Accurate estimation of neural population dynamics without spike sorting

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A central goal of systems neuroscience is to relate an organism's neural activity to behavior. Such efforts often begin by reducing the dimensionality of data to extract dominant neural population dynamics that could underlie task performance. A major hurdle to these analyses involves spike sorting, or extracting individual units from mixed activity on recording electrodes. This hurdle becomes more severe as the number of recorded neurons increases. Here, we investigate whether spike sorting itself may even be a necessary first step to accurately estimating neural population dynamics.

We re-analyzed data from three previous electrophysiological studies involving primate motor cortical dynamics of hundreds of neurons during reaching behaviors, as well as conducted a new study involving neuropixel probe measurements. In all cases, we found that both neural population dynamics and the scientific conclusions reached are quite similar using multi-unit threshold crossings instead of sorted neurons. Moreover we developed a quantitative theory, based on random projections, to explain the finding that mixing individual neurons on the same electrode does not significantly impair the estimation accuracy of neural population dynamics. Our theory predicts quantitative scaling laws for the estimation error: it should scale inversely with the number of electrodes, and logarithmically with the length, number and curvature of neural population trajectories. We successfully verified these theoretically predicted scaling laws in all four experiments.

Overall, our combined theory and experiment provides a conceptual framework, based on random projection theory, to uncover experimental regimes in which spike-sorting need not be necessary for understanding neural population dynamics. In terms of future impact, these findings may unlock existing data for new analyses without time-consuming or error-prone sorting, inform the design and clinical use of new wireless, low power, limited bandwidth electrode arrays, and enable new science with arrays that do not afford high quality spike sorting.

Significance: The process of spike sorting is a laborious task. For a typical experiment, composed of several hours of neural and behavioral recordings, manually spike sorting even 100 channels can take a skilled researcher several hours, and different human experts often arrive at different results. Automatic methods show promise, but are computationally intensive, sensitive to changes in waveform due to electrode drift, and typically have no ground truth data to validate the results. Thus by demonstrating experimentally that spike sorting need not be necessary for uncovering population dynamics, and developing theory for when this is the case, our work can have substantial impact on future electrophysiology studies in terms of both reduced labor and unlocked potential.

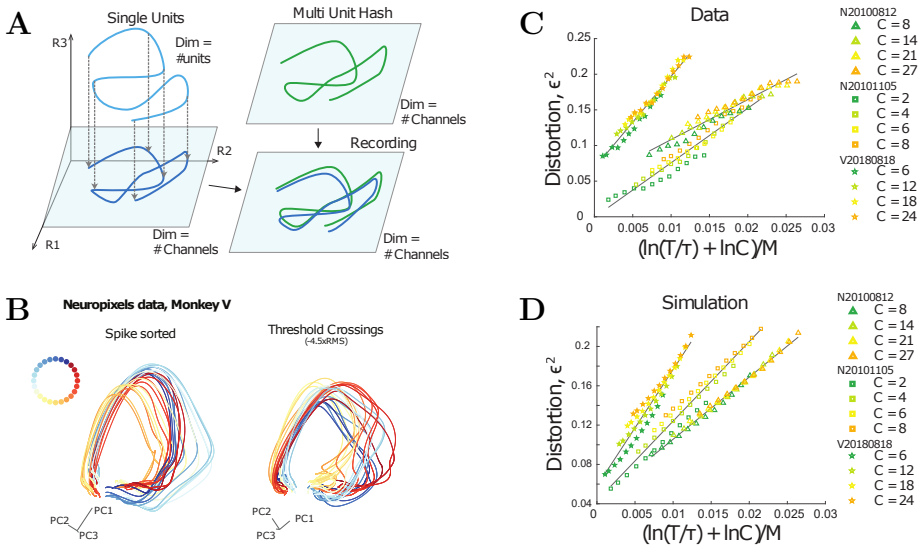

Figure 1: **A**. Schematic description of the link between spike-sorting and linear projections. **B**. Neural trajectories with and without spike sorting. **C**. Scaling law relating manifold estimation error to manifold complexity. **D**. Comparison with numerical simulations using random neural trajectories and random projections, sampled to mimic the statistics of neural data.

