

BOOTSTRAP AND PERMUTATION TESTS OF INDEPENDENCE FOR POINT PROCESSES¹

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Motivated by a neuroscience question about synchrony detection in spike train analysis, we deal with the independence testing problem for point processes. We introduce nonparametric test statistics, which are rescaled general U -statistics, whose corresponding critical values are constructed from bootstrap and randomization/permutation approaches, making as few assumptions as possible on the underlying distribution of the point processes. We derive general consistency results for the bootstrap and for the permutation w.r.t. Wasserstein's metric, which induces weak convergence as well as convergence of second-order moments. The obtained bootstrap or permutation independence tests are thus proved to be asymptotically of the prescribed size, and to be consistent against any reasonable alternative. A simulation study is performed to illustrate the derived theoretical results, and to compare the performance of our new tests with existing ones in the neuroscientific literature.

1. Introduction. Inspired by neuroscience problems, the present work is devoted to independence tests for point processes. The question of testing whether two random variables are independent is of course largely encountered in the statistical literature, as it is one of the central goals of data analysis. From the historical Pearson's chi-square test of independence (see [49, 50]) to the modern test of [27] using kernel methods in the spirit of statistical learning, many nonparametric independence tests have been developed for real valued random variables or even random vectors. Among them, of particular interest are the tests based on the randomization/permutation principle introduced by Fisher [23], and covered thereafter in the series of papers by Pitman [55, 56], Scheffe [66], Hoeffding [37], for

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instance, or bootstrap approaches derived from Efron's [21] "naive" one. Note that permutation and bootstrap-based tests have a long history of applications, of which independence tests are just a very small part (see, e.g., [22, 52, 61, 62] for some reviews, or [3, 24, 41, 43, 44] for more recent works). Focusing on independence tests, two families of permutation or bootstrap-based tests may be distinguished at least: the whole family of rank tests including the tests of Hotelling and Pabst [39], Kendall [42], Wolfowitz [72] or Hoeffding [35] on the one hand, the family of Kolmogorov–Smirnov type tests, like Blum, Kiefer and Rosenblatt's [11], Romano's [62] or van der Vaart and Wellner's [70] ones on the other hand.

To describe the properties of these tests, let us recall and fix a few definitions, which are furthermore used throughout this article. Tests are said to be *nonparametric* if they are free from the underlying distribution of the observed variables. For any prescribed α in $(0, 1)$, tests are said to be *exactly of level α* if their first kind error rate is less than or equal to α whatever the number of observations. This is a nonasymptotic property. Tests are also said to be *asymptotically of size α* if their first kind error rate tends to α when the number of observations tends to infinity. They are said to be *consistent* against some alternative if, under this alternative, their second kind error rate tends to 0 or equivalently their power tends to 1, when the number of observations tends to infinity. Finally, *bootstrap* refers here to bootstrap with replacement. It is thus different from *permutation*, which appears sometimes in the literature as bootstrap without replacement. In this respect, the above mentioned tests of independence are all nonparametric and asymptotically of the prescribed size. Moreover, the tests based on permutation are exactly of the desired level. Some of these tests are proved to be consistent against many alternatives, such as Hoeffding's [35] one and the family of Kolmogorov–Smirnov type tests.

Detecting dependence is also a fundamental old point in the neuroscientific literature (see, e.g., [26]). The neuroscience problem we were initially interested in consists in detecting interactions between occurrences of action potentials on two different neurons simultaneously recorded on n independent trials, as described in [29]. Each recorded set of time occurrences of action potentials for each neuron is usually referred to as a spike train, the spikes being the time occurrences themselves. It is commonly accepted that these spikes are one of the main components of the brain activity (see [68]). So, when observing two spike trains coming from two different neurons, one of the main elementary problem is to assess whether these two spike trains are independent or not. Unfortunately, even if the real recordings of spike trains are discretized in time, and thus belong to finite dimensional spaces, due to the record resolution, the dimension of these spaces is so huge (from ten thousand up to one million) that it is neither realistic nor reasonable to model them by finite dimensional variables, and to apply usual independence tests. Several methods, such as the classical Unitary Events method (see [29] and the references therein), consist in binning the spike trains at first in order to deal with vectorial data with reduced dimension. However, it has been shown

that these dimension reduction methods involve an information loss of more than 60% in some cases, making this kind of preprocessing quite proscribed despite its simplicity of use. It is therefore more realistic and reasonable to model recordings of spike trains by finite point processes, and to use independence tests specifically dedicated to such point processes. Asymptotic tests of independence between point processes have already been introduced in [69], but in the particular case of homogeneous Poisson processes. Such a parametric framework is necessarily restrictive and even possibly inappropriate here, as the very existence of any precise underlying distribution for the point processes modelling spike train data is subject to broad debate (see [57, 58]). We thus focus on nonparametric tests of independence for point processes. In this spirit, particular bootstrap methods under the name of *trial-shuffling* have been proposed in [53, 54] for binned data with relatively small dimension, without proper mathematical justification. Besides the loss of information that the binning data pre-processing involves, it appears that the test statistics chosen in these papers do not lead to tests of asymptotic prescribed size as shown by our simulation study.

We here propose to construct new nonparametric tests of independence between two point processes, from the observation of n independent copies of these point processes, with as few assumptions as possible on their underlying distributions. Our test statistics are based on U -statistics (see [67], Chapter 5, for a key reference on U -statistics). The corresponding critical values are obtained from bootstrap or permutation approaches. It has been acknowledged that when both bootstrap and permutation approaches are available, permutation should be preferred, since the corresponding tests are exactly of the desired level ([22], page 218). Nevertheless, we keep investigating them together, as bootstrap methods—through *trial-shuffling*—are the usual references in neuroscience. Moreover, for specific U -statistics, the corresponding tests share the same properties: both are proved to be asymptotically of the prescribed size and consistent against any reasonable alternative, despite the fact that different tools are used to obtain these results. Indeed, the distance between the bootstrapped distribution and the initial distribution under independence is here directly studied for the bootstrap approach, unlike the permutation approach. Finally, both procedures have good performance in practice when the sample size is moderate to small, as is often the case in neuroscience due to biological or economical reasons.

As U -statistics are usual tools for nonparametric statistical inference, many works deal with the application of bootstrap or permutation to U -statistics. From the original work of Arvesen [8] about the jackknife of U -statistics, to the recent one of Leucht and Neumann [45], several papers [4, 9, 15, 18] have been devoted to the general problem of bootstrapping a U -statistic. The use of bootstrap or permutation of U -statistics is specially considered in testing problems [16, 38], in particular in dependence detection problems with the Kolmogorov–Smirnov type tests cited above [62, 70].

But all those works exclusively focus on U -statistics of i.i.d. real valued random variables or vectors. To our knowledge, there is no previous work on the bootstrap or permutation of general U -statistics for i.i.d. pairs of point processes, as considered in the present paper. The main difficulty thus lies in the nature of the mathematical objects we handle here, that is, point processes and their associated point measures which are random measures. The proofs of our results, although inspired by Romano's [60, 62] work and Hoeffding's [37] precursor results on the permutation, are therefore more technical and complex on many aspects detailed in the sequel. In addition, we aim at obtaining the asymptotic distribution of the bootstrapped or permuted test statistics under independence, but also under dependence (see Theorems 3.1 and 4.1). Concerning the permutation approach, such a result is, as far as we know, new even for more classical settings than point processes. It thus partially solves a problem stated as an open question in [70].

This paper is organized as follows.

We first present in Section 2 the testing problem, and introduce the main notation. Starting from existing works in neuroscience, we introduce our test statistics based on general kernel-based U -statistics.

Section 3 is devoted to our bootstrap approach and new general results about the consistency of the bootstrap for the considered U -statistics, expressed in terms of Wasserstein's metric as in [9]. The convergence is studied under independence as well as under dependence. The corresponding bootstrap independence tests are therefore shown to be asymptotically of the desired size, and consistent against any reasonable alternative. The impact of using Monte Carlo methods to approximate the bootstrap quantiles is also investigated in this section.

Section 4 is devoted to the permutation approach which leads, by nature, to nonparametric independence tests exactly of the desired level, and this, even when a Monte Carlo method is used to approximate the permutation quantiles. We then give new general results about the consistency of the permutation approach when the kernel of the U -statistic has a specific form. These results are still expressed in terms of Wasserstein's metric. As a consequence, the corresponding permutation independence tests are proved to satisfy the same asymptotic properties as the bootstrap ones under the null hypothesis as well as under the same alternatives.

As a comparison of the performance of our tests with existing ones in neuroscience, especially when the sample sizes are moderate or even small, a simulation study is presented in Section 5.

A conclusion is given in the last section.

Finally, all proofs and some additional technical results can be found in the supplementary material [2].

2. From neuroscience interpretations to general test statistics.

2.1. *The testing problem.* Throughout this article, we consider finite point processes defined on a probability space $(\Omega, \mathcal{A}, \mathbb{P})$ and observed on $[0, 1]$, that is, random point processes on $[0, 1]$ whose total number of points is almost surely finite

(see [17], e.g.). Typically, in a neuroscience framework, such finite point processes may represent spike trains recorded on a given finite interval of time, and rescaled so that their values may be assumed to belong to $[0, 1]$. The set \mathcal{X} of all their possible values consists of the countable subsets of $[0, 1]$. It is equipped with a metric $d_{\mathcal{X}}$ that we introduce in (3.3). This metric, issued from the Skorohod topology, makes \mathcal{X} separable and allows us to define accordingly Borelian sets on \mathcal{X} and by extension on \mathcal{X}^2 through the product metric.

The point measure dN_x associated with an element x of \mathcal{X} is defined for all measurable real-valued function f by $\int_{[0,1]} f(u) dN_x(u) = \sum_{u \in x} f(u)$. In particular, the total number of points of x , denoted by $\#x$, is equal to $\int_{[0,1]} dN_x(u)$. Moreover, for a finite point process X defined on $(\Omega, \mathcal{A}, \mathbb{P})$ and observed on $[0, 1]$, $\int f(u) dN_X(u)$ becomes a real random variable, defined on the same probability space $(\Omega, \mathcal{A}, \mathbb{P})$.

