Detection of dependence patterns with delay

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Biological context

- **Neural network:** Interacting cells.
- **Information transport via electric pulses:** action potentials.
Biological context

- Neural network: Interacting cells.
- Information transport via electric pulses: action potentials.

After preprocessing, we dispose of $M$ trials of simultaneously recorded spike trains.
- The synchronization phenomenon can occur during sensory-motor tasks.
- The repetition of a given task may give birth to neuronal assemblies.

**Goal**

Detection of synchronizations.
Statistical analysis

- Cross-correlogram (Perkel et al., '67).
- Peristimulus time histogram (PSTH, (Aertsen et al., '89)).
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- Unitary events (Grün, '96).
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**UE method**
- Unitary event: spike synchrony that recurs more often than expected.
- The test statistic is based on the *number of coincidences*.
  - Introduced in the PhD thesis of S. Grün ('96).
  - Applied to time discrete data.
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**GAUE method for two neurons (Tuleau-Malot et al., 2014)**

- Notion of coincidence transposed to the continuous time framework.
- Independence test between Poisson processes based on this new notion.
Notion of delayed coincidences

- $N_1, \ldots, N_n$ are point processes on $[a, b]$.
- $\mathcal{I} \subset \{1, \ldots, n\}$ is a set of indices.
Notion of delayed coincidences

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**Definition**

The *delayed coincidence count* of delay $\delta < (b - a)/2$ is

$$X_J := \int_{[a,b]^J} 1_{\max_{i \in \{1, \ldots, J\}} x_i - \min_{i \in \{1, \ldots, J\}} x_i \leq \delta} N_{i_1}(dx_1) \ldots N_{i_J}(dx_J).$$

Neuron 1
Neuron 2
Neuron 3

\[ a \quad \quad b \]
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**Diagram**

- Neuron 1
- Neuron 2
- Neuron 3

a b
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**Definition**

The general coincidence count is

$$X_{\mathcal{J}} := \int_{[a,b]^J} c(x_1, \ldots, x_J) \ N_{i_1}(dx_1) \cdots N_{i_J}(dx_J).$$
Notion of delayed coincidences

- $N_1, \ldots, N_n$ are point processes on $[a, b]$.
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**Definition**

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**Goal:** Test $\mathcal{H}_0$ against $\mathcal{H}_1$

$$\begin{cases} 
\mathcal{H}_0 : \text{ The processes } N_j, j \in \mathcal{J} \text{ are independent;} \\
\mathcal{H}_1 : \text{ The processes } N_j, j \in \mathcal{J} \text{ are not independent.}
\end{cases}$$
Asymptotic properties

Let $(N_1^{(k)}, \ldots, N_n^{(k)})_{1 \leq k \leq M}$ denote a $M$-sample. We compare two estimates.

- CLT $\Rightarrow \sqrt{M} \frac{\bar{m} - \mathbb{E}[X_{\mathcal{J}}]}{\sqrt{\text{Var}(X_{\mathcal{J}})}} \xrightarrow{M \to \infty} \mathcal{N}(0,1)$, where $\bar{m} = \frac{1}{M} \sum_{k=1}^{M} X_{\mathcal{J}}^{(k)}$. 
Asymptotic properties

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- CLT \(\Rightarrow \sqrt{M} \frac{\bar{m} - \mathbb{E}[X_J]}{\sqrt{\text{Var}(X_J)}} \xrightarrow{M \to \infty} N(0, 1)\), where \(\bar{m} = \frac{1}{M} \sum_{k=1}^{M} X_J^{(k)}\).

- If \(N_1, \ldots, N_n\) are Poisson processes with intensities \(\lambda_1, \ldots, \lambda_n\), then
  \[
  \begin{cases}
  \mathbb{E}[X_J] = m_0((\lambda_i)_i) \\
  \text{Var}(X_J) = \nu_0((\lambda_i)_i)
  \end{cases}
  \text{ under } \mathcal{H}_0.
  \]

- Let us denote
  \[
  \hat{\lambda}_i := \frac{1}{M} \sum_{k=1}^{M} \frac{N_i^{(k)}([a, b])}{b - a}
  \quad \text{and} \quad
  \begin{cases}
  \hat{m}_0 = m_0((\hat{\lambda}_i)_i) \\
  \hat{\nu}_0 = \nu_0((\hat{\lambda}_i)_i).
  \end{cases}
  \]

- Plug-in step (delta method + Slutsky) \(\Rightarrow \sqrt{M} \frac{\bar{m} - \hat{m}_0}{\hat{s}^2} \xrightarrow{M \to \infty, \mathcal{H}_0} N(0, 1)\) where
  \[
  \hat{s}^2 = \hat{\nu}_0 - (b - a)^{-1} \hat{m}_0^2 \left( \sum_{j \in J} \hat{\lambda}_j^{-1} \right).
  \]
Definition

Denote \( z_\alpha \) the \( \alpha \)-quantile of the standard Gaussian distribution. Then the symmetric test \( \Delta_\alpha \) rejects \( H_0 \) when \( \bar{m} \) and \( \hat{m}_0 \) are too different, that is when

\[
\left| \sqrt{M} \frac{(\bar{m} - \hat{m}_0)}{\sqrt{\hat{\sigma}^2}} \right| > z_{1-\alpha/2}.
\]

Theorem

If \( N_1, \ldots, N_n \) are homogeneous Poisson processes, the test \( \Delta_\alpha \) is of asymptotic level \( \alpha \).
Simulation procedure

1. Generate a set of random parameters \((b - a, (\lambda_i)_i)\) according to the appropriate Framework;
2. Use this set (and \(\delta = 10\text{ms}\)) to generate \(M\) trials;
3. Compute the different statistics;
4. Repeat steps 1 to 3 a thousand times.
- $n = 4$ neurons. $I = \{1, 2, 3, 4\}$;
- $b - a \sim \mathcal{U}([0.2, 0.4])$;
- Independent intensities. $\lambda_i \sim \mathcal{U}([8, 20\text{Hz}])$;
- $M = 50$ (Figure C).
Add an injection process $\tilde{N}$. Intensity: 0.3Hz.

$\alpha = 0.05$.

$M = 50$ (Figure B).
Hawkes processes ('71)

- More realistic than Poisson processes (Goodness of fit tests, Reynaud-Bouret et al., '14).
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- Form of the intensity:

\[
\lambda_t^j = \max \left(0, \mu_j + \sum_{i=1}^{n} \int_{s<t} h_{ij}(t-s) N^j_i(ds) \right).
\]

- Spontaneous rate \( \mu_j \geq 0 \).

- Interaction function \( h_{ij} \): influence of neuron \( i \) over neuron \( j \).
  - Either excitatory or inhibitory phenomena.
  - Strict refractory period. \( (h_{ii} \ll 0) \)
- $n = 4$ neurons. $\mathcal{J} = \{1, 2, 3, 4\}$;
- $b - a \sim \mathcal{U}([0.2, 0.4])$;
- Independent spontaneous intensities. $\mu_i \sim \mathcal{U}([8, 20\text{Hz}])$;
- Auto-interaction functions $h_{ii}$ to model refractory period of 3ms.
- $M = 50$ (Figure C).
Add interaction functions according to the graph. Range: 5ms.

- $\alpha = 0.05$.
- $M = 50$ (Figure B).
Simulations

Rate of dependence detection
Overview

- Independence test over any subset of \( n \) neurons.
- Multiple testing over the subsets.
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- Independence test over any subset of $n$ neurons.
- Multiple testing over the subsets.

Outlook:
- Find the asymptotic for Hawkes processes.
- R package.