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Information geometric analysis for multi-neuronal spike trains
- Estimation of directional interaction and direct/indirect synaptic connections -

Understanding how the brain works is one of the most challenging questions of modern science. It is important not only for expanding the frontier of our scientific knowledge, but also for developing a more effective treatment for neuronal diseases.

The brain is composed of a large number of neurons. Most neurons interact with other neurons via action potentials (spikes), and have the tendency to form cell-assemblies (*1*) that can be organized dynamically through information processing in the brain. To study these group dynamics and their role in cognitive functions, it is important to record simultaneously from as many neurons as possible from behaving animals (*2*). Due to recent technological developments, multi-electrode recordings have become an increasingly widespread tool in electrophysiology, enabling the recording of spiking activity from tens to hundreds of neurons simultaneously (*3*) (see Figure 1).

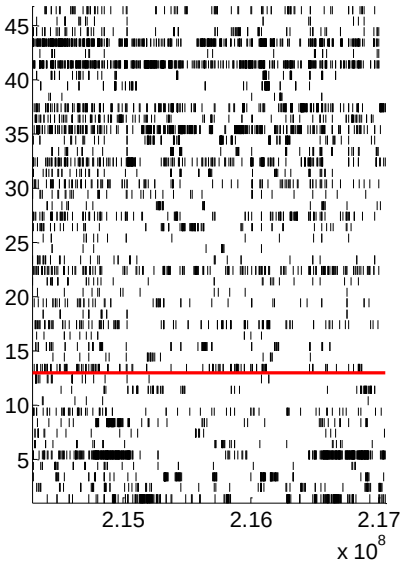

Figure 1: Multi-neuronal spiking activity. The x-axis and y-axis represent recording time (in microseconds) and simultaneously recorded neurons, respectively. Each small vertical bar represents the timing of spikes. The neurons 1 to 12 (below the red line) were recorded from the medial prefrontal cortex. The neurons 13 to 46 (above the red line) were recorded from CA1 of the hippocampus.

Recording from many neurons simultaneously generates a large amount of high-dimensional data. The major challenge is to develop analysis methods that provide information about how the neural dynamics change with experience. This is critical for understanding how information is processed in the brain. Furthermore, since many neuronal diseases exhibit abnormal neuronal activity, this analysis would be beneficial in clinical settings.

Multi-neuronal spike patterns have been analyzed using various statistical methods (*4-15*), but **the quantification of their correlation** and **estimation of possible changes occurring in the underlying neural networks** have remained difficult problems. To this end, information geometry (IG) (*16*), based on the theory of differential geometry, has been proposed as a powerful tool for analyzing neuronal activity (*17-29*).

For **the quantification of correlations between neurons**, the IG approach provides an effective way to estimate interactions independently from changes in the firing rates of neurons (*17, 18, 28*). This property is made possible by the orthogonal decomposition of neuronal interactions by IG, but it is not possible in other conventional correlation measures such as covariance and correlation coefficient (*28*). For the **estimation of possible changes in the underlying networks**, the IG approach provides a direct relationship between the IG measures and the synaptic connection strengths (*20, 25*). Mathematically, it can written as: $IG\ measure \propto (W_{ij} + W_{ji})$ where W_{ij} (W_{ji}) represents a synaptic connection from one neuron j (i) to another neuron i (j). Other conventional correlation measures do not have this relationship. This property is especially useful because it allows for estimation of the connection weights from extracellulary recorded spike data (see Figure 1).

The IG approach is a very promising method for spike train analysis. However, two important problems need to be addressed regarding this method.

Problem 1 – The IG measure and a directional interaction
Previous studies (*20, 25*) investigated the relationship between IG measures and the synaptic connections using coincident (lag-zero) spiking activity. That is, the value of the IG measure corresponds to the sum of two connections (as seen above), and it is not able to differentiate a directional effect of connections. By extending the IG method to take into account lagged spiking activities, it is expected that IG is capable of estimating a directional synaptic interaction. Therefore, this extension would make the IG approach applicable for the investigation of the direct causal relationship between neuronal activities.

Problem 2 – The IG measure and direct/indirect synaptic interactions
The result that the IG measure corresponds to the sum of connections was obtained with the assumption that axonal or synaptic delays do not exist between neurons. That is, both direct (mono-synaptic) and indirect (poly-synaptic) influences show up on the target neuron at the same time. This makes it difficult for the IG measure to differentiate between direct and indirect interactions. By analyzing spike trains generated by a neural network model with delayed connections, the time-lagged IG analysis (as seen in Problem 1) with varying bin sizes is expected to differentiate between direct and indirect synaptic interactions. This would allow the IG approach to estimate a change in mono-synaptic (direct) connections which would provide a significant contribution to the study of learning and memory.

To summarize the approaches, these questions can be investigated by using numerical simulations of neural networks. In Problem 1, spike trains are generated by neural network models. We could use a simple binary state neuron model (Hopfield type network (*30*)), spiking neuron model (*31*), or biologically plausible Hodgkin-Huxley type neuron model (*32, 33*), depending on the expertise of the workshop attendees. The generated spike trains will be analyzed by the time-lagged IG method. For Problem 2, we will extend the neural network model to include axonal/synaptic delays. Then we will vary the bin size when we convert spike trains into discrete binary numbers (1 for existence of spikes and 0 for no spikes). The different bin size is considered to correspond to different connection effects. For example, a one to two microsecond bin would correspond to mono-synaptic connections, while a larger bin size would include more poly-synaptic influences.

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