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Unitary Event Analysis

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Definition

The unitary event (UE) analysis is a statistical method that detects conspicuous patterns of synchronous spiking activity among simultaneously recorded spike trains. Significant patterns are identified by comparison of their occurrence counts to the null hypothesis of statistical independence based on the activity of the neurons.

Detailed Description

It has been proposed that cortical neurons organize dynamically into functional groups ("cell assemblies") by the temporal structure of their joint spiking activity. The unitary event analysis method is designed to detect such patterns of coincident spiking activity occurring more often than expected by chance among simultaneously recorded single neurons. To this end, the spiking activity of all simultaneously recorded neurons is represented, after appropriate time discretization (e.g., $h = 1$ ms), as parallel sequences of zeros and ones, "1" indicating the existence of at least one spike (clipping) and "0" the absence of spikes (Fig. 1a). From this representation, the number of occurrences for each of the individual 0–1 patterns across the neurons is counted. There are at most different 2^N different coincidence patterns in data of N simultaneously observed neurons. Due to the finite recording time and the dominance of zeros, however, the actual number of different coincidence patterns found is typically much lower. A unique index k is assigned to each existing pattern based on some arbitrary sorting. Next, for each pattern k, the number of occurrences termed the empirical count is determined. To derive the *significance* of a pattern k, the p-value of its number of occurrences is calculated by comparison to the probability distribution derived under the null hypothesis of statistical independence of the processes. The distribution can either, under certain conditions, be assumed and adjusted by parameters estimated from the data (parametric approach) or can be derived with Monte Carlo methods by the generation of surrogate data on the basis of the original data (nonparametric approach).

The parametric approach has the following assumptions: (a) the firing rates are stationary within the time span of the observation T, and (b) the processes have Poisson properties. Then the expected number of occurrences of a pattern k can *analytically* be calculated based on the firing rates of the neurons. For each neuron i, the probability of firing within a bin p_i is derived by dividing the number of bins occupied by a spike c_i by the total number of bins in T, i.e., T/h, with h the bin width. The joint probability for pattern k, P^k_{exp}, to occur by chance is then calculated as the product of the firing probabilities p_i for the neurons contributing a spike in pattern k and probabilities $1 - p_i$ for neurons contributing a 0 to the pattern. The expected number of occurrences of pattern k is derived as

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$n^k_{\text{exp}} = P^k_{\text{exp}} \cdot T/h$. This quantity defines the mean of the Poisson distribution that is used to estimate the significance of the pattern by calculation of its p-value, i.e., the area under the distribution from n^k_{emp} to infinity. If the p-value is smaller or equal to a predefined significance level α, the pattern is considered to occur significantly more often than by chance. If the p-value is larger or equal to $1 - \alpha$, the pattern is occurring significantly less often than expected. The p-value may be expressed as the surprise measure (Fig. 1c), a logarithmic transformation of the p-value (Grün et al. 2002a) for better visualization (Fig. 2c).

Often experimental data exhibit violations of the above assumptions, i.e., firing rates may change even on a short timescales or spike trains deviate from Poisson statistics. In the latter case, the coincidence distribution is not well described anymore by a Poisson distribution (e.g., Pipa et al. 2013), since the process type influences the distribution. If firing rate changes are not properly considered, the estimated mean of the distribution may not be correct. If such cases are ignored, this may lead to false-positive outcomes and wrong interpretation of the data (Grün 2009; Grün et al. 2010). Thus, an alternative approach for the estimation of the significance is based on a numerical (Monte Carlo) method, in which the original data are manipulated to destroy potential spike synchrony but conserve all other features of the spike trains. One example is spike dithering, i.e., the random displacement of each individual spike within a small time window (e.g., Pipa et al. 2003; for details and alternative approaches, see Louis et al. 2010a, b). The resulting surrogate data are then analyzed like the original data for the number of occurrences of patterns of interest. Pattern counts from many repetitions of this procedure realizing the null hypothesis of independence form the distribution, which is then used for the significance estimation of the empirical pattern count.

When aiming at the analysis of the correlation structure of the neuronal spiking activity in relation to behavior, which is dynamic by nature, the analysis has to be performed in a time-dependent manner. Also the firing rates typically change in time which needs to be accounted for. Therefore, the UE analysis is applied within a time window of length T (i.e., 100 ms duration) that is slid along the data (for proper choice of the analysis window, see Grün et al. 2002b). This enables the study of the dynamics of the correlation structure. It was found in a number of studies that spike synchronization modulates in time in relation to the behavioral context (e.g., Riehle et al. 1997; Grün et al. 1999; Riehle et al. 2000; Maldonado et al. 2008; Kilavik et al. 2009; Ito et al. 2011).

The experiments are typically repeated over several trials to improve the statistics of the analysis. For this purpose, the trial data are aligned to an (behavioral) event of interest. The analysis window is then slit along the aligned data, and at each window position, the data of the same time segment are jointly considered. The empirical pattern counts are derived by summing the occurrence counts of

