Low-frequency local field potentials and spiking activities encode delayed reach-to-grasp task kinematics in primary motor and dorsal or ventral pre-motor cortices

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Electroencephalogram (EEG) is a way to measure electrical activity of the brain but the poor spatial resolution limits us to record activity of a-single neuron. Local Field Potential (LFP) is a technique that by using electrode arrays can record in depth. Using LFPs we can decode each neuron's behaviour and see what is it that each neuron is responsive to. Here we demonstrated that LFPs recorded from Primary Motor and Dorsal-Ventral Pre-Motor Cortices will have a significant low frequency component on the onset of a hand movement of a monkey and an averaged increased firing rate at this onset. We also show that some neurons are responsible for encoding different types of kinematics.

Motor Cortex | Local Field Potential | Reach-to-Grasp | M1 and PMd

1 | Introduction

The local field potential (LFP) is an intracereberal measuring method of brain activity that reflects the neural activities of an specific area in the brain. The LFP is recorded using different configurations, ranging from single-electrode recordings to multi-electrode arrays. In contrast to LFPs, the electroencephalogram (EEG) samples large populations of neurons. A prominent feature of motor cortex field potentials during movement is low frequency local field potentials (1). Also, It has been shown that the reach and grasp kinematics are encoded in the spiking activities recorded from neurons in primary motor cortex (M1) and dorsal pre-motor cortext (PMd) (2). Previous studies has reported hand and finger kinematics are accurately encoded in LFPs from M1 area. There are also different other patterns that are reported to be encoded in the LFPs of this area like different grasp types. In this study, we have been evaluating if grasp type and grasp force is encoded in LFPs of M1 or not in a reach and grasp task on a Macaque Monkey.

2 | Results

As the data is collected from motor cortex, we are expecting to get a significant difference when the Monkey do a motor activity. In our experiment (see the "Methods" section for details), the Monkey moves his hand to grasp at the SR-ONSET. So our time of interest is around SR-ONSET.To test our hypothesis, various techniques are used which we will go over their results step by step.

2.1 | Raster Plot Raster Plot is a technique to show spike times of neurons during a period of time. As you can see (Fig.1), the firing rate of some neurons increase after the SR-ONSET and some neurons' firing rate don't change. Here we probably can get that some neurons are more responsible for encoding. we will study this more accurately on next sections.

2.2 | PETH Pre Event Time Histogram (PETH) is a tool to plot the firing rate of some neurons during a period of time. Supporting the Raster Plot report, we can see increased firing rate after SR-ONSET (Fig.2). The PETH plot is calculated using a moving window with a length of 300 samples and averaged on all 271 neurons over one trial. We can also average over all trials which will remove some noisy artifacts but since the SR time is different for the trials and we wanted to have a PETH over all of the trial time, we did not do averaging over trials in this part. We will see an average PETH over trials in next sections.

2.3 | ISI Interspike Interval (ISI) distribution of a neuron is plotted and as you can see they have a gamma distribution (Fig.3). The refractory period is the reason of this gamma distribution. As we know, a neuron can't fire faster than a maximum rate since the biological process of the Na^+ Channels require a time to go to its normal state. But in the second plot (Fig.3), we can see that the exponential distribution is a good approximation for the ISI and due to that, neuron's firing is a Poisson point process.

2.4 | Hypothesis As the Raster Plots and the PETHs reported, it seems that the firing rate of the Motor Cortex neurons will be increased at the SR-ONSET for a while. Since the task is a motor task and we are acquiring data from motor cortex, it is logical to say we have more activity at the SR-ONSET. But are we sure? Can we only accept this hypothesis from 2 raster plots and PETHs? No, we should do a statistical analysis (t-test, (3)) and reject a null hypothesis. So, the null hypothesis will be "Motor Cortex neurons' activity won't increase after the movement of the Macaque's hand (SR-ONSET)". Since on the other event's, the Macaque is held steady and doesn't have any movements, we don't see any significant difference and actually before the SR event would be our baseline from now on.

2.5 | Statistical Analysis In order to accept our alternate hypothesis, we have to reject the null hypothesis which we defined in part.2.4. To do that, we are going to use Student's t-test. At first, we calculate the firing rate over all neurons in the baseline period. Baseline starts at TS-ONSET and continues up to SR-ONSET on each trial. Then, the firing rate over all

