Low Dimensionality, High Robustness in Neural Population Dynamics

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Neuronal populations respond within a small number of relevant dimensions. New research by Trautmann et al. (2019) shows that spike sorting is not necessary to extract the important features of this low-dimensional population signal. Combined responses of multiple neurons (multiunit activity) only generate small changes in the extracted signals.

Neural population dynamics do condense to a few meaningful signals. Several thousands of single-neuron responses give rise to a small number of significant population dynamics ("*E pluribus pauca*"). Low dimensionality of neural data appears to be a general biological feature, observed in several experiments and animal models (Gao and Ganguli, 2015; Kobak et al., 2016; Rossi-Pool et al., 2017). Further, the dimension-reduced representation of the neural data across time constitutes a surface with smooth curvature (manifold). In recent years, different dimensionality reduction methods have been employed to infer the relevant latent population signals. Neural responses at a macroscopic level have helped neuroscientists to infer computational principles hidden in the heterogeneous activity of single neurons (Ames et al., 2014; Churchland et al., 2012; Kaufman et al., 2014; Rossi-Pool et al., 2019). This means that structures and invariant features of the data emerge by zooming out from single-neuron responses. However, what are the biological implications of the low dimensionality and smooth curvature of the population dynamics?

In general, population analyses employ a weighted sum of single-unit activity to compute the meaningful population signals from data. Therefore, to obtain each component of the population dynamics, different weights (importance) are given to each individual neuron of the network. Multiunit activity, recorded with a simple voltage threshold at each single channel, randomly combined activity from several neurons (Figure 1A). Notably, single neurons with analogous

or different coding dynamics (high tuning correlation) are mixed spatially (see Figure S2 in Trautmann et al., 2019). Then, each multiunit response constitutes a random selection of single units that could be compelling for the same or different population components. Considering that the neural response is low dimensional, is it possible to obtain population dynamics employing multiunit instead of single-unit activity?

In this issue of *Neuron*, Trautmann et al. (2019) address this question, offering important new evidence of the robustness of population dynamics. The authors found that spike sorting is not necessary to accurately determine which population signals are most meaningful. To endorse this claim, they replicate results from three previous studies, originally spike sorted (Ames et al., 2014; Churchland et al., 2012; Kaufman et al., 2014) but now directly using the unsorted multiunit activity. Notably, they were able to extract population signals, employing threshold-crossing multiunit activity, with only minor differences with respect to the signals found in the previous studies. When dimensionality reduction methods are applied to random linear combinations of single-unit responses, they yield analogous neural trajectories. Equivalent hidden population responses emerged from both approaches (Figure 1A). Not only do these results have great implications for facilitating future population studies, they also provide new evidence of the robustness and stability of population signals. Moreover, multiunit responses include hash activity that cannot be sorted into isolated neurons. This unsort-

able activity could carry relevant signals that increase the statistical power of the population analysis.

In addition to the previously recorded neurons, the authors collected new neural data using silicon Neuropixels probes during a motor reaching task. Employing this new high-density recording technique (∼20 μm site spacing), Trautmann et al. (2019) were able to sort hundreds of single neurons per trial. Again, the same population dynamics were obtained with the well-isolated single neurons. Importantly, their results suggest that more independent observations of the neural population are fundamental to compute the important aspect of the network. Contrary to that, redundancy given by high-density electrodes will not improve accuracy to infer the underlying neural signals. However, the authors used this new recording technique to provide significant additional evidence that nearby neurons do not share similar tuning properties. The results show that there are no spatially organized clusters of neurons with similar selectivity. This finding opens new questions that could be tackled with these high-density recordings. Is noise correlation higher between nearby neurons? Is there any relationship between distance, tuning, and noise correlation? These important questions could help to understand the underlying architecture of neural microcircuits.

