

Surrogate methods for spike pattern detection in non-Poisson data

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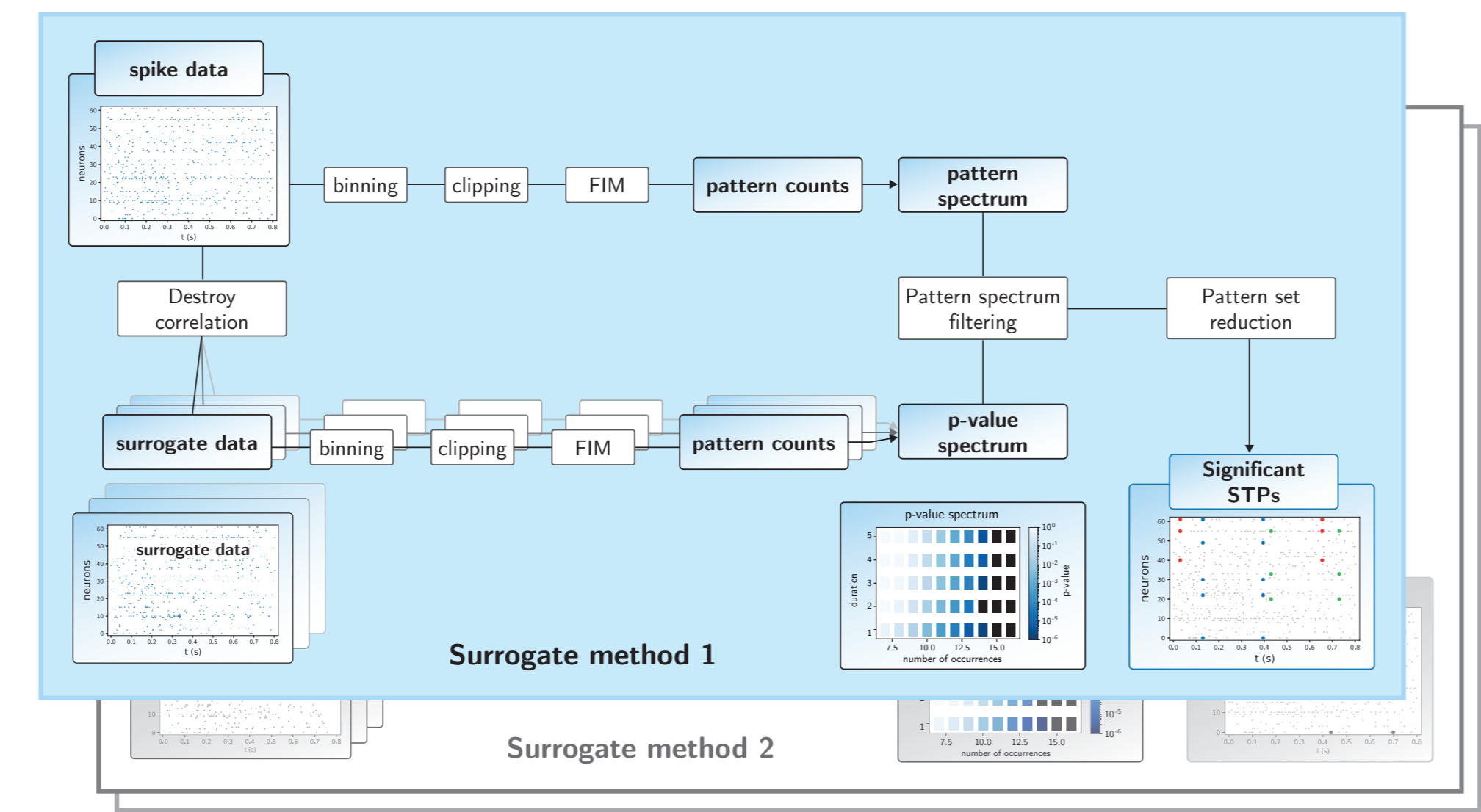
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Context

Detection of significant correlated neuronal activity, which is thought to be a signature of cell-assembly activity [1, 2], is a challenging endeavor from a statistical perspective. To identify active cell assemblies, we have developed a method, **SPADE** [3, 4, 5], that detects **spatio-temporal spike patterns** with millisecond precision and tests them for significance.

