

Revealing cell types *in vivo* via dimensionality reduction and graph clustering of spike waveforms

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Background

Brain areas are thought to contain a wide variety of cell types with distinct roles

Current in-vivo methods that operate only on waveform features can only differentiate between broad- (**BS**) and narrow-spiking (**NS**) neurons.

We need new methods for accessing and understanding diversity

Our new non-linear dimensionality reduction and clustering method (WaveMAP) better reveals candidate cell classes *in vivo*.

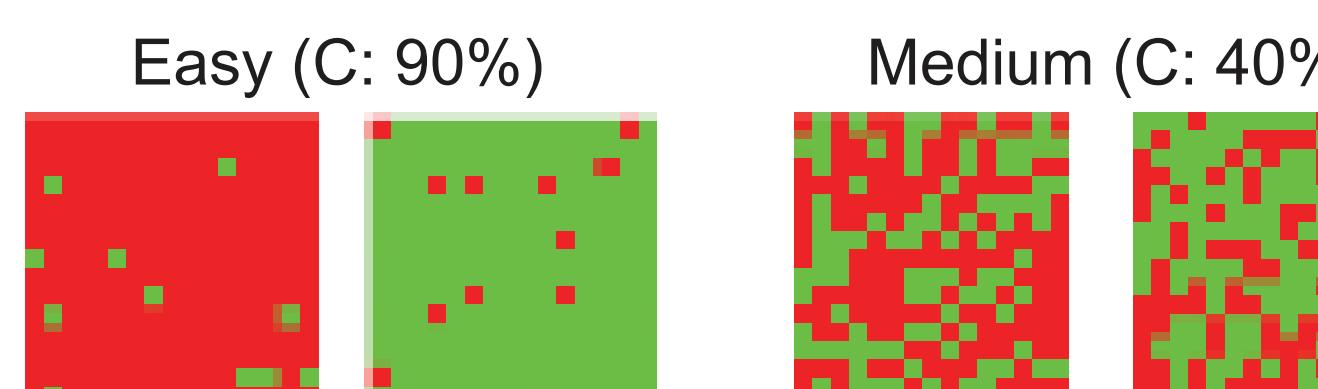
Introduction

Single neuron extracellular waveforms recorded in pre-motor cortex while a monkey performed a decision-making task [1]. ►