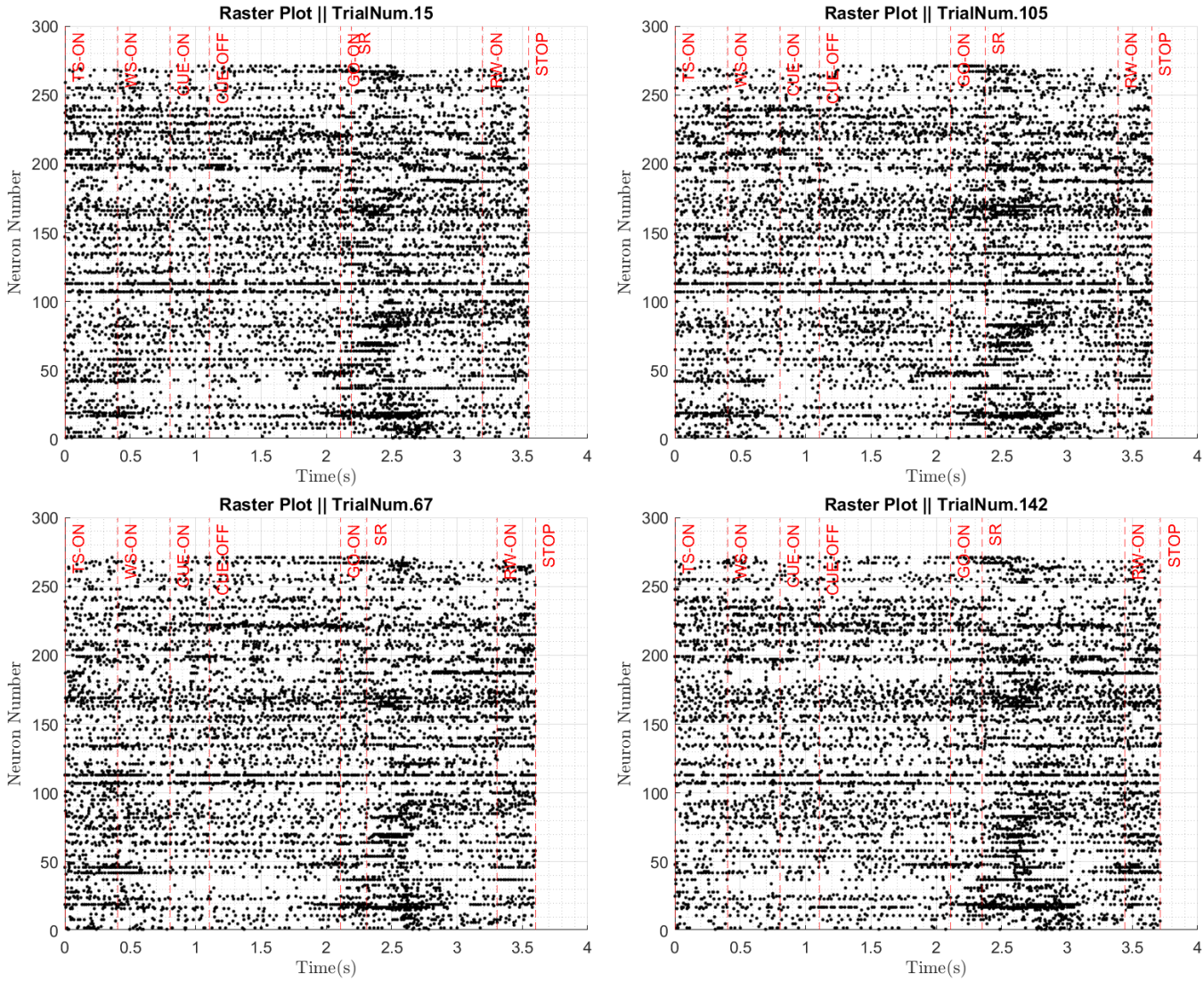

Fig. 1. Raster Plot for all 271 neurons for 4 different trials

neurons is calculated at the period of interest (SR-ONSET to RW-ONSET). Then we run a two-sample t-test on both distributions to check whether they are same distributions or not. As you can see the distributions (Fig.4), they seems completely different distributions. The null hypothesis

df=141	Critical t-value	t-value	p-value(0.95)
1. t-test	1.65	75.43	7.34e-116

t-test result

2.6 | Statistical Analysis on Fano Factor Fano Factor is a measure of dispersion. Here we calculate averaged Fano factor on all neurons for each trial. If we run a t-test on the two distributions, it will tell us that these distributions are different (Fig.4). As you can see in Fig.5, trials on SR-ONSET have more Fano factor values. It is logical since we have more dispersion in SR-ONSET window to the RW-ONSET. It's because neurons have both high firing rate and baseline firing rate in this period.

df=141	Critical t-value	t-value	p-value(0.95)
1. t-test	1.65	-20.6	2.38e-44

Fano Factor t-test result

2.7 | Encoding Up to now, we have shown that motor cortex neurons will have an increased averaged activity after hand movement of the Macaque (SR-ONSET) but do all of this neurons act like each other? The answer is no! We probably have different neurons acting differently. Some neurons can just have a baseline firing rate and don't even change its behaviour at the SR-ONSET. Some neurons will decrease their firing rate at the SR-ONSET, Also, there are some neurons that just response to one kinds of the trials (see the "Methods" section for details). The goal of this part is to find neurons responsible for encoding these 4 kinds of trials. To show this, we use different methods such as Raster Plot, Firing Rate Plot and PETH.

