Spike Train Distance

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Synonyms

Spike metric

Definition

A "spike train distance" is a means for comparing two sequences of stereotyped events. The term "spike metric" refers to a spike train distance that, additionally, has the formal mathematical properties of a metric. Spike train distances have broad application in neuroscience, since the action potentials emitted

by a neuron or set of neurons can be regarded as a sequence of stereotyped events; we briefly survey these applications here.

Detailed Description

Spike train distances are rules for assigning a notion of distance, or dis-similarity, to pairs of event sequences. In contrast to most quantitative approaches to the analysis of scientific data, the framework of spike train distances does not make the implicit assumption that the objects of interest (i.e., the event sequences) can be thought of as vectors. In many cases, including the earliest examples of spike train distances (van Rossum 2001, Victor & Purpura 1996, Victor & Purpura 1997), these distances also satisfy the formal mathematical requirements a "metric" (see below). In this case, the event sequences may be considered elements in a "metric space." A metric space is a topological space that is more general than a vector space. A metric space must have a notion of distance, but it need not have coordinates, nor allow for addition, scalar multiplication, or the measurement of angles.

Two considerations give this general framework a special flavor when applied to neural data. The first consideration is mathematical: for event sequences, it is natural to think of the topology as combining a discrete component with a continuous component. The discrete component is that the number of events in a spike train must be an integer; the continuous component is that each of these events can occur across a continuum of times. The second consideration is biological: much is known about the physiology of neurons and neural circuits, and spike train distances are typically designed with the goal of capturing the biologically significant aspects of neuronal activity.

As detailed below, two contrasting ideas concerning the biological meaning of a spike train serve as anchor points: (a) the firing events in a spike train might serve primarily as a means to represent an underlying firing rate vs. (b) the times of these firing events might have individual significance, enabling neural computations to be based on coincident firing events across neurons and other aspects of fine temporal structure.

Notation

A spike train – the sequence of action potentials emitted by one or more neurons – is formalized as a sequence of stereotyped events, called spikes, that occur during a fixed observation period $[0, T]$. That is, a spike train A is represented by an ascending sequence of real numbers $t_1^A, \ldots, t_{M(A)}^A$ in $[0, T]$, where t_j^A (or simply t_j) is the time of occurrence of the j th spike, and $M(A)$ is the total number of spikes (which may be 0).

The above applies to a setting in which all spikes originate from a single neuron, or in which the identity of the neurons that generate the individual spikes is not distinguished. It is readily extended to a setting in which the neural activity arises from R different neurons, and the neuron of origin of each event is known: the sequence of times $t_1, \ldots, t_{M(A)}$ is associated with a sequence of labels $a_1, \ldots, a_{M(A)}$, each drawn from a set of tags $\{1, \ldots, R\}$. Thus, spike trains are regarded as a sample drawn from a **point process** (activity of one neuron) or a **labeled point process** (activity of several neurons).

Formal Definition

A spike train distance is a mapping D from the set of spike trains to the non-negative real numbers that meets the three requirements of a topological **metric**:

$$\text{Non-negativity: } D(A,B) \geq 0 \text{, and } D(A,B) = 0 \text{ only if } A = B \qquad (1)$$

$$\text{Symmetry: } D(A,B) = D(B,A) \qquad (2)$$

$$\text{Triangle inequality: } D(A,C) \leq D(A,B) + D(B,C) \qquad (3)$$

The symmetry property (Eq. (2)) and the triangle inequality (Eq. (3)) are critical to give the metric the properties that one expects from a distance based on paths between points. Specifically, the symmetry property means that the shortest path between two points does not depend on the direction of travel, and the triangle inequality means that the shortest path between two points (A and C) cannot be any longer than a path that is constrained to stop at a particular intermediate point B. However, the non-negativity property (Eq. (1)) is less crucial, and is frequently relaxed to omit the "only if" clause – in which case, D is formally a **pseudometric**. In this case, the space of spike trains can be partitioned into equivalence classes of spike trains that are at distances of zero from each other, and D acts as a metric on these equivalence classes. The "spike count distance," formalized following Eq. (11), is a simple example of a pseudometric; spike trains with the same number of spikes fall into an equivalence class.

Constructing Spike Train Distances

Spike train distances can be organized into several families. The most straightforward family is based on embedding: spike train distances are defined by mapping the spike trains into a vector space, and then adopting the vector space distance. Since the vector space distance is a metric, the resulting spike train distance is also guaranteed to be a metric.