Color coherence modulates the difficulty of the trial. ▼

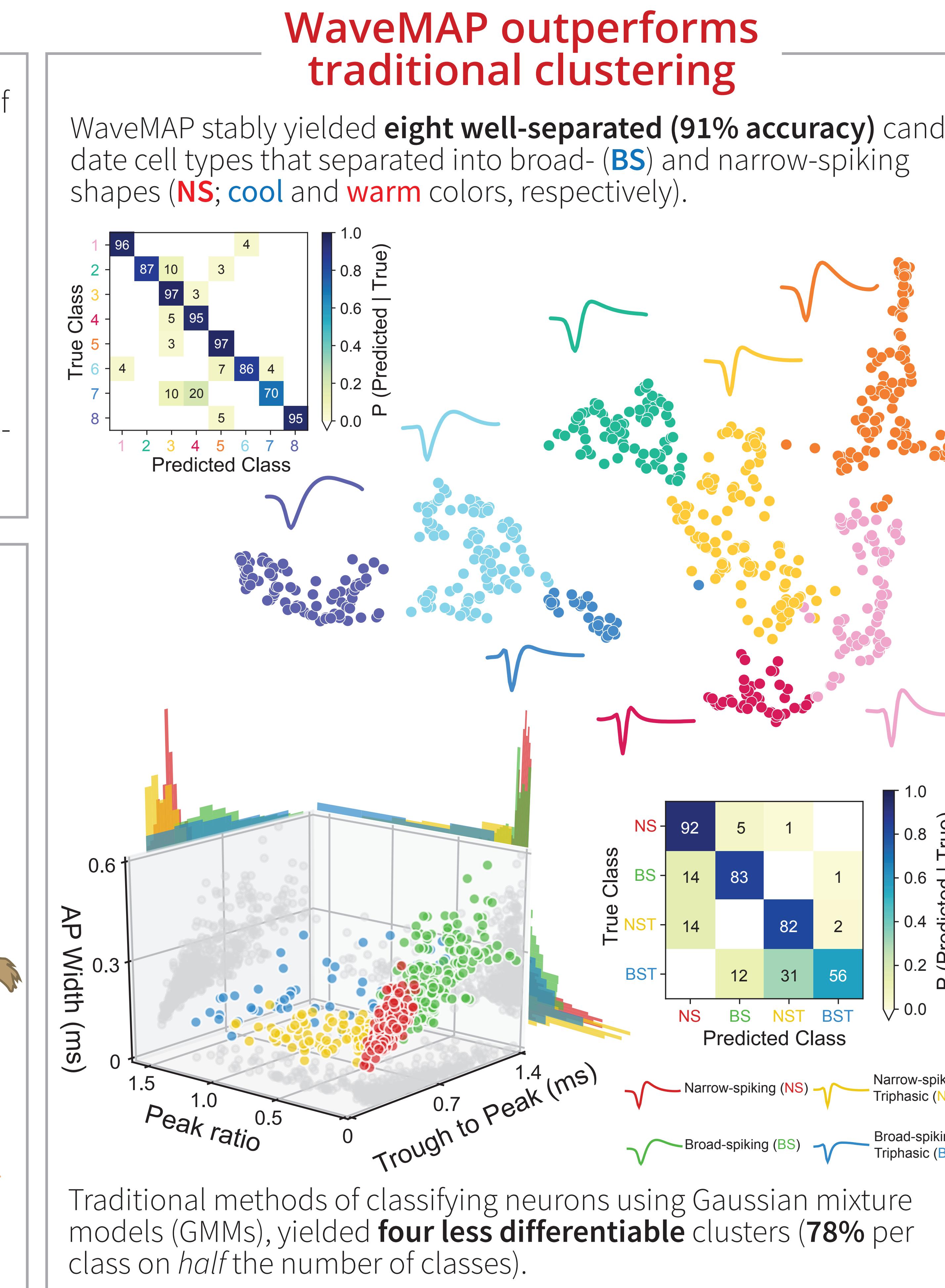
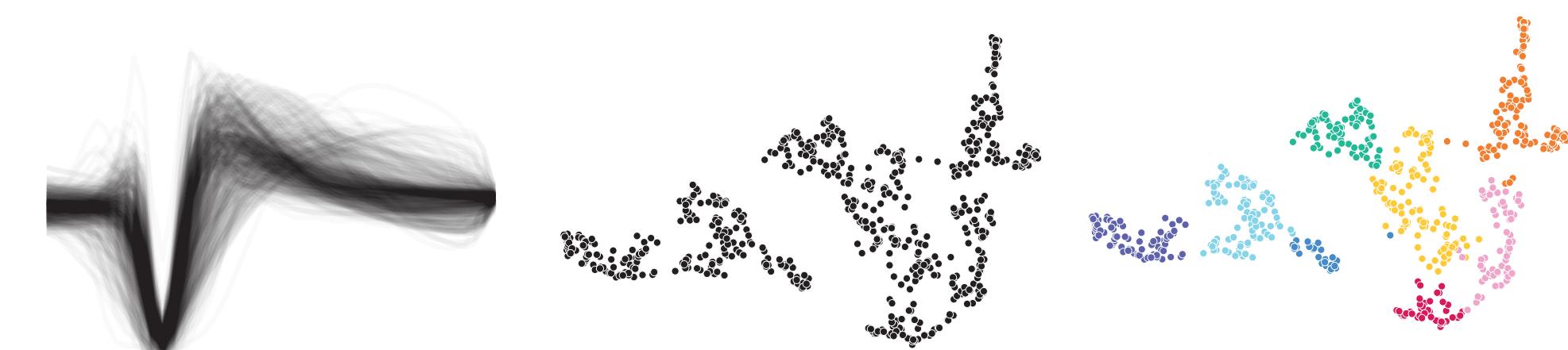
$$\text{color coherence } (C) = \frac{|R-G|}{R+G} \times 100$$

