Metric-space Analysis of Multineuronal Responses: Algorithmic Improvements Allow for Extension to Multiple Neurons

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INTRODUCTION: Why use a metric space method to estimate information?

For neural systems, the "transmitted information" (Shannon) is the extent to which observation of a neural response reduces the uncertainty about the stimulus. Straightforward estimation of transmitted information requires experimental estimation of the probabilities of all joint stimulus-response events.

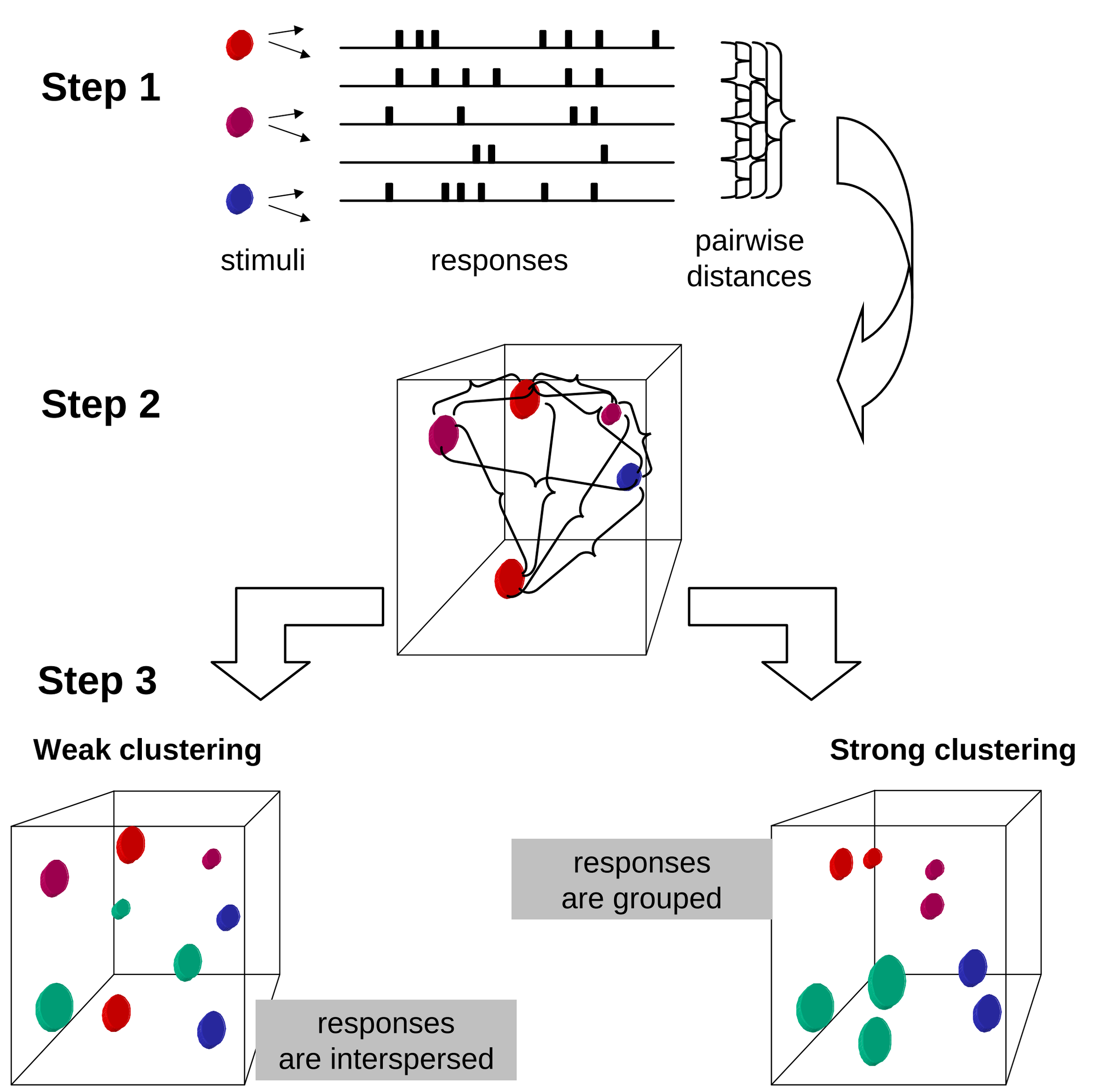
The difficulty with this approach is that, in principle, each different spike train configuration constitutes a different "response." Thus, the number of possible "responses" may be astronomically large, especially for multineuronal activity. When the set of possible responses is severely undersampled, biases in the estimates of response probabilities can dominate the estimates of information. Without an *a priori* notion of when two spike train configurations are sufficiently similar so as to be considered identical, any variation in a response must be considered as a possible carrier of information.