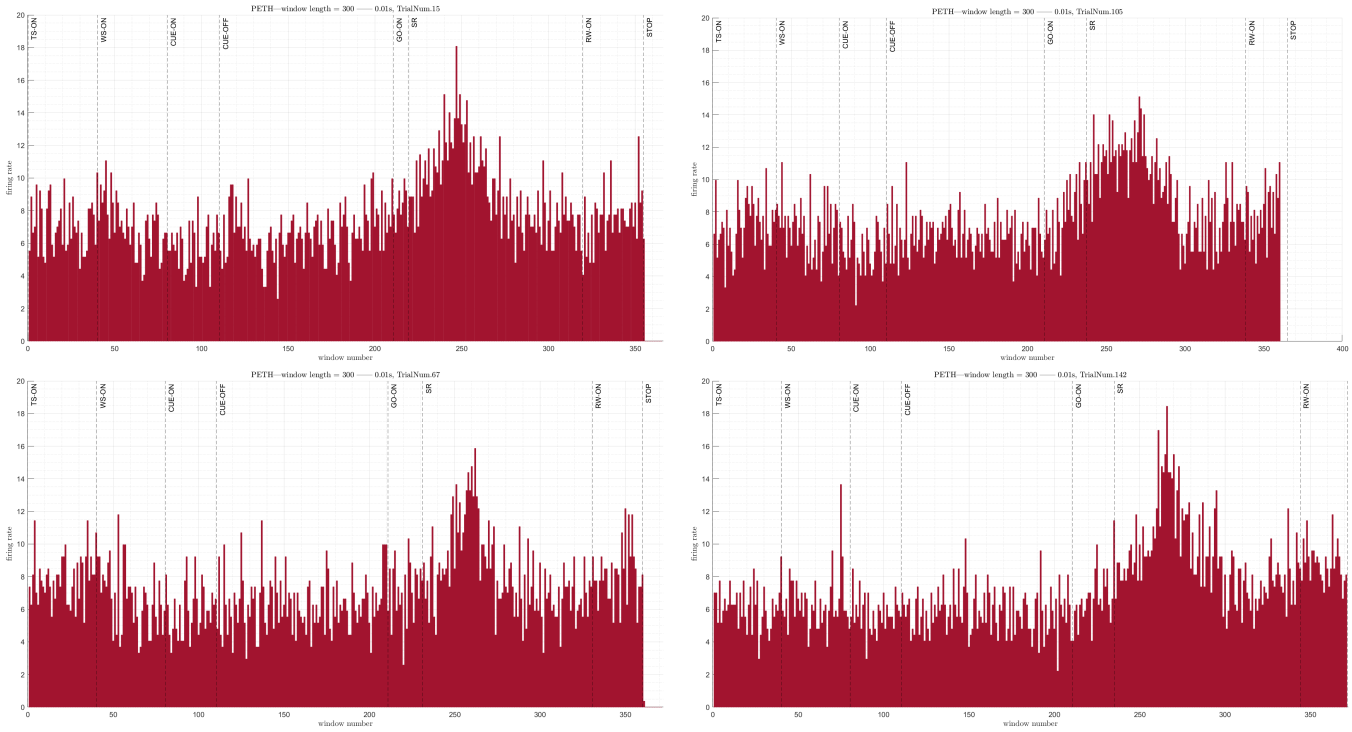

Fig. 2. PETH over all 271 neurons on 4 different trials

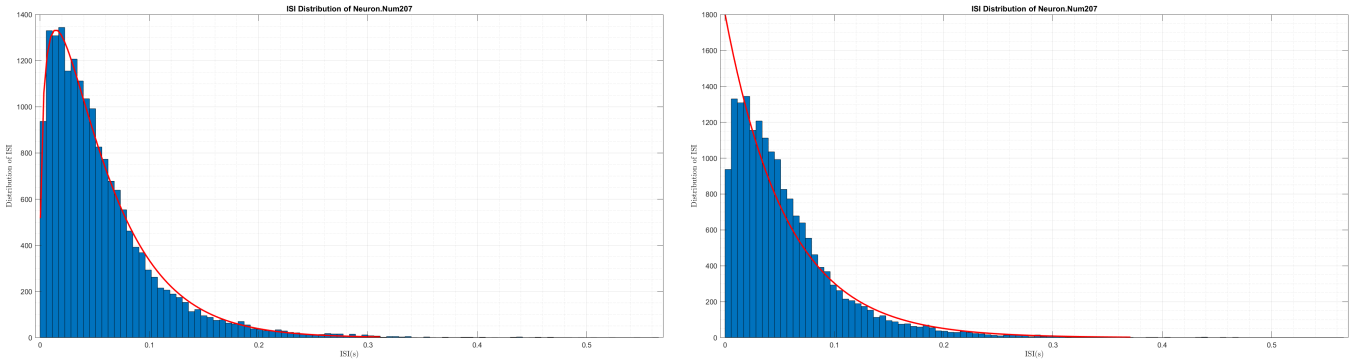

Fig. 3. ISI distribution and fitting

2.7.1 | Encoding-RasterPlot Here we plot Raster Plot on 4 different trials with different kinds (Fig.5). As you can see, at the SR-ONSET, not all neurons act like each other. If we focus more on the plots, we can see that some neurons will increase their firing rate for just some kinds of the trials but it‘s not recognizable with direct eye. So what we are going to do is to plot firing rate of each neuron averaged on all trials just in the window of interest (SR-ONSET to RW-ONSET) to remove artifacts.

