Title: A Simulation Model of Neural Activity during Hand Reaching Movement

Authors: Sohrab Saberi Moghadam\textsuperscript{1*}, Mahsa Behroozi\textsuperscript{2}

\textsuperscript{1} Amol University of Special Modern Technologies, Amol, Iran.
\textsuperscript{2} Iran University of Science and Technology, Tehran, Iran.

* Corresponding author. E-mail address: sohrab.saberimoghadam@unil.ch (S Saberi-Moghadam)

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Abstract

Neural response is a noisy random process. The neural response to a sensory stimulus is completely equivalent to a list of the spike times in the spike train. In previous studies, decrease of neuronal response variability was observed in various areas of the cortex during motor preparatory in reaching task. The reasons of reduction in neural variability (NV) is unknown whether it could be influenced by increasing the firing rate or it might be a result of the intrinsic characteristic of cells during the reaction time (RT). For this purpose, a neural response function with an underlying deterministic instantaneous firing rate signal and a random Poisson process spike generator is simulated in this paper. Neural simulation can help us understand relationships between complex data structures of cortical activities and their stability in details during motor intention in arm-reaching tasks. The our measurements showed a similar pattern of results to cortex, a sharp reduction of normalized variance of simulated spike trains across all trials. We also reported that there is a reverse relationship between activity and normalized variance. This study could be applied to neural engineering and brain machine interfaces as a means of controlling external devices such as the movement of a robot arm.

Keywords: Poisson model of neural activity, neural variability, hand movement, cortex.
Highlights

- Simulation of neural spike trains in cerebral cortex during a reach-to-grasp task performed by a monkey.
- Definition of neural mechanisms and trial-to-trial variability in execution of movements by simulation model of spike trains as neural activity and measured normalized variance as neural variability.
- Reduction of simulated neural variability in comparison with similar behavior in real variation of cortical activity after target onset or before movement.

Plain Language Summary:

The brain activities are not identical in repeated trials during the motor preparation and hand movements. This variation of cortical neural responses could be resulted from internal and external properties of individual neurons or neural populations. The stimulus onset reduces neural cortical variability during the hand movement. If this reduction is coordinated to variability in the sensorimotor neural population, then the observational error movement should have represented low values. To understand the mechanism of reduction, the neural response has been simulated as a random Poisson process spike generator with or without noise. The simulation model showed a decrease in variability of simulated neural responses with noise after the target onset but no changes of activity was observed in the absence of noise. The simulation of this mechanism gives a great opportunity for a better understanding of the neurophysiological substrate of the neurodegenerative diseases and mental disorders. The application of neural variability in the prediction of hand movements control could be supportive in brain machine interfaces for stroke patients’ paralysis and even neuro-feedback therapy. The control of hand movement could be modeled in a closed loop neural circuit with added noise and neural variability.
1. Introduction

Cortical cells receive inputs from many sources and the distribution of post-synaptic potentials are Poisson-like (Anderson, Carandini, & Ferster, 2000; Carandini, 2004). The brain activity is inherently variable, as it is its output in the form of motor behavior. The response of cortical neurons to an identical stimulus repeated over time exhibits a large variability in spiking activity. The neural variability (NV) is characterized by the ratio of variance to the mean of spike density function across repeated trials (Churchland et al., 2010; Shadlen & Newsome, 1998; Teich, Heneghan, Lowen, Ozaki, & Kaplan, 1997). Assuming that pure Poisson distribution with an independent information follows the firing rate between spikes, the measured NV equals unity and for contaminated neural spike activity by additive noise the latter being exceed unity (Geisler et al., 2005; Mazurek & Shadlen, 2002; Shadlen & Newsome, 1998). Above all the stimulus-driven neural response as a noisy Poisson activity reduces the neural variability across cortical areas (Churchland et al., 2010). The exponential Poisson distribution of the neural response would be formed to a more regular compact pattern by increasing the firing rate and the refractoriness together (Maimon & Assad, 2009). During delayed reach-task, an increase in the firing rate after the target presentation would present a sharp decrease in variability during motor intention in the dorsal premotor cortex of monkey (Churchland, Byron, Ryu, Santhanam, & Shenoy, 2006). Briefly, researchers design behavioral task for monkeys. Monkeys were trained to sit in a primate chair to perform a set of arm-reaching tasks. Every task consists of several trials and each trial starts with a stimulus onset (for example central spot on the screen) and ended with a juice reward if successful. (Figure 1)
**Figure 1.** The monkey was trained for arm-reaching task. After training, long-term neural recordings in behaving animals were collected for pre-processing.

