Analysis of higher-order correlations in multiple parallel processes

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Abstract

The 'unitary event' method analyzes multiple spike trains to identify neuronal groups whose coherent activity does not conform with full independence. Here we distinguish 'genuine' coincidences from those due to subgroup correlations. The introduced model describes a neuron's firing as a superposition of independent and stationary Bernoulli processes, each representing the synchronous activity of one of all possible subsets of neurons. Using maximum likelihood and normal approximation, genuine correlations are identified under a null-hypothesis that respects lower-order correlations. An extended model analyzes jittered coincidences with the method of moments. Evaluation of both approaches includes test power and adequateness of significance levels.

Key words: spike synchronization, higher-order correlation, significance, test power

1 Introduction

The hypothesis that temporally structured coherent firing is an indication of assembly activity motivates the analysis of (near-)coincident firing activity observed in simultaneously recorded spike trains. The 'unitary event' method [1–3] analyzes the probability of coincident spiking of groups of neurons based on the null-hypothesis of full independence of the processes. Detection of unitary events implies existence of correlations between the processes. However, deviation from expectation due to a correlation caused by a subgroup of neurons is not identified. The work presented here focuses on the identification of 'genuine' higher-order correlations defined here as the coincidences that cannot be explained by a chance co-activation of lower-order correlations.

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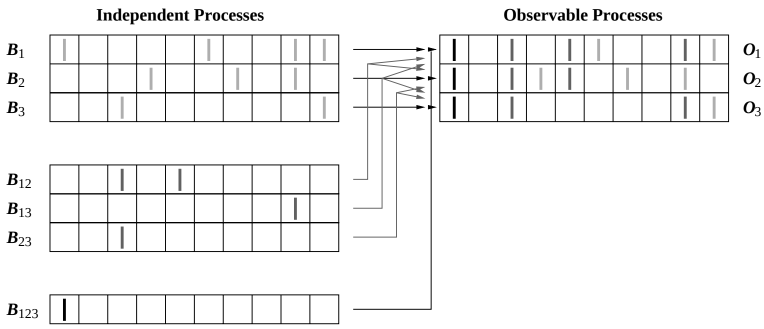

Fig. 1. Model illustrated for 3 neurons. Observed spiking activity (O_1, O_2, O_3) results from a superposition of several 'basic' independent processes: the neurons' background activity: B_1, B_2, B_3, and correlation processes between pairs B_{12}, B_{13}, B_{23} and all three neurons B_{123}. Thus, a certain spike-pattern at a time can be due to several different 'basic events'.

2 The Model

We use a model that regards firing activity of each neuron to be describable as a superposition of independent and stationary Bernoulli processes (Fig. 1). Observable processes (O_1, O_2 etc.) are distinguished from underlying basic processes of which there are independent 'background' processes (B_1, B_2 etc. with firing probabilities λ_1, λ_2 etc.) and correlation processes (B_{12}, B_{13}, B_{23} with coincidence rates $\lambda_{12}, \lambda_{13}, \lambda_{23}$ etc. and B_{123} with rate λ_{123}) producing coincidences among all possible (sub)groups of neurons.

3 Maximum-Likelihood Estimation of Parameters

The first goal is to estimate the parameters of the underlying processes based only on the observable processes. Coding the occurrence of a spike in a bin as a one and a non-spike as a zero [2], the sufficient statistics for a piece of data are the numbers of all 2^N possible observable binary vectors of length n (number of neurons) observed in T time steps (time resolution assumed to be 1ms). In the 2-neurons-case, we simply need to count the following patterns:

$$S_{ij} = \sum_{t=1}^{T} I(O_1(t) = i, O_2(t) = j), \qquad i, j \in \{0, 1\} \tag{1}$$

$S_{00}, S_{01}, S_{10}, S_{11}$. To estimate the parameters λ_1, λ_2 and λ_{12}, we use the maximum likelihood (ML) principle. The estimators are chosen such that they maximize the likelihood of the given data piece. For $n = 2$, the likelihood function L is the following:

$$L(\lambda_1, \lambda_2, \lambda_{12}) = p_{00}^{S_{00}} \cdot p_{10}^{S_{10}} \cdot p_{01}^{S_{01}} \cdot p_{11}^{S_{11}}, \tag{2}$$

where p_{ij} with $i, j \in \{0, 1\}$ indicates the probability to find i in process O_1 and j in process O_2 at any arbitrary point in time, e.g.