2.7.2 | Encoding-Firing Rate plot To remove artifacts and get a better visualisation, we did averaging on window of interest of all trials of 4 kinds. (Fig.6) shows the firing rates. As the figure shows, it seems that the neuron number 17 is responsible for separating "PG-SG" trials and encoding "PG"s and neuron 113 is responsible for separating "HF-LF" trials and encoding "HF"s.

2.7.3 | Encoding-PETH Another thing that we can do, is plotting firing rate of the neuron 17 and 113, averaged over all trials from 0.5 seconds before SR-ONSETs to 1.5 seconds after SR-ONSETs. As the firing rate of the neuron 17 is showing, it is clearing doing encoding for "PG"s but the plot of neuron 113 won‘t tell us anything as maybe it is not a good method to show the difference between the different kinds of trials.

2.8 | Time-Frequency Analysis of LFP signals Using Morse wavelet transform on averaged LFP signals on each 4 kinds of trials and all 96 channels, we get the time-frequency response of LFP signals. After baseline normaliztion, we plot the wavelet transform of the averaged LFP of each kind (Fig.8). The result report low frequency (f $<$ 10Hz) high activity after the SR-ONSET which supports the reports from other literature. As we can see, "LF" trials have more magnitude in the time and frequency of interest. This can be a feature work

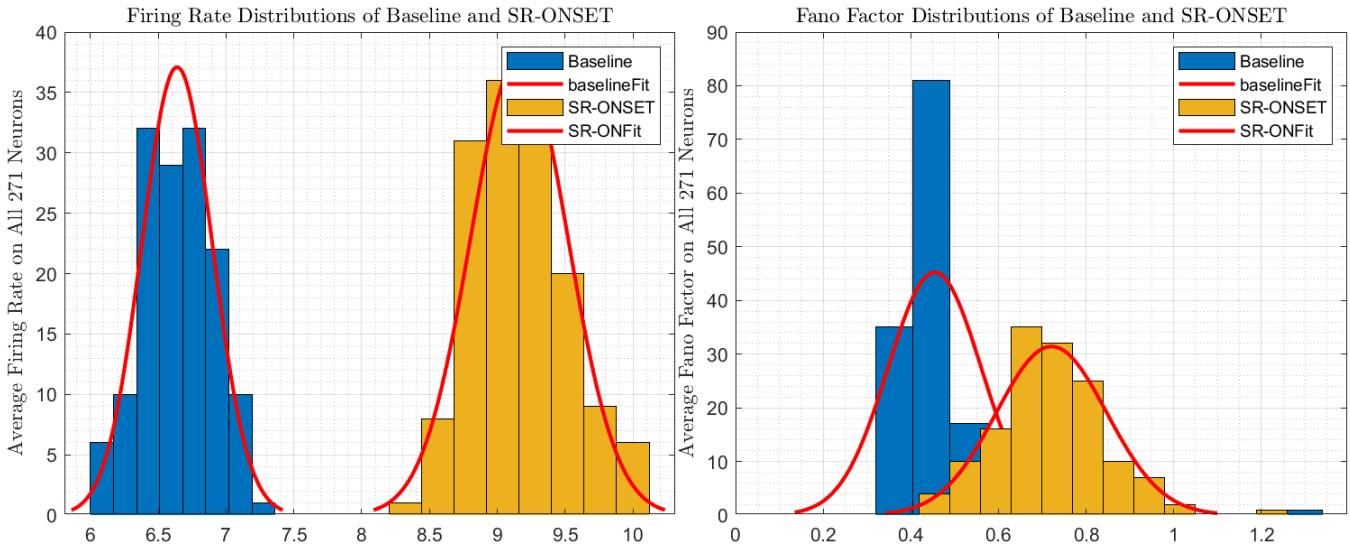

Fig. 4. t-test results for a. Firing rate and b.Fano factor, baseline vs SR-ONSET

