# 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. Evaluation of the approach 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 [2,3] 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 (Fig. 1). The order of a genuine correlation is the number of neurons involved in a common process.

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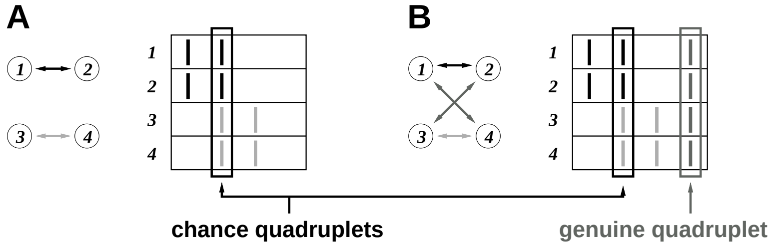


Fig. 1. Illustration of coincidence quadruplets originating in genuine quadruplet correlations and chance quadruplets. In (A) a system is assumed that contains only pairwise correlations between neurons 1-2 and 3-4, which may lead to chance co-activation of both subgroups of neurons. These by chance quadruplets have to be distinguished from genuine quadruplets that originate from four neurons being involved in a common process (B). Coexistence of involvements in processes of different neuron compositions is possible.

## 2 The Model

As the basis for our study of higher-order correlations we define a model of independent interaction processes (MIIP) that regards firing activity of each neuron to be describable as a superposition of independent and stationary Bernoulli processes (Fig. 2). 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 $\lambda_1$, $\lambda_2$ etc.) and correlation processes ($B_{12}$, $B_{13}$, $B_{23}$, $B_{123}$ etc. with coincidence rates $\lambda_{12}$, $\lambda_{13}$, $\lambda_{23}$, $\lambda_{123}$ etc.) producing coincidences among all possible subgroups of neurons.

## 3 Analysis Method

The first goal is to estimate the parameters of the underlying Bernoulli processes based only on the observable processes. We do this using the maximum-likelihood (ML) principle. The estimates are chosen such that they maximize the likelihood of the given data piece. Coding the occurrence of a spike in a bin as a one and a non-spike as a zero, the sufficient statistics for a piece of data are the numbers of all $2^n$ possible observable binary vectors of length $n$ across the $n$ neurons observed in the $T$ time steps (time resolution here assumed to be 1 ms).
The ML-estimates of the basic processes' firing probabilities for any number of neurons can be derived with the following formula: Let $N := \{1, \ldots, n\}$ be the set of neurons, $M, M_0 \subseteq N$, and $S_M := \sum_{t=1}^{T} I(\{O_i(t) = 0 \quad \forall i \in N - M\})$ the pattern counts of all possible subsets $M \subseteq N$ then

$$1 - \widehat{\lambda}_{M_0} = \frac{\prod_{M \subseteq M_0,\, |M| \neq |M_0| \mathrm{mod}\, 2} S_M}{\prod_{M \subseteq M_0,\, |M| = |M_0| \mathrm{mod}\, 2} S_M} \qquad (1)$$

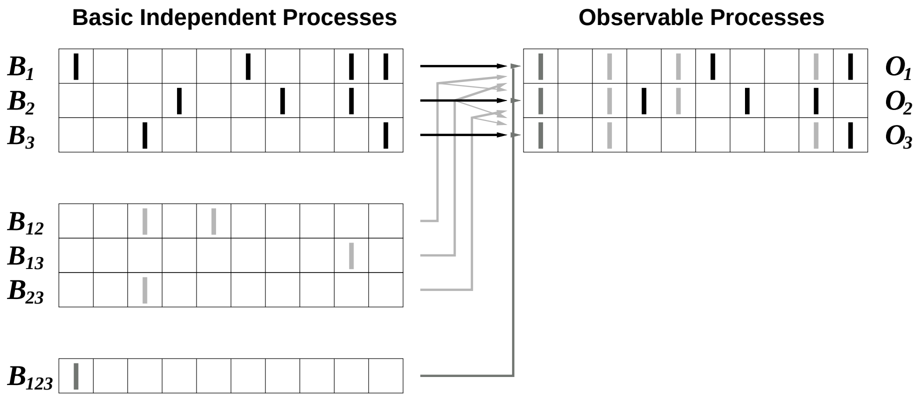


Fig. 2. MIIP illustrated for 3 neurons. Observed spiking $(O_1, O_2, O_3)$ results from several 'basic' independent processes: the neurons' background activity $(B_1, B_2, B_3)$, correlation processes between pairs $B_{ij}$ and of all three neurons $B_{123}$. Thus, a certain spike-pattern at a time can be due to several different 'basic events', i.e. firing patterns of the basic processes.