$$p_{00} = (1 - \lambda_1)(1 - \lambda_2)(1 - \lambda_{12}) \tag{3}$$

Setting the first partial derivatives of L equal to zero and controlling for negativeness of the second derivatives, one finds the ML-estimators. The formula can be

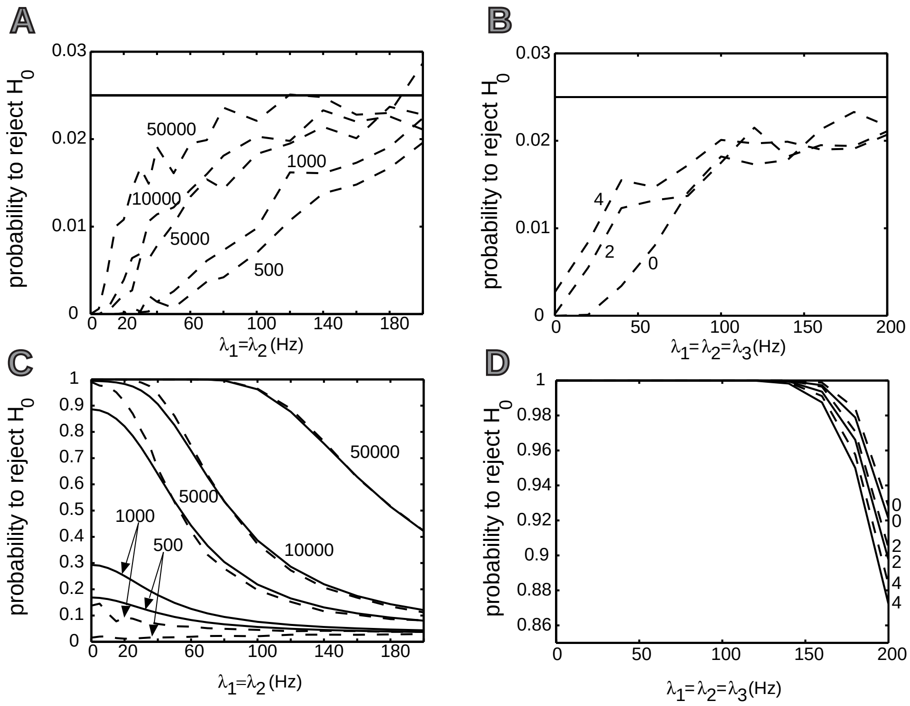

Fig. 2. Comparison of empirical significance level and test power to asymptotical levels. Empirical values are extracted as the relative number of significant experiments out of 10^4. (A), (B): Empirical significance level (dashed) as a function of background rate (solid line: predefined asymptotical significance level $\alpha = 0.025$). (A) $n = 2$, $\lambda_{12} = 0$, for different lengths T of the data segment (indicated by numbers). (B): $n = 3$, $T = 5 \cdot 10^4$, for different pair correlation rates $\lambda_{12} = \lambda_{13} = \lambda_{23} = 0, 2, 4$ Hz $\lambda_{123} = 0$. (C), (D): Empirical (dashed) and asymptotical (solid) test power. (C) $n = 2$, $\lambda_{12} = 2$ Hz for different lengths of the data segment (parameters as in (A)); (D) $n = 3$, $\lambda_{123} = 2$ Hz, $T = 5 \cdot 10^4$, pair correlation rates as in (B).

generalized for any number of neurons (see also [6]).
Let $N := \{1, ..., n\}$ be the set of neurons, $M, M_0 \subseteq N$, and
$S_M := \sum_{t=1}^{T} I(\{O_i(t) = 0 \quad \forall i \in N - M\})$ for $M \subseteq N$, then

$$1 - \widehat{\lambda}_{M_0} = \frac{\prod_{M \subseteq M_0,\ |M| mod 2 \neq |M_0| mod 2} S_M}{\prod_{M \subseteq M_0,\ |M| mod 2 = |M_0| mod 2} S_M} \tag{4}$$

Thus, we can estimate the probability of coincident firing of every specified subset of the observed neurons.