As the authors assert across the manuscript, these results are restrained to population analysis. Crucial to this point, there are still many important questions to be addressed with single units. To evaluate individual cells' properties, like tuning to
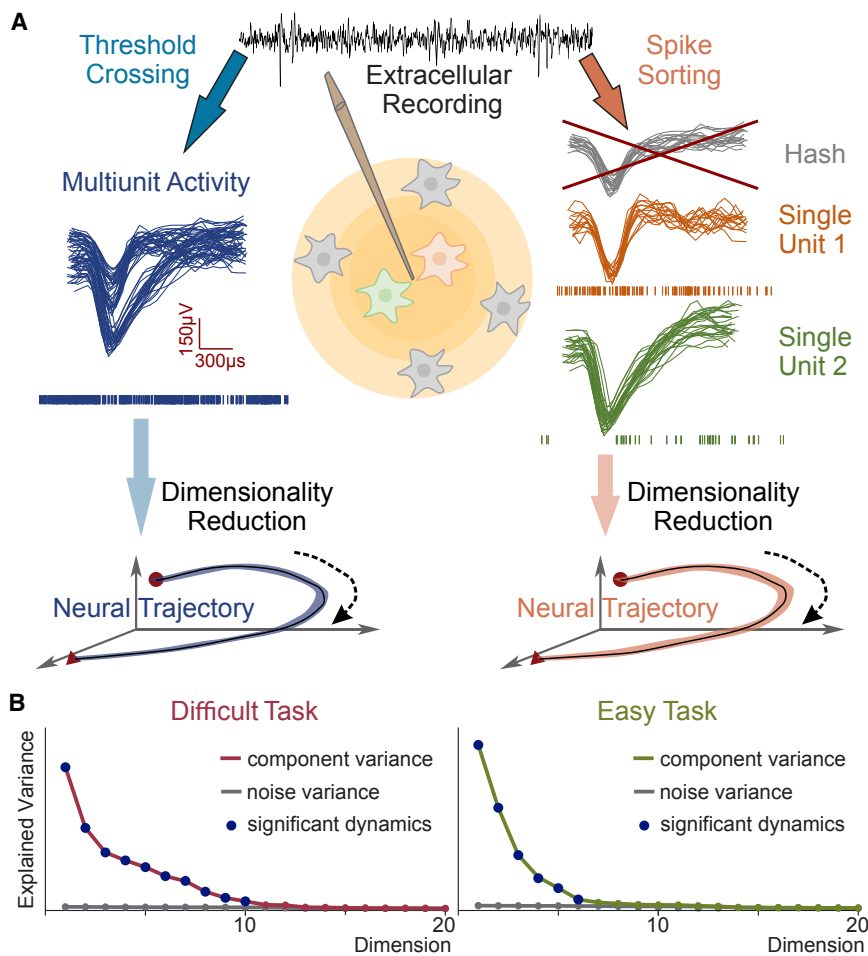
Figure 1. Single-Unit Versus Multiunit Activity in Low-Dimensional Neural Trajectories
(A) Single-unit activity obtained with spike sorting or multiunit activity obtained from threshold crossing gives rise to similar neural dynamics. Note that in the single-neuron approach, hash activity is discarded. (B) Easy and difficult tasks exhibit low dimensionality. Few significant dynamics explain most of the variance. A more difficult task displays more significant dynamics (above noise) than an easier task.

gest that dimensionality is associated with the complexity of the task (Rossi-Pool et al., 2017, 2019). When a task is too easy, the number of relevant dimensions decreases (Figure 1B). Note that to consider a neural dimension as significant, its explained variance should be higher than the noise variance associated with this component. Markedly, several tasks have shown that many significant dimensions and most of the network variance is captured by pure temporal latent signals (Kobak et al., 2016). These timing signals could be understood as a necessary substrate on which parameter coding responses can develop (Rossi-Pool et al., 2019).

Another important problem to be answered in future research is the relevance of the population-level responses. Do population responses reveal fundamental processes of brain circuits or do they only represent suitable pictures of their dynamics? Are the population responses, calculated with dimensional reduction approaches, still meaningful when the task is much more complex? Is it possible to establish an electrophysiological relationship between population signals and the oscillatory activity computed with local field potentials, which is considered to measure the level of synchronization of neural activity? These and other important questions are still open for future studies.

