Behavior specific rate latency ordering of simultaneously recorded neurons

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Introduction

Rate Latency Ordering

- Previous studies on single cells have revealed much about how the firing rate of individual neurons is modulated by sensory external stimuli and in relation to movement [5]
- For several areas of the cerebral cortex, it is well established that neuron rate latencies have a role in coding information [4, 3]
- Studies based on simultaneous recording have shown the existence of stereotypical sequences of activations (latencies pattern) [4, 3]

Aim of the Analysis

- When neurons in the motor cortex change their rates in relation to motor action, the rate latencies are different across neurons.
- Here we aim to answer the following questions:
  - are single neuron latencies specific to the motor behavior?
  - is the order of the latencies of different neurons consistent across trials?
  - Is that order specific to the motor behavior?

Method: Experiment

Reach to Grasp Experiment [2]

- Two macaque monkeys (N and L) were trained to perform a reach-to-grasp task [2], where the monkeys were required to reach to an object, hold it with a specific grip type (side grip (SG) or precision grip (PG)), and pull it at a specific force level (high force (HF) or low force (LF))
- Behavioral protocol (**Fig. 1**):
  - the monkey initiates a trial (TS) by pressing a lever
  - at $800ms$ after TS (C-ON), CUE is presented for $300ms$ (up to C-OFF), informing the monkey about the grip type (PG or SG)
  - after C-OFF, monkey waits for GO for $1000ms$ (DELAY)
  - GO informs about the force to be applied (HF or LF) and also serves as the go-signal for the monkey to initiate the movement
  - after GO, the monkey releases the lever (SR) and reaches the object (OT)

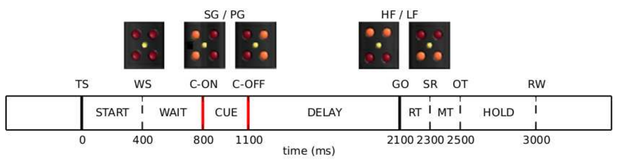

Figure 1. Experimental protocol: Illustration of experimental and behavioral events in a trial of the reach to grasp experiment

Recording

- Multi-channel extra-cellular recordings (Utah array) from premotor (PM) and primary motor (M1) cortices in macaque monkeys
- in the current study, we analyzed the following datasets:
  - monkey N: session i140307
    - 141 trials (35 of SGHF, SGLF, PGLF, 36 of PGHF)
    - 156 single units isolated
  - monkey L: session l101220
    - 144 trials (33 of SGLF, PGHF, PGLF, 42 of SGHF)
    - 107 single units isolated

Method: Single Trial Estimation of Latency

Task: estimation of rate peak latencies on single neuron spiking activity in single trials

Rate estimation: Kernel density

We estimate the firing rate by convolving the spike trains of each neuron with a kernel [7]. This allows both an estimation based on single trials and to obtain the firing rate as a continuous function of time

Rate Change Detection: Threshold Crossing [1]

For detection of the rate change, we first define a baseline period in which we estimate the mean (λ_b) and the standard deviation (SD_b) of the firing rate. These estimates are used to define 2 thresholds: $T_{onset} = \lambda_b + 3SD_b$ and $T_{peak} = \lambda_b + 3.72SD_b > T_{onset}$ (Fig. 2). Using these thresholds, first we detect the intervals within which the rate is above T_{onset}. Then for each interval we check if the maximum firing rate is higher than T_{peak}, and if this interval is longer than a pre-defined time duration (here we used $50ms$). Finally, any intervals satisfying these 2 conditions are considered as significant rate change periods. We define the latency $l^{i,j}$ of neuron j in trial i as the timing of the maximum firing rate within the first detected rate change period (Fig. 3). For each trial i we define the latency vector $\overrightarrow{L}_i = [l^{i,1}, .., l^{i,n}]$ and the population latency as its mean $\mu_i = \sum_j l^{i,j}/n$.

In our application of the method to the data we set the baseline period within DELAY, i.e., between $1100ms$ and $1950ms$ after the trial start. We exclude the last $150ms$ of the delay period in order to avoid the influence of neurons increasing the firing rate before the GO signal.

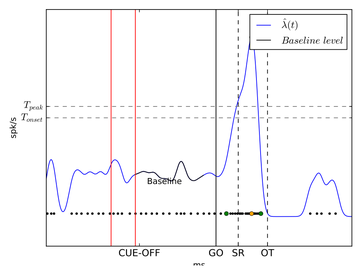

Figure 2. (left) Example application of the rate change detection method to a single trial train (green dots: onset latency and offset, yellow dot: peak latency)

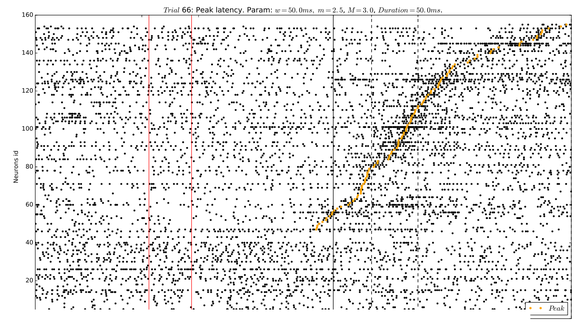

Figure 3. (right) Raster plot for 1 single trials and 156 neurons. For 80/156 neurons a rate change was detected (red dots). The neurons are order on the y-axis according to increasing latency.