4 Significance and Test power

To decide whether all observed coincidences are chance coincidences, we derived the distribution of the estimates under the null-hypothesis that only lower-order correlations exist. The procedure is demonstrated here for $n = 2$ and can be extended to any number of neurons. For $n = 2$, H_0 is equivalent to independence of the processes, and the interesting parameter is λ_{12}. Assuming asymptotically normal distribution of the counts S_{ij}, the asymptotical variance of the estimator of the coincidence rate $\widehat{\lambda}_{12}$ is:

$$\sigma^2(\widehat{\lambda}_{12}) \doteq \frac{(1-\lambda_{12})(\lambda_{12}(1-\lambda_1)(1-\lambda_2)+\lambda_1\lambda_2)}{T(1-\lambda_1)(1-\lambda_2)} \tag{5}$$

We can thus z-transform $\widehat{\lambda}_{12}$ to get a standard-normally distributed random variable. Setting a significance level (e.g. $\alpha = 0.025$) for the test, we can compute the asymptotical test power, which is the probability to correctly reject a false H_0 in favor of the true alternative hypothesis, i.e. to 'detect' higher-order coincidences:

$$0.975 = P(\frac{\widehat{\lambda}_{12}}{\widehat{\sigma}(\widehat{\lambda}_{12})} > 1.96) \doteq P(Z > 1.96 - \frac{\lambda_{12}}{\sigma(\widehat{\lambda_{12}})}) \tag{6}$$

By rearrangement of the latter and insertion of (5) the minimal number of time steps required to reach a requested level of the test power can be calculated.

5 Comparison with Simulations

Using simulations of spike trains, we tested the empirical significance level and test power and compared the results to the asymptotical levels (Fig. 2). Simulation experiments consisting of parallel spike trains, that were generated according to the model by 'injecting' coincidences [4,2] of given rates, were analyzed for coincident events of the order under investigation. The percentage of significant experiments yields the probability reject to H_0. In case of no injection of coincidences of the evaluated order, this yields the empirical significance level (Fig. 2A,B), whereas for injected coincidences it yields the test power (Fig. 2C,D). For relatively short data segments ($T < 10^4$), the empirical significance turns out to be smaller than the applied significance level. For larger T, the given significance level is approached from below for increasing rates, i.e. the test is conservative as long as the asymptotics are not reached. The test power decreases with increasing background rates. The asymptotical test power (solid line in Fig. 2C,D) describes the empirical test power (dashed line in Fig. 2C,D) quite well, however deviates in case of $n = 2$ for small numbers of time steps T. For $n = 3$, the test power is maximal up to large background rates (up to 150 Hz) before dropping rapidly. The larger the coincidence rates of order 2, the faster the decrease.

6 Model-Extension: 'Jittered' Coincidences

Experimental data indicate that synchronous spiking activity may occur with a small temporal jitter up to a few ms (e.g. [4,9]). To account for such 'jittered' coincidences, we extend the model, and allow for additional independent processes, each accounting for one specific time delay of near-coincidences. For each specific time delay $j \in \{1, ..., J\}$ and subgroups of neuron $M_0 \subseteq N$, $\mid M \mid \leq 2$ one additional independent Bernoulli process is introduced with rate $\mu_1^{M_0}, ..., \mu_J^{M_0}$ (Fig. 3). Here we discuss the symmetrical case $\mu_j = \mu_{j'}\ \forall j = 1, ..., J$ for $n = 2$. The asymmetrical case can be treated analogously. Due to dependencies between time steps introduced by the jittered coincidences, the sufficient statistics are more complex. With the method

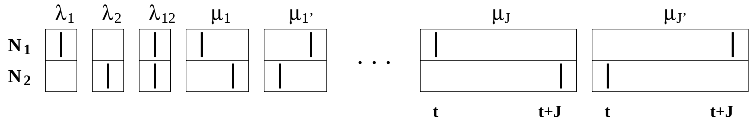

Fig. 3. Sketch (shown for $n = 2$) of the extended model including jittered coincidence patterns. Additional basic processes with rates $\mu_1, ..., \mu_J$ are considered, representing processes for near-coincidences of a given time offset J.

