

Detecting pairwise correlations in spike trains: an objective comparison of methods and application to the study of retinal waves

Mathematical details

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1 Correlation index is confounded by firing rate

In this section we derive Equation 2 from the paper which is used to show that the correlation index is confounded by firing rate. To make this document self-contained we reproduce the formula for the correlation index $i_{A,B}$ between spike trains A and B. Here, the vectors \mathbf{a} and \mathbf{b} represent the spike times of neurons A and B; a_i is the i th spike in train A and b_j is the j th spike in train B.

$$i_{A,B} = \frac{N_{A,B}T}{N_A N_B 2\Delta t} \quad (1)$$

where

$$N_A = |\mathbf{a}| \text{ (total number of spikes of A in recording),}$$

$$N_B = |\mathbf{b}|,$$

$$T = \text{length of recording,}$$

$$\Delta t = \text{synchronicity window,}$$

and $N_{A,B}$ is the number of spike pairs where a spike from train A falls within $\pm\Delta t$ of a spike from train B:

$$N_{A,B} = \sum_{i=1}^{N_A} \sum_{j=1}^{N_B} \mathbb{1}_{\Delta t}(|a_i - b_j|)$$

where

$$\mathbb{1}_{\Delta t}(x) = \begin{cases} 1 & \text{if } x \leq \Delta t \\ 0 & \text{otherwise} \end{cases}$$

No one statistical model is able to recreate the full range of observed spiking patterns, so a general proof that the correlation index is dependent on firing rate is not possible. Instead we assume a simple model for firing times and use this as a counter example to the statement “the correlation index is in general independent of firing rate”.

The model is as follows: the spikes of neurons A and B form a Poisson process with rates λ_A, λ_B respectively. A set proportion of these spikes occur in both trains (i.e. each train fires a spike synchronously with the other), these occur with rate $\lambda_S \leq \lambda_A, \lambda_B$. We derive an expression for the correlation index under this model and show that it is dependent on firing rate.

The recording time T and synchronicity window Δt are independent parameters (i.e. they cannot be evaluated in terms of firing rates). The expected values of N_A and N_B are as follows:

$$N_A = \lambda_A T$$

$$N_B = \lambda_B T$$

The calculation of the remaining term, $N_{A,B}$, is non-trivial. We use the following results for Poisson processes (Kingman, 1992):

- **Superposition:** If X and Y are two independent Poisson processes with respective rates λ_X and λ_Y then X+Y is a Poisson process with rate $\lambda_X + \lambda_Y$.
- **Decomposition:** To decompose this composite process into two processes with identical statistics to X and Y (i.e. two Poisson processes with rates λ_X and λ_Y), it suffices to generate a series of Poisson events with rate $\lambda_X + \lambda_Y$ and assign each event as type X with probability $\frac{\lambda_x}{\lambda_x + \lambda_y}$ and as type Y with probability $\frac{\lambda_y}{\lambda_x + \lambda_y}$.

It follows from the above that the synchronous spikes in our model form a Poisson process with rate λ_S . The expected number of synchronous spikes is therefore $\lambda_S T$. This

contributes to $N_{A,B}$ since each of these is one spike pair where a spike from A falls within $\pm\Delta t$ of a spike from B. There is also a second contribution to $N_{A,B}$ from cases where spikes from different processes (i.e. any combination except A and A, and B and B) fall within $\pm\Delta t$ of each other. We denote the expected number of such spike pairs C and then:

$$N_{A,B} = \lambda_S T + C \quad (2)$$

To evaluate C we consider the system as a decomposition of a master Poisson process with rate $\lambda = \lambda_A + \lambda_B - \lambda_S$. Events are assigned as A only (A) with probability $\frac{\lambda_A - \lambda_S}{\lambda}$, B only (B) and synchronous (S) with probabilities given similarly. By considering the master process we can work out the probability of spikes from each combination of trains falling within $\pm\Delta t$ of each other by calculating the probability that *any* spikes fall within $\pm\Delta t$ of each other and then multiplying this by the probability of them being from the correct combinations.

