Rotational dynamics versus sequence-like responses

Mikhail A Lebedev[1,2]

[1]Center for Bioelectric Interfaces of the Institute for Cognitive Neuroscience of the National Research University Higher School of Economics, Moscow, Russia

[2]Department of Information and Internet Technologies of Digital Health Institute, I.M. Sechenov First Moscow State Medical University, Moscow, Russia

Abstract

In a recent review, Vyas et al. commented on our previous observations regarding the presence of response sequences in the activity of cortical neuronal population and the contribution of such sequences to rotational dynamics patterns revealed with jPCA. Vyas et al. suggested that rotations generated from sequence-like responses are different from the ones arising from empirical neuronal patterns, which are highly heterogeneous across motor conditions in terms of response timing and shape. Here we clarify our previous findings and present new results showing that empirical population data contain plentiful neuronal responses whose temporal structure persists across conditions. The more complex, heterogeneous responses also contain temporal structure that persists within clusters of conditions. Both consistent and heterogeneous responses contribute to rotational dynamics; therefore, these contributions should be considered when interpreting population rotations. Overall, we do not see any principal contradiction between the neural population dynamics framework and our results pertaining to sequence-like responses. Yet, questions remain regarding the conclusions that can be drawn from the analysis of low-dimensional representations of neuronal population data.

Introduction

Last year, we published an analysis (Lebedev, Ossadtchi et al. 2019) of multichannel recordings of single-unit activity from monkey motor cortex, which Churchland, Shenoy and their colleagues had made available online (https://www.dropbox.com/sh/2q3m5fqfscwf95j/AAC3WV90hHdBgz0Np4RAKJpYa?dl=0) and which they had originally used to develop the concept of rotational dynamics – a fundamental type of neuronal processing in many species according to their theory (Churchland, Cunningham et al. 2012). In the rotational dynamics approach, multidimensional neuronal data are processed with a linear transform, called jPCA, that generates a set of circular trajectories, one trajectory per condition. (Each condition corresponds to an arm reaching movement with a unique path.) If the rotational components obtained with this method account for a substantial percentage of variance in the data, this is taken as a proof that the neuronal population acts as a dynamical system:

$$\dot{X} = M_{skew}X \tag{1}$$

where X is a six-dimensional vector of principal components obtained from neuronal population activity, $\dot{X}$ is its time derivative. Matrix M_{skew} has imaginary eigenvalues, which corresponds to a rotation of X around the center of coordinates (Garfinkel, Shevtsov et al. 2017).

Given that Xrotates, its coordinates are oscillating functions of time, and there is a temporal lag (or phase shift) between these functions. In our previous article (Lebedev, Ossadtchi et al. 2019), we hypothesized that similar temporal lags could be present in the neuronal population data before it has been processed with jPCA. To

test this hypothesis, we plotted population perievent time histograms (PETHs) for different conditions, where neurons were sorted by the time of peak activity taken from the cross-condition average PETHs. With this simple procedure, we found a temporal sequence of neuronal responses during the arm reaching task. This sequence persisted across 108 conditions with some variability (see Figure 2 in Lebedev, Ossadtchi et al. (2019)). Based on this observation, we argued that sequence-like responses could be the cause of the rotational dynamics revealed with jPCA. To tackle this idea further, we showed that rotational patterns could be easily obtained with jPCA from a rather arbitrary simulation of neuronal responses that incorporated a requirement that the responses be arranged in a temporal sequence but did not mimic any representation of movement. We concluded that jPCA reveals sequence-like dynamics in neuronal population data, but we were skeptical regarding Churchland's claim that this method elucidates a fundamental mechanisms of cortical motor control.

Recently, the Shenoy group published a new review on neural population dynamics (Vyas, Golub et al. 2020) where they covered rotational dynamics and commented on our article. These comments prompted us to provide several clarifications and to conduct additional analyses.