of moments it is possible to derive estimates for the rate parameters $\lambda_1, \lambda_2, \lambda_{12}$ and $\mu_1, ..., \mu_J$. For any fix $t \in \{1, ..., T\}$ holds

$$p_{0+} := P(O_1(t) = 0) = (1 - \lambda_1)(1 - \lambda_{12})(1 - \mu_1)^2 \tag{7}$$

$$p_{+0} := P(O_2(t) = 0) = (1 - \lambda_2)(1 - \lambda_{12})(1 - \mu_1)^2 \tag{8}$$

$$p_{00} := P(O_1(t) = 0 \wedge O_2(t) = 0) = (1 - \lambda_1)(1 - \lambda_2)(1 - \lambda_{12})(1 - \mu_1)^4 \tag{9}$$

which implies

$$(1 - \lambda_{12}) = \frac{p_{0+}p_{+0}}{p_{00}} \tag{10}$$

With $p_j := P[O_i(t) = O_i(t + 1) = ... = O_i(t + j) = 0, \quad i = 1, 2]$ for any $t \in \{1, ..., T - j\}$, $j = 1, ..., J$ and with $p_0 := 1$, it follows

$$(1 - \mu_j) = \frac{p_j}{\sqrt{p_{j-1}p_{j+1}}} \quad \text{and} \quad (1 - \lambda_1) = \frac{p_{J+1}}{p_J p_{+0}} \tag{11}$$

Only the estimator of the background rates depends on J. We propose to estimate the probabilities on the basis of disjunct (for p_{0+}, p_{+0}, p_{00}) or overlapping (for $p_j, j = 2, \cdots, J$) intervals, because the dependencies between time steps are relatively small. To get a significance value for the existence of jittered coincidences, one can perform similar tests as described for the non-jittered case. As a test value, we propose the quotient of the sum of the estimated coincidence probabilities and its standard deviation, which we derive from simulations. As we usually do not know the maximal existent time shift J of coincidences in the data, we compare the performance of different test values

$$Z_{jit} = t_{jit}/\sigma(t_{jit}), \text{ with } t_{jit} = \widehat{\lambda}_{12} + \sum_{j=1}^{jit} \widehat{\mu_j}, jit = 0, \cdots, 5 \tag{12}$$

on data with different J. Fig. 4 illustrates the test power of the different tests when applying onto data with different J ($J = 0, \cdots, 5$). For constant J, the test power is maximal for test values Z_{jit} for $jit = J$ (cmp. [4]).

7 Summary and Conclusions

We presented approaches for identification of higher-order correlations as expressed by the existence of higher-order coincidences in multiple parallel spike trains. For the investigation of correlation within a set of parallel processes we formulated a model that is composed of a set of independent processes each of which is representing a process for coincidences of different order and composition. Using maximum likelihood estimates and their asymptotical variance we derived estimates to identify 'genuine' higher-order coincidences (cmp. [7,6,5,8]). In a second step, the model

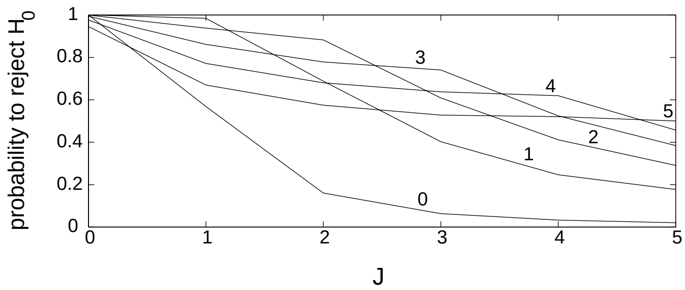

Fig. 4. Test power as a function of jitter J in the data for $\lambda_1 = \lambda_2 = 50$ Hz, $\lambda_c := \lambda_{12} + \sum_{j=1}^{J} \mu_j = 6$ Hz, $\lambda_{12} = \mu_j \quad \forall j = 1, \cdots, J$, $T = 10^4$, in 10^4 experiments. The graphs show the test power of tests using different test values Z_{jit}, with $jit = 0, \cdots, 5$ the maximal jitter assumed in the model. The empirical significance levels correspond to the predefined level (here $\alpha = 0.025$).

was extended for near-coincidences, i.e. coincidences that have a small temporal jitter. For each time offset of near-coincident events we introduced an additional independent process. Using the method of moments, parameters can be reliably estimated. For a given temporal jitter in the data, the test power is maximal for the corresponding jitter included in the test statistics. The approach was demonstrated for two parallel processes, however can be extended to systems of larger number of parallel processes.

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