An alternative approach is to parameterize the problem by a set of "metrics" that explicitly quantify the extent to which two responses are similar. This ameliorates the undersampling problem, but is computationally intensive. We present algorithms that make this approach feasible for the study of 3 or more neurons.

THE METRIC SPACE ALGORITHM: AN OVERVIEW

For each metric (notion of distances between spike trains)...

- Calculate pairwise distances between all responses to all stimuli.
- Construct a response space from the pairwise distances.
- Quantify degree of clustering via the "confusion matrix"
- Repeat the above for each metric



Information (H) = row entropy + column entropy - table entropy

Weak clustering (assigned stimulus across, actual stimulus down):

1	1		1
	1	2	
1	1	1	1
2			

most nonzero entries are off-diagonal
***H* is low**

Strong clustering (assigned stimulus across, actual stimulus down):

1	1		1
	2	1	
	1	3	
			2

most nonzero entries are diagonal
***H* is high**

METRIC SPACE METHOD FOR

SINGLE-NEURON RESPONSES

A single parameter, q, expresses the sensitivity of the distance to the timing of individual spikes. The distance $D_q(A,B)$ between two spike trains A and B is the least total cost of *any* sequence of allowed transformations from A to B. The allowed transformations consist of:

insert a spike: cost=1
delete a spike: cost=1
shift a spike in time by ΔT: cost = $q\,\Delta T$

With this notion of distance, spike trains are similar only if spikes occur at similar times (i.e., within $1/q$ sec). A spike count code corresponds to q=0 (i.e., timing is irrelevant).

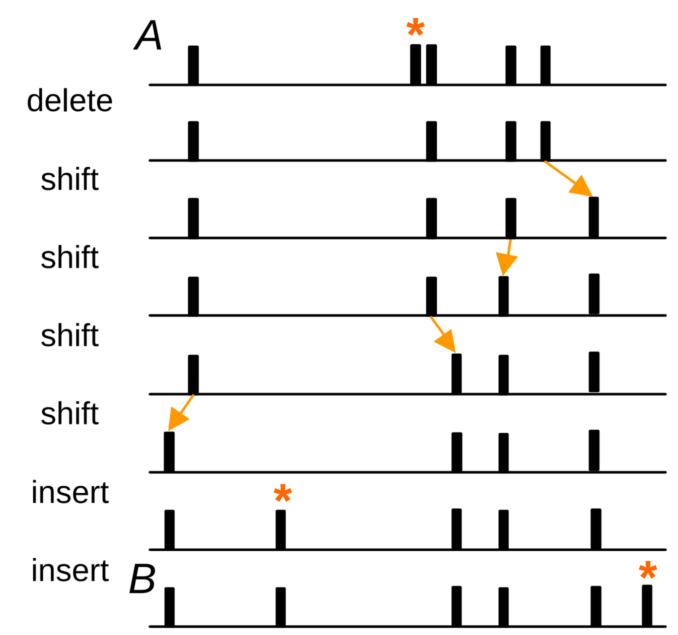
Efficient calculation of distances

In a sequence of transformations that realizes the minimal total cost, "world lines" of each spike cannot cross.