We note that multiple spikes can occur within $\pm\Delta t$ of each other, not just pairs and so our calculations need to be recursive, that is we have to consider the case when n successive inter-spike-intervals (ISIs) sum to less than Δt and sum the contributions from all n . We also have to be careful not to double-count events: if we consider all the spike pairs formed when n inter-spike-intervals sum to less than Δt then most of those spike pairs will have been covered in the previous cases $n = 1 \dots n - 1$. The only pair not already counted is the pair formed by the first and last spikes. Therefore, for arbitrary n , the expected number of new spike pairs (C_n) is:

$$C_n = I_n(\Delta t) P_n S_n \quad (3)$$

where

$I_n(\Delta t)$ = probability that n successive ISIs sum to $\leq \Delta t$,

P_n = probability that outer two spikes are not both A or both B (can be synchronous),

S_n = number of n successive ISIs in the recording.

and

$$C = \sum_{n=1}^{\infty} C_n$$

We find each quantity in turn:

I_n(Δt): Let the *i*th ISI in the master train be Z_i . Since the master train is a Poisson process with rate λ :

$$Z_i \sim \text{Exponential}(\lambda) \quad (4)$$

and

$$\sum_{i=1}^k Z_i \sim \text{Erlang}(k, \lambda) \quad (5)$$

(Kingman, 1992) where the cumulative distribution function of the Erlang distribution is:

$$\text{ErlangC}(z; k, \lambda) = 1 - \sum_{n=0}^{k-1} \frac{1}{n!} e^{-\lambda z} (\lambda z)^n \quad (6)$$

The probability of n ISIs summing to less than Δt is then given by:

$$I_n(\Delta t) = \text{ErlangC}(\Delta t; n, \lambda) \quad (7)$$

P_n: The combinations of spikes which will contribute a spike pair to $N_{A,B}$ are as follows: AB(BA),AS(SA),BS(SB). Combinations in brackets occur with the same probability as their counterpart outside the brackets. The combination SS will contribute *two* spike pairs to $N_{A,B}$ so to account for this we multiply its probability by two (meaning that P_n is not strictly a probability). To simplify the notation we introduce the following:

$$\lambda_{A'} = \lambda_A - \lambda_S$$

$$\lambda_{B'} = \lambda_B - \lambda_S$$

and P_n is then given by:

$$P_n = \frac{2\lambda_S^2 + 2\lambda_S\lambda_{A'} + 2\lambda_S\lambda_{B'} + 2\lambda_{A'}\lambda_{B'}}{\lambda^2} \quad (8)$$

This is independent of n so we drop the subscript, $P_n = P$. This simplifies to

$$P = \frac{2\lambda_A\lambda_B}{(\lambda_A + \lambda_B - \lambda_C)^2} \quad (9)$$

S_n: The number of n successive ISIs in the recording is $\lambda T - n$ (λT is the total number of spikes in the recording).

We substitute these three terms into Equation 3 to find C_n and sum over all n to find C :

$$C = \sum_{n=1}^{\lambda T} (\lambda T - n) \text{ErlangC}(\Delta t; n, \lambda) P \quad (10)$$

for simplicity, we leave this in terms of P . Then,

$$N_{A,B} = \lambda_S T + \sum_{n=1}^{\lambda T} (\lambda T - n) \text{ErlangC}(\Delta t; n, \lambda) P \quad (11)$$

Having found $N_{A,B}$, the correlation index is:

$$i_{a,b} = \frac{\left(\lambda_S T + \sum_{n=1}^{\lambda T} (\lambda T - n) \text{ErlangC}(\Delta t; n, \lambda) P \right) T}{(\lambda_A T)(\lambda_B T) 2\Delta t} \quad (12)$$

This expression is clearly dependent on rate which is what we set out to show. We now simplify it to gain an understanding about the strength of the dependency and how it varies with rate.

We first simplify C :

$$C = \sum_{n=1}^{\lambda T} (\lambda T - n) \text{ErlangC}(\Delta t; n, \lambda) = \sum_{n=1}^{\lambda T} (\lambda T - n) \left(1 - \sum_{i=0}^{n-1} \frac{1}{i!} e^{-\lambda \Delta t} (\lambda \Delta t)^i \right) \quad (13)$$