A pair $X = (X^1, X^2)$ of finite point processes defined on $(\Omega, \mathcal{A}, \mathbb{P})$ and observed on $[0, 1]$, has joint distribution P , with marginals P^1 and P^2 if $P(\mathcal{B}) = \mathbb{P}(X \in \mathcal{B})$, $P^1(\mathcal{B}^1) = \mathbb{P}(X^1 \in \mathcal{B}^1)$, and $P^2(\mathcal{B}^2) = \mathbb{P}(X^2 \in \mathcal{B}^2)$, for every Borelian set \mathcal{B} of \mathcal{X}^2 , and all Borelian sets $\mathcal{B}^1, \mathcal{B}^2$ of \mathcal{X} .

Given the observation of an i.i.d. sample $\mathbb{X}_n = (X_1, \dots, X_n)$ from the same distribution P as X , with $X_i = (X_i^1, X_i^2)$ for every $i = 1, \dots, n$, we aim at testing (H_0) X^1 and X^2 are independent against (H_1) X^1 and X^2 are not independent, which can also be written as

$$(H_0) P = P^1 \otimes P^2 \quad \text{against} \quad (H_1) P \neq P^1 \otimes P^2.$$

2.2. *Independence test based on coincidences in neuroscience.* In the neuroscience issue which initially motivated this work, the i.i.d. sample $\mathbb{X}_n = (X_1, \dots, X_n)$ models pairs of rescaled spike trains issued from two distinct and simultaneously recorded neurons during n trials. Those data are usually recorded on living animals that are repeatedly subject to the same stimulus or that are repeatedly executing the same task. Because there are periods of rest between the records, it is commonly admitted that the n trials are i.i.d. and that the considered i.i.d. sample model is actually realistic. Then the main dependence feature that needs to be detected between both neurons corresponds to synchronization in time, referred to as coincidences [29]. More precisely, neuroscientists expect to detect if such coincidences occur significantly, that is more than what may be due to chance. They speak in this case of a detected synchrony.

In [69], the notion of coincidence count between two point processes X^1 and X^2 with delay δ ($\delta > 0$) is defined by

$$(2.1) \quad \varphi_{\delta}^{\text{coinc}}(X^1, X^2) = \int_{[0,1]^2} \mathbb{1}_{|u-v| \leq \delta} dN_{X^1}(u) dN_{X^2}(v) = \sum_{u \in X^1, v \in X^2} \mathbb{1}_{|u-v| \leq \delta}.$$

Notice that other coincidence count functions have been used in the neuroscience literature such as the binned coincidence count function (i.e., based on

binned data) introduced in [28] or its shifted version [30] (see also [69] for explicit formulae). A further example of possible function used to detect dependence in neuroscience (see [65]) is of the form

$$(2.2) \quad \varphi^w(X^1, X^2) = \int_{[0,1]^2} w(u, v) dN_{X^1}(u) dN_{X^2}(v).$$

Under the assumption that both X^1 and X^2 are homogeneous Poisson processes, the independence test of [69] rejects (H_0) when a test statistic based on $\sum_{i=1}^n \varphi_\delta^{\text{coinc}}(X_i^1, X_i^2)$ is larger than a given critical value. This critical value is deduced from the asymptotic Gaussian distribution of the test statistic under (H_0) . The test is proved to be asymptotically of the desired size, but only under the homogeneous Poisson processes assumption. However, it is now well known that this assumption, as well as many other model assumptions, fails to be satisfied in practice for spike trains (see [57, 58]).

2.3. *General U-statistics as independence test statistics.* In the parametric homogeneous Poisson framework of [69], the expectation of $\varphi_\delta^{\text{coinc}}(X_i^1, X_i^2)$ has a simple expression as a function of δ and the intensities λ_1 and λ_2 of X^1 and X^2 . Since λ_1 and λ_2 can be easily estimated, an estimator of this expectation can thus be obtained using the plug-in principle, and subtracted from $\varphi_\delta^{\text{coinc}}(X_i^1, X_i^2)$ to lead to a test statistic with a centered asymptotic distribution under (H_0) .

In the present nonparametric framework where we want to make as few assumptions as possible on the point processes X^1 and X^2 , such a centering plug-in tool is not available. We propose using instead a self-centering trick, which amounts, combined with a rescaling step, to the statistic

$$(2.3) \quad \frac{1}{n(n-1)} \sum_{i \neq i' \in \{1, \dots, n\}} (\varphi_\delta^{\text{coinc}}(X_i^1, X_i^2) - \varphi_\delta^{\text{coinc}}(X_i^1, X_{i'}^2)).$$

It is clear that the function $\varphi_\delta^{\text{coinc}}$ used in [69] suits the dependence feature the neuroscientists expect to detect in a spike train analysis. However, it is not necessarily the best choice for other kinds of dependence features to be detected in a general point processes analysis. Note furthermore that the statistic (2.3) can be written as a U -statistic of the i.i.d. sample $\mathbb{X}_n = (X_1, \dots, X_n)$ with a symmetric kernel, as defined by Hoeffding [34].

Let us therefore consider the general independence test statistics which are U -statistics of the form

$$(2.4) \quad U_{n,h}(\mathbb{X}_n) = \frac{1}{n(n-1)} \sum_{i \neq i' \in \{1, \dots, n\}} h(X_i, X_{i'}),$$

where $h : (\mathcal{X}^2)^2 \rightarrow \mathbb{R}$ is a symmetric kernel such that

$$(\mathcal{A}_{\text{Cent}}) \quad \left| \begin{array}{l} \text{For all } n \geq 2, U_{n,h}(\mathbb{X}_n) \text{ is zero mean under } (H_0), \\ \text{that is, for } X_1 \text{ and } X_2, \text{ i.i.d. with distribution } P^1 \otimes P^2 \text{ on } \mathcal{X}^2, \\ \mathbb{E}[h(X_1, X_2)] = 0. \end{array} \right.$$

In the sequel, we call *Coincidence case* the case where $h = h_{\varphi_\delta^{\text{coinc}}}$, with

$$(2.5) \quad \begin{aligned} h_{\varphi_\delta^{\text{coinc}}}(x, y) = & \frac{1}{2}(\varphi_\delta^{\text{coinc}}(x^1, x^2) + \varphi_\delta^{\text{coinc}}(y^1, y^2) \\ & - \varphi_\delta^{\text{coinc}}(x^1, y^2) - \varphi_\delta^{\text{coinc}}(y^1, x^2)), \end{aligned}$$

so that $U_{n, h_{\varphi_\delta^{\text{coinc}}}}(\mathbb{X}_n)$ is equal to the statistic (2.3).

A more general choice, which of course includes the above *Coincidence case*, is obtained by replacing $\varphi_\delta^{\text{coinc}}$ by any generic integrable function φ . This is the *Linear case*. For any integrable function φ , the kernel h is then taken equal to h_φ , with

$$(2.6) \quad h_\varphi(x, y) = \frac{1}{2}(\varphi(x^1, x^2) + \varphi(y^1, y^2) - \varphi(x^1, y^2) - \varphi(y^1, x^2)).$$

This example is of utmost importance in the present work since it provides a first proved case of consistency for the permutation approach under the null hypothesis as well as under the alternative (see Theorem 4.1). In this case, note that $(\mathcal{A}_{\text{Cent}})$ is straightforwardly satisfied, that is, $U_{n, h_\varphi}(\mathbb{X}_n)$ is zero mean under (H_0) . Note furthermore that $U_{n, h_\varphi}(\mathbb{X}_n)$ is an unbiased estimator of

$$\int \int \varphi(x^1, x^2)(dP(x^1, x^2) - dP^1(x^1) dP^2(x^2)),$$

without any assumption on the underlying point processes. This is therefore a reasonable independence test statistic. If X^1 and X^2 were finite dimensional variables with continuous distributions w.r.t. the Lebesgue measure, this test statistic would be closely related to generalized Kolmogorov–Smirnov tests of independence. For instance, the test statistics of Blum, Kiefer and Rosenblatt [11], Romano [62], van der Vaart and Wellner in [70] are equivalent to $\sqrt{n} \sup_{v^1 \in \mathcal{V}^1, v^2 \in \mathcal{V}^2} |U_{n, h_{\varphi_{(v^1, v^2)}}}(\mathbb{X}_n)|$, where, respectively:

- $\mathcal{V}^1 = \mathcal{V}^2 = \mathbb{R}$ and $\varphi_{(v^1, v^2)}(x^1, x^2) = \mathbb{1}_{]-\infty, v^1]}(x^1) \mathbb{1}_{]-\infty, v^2]}(x^2)$,
- \mathcal{V}^1 and \mathcal{V}^2 are countable V.-C. classes of subsets of \mathbb{R}^d , and $\varphi_{(v^1, v^2)}(x^1, x^2) = \mathbb{1}_{v^1}(x^1) \mathbb{1}_{v^2}(x^2)$,
- \mathcal{V}^1 and \mathcal{V}^2 are well-chosen classes of real-valued functions, and $\varphi_{(v^1, v^2)}(x^1, x^2) = v^1(x^1) v^2(x^2)$.

Note also the work of [46] based on integrals instead of the supremum of similar quantities with $\varphi_{(v^1, v^2)}(x^1, x^2) = e^{iv^1 x^1} e^{iv^2 x^2}$. Thus, to our knowledge, the existing test statistics are based on functions φ of product type. However, as seen in Section 2.2, when dealing with point processes, natural functions φ , as for instance $\varphi_\delta^{\text{coinc}}$, are not of this type.

2.4. *Nondegeneracy of the U -statistics under (H_0) .* Following the works of Romano [62] or van der Vaart and Wellner [70], the tests we propose here are based on bootstrap and permutation approaches for the above general U -statistics. Most of the assumptions on h depend on the chosen method (permutation or bootstrap) and are postponed to the corresponding section. However, another assumption is common, besides $(\mathcal{A}_{\text{Cent}})$:

$$(\mathcal{A}_{\text{nondeg}}) \quad \left| \begin{array}{l} \text{For all } n \geq 2, U_{n,h}(\mathbb{X}_n) \text{ is nondegenerate under } (H_0), \\ \text{that is, for all } X_1 \text{ and } X_2, \text{ i.i.d. with distribution } P^1 \otimes P^2 \text{ on } \mathcal{X}^2, \\ \text{Var}(\mathbb{E}[h(X_1, X_2)|X_1]) \neq 0. \end{array} \right.$$

This assumption is needed in all results with weak convergence to a Gaussian limit, as its variance has to be strictly positive (see, e.g., Proposition 3.5 or Theorem 4.1). Since under (H_0) , $U_{n,h}(\mathbb{X}_n)$ is assumed to have zero mean, it is degenerate under (H_0) if and only if for X with distribution $P^1 \otimes P^2$ and for $P^1 \otimes P^2$ -almost every x in \mathcal{X}^2 , $\mathbb{E}[h(x, X)] = 0$.