Easy (C: 90%)



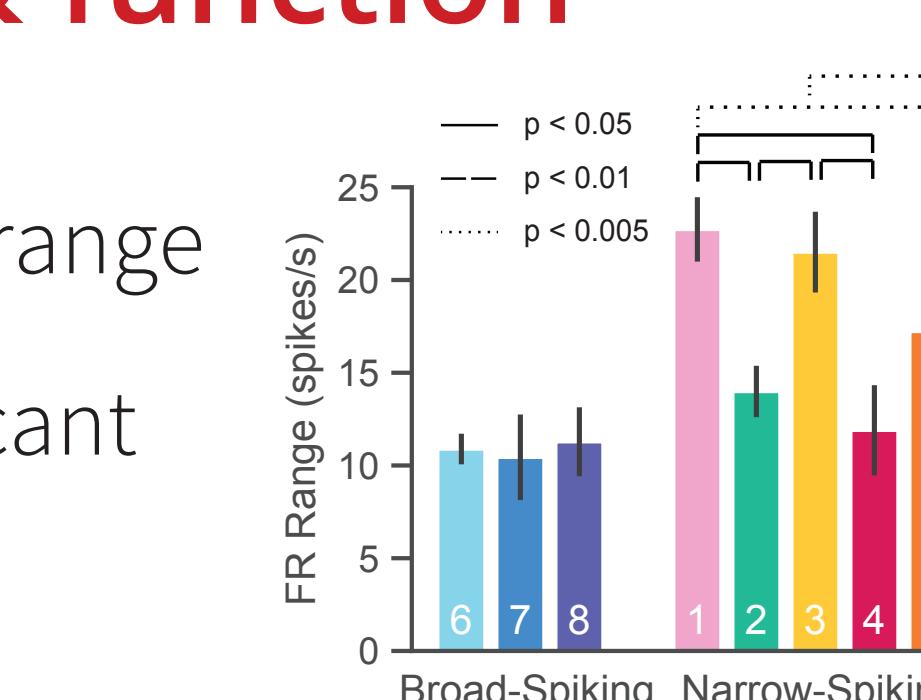
Normalized Waveforms

→ UMAP Projection → Louvain Clustering

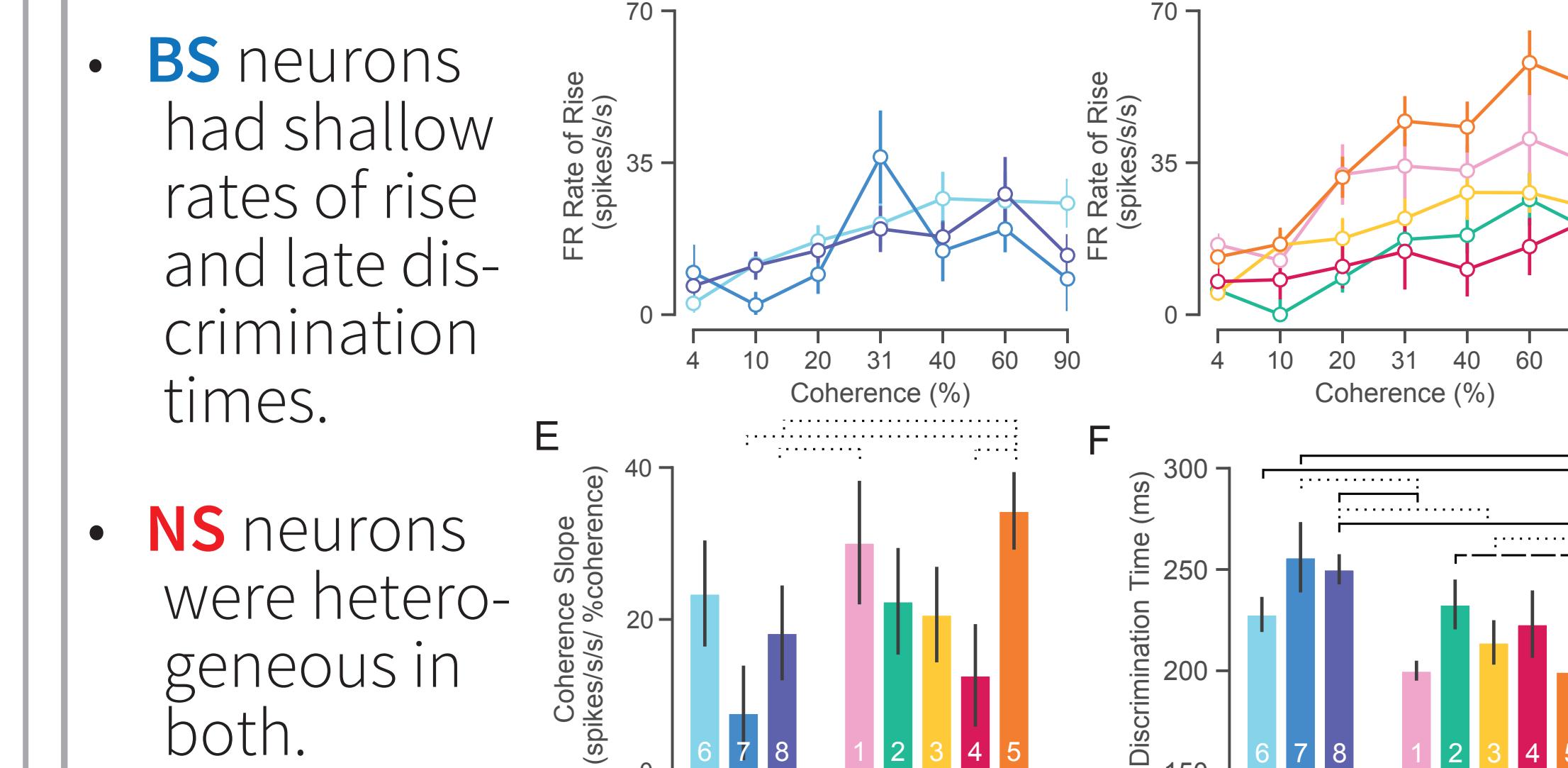


Clusters are distinct in physiology & function

- **BS** neurons were low in FR range
- **NS** neurons showed significant heterogeneity.



