A Novel Analysis Framework for Characterizing Ensemble Spike Patterns Using Spike Train Clustering and Information Geometry

Peter Lipa[1*], Masami Tatsuno[1], Shun-ichi Amari[2], Bruce L. McNaughton[1] and Jean-Marc Fellous[1]

[1]ARL Neural Systems Memory and Aging, Univ Arizona, Tucson, AZ [2]RIKEN BSI, Wako-shi, Saitama, Japan

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ABSTRACT

Presently, hundreds of neurons can be recorded simultaneously from different brain areas of behaving animals. It is conjectured that multi-neuronal spike-synchronization patterns ('assemblies') emerge dynamically and may play an important role in cognitive functions. Their detection has proven difficult because they are hidden among the overall recorded neuronal groups. Furthermore, the quantification of their significance has also proven difficult because correlation due to spike-timing relations among neurons cannot be easily separated from correlation due to mean firing rate modulations of individual neurons.

We propose a novel analysis framework for the characterization of multi-neuronal spike patterns that resolves these difficulties by integrating two independently developed analysis methods based on 'spike train clustering' and 'information geometry'. With the former method, neuronal subgroups that exhibit synchrony are first identified. With the latter method, 'pure' correlations due to spike-timing relationships among neurons in those neuronal subgroups are separated from correlations due to mean firing rate modulations.

We examined the proposed method using ensemble spike trains that were generated by recurrent networks of biophysical model neurons connected by AMPA and GABAA synapses. Correlation was introduced by either common external inputs or by the modulation of specific intrinsic connections. The spike train clustering method identified subgroups of synchronized neurons successfully and dramatically reduced the number of neuron pairs that needed to be analyzed. Information geometry applied on these subgroups successfully detected pure, rate-independent correlations. The advantages of using information geometry over the conventional correlation measures such as the correlation coefficient were also examined. These results indicate that spike train clustering and information geometry are potentially powerful tools for the detection and analysis of multi-neuronal spike patterns.

INTRODUCTION

Two open problems in the analysis of spatio-temporal spike patterns

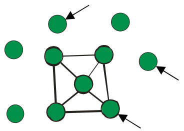
1) Systematic detection of neuronal clusters

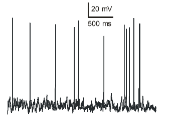
- In the course of information processing, neurons form clusters of functionally related units.
- In general, the neuronal clusters are not apparent but rather hidden among the populations of recorded neurons.
- Development of a systematic detection method of neuronal clusters is, therefore, a critical step towards the analysis of multi-neuronal spike patterns.

2) Separation of contributions from neuronal interactions and from mean firing rate modulations to correlation

- The separation of neuronal interactions from mean firing rate modulation is another important issue.
- The cross-correlogram and the Pearson correlation coefficient, however, are affected by the mean firing rate (Tatsuno et al., 2006).
- An alternative correlation measure that is capable of estimating correlations independently from mean firing rate modulations is, therefore, highly desired.

SPIKE TRAIN CLUSTERING





● = I_{Na}, I_{Kdr}, I_{ahp}, I_{Ca}, Ca_{pump}

Modeling Methods

- We use one compartment cells, with parameters corresponding to a typical cortical neuron.
- Synaptic potentials follow an exponential decay time course. No short term synaptic dynamics were included. Synaptic conductances were tuned to generate EPSPs between 0.1 (weak) and 5 (strong) mV.
- Independent excitatory and inhibitory background noise was provided to each neuron separately and followed Ornstein-Uhlenbeck processes as previously described (Destexhe et al. 2001). Membrane fluctuations were adjusted to yield 1 (small) to 15 (large) mV peak-peak amplitudes.
- All simulations were performed using NEURON.

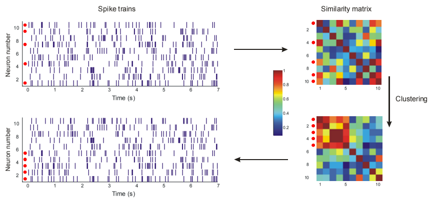
Clustering Methods

We use a modified fuzzy-clustering method, as previously described (Fellous et al., 2004). Briefly:

1- The spike train of each neuron is convolved with a Gaussian (3 ms width).
2- The similarity matrix between spike trains is constructed.
3- Each column of the matrix is a vector V_i.
4- Iterative procedure aimed at minimizing the objective function $O_f(U,V)$ for K clusters, N vectors (neurons). C_j are the cluster centers, u_{ij}^f are the membership weights, and f is the fuzzy factor (>1).

$$O_f(U,V) = \sum_{i=1}^{N}\sum_{j=1}^{K} u_{ij}^f \| V_i - C_j \|^2$$

● = Neuron belonging to the ensemble



INFORMATION GEOMETRY

What is Information Geometry?