In the *Linear case*, this condition implies a very particular link between φ and the distribution of the bivariate point process X , which is unknown. The following result gives some basic condition to fulfill $(\mathcal{A}_{\text{nondeg}})$ when φ is the coincidence count function.

PROPOSITION 2.1. *If the empty set is charged by the marginals, that is, if $P^1(\{\emptyset\}) > 0$ and $P^2(\{\emptyset\}) > 0$ and if $\varphi_\delta^{\text{coinc}}(X_1, X_2)$ [see (2.1)] is not almost surely null under (H_0) , then when h is given by (2.5), $(\mathcal{A}_{\text{nondeg}})$ is satisfied.*

The proof can be found in the supplementary material [2] together with a more informal discussion on the *Linear case* with $\varphi = \varphi^w$ as given by (2.2).

With respect to neuronal data, assuming that the processes may be empty is an obvious assumption as there often exist trials (usually short) where, just by chance, no spikes have been detected. Moreover, practitioners usually choose δ large enough such that coincidences are observed in practice and, therefore, $\varphi_\delta^{\text{coinc}}(X_1, X_2)$ is not almost surely null. Hence, in practice, the nondegeneracy assumption is always satisfied in the *Coincidence case*.

Throughout this article, $(X_i)_i$ denotes a sequence of i.i.d. pairs of point processes, with $X_i = (X_i^1, X_i^2)$ of distribution P on \mathcal{X}^2 , whose marginals are P^1 and P^2 on \mathcal{X} . For $n \geq 2$, let $\mathbb{X}_n = (X_1, \dots, X_n)$ and $U_{n,h}(\mathbb{X}_n)$ as in (2.4), with a fixed measurable symmetric kernel h satisfying $(\mathcal{A}_{\text{Cent}})$. To shorten mathematical expression, $U_n(\mathbb{X}_n)$ refers from now on to $U_{n,h}(\mathbb{X}_n)$.

3. Bootstrap tests of independence. Since the distribution of the test statistic $U_n(\mathbb{X}_n)$ is not free from the unknown underlying marginal distributions P^1 and P^2 under the null hypothesis (H_0) , we turn to a classical bootstrap approach, which aims at mimicking it, for large, but also moderate or small sample sizes.

To describe this bootstrap approach, and to properly state our results, we give below additional notation and discuss the main assumptions.

3.1. *Additional notation: Bootstrap and convergence formalism.* For j in $\{1, 2\}$, let P_n^j be the empirical marginal distribution defined by

$$(3.1) \quad P_n^j = \frac{1}{n} \sum_{i=1}^n \delta_{X_i^j}.$$

A bootstrap sample from \mathbb{X}_n is denoted by $\mathbb{X}_n^* = (X_{n,1}^*, \dots, X_{n,n}^*)$, with $X_{n,i}^* = (X_{n,i}^{*1}, X_{n,i}^{*2})$, and is defined as an n i.i.d. sample from the distribution $P_n^1 \otimes P_n^2$. Then, the bootstrap distribution of interest is the conditional distribution of $\sqrt{n}U_n(\mathbb{X}_n^*)$ given \mathbb{X}_n to be compared with the initial distribution of $\sqrt{n}U_n(\mathbb{X}_n)$ under (H_0) . To state our convergence results as concisely as possible, we use the following classical formalism:

- For any functional $Z : (\mathcal{X}^2)^n \rightarrow \mathbb{R}$, $\mathcal{L}(Z, Q)$ denotes the distribution of $Z(\mathbb{Y}_n)$, where \mathbb{Y}_n is an i.i.d. sample from the distribution Q on \mathcal{X}^2 . In particular, the distribution of $\sqrt{n}U_n(\mathbb{X}_n)$ under (H_0) is denoted by $\mathcal{L}(\sqrt{n}U_n, P^1 \otimes P^2)$.
- If the distribution $Q = Q(W)$ depends on a random variable W , $\mathcal{L}(Z, Q|W)$ is the conditional distribution of $Z(\mathbb{Y}_n)$, \mathbb{Y}_n being an i.i.d. sample from the distribution $Q = Q(W)$, given W .

In particular, the conditional distribution of $\sqrt{n}U_n(\mathbb{X}_n^*)$ given \mathbb{X}_n is denoted by $\mathcal{L}(\sqrt{n}U_n, P_n^1 \otimes P_n^2 | \mathbb{X}_n)$.

- “ Q -a.s. in $(X_i)_i$ ” at the end of a statement means that the statement only depends on the sequence $(X_i)_i$, where the X_i ’s are i.i.d. with distribution Q , and that there exists an event \mathcal{C} only depending on $(X_i)_i$ such that $\mathbb{P}(\mathcal{C}) = 1$, on which the statement is true. Here, Q is usually equal to P .
- “ $Q_n \xrightarrow[n \rightarrow +\infty]{} Q$ ” means that the sequence of distributions $(Q_n)_n$ converges towards Q in the weak sense, that is for any real valued, continuous and bounded function g , $\int g(z) dQ_n(z) \xrightarrow[n \rightarrow +\infty]{} \int g(z) dQ(z)$.
- As usual, $\mathbb{E}^*[\cdot]$ stands for the conditional expectation given \mathbb{X}_n .

One of the aims of this work is to prove that the conditional distribution $\mathcal{L}(\sqrt{n}U_n, P_n^1 \otimes P_n^2 | \mathbb{X}_n)$ is asymptotically close to $\mathcal{L}(\sqrt{n}U_n, P^1 \otimes P^2)$. Following the historical paper by Bickel and Freedman [9], the closeness between these two distributions, which are both distributions on \mathbb{R} , is here measured via the \mathbb{L}^2 -Wasserstein’s metric (also called Mallows’ metric):

$$(3.2) \quad d_2^2(Q, Q') = \inf\{\mathbb{E}[(Z - Z')^2], (Z, Z') \text{ with marginals } Q \text{ and } Q'\},$$

for all the distributions Q, Q' with finite second-order moments. Recall that convergence w.r.t. d_2 is equivalent to both weak convergence and convergence of second-order moments.

3.2. *Main assumptions.* The random variables we deal with are not real-valued variables but point processes, so the assumptions needed in our results may be difficult to interpret in this setting. We therefore devote this whole section to their description and discussion.

In addition to Assumption $(\mathcal{A}_{\text{Cent}})$, we need its following empirical version:

$$(\mathcal{A}_{\text{Cent}}^*) \quad \left\{ \begin{array}{l} \text{For } x_1 = (x_1^1, x_1^2), \dots, x_n = (x_n^1, x_n^2) \text{ in } \mathcal{X}^2, \\ \sum_{i_1, i_2, i'_1, i'_2=1}^n h((x_{i_1}^1, x_{i_2}^2), (x_{i'_1}^1, x_{i'_2}^2)) = 0. \end{array} \right.$$

Notice that this assumption, as well as $(\mathcal{A}_{\text{Cent}})$, is fulfilled in the *Linear case* where h is of the form h_φ given by (2.6), but $(\mathcal{A}_{\text{Cent}}^*)$ does not imply that h is of the form h_φ (see the supplementary material [2] for a counterexample).

Moment assumptions. Due to the \mathbb{L}^2 -Wasserstein's metric used here to study the consistency of the bootstrap approach, moment assumptions are required. In particular, the variance of $U_n(\mathbb{X}_n)$ should exist, that is,

$$(\mathcal{A}_{\text{Mmt}}) \quad \left\{ \begin{array}{l} \text{For } X_1 \text{ and } X_2, \text{ i.i.d. with distribution } P \text{ on } \mathcal{X}^2, \\ \mathbb{E}[h^2(X_1, X_2)] < +\infty, \end{array} \right.$$

and more generally we need

$$(\mathcal{A}_{\text{Mmt}}^*) \quad \left\{ \begin{array}{l} \text{For } X_1, X_2, X_3, X_4 \text{ i.i.d. with distribution } P \text{ on } \mathcal{X}^2, \\ \text{and for } i_1, i_2, i'_1, i'_2 \text{ in } \{1, 2, 3, 4\}, \\ \mathbb{E}[h^2((X_{i_1}^1, X_{i_2}^2), (X_{i'_1}^1, X_{i'_2}^2))] < +\infty. \end{array} \right.$$

Notice that when $(\mathcal{A}_{\text{Mmt}}^*)$ is satisfied, this implies that:

- $(\mathcal{A}_{\text{Mmt}})$ is satisfied (taking $i_1 = i_2, i'_1 = i'_2$, and $i'_1 \neq i_1$),
- for $X \sim P, \mathbb{E}[h^2(X, X)] < +\infty$ (taking $i_1 = i_2 = i'_1 = i'_2$),
- for X_1, X_2 i.i.d. with distribution $P^1 \otimes P^2, \mathbb{E}[h^2(X_1, X_2)] < +\infty$ (taking i_1, i_2, i'_1, i'_2 all different).

A sufficient condition for $(\mathcal{A}_{\text{Mmt}}^*)$ and $(\mathcal{A}_{\text{Mmt}})$ to be satisfied is that there exist positive constants α_1, α_2, C such that for every $x = (x^1, x^2), y = (y^1, y^2)$ in $\mathcal{X}^2, |h(x, y)| \leq C((\#x^1)^{\alpha_1} + (\#y^1)^{\alpha_1})(\#x^2)^{\alpha_2} + (\#y^2)^{\alpha_2}$, with $\mathbb{E}[(\#X^1)^{4\alpha_1}] < +\infty$ and $\mathbb{E}[(\#X^2)^{4\alpha_2}] < +\infty$.

In the *Linear case* where h is of the form h_φ given by (2.6), a possible sufficient condition is that there exist some positive constants α_1, α_2 and C such that for every x^1, x^2 in $\mathcal{X}, |\varphi(x^1, x^2)| \leq C(\#x^1)^{\alpha_1}(\#x^2)^{\alpha_2}$, with $\mathbb{E}[(\#X^1)^{4\alpha_1}] < +\infty$ and $\mathbb{E}[(\#X^2)^{4\alpha_2}] < +\infty$. In particular, in the *Coincidence case*, the coincidence count function $\varphi_\delta^{\text{coinc}}$ satisfies: for every x^1, x^2 in $\mathcal{X}, |\varphi_\delta^{\text{coinc}}(x^1, x^2)| \leq (\#x^1)(\#x^2)$. So, $(\mathcal{A}_{\text{Mmt}}^*)$ and $(\mathcal{A}_{\text{Mmt}})$ are satisfied as soon as $\mathbb{E}[(\#X^1)^4] < +\infty$ and $\mathbb{E}[(\#X^2)^4] < +\infty$.