However, spike train distances need not be derived from distances in vector spaces. In cost-based distances, a set of simple transformations of spike trains is specified, along with their (non-negative) costs. The spike train distance is then defined as the minimal total cost of transforming one spike train into another. Because the distance is defined in terms of a minimum-cost path of transformations, these distances are guaranteed to be metrics. Other families of distances include time-resolved and timescale-independent spike train distances, described below; many of these are not metrics.

Spike Train Distances Based on Embedding

In the embedding construction, spike trains are first mapped into a **normed vector space** V via a mapping f. Since the vector space norm $\|u\|$ provides a metric on vectors via $D(u,v) = \|u - v\|$, mapping spike trains into vectors yields a metric on the spike trains:

$$D(A,B) = \|f(A) - f(B)\| \qquad (4)$$

The nature of the mapping f from the space of spike trains to the vector space is critical. Typically, this mapping respects an additive structure on the spike trains: that is, if $A + B$ denotes the spike train that results from superimposing A and B (with suitable provision made for coincident spikes), then $f(A+B) = f(A) + f(B)$. For such embeddings, then resulting metric is unchanged by parallel translation:

$$D(A + C, B + C) = D(A, B) \tag{5}$$

Spike train distances in this class generally emphasize either the continuous aspect of spike train topology or its discrete aspect. The family of distances introduced by van Rossum (van Rossum 2001) is a prototypical example of the former. We consider first the case of an unlabeled spike train, which here is regarded as a sequence of delta functions. The target vector space consists of scalar functions of time (considered as a continuous variable), and the embedding f consists of a convolution by a kernel function $K(t)$:

$$f(A)(t) = \int_{-\infty}^{\infty} K(t - \tau) \sum_{j=1}^{M(A)} \delta(\tau - t_j^A) d\tau \tag{6}$$

Since the mapping in Eq. (6) from the spike train A to the vector space element $f(A)$ is linear, it follows that the resulting metric, defined by Eq. (4), is unchanged by parallel translation (as in Eq. (5)).

Typically the kernel function K in Eq. (6) includes a parameter that expresses the temporal resolution of the comparison between two spike trains, e.g.,

$$K(t) = \frac{1}{t_0} e^{-t/t_0} \quad (t \geq 0). \tag{7}$$

If spikes in train A and train B are matched within this resolution, i.e., if $\left| t_j^A - t_j^B \right| \ll t_0$, then the spike train distance between A and B will be small. Gaussians, boxcars, and similar non-negative windowing functions are also reasonable choices for K. These embedding functions are conventionally used in conjunction with an L^p norm for the target vector space,

$$\| f(A) \| = \left(\int_{-\infty}^{\infty} |f(A)(t)|^p dt \right)^{1/p}, \tag{8}$$

usually with $p = 2$ (the Euclidean norm). Thus, the net result of a linear embedding followed by the vector space norm provides a Euclidean geometry on spike trains.

To extend this kind of spike train distance to the multineuronal setting (R labeled neurons), the target vector space is taken to be vector-valued functions of time (Houghton & Sen 2008), and the norm is the L^2-norm on the space of vector-valued functions. To define the embedding function f, vectors $\vec{v}_l$ (typically, unit vectors) are assigned to each of the R labels. With this assignment,

$$f(A)(t) = \int_{-\infty}^{\infty} K(t - \tau) \sum_{j=1}^{M(A)} \vec{v}_{a(j)} \delta(\tau - t_j^A) d\tau \tag{9}$$

Thus, the j th event, a spike on neuron $a(j)$ at time t_j, is mapped to a bump (the kernel shape) "pointing" in the direction $\vec{v}_{a(j)}$ that has been assigned to neuron $a(j)$. The angles between the vectors $\vec{v}_l$ correspond to the extent to which the spike train distance is sensitive to the label associated with each spike. An alternative approach is to define multidimensional kernels that spill over from one neuron's spike train to another's (Tezuka 2014, Tezuka 2018).

In the above examples, the embeddings are linear, and, moreover, time-reversal (formally, replacing each t_j with $T - t_{M(A)+1-j}$) has no effect on the resulting distances. Neither of these properties is needed for an embedding to yield a metric; in fact, there are biological motivations to consider distances that derive from embeddings but lack these properties. For example, as a consequence of synaptic facilitation and depression (Sen et al. 1996), the effect of a spike on a post-synaptic neuron depends on how much time

has elapsed since the previous spike. This dependence can be incorporated into an embedding function (Brasselet et al. 2011a, Houghton 2009), conferring on it both nonlinearities and time-reversal asymmetries.

