brochier et al. 2018. Data from the lab of Thomas Brochier, INT Marseille.

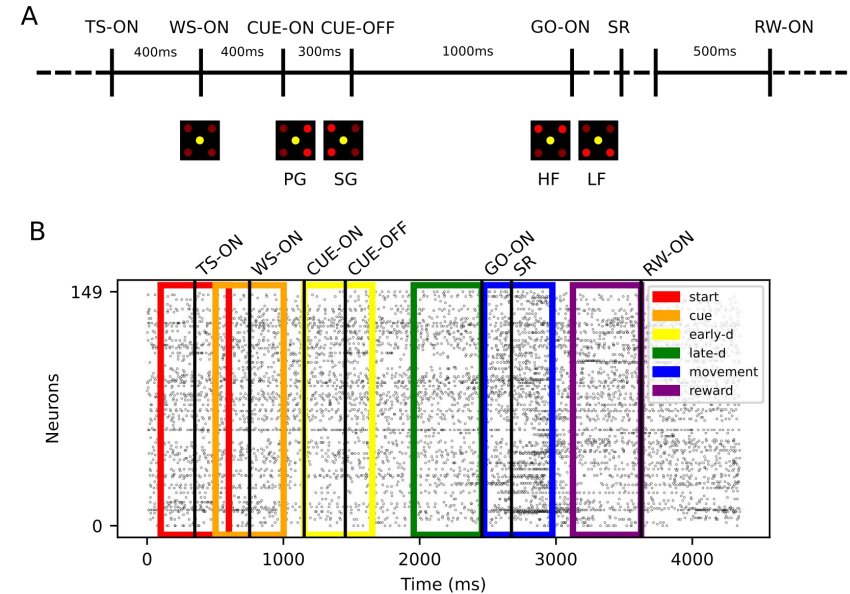
# SPADE analysis of experimental data

- 2 monkeys
- 9/10 sessions per monkey (15min per session)
- 4 trial types (SGHF, SGLF, PGHF, PGLF)
- Separately analyzed
- Quasi time-resolved analysis
  - into behaviorally relevant epochs

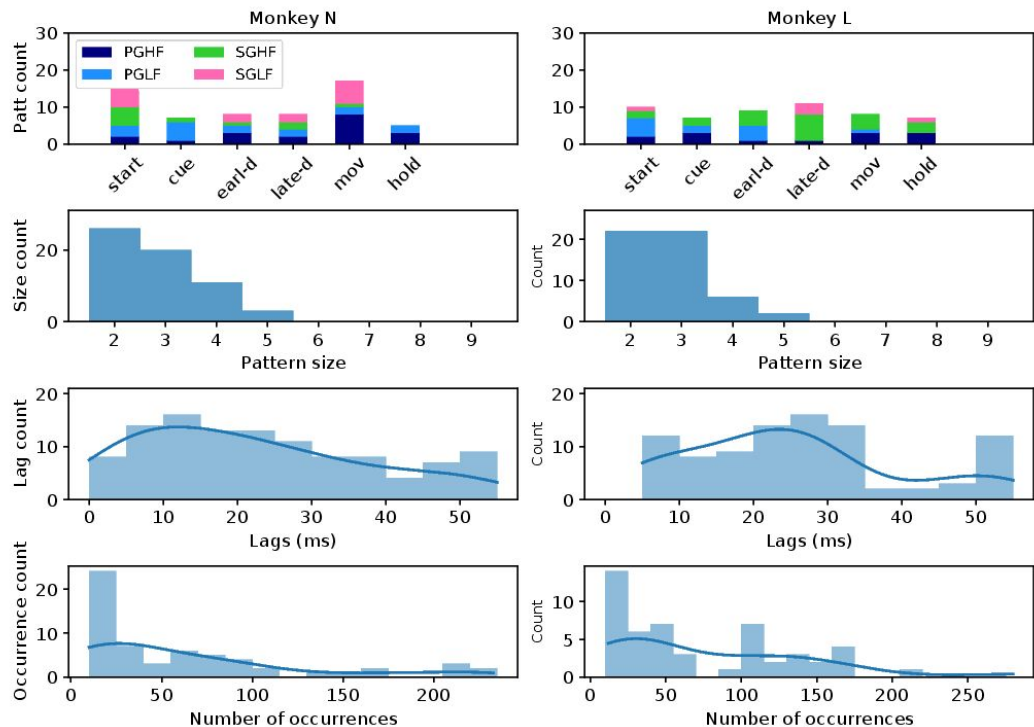
## SPADE parameters:

Max pattern duration: 60ms, temporal precision (bin size): 5ms,

Surrogate technique: trial shifting (25ms),  $\alpha$ : 0.05



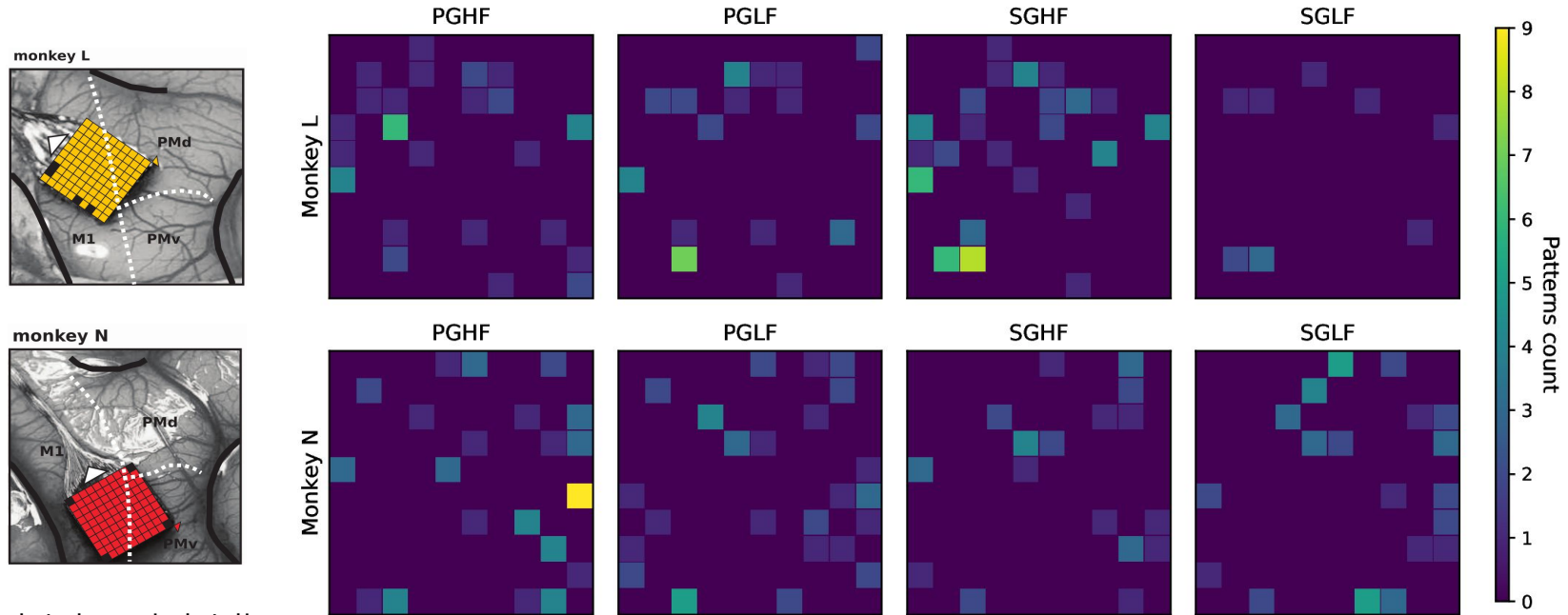
# Analysis of Spatio-Temporal Patterns of experimental parallel spike trains with SPADE: Pattern statistics



Pattern statistics for both monkeys across sessions.

- A. Pattern counts across behavioral epochs:
  - ~60 patterns per monkey
  - patterns occur in all phases of behavior and all trial types
- B. Pattern size:
  - 2-5 neurons per pattern
- C. Pattern lags:
  - max temporal duration = 60ms
- D. Number of pattern repetitions:
  - min: 10 to max. 250 occurrences, depending on size

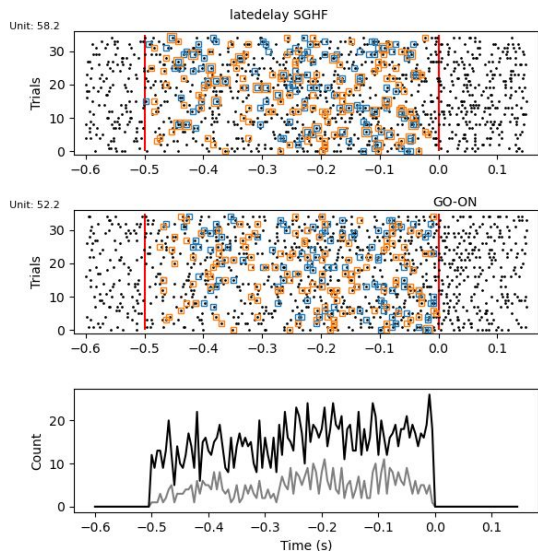
# Spatial distribution of Spatio-temporal spike patterns on the Utah array