(see also e.g. [10]). Thus, we can estimate the probability of coincident firing of every specified subset of the observed neurons. Equation (1) together with the $\delta$-Method (e.g. [1]) first imply asymptotic normality of all ML-estimates of the basic processes' parameters due to asymptotic normality of the counts $S_M$. One can secondly use the $\delta$-Method to get the asymptotic variance. We need to assign an index $i \in \{1, 2, \ldots, 2^{|M_0|}\}$ to each of the sets $M \subseteq M_0$ , such that $S_i := S_M$, where $i \neq j$ for $M \neq M'$. Let the relative frequencies of the events $\widehat{p}_i := \frac{S_i}{T}$ be the estimates for the corresponding probabilities. Writing the right hand side of formula (1) as a function $f(p_i)_{i=1,2,\ldots,2^{|M_0|}}$ of the probabilities $p_i$ and deriving the asymptotic covariance matrix $\Sigma = (\sigma_{ij}) = \frac{1}{T}\mathrm{Cov}(S_i, S_j)$, the asymptotic variance of $\widehat{\lambda}_{M_0}$ can be written as

$$\sigma^2(\widehat{\lambda}_{M_0}) = \frac{1}{T} \sum_{k,k'=1}^{2^n-1} \sigma_{kk'} \left(\frac{\partial f}{\partial p_k}\right) \left(\frac{\partial f}{\partial p_{k'}}\right) \tag{2}$$

We can thus Z-transform the ML-estimate to get a standard normally distributed random variable Z. Choosing a significance level for the test (e.g. 2.5%), we can compute the asymptotic test power, which is the probability to correctly reject a false $H_0$ (i.e. absence of the one inspected genuine higher-order correlation) in favor of the true alternative hypothesis, i.e. to detect higher-order coincidences.

$$\text{test power} = P\left(\frac{\widehat{\lambda}}{\widehat{\sigma}(\widehat{\lambda})} > 1.96\right) \doteq P\left(Z > 1.96 - \frac{\lambda}{\sigma(\widehat{\lambda})}\right) \tag{3}$$

By rearrangement of (3) and insertion of (2), the minimal number of time steps required to reach a requested level of the test power can be calculated.

### *3.1 Illustration for n=2*

We now want to illustrate the proposed method for two parallel processes. In the 2-neurons-case, we simply need the counts $S_{00} := S_{\{\}}, S_{0+} := S_{\{2\}}$ and $S_{+0} := S_{\{1\}}$

of the corresponding patterns. We have

$$p_{00} := P(O_1 = O_2 = 0) = (1-\lambda_1)\cdot(1-\lambda_2)\cdot(1-\lambda_{12}) \tag{4}$$
$$p_{0+} := P(O_1 = 0) = (1-\lambda_1)\cdot(1-\lambda_{12}) \tag{5}$$
$$p_{+0} := P(O_2 = 0) = (1-\lambda_2)\cdot(1-\lambda_{12}) \tag{6}$$

This gives us the following formulas for the underlying parameters:

$$1-\lambda_1 = \frac{p_{00}}{p_{+0}}, \quad 1-\lambda_2 = \frac{p_{00}}{p_{0+}}, \quad 1-\lambda_{12} = \frac{p_{0+}p_{+0}}{p_{00}} \tag{7}$$

The counts $S_{ij}$ of all possible patterns follow a multinomial distribution, which implies that the ML-estimates of the probabilities used in equation (7) are just the relative frequencies of the corresponding events, leading to equation (1).
To decide whether all observed coincidences are chance coincidences, we derive the distribution of the estimates under the null-hypothesis that only lower-order correlations exist. For $n = 2$, $H_0$ is equivalent to independence of the processes, and the interesting parameter is $\lambda_{12}$. According to equation (2), the asymptotic variance of $\widehat{\lambda}_{12}$ is

$$\sigma^2(\widehat{\lambda}_{12}) = \frac{(1-\lambda_{12})(\lambda_{12}(1-\lambda_1)(1-\lambda_2)+\lambda_1\lambda_2)}{T(1-\lambda_1)(1-\lambda_2)} \tag{8}$$

We can thus make a test by Z-transforming the estimate $\widehat{\lambda}_{12}$. For more than two neurons, one can proceed analogously by applying equations (1) and (2). This allows to parallely and independently investigate all subgroup correlations of interest, irrespective of their order.