Spike train distances based on an embedding can also emphasize their discrete aspect. Specifically, a spike train can be discretized into "bins" of width ΔT (typically chosen to be short enough so that no bin contains more than two spikes) and then regarded as a binary sequence. The Hamming distance between two discretized spike trains (i.e., an L^1 distance in a vector space of dimension $T/\Delta T$) is a spike train distance. The main distinction is that in contrast to the kernel-based distances discussed above, spike trains that have spikes in different bins are regarded as equally distant, regardless of whether or not the times of occurrence of the spikes are close.

Embeddings can also be used to construct measures of spike train *similarity* (i.e., measures that decrease as spike trains become more dissimilar), via the normalized inner product

$$\rho(A, B) = \frac{\langle f(A), f(B) \rangle}{\|f(A)\| \|f(B)\|},$$

(10)

where $\langle u, v \rangle$ is the inner product in the vector space V and $\|v\| = \sqrt{\langle v, v \rangle}$ is the corresponding norm. These similarity measures have an exact correspondence to a spike train distance, as $\cos^{-1}(\rho(A, B))$ is a metric – namely, the geodesic distance between the unit vectors in the direction of $f(A)$ and $f(B)$ on the unit sphere. The Haas and White measure (Haas & White 2002) uses an exponential kernel for the embedding (Eq. (6)); the Schreiber measure (Schreiber et al. 2003) uses a Gaussian kernel. Since these measures are normalized for the spike count of the individual spike trains, they are only sensitive to temporal pattern, and a provision needs to be made for the empty spike train.

Cost-Based Spike Train Distances

While distances constructed via vector space embeddings focus on either the continuous or discrete aspects of the topology of spike trains, cost-based distances attempt to combine these two facets.

The prototypical example was introduced by Victor and Purpura, the "spike time" distance (Victor & Purpura 1997). As is the case for the other distances in this class, the key ingredient is a set of elementary transformations between spike trains, each of which is assigned a cost. Once the elementary transformations have been specified, the distance between two spike trains is the minimal total cost required to transform one spike train into another. That is, the distance $D(A, B)$ is defined as

$$D(A, B) = \min \sum_{k=0}^{K} c(X_k, X_{k+1}),$$

(11)

where $X_0, ..., X_K$ is a sequence of spike trains with $X_0 = A$ and $X_K = B$ and each successive spike train linked to the next by an elementary transformation of cost $c(X_k, X_{k+1}) = c(X_{k+1}, X_k)$. For the specific case of the spike time distance, the elementary transformations consist of (i) inserting a spike into a spike train, (ii) deleting a spike from a spike train, and (iii) shifting a spike in time. Inserting or deleting a spike is assigned a cost of 1; shifting a spike by an amount of time Δt is assigned a cost $q|\Delta t|$. The parameter q plays the same role as the parameter $1/\Delta t_0$ for the kernel-based distances: as q increases (or as Δt_0 decreases), the distance becomes progressively more sensitive to fine timing differences. For $q = 0$, the distance is entirely insensitive to timing differences (so, formally, it is a pseudometric), since spikes can

be moved "for free." In this limit, the distance which is often called the "spike count distance" is simply the difference in spike counts, $D(A,B) = |M(A) - M(B)|$.

The choice of elementary transformations determines the qualitative nature of the distance. A contrasting example of the spike time distance is the "interspike interval" distance (Victor & Purpura 1997), in which the elementary transformations act on interspike intervals, rather than on the spike times themselves. Since changing the length of one interspike interval shifts the time of all successive spikes, two spike trains can be close in terms of the spike interval distance, but not in terms of the spike time distance. Thus, these distances confer different topologies on the space of spike trains: the topology of the spike time distance is equivalent to that of the van Rossum distance (Eq. (6)) with a typical kernel, but the topology of the spike interval distance is not. Additionally, the spike time distance is invariant under parallel translation (adding a common spike train to the spike trains being compared, as in Eq. (5), while the spike interval distance is not. Cost-based distances are typically non-Euclidean (Aronov & Victor 2004, Dubbs et al. 2010).