For the fate of the last spikes in trains A and B the only three remaining possibilities are:
- The last spike in train A is deleted.
- The last spike in train B is inserted.
- These spikes are linked by a shift.

$$D_q(A_m,B_n)=\min\{\,D_q(A_{m-1},B_n)+1,\; D_q(A_m,B_{n-1})+1,\; D_q(A_{m-1},B_{n-1})+q|t_m(A)-t_n(B)|\,\},$$

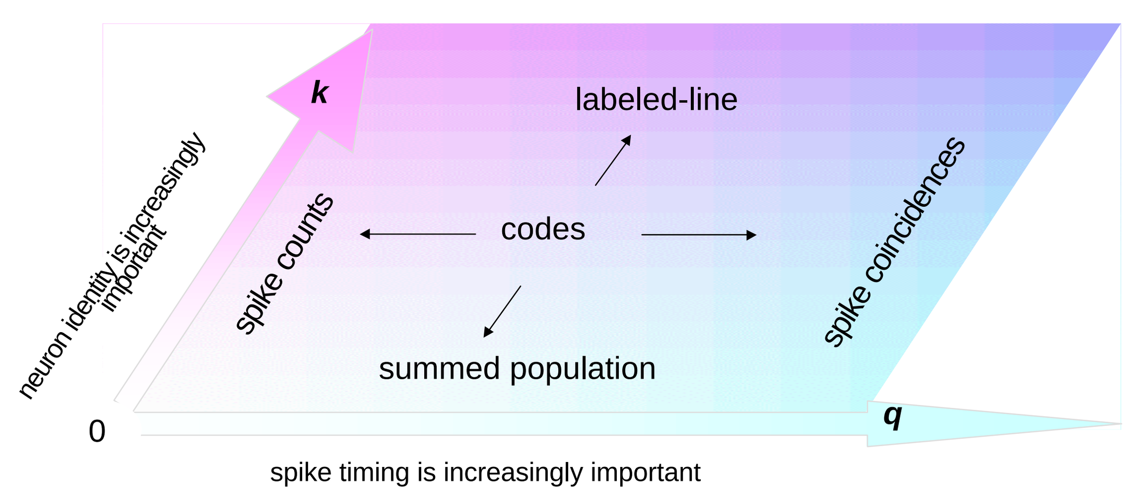
where
A_m = train of the first m spikes of A, etc.,
$t_m(A)$ = the time of the mth spike of A, etc.



The resulting dynamic programming algorithm has a running time, T, proportional to the product of the number of spikes in each response. For an average N spikes per response

$$T \sim n_A * n_B \sim N^2$$

A 2-PARAMETER FAMILY OF CODES AND METRICS

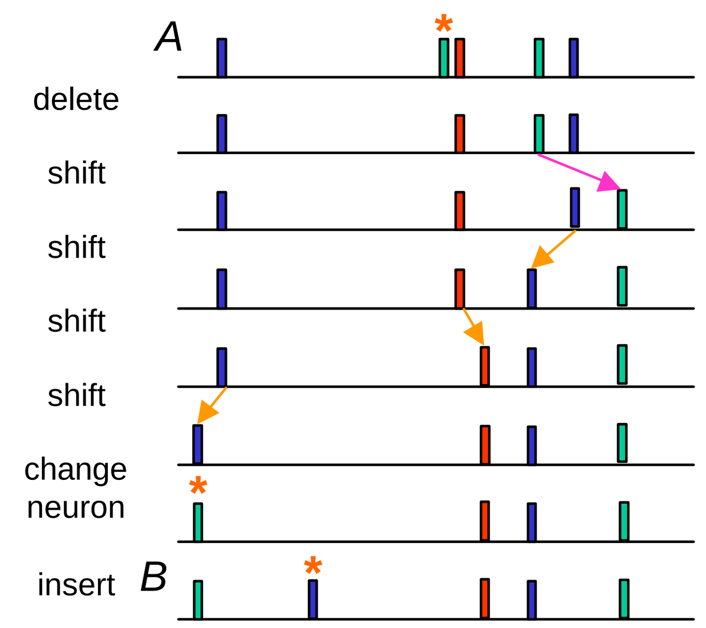


MULTI-NEURON RESPONSES

Several neurons' joint response is considered to be a single sequence of labeled events, with label indicating neuron of origin (shown below as color.) The distance between two *multineuronal* responses, A and B, is defined similarly to the single-neuron case, but a second parameter, k, is added that expresses the sensitivity of the distance $D_{q,k}(A,B)$ to the neuron of origin of spikes. The new transformation is:

change spike label (neuron of origin): cost=k

At the two extremes:
k=0, neuron of origin is ignored ("summed population code").
k=2, neuron of origin is fully considered ("labeled line code").