## 4 Comparison with Simulations

Using simulated spike trains, we tested the empirical significance and test power and compared the results to the asymptotic levels (Fig. 3). Simulation experiments consisting of parallel spike trains, that were generated according to the model (Fig. 2) by 'injecting' coincidences [2,4] of given rates, were analyzed for coincident events of the order under investigation. The percentage of the number of significant experiments in relation to the total number of performed experiments yields the probability to reject $H_0$. In case of no injection of coincidences of the evaluated order, this yields the empirical significance (Fig. 3A,B), whereas for injected coincidences it yields the test power (Fig. 3C,D). For relatively short data segments (e.g. $T = 10^4$, black lines in Fig. 3A,B) and small background rates, the empirical significance (solid lines in Fig. 3A,B) turns out to be smaller than the applied significance level (dashed lines in Fig. 3A,B). For larger $T$ (grey lines in Fig. 3A,B), 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 rates of the background, and in case of $n > 2$, also with increasing coincidence rates of lower order than evaluated. The asymptotic test power (dashed curves in Fig. 3C,D) describes the empirical test power (solid curves in Fig. 3C,D) quite well. For $n = 2$ and $n = 3$, the test power decreases with increasing background rates. For $n = 3$, the larger the coincidence rate of order 2, the faster the decrease.