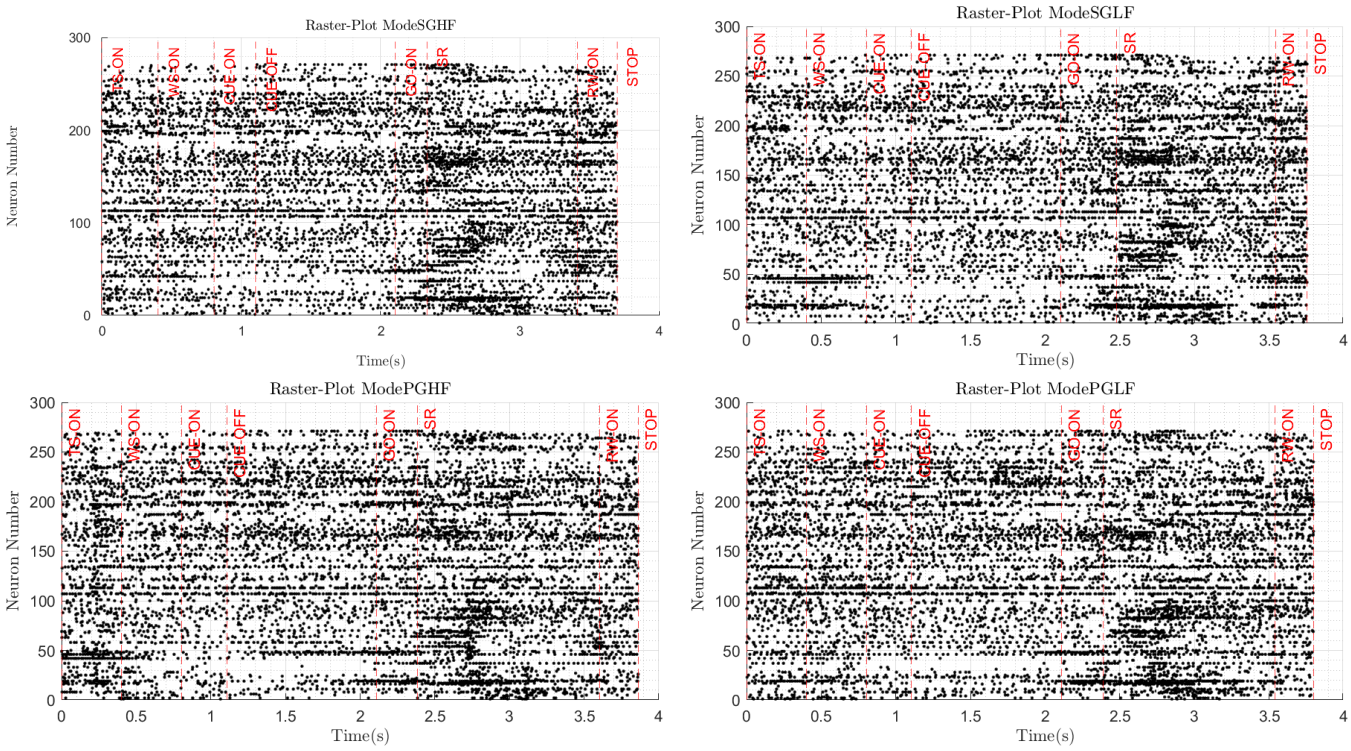

Fig. 5. Raster plot for all 271 neurons over 4 different types of trials

that why "LF"s have lower magnitude than "HF"s in the time and frequency of interest? Do they have a reverse connection?

3 | Materials and Methods

3.1 | Subject All animal procedures were approved by the local ethical committee (C2EA 71; authorization A1/10/12) and conformed to the European and French government regulations. We here just did analysis on the male monkey which were trained to do the delayed reach-to-grasp task for reward (apple sauce). The training of the monkey finished when he did the task in more than 85 percent of the trials. (4)

3.2 | Data Acquisition Data is recorded from motor cortex (Fig.9) of a Macaque Monkey using implanted 10×10 electrode arrays with a sample rate of 1 KHz during reach-to-grasp task. The electrode array was implanted along the central sulcus and overlapping the putative border (dotted line) M1 and PMd or PMv of the right hemisphere. (4)

3.3 | Dataset The dataset include LFP signal of 96 channels with a sampling rate of 1KHz and time of spikes of