Cost-based distances are also applicable to the multineuron setting (Aronov et al. 2003). For the spike time distance, a straightforward approach is to include an elementary transformation that assigns a cost to changing the neuronal label associated with a spike. Parametric variation of this cost changes the character of the distance from one that is sensitive to overall population activity (low cost to change the label) to one that is sensitive to cross-population patterns (high cost to change the label).

For cost-based distances, the overall distance and the costs associated with elementary transformations can be interpreted in terms of a generative model for spike trains (Dauwels et al. 2009). Cost-based distances can also be formulated in terms of "alignments" between spikes, rather than transformations (Dubbs et al. 2010).

The above constructions can be generalized in many ways. To name a few, normalization by spike count can be applied; the costs of each transformation (Victor et al. 2007) or alignment (Dubbs et al. 2010) can be transformed by a power law prior to summation; elementary transformations sensitive to burst structure can be added (Victor & Purpura 1997); and different kinds of elementary transformations can be combined.

Timescale-independent Spike Train Distances

Complementary to the timescale dependent approaches, in recent years spike train distances have been proposed which are timescale and thus parameter free since they always adapt to the local firing rate. While not allowing the functional characterization and precision analysis described above, single-valued methods give an objective and comparable estimate of neuronal variability (Chicharro et al. 2011). Measures in this group include the ISI-distance (Kreuz et al. 2007), the SPIKE-distance (Kreuz et al. 2013), and SPIKE-synchronization (Kreuz et al. 2015).

ISI-distance and SPIKE-distance

The ISI-distance D_I and the SPIKE-distance D_S rely on instantaneous values in the sense that in a first step the sequences of discrete spike times are transformed into continuous dissimilarity profiles $I(t)$ and $S(t)$. For the ISI-distance (Kreuz et al. 2007) the dissimilarity profile is derived from the interspike intervals, while in the case of the SPIKE-distance (Kreuz et al. 2013) it is extracted from differences between the spike times of the two spike trains. Both distances are then defined as the temporal average of the respective dissimilarity profile, e.g., for the SPIKE-distance

$$D_S = \frac{1}{T} \int_{t=o}^{T} S(t)dt. \tag{12}$$

The two dissimilarity profiles rely on three piecewise constant quantities which for each neuron ($X = A$ or $X = B$ below) are assigned to every time instant between 0 and T. These are the time of the preceding spike

$$t_P^X(t) = \max(t_i^X \mid t_i^X \leq t), \tag{13}$$

the time of the following spike

$$t_F^X(t) = \min(t_i^X \mid t_i^X > t), \tag{14}$$

and the interspike interval

$$z_{ISI}^X(t) = t_F^X(t) - t_P^X(t). \tag{15}$$

The ambiguity regarding the definition of the very first and the very last interspike interval is resolved by means of auxiliary spikes (Kreuz et al. 2015).

ISI-distance
The ISI-distance (Kreuz et al. 2007) is a time-resolved, symmetric, and timescale-adaptive measure of the relative firing rate pattern, defined as the ratio between the instantaneous interspike intervals $z_{ISI}^A(t)$ and $z_{ISI}^B(t)$ is calculated according to:

$$I(t) = \frac{\mid z_{ISI}^A(t) - z_{ISI}^B(t) \mid}{\max(z_{ISI}^A(t), z_{ISI}^B(t))}. \tag{16}$$

This quantity is 0 when the ISI's in the two spike trains are equal, and approaches -1 and 1, respectively, if the first or the second spike train is much faster than the other. Since both directions of deviation from identical ISIs are equally important, the ISI-distance is calculated by temporal averaging over the absolute values $|I(t)|$ in Eq. (12).

SPIKE-distance
The ISI-distance relies on the relative length of simultaneous interspike intervals and is thus capable to quantify similarities in the neurons' firing rate profiles. However, it is not optimally suited to track synchrony that is mediated by spike timing. This issue is addressed by the SPIKE-distance (Kreuz et al. 2013) which combines the properties of the ISI-distance with a specific focus on spike timing.
The dissimilarity profile of the SPIKE-distance is based on differences between the spike times in the two spike trains. It is calculated in two steps: First, for each spike, the distance to the nearest spike in the other spike train is calculated. Then, for each time instant, the relevant spike time differences are selected, weighted, and normalized. Here 'relevant' means 'local,' i.e., each time instant is uniquely surrounded by four corner spikes: the preceding spike of the first spike train t_P^A, the following spike of the first spike train t_F^A, the preceding spike of the second spike train t_P^B, and, finally, the following spike of the second spike train t_F^B. Each of these corner spikes can be identified with a spike time difference, for example, for the previous spike of the first spike train