Massively-parallel spike train recordings are discretized to 0-1 bins (*clipping*), allowing us to extract pattern candidates using Frequent Itemset Mining [6]. **Surrogate spike trains** are then used to generate a null hypothesis of conditional independence given firing rates. The pattern candidates are tested for significance by comparing them to the patterns found by applying the mining algorithm to the surrogate spike trains.

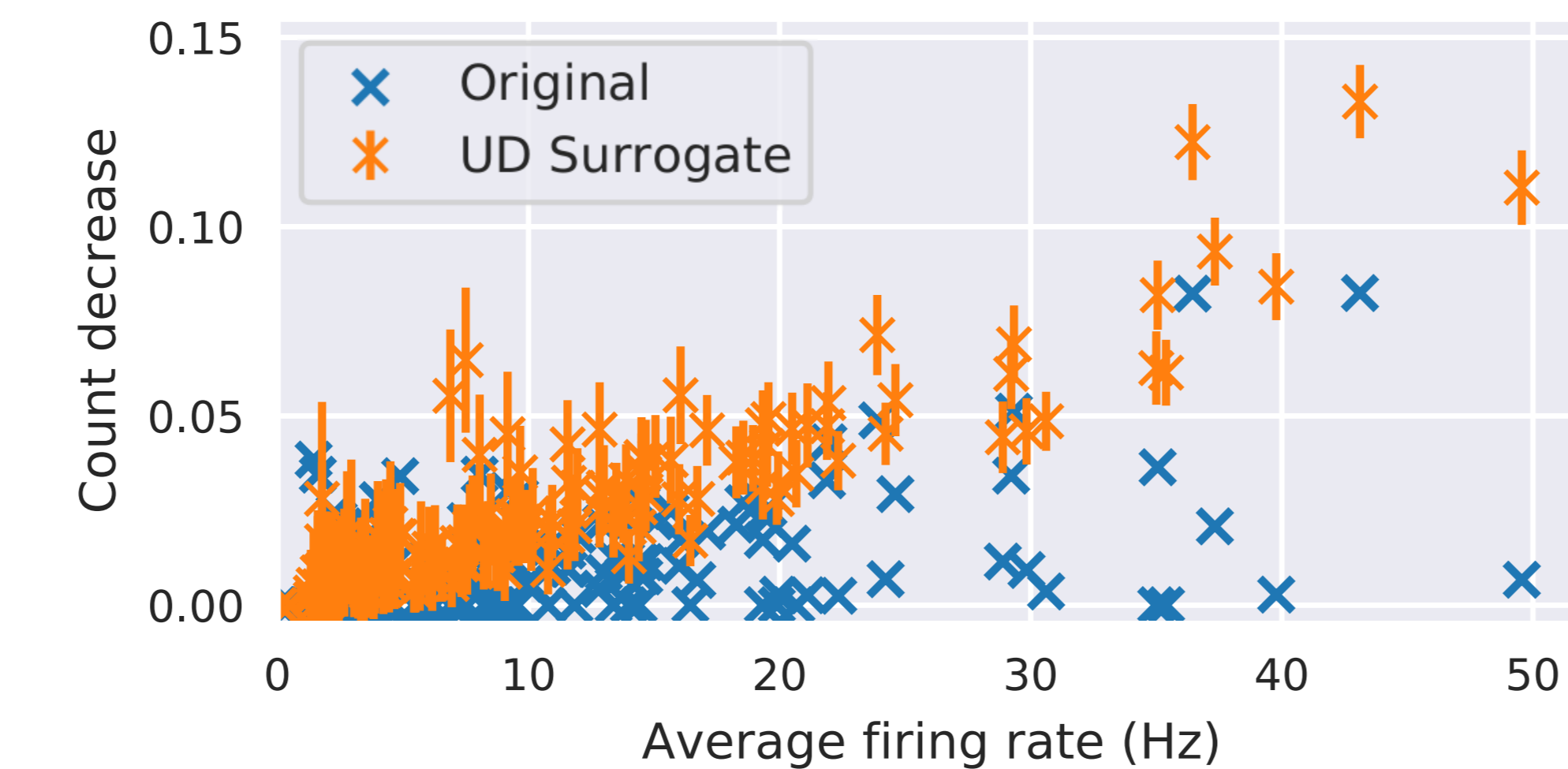


SPADE analysis workflow. The figure shows the sequence of analysis steps of SPADE from the original data to the final significant spatio-temporal patterns.

Spike count reduction due to uniform dithering

A classical choice for surrogate data to implement the null hypothesis is **uniform dithering** (UD). Each surrogate spike train is a copy of the original one, with each spike displaced according to a uniform distribution (typically ± 25 ms). Relevant aspects *opposing* the use of uniform dithering are

- that a possible refractory period of the spike trains is not preserved,
- the ISI distribution approaches that of a Poisson process,
- and after clipping there are fewer spikes in the surrogates than in the clipped original spike trains.



Spike count reduction in an experimental session [7] before and after UD. Each dot represents a single unit.