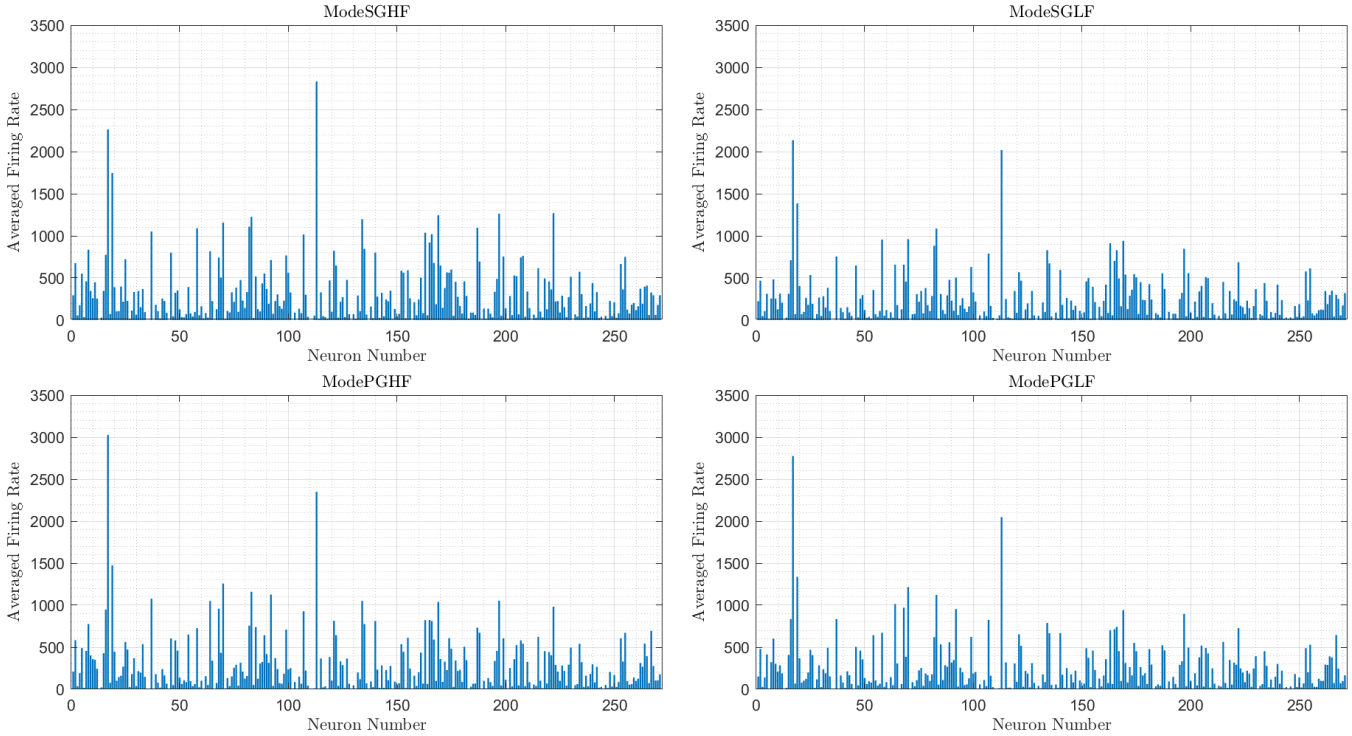

Fig. 6. Averaged Firing rate of 271 neurons on SR-ONSET window over all trials

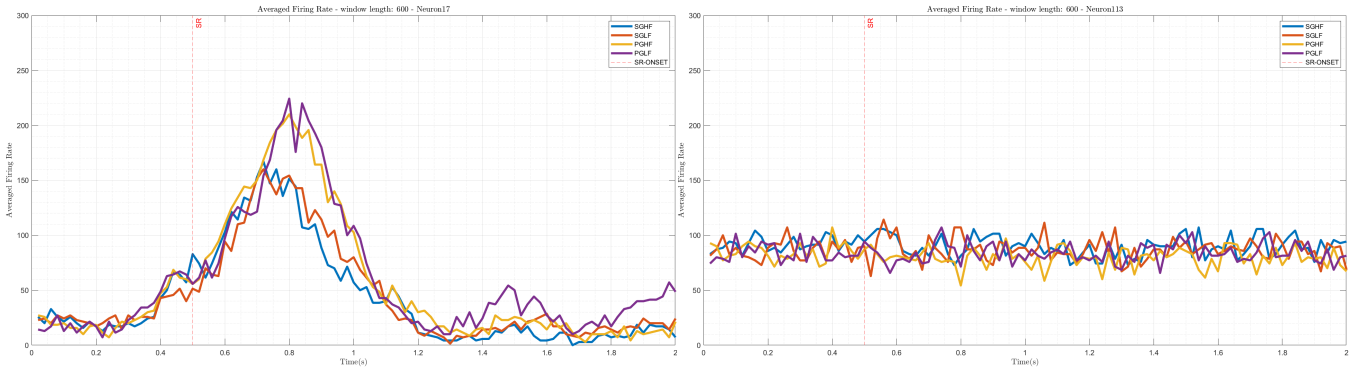

Fig. 7. Firing rate of neurons 17, 113 in window time of interest

271 neurons covered by the 10×10 electrode arrays with a sampling rate of 30KHz. Some of the events in dataset were errors that were removed at the beginning of the code. The preprocessed dataset is available in the zip file alongside this paper. Also, there were some trials without RW-ON event which are stored in another variable in case they were needed for feature works and we didn't use them in our analysis. At total, we have 142 trials.

3.4 | Task During each trial, the monkey had to grasp the object using a side grip (SG) or a precision grip (PG). In "SG", monkey places the tip of thumb and lateral surface of the other fingers were placed on the right and the left sides of the object. In "PG", monkey places the tips his index and thumb in groove on the upper and lower side of the object. The monkey had to pull the object towards him against one of two possible loads requiring either a high or low pulling force (HF and LF, respectively). So the monkey had to do four different types of trials (SG-LF, SG-HF, PG-LF, PG-HF). Monkey were ordered to do each type of the trials before the SR-ONSET by some LEDs. TS-ON label is the start of the task, and then after 400ms, we have WS-ON which is the start of the trail. Then, we have the CUE-ON and CUE-OFF which specifies the "PG-SG" for the monkey which it lasts 300ms. Then, we have GO-ON which specifies the "HF-LF" for the monkey and after that we have SR-ONSET that the monkey can moves his hand to do the task and after that gets reward at the RW-ON and WS-OFF is the end of the trial (Fig.10). (4)

3.5 | Analysis In this research we used raster plots, PETHs, firing rate plots and time-frequency analysis using Morse wavelet transform and baseline normaliztion.