Methods: The process of spike sorting changes the data dimensionality from the number of recording channels to the total number of isolatable neurons observed in the experiment (Fig 1A). Here, we propose to bypass this sorting step prior to population-level analyses. Starting with multi-unit threshold crossings, the multiple neurons present on each channel are linearly summed prior to performing a second linear operation via dimensionality reduction. We will find that the resulting manifold of neural population activity closely resembles that found with sorted neurons, as shown schematically in Fig 1B.

We tested whether combining multiple units prior to applying dimensionality reduction algorithms adds significant distortion to the reduced-dimensionality estimates of neural state using a combination of empirical data, simulations, and theory. We used Neuropixels probes to record from populations of several hundred neurons simultaneously in dorsal premotor (PMd) and primary motor (M1) cortex, and found that neural trajectories are only minimally distorted when starting from multi-unit threshold crossings or simulated multi-unit channels. In addition, we replicated analyses from three previously published studies of primate motor cortical control of arm movements [1–3] using multi-unit threshold crossings (i.e., the linear combination of a small number of neurons as well as multi-unit 'hash').

This success can be explained by the theory of random projections from high dimensional statistics (e.g., [4–8]), which demonstrates that the geometry of a low dimensional manifold embedded in a high dimensional space can be accurately recovered without measuring all of the high-dimensional coordinates. Instead, it is sufficient to measure a small number of noisy, random linear combinations (i.e., projections) of these coordinates [5].

In the spike-sorting context, (1) the low dimensional manifold is the set of neural population trajectories; (2) the coordinates of the high dimensional space are the set of firing rates of all individual neurons relevant to the behavior; and (3) the noisy projections of these coordinates are the activities measured across the electrodes, which each detect a linear combination of a small number of neurons near that electrode as well as smaller spikes that cannot be resolved into a single neuron, also referred to as "hash" (Fig 1A). The error in estimating neural population dynamics extracted from sorted versus unsorted data can be derived from the theory of random projections. We find quantitative scaling laws for how this similarity depends on the complexity of the population dynamics themselves, which match experiment (Fig 1CD). In more detail, we quantify the similarity of the spike sorted vs. unsorted data with a single distortion measure ϵ, defined as

$$\epsilon = \min_{\lambda} \left\{ \max_{\mathbf{x}_1, \mathbf{x}_2} \left\{ \frac{\lambda \left\| \mathbf{A}(\mathbf{x}_1 - \mathbf{x}_2) \right\|}{\left\| \mathbf{x}_1 - \mathbf{x}_2 \right\|} - 1 \right\} \right\},$$

where $\mathbf{A}$ is the projection matrix from neurons to electrodes and $\mathbf{x}_1, \mathbf{x}_2$ are two points on the low dimensional manifold of neural trajectories. ϵ is the worst- case fractional change in length, up to an overall scale factor. We quantify the complexity of the population dynamics in terms of the duration, T, the number of task conditions, C, and the temporal correlation length, τ. Random projection theory predicts that ϵ^2 should scale inversely with the number of electrodes M, and logarithmically with C, T, and $1/\tau$. We verified these scaling laws *both* in data and simulations (Fig.1CD). For simulations, we performed the same analyses with simulated projections (with the same statistics as data) on simulated neural trajectories (with the same second-order statistics as data).

Overall, this theory thus reveals quantitative scaling regimes in which spike-sorting is not necessary for recovering population dynamics. In essence, if neural trajectories are not too long (small T), not too curved (large τ), and not too large in number (small C), and if the number of electrodes is enough (large M), then one can avoid spike-sorting while still accurately obtaining population dynamics.

[**1**] KC Ames, SI Ryu, and KV Shenoy, *Neuron* **81**.2 (2014), pp. 438–451. [**2**] MM Churchland et al., *Nature* **487**.7405 (2012), pp. 51–56. [**3**] MT Kaufman et al., *Nature Neuroscience* **17**.3 (2014), pp. 440–448. [**4**] S Dasgupta and A Gupta, *Random Struct. Algorithms* **22**.1 (2003), pp. 60–65. [**5**] S Ganguli and H Sompolinsky, *Annu. Rev. Neurosci.* **35** (2012), pp. 485–508. [**6**] M Advani, S Lahiri, and S Ganguli, *J. Stat. Mech.* **2013**.03 (2013), P03014. [**7**] P Gao et al., (2017) . BioRxiv: 214262. [**8**] S Lahiri, P Gao, and S Ganguli, *Arxiv* (2016) . arXiv:1607.04331 [stat.ML].