Statistical method for detection of firing rate changes in spontaneously active neurons

Andrej Blejec

National Institute of Biology

Vecna pot 111, SI-1000 Ljubljana, Slovenia

Abstract

We present a simple statistical method for detection and identification of firing rate changes in spontaneously active neurons. Spontaneously active neurons (such as olfactory neurons) can be, in response to stimulation, either excited or suppressed and thus increase or decrease the spike firing rate. The described method, here called Cumulative Slope Analysis, is based on the detection of changes in slope of cumulative spike time distribution and efficiently detects excitations and suppressions. Using the simulated spike trains we examined the methods Type I error and power in relation to recorded number of spikes, response strength and duration.

Keywords: Spike train analysis; Cumulative distribution function; Firing rate; Spontaneous activity; Olfaction

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1. Introduction

Single olfactory receptor cell responds to chemical stimulation with either decreased (suppression) or increased (excitation) action potential firing rates. Most olfactory receptor cells respond to several different chemical stimuli. To understand the quantitative properties of the olfactory code composed of receptor cell activities, one needs to know the activity of a large number of olfactory receptor neurons. Detection of either excited or inhibited responses of the follower mitral cells is also very important in understanding nerve code of olfactory stimuli in the second layer of the olfactory network.

Here we first present the method, based on the changes of spike times cumulative distribution slopes, for rapid and reliable detection of neuron's firing rate changes. Next we describe the simulated spike trains used to asses method Type I error and power. Then we show some results from studies of olfactory neurons responses

2. Method description

A spike train, shown as a raster plot on Fig. 1., can be considered as a sequence of discrete spike events (or simply events) with occurring times $\{t_i\}$, $i = 1, 2, \ldots, n$. Cumulative distribution function at time t_i is defined as a number of events prior and up to t_i or rank(t_i) = i and is strictly increasing step function changing at times t_i in steps of 1. Cumulative distribution is plotted by plotting rank(t_i) = i as ordinate against event time t_i as abscisa (Fig. 1.). The slope of cumulative distribution changes with density of events and is equal to density of events (per unit time) or firing rate. For each reference

event t_i an *neighborhood* ($W_{i,j}$) is defined as interval (t_{i-j-1} , t_{i+j}] that contains $J = 2j+1$ events and has duration $T_i = t_{i+j} - t_{i-j-1}$. Local linear regression, based on events in neighborhoods $W_{i,j}$ may be used to estimate the cdf slope. At any spike time t_i the regression line slope b_i estimates the density of events at reference time t_i (Fig. 1.).

The distribution of firing rates (slopes b_i) of spontaneous activity prior to stimulus application serves as the basis for comparing activity during stimulus application with basal spontaneous activity. Slopes of the cdf are non-negative so the distribution of slopes during spontaneous activity is positively asymmetric. Quantile values Q_α and $Q_{1-\alpha}$ (for example, percentiles C_5 and C_{95}), can be used to predict expected slopes during spontaneous activity. On the basis of these control limits, three possible decisions can then be made:

a) if firing rates during stimulus application are higher than $Q_{1-\alpha}$ the activity is identified as 'excitation' (E),

b) if firing rates are lower than Q_α the activity is identified as 'suppression' (S), and

c) if firing rates are between the control limits the activity cannot be distinguished from the spontaneous (basal) activity ('no response', N).

The first two decision rules could incorrectly identify a response when none has occurred (Type I error). The last decision rule could also possibly fail to detect a response when one has occurred (Type II error).

3. Rate functions used in Computer simulation

To asses Type I error and power we employed computer intensive analyses of simulated spike trains based on rate functions [2]

$$\rho_{b,A,w}(t) = b + A\beta_{\tau_1,\tau_2}(t - t_0)$$

where b is baseline spontaneous activity firing rate, A measures the response strength as a maximal change of firing rate during response, t_0 denotes the time of response onset. Normalized response function β_{τ_1,τ_2} is defined as

$$\beta_{\tau_1,\tau_2}(t) = \begin{cases} \beta_0(e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}}) & t \geq 0 \\ 0 & t < 0 \end{cases}$$