After rearrangement involving rewriting the double sums into single sums:

$$C = \frac{\lambda T(\lambda T - 1)}{2} (1 - e^{-\lambda \Delta t}) \sum_{n=0}^{\lambda T} \frac{1}{n!} (\lambda \Delta t)^n + (\lambda^2 T \Delta t - \lambda \Delta t + \frac{\lambda^2 \Delta t^2}{2}) e^{-\lambda \Delta t} \sum_{n=0}^{\lambda T} \frac{1}{n!} (\lambda \Delta t)^n \quad (14)$$

writing

$$e^{-\lambda\Delta t} \sum_{n=0}^{\lambda T} \frac{1}{n!} (\lambda\Delta t)^n = e^{-\lambda\Delta t} \left(e^{\lambda\Delta t} - \sum_{n=\lambda T+1}^{\infty} \frac{1}{n!} (\lambda\Delta t)^n \right) \quad (15)$$

$$= 1 - e^{-\lambda\Delta t} \sum_{n=\lambda T+1}^{\infty} \frac{1}{n!} (\lambda\Delta t)^n \quad (16)$$

we assume that

$$1 - e^{-\lambda\Delta t} \sum_{n=\lambda T+1}^{\infty} \frac{1}{n!} (\lambda\Delta t)^n \approx 1 \quad (17)$$

which is true if the following hold:

- $\lambda\Delta t \leq 1$. This holds within experimentally observed ranges since λ is $O(1)$ Hz and typically $\Delta t = 0.05 - 0.1$ s.
- λT is sufficiently large. This also holds within experimentally observed ranges, for instance if $\lambda = 1$ Hz, $\Delta t = 0.1$ s and $T = 4$ s then Equation 16 is equal to 0.9999999 (7 d.p). Since T is typically $O(1000)$ s, in practice this approximation will be even more accurate.

If the above holds, then

$$C \approx \lambda^2 T \Delta t - \lambda \Delta t - \frac{\lambda^2 \Delta t^2}{2} \quad (18)$$

Using this approximation:

$$i_{AB} \approx (\lambda_S T + (\lambda^2 T \Delta t - \lambda \Delta t - \frac{\lambda^2 \Delta t^2}{2}) P) \frac{1}{\lambda_A \lambda_B T 2 \Delta t} \quad (19)$$

substituting in our expression for P and simplifying gives us the form of Equation 2 in the paper:

$$i_{A,B} = \frac{\lambda_S}{2\Delta t \lambda_A \lambda_B} + 1 - \frac{1}{(\lambda_A + \lambda_B - \lambda_S) T} - \frac{\Delta t}{2T} \quad (20)$$

In the paper we use the sub-case of auto-correlation $\lambda = \lambda_A = \lambda_B = \lambda_S$ to illustrate the dependence on firing rate. In this case:

$$i_{A,B} = \frac{1}{\lambda} \left(\frac{1}{2\Delta t} - \frac{1}{T} \right) + \left(1 - \frac{\Delta t}{2T} \right) \quad (21)$$

Both the term in $\frac{1}{\lambda}$ and the second term are positive since $\Delta t \leq 1$ (within experimentally observed ranges) and $T = O(1000)$ s. Therefore increasing λ decreases the correlation index.

2 Normalisation of the Spike Time Tiling Coefficient

In this section we justify the form of the normalisation of the Spike Time Tiling Coefficient. To make this self contained, we reproduce the formula for the Spike Time Tiling Coefficient C from Figure 1 of the paper:

$$C = \frac{1}{2} \left(\frac{P_A - T_B}{1 - P_A T_B} \right) + \frac{1}{2} \left(\frac{P_B - T_A}{1 - P_B T_A} \right)$$

where

P_A =The proportion of spikes in train A which fall within $\pm\Delta t$ of any spike in train B,

P_B =the proportion of spikes in train B which fall within $\pm\Delta t$ of any spike in train A,

T_A =the proportion of the recording time which falls within $\pm\Delta t$ of any spike in train A,

T_B =the proportion of the recording time which falls within $\pm\Delta t$ of any spike in train B.

The rationale behind this is that we would expect the proportion of spikes in A which fall within $\pm\Delta t$ of any spike in B *by chance* to be equal to the proportion of the recording time which falls within $\pm\Delta t$ of any spike from B. The quantity $P_A - T_B$ will therefore be positive/negative if this happens more/less than expected by chance which is indicative of positive/negative correlation. It does not, however, possess the following necessary qualities:

- **N1:** The measure should be symmetric i.e. $C(A, B) = C(B, A)$.
- **N4:** The measure should be bounded taking a value of +1 when the spike trains are identical, with a value of zero corresponding to no correlation and -1 corresponding to anti-correlation.

We normalise this quantity to ensure it has property N4 and then take the mean of the two directed variants to ensure it satisfies property N1 (hence the factor $\frac{1}{2}$).