Empirical observations versus modelling

In their review, the Shenoy group wrote (Vyas, Golub et al. 2020):

> *"While it is possible to obtain rotation-like features from non-dynamical models [e.g., sequence-like responses (Lebedev et al. 2019)], such rotations are dissimilar from those observed empirically (Michaels et al. 2016)."*

Here, we would like to clarify that we did not advocate any non-dynamical model that would oppose the dynamical-system framework of Shenoy and his colleagues. In fact, we did not propose any physiologically plausible neuronal model at all, which is very different from the simulations run by Michaels, Dann et al. (2016) where they compared representational and dynamical models. We started with analyzed Churchland's data (i.e., empirical observations), where we found evidence of sequence-like responses. This finding is not new; several previous studies reported similar neuronal patterns (Georgopoulos, Kalaska et al. 1982, Luczak, Barthó et al. 2007, Lebedev, O'Doherty et al. 2008). What is novel is the observation that response sequences are preserved across different movement conditions. This is somewhat surprising for motor cortical activity, which typically closely matches movement kinematics. It is tempting to interpret such sequence of motor cortical responses in terms of consecutive processing stages, but we also think that the dynamical-system explanation proposed by the Shenoy group has merits.

As to the comparison of representational and dynamical models conducted by Michaels, Dann et al. (2016), we consider their work an effort in the right direction but we have little to add to this topic simply because we did not examine how the neurons in Churchland's dataset encode motor parameters. (And we could not because the dataset does not contain kinematics data.) Yet, there appears an important point of agreement between us and Michaels and his colleagues, as they concluded that "incorporating variable latency offsets between neural activity and kinematics is sufficient to generate rotational dynamics at the level of neural populations". The same judgment was expressed by the reviewer of our manuscript who wrote that it was obvious that "state-space rotation is equivalent to a preserved sequence of neural activity". Since there appears to be a consensus on the issues of sequences producing rotations and sequences being present in empirical data, we suggest that "sequence-like responses" should not be considered as something completely different from a "dynamical model" or an "empirical observation". We instead suggest that an investigation of response sequences should be viewed as a complementary analysis to the population methods that reduce data dimensionality, such as jPCA.

Looking into how response sequences (taken from experimental data or simulated) could be helpful to validate the results obtained with jPCA and similar methods, which are often hard to interpret. For instance, we described cases where there was a clear sequence in neuronal responses but jPCA did not return rotations because

it incorporated a subtraction of cross-condition mean response (Lebedev, Ossadtchi et al. 2019). Algorithmic components of this kind could significantly alter the results an mislead a researcher that relies exclusively on a complicated population analysis. For instance, Michaels, Dann et al. (2016) permutated their data and then generated rotational patterns – a procedure that could have resulted data that was ill conditioned for jPCA. Yet, they drew their conclusion from the state-space plots.

Consistent versus heterogeneous responses

The second point made by the Shenoy group was the following:

> *Perhaps more critically, the hypothesis of sequence-like responses does not account for single-neuron responses, which are typically multiphasic and/or peak at different times for different conditions (e.g., Churchland et al. 2012, figure 2).*

Figure 2 in Churchland, Cunningham et al. (2012) indeed illustrates ten neurons (selected from the data of four monkeys) whose responses are variable across conditions. Yet, one can notice in the same figure (also see their Supplementary Figure 11a) that the responses of the illustrated neurons contain groups of responses that are consistent for a cluster of trials and sometimes become inverted (e.g. inhibition versus excitation) for another cluster of trials while the response time does not change. Such clusters of trials could contain response sequences that are then converted into curved trajectories by jPCA. (We did not examine this possibility, but it could be assessed in the future.) As to the multiphasic responses, the way they are handled by jPCA depends on many factors, most importantly on the correlation between the neurons in the population. For instance, one response phase could be highly correlated with the responses of other neurons, so it will be emphasized by jPCA. Overall, we agree with Shenoy and his colleagues that the contribution to rotational dynamics from the neurons with high variability across conditions is an interesting issue, but we doubt that the activity of these neurons is completely void of sequences. While this issue deserves a separate analysis, neurons with high cross-condition variability introduce only a small "noise" in the otherwise consistent sequence of neuronal responses visible in Churchland's data (see Figure 2 in Lebedev, Ossadtchi et al. (2019)).

Neurons with high cross-condition variability are only part of the story. Neurons with consistent responses are the second part. To identify these neurons, we quantified cross-condition consistency of PETHs as the correlation for pairs of PETHs from different conditions. This metric detected similar PETH shapes (i.e. similar response times) while ignoring the differences in amplitude. We calculated the correlation coefficients for all possible PETH pairs and then used the mean of these values as a measure of consistency for each neuron. The mean correlation coefficient ranged from 0.03 to 0.99 for different neurons (N=218), with the median of 0.41. Figure 1 illustrates top twenty neurons with the best consistency by this metric. Mean correlation coefficient was greater than 0.90 for all of them. PETHs for individual neurons (Figure 1A) confirm that the shape of responses was highly consistent across conditions. Furthermore, after these neurons were sorted by the time of peak response, their population PETHs revealed a temporal sequence that was preserved across conditions (Figure 1B). Peak response time was under 150 ms relative to movement onset for these neurons. jPCA with (Figure 1D) and without (Figure 1C) mean PETH subtraction revealed rotations. The rotations were similar for all trials when mean PETH was not subtracted, and two clusters of curved trajectories (colored red and green by Churchland's script) occurred when mean PETH was subtracted. We previously expressed concerns about the subtraction step (Lebedev, Ossadtchi et al. 2019), so it is not clear whether these two clusters represent any meaningful result.