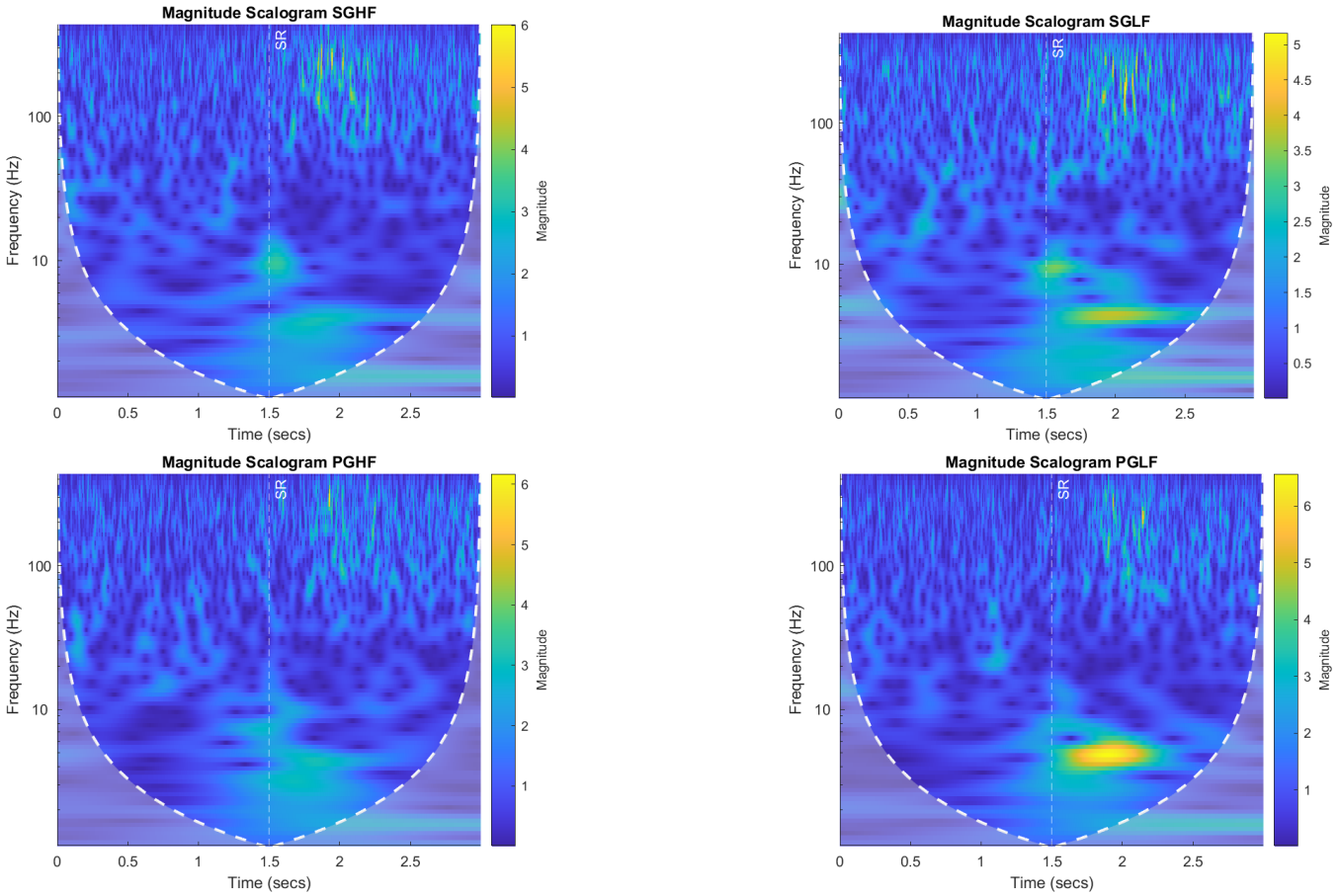

Fig. 8. Magnitude of the wavelet transform of LFP signals over all trials and neurons for four different types of trials

4 | Discussion

Motor cortex is an area in cerebral cortex of the brain which is involved in the planning, control, and execution of voluntary movements. In this research, we showed that at the onset of a voluntary movement (grasping), the neurons in M1 and PMd area covered by our electrode arrays, will have an increased firing rate. We also showed that all the neurons don't have the same behaviour and each of them do a specific thing. As in this research, Some neurons are responsible for "SG-PG" encoding of the movement and some are responsible for "HF-LF" encoding. Some neurons are just sensitive to movement, no matter what type of movement it is going to be and some will have decreased firing rate after movement. We also show that LFPs recorded from motor cortex neuron will have an low frequency at the SR-ONSET.

Maybe one of the shortcomings of our approaches is in analysis that we have used moving windows which may have caused missing of some details. By the way, our results including neurons responsible for type of movement and low frequency components are supported by previous papers' works which you can find those papers in references.

Analysing why the frequency component, in the window of interest in time-frequency response of "LF"s are stronger than "HF"s can be a future work. We can also include different types of movements and find other neurons responsibilities. As we know, neurons can handle more than one responsibility and maybe in future works we can detect new responsibilities even for neurons that we know what they do!

