Estimation of inhibitory response latency: the problem of detecting non-spikes

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Response latency denotes the time delay between the stimulus onset and the beginning of the evoked response. It is believed to contain important information for the understanding of the temporal code. In the last twenty years, many methods dealing with latency estimation from experimental data were proposed (e.g. [1], [3]). As in practice the studied responses are mostly excitatory, these methods are usually based on looking for extra spikes evoked by the stimulation or searching for a significant increase in the estimated firing rate. By contrast, the possibility of an inhibitory response has been rather neglected and since it is characterised by suppression of neuronal activity, many common methods, when applied in such a case, give poor results or cannot deal with this situation at all. We aim to illustrate and to extend results presented in our paper [4], where we focused on latency estimation if the applied stimulus is known to evoke inhibitory response.

Our approach modifies the concept used in [5], [6] and [7], thus the derived estimators are based on measurements of the time interval between the stimulus onset and the first consecutive spike observed in repeated trials and do not require whole spike trains like many traditional approaches. This is especially suitable if the response consists only of a few spikes. A fraction of the observed first spikes might be a result of spontaneous activity, which lasts up to the beginning of the response, therefore a reliable estimation method must take this into account. The novelty of our methodology is that instead of identifying spikes evoked by the stimulus, it is based on detecting and analysing spikes, before which at least one hypothetical spontaneous spike was suppressed as a result of the stimulation.

Because we employ mostly the parametric approach, several parametric models are proposed. All of them consider spike trains as stochastic point processes. Specifically, spontaneous activity is described by a renewal process and three different simplified scenarios, what might the intervention cause, are proposed. The key quantity in the models is the time from the stimulus onset to the first subsequent spike. The first class of models assumes that the beginning of the response evokes a change in the distribution of the point process, which is independent of the past spikes. The second class assumes that the stimulus delays the first spike after the beginning of the response by a positive random quantity. The third type of models uses the concept of selective interaction [2], which directly describes the mechanism of spikes suppression, since it models incoming excitatory and inhibitory pulses and states a simple rule how the outcome is generated based on their interaction. In the models, we consider not only latency that is constant across repeated trials, but also allow for latency being a random variable.

Based on the proposed models, the probabilistic characteristics of the time to the first spike (moments, the probability density function, its Laplace transform and the cummulative distribution function) are calculated. They are subsequently utilized when implementing estimation methods, such as the maximum-likelihood method, the method of moments and the method using Laplace transform of a probability density function. Besides these, we found that a nonparametric method proposed in [6] can be easily modified for our purposes, if the latency is known to be constant.

References

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