Such moment bounds for the total number of points of the processes are in fact satisfied by many kinds of point processes: discretized point processes at resolution $0 < r < 1$ (see [69] for a definition), which have at most $1/r$ points, Poisson processes, whose total number of points obeys a Poisson distribution having exponential moments of any order and point processes with bounded conditional intensities, which can be constructed by thinning homogeneous Poisson processes (see [48]). Similar moment bounds can also be obtained (see [32]) for linear stationary Hawkes processes with positive interaction functions that are classical models in spike train analysis (see, e.g., [51, 69]). This finally may be extended to point processes whose conditional intensities are upper bounded by intensities of linear stationary Hawkes processes with positive interaction functions, by thinning arguments. This includes more general Hawkes processes (see [14]) and in particular Hawkes processes used to model inhibition in spike train analysis (see [32, 58, 59, 69]).

Continuity of the kernel. The set \mathcal{X} can be embedded in the space \mathcal{D} of càdlàg functions on $[0, 1]$ through the identification

$$N : x \in \mathcal{X} \mapsto \left(N_x : t \mapsto \int_0^t \mathbb{1}_{u \leq t} dN_x(u) \right) \in \mathcal{D}.$$

Notice that the quantity N_x is actually the counting process associated with x (see [13], e.g.): at time t , $N_x(t)$ is the number of points of x less than t . Now consider the uniform Skorohod topology on \mathcal{D} (see [10]), associated with the metric $d_{\mathcal{D}}$ defined by

$$d_{\mathcal{D}}(f, g) = \inf \left\{ \varepsilon > 0; \exists \lambda \in \Lambda, \left\{ \begin{array}{l} \sup_{t \in [0,1]} |\lambda(t) - t| \leq \varepsilon, \\ \sup_{t \in [0,1]} |f(\lambda(t)) - g(t)| \leq \varepsilon \end{array} \right\} \right\},$$

where Λ is the set of strictly increasing, continuous mappings of $[0, 1]$ onto itself. Notice that here, λ represents a uniformly small deformation of the time scale. Thanks to the identification N above, \mathcal{X} can then be endowed with the topology induced by $d_{\mathcal{X}}$ defined on \mathcal{X} by

$$(3.3) \quad d_{\mathcal{X}}(x, x') = d_{\mathcal{D}}(N(x), N(x')) \quad \text{for every } x, x' \text{ in } \mathcal{X}.$$

As an illustration, if x and x' are in \mathcal{X} , for ε in $(0, 1)$, $d_{\mathcal{X}}(x, x') \leq \varepsilon$ implies that x and x' have the same cardinality, and for k in $\{1, \dots, \#x\}$, the k th point of x is at distance less than ε from the k th point of x' . Since $(\mathcal{D}, d_{\mathcal{D}})$ is a separable metric space, so are $(\mathcal{X}, d_{\mathcal{X}})$, $(\mathcal{X}^2, d_{\mathcal{X}^2})$, where $d_{\mathcal{X}^2}$ is the product metric defined from $d_{\mathcal{X}}$ (see [19], page 32), and $(\mathcal{X}^2 \times \mathcal{X}^2, d)$, where d , the product metric defined from $d_{\mathcal{X}^2}$, is given by

$$(3.4) \quad d((x, y), (x', y')) = \sup \left\{ \sup_{j=1,2} \{d_{\mathcal{X}}(x^j, x'^j)\}, \sup_{j=1,2} \{d_{\mathcal{X}}(y^j, y'^j)\} \right\},$$

for every $x = (x^1, x^2)$, $y = (y^1, y^2)$, $x' = (x'^1, x'^2)$, $y' = (y'^1, y'^2)$ in \mathcal{X}^2 . The kernel h chosen to define the U -statistic $U_n(\mathbb{X}_n)$ in (2.4) should satisfy

$$(\mathcal{A}_{\text{Cont}}) \quad \left\{ \begin{array}{l} \text{There exists a subset } \mathcal{C} \text{ of } \mathcal{X}^2 \times \mathcal{X}^2, \text{ such that} \\ \text{(i) } h \text{ is continuous on } \mathcal{C} \text{ for the topology induced by } d, \\ \text{(ii) } (P^1 \otimes P^2)^{\otimes 2}(\mathcal{C}) = 1. \end{array} \right.$$

Here are some examples in the *Linear case* for which $(\mathcal{A}_{\text{Cont}})$ holds.

PROPOSITION 3.1. *Let $w : [0, 1]^2 \rightarrow \mathbb{R}$ be a continuous integrable function. Then the kernel h_{φ^w} defined on $\mathcal{X}^2 \times \mathcal{X}^2$ by (2.2) and (2.6) is continuous w.r.t. the topology induced by d , defined by (3.4).*

The above result does not apply to $h_{\varphi_\delta^{\text{coinc}}}$ but the following one holds.

PROPOSITION 3.2. *The coincidence count kernel $h_{\varphi_\delta^{\text{coinc}}}$ defined on $\mathcal{X}^2 \times \mathcal{X}^2$ by (2.1) and (2.6) is continuous w.r.t. the topology induced by d , on*

$$(3.5) \quad \begin{aligned} \mathcal{C}_\delta = \{ & ((x^1, x^2), (y^1, y^2)) \in \mathcal{X}^2 \times \mathcal{X}^2; \\ & (\{x^1\} \cup \{y^1\}) \cap (\{x^2 \pm \delta\} \cup \{y^2 \pm \delta\}) = \emptyset \}. \end{aligned}$$

As suggested in [69], when dealing with discretized point processes at resolution r , the right choice for δ is $kr + r/2$ for an integer k , so $(P^1 \otimes P^2)^{\otimes 2}(\mathcal{C}_\delta) = 1$, and $h_{\varphi_\delta^{\text{coinc}}}$ satisfies $(\mathcal{A}_{\text{Cont}})$. Furthermore, when dealing with independent point processes with conditional intensities, those processes may be constructed by thinning two independent Poisson processes X and X' . Hence, in this case, the probability $(P^1 \otimes P^2)^{\otimes 2}$ of \mathcal{C}_δ in (3.5) is larger than $\mathbb{P}(X \cap (X' \pm \delta) = \emptyset)$, whose value is 1. So when dealing with point processes with conditional intensities, $h_{\varphi_\delta^{\text{coinc}}}$ also satisfies $(\mathcal{A}_{\text{Cont}})$.

3.3. *Consistency of the bootstrap approach.* The validity of the bootstrap approach for our independence tests is due to the following consistency result.

THEOREM 3.1. *For every $n \geq 2$, let P_n^j for $j = 1, 2$ be the empirical marginal distributions defined by (3.1). Then, under $(\mathcal{A}_{\text{Cent}})$, $(\mathcal{A}_{\text{Cent}}^*)$, $(\mathcal{A}_{\text{Mmt}}^*)$ and $(\mathcal{A}_{\text{Cont}})$,*

$$d_2(\mathcal{L}(\sqrt{n}U_n, P_n^1 \otimes P_n^2 | \mathbb{X}_n), \mathcal{L}(\sqrt{n}U_n, P^1 \otimes P^2)) \xrightarrow[n \rightarrow +\infty]{} 0, \quad P\text{-a.s. in } (X_i)_i.$$

The proof follows similar arguments to the ones of [9] for the bootstrap of the mean, or to [18] and [45] for the bootstrap of U -statistics. The main novel point here consists in using the identification (3.4) and the properties of the separable Skorohod metric space $(\mathcal{D}, d_{\mathcal{D}})$, where weak convergence of sample probability

distributions is available (see [71]). This theorem derives in fact from the following two propositions which may be useful in various frameworks. The first one states a nonasymptotic result, while the second one gives rather natural results of convergence.

PROPOSITION 3.3. *Under $(\mathcal{A}_{\text{Cent}}), (\mathcal{A}_{\text{Cent}}^*), (\mathcal{A}_{\text{Mmt}}^*)$, with the notation of Theorem 3.1, there exists an absolute constant $C > 0$ such that for $n \geq 2$,*

$$d_2^2(\mathcal{L}(\sqrt{n}U_n, P_n^1 \otimes P_n^2 | \mathbb{X}_n), \mathcal{L}(\sqrt{n}U_n, P^1 \otimes P^2)) \leq C \inf \left\{ \mathbb{E}^*[(h(Y_{n,a}^*, Y_{n,b}^*) - h(Y_a, Y_b))^2], Y_{n,a}^* \sim P_n^1 \otimes P_n^2, Y_a \sim P^1 \otimes P^2, \right. \\ \left. \text{and } (Y_{n,b}^*, Y_b) \text{ is an independent copy of } (Y_{n,a}^*, Y_a) \right\}.$$

COMMENT. In the above proposition, the infimum is taken over all the possible distributions of $(Y_{n,a}^*, Y_a)$ having the correct marginals, $(Y_{n,b}^*, Y_b)$ being just an independent copy of $(Y_{n,a}^*, Y_a)$. In particular, $Y_{n,a}^*$ is not necessarily independent of Y_a .

PROPOSITION 3.4. *If $\mathbb{E}[|h(X_1, X_2)|] < +\infty$, then*

$$(3.6) \quad U_n(\mathbb{X}_n) \xrightarrow[n \rightarrow +\infty]{} \mathbb{E}[h(X_1, X_2)] = \int h(x, x') dP(x) dP(x'),$$

P-a.s. in $(X_i)_i$.

Under $(\mathcal{A}_{\text{Mmt}}^)$, one moreover obtains that P-a.s. in $(X_i)_i$,*

$$\frac{1}{n^4} \sum_{i,j,k,l=1}^n h^2((X_i^1, X_j^2), (X_k^1, X_l^2)) \xrightarrow[n \rightarrow +\infty]{} \mathbb{E}[h^2((X_1^1, X_2^2), (X_3^1, X_4^2))].$$

3.4. *Convergence of cumulative distribution functions (c.d.f.) and quantiles.* As usual, $\mathcal{N}(m, v)$ stands for the Gaussian distribution with mean m and variance v , $\Phi_{m,v}$ for its c.d.f. and $\Phi_{m,v}^{-1}$ for its quantile function. From the results of Rubin and Vitale [64], generalizing Hoeffding’s [34] decomposition of nondegenerate U -statistics to the case where the X_i ’s are not necessarily real valued random vectors, a central limit theorem for $U_n(\mathbb{X}_n)$ can be easily derived. It is expressed here using the \mathbb{L}^2 -Wasserstein’s metric, and is thus slightly stronger than the one stated in equation (1.1) of [40].