Thus, the statement is inexact that single-neuron responses are "typically multiphasic and/or peak at different times for different conditions". Churchland's data include neurons with both consistent and heterogeneous responses. The contribution to rotations of both types of neurons should be assessed for better understanding of rotational dynamics.

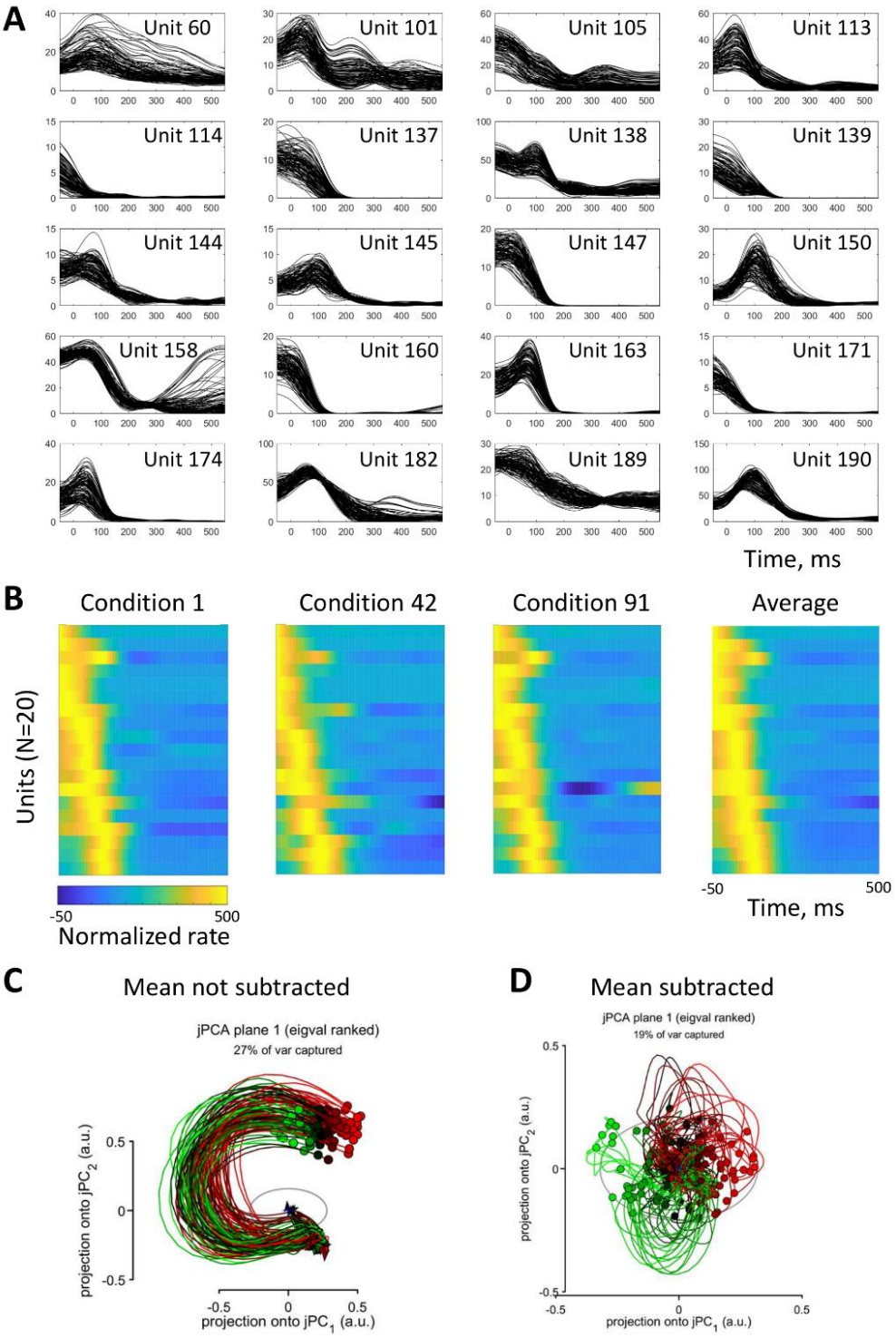

Figure 1. PETHs and jPCA plots for twenty neurons with the highest consistency of PETH shape across conditions. A: PETHs. Each box displays PETHs from different conditions for a single neuron. B: Population PETHs for three representative conditions (left) and the across-condition average PETH (right). Neurons are sorted by the time of peak response derived from the average PETH. C: State-space trajectories for jPCA without the subtraction of mean PETH. D: Trajectories for jPCA with mean PETH subtracted.

Discussion

Here we responded to the comments of the Shenoy group made in their recent review of neural population dynamics (Vyas, Golub et al. 2020). These comments regarded the role of sequence-like responses in the origin of rotational dynamics. Rotational dynamics was originally described by Churchland, Cunningham et al. (2012). They used jPCA method to extract rotational patterns from neuronal population activity and argued that the existence of such patterns constitutes a proof that monkey motor cortex acts like a dynamical system. While the dynamical system idea is currently popular, we think that the results generated with dimensionality reduction methods need scrutiny, particularly with respect to their relationship to the activity patterns of individual neurons within the population. We previously contributed to this consideration by making an observation that Churchland's data contain response sequences that persist across different movements (conditions) and showing that population-level rotations can be obtained from such sequences (Lebedev, Ossadtchi et al. 2019).

In their response to our work, the Shenoy group was skeptical regarding response sequences being the main cause of rotational dynamics. They also called sequence-like responses a non-dynamical model even though their own data contain such sequences. In this paper, we provided additional evidence showing that Churchland's dataset contains neurons whose response timing is highly consistent across conditions (Figure 1). Previously the Shenoy group emphasized that motor cortical neurons have heterogeneous response patterns and did not describe the neurons with consistent responses.