The work of Trautmann et al. (2019) leads the way to some other important, unresolved questions. Which are the biological reasons to have population neural responses with low dimensionality and high robustness? One possible hypothesis is that neurons from a downstream area could obtain the relevant neural information from upstream areas combining randomly single-unit activity. This population feature could help to facilitate communication across brain areas. Another complementary hypothesis is that low dimensionality gives stability and redundancy to the network. Once a complex task is learned, the neuronal population response could be prone to tolerate perturbation in its dynamic. However, under this stability, how do the networks learn a completely new task or variations of a previously acquired task? Is the dimensionality of the population higher when the subject is being trained

a stimulus parameter, spike sorting is still imperative. Studies based on single units are extremely important to understand the basic operations employed by neuronal circuits. Some of the most profound understandings of the neural mechanisms of working memory and decision making were obtained from studies of single-neuron activity across brain areas (Hernández et al., 2010). Furthermore, to our knowledge, there are no population-level studies analyzing neural features across areas.

To give a deeper interpretation of their results, the authors apply the theory of random projections (Ganguli and Sompolinsky, 2012). This theory is pertinent when a low-dimensional neural response

is enclosed in a high-dimensional space. In this case, each single-neuron activity represents one axis of the high-dimension space. While the number of significant dimensions in a neural state is around ten, the number of recorded neurons could be on the order of thousands (Gao and Ganguli, 2015). Under these circumstances, recording small numbers of random linear combinations of single-neuron activity (multiunit activity) is enough to extract the meaningful population responses (Figure 1). Applying this theory, Trautmann et al. (2019) show that higher-dimensional neural data require a larger number of multiunit channels to properly estimate the population dynamics. Importantly, recent results suggest that

in a new task? New experiments, computational analyses, and theoretical biology developments are necessary to clear up these propositions.

To conclude, Trautmann et al. (2019) present a meticulous study showing how dimensionality reduction methods can be employed with multiunit instead of single-unit activity, and by doing so, they provide new evidence to the actual debate about the functional roles of dimensionality, robustness, stability, and redundancy of neural network dynamics.

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How to Break a Fever: A Feedback Circuit for Body Temperature Control

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Body temperature control is a critical brain function. In this issue of *Neuron*, Wang et al. identify a negative feedback circuit in mouse preoptic area of the hypothalamus that regulates body temperature to counter fever.

Body temperature regulation is a fundamental homeostatic function in mammals. The maintenance of a constant body core temperature (T_c) at approximately 37°C is controlled by a central nervous network in an orchestrated manner. The thermoregulation system also plays a key role in host defense against pathogens through elevation of T_c, a response called fever. How is this accomplished? As a concept, the thermoregulation system consists of three components: sensory afferents, the central integration center, and command outputs (Morrison and Nakamura, 2019). The thermoregulatory center in the brain receives information through sensory afferents from thermoreceptors in the skin to detect ambient temperature and from thermoreceptors in viscera, muscle, spinal cord, and brain to detect body temperature. The thermal information is integrated in the thermoregulatory center, and then the center provides commands to thermoeffectors to control heat production or heat loss (Morrison and Nakamura, 2019). Work in the past decade has greatly advanced our understanding of the role of the temperature-sensitive TRP (transient receptor potential) family of cation channels in cutaneous thermosensation, particularly heat sensation (Dhaka et al., 2006). However, the molecular and cellular mechanisms underlying body temperature regulation in the brain remain largely unknown.

In mammals, the preoptic area (POA), located in the rostral pole of the hypothalamus, is thought to function as the thermoregulatory center in which a variety of thermal information, including ambient and body temperature, is integrated for the maintenance of temperature homeostasis (Morrison and Nakamura, 2019) (Figure 1). In their classic work in 1938, Magoun and colleagues precisely defined the thermosensitive area in the POA (Magoun et al., 1938). Later, single-unit studies in 1960s to 1980s showed that about 30% of POA neurons are warm-sensitive, 10%