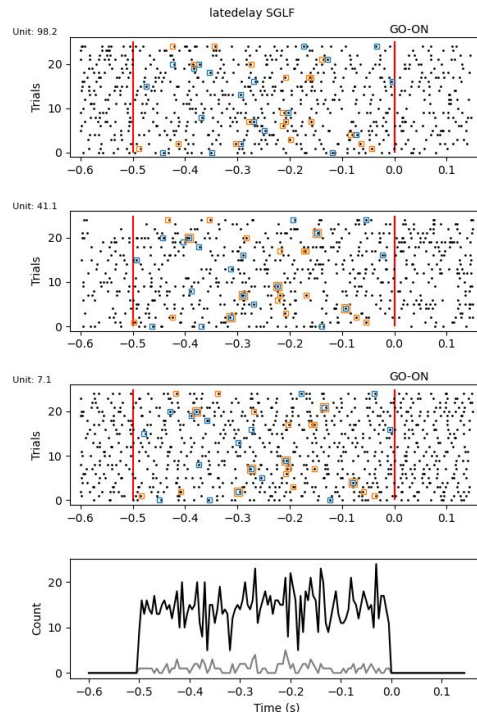
Utah electrode arrays implanted in Monkey L and N. Figure adapted from Brochier et al. 2018

# Spatio-temporal patterns may share individual spikes

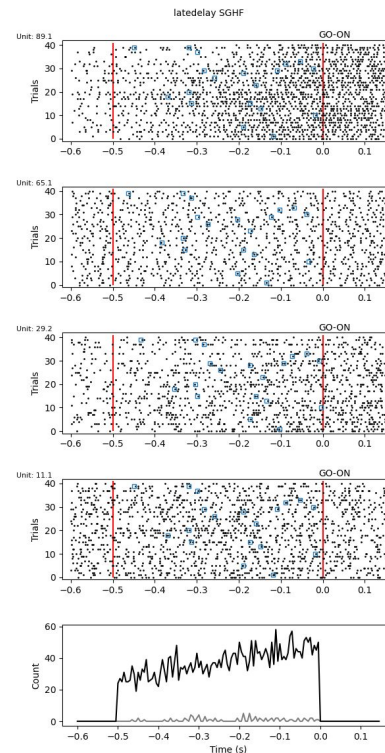
Order of correlation 2



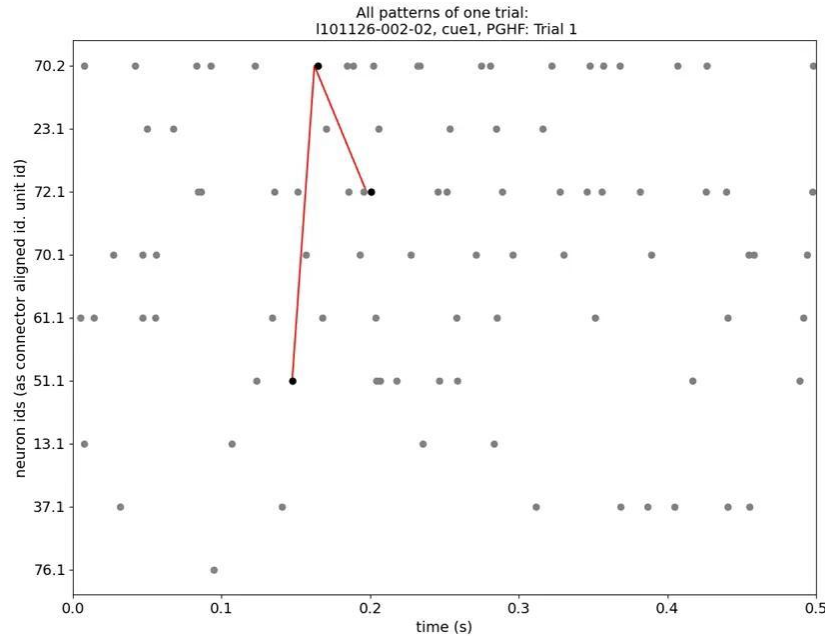
Order of correlation 3



Order of correlation 4



# Analysis of Spatio-Temporal Patterns of experimental parallel spike trains with SPADE

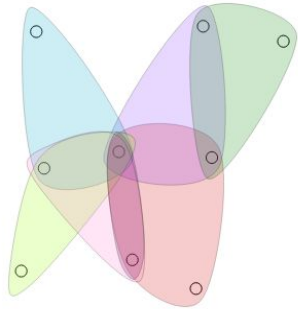


- Shown: neurons involved in patterns. Video shows single trials in succession
  - Patterns are **strictly specific** to the specific condition
  - Different neuronal compositions and different lags
- **STPs are specific to behavior**

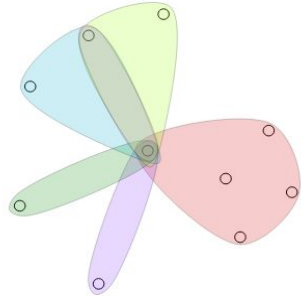
# Hub neurons in patterns

Spatio Temporal Patterns share neurons

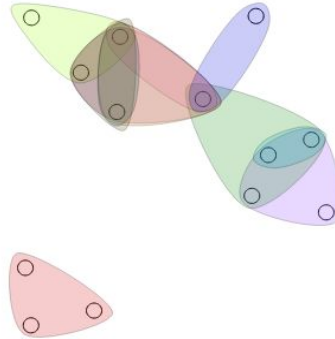
→ might be central for the network coordination



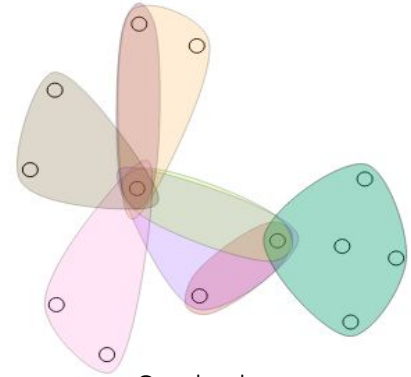
Session i101006



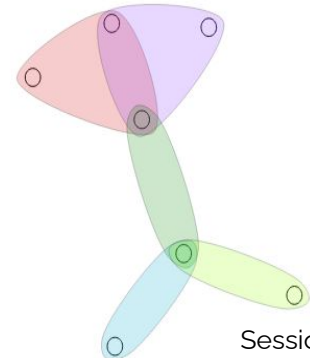
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Session i140718



Session i140703



Session i140701

# Conclusions

- We hypothesize that assembly activity is expressed by the occurrence of **precise spatio-temporal patterns of spikes** emitted by neurons that presumably are members of an assembly
- We **developed a method, called SPADE, detecting significant spatio temporal patterns** in massively parallel spike trains