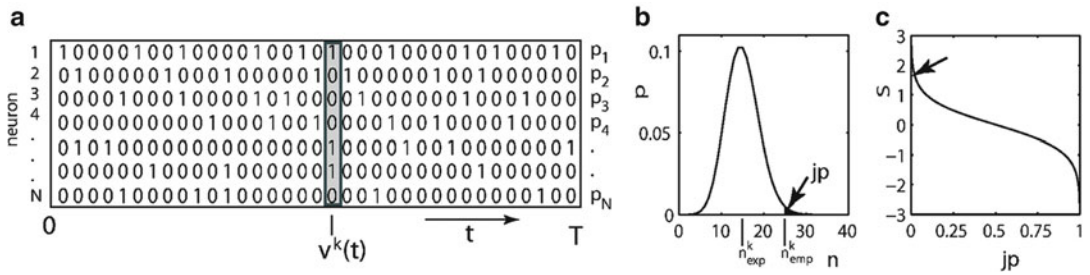

Fig. 1 Binary data representation of N parallel spike trains within a data stretch of T bins of width h. (b) Distribution of coincidences given the expected number n_{exp}. Significance (p-value, *black area*) of the number of empirically found coincidences n_{emp}. (**c**) Transformation of the p-value into the surprise measure S. The *arrow* indicates the surprise value corresponding to the identified p-value (jp) in b (Modified from Grün (2009))

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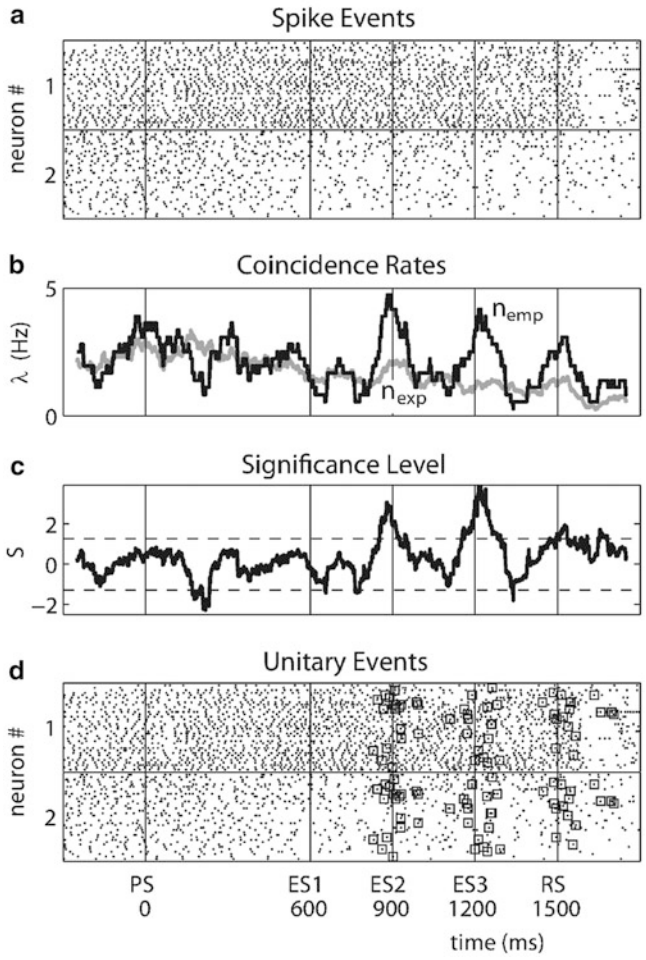

Fig. 2 Temporal modulation of synchronous activity. UE analysis of two simultaneously recorded single neurons from motor cortex of awake behaving monkey. The monkey was involved in a delayed pointing task, where the duration of the preparation period (after PS) to the requested movement (*RS*) was selected randomly from four possible durations (600, 900, 1200, 1500 ms) from trial to trial. Here trials (36) with the longest duration (1,500 ms) were pooled. (**a**) Raster displays of spike discharges of two neurons. (**b**) Comparison of measured (*black*) and expected (*gray*) coincidence rates. Allowed coincidence width ±2 ms. (**c**) Surprise as a function of trial time. (**d**) Dot display with unitary events (*squares*) detected based on a significance level of $\alpha = 0.05$, in sliding windows of T = 100 ms (Modified from Riehle et al. (1997))

the same pattern in the different trials to provide the empirical count $\tilde{n}^k_{\text{emp}} = \sum_j n^{k,j}_{\text{emp}}$. In the parametric approach, the expected number is calculated trial by trial and then summed to the total number $\tilde{n}^k_{\text{exp}} = \sum_j n^{k,j}_{\text{exp}}$ providing the mean of the distribution as introduced above. Taking the sum instead of an estimate based on average firing rates across trials has the advantage to account for cross-trial non-stationarities in the firing rates (Grün et al. 2003). For the nonparametric approach, the count across trials is compared to the count distribution derived from surrogates by the sum of counts of the surrogates across the trials. For population measures, i.e., for statistics of the data across several sessions, one may proceed by adding more trial data, however now resulting from the different sessions (see for details Kilavik et al. 2009).

This method is not designed to detect higher-order correlations, since the null hypothesis is statistical independence. Shimazaki et al. (2012) extended the approach within the information geometry framework. This identifies in a time-dependent manner higher-order spike correlation

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patterns. The analyses of massively parallel spike data (e.g., in the range of 100 neurons) require statistical methods that either ignore the individual spike patterns (e.g., Staude et al. 2010a, b) or pool across patterns to avoid severe multiple testing problems (Picado-Muiño et al. 2013; Torre et al. 2013).

Cross-References

- ▶ Correlation Analysis of Parallel Spike Trains
- ▶ Estimation of Neuronal Firing Rate
- ▶ Gravity Analysis of Parallel Spike Trains
- ▶ Information Geometry as Application to Point Processes
- ▶ Joint-Peri Stimulus Time Histogram (JPSTH)
- ▶ Significance Evaluation
- ▶ Spike Train
- ▶ Surrogate Data for Evaluation of Spike Correlation

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