$$\Delta t_P^A = \min_k \left(\left| t_P^A - t_k^B \right| \right) \tag{17}$$

and analogously for t_F^A, t_P^B, and t_F^B.
For each spike train separately, a locally weighted average is employed. The weighting factors ensure that the differences for the closer spike dominate: the weighting factors depend on

$$z_P^A(t) = t - t_P^A(t) \tag{18}$$

and

$$z_F^A(t) = t_F^A(t) - t, \tag{19}$$

the intervals to the previous and the following spikes for each neuron. The local weighting for the spike time differences of the first spike train reads

$$S_A(t) = \frac{\Delta t_P^A(t) z_F^A(t) + \Delta t_F^A(t) z_P^A(t)}{z_{ISI}^A(t)} \tag{20}$$

For the second spike train $S_B(t)$ is obtained analogously.

Averaging over the two spike train contributions and normalizing by the mean interspike interval yields

$$S'(t) = \frac{S_A(t) + S_B(t)}{2 \left\langle z_{ISI}^X(t) \right\rangle_{X=A,B}} \tag{21}$$

This quantity weights the spike time differences for each spike train according to the relative distance of the corner spike from the time instant under investigation. Averaging over this dissimilarity profile $S'(t)$ according to Eq. (12) yields the rate-independent SPIKE-distance (RI-SPIKE-distance) D_S^{RI} (Satuvuori et al. 2017), which completely disregards any rate differences between the two spike train and thus focuses purely on spike timing information.

In order to also account for differences in firing rate, in a last step the two contributions from the two spike trains are locally weighted by their instantaneous interspike intervals. This leads to the dissimilarity profile of the SPIKE-distance

$$S(t) = \frac{S_A(t) z_{ISI}^B(t) + S_B(t) z_{ISI}^A(t)}{2 \left\langle z_{ISI}^X(t) \right\rangle_{X=A,B}^2} \tag{22}$$

which is thus sensitive to both spike rate and spike timing (Satuvuori & Kreuz 2018).

The dissimilarity profiles of both the ISI-distance and the SPIKE-distance and thus both distances are bounded in the interval $[0,1]$. For the ISI-distance the minimum value 0 is obtained for any periodic spike trains with the same period. Thus the ISI-distance is a pseudo-metric, in which all spike trains with a certain constant interspike interval, but overall time shifts form the equivalence classes (Mulansky et al. 2015). On the other hand, for the SPIKE-distance the value 0 is indeed obtained only for perfectly identical spike trains, but it is possible to construct examples that violate the triangle equality (Mulansky et al. 2015), so the SPIKE-distance is not a metric.

For both distances there exists a straightforward extension to estimate the time-resolved level of dissimilarity within a group of spike trains (Kreuz et al. 2009, Kreuz et al. 2013). It is the straightforward average over all pairs of spike trains, but in these cases the averaging can be performed locally, e.g., for the SPIKE-distance:

$$S^a(t) = \frac{1}{N(N-1)/2} \sum_{n=1}^{N-1} \sum_{m=n+1}^{N} S^{mn}(t). \tag{23}$$

SPIKE synchronization

SPIKE synchronization (Kreuz et al. 2015) acts as coincidence detectors and quantifies the level of synchrony from the number of quasi-simultaneous appearances of spikes. It is a measure of similarity, i.e. for identical spike trains it yields not its minimum value 0 but its maximum value 1.

The calculation consists of two steps, coincidence detection and a combination of normalization and windowing. The first step builds on the same bivariate and adaptive coincidence detection that was used for event synchronization (Quian Quiroga et al. 2002). The temporal resolution can be adjusted with a coincidence window of fixed size τ, but in the parameter- and timescale-free main variant the maximum

time lag τ_{ij} up to which two spikes t_i^A and t_j^B are considered to be synchronous is adapted to the local spike rates according to

$$\tau_{ij} = \frac{1}{2}\min[t_{i+1}^A - t_i^A, t_i^A - t_{i-1}^A, t_{j+1}^B - t_j^B, t_j^B - t_{j-1}^B] \tag{24}$$

The coincidence criterion can be quantified by means of a coincidence indicator

$$C_i^A = \begin{cases} 1 & \text{if } \min_j(|t_i^A - t_j^B|) < \tau_{ij}^{A,B} \\ 0 & \text{otherwise} \end{cases} \tag{25}$$

(and analogously for C_j^B), which assigns to each spike either a one or a zero depending on whether it is part of a coincidence or not. Here the minimum function takes already into account that a spike can at most be coincident with one spike in the other spike train. If a spike is exactly in between two spikes from the other spike train, this is not considered a coincidence.