Surrogate Techniques

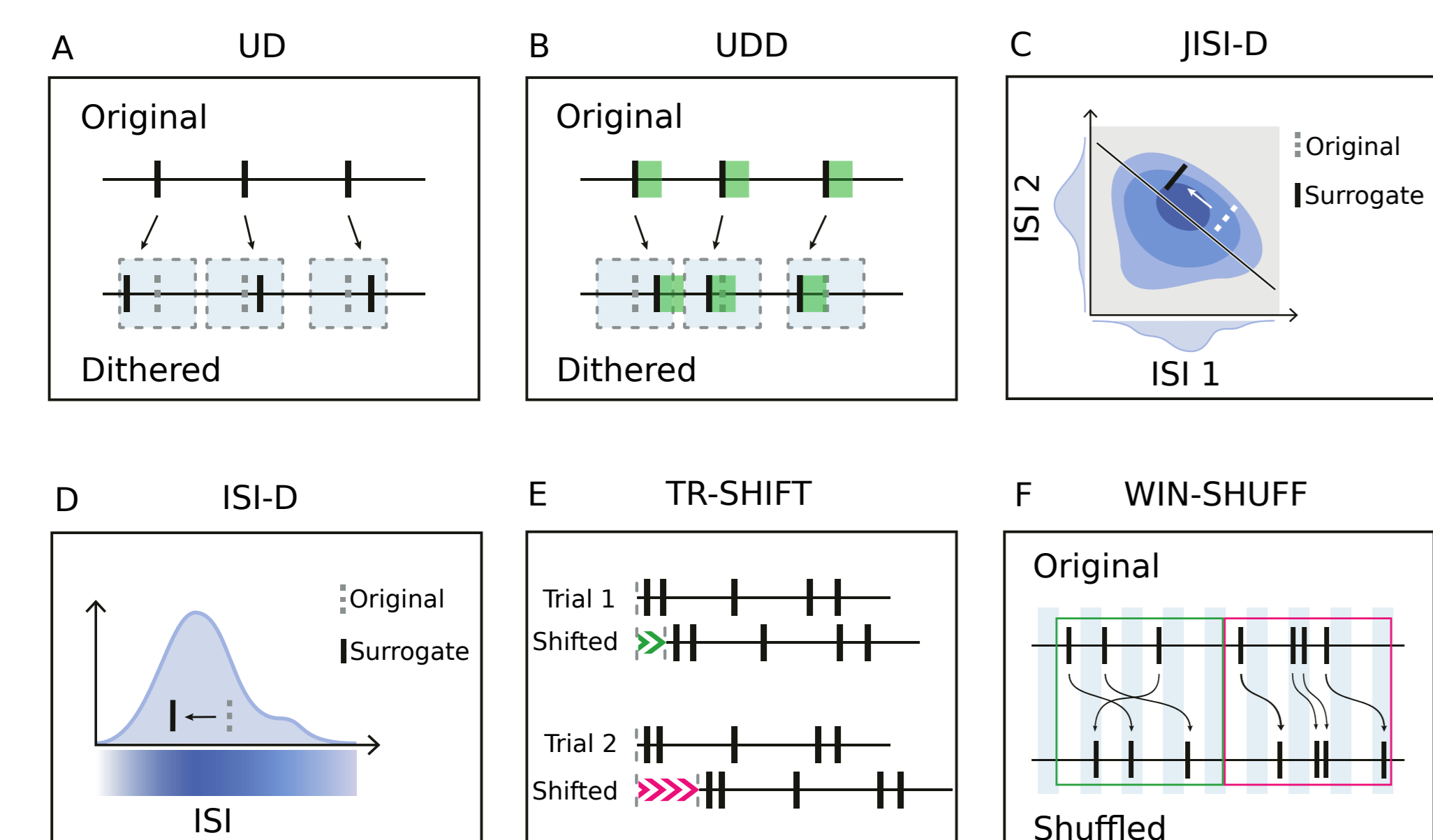


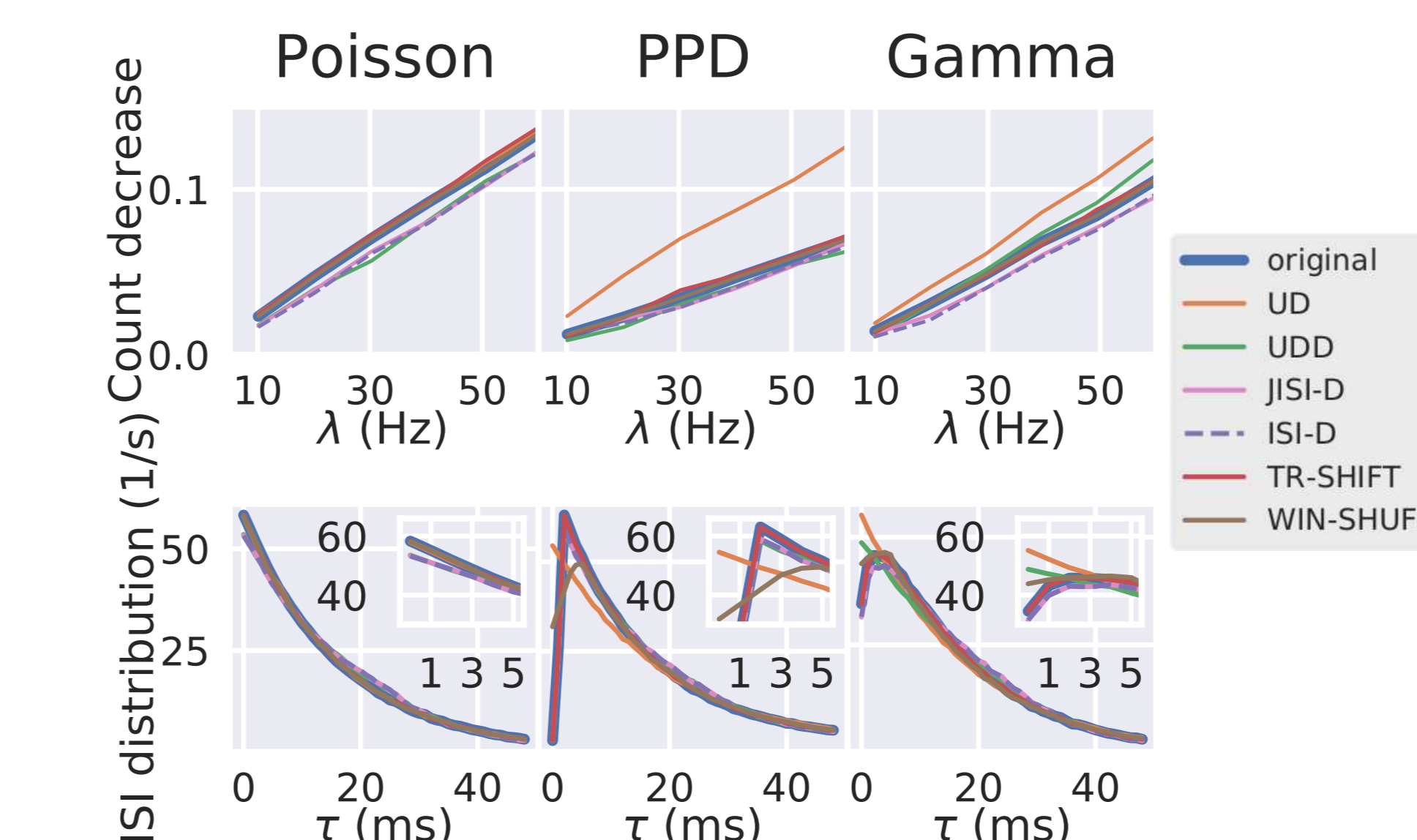
Illustration of the different surrogate methods: A Uniform Dithering (UD) [8, 9], B Uniform dithering with dead time (UDD), C Joint ISI-Dithering (JISI-D) [10], D ISI-Dithering (ISI-D), E Trial Shifting (TR-SHIFT) [8, 9], F Window Shuffling (WIN-SHUFF)