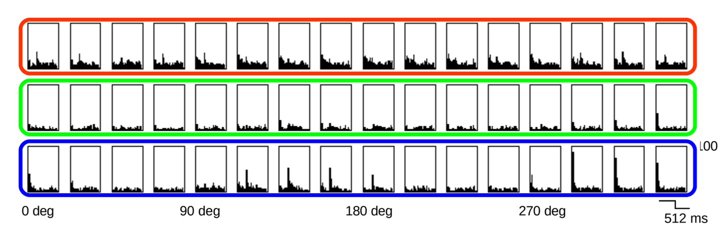
"World lines" of spikes can cross (e.g., purple arrow,left) because of the added penalty (k) for aligning spikes from different neurons.

There are multiple alternative fates for the last spike in either train, including deletion, or being linked to the last spike *of any neuron* in the other response.

Here, T is proportional to the product of the number of spikes in each neuron in each response. For L neurons with an average N spikes each ,

$$T \sim (n_{A,1} * n_{A,2} * \ldots * n_{A,L}) * (n_{B,1} * n_{B,2} * \ldots * n_{B,L}) \sim N^{2L}$$

ANALYSIS OF SPATIAL PHASE RESPONSES IN MACAQUE VISUAL CORTEX

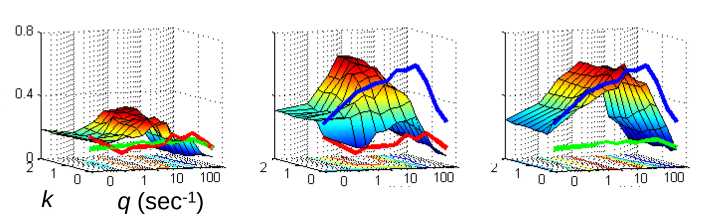


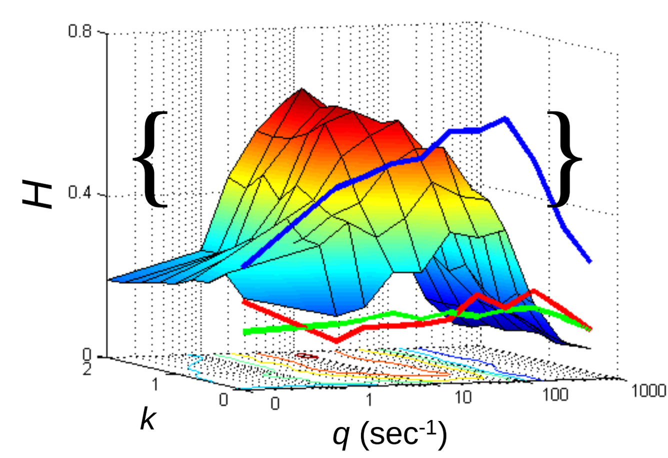
Responses of three neurons (simultaneously recorded with a tetrode) to pattern-appearance gratings, as a function of spatial phase

Pairwise analyses

Data from Aronov et al., 2003

Greater information when neural identity is retained (k>0) than when neurons are pooled (k=0); meaningful resolution ca. 50 ms ($q_{max} \approx 20$).