where $\tau_1 > \tau_2 > 0$ are fall and raise time constants and $\beta_0 = (\tau_1 / \tau_2)^{(\tau_1+\tau_2)/(\tau_1-\tau_2)}$ is normalizing parameter. Function $\beta_{\tau_1,\tau_2}(t)$ is normalized to have a unit maximum value between 0 and its standard width given by $w = \sqrt{\tau_1^2 + \tau_2^2}$ .The family of rate functions $\rho_{b,A,w}$ can be used to simulate excitations (A>0), suppressions (A<0) as well as no change from basal firing rate b (A=0). The temporal extend of respose can be described with w and response relative strength by A/b. Sets of N=100 simulated spike trains for different combinations of parameters b, A, and w were analyzed by the CSA method, programmed in S-PLUS.

4. Simulation results

Fig 2. shows the results of CSA power determination for different combinations of basal spontaneous activity b and response strength A. The power increases with increasing absolute response intensity A (signal), but decreases with increasing basal spontaneous activity b (noise) (Fig 2a). Plotting the same results shows, that power basically depends on relative intensity of response A/b and increases with absolute relative intensity (Fig. 2a). The power of response detection with CSA shows similar pattern for response duration w and increases with increasing response duration w for both, excitations and suppressions.

5. Application to experimental data

Fig. 3 and 4 show the results of CSA application to experimental data. Data were recorded extracelulary from mitral cells in olfactory bulb of goldfish (*Carassius auratus*) briefly exposed to pheromone mixtures [1]. Brief excitation is detected and shown on Fig. 3. while mixed response (suppression followed by an excitation) is shown on Fig. 4.

6. Conclusion

Cumulative slope analysis (CSA) is simple and efficient method for detection of firing rate changes in spontaneously active neurons. Compared to usually used peri-stimulus histograms it avoids problems with binning of data. CSA is able to detect both possible types of responses, excitation and suppression. The power of CSA mostly depends on the relative intensity of response and response duration. The pre-stimulus

recording, on which the control limits are based should contain sufficient number of spikes which means that pre-stimulus recordings should be longer for neurons with low spontaneous firing rate. CSA was successfully used in analysis of responses of olfactory receptor neurons in fishes [1, 3, 4]. The method is implemented in S-PLUS, and is suitable for rapid analysis of batches of recordings.

Acknowledgments

The author is grateful to Tine Valentincic, Peter Sorensen, and Leah Hanson for helpful discussions and provided data. The work was supported by the MSNZ grant J1-3366 and SLO/US-18/2002.

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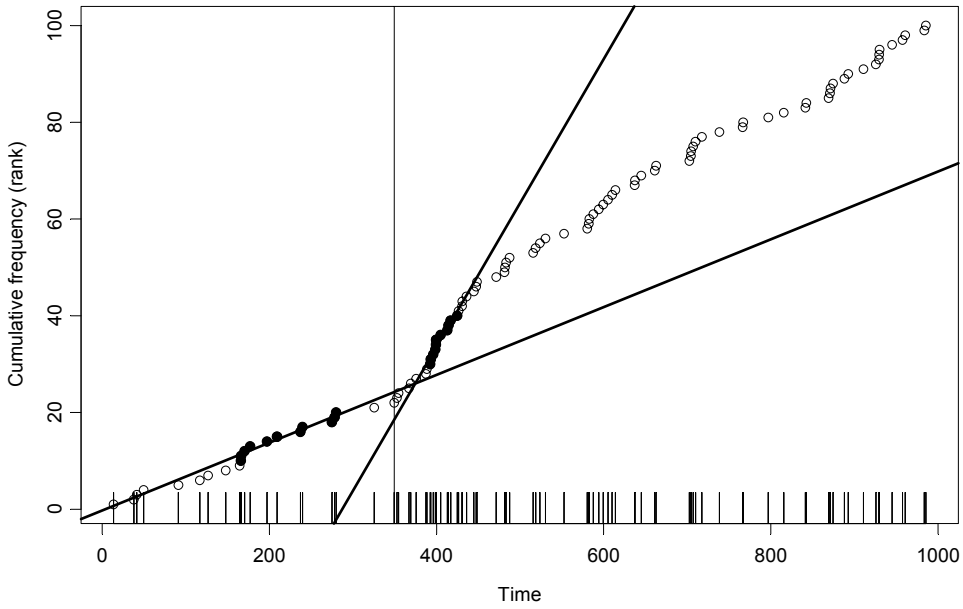

Fig. 1. Cumulative distribution (○) of excitation (simulated data) after stimulus application at time 350 (vertical line). Local linear regression lines (slanted lines), based on neighborhood data (●).