References

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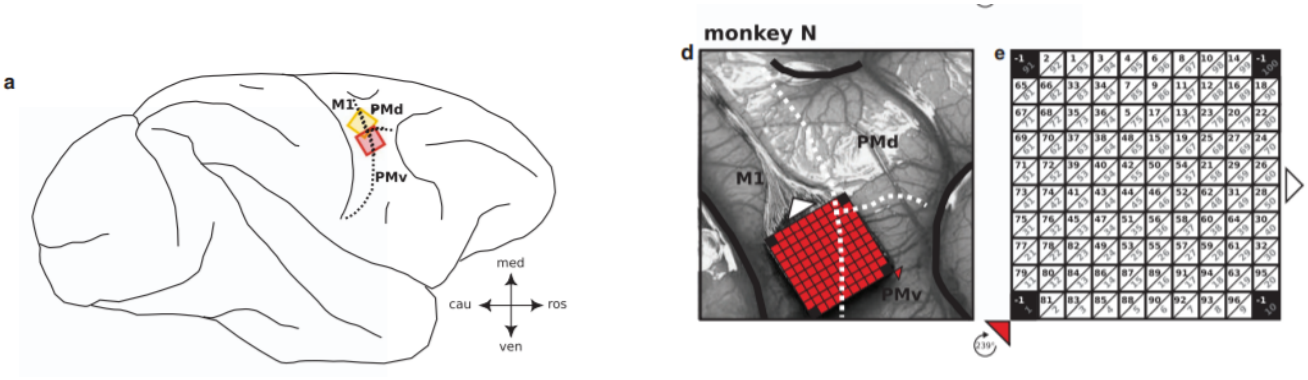

Fig. 9. Electrode Placement

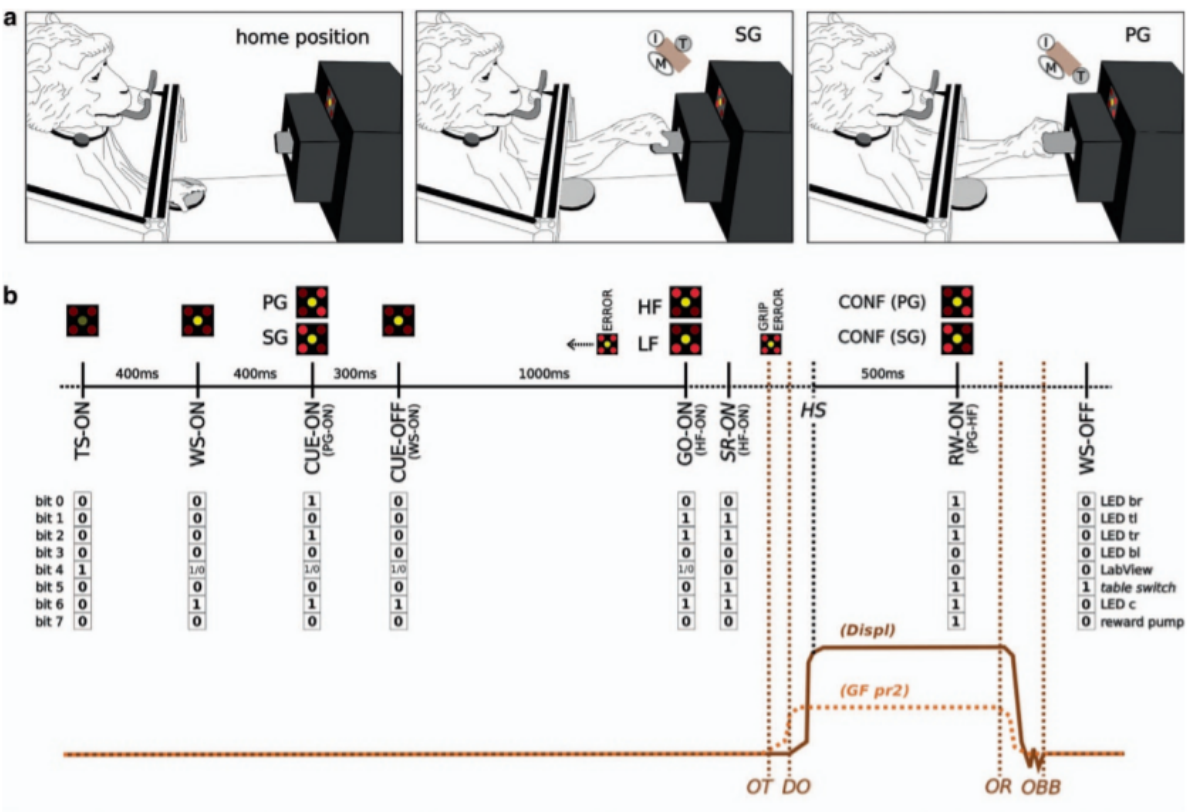

Fig. 10. Reach-to-Grasp motor task timeline