The extension to the case of one group of more than two spike trains is straightforward. After performing bivariate coincidence detection for every pair of spike trains, for each spike of every spike train a normalized coincidence counter

$$C_i^A = \frac{1}{N-1}\sum_{X \neq A} C_i^{A,X} \tag{26}$$

is obtained by averaging over all $N-1$ bivariate coincidence indicators involving the spike train A. This way for both the bivariate and the multivariate case we have defined a coincidence counter for each individual spike in every spike train. In order to obtain one combined similarity profile, we pool the spikes of all the spike trains as well as their coincidence counters by introducing one overall spike index j. In case there exist exact matches (perfectly coincident spikes), j counts over all of these spikes. From this discrete set of coincidence counters C_j, the SPIKE-Synchronization profile $C(t_j)$ is obtained via $C(t_j) = C(j)$. Finally, SPIKE-Synchronization is defined as the average value of this profile

$$S_C = \frac{1}{M}\sum_{j=1}^{M} C(t_j) \tag{27}$$

with $M = \sum_X M(X)$ denoting the total number of spikes in the pooled spike train.

The interpretation is very intuitive: SPIKE-Synchronization quantifies the overall fraction of coincidences. It is zero if and only if the spike trains do not contain any coincidences, and reaches one if and only if each spike in every spike train has one matching spike in all the other spike trains. SPIKE-Synchronization is complementary to the distances described above. It is a measure of spike matching based on a binary coincidence criterion. If converted from a measure of similarity into a measure of distance (by considering $1 - S_C$), it would remain symmetric, but it would fail to be a metric.

This is because of the binariness of the coincidence criterion: there are non-identical spike trains that would have a distance of zero (violating Eq. (1)), and it is possible to construct violations of the triangle inequality (Eq. (3)) (Mulansky et al. 2015). SPIKE-Synchronization is complemented by SPIKE-order and Spike Train Order (Kreuz et al. 2017), two indicators that allow to sort spike trains from leader to follower and to quantify the consistency of the temporal leader-follower relationships for both the original and the optimized sorting.

All three of these timescale-independent approaches (the ISI-distance, the SPIKE-distance and SPIKE-Synchronization) have recently been adapted for data containing multiple timescales by adding a notion of the relative importance of local differences compared to the global time scales (Satuvuori et al. 2017).

Other timescale-independent measures

The modulus- and the max-metric (Rusu & Florian 2014) form another family of metrics which is timescale free as well and can also be turned into a time-resolved profile. Both measures are more sensitive to large-scale temporal structure and less sensitive to spike counts and to fine structure within bursts. The most recent proposal in this group is Spike-contrast, a further timescale independent and multivariate measure of spike train synchrony (Ciba et al. 2018). It mostly yields very similar results to the SPIKE-distance, however, it is complementary since it does not provide a time-resolved dissimilarity profile but instead a synchrony curve as a function of bin size (one of several parameters).

Other Types of Spike Train Distances

There are several useful spike train distances that do not fall into these major categories. The family of metrics proposed in (Wu & Srivastava 2011) resembles an embedding-based metric in that the spike trains are mapped to functions using a kernel; however, these metrics also allow for time to be warped for one spike train relative to the other to bring them into better alignment. In a manner which is reminiscent of a cost-based metric, this warping is associated with a penalty. This metric facilitates the calculation of a "mean spike train," something that can also be calculated using an embedding-based metric (Julienne & Houghton 2013).

The Hunter-Milton measure compares spike times in one train with the nearest spike times in the other (Hunter & Milton 2003). A choice of scale parameter is required. Lyttle and Fellous have proposed metrics to specifically assess the similarity of spike trains with either common silent periods or bursts (Lyttle & Fellous 2011). Both metrics can be adapted to the dataset by means of several parameters. Finally, the "coincidence factor," while not a distance, has also been used to compare discretized spike trains based on a normalized count of coincidences (Jolivet et al. 2008, Kistler et al. 1997).