Information Geometry (IG) was developed to study geometrical properties of the parameter space of families of probability distributions. It has been shown that IG can provide a useful tool for spike train analysis because of the following properties (Amari, 2001; Nakahara and Amari, 2002; Tatsuno and Okada, 2004):

- Neuronal interactions can be decomposed into an 'orthogonal' sum of pairwise, triplewise and further higher order interactions.
- Mutual information between neuronal interactions and external parameters such as stimuli or animal behavior can be estimated.
- The biologically plausible null-hypothesis can be used in statistical tests.
- IG measures can be related to synaptic weights and amount of external inputs.

Construction of information geometric measures (2 neuron case)

1. Convert spike trains to binary trains using a small bin. '1' represents an existence of a spike and '0' represents no spike in the bin.
2. Count the occurrence of one of the four mutually exclusive spike patterns at each bin: (Neuron #1, Neuron #2) = (0,0), (0,1), (1,0) and (1,1).
3. Repeat the counting procedure over all trials, and calculate the probability of each spike pattern.
4. Use the log-linear model to express probability.
5. The coefficient of the second order term gives interaction between two neurons measured by information geometry

x: 0 0 1 0 1 0 1 0
y: 0 1 0 0 1 0 0 0
n_{00} n_{01} n_{10} n_{00} n_{11} n_{00} n_{10} n_{00}

$$p_{00} = \frac{n_{00}}{n},\ p_{01} = \frac{n_{01}}{n},\ p_{10} = \frac{n_{10}}{n},\ p_{11} = \frac{n_{11}}{n}$$

where $n = \sum_{i,j} n_{ij}$

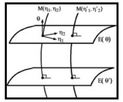
$$\log p_{xy} = \theta_1 x + \theta_2 y + \theta_{12} xy - \psi$$

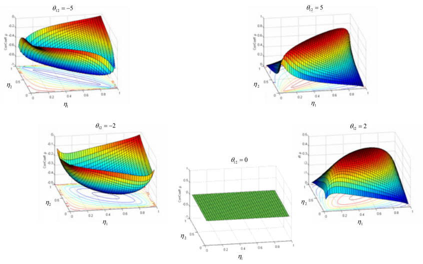
where

$$\theta_1 = \log\frac{p_{10}}{p_{00}},\quad \theta_2 = \log\frac{p_{01}}{p_{00}},\quad \theta_{12} = \log\frac{p_{11}p_{00}}{p_{01}p_{10}},\quad \psi = -\log p_{00}$$

Comparison between IG Measure and Corr. Coeff.

The traditional method often uses correlation coefficient ρ to represent interaction between two neurons. Together with firing rate parameters η_1 and η_2, $(\eta_1, \eta_2; \rho)$ forms a 3 dimensional space. However, (η_1, η_2) and ρ are not orthogonal, meaning that ρ is affected by firing rate modulation. Information geometry proposes to use θ_{12} instead of ρ because θ_{12} is orthogonal to (η_1, η_2), and therefore it represents 'pure' two neuron interaction. The following figures show how ρ is affected by firing rate modulation when θ_{12} is fixed at -5, -2, 0, 2 and 5.



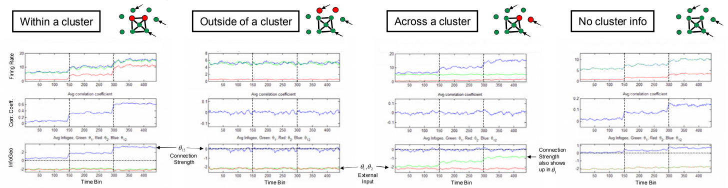


SPIKE TRAIN CLUSTERING & INFORMATION GEOMETRY

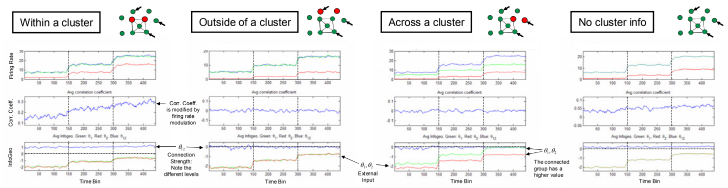
Application of spike train clustering & information geometry to simulated data

- 10 spike trains were generated from fully connected 5 neurons and from 5 independent neurons. In scenario (A), the connection strength within the cluster was modified. In scenario (B), the external inputs to all 10 neurons were modified.
- In both scenarios (A) and (B), the clustering method successfully identified the connected subgroup.
- Information geometry was then applied to the clustered neuron groups. The method successfully detected 'pure' interactions which are independent from firing rate modulation. In addition, the method was able to identify possible changes (i.e., modification of connection strength and external inputs) that take place at the network level. In general, if the spike trains were not clustered beforehand, such analysis would not be practical.

Scenario (A): Connection strength is modified



Scenario (B): External input is modified



CONCLUSIONS

- **We propose a novel analysis framework for ensemble spike patterns by combining 'spike train clustering' and 'information geometry'.**
- **The clustering method successfully and efficiently identifies a subgroup of neurons that are characterized by partial synchrony. The method dramatically reduces the number of neurons that need to be analyzed.**
- **The information geometric method successfully detects 'pure' neuronal interactions that are independent from firing rate modulation. In addition, the method is able to separate connection strength change from external input modulation.**
- **The proposed approach provides a powerful analysis tool for multi-unit recordings.**

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