- We **analyzed N=19 experimental sessions** with SPADE consisting of about 100 parallel spike trains recorded by a 10x10-electrode Utah array in the pre-/motor cortex of two macaque monkeys performing a reach-to-grasp task
- Our results show that **spatio temporal patterns occur in all phases of the behavior**
- Patterns are specific to a behavioral condition, suggesting that **different assemblies are activated for each specific behavioral context**

# Thanks for listening



**Group of Statistical Neuroscience, Institute of Neuroscience and Medicine 6 (INM-6), Jülich Research Center**

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- Prof. Dr. Sonja Grün
- Prof. Dr. Günther Palm
- Peter Bouss
- Dr. Alexa Riehle
- Dr. Thomas Brochier



Surrogate techniques and SPADE are on **elephant!**  
[elephant.readthedocs.io](http://elephant.readthedocs.io)

## References

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- Quaglio P, Yegenoglu A, Torre E, Endres DM, Grün S. Frontiers in computational neuroscience. 2017
- Brochier T, Zehl L, Hao Y, Duret M, Sprenger J, Denker M, Grün S, Riehle A. Scientific data. 2018
- Stella A, Quaglio P, Torre E, Grün S. Biosystems. 2019
- Stella A, Bouss P, Palm G, Grün S. In preparation
- Pormann F, Pilz S, Stella S, Kleinjohann A, Denker M, Hagemeyer J, Rückert J. Submitted

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# Analysis of Spatio-Temporal Patterns of experimental parallel spike trains with SPADE

Different distribution of participation of neurons per Monkey

- higher rate for monkey L (left) ~ 8%
- lower rate for monkey N ~ 25%