PROPOSITION 3.5. *Assume that h satisfies $(\mathcal{A}_{\text{nondeg}}), (\mathcal{A}_{\text{Cent}})$ and $(\mathcal{A}_{\text{Mmt}})$. Let $\sigma_{P^1 \otimes P^2}^2$ be defined by*

$$(3.7) \quad \sigma_{P^1 \otimes P^2}^2 = 4 \text{Var}(\mathbb{E}[h(X_1, X_2) | X_1]),$$

when X_1 and X_2 are $P^1 \otimes P^2$ -distributed. Then

$$d_2(\mathcal{L}(\sqrt{n}U_n, P^1 \otimes P^2), \mathcal{N}(0, \sigma_{P^1 \otimes P^2}^2)) \xrightarrow{n \rightarrow +\infty} 0.$$

COMMENTS. (i) Notice that $(\mathcal{A}_{\text{nondeg}})$ is equivalent to $\sigma_{P^1 \otimes P^2}^2 > 0$. In the case where $(\mathcal{A}_{\text{nondeg}})$ does not hold, that is, if $\sigma_{P^1 \otimes P^2}^2 = 0$, the quantity $\sqrt{n}U_n(\mathbb{X}_n)$ tends in probability towards 0. In this case, Theorem 3.1 implies that the two distributions $\mathcal{L}(\sqrt{n}U_n, P_n^1 \otimes P_n^2 | \mathbb{X}_n)$ and $\mathcal{L}(\sqrt{n}U_n, P^1 \otimes P^2)$ are not only close, but that they are actually both tending to the Dirac mass in 0. Indeed, degenerate U -statistics of order 2 have a faster rate of convergence than \sqrt{n} (see [5], e.g., for explicit limit theorems). So in this degenerate case, one could not use $\sqrt{n}U_n(\mathbb{X}_n)$ as a test statistic anymore (without changing the normalization). But as mentioned above, $(\mathcal{A}_{\text{nondeg}})$ is usually satisfied in practice (see Section 2.4 for the *Coincidence case*).

(ii) Let us introduce, as in [40], an estimator of $\sigma_{P^1 \otimes P^2}^2$, but which is here corrected to be unbiased under (H_0) , namely

$$\hat{\sigma}^2 = \frac{4}{n(n-1)(n-2)} \sum_{i,j,k \in \{1, \dots, n\}, \# \{i,j,k\} = 3} h(X_i, X_j)h(X_i, X_k),$$

and the statistic

$$(3.8) \quad S_n = \sqrt{n}U_n(\mathbb{X}_n) / \hat{\sigma}.$$

From Proposition 3.5 combined with Slutsky’s lemma and the law of large numbers for U -statistics of order 3, one easily derives that under (H_0) , S_n converges in distribution to $\mathcal{N}(0, 1)$. This leads to a rather simple but asymptotically satisfactory test: the test which rejects (H_0) when $|S_n| \geq \Phi_{0,1}^{-1}(1 - \alpha/2)$ is indeed asymptotically of size α . It is also consistent against any reasonable alternative P , satisfying $(\mathcal{A}_{\text{Mmt}})$ and such that $\mathbb{E}[h(X, X')] \neq 0$, for X, X' i.i.d. with distribution P . Such a purely asymptotic test may of course suffer from a lack of power when the sample size n is small or even moderate, which is typically the case for the application in neuroscience described in Section 2 for biological reasons (from few tens up to few hundreds at best). Though the bootstrap approach is mainly justified by asymptotic arguments, the simulation study presented in Section 5 shows its efficiency in a nonasymptotic context, compared to this simpler test.

As Proposition 3.5 implies that the limit distribution of $\sqrt{n}U_n(\mathbb{X}_n)$ has a continuous c.d.f., the convergence of the conditional c.d.f. or quantiles of the considered bootstrap distributions holds. Note that these conditional bootstrap distributions are discrete, so the corresponding quantile functions are to be understood as the generalized inverses of the cumulative distribution functions.

COROLLARY 3.1. For $n \geq 2$, with the notation of Theorem 3.1, let \mathbb{X}_n^* be a bootstrap sample, that is, an i.i.d. n -sample from the distribution $P_n^1 \otimes P_n^2$. Let \mathbb{X}_n^\perp be another i.i.d. n -sample from the distribution $P^1 \otimes P^2$ on \mathcal{X}^2 . Under $(\mathcal{A}_{\text{nondeg}})$ and the assumptions of Theorem 3.1,

$$\sup_{z \in \mathbb{R}} |\mathbb{P}(\sqrt{n}U_n(\mathbb{X}_n^*) \leq z | \mathbb{X}_n) - \mathbb{P}(\sqrt{n}U_n(\mathbb{X}_n^\perp) \leq z)| \xrightarrow{n \rightarrow +\infty} 0, \quad P\text{-a.s. in } (X_i)_i.$$

If moreover, for η in $(0, 1)$, $q_{\eta,n}^*(\mathbb{X}_n)$ denotes the conditional η -quantile of $\sqrt{n}U_n(\mathbb{X}_n^*)$ given \mathbb{X}_n and $q_{\eta,n}^\perp$ denotes the η -quantile of $\sqrt{n}U_n(\mathbb{X}_n^\perp)$,

$$(3.9) \quad |q_{\eta,n}^*(\mathbb{X}_n) - q_{\eta,n}^\perp| \xrightarrow{n \rightarrow +\infty} 0, \quad P\text{-a.s. in } (X_i)_i.$$

3.5. Asymptotic properties of the bootstrap tests. We are interested in the asymptotic behavior of sequences of tests all based on test statistics of the form $\sqrt{n}U_n(\mathbb{X}_n)$. The bootstrap approach, whose consistency is studied above, allows to define bootstrap-based critical values for these tests. Note that the permutation approach studied in Section 4 is based on the same test statistics, but with critical values obtained by permutation. Hence, we introduce here a condensed and common formalism for the upper-, lower- and two-tailed tests considered in this work, taking into account that the only change in our two considered approaches concerns the critical values. This will help to state our results in the shortest manner.

Let α be fixed in $(0, 1)$, and q be a sequence of upper and lower critical values:

$$q = (q_{\alpha,n}^+(\mathbb{X}_n), q_{\alpha,n}^-(\mathbb{X}_n))_{n \geq 2}.$$

From this sequence q , let us now define the family $\Gamma(q)$ of three sequences of tests $\Delta^+ = (\Delta_{\alpha,n}^+)_{n \geq 2}$, $\Delta^- = (\Delta_{\alpha,n}^-)_{n \geq 2}$, and $\Delta^{+/-} = (\Delta_{\alpha,n}^{+/-})_{n \geq 2}$, where

$$(3.10) \quad \begin{cases} \Delta_{\alpha,n}^+(\mathbb{X}_n) = \mathbb{1}_{\sqrt{n}U_n(\mathbb{X}_n) > q_{\alpha,n}^+(\mathbb{X}_n)} & \text{(upper-tailed test),} \\ \Delta_{\alpha,n}^-(\mathbb{X}_n) = \mathbb{1}_{\sqrt{n}U_n(\mathbb{X}_n) < q_{\alpha,n}^-(\mathbb{X}_n)} & \text{(lower-tailed test),} \\ \Delta_{\alpha,n}^{+/-}(\mathbb{X}_n) = \max(\Delta_{\alpha/2,n}^+(\mathbb{X}_n), \Delta_{\alpha/2,n}^-(\mathbb{X}_n)) & \text{(two-tailed test),} \end{cases}$$

the last test being implicitly defined by the corresponding choices in $\alpha/2$.

Of course, q , $\Gamma(q)$, as well as Δ^+ , Δ^- and $\Delta^{+/-}$, depend on the choice of α , but since α is fixed at the beginning, to keep the notation as simple as possible, this dependence is, like the one in h , omitted in the notation.

Depending on the choice of q , the classical asymptotic properties that can be expected to be satisfied by $\Gamma(q)$ are $(\mathcal{P}_{\text{size}})$ and $(\mathcal{P}_{\text{consist.}})$ defined by

$$(\mathcal{P}_{\text{size}}) \quad \left| \begin{array}{l} \text{Each } \Delta = (\Delta_{\alpha,n})_{n \geq 2} \text{ in } \Gamma(q) \text{ is asymptotically of size } \alpha, \\ \text{that is, } \mathbb{P}(\Delta_{\alpha,n}(\mathbb{X}_n) = 1) \xrightarrow{n \rightarrow +\infty} \alpha \text{ if } P = P^1 \otimes P^2; \end{array} \right.$$

$$(\mathcal{P}_{\text{consist.}}) \left\{ \begin{array}{l} \text{Each } \Delta = (\Delta_{\alpha,n})_{n \geq 2} \text{ in } \Gamma(q) \text{ is consistent,} \\ \text{that is, } \mathbb{P}(\Delta_{\alpha,n}(\mathbb{X}_n) = 1) \xrightarrow{n \rightarrow +\infty} 1, \text{ for every } P \text{ such that} \\ \bullet \int h(x, x') dP(x) dP(x') > 0 \text{ if } \Delta = \Delta^+, \\ \bullet \int h(x, x') dP(x) dP(x') < 0 \text{ if } \Delta = \Delta^-, \\ \bullet \int h(x, x') dP(x) dP(x') \neq 0 \text{ if } \Delta = \Delta^{+/-}. \end{array} \right.$$

Following Corollary 3.1, our bootstrap tests family is defined from (3.10) by $\Gamma(q^*)$, with

$$(3.11) \quad q^* = (q_{1-\alpha,n}^*(\mathbb{X}_n), q_{\alpha,n}^*(\mathbb{X}_n))_{n \geq 2}.$$

THEOREM 3.2. *Let $\Gamma(q^*)$ be the family of tests defined by (3.10) and (3.11). If $(\mathcal{A}_{\text{nondeg}})$, $(\mathcal{A}_{\text{Cent}})$, $(\mathcal{A}_{\text{Cent}}^*)$, $(\mathcal{A}_{\text{Mmt}}^*)$ and $(\mathcal{A}_{\text{Cont}})$ hold, then $\Gamma(q^*)$ satisfies both $(\mathcal{P}_{\text{size}})$ and $(\mathcal{P}_{\text{consist.}})$.*

COMMENTS. In the *Linear case* where h is equal to h_φ defined by (2.6), $\int h(x, x') dP(x) dP(x') = \int \varphi(x^1, x^2)[dP(x^1, x^2) - dP^1(x^1) dP^2(x^2)]$. This means that under the assumptions of Theorem 3.2, the two-tailed test of $\Gamma(q^*)$ is consistent against any alternative such that $\int \varphi(x^1, x^2) dP(x^1, x^2)$ differs from what is expected under (H_0) , that is, $\int \varphi(x^1, x^2) dP^1(x^1) dP^2(x^2)$.