After designing a behavioral task and training the monkeys for specific experiment, the neural data could be recorded. There are several methods for recording the neural activity. For instance, the extracellular activity was recorded with electrodes (glass-coated tungsten-platinum fibers; 1–2 M_ impedance at 1 kHz) by using a Thomas Recording system.

In our study, the neural Poisson distribution time locked to the target onset is simulated. Indeed, the struggle was the quantification of a relationship between the simulated neural Poisson spike process and the measured neural variability. There are several rate coding methods to measure firing rate of single cells or population activity. The endogenous activity of a time varying cell as a stimulus response is a spike density function (SDF). SDF for each movement direction and cell have been calculated, by firstly, operating spike timing alignments to the onset of the hand movement periods or the target presentation in trials respectively. Secondly, Spikes were replaced by a Gaussian function with a width (SD) of 30ms and a full area of 1. A continuous signal (firing rate) was observed as a result and after the normalization considering the trials numbers, in order to produce the SDF for each cell and movement conditions. To compute the mean firing rate, we also averaged SDFs across trials for each movement direction (Saberi-Moghadam, Ferrari-Toniolo, Ferraina, Caminiti, & Battaglia-Mayer, 2016).

**Method**

**Neural variability measurements**

The first and second order moment statistics were applied to estimate the mean and variance parameters of neuronal responses. The Normalized Variance (NV) which is the time function of trial-to-trial variability, is defined as the variance-to-mean ratio of spike density function across trials. This method is proposed by (Churchland, Afshar, et al., 2006) with the following formula:

\[(1)\]
\[ NV(t) = k \times \frac{\varepsilon + Var(SDF(t))}{k\varepsilon' + Mean(SDF(t))} \]

Where \( \varepsilon = \varepsilon' = 0.01 \) and \( k = 0.1 \).

To prevent the ratio of NV from becoming zero in the dominator in some cases; the constant value \( k\varepsilon' \) was added. Based on the assumption that a neural activity is commonly generated as Poisson process, the mean values of the firing activity and variance are identical and thus NV is unity. This value of fraction could be changed depending on the internal and external states of the individual and population neurons.

**Simulation**

Neural activity of each neuron in contact with the neural network in various areas of the cortex exhibits chaotic patterns, which implies the intrinsic and extrinsic characteristics of that cell. Therefore, in order to detect the characteristics of a cell for repeated trials (in random responses to the same stimulus), firing rates were simulated (equal to SDF) in two types of pure Poisson distribution of firing rates and pure Poisson activities by adding a random noise (noisy Poisson distribution). The aforementioned random noise contains random numbers that follow a Gaussian distribution. The Pure Poisson distribution is a set of Poisson random numbers generating random numbers from the Poisson distribution with an average number of occurrences \( \mu \) over a period. Poisson distribution \( P(X) \) is an event with a small probability of occurrence and a large number of independent trials taking place. The obtained NV has shown different behaviors for each group. In order to use the Poisson spike generator in a simulation, a model neuron is required. The Probability of spikes for a Poisson distribution is:

\[ P(X = k) = \frac{(e^{-\mu} \cdot \mu^k)}{k!} \]

Where \( \mu \) is the average number of spikes per intervals, \( e \) is the Euler's number and the \( X \) parameter is a Poisson random variable that takes non-negative discrete values 0, 1, 2...
Results

Neural variability vs. firing rate

To determine the relation between NV and firing rates, the mean firing rate of simulated activity has been computed firstly. Then the normalized value of neural response was found through calculating maximum value of firing rate. In the next step the normalized value of amplitude of neural response was divided into three levels which are the maximum value of response, (0.8-1)% of maximum value, (0.5-0.8)% of maximum and less than 50% and finally the distribution value of NV related to each level was found.