Conclusions

We investigated the effect of surrogate methods used for significance analysis of spatio-temporal spike patterns. First, we observed that using uniform dithering together with spike train discretization yield a *spike count mismatch* between original spike trains and surrogate data. We further analyzed this aspect on three different spike train models, highlighting the relevance of the dead time. Analyzing *realistic* artificial data, we showed that the proposed surrogate alternatives yield a low false positive count. Given that the results are consistent between the techniques, we recommend using **trial-shifting** as method of choice. It is the simplest employed method, best preserving all statistical features.

Analysis of stationary test data

To evaluate the properties of the different surrogate techniques for use in the null hypothesis, we first examine the effect of these techniques on spike trains modeled using three renewal point process models: Poisson process, Poisson process with dead time (PPD; $d = 1.6$ ms; [11]), and gamma process ($\gamma = 1.23$).



Analysis of surrogate statistics. The upper panel shows the spike count decrease for the different surrogate techniques (color), and spike train models (left to right). The lower panel shows the surrogate ISI distributions.

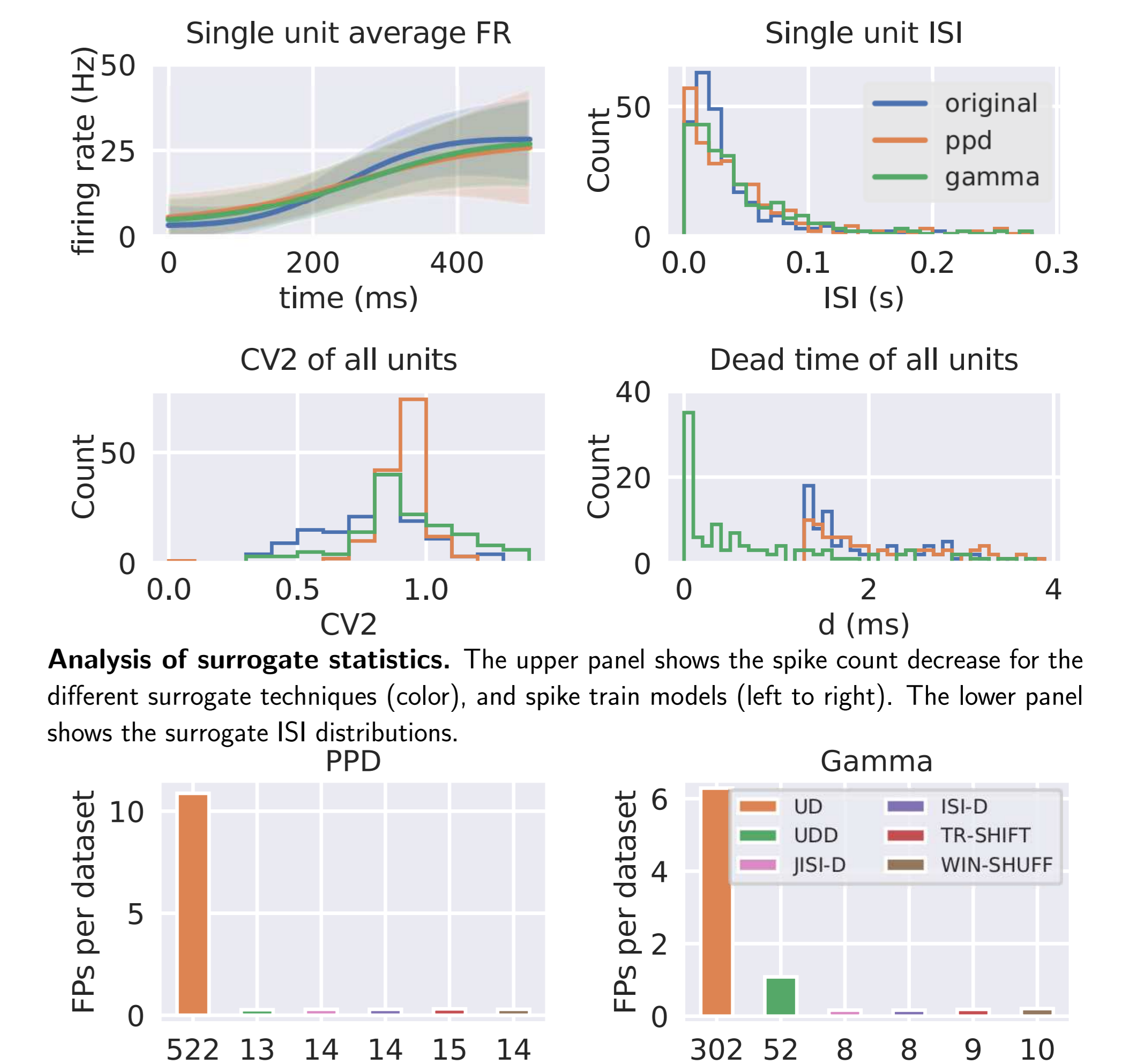
The first result of this study is that all surrogate spike trains follow very closely the spike count decrease and the ISI distribution of the original spike trains, with some deviations for UDD, JISI-D and ISI-D. Considering the PPD process, we notice how much the surrogates of UD differ from all others, both in spike count decrease and ISI distribution. The effect on the spike count decrease is very similar to what we have already observed in the experimental data. We conclude that when spike trains are *clipped*, the consideration of the **dead time** is of central importance. Finally, also for the gamma process, i.e., regular spike trains, we observe that the spike count decrease is highest for UD.

Analysis of non-stationary test data

After analyzing the statistical properties of stationary surrogate spike trains, we go a step further to consider non-stationary, independent, artificial data whose properties follow those of experimental data (two sessions of two different macaque monkeys, pre-/motor cortex [7]). Thus, we can check how far the different surrogate techniques lead to false positive spike patterns in the context of realistic data.

Characteristics of the artificial data:

- Same number of neurons as in experimental data.
- Models are non-stationary PPD and gamma processes.
- The firing rate profiles are estimated from each single unit using optimized kernel density estimation [12].
- The dead time for PPD, and shape factor for gamma are both estimated from each single experimental unit.



Analysis of surrogate statistics. The upper panel shows the spike count decrease for the different surrogate techniques (color), and spike train models (left to right). The lower panel shows the surrogate ISI distributions.

False positive results of analysis of artificial data.

From the analysis regarding false positives on the artificial data, we conclude that:

- Uniform dithering yields many false positives for data that either has a dead time, or is regular.
- All alternative surrogate methods have a **stable low number of false positives** (except UDD on gamma data).
- Further, the false positive patterns are mostly *consistent* across surrogate techniques.

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