(i) In particular, in the *Coincidence case* where h is equal to $h_{\varphi_\delta^{\text{coinc}}}$ defined by (2.5), the assumptions of Theorem 3.2 are fulfilled for instance if X^1 and X^2 are discretized at resolution r , with $\delta = kr + r/2$ for some integer k , or if X^1 and X^2 have bounded conditional intensities, with δ large enough so that $\varphi_\delta^{\text{coinc}}(X^1, X^2)$ is not a.s. null. Theorem 3.2 means in such cases that the corresponding two-tailed test is asymptotically of power 1, for any alternative P such that $\int \mathbb{1}_{|v-u| \leq \delta} \mathbb{E}[dN_{X^1}(u) dN_{X^2}(v)] \neq \int \mathbb{1}_{|v-u| \leq \delta} \mathbb{E}[dN_{X^1}(u)] \mathbb{E}[dN_{X^2}(v)]$. Note that no δ ensuring this condition can be found if heuristically, the repartition of the delays $|v - u|$ between points of X^1 and X^2 is the same under (H_0) and under (H_1) . For neuroscientists, it means that the cross-correlogram (histogram of the delays, classically represented as a first description of the data) does not show different behaviors in the dependent and independent cases. This would only occur if the dependence could not be measured in terms of delay between points.

(ii) Furthermore, when φ is equal to φ^w defined by (2.2) with a continuous integrable function w (see Proposition 3.1), Theorem 3.2 means that the corresponding two-tailed test is consistent against any alternative such that $\beta_w = \int w(u, v) (\mathbb{E}[dN_{X^1}(u) dN_{X^2}(v)] - \mathbb{E}[dN_{X^1}(u)] \mathbb{E}[dN_{X^2}(v)]) \neq 0$. For the function w chosen in [65] and under specific Poisson assumptions, β_w is linked to a coefficient in the Haar basis of the so-called interaction function, which measures the dependence between both processes X^1 and X^2 . Working nonasymptotically, one of the main results of [65] states, after reformulation in the present setting, that if β_w is larger than an explicit lower bound, then the second kind error rate of

the upper-tailed test is less than a prescribed β in $(0, 1)$. Theorem 3.2 thus generalizes the result of [65] to a set-up with much less restrictive assumptions on the underlying stochastic models, but in an asymptotic way.

Whereas the above family of bootstrap tests $\Gamma(q^*)$ involves an exact computation of the conditional quantiles $q_{\eta,n}^*(\mathbb{X}_n)$, in practice, these quantiles are approximated by a Monte Carlo method. More precisely, let $(B_n)_{n \geq 2}$ be a sequence of possible numbers of Monte Carlo iterations, such that $B_n \rightarrow_{n \rightarrow +\infty} +\infty$. For $n \geq 1$, let $(\mathbb{X}_n^{*1}, \dots, \mathbb{X}_n^{*B_n})$ be B_n independent bootstrap samples from \mathbb{X}_n . Set $(U^{*1}, \dots, U^{*B_n}) = (U_n(\mathbb{X}_n^{*1}), \dots, U_n(\mathbb{X}_n^{*B_n}))$, and introduce its corresponding order statistic $(U^{*(1)}, \dots, U^{*(B_n)})$. The considered family of Monte Carlo bootstrap tests is then defined from (3.10) by $\Gamma(q_{MC}^*)$, with

$$(3.12) \quad q_{MC}^* = (\sqrt{n}U^{*(\lceil(1-\alpha)B_n\rceil)}, \sqrt{n}U^{*(\lfloor\alpha B_n\rfloor+1)})_{n \geq 2}.$$

PROPOSITION 3.6. *Let $\Gamma(q_{MC}^*)$ be the family of Monte Carlo bootstrap tests defined by (3.10) and q_{MC}^* in (3.12). Under the same assumptions as in Theorem 3.2, then $\Gamma(q_{MC}^*)$ also satisfies both (\mathcal{P}_{size}) and $(\mathcal{P}_{consist.})$.*

4. Permutation tests of independence.

4.1. *The permutation approach and its known nonasymptotic properties.* Consider a random permutation Π_n , uniformly distributed on the set \mathfrak{S}_n of permutations of $\{1, \dots, n\}$, and independent of \mathbb{X}_n . Then a permuted sample from \mathbb{X}_n is defined by $\mathbb{X}_n^{\Pi_n} = (X_1^{\Pi_n}, \dots, X_n^{\Pi_n})$ with $X_i^{\Pi_n} = (X_i^1, X_{\Pi_n(i)}^2)$. In the same formalism as for the bootstrap approach, for $n \geq 2$ and η in $(0, 1)$, let $q_{\eta,n}^*(\mathbb{X}_n)$ denote the η -quantile of $\mathcal{L}(\sqrt{n}U_n, P_n^*|\mathbb{X}_n)$, where P_n^* stands for the conditional distribution of $\mathbb{X}_n^{\Pi_n}$ given \mathbb{X}_n . The family of permutation tests is then defined by $\Gamma(q^*)$ [see (3.10)], with

$$(4.1) \quad q^* = (q_{1-\alpha,n}^*(\mathbb{X}_n), q_{\alpha,n}^*(\mathbb{X}_n))_{n \geq 2}.$$

As for the bootstrap approach, in practice, the sequence of quantiles q^* is approximated by a Monte Carlo method. So, let $(B_n)_{n \geq 2}$ be a sequence of numbers of Monte Carlo iterations, such that $B_n \xrightarrow{n \rightarrow +\infty} +\infty$. For $n \geq 1$, let $(\Pi_n^1, \dots, \Pi_n^{B_n})$ be a sample of B_n i.i.d. random permutations uniformly distributed on \mathfrak{S}_n . Set $(U^{*1}, \dots, U^{*B_n}) = (U_n(\mathbb{X}_n^{\Pi_n^1}), \dots, U_n(\mathbb{X}_n^{\Pi_n^{B_n}}))$ and $U^{*B_n+1} = U_n(\mathbb{X}_n)$, the U -statistic computed on the original sample \mathbb{X}_n . The order statistic associated with $(U^{*1}, \dots, U^{*B_n+1})$ is denoted as usual by $(U^{*(1)}, \dots, U^{*(B_n+1)})$. The considered family of Monte Carlo permutation tests is then defined from (3.10) by $\Gamma(q_{MC}^*)$, with

$$(4.2) \quad q_{MC}^* = (\sqrt{n}U^{*(\lceil(1-\alpha)(B_n+1)\rceil)}, \sqrt{n}U^{*(\lfloor\alpha(B_n+1)\rfloor+1)})_{n \geq 2}.$$

The main advantage of the above families of permutation tests is that any test $\Delta_{\alpha,n}$ from either $\Gamma(q^*)$ or $\Gamma(q_{MC}^*)$ is exactly of the desired level α , that is,

$$(4.3) \quad \text{if } P = P^1 \otimes P^2, \quad \mathbb{P}(\Delta_{\alpha,n}(\mathbb{X}_n) = 1) \leq \alpha.$$

Such nonasymptotic results for the permutation tests are well known (see, e.g., [63], Lemma 1 and [52]). Though similar results are since recently available for bootstrap tests in other settings [6, 7, 20, 25], there is no known exact counterpart for the bootstrap in the present context.

4.2. *Consistency of the permutation approach.* In this section, we focus on the *Linear case* where h is of the form h_φ for some integrable function φ , as defined in (2.6). Indeed, it is the most general case for which we are able to prove a combinatorial central limit theorem under any alternative as well as under the null hypothesis (Theorem 4.1). Hence in this section, U_n refers to U_{n,h_φ} . Notice that the centering assumption $(\mathcal{A}_{\text{Cent}})$ is then always satisfied by $U_n(\mathbb{X}_n)$. We here only need the following moment assumption:

$$(\mathcal{A}_{\varphi,\text{Mmt}}) \quad \left\{ \begin{array}{l} \text{For } (X^1, X^2) \text{ with distribution } P \text{ or } P^1 \otimes P^2 \text{ on } \mathcal{X}^2, \\ \mathbb{E}[\varphi^4(X^1, X^2)] < \infty. \end{array} \right.$$

Though we have no exact counterpart of Theorem 3.1 for our permutation approach, the following result combined with Proposition 3.5 gives a similar result.

THEOREM 4.1. *For all $n \geq 2$, let P_n^* be the conditional distribution of a permuted sample given \mathbb{X}_n . In the Linear case where the kernel h is of the form (2.6) for an integrable function φ , under $(\mathcal{A}_{\text{nondeg}})$ and $(\mathcal{A}_{\varphi,\text{Mmt}})$, with the notation of Section 3,*

$$(4.4) \quad d_2(\mathcal{L}(\sqrt{n}U_n, P_n^*|\mathbb{X}_n), \mathcal{N}(0, \sigma_{P^1 \otimes P^2}^2)) \xrightarrow[n \rightarrow +\infty]{\mathbb{P}} 0,$$

where $\xrightarrow{\mathbb{P}}$ stands for the usual convergence in \mathbb{P} -probability.

COMMENTS. As pointed out above, unlike the bootstrap approach, the conditional permutation distribution of the test statistic is not here directly compared to the initial distribution of the test statistic under the null hypothesis. It is in fact compared to the Gaussian limit distribution of the test statistic under the null hypothesis, when the nondegeneracy assumption $(\mathcal{A}_{\text{nondeg}})$ holds. Moreover, the convergence occurs here in probability and not almost surely, but note that no continuity assumption for the kernel h_φ is used anymore. The price to pay is that the moment assumption is stronger than the one used for the bootstrap. This assumption, due to our choice to use an existing central limit theorem for martingale difference arrays in the proof, is probably merely technical and maybe dispensable. Indeed, the result of Theorem 4.1 is close to asymptotic results for permutation known as

combinatorial central limit theorems [36, 52], where this kind of higher moment assumption can be replaced by some Lindeberg conditions [31, 33, 47]. However, all these existing results can only be applied directly in our case either when $(X_i)_i$ is deterministic or under the null hypothesis. To our knowledge, no combinatorial central limit theorem has been proved for nondeterministic and nonexchangeable variables, like here under any alternative.