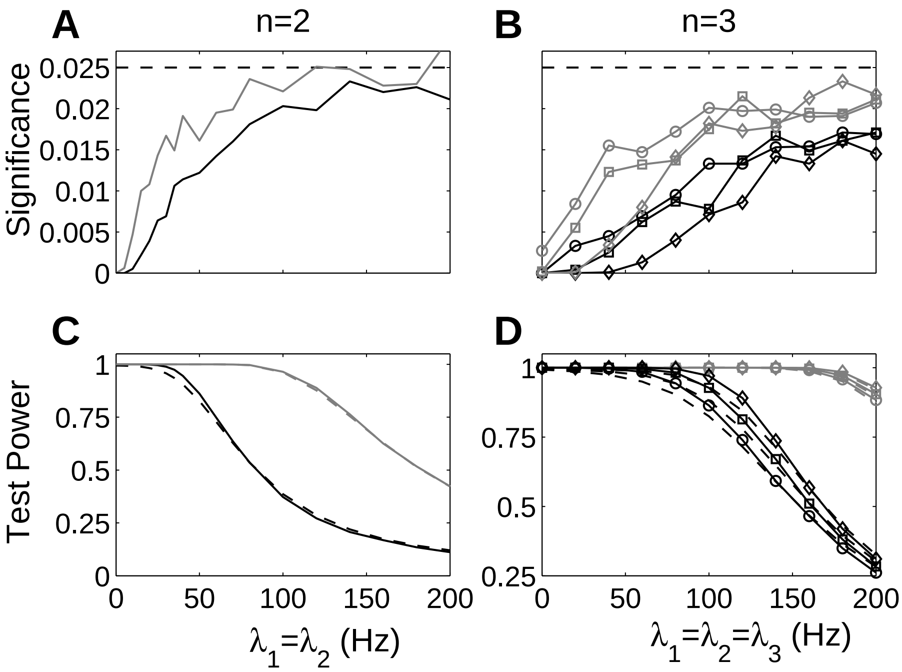


Fig. 3. Comparison of empirical significance level (A,B) and test power (C,D) to asymptotic levels as a function of background rate level. Empirical values are extracted as the relative number of significant experiments out of $10^4$. The number of time steps considered are indicated by the color of the graphs (black: $T = 10^4$, grey: $T = 5 \cdot 10^4$). (A) For $n = 2$ the empirical significance level ($\lambda_{12} = 0$ Hz) is illustrated as a function of background rates ($\lambda_1 = \lambda_2$). (B) For $n = 3$, the empirical significance level ($\lambda_{123} = 0$ Hz) is in addition shown for different pairwise coincidence rate levels ($\lambda_{12} = \lambda_{13} = \lambda_{23}$ chosen as 0 Hz ($\diamond$), 2 Hz ($\square$) and 4 Hz ($\circ$)). In both cases, the significance level is 2.5% (dashed lines). Empirical (solid) and asymptotic (dashed) test power (C) for $n = 2$ with $\lambda_{12} = 2$ Hz, and (D) for $n = 3$ with $\lambda_{123} = 2$ Hz, other parameters and coding as in (A,B).

## 5 Conclusions and Outlook

We presented an approach for the identification of genuine 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 asymptotic variance we developed a method to identify 'genuine' higher-order correlations. It proved to be conservative as long as the asymptotics do not hold and allows to parallely and independently investigate all subgroup correlations of interest.
The approach is related to methods that use log-linear models (cmp. [5–8]) due to similarity of estimates. Still, in the proposed information-geometric measures it is not possible to distinguish between different subgroups of a given number of elements. Those approaches are extremely useful if one is interested in the existence of

correlations of a given order. However, if we would like to identify the group(s) of neurons that are involved in the computation of a specific task ('assembly hypothesis'), we need to explicitly identify the special subgroups that express correlations. All approaches discussed are restricted to the analysis of exact coincidences. As experimental data indicate that synchronous spiking activity may occur with a small temporal jitter up to a few ms (e.g. [4,9]), we currently work at an extension of the model for near-coincidences, i.e. coincidences with a small temporal jitter. The basic idea is to introduce additional independent processes per time offset, subgroup of neurons and order of spikes [11]. The approach can be extended to systems of more than two parallel processes.
As the analysis of higher-order correlations in itself implies an exponential increase in the number of parameters if one wants to separately consider all different subgroups of neurons, one needs to find means to reduce the parameter space. Furthermore, for an application onto experimental data, problems of nonstationarity and jitter size need to be considered carefully and are addressed in current projects.

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## References

[1] Y. Bishop, S. E. Fienberg, P. W. Holland, Discrete multivariate analysis. Theory and practice. Cambridge, Massachusetts, London: MIT Press (1991)

[2] S. Grün, M. Diesmann, A. Aertsen, 'Unitary Events' in multiple single-neuron activity. I. Detection and significance, Neural. Comp. 14 (2002) 43–80.

[3] S. Grün, M. Diesmann, A. Aertsen, 'Unitary Events' in multiple single-neuron activity. II. Non-Stationary data, Neural. Comp. 14 (2002) 81–119.

[4] S. Grün, M. Diesmann, F. Grammont, A. Riehle, A. Aertsen, Detecting unitary events without discretization of time, J. Neurosci. Meth. 94 (1999) 67–79.

[5] R. Gütig, A. Aertsen, S. Rotter, Analysis of higher-order neuronal interactions based on conditional inference, Submitted

[6] L. Martignon, G. Deco, K. Laskey, M. Diamond, W. Freiwald, E. Vaadia, Neural coding: Higher-order temporal patterns in the neurostatistics of cell assemblies, Neural. Comp. 12 (2000) 2621–2653.

[7] L. Martignon, H. von Hasseln, S. Grün, A. Aertsen, G. Palm, Detecting higher-order interactions among the spiking events in a group of neurons, Biol. Cybern. 73 (1995) 69–81.

[8] H. Nakahara, S. Amari, Information-geometric decomposition in spike analysis, In Diettrich T.G. and Tresp V. (eds.), NIPS, vol. 14, in press. MIT Press: Cambridge, 2002.

[9] L. G. Nowak, M. H. Munk, J. I. Nelson, A. James, J. Bullier, Structural basis of cortical synchronization. i. three types of interhemispheric coupling., J. Neurophysiol. 74 (1995) 2379–2400.

[10] C. J. Preston, Gibbs states on countable sets. London: Cambridge University Press (1974)

[11] G. Schneider, Analysis of Higher-Order Coincident Activity in Multiple Parallel Processes, Diploma Thesis, Mathematics Dept., JW Goethe-University Frankfurt/Main, 2002