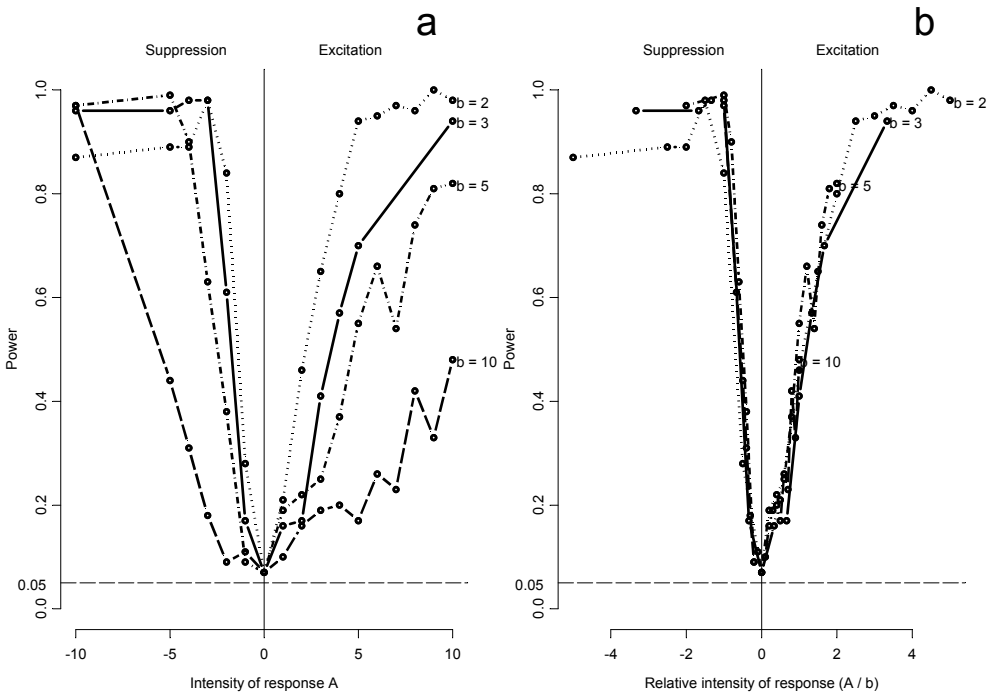

Fig. 2. Power versus strength of response *A* (a) and relative intensity of response *A*/*b* (b) for various basal firing rates *b* = 2, 3 ,5 ,10 and α=0.05 (dashed lines).