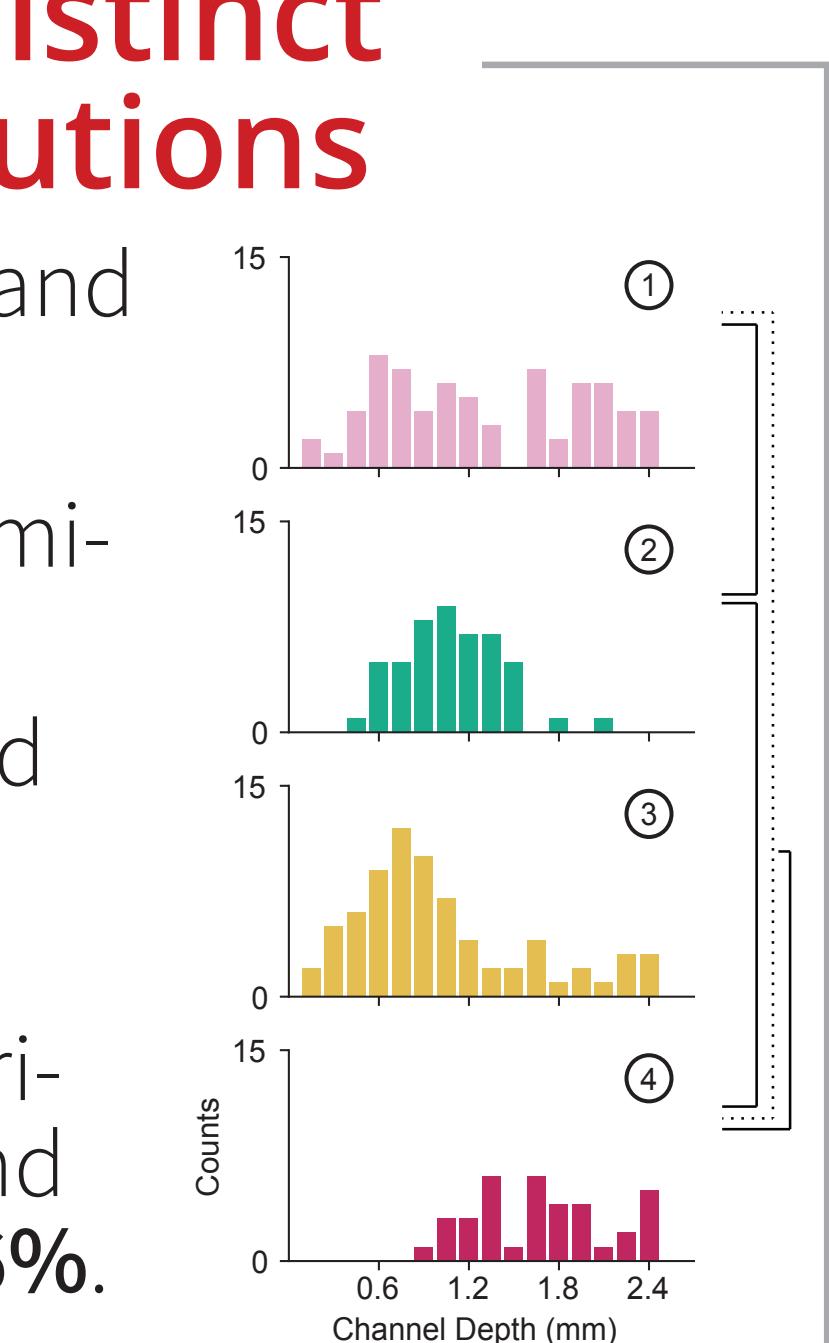
Discrimination time is the time point, within a trial, at which reach direction can be decoded from a neuron.