Results

Single Unit Analysis

- We consider the cell to be active if we can detect a latency in at least 90% of the trials of same grip condition
- The majority of neurons were active in both PG and SG trials ($42/156$ N, $42/107$ L).
- For cells active in both grip conditions (e.g., figure 4), we ask if the peak latency varies for different grip conditions (2way ANOVA PG vs SG) ($11/42$ N, $16/42$ L, $p < 0.05$)

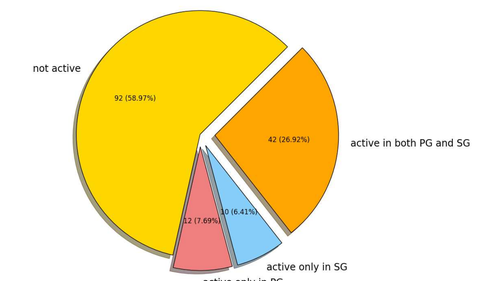

Figure 4. Portion of neurons active in during movement

Rank order correlation in same behavioral condition [4]

- To quantify the similarity of latency order vectors in a pair of trials we use the pairwise Spearman rank correlation coefficient ρ defined as:

$$\rho(\overrightarrow{L}_i, \overrightarrow{L}_{i'}) = 1 - \frac{\sum_{i=j}^{n} d_j^2(\overrightarrow{L}_i, \overrightarrow{L}_{i'})}{n(n^2-1)}$$

  where $d_j = rk(l^{i,j}) - rk(l^{i',j})$ and $rk(l^{i,j})$ indicates the position of $l^{i,j}$ (latency of neuron j in trial i) in the ordered vector $\overrightarrow{L}_i$
- The blue (green) histogram represents the values $\rho(\overrightarrow{L}_i, \overrightarrow{L}_{i'})$, for PG (SG) trials i, i' (same type). The underlying shaded histograms are obtained from trials shuffled surrogates.
- For trials of same grip modality, the distribution of rank similarity values is significantly higher (Mann Wihtney U-test) than the null distribution obtained from surrogates ($p < 0.0001$ N and L)

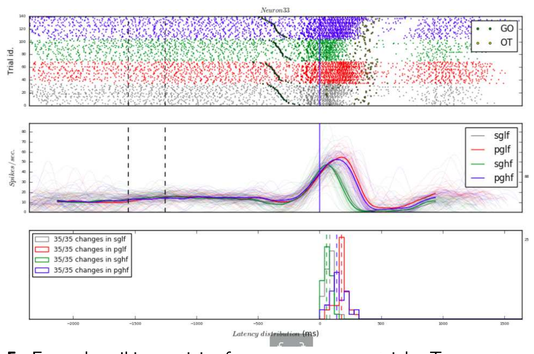

Figure 5. Example spiking activity for a neuron across trials. Top: raster, middle: firing rates, bottom: latency distributions

Rank correlation specific to behavior condition [3]

- The yellow histograms represent the values $\rho(\overrightarrow{L}_j, \overrightarrow{L}_i)$, for PG trials i and SG trials j (different type)
- This distribution seems to be shifted to smaller values compared to the one obtained from values of rank similarity of trials of same type
- The rank order seems therefore specific to the grip: green (blue) vs yellow $p < 0.001$ ($p < 0.001$) N, green vs yellow $p < 0.001$ L

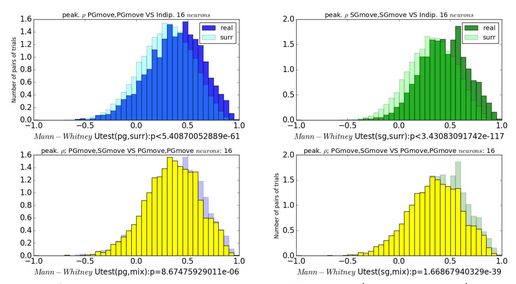

Figure 6. Histograms of Spearman ρ. Top left (bottom right): rank similar (SG) trials. Bottom left and right: rank similarity between PG and SG tri monkey L, right: monkey N.

Conclusion

- About half of the cells show rate changes in relation to grip. One third of those show a specific latency difference with respect to PG and SG.
- The order of single trial neuronal latencies is consistent across same behavior (SG or PG).
- The latency ordering is significantly different in SG and PG. Thus, latency ordering across neurons changes as a function of behavior and cannot merely be a result of neuronal connectivity.

Outlook

- Relating single unit latency and latency orders across neurons to behavioral performance.
- Meta analysis across many sessions of both monkeys.
- Evaluate the specific role of ramping neurons during delay period.

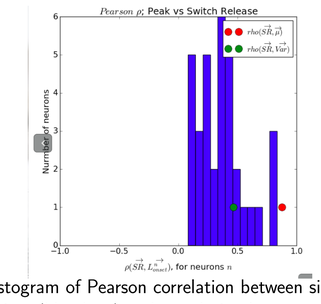

Figure 6. Histogram of Pearson correlation between single unit latency and reaction time (blue bars) and population latency and reaction time

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