The above result is thus one of the newest results presented here and its scope is well beyond the only generalization to the point processes setting. Indeed, because it holds not only under (H_0) but also under (H_1) , it goes further than any existing one for independence test statistics such as the ones of Romano [62]. The behavior under (H_1) of the permuted test statistic of van der Vaart and Wellner was also left as an open question in [70].

The proof is presented in the supplementary material [2].

From Theorem 4.1, we deduce the following corollary.

COROLLARY 4.1. *Under the assumptions of Theorem 4.1 and with the notation of Proposition 3.5, for η in $(0, 1)$,*

$$q_{\eta,n}^*(\mathbb{X}_n) \xrightarrow[n \rightarrow +\infty]{\mathbb{P}} \Phi_{0,\sigma_{p^1 \otimes p^2}}^{-1}(\eta).$$

4.3. Asymptotic properties of the permutation tests. As for the bootstrap tests, we obtain the following result.

THEOREM 4.2. *Let $\Gamma(q^*)$ and $\Gamma(q_{MC}^*)$ be the families of permutation and Monte Carlo permutation tests defined by (3.10) combined with (4.1) and (4.2), respectively. In the Linear case, if $(\mathcal{A}_{\text{nondeg}})$ and $(\mathcal{A}_{\varphi, \text{Mmt}})$ hold, then $\Gamma(q^*)$ and $\Gamma(q_{MC}^*)$ both satisfy $(\mathcal{P}_{\text{size}})$ and $(\mathcal{P}_{\text{consist.}})$.*

5. Simulation study. In this section, we study our testing procedures from a practical point of view, by giving estimations of the size and the power for various underlying distributions that are coherent with real neuronal data. This allows to verify the usability of these new methods in practice, and to compare them with existing classical methods. A real data sets study and a more operational and complete method for neuroscientists derived from the present ones is the subject of [1]. The programs have been optimized, parallelized in C++ and interfaced with R. The code is available at <https://github.com/ybouret/neuro-stat>.

5.1. Presentation of the study. All along the study, h is taken equal to $h_{\varphi_\delta^{\text{coinc}}}$ [see (2.5)], where $\varphi_\delta^{\text{coinc}}$ is defined in (2.1) and $\alpha = 0.05$. We only present the results for upper-tailed tests, but an analogous study has been performed for lower-tailed tests with similar results. Five different testing procedures are compared.

5.1.1. *Testing procedures.*

(CLT) Test based on the central limit theorem for U -statistics (see Proposition 3.5) which rejects (H_0) when the test statistic S_n in (3.8) is larger than the $(1 - \alpha)$ -quantile of the standard normal distribution.

(B) Monte Carlo bootstrap upper-tailed test of $\Gamma(q_{MC}^*)$ [(3.10) and (3.12)].

(P) Monte Carlo permutation upper-tailed test of $\Gamma(q_{MC}^*)$ [(3.10) and (4.2)].

(GA) Upper-tailed tests introduced in [69], Definition 3, under the notation $\Delta_{GAUE}^+(\alpha)$, based on a Gaussian approximation of the total number of coincidences.

(TS) Trial-shuffling test based on a Monte Carlo approximation of the p -value introduced in [53], equation (3), but adapted to the present notion of coincidences. This test is the reference distribution-free method for neuroscientists. More precisely, let $C(\mathbb{X}_n) = \sum_{i=1}^n \varphi_\delta^{\text{coinc}}(X_i^1, X_i^2)$ be the total number of coincidences of \mathbb{X}_n . The trial-shuffling method consists in uniformly drawing with replacement n i.i.d. pairs of indices $\{(i^*(k), j^*(k))\}_{1 \leq k \leq n}$ in $\{(i, j), 1 \leq i \neq j \leq n\}$, and considering the associated TS -sample $\mathbb{X}_n^{TS} = ((X_{i^*(k)}^1, X_{j^*(k)}^2))_{1 \leq k \leq n}$. The Monte Carlo p -value is defined by $\alpha_B^{TS} = \frac{1}{B} \sum_{b=1}^B \mathbb{1}_{C(\mathbb{X}_n^{TS,b}) \geq C(\mathbb{X}_n)}$, where $\mathbb{X}_n^{TS,1}, \dots, \mathbb{X}_n^{TS,B}$ are B independent TS -samples, and the test rejects (H_0) if $\alpha_B^{TS} \leq \alpha$. This procedure is therefore close in spirit to our bootstrap procedure except that it is applied on a noncentered quantity under (H_0) , namely $C(\mathbb{X}_n)$.

The number B of steps in the Monte Carlo methods is taken equal to 10,000.

5.1.2. *Simulated data.* Various types of point processes are simulated here to check the distribution-free character of our approaches and to investigate their limits. Of course, each of the considered point processes satisfies the moment assumptions on the number of points so that the theorems in this article can be applied. From now on and to be coherent with the neuroscience application which originally motivated this work, the point processes are simulated on $[0, 0.1]$. Indeed the following experiments have been done to match neurophysiological parameters [28, 69] and the classical necessary window for detection is usually.

Estimation of the size. The three data sets simulated under (H_0) consist of i.i.d. samples of pairs of independent point processes. For simplicity, both processes have the same distribution, though this is not required.

Exp. A. Homogeneous Poisson processes on $[0, 0.1]$ with intensity $\lambda = 60$.

Exp. B. Inhomogeneous Poisson processes with intensity $f_\lambda : t \in [0, 0.1] \mapsto \lambda t$ and $\lambda = 60$.

Exp. C. Hawkes processes as detailed in [69], that is, point processes with conditional intensity $\lambda(t) = \max(0, \mu - \int_0^t \nu \mathbb{1}_{[0,r]}(t-s) dN_X(s))$, for t in $[0, 0.1]$, with spontaneous intensity $\mu = 60$, refractory period $r = 0.001$, and $\nu > \mu$ such

that for all point T in X and t in $]T, T + r]$, $\lambda(t) = 0$. This choice of ν prevents two points to occur at a distance less than the refractory period r to reflect typical neuronal behavior. This model is also sometimes called Poisson process with dead time.

Study of the power. The three data sets simulated under (H_1) are such that the number of coincidences is larger than expected under (H_0) . The models (injection or Hawkes) are classical in neuroscience and already used in [29, 69].

Exp. D. Homogeneous injection model. $X^1 = X_{\text{ind}}^1 \cup X_{\text{com}}$ and $X^2 = X_{\text{ind}}^2 \cup X_{\text{com}}$, X_{ind}^1 and X_{ind}^2 being two independent homogeneous Poisson processes with intensity $\lambda_{\text{ind}} = 54$, X_{com} being a common homogeneous Poisson process with intensity $\lambda_{\text{com}} = 6$, independent of X_{ind}^1 and X_{ind}^2 .

Exp. E. Inhomogeneous injection model. Similar to *Exp. D*, X_{ind}^1 and X_{ind}^2 being two independent inhomogeneous Poisson processes with intensity $f_{\lambda_{\text{ind}}}$ (see *Exp. B*), $\lambda_{\text{ind}} = 54$, X_{com} being a homogeneous Poisson process with intensity $\lambda_{\text{com}} = 6$, independent of X_{ind}^1 and X_{ind}^2 .

Exp. F. Dependent bivariate Hawkes processes. The coordinates X^1 and X^2 of a same pair respectively have the conditional intensities

$$\lambda^1(t) = \max \left\{ 0, \mu - \int_0^t \nu \mathbb{1}_{]0,r]}(t-s) dN_{X^1}(s) + \int_0^t \eta \mathbb{1}_{]0,u]}(t-s) dN_{X^2}(s) \right\},$$

$$\lambda^2(t) = \max \left\{ 0, \mu - \int_0^t \nu \mathbb{1}_{]0,r]}(t-s) dN_{X^2}(s) + \int_0^t \eta \mathbb{1}_{]0,u]}(t-s) dN_{X^1}(s) \right\},$$

with the spontaneous intensity $\mu = 54$, the interaction intensity $\eta = 6$ in the period designated by $u = 0.005$ and the refractory period designated by $r = 0.001$ with $\nu \gg \mu + \eta u$ such that once again, $\lambda^j(t)$ is null on each $]T, T + r]$, for T in X^j . We arbitrarily took $\nu = 50(2\mu + \eta)$.

5.2. Results.

Varying number of trials n. In Figure 1, the delay is fixed at $\delta = 0.01$ and the number n of trials varies in $\{10, 20, 50, 100\}$. Note that when the number of trials is too small ($n = 10$), the estimated variance in (CLT) is sometimes negative, therefore, the test cannot be implemented.

The left-hand side of Figure 1 corresponds to estimated sizes. On the one hand, one can see in the case of homogeneous Poisson processes (*Exp. A*) and in the case of refractory Hawkes processes (*Exp. C*) that the methods (CLT), (B), (P) and (GA) are quite equivalent, but the size (first kind error rate) seems less controlled in the bootstrap approach (B) especially for small numbers of trials. Yet, one can see the convergence of the size of the bootstrap test towards α as the number of trials goes to infinity, which illustrates Proposition 3.6. Note that the (CLT) test