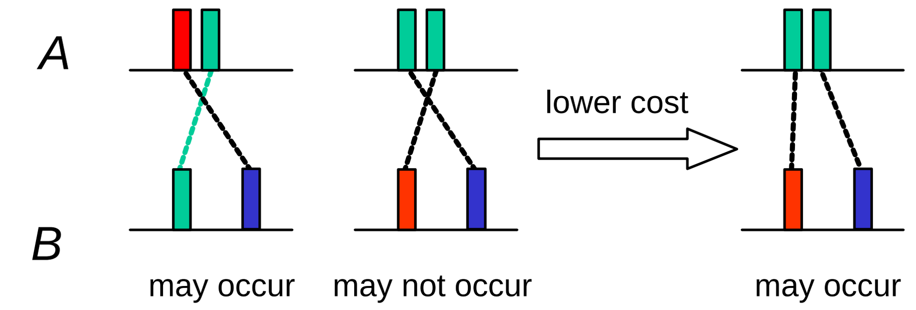
Analysis of coding by the triplet

Qualitatively similar to pairwise analysis: greater information when neural identity retained (k>0) than when neurons are pooled (k=0); meaningful resolution ca. 50 ms ($q_{max} \approx 20$).

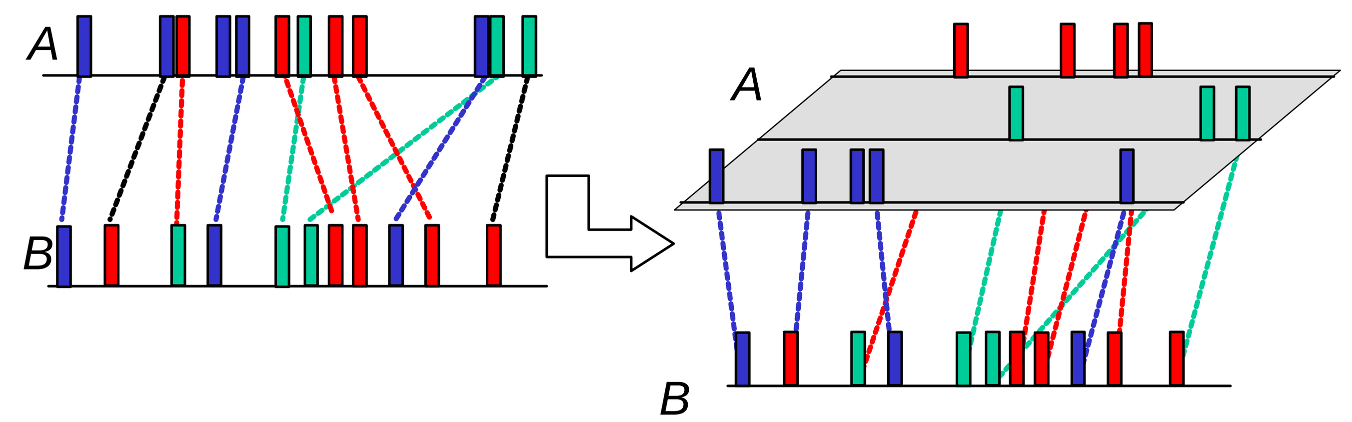
Adding a third neuron only increases information if k is near 2.

MAJOR IMPROVEMENT: $N^{2L} \rightarrow N^{L+1}$

Key observation:
world lines of spikes from same neuron in either response cannot cross for minimizing set of transformations.



Thus, the non-crossing property can be recovered by separating **one** of the two responses into its components:



The resulting dynamic programming algorithm's running time, T, is now proportional to the total number of spikes in the separated response instead of the number of spikes in each neuron. For L neurons, with an average N spikes each:

$$T \sim (n_{A,1} + n_{A,2} + \ldots + n_{A,L}) * (n_{B,1} * n_{B,2} * \ldots * n_{B,L}) \sim N^{L+1}$$

FURTHER IMPROVEMENT: PARALLEL COMPUTATION

The above dynamic programming algorithm can be modified to calculate the minimum total distance required to align the two responses exactly, given a prescribed number of spikes that are matched, and a prescribed number of changes of neuron of origin. This adds a factor of N^2 to running time. However, from this calculation, the distances for *all* values of q and k can be calculated rapidly and in parallel.

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http://www-users.med.cornell.edu/~jdvicto/pubalgor.html to download software

http://www-users.med.cornell.edu/~jdvicto/metricdf.html for background on the metric space method

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