Clusters have distinct laminar distributions

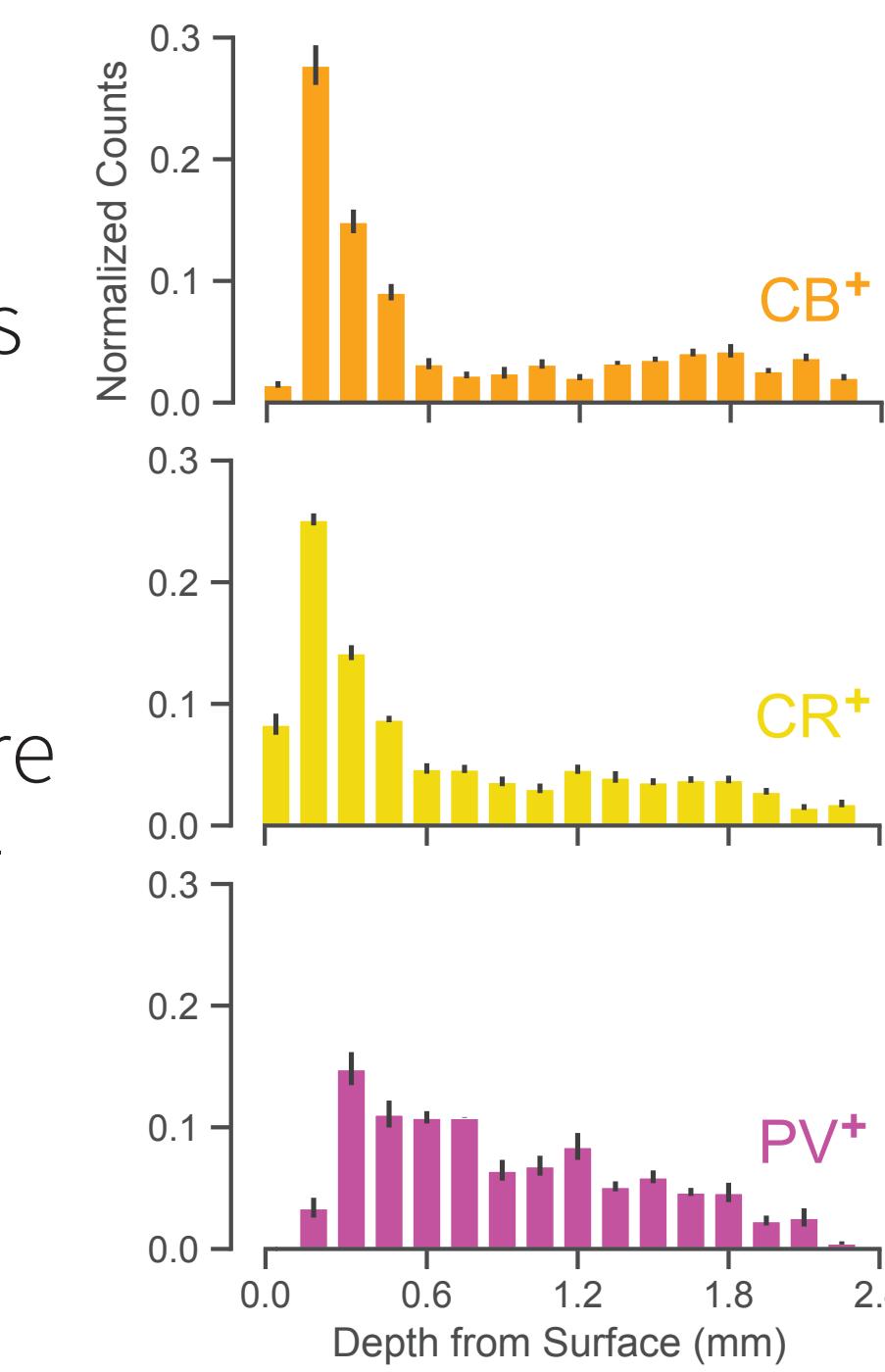
Focusing on four **NS** neurons (**BS** and **5** all had broad distributions), ►

- **NS** neurons each had unique laminar distributions
- No unique laminarities are found with traditional methods
- Depth with WaveMAP explained **7.6%** of discrimination time variance vs. traditional methods and depth which only explained **4.6%**.



Cluster laminarity matches cell types

- **CB⁺** and **CR⁺** cells are superficial like cluster **3**.
- **PV⁺** cells are more diffuse like cluster **1**.



Takeaways

- WaveMAP produced more clusters that were better separable than traditional methods.
- Clusters had significant differences in physiology, function, and laminarity not seen with traditional methods.
- WaveMAP explains more functional variance than traditional methods.
- We uncovered **NS** cells with properties matching excitatory neurons.

[1] Chandrasekaran, C., Peixoto, D., Newsome, W. T. & Shenoy, K. V. Laminar differences in decision-related neural activity in dorsal premotor cortex. *Nature Comms* 8, 614 (2017).

[2] McInnes, L. & Healy, J. UMAP: Uniform Manifold Approximation and Projection for Dimension Reduction. *arXiv* (2018).

[3] Blondel, V. D., Guillaume, J.-L., Lambiotte, R. & Lefebvre, E. Fast unfolding of communities in large networks. *arXiv* (2008).