Figure 2. The different levels of maximum values (spike count from random Poisson spike trains) for each associated neural variability across trials. There is a reverse relationship between the firing rate and normalized variance. The neural variability is declined by increasing the level of firing rate.
Neural variability in DR tasks

The previous studies demonstrate the temporal evolution NV (±, computed across individual cells and target directions) declined significantly in frontal areas after the target presentation or before the movement onset. Indeed. In order to overcome unreliable statistical results across repeated trials, selected neurons and all direction were pooled. The neural signal and neural variability was averaged across all trials and direction. This strength of NV reduction in Frontal lobe could be a result of an increase in activity only within specific time windows that depends on the considered area. In our study, simulated level of neural activity is changing during time course of a behavior (Figure 3). The result demonstrates reduction of variation in time windows. It confirmed that neural variability is a time course of neural activity to predict or code events.
Figure 3. Time course of the simulated spike train (firing rate) and variability in an inhomogeneous Poisson distribution. NV, aligned to the target presentation, is declined by the change in the population neural activity represented in the form of population spike density function or firing rate.

3.3 Simulated neural activity and variability

The simulation in Figure 4 illustrates the neural activity and variability for a neuron with Poisson spiking statistics. An inhomogeneous Poisson model (time varying) is used to generate spike trains for 100 trials and 1ms duration which we showed in raster plots 50 trials in Figure 4.A and 40 trials Figure 4.B. The pure Poisson distribution of spike activities shows linear effects between the variance and mean values of the firing rate that leads to a neural variability equal to one (Figure 4.A & Figure 4.C). If the simulated neural response is contaminated by the random noise with a random poison distribution, the nonlinear effects between the mean and variance cause the NV to become greater than one (Figure 4.B & Figure 4.D). In fact, the NV is sensitive to small changes of contaminated signals and it decreases by increasing the neural activity in a noisy Poisson distribution. This decline results in the change of the activity and the internal states of neurons in the population level of neural networks.

3.4 Neural variability as a predictor of behavior

In Figure 5, a closed loop of neural circuits of a motor plan is shown. In the block diagram the neural variability can be supposed as a disturbance, the motor cortex in spiking neural network controller controls the complex motor information, and the output of motor command decodes the motor intention.
Figure 4. A Poisson model of a spike generator for 100 trials and 1000ms. (A) a raster plot of pure Poisson and (B) noisy distribution (C) Pure Poisson of the firing rate (FR) and the relevant neural variability. There is no change of neural variability (close to unity) even after a rise in the firing rate. (D) Noise contaminated firing rate and the relevant neural variability. In this case the NV increased having more changes after the jumps of the firing rates.

The copy of movement compared with an electrical stimulation (an input of a closed loop system). The neural variability method could be applied in brain machine interfaces to support neurodegenerative diseases such as optic ataxia in human and animal researches to obtain a better understanding of the performance of this closed loop neural circuits in the cortex, a mutual connection between the motor and the parietal cortex.

4. Discussion

No single study has been performed on simulated neural variability to characterize the role of the noise in the brain. This study confirms that the neural variability as an internal-external state of noise in the brain was a function of modulations of trial-to-trial firing rate variability on the single and population level in the parietal, dorsal premotor and motor cortices. In real data, the across-trial variability of firing rates through the normalized variance was measured firstly. In all
the frontal and parietal areas studied, after target presentation a significant decline of NV was observed.

Figure 5. Block diagram of a closed loop neural circuit of the motor planning cortex: The neural variability is a disturbance or noise (target value) in this system and a sensory feedback (forward model) to compare the change status (movement) and the desired motor plan (target position).

The closed loop system in the motor cortex controls the motor plan.

To assess the dependency between the activity and the temporal or non-temporal pattern variability across repeated trials spike trains designed through a random process were simulated where generated Pure Poisson distribution with no change of variability. By adding the noise to signal, normalized variance was increased across contaminated trials. Moreover, the significant increment of the averaged noisy activity (by supposing time locked to the stimulus onset) appeared a predominant impact on relative and absolute refractory periods of neuronal responses and a sharp decline of normalized variance on time patterns. It could be concluded that the neural variability associated to the composition of a motor plan describes the task events and the behavioral performance of the animal in a satisfactory way. Moreover, there is a strong correlation between the neural and movement variability where the NV could predict the temporal evolution of movement planning and behaviors in human. However, the mechanisms underlying the temporal variability of the neural planning in the human motor cortex and its characteristic changes in mental disorders could be related to the neurophysiological substrate of the disorder. By improving this method as a scanner of the neural firing rate in the cortex, other forms of bio-signals in the other areas of the brain might also have potentials as a predictor of the behavior. These results could be related to the neurophysiological substrate of the disorder. To
study this active inhibition notion, active task involvement is necessary to imply an interactive task performance. By improving the therapy with the aforementioned suggestions, other forms of neuro-feedbacks might also have potentials as a treatment for ADHD.

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