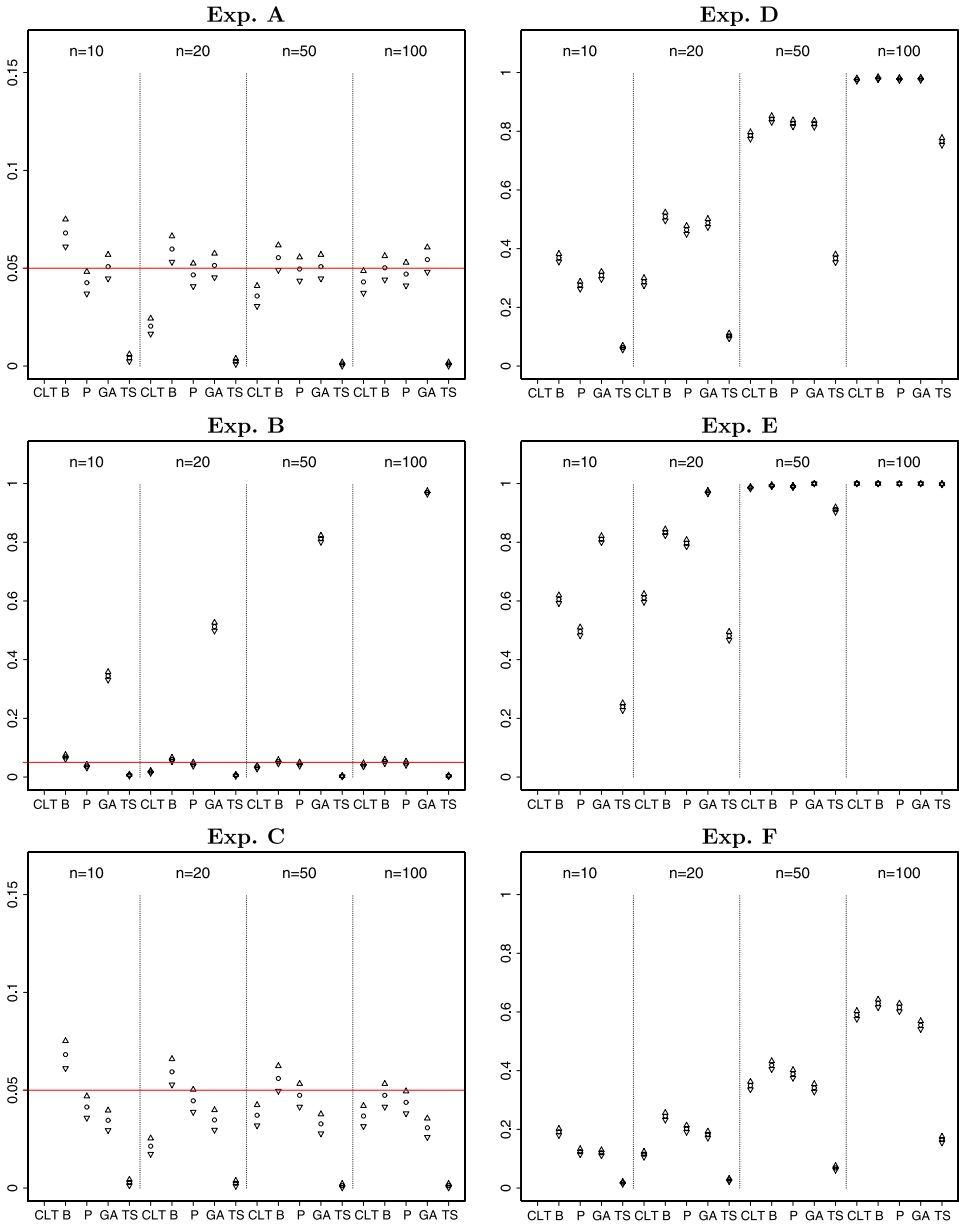


FIG. 1. Estimated sizes and powers for various numbers of trials n , all the tests being performed with a level $\alpha = 0.05$. The circles represent the percentage of rejection on 5000 simulations for each method, the triangles represent the corresponding endpoints of a 95% confidence interval. The corresponding experiments are described in Section 5.1.2.

also has a well controlled size even if it cannot be used for very small n . On the other hand, in the case of inhomogeneous Poisson processes (Exp. B), one can

see that the (GA) test has a huge size and is thus inadequate here. Indeed, it is based on the strong assumption that the data are homogeneous Poisson processes though they are in fact strongly nonstationary. The test tends thus to reject the independence null hypothesis even when the data are independent. Finally, in the three considered cases, the (TS) approach has a very small size, and is thus too conservative as one can see in the power study. The study of [1] shows that this lack of performance is due to the fact that the (TS) approach is applied here on a not correctly centered quantity.

The right-hand side of Figure 1 corresponds to estimated powers, which increase as n grows. This is in line with the consistency of the tests. Now, as it could be expected when looking at its estimated sizes, for the (TS) approach, the estimated powers are distinctly lower than the ones for the other methods, which confirms its conservative behavior. The other approaches are more similar in *Exp. D* or *Exp. F* though (B) clearly seems to outperform all tests, but at the price of a less controlled size. Note that in the inhomogeneous case (*Exp. E*), (GA) seems to have the best power, but this time, at the price of a totally uncontrolled size.

This part of the simulation study illustrates the convergences of the size and the power of the bootstrap and permutation tests introduced here. The permutation approach seems to actually guarantee the best control of the size as expected, as compared with the bootstrap approach. Nevertheless, both approaches are quite effective for any considered kind of point processes and any sample size, unlike the (GA) test which has very restrictive assumptions. The reference method (TS) for neuroscientists is clearly too conservative. Moreover, the (CLT) test seems to have also satisfying results, but with a slower convergence than the (B) and (P) tests. This seems to illustrate that the conditional bootstrap and permutation distributions give better approximations of the original one under independence than a simple central limit theorem. This phenomenon is well known as the second-order accuracy of the bootstrap in more classical frameworks.

Varying delay δ . We now investigate the impact of the choice for the delay δ by making δ vary in $\{0.001, 0.005, 0.01, 0.02\}$ for a fixed number of trials $n = 50$. The results for the sizes being similar to the previous study, only the estimated powers are presented in Figure 2.

On the top row of Figure 2, the same process is injected in both coordinates: the coincidences are exact in the sense that they have no delay. Therefore, the best choice for the delay parameter δ is the smallest possible value: the obtained power is 1 for very small δ 's (e.g., $\delta = 0.001$) and then decreases as δ increases. On the contrary on the bottom row, it can be noticed that the highest power is for $\delta = 0.005$ which is the exact length of the interaction period u . Once again, the (TS) method performs poorly, as does the (CLT) method. The three other methods seem to be quite equivalent except in the inhomogeneous case (*Exp. E*) where the (GA) method has a power always equal to 1, but at the price of an uncontrolled size.

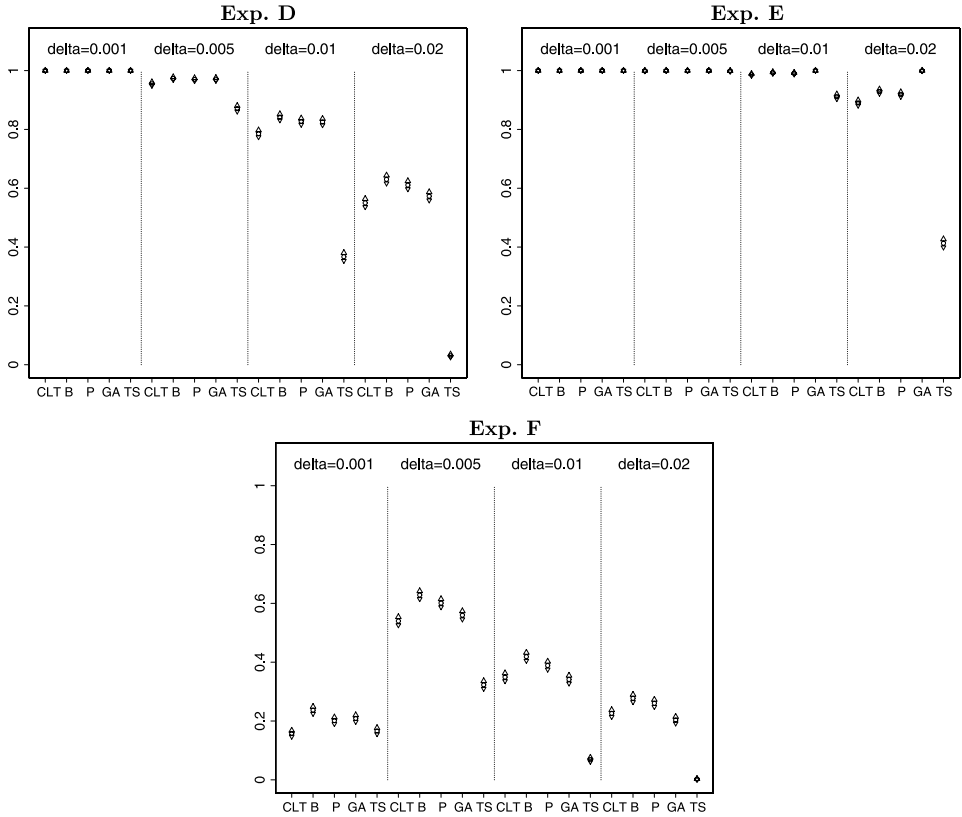


FIG. 2. Estimated powers for different δ . Same convention as in Figure 1.

6. Conclusion. In the present paper, we have introduced nonparametric independence tests between point processes based on U -statistics. The proposed critical values are obtained either by bootstrap or permutation approaches. We have shown that both methods share the same asymptotic properties under the null hypothesis as well as under the alternative. From a theoretical point of view, the main asymptotic results (Theorems 3.1 and 4.1) have almost the same flavor. However, there are additional assumptions in the permutation case which make the bootstrap results more general (despite the additional continuity assumption, which is very mild). From a more concrete point of view, it is acknowledged (see, e.g., [22]) that permutation should be preferred because of its very general nonasymptotic properties (4.3). This is confirmed by the experimental study, where clearly permutation leads to a better first kind error rate control. However, both approaches perform much better than a naive procedure, based on a basic application of a central limit theorem, when the number of observation is small. They also outperform existing procedures of the neuroscience literature, namely [69], which assumes the point processes to be homogeneous Poisson processes and the trial-shuffling procedures [53, 54], which are biased bootstrap variants applied on a noncentered quantity.

One of the main open questions with respect to the existing literature is whether our results can be extended to test statistics as $\sup_h U_{n,h}$. A first obstacle to this question lies in the nature of the observed random variables (point processes) and the fact that controlling such a supremum leads to controlling the whole U -process. This difficulty can probably be overcome, since the asymptotic Gaussian behavior of similar statistics has already been proved in general spaces under (H_0) for product type kernels (see [12]). The study of such behavior under (H_1) is surely much more complex. A second obstacle comes from a more practical aspect. In neuroscience, and in the particular case of coincidence count, the use of $\sup_\delta U_{n,h}^{\text{coinc}}_{\phi_\delta}$ leads to the following fundamental problems. On the one hand, such a statistic may not be computable if δ varies in a too large space, typically $[0, 1]$. On the other (more important) hand, neuroscientists are especially interested in the value of δ which leads to a rejection, since it actually provides the delay of interaction (see also Section 5). In this respect, our work in [1] involves multiple testing aspects, which may answer this issue.

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SUPPLEMENTARY MATERIAL

Technical results and proofs of “Bootstrap and permutation tests of independence for point processes” (DOI: [10.1214/15-AOS1351SUPP](https://doi.org/10.1214/15-AOS1351SUPP); .pdf). This Supplement consists of all the proofs. It also contains some additional results about nondegeneracy and the empirical centering assumption.

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