For the highly consistent neurons, a sequence of responses can be easily revealed with a simple analysis of response peak timing. These neurons fit Churchland's original description of "an unexpected yet surprisingly simple structure in the population response" as they exhibit remarkably similar responses for all arm-movement conditions. Yet, Churchland, Shenoy and his colleagues have expressed dissatisfaction with this simple population pattern (Churchland, Cunningham et al. 2012) because it corresponds to "rotations that are similar for all conditions". They reasoned that "in such cases one fails to gain multiple views of the underlying process, making it difficult to infer whether rotations are due to dynamics or to more trivial possibilities". We respectfully disagree with this assessment because, in our opinion, cross-condition consistency fits the dynamical system framework quite well. For example, Figure 1C depicts state-space trajectories for the neurons with consistent responses. These trajectories resemble the state diagram for a pendulum (see Figure 1c in (Vyas, Golub et al. 2020)), and even a dependence of the trajectory on the initial state can be noticed.

The other point of disagreement is related to the way Churchland et al. dealt with "rotations that are similar for all conditions". To remove these rotations, they subtracted cross-condition mean PETHs from the PETHs for each condition. In the case of the neurons with consistent responses, this procedure simply removes most of the data and leaves noise (e.g. compare Figure 1C and Figure 1D), so it is unclear what one is supposed to gain with this method. The gain is not clear either for the neurons that are "multiphasic and/or peak at different times for different conditions". In this case, mean PETH is likely to be highly noisy. Additionally, mean PETH could be dominated by the strongest responses contributed by a few conditions (e.g. preferred-direction response). Then, the procedure of subtracting the mean may kill the purpose: instead of becoming less similar, responses become more similar because of the introduction of a common signal. (Neuronal recordings sometimes have this problem if there is a prominent signal on the reference electrode.) In addition to these considerations, it is unclear how a dynamical system defined by equation 1 could perform subtraction of the mean PETH.

The point the Shenoy group made about the neurons with heterogeneous responses merits a special consideration. Intuitively, some form of sequence should be present in the responses of these neurons (otherwise, how would jPCA detect it), but a simple analysis like the one we conducted to produce Figure 1B would not work. A more insightful analysis should be conducted in the future.

Overall, we do not see any principal controversy between the neural population dynamics framework (Vyas, Golub et al. 2020) and our results pertaining to sequence-like responses. Yet, in our opinion, questions remain regarding the interpretation of low-dimensional representations of neuronal population data.

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