For simplicity, we consider one of the directed variants and define:

$$f(P_A, T_B) = \frac{P_A - T_B}{1 - P_A T_B}$$

In order to fulfil N4, the following is needed (where $0 \leq P_A \leq 1$, $0 \leq T_B \leq 1$):

1. $f(1, T_B) = 1$. This ensures that auto-correlations always take the value +1.
2. $f(0, 1) = -1$. Ensures that the most anti-correlated patterns take value -1.
3. $f(P_A, T_B) = 0$, if $P_A = T_B$ ($P_A \neq 1, T_B \neq 1$). Ensures that uncorrelated spikes take value zero.
4. $f(P_A, T_B) > 0$ if $P_A > T_B$ and $f(P_A, T_B) < 0$ if $P_A < T_B$. Ensures that the measure is positive/negative for positive/negative correlation.

The following two properties must also hold since they are implicitly implied by the notion of a correlation measure:

5. $f(P_A, T_B)$ must be monotonically increasing in P_A for $P_A \neq 1, T_B \neq 1$.
6. $f(P_A, T_B)$ must be monotonically decreasing in T_B for $P_A \neq 1, T_B \neq 1$.

i.e. if the correlation increases, so does f , if it decreases, so does f .

Properties One, Two and Three are trivially satisfied. We note that for $P_A \neq 1, T_B \neq 1$, $1 - P_A T_B > 0$ so property Four is also satisfied. Note also:

$$\frac{\partial f}{\partial P_A} = \frac{1 - T_B^2}{(1 - P_A T_B)^2}$$

which is positive within the ranges of P_A and T_B , so f increases monotonically with P_A (property Five) and

$$\frac{\partial f}{\partial T_B} = \frac{P_A^2 - 1}{(1 - P_A T_B)^2}$$

which is negative within the ranges of P_A and T_B , so f decreases monotonically with T_B (property Six).

Therefore f satisfies all required properties and the normalisation is appropriate.

Alternative normalisations

We note that this is not the only possible normalisation of the Spike Time Tiling Coefficient. Other normalisations exist which have all the properties listed above, for instance $2 - P_A - T_B$. Using another normalisation factor which has these properties will not change whether the Spike Time Tiling Coefficient possess all the necessary and desired properties. However, the sensitivity of the measure to changes in values of P_A and T_B does change for different normalisations. This is important as it will affect how big a change in firing patterns is needed to affect a noticeable change in the Spike Time Tiling Coefficient which should be as sensitive as possible to changes within the experimentally observed ranges of P_A and T_B . The version in the paper was chosen as we found it to be sensitive to small changes in these values.

To illustrate this, we briefly compare the sensitivity of f with that of the following differently normalised Spike Time Tiling Coefficient, g :

$$g(P_A, T_B) = \frac{P_A - T_B}{2 - P_A - T_B}$$

It is important that the measure is sensitive to changes within the experimentally observed ranges of values. The values of P_A typically take all values in the range $0 - 1$, but the distribution is highly skewed towards small values and values of T_B are usually small (Figure 1). We therefore want our coefficient to be as sensitive as possible to changes within this range and since within it $f(P_A, T_B)$ is more sensitive than $g(P_A, T_B)$ (Figure 2), f is preferred.

References

- Kingman C (1992) *Poisson Processes*, Vol. 3 Clarendon Press.
- Kirkby LA, Feller MB (2013) Intrinsically photosensitive ganglion cells contribute to plasticity in retinal wave circuits. *Proc Natl Acad Sci USA* 110:12090–12095.