Applications: Analytical Methods

Spike train distances are the starting point for many analysis and modeling strategies. The distinctive feature of this starting point (i.e., considering spike trains to be event sequences, vs. considering them to be vectors) is that it allows for a much more flexible kind of geometry, and focuses on intrinsic relations between spike trains, rather than a coordinate system for them. As we describe below, this enables a variety of approaches to exploratory data analysis, neural coding, and model testing. We first survey these approaches according to the type of analysis, and then describe some examples of these applications in neuroscience and behavior. For earlier reviews, see (Houghton & Victor 2011, Victor 2005, Victor & Purpura 2010).

Dimension reduction

A main challenge in analyzing neural data is its high dimensionality. Thus, as a first step in exploratory analysis or data visualization, it is often helpful to construct a low-dimensional representation of a dataset that preserves key aspects of its structure. From the spike train distance viewpoint, the central goal is to preserve similarity; thus, the crucial requirement in dimensional reduction is to preserve the metric.

The classical approach to accomplishing this is standard multidimensional scaling (Kruskal & Wish 1978), which can be directly applied to spike metrics. Multidimensional scaling is algebraically related to principal components analysis, but in multidimensional scaling, there is no need to identify coordinates or to conceptualize the spike trains as points in a vector space. When applied to a cost-based distance, multidimensional scaling approach often leads to a representation of the neural responses that recapitulates the geometry of the domain being represented (e.g., spatial phase (Aronov et al. 2003) or sound location (Victor & Purpura 1997)).

The global geometry of cost-based distances is typically non-Euclidean (Aronov & Victor 2004). As a consequence, standard multidimensional scaling can at best approximate these (and perhaps other) spike train distances. One approach to this problem is to apply multidimensional scaling to a monotonic function of the distance (such as d^p for $0 < p < 1$), rather than the raw distances themselves. For a sufficiently small but data-dependent p, these derived distances can be exactly embedded into a Euclidean space. An alternative approach is to seek an embedding that focuses on local geometry: the isomap (Tenenbaum et al. 2000) or local linear embedding (Roweis & Saul 2000) approaches can be used to expand a locally-Euclidean representation to a non-Euclidean manifold. The t-distributed stochastic neighbor embedding (t-SNE) is another such non-linear dimensional reduction approach, which is particularly suitable for sampled data and also focuses on local geometry. Specifically, combining spike train metrics with t-SNE (van der Maaten & Hinton 2008) has been found to be effective for single-neuron and multineuronal datasets (Vargas-Irwin et al. 2015), as well as for non-neural data -- bat biosonar, an acoustic emission that can be considered as a sequence of pulses (Accomando et al. 2018).

Information-theoretic analysis

Spike train distances are also the starting point for information-theoretic analyses of neural coding. For example, they can be used as a way to estimate the **mutual information** between a set of stimuli and a set of responses, by determining the extent to which neural responses to a set of stimuli form reliable clusters. The dependence of this estimate on the kind of spike train distance used (e.g., one that is sensitive to spike times, vs. spike intervals, or the degree of temporal precision of the distance) points to the features of the neural response that carries the information (Satuvuori & Kreuz 2018, Victor & Purpura 1997). Spike train distances can also be combined with the Kozachenko-Leonenko estimator (Kozachenko & Leonenko 1987) to provide estimates of mutual information, without the need for explicit clustering (Houghton 2015, Shapira & Nelken 2013). It is important to note, however, that these approaches typically yield underestimates of mutual information, since they focus on a single timescale, and use a very limited number of parameters to describe the possible relationships between spike trains (Lopes-dos-Santos et al. 2015).

Model evaluation

Spike train distances provide a way to measure the quality of a neural model, by determining the distance between experimentally observed spike trains and models of them (Kameneva et al. 2015). Extending this idea, a spike time distance can also be used as a cost function to be minimized by adjusting model parameters (Lynch & Houghton 2015), or as a cost function to drive learning algorithms that shape artificial networks to process temporal patterns (Florian 2012). They can also provide a way to quantify whether a model accounts for neuronal variability, by determining the distances between members of a

set of spike trains that represent samples of spontaneous activity or samples of responses to the same stimulus.