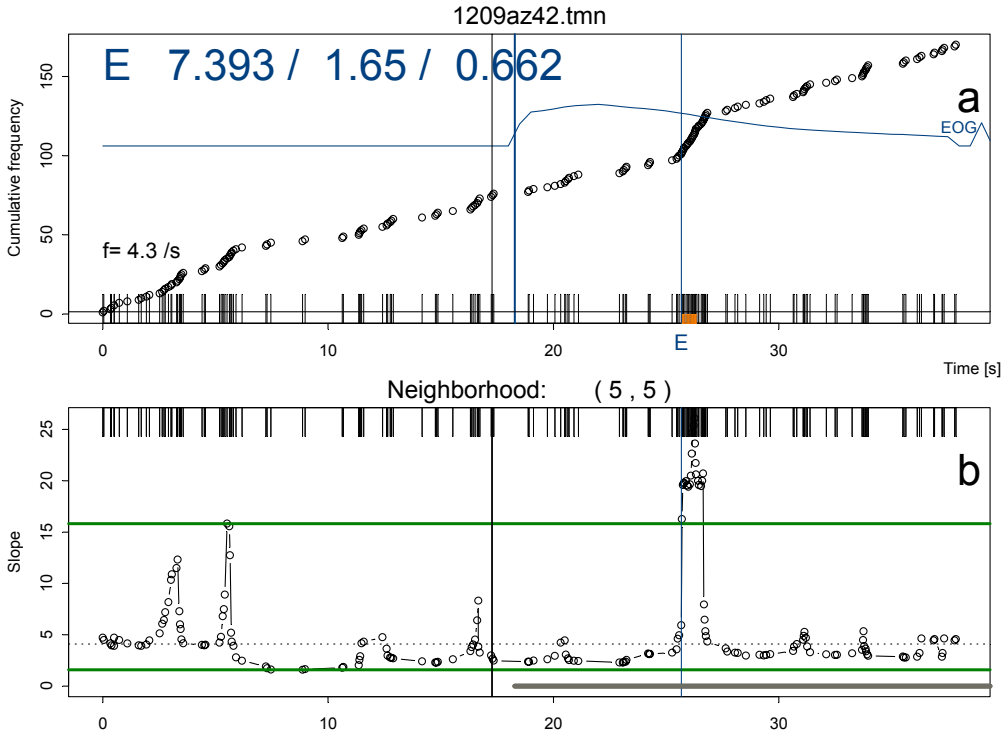

Fig. 3. CSA analysis of extracelulary recording from mitral cell in olfactory bulb of goldfish (*Carassius auratus*) briefly exposed to pheromone mixtures shows excitation (E) 7.393 s after stimulus application, estimated relative intensity1.65, and duration 0.662s. Cumulative distribution (a) and estimated slopes (b) with control limits (horizontal lines) and median slope (dotted horizontal line).

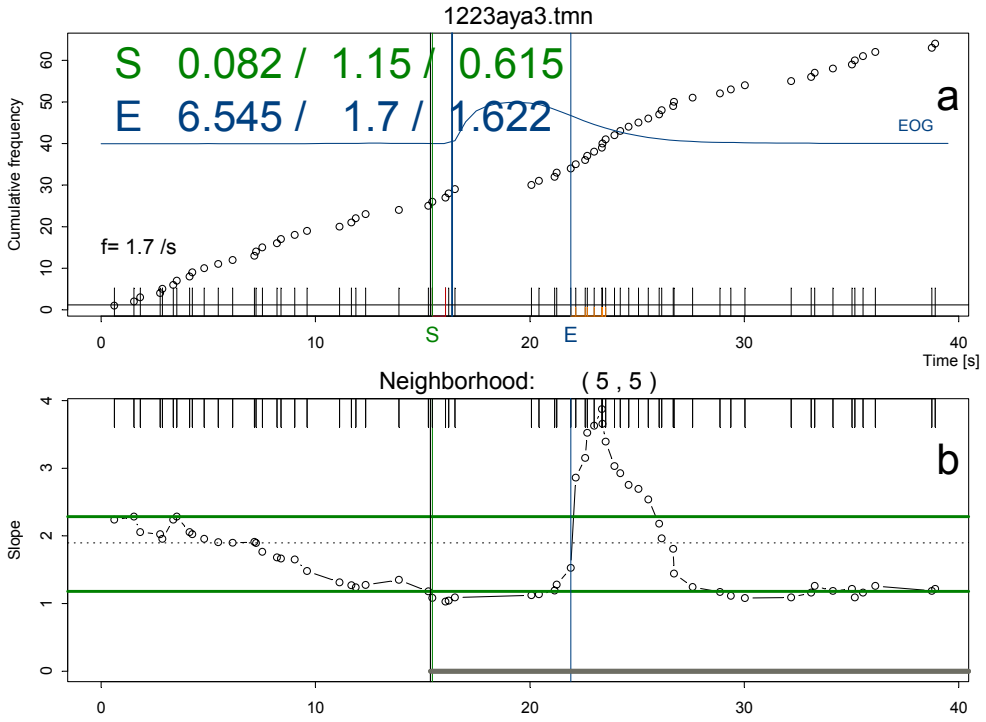

Fig. 4. CSA analysis of extracelulary recording from mitral cell in olfactory bulb of goldfish (*Carassius auratus*) briefly exposed to pheromone mixtures shows suppression (S) 0.082s after stimulus application and excitation (E) 6.545s after stimulus application. Cumulative distribution (a) and estimated slopes (b) with control limits (horizontal lines) and median slope (dotted horizontal line).