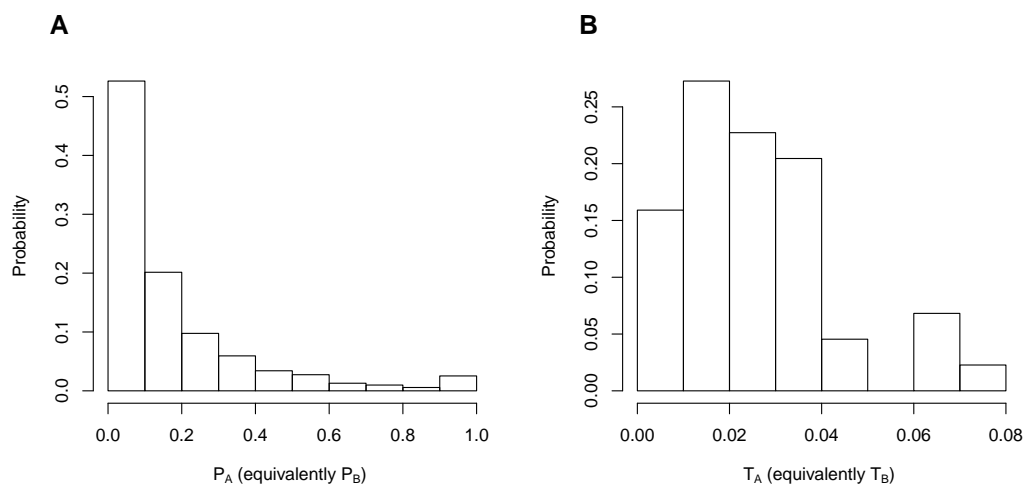


Figure 1: **Experimentally observed distributions of P_A and P_B are skewed towards low values and values of T_A and T_B are low.** A: Histogram of the values of P_A (or equivalently P_B) from a recording of spontaneous retinal activity in P5 wild type mouse from Kirkby and Feller (2013). Note the local maximum at P_A or $P_B = 1$, which are the values of the auto-correlations. B: Histogram of the values of T_A (or equivalently T_B) from the same recording. This recording has duration 998.1 s, 44 electrodes and mean firing rate 0.28 Hz. In both panels $\Delta t = 0.1$ s as in the original publication.

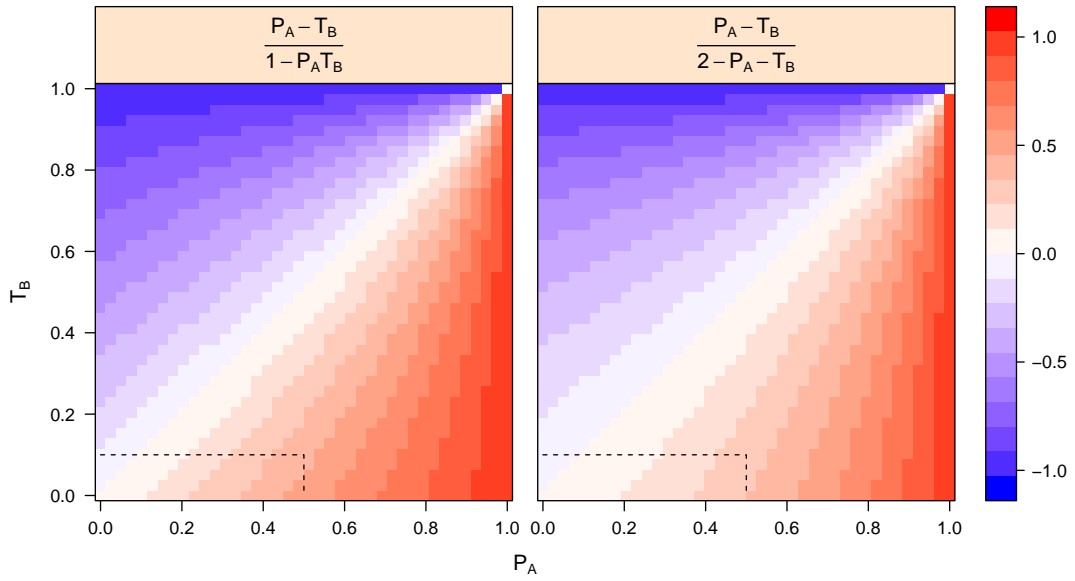


Figure 2: **The form of normalisation affects the sensitivity of the Spike Time Tiling Coefficient to changes in P_A and T_B .** A: Heatmap of f (one half of the Spike Time Tiling Coefficient with denominator $1 - P_A T_B$) for $0 \leq P_A \leq 1$, $0 \leq T_B \leq 1$. Changes in colour show changes in contours of f . The sensitivity of f (and therefore the sensitivity of the Spike Time Tiling Coefficient) to changes in the values of P_A and T_B can be seen by the widths of the contours- narrower contours show higher sensitivity. Since typically T_B is small and the distribution of P_A is skewed towards small values, the sensitivity of the Spike Time Tiling Coefficient in this region (marked with a black dotted-line) is most crucial. B: Same as A but with f replaced by g (one half of the Spike Time Tiling Coefficient with denominator $2 - P_A - T_B$).