Applications to Neuroscience

As spike train metrics are metrics on sequences of events, they can be applied to any problem where the data are sets of event sequences. However, they are primarily designed to express the metric structure of spike trains that is functionally or mechanistically relevant, and are most often applied to the analysis of electrophysiological data.

One frequent application is as a tool for quantifying how information is coded in spike trains. In describing the different spike train metrics it has been noted that they often have a parameter interpolating between a spike count pseudometric and metrics in which the precise timing of individual spikes is very significant. In the case of the embedding metrics, this parameter is the width of the kernel used in the embedding, for example, if the kernel is given by Eq. (7), it is t_0; in the case of the cost based metric, it is q, the cost of moving a spike (see discussion following Eq. (11)). This parameter can be fitted to stimulus-evoked spike train data by choosing the value where the metric-based clustering best matches clustering according to stimulus. This gives an indication of the temporal scale relevant to the coding of information about the stimulus in the spike trains. This approach was used, for example, in analyzing visual responses in V1, V2 and V3 in monkey in (Victor & Purpura 1996) and in analyzing auditory responses in zebra finch in (Narayan et al. 2006). Another approach is used in (Brasselet et al. 2009, Brasselet et al. 2011b) where a metric analysis combined with a novel definition of mutual information is used to argue for the primacy of the latency of first spike in encoding tactile information in human microneurography data.

In multineuronal spike train metrics, there is often a parameter which specifies how significant the individual neurons are in coding; this parameter interpolates between a population code where the identity of the neuron firing a spike has no effect on the distance, and a "labeled line code" where the spike train distance between a pair of multineuron spike trains is effectively the sum of the distances between the individual pairs of spike trains for individual neurons. This was used, for example, in (Clemens et al. 2011) to analyze the degree of population coding of auditory information in grasshoppers.

These applications all compare responses by the same neuron, or neurons, across different stimuli. Another application of spike train metrics is the detection of cell assemblies, this involves comparing the spiking responses of different neurons to the same stimulus (Humphries 2011, Humphries 2017): roughly, a network is formed whose nodes correspond to neurons and the links to a measure of similarity derived from a spike train metric, assemblies are then identified using community detection algorithms. This approach has been applied to CA3 in hippocampus (Li et al. 2010), to reaching tasks in monkey (Newman et al. 2011), and similar ideas can be applied to recordings of activity in the retina (Cutts & Eglen 2014). In (Kreuz et al. 2013), the SPIKE-distance is used to study synchrony between recording sites in data recorded from epilepsy patients. It is demonstrated that during ictal periods, there is an elevated level of neuronal synchrony in the hemisphere containing the seizure focus.

Computation of Spike Distances

Computation of distances based on embeddings is straightforward, as the essential steps are convolution and pairwise multiplication. Houghton and Kreuz (Houghton & Kreuz 2012) introduced a markage trick which reduces the computational cost for the regular van Rossum metric between two spike trains of

similar length, $M(A) \sim M(B)$, to order $M = M(A) + M(B)$ from order M^2. The same markage trick can also be used for the multineuron extension.

For cost-based distances, dynamic programming algorithms modeled after alignment algorithms for genetic sequences (Needleman & Wunsch 1970, Sellers 1974) provide an efficient way to identify the minimal-cost sequence of transformations in the single-neuron setting and for settings with a small number of neurons.   The number of computations is approximately $O(N^2)$ for unlabeled spike trains containing N events and $O(N^{R+1})$ when R neurons (labels) are present. These algorithms extend to enable simultaneous computation of distances for all values of its parameters (cost to move a spike, cost to change a label) (Victor et al. 2007). For the single-neuron scenario and single values of the cost parameter, a graph-theoretic approach based on the "Hungarian" algorithm may provide improved performance (Dubbs et al. 2010). For five or more neurons, an incremental matching algorithm (Diez et al. 2012) is the most efficient approach currently available; the computational complexity (specifically, the number of computations required) scales approximately as N^6, independent of the number of neurons.

Finally, the calculation of the time-resolved and timescale independent spike train distances is very straightforward since it involves only simple arithmetic. Computational complexity for the ISI-distance and the SPIKE-distance is $O(N)$; for SPIKE-Synchronization it is $O(N^2)$.

Cross-References/Related Terms

Edit length distances

Point processes

Earth mover distance

Metric space analysis of neural information flow

Spike train

Spike train analysis: overview

Correlation analysis of parallel spike trains

Statistics of inter-spike intervals

Further Reading

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