Identifying distinct neural features between the initial and corrective phases of precise reaching using AutoLFADS

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Abstract

Many initial movements require subsequent corrective movements but how motor cortex transitions to make corrections and how similar the encoding is to initial movements is unclear. We recorded a large population of neurons during a precision reaching task across multiple sessions to examine the neural space during not only initial movements but also subsequent corrective movements. AutoLFADS, an auto-encoder based deep-learning model, was applied to analyze individual corrective movements unique to any given trial and to stitch across sessions into a single, common neural space. Several locations in the neural space where corrective submovements originated after the initial reaches were identified and were different than the baseline firing rate before initial movements. The neural trajectories for corrective submovements were organized according to both their starting position as well as reach direction but varied with several local domains rather than a single global space. Decoding of reach velocity generalized poorly from initial to corrective submovements and corrective decoding was relatively poor. To improve corrective movement decoding, we demonstrate that a state-dependent decoder incorporating where in the neural space a correction was initiated improved performance, highlighting the diverse neural features of corrective movements during a precision reaching task.

Significance Statement

We analyzed the underlying submovement neural dynamics during precision reaches on a single-trial basis using an auto-encoder based deep-learning model, AutoLFADS. Our study shows distinct neural dynamics between initial and corrective submovements. We demonstrate unique neural features of both position and reach direction and the importance of considering the specific states within the neural space when decoding corrective submovements. Our study highlights the significance of AutoLFADS in revealing single-trial population dynamics and demonstrates the need to account for state-specific strategies when decoding neural activity during complex motor tasks.

Introduction

Classic approaches to studying neural control of movements probe a small fraction of the behaviors critical to daily life. This limitation is often analytical, as standard approaches for interpreting neural activity rely on averaging responses across repeated behavioral trials (Pruszynski and Zylberberg, 2019). While trial-averaging helps provide robustness to highly variable neuronal responses on individual trials,

it requires studying behaviors with repeated trial structure and a high degree of similarity across trials. This strategy becomes limiting as we begin to study the neuronal processes for behaviors of increased complexity. If we wish to study sensorimotor control with the richness and complexity of natural behaviors, we must characterize neural systems on a single-trial level to understand how populations of neurons take in new sensory information combined with previous motor errors to plan, update, and generate movements.

Although common in natural reaching behavior, neuronal processes for corrective movements are understudied. Subjects often generate corrective movements during precise reaches with online error correction required to compensate for sensorimotor noise (Abrams et al., 1990; Sainburg et al., 1999; Elliott et al., 2010). In a traditional velocity-encoding model of neural activity (Moran and Schwartz, 1999), one would expect activity to return to a baseline state during the low-speed period and then encode the smaller corrective movements with similar tuning but smaller amplitude changes in firing rate with separate and additive tuning for posture (Wang et al., 2007). However, the temporal dynamics of the neural population may instead depend on the initial reaching movement and not return to a common baseline state (Albert et al., 2020). Additionally, given the high dimensionality of the neural population (Yu et al., 2007; Cunningham and Yu, 2014), corrective movements may not encode as smaller initial movements but instead have distinct neural features for subpopulations of individual neurons (Evarts et al., 1983). A more complete description of motor encoding requires examining not just initial, instructed movements but also how brain areas represent online corrections of movement.

When a subject reaches for but misses a target due to motor error, the corrective submovements are heterogeneous. Correction may be needed from many different postures and require movement in any direction, necessitating a unique, state-dependent correction from an initial reach. This behavioral variability may reflect greater heterogeneity in the underlying neural processes not fitting neatly into a single kinematic encoding scheme such as a single velocity or force-based space. Analyzing the associated neural data via trial-averaging would require assumptions about which corrective behaviors lead to similar neural activity and risks obscuring the neural processes of interest. Thus, single-trial neural analysis strategies are required to uncover the neural patterns of corrective submovements. Since current experimental methods only record from a small sampling of neurons and the neuron's firing rates have stochastic features, the raw data of estimated firing rates on a single trial can be challenging to

interpret. However, most movements including corrective movements tend to include discrete submovements (Paninski et al., 2004; Fishbach et al., 2007; Hatsopoulos et al., 2007). Our recent work has identified consistent and distinct peaks in speed that define separate initial and corrective submovements (Rouse et al., 2022) and that condition-invariant neural activity previously described by others (Kaufman et al., 2016; Kobak et al., 2016) define these submovements. With advanced statistical and machine learning methods, one might better infer the latent state of the neural population on any single trial and within each submovement.

Additionally, neural recording interfaces can be unstable, such as movements of the electrode tip relative to the recorded neurons, which prevents consistent recording from the exact same neurons across recording sessions (Chestek et al., 2011; Fraser and Schwartz, 2012; Perge et al., 2013). These instabilities limit the total number of trials with a given behavior we can observe for any given neuron. Thus, for behaviors with a high degree of heterogeneity, such as corrective movements, it becomes challenging to gather sufficient data within a single recording session to characterize the neural and behavioral spaces of interest. As a result, any analysis of highly variable corrective movements will also require analysis techniques that “stitch” recording sessions together into a common representation of neural activity (Turaga et al., 2013; Nonnenmacher et al., 2017; Pandarinath et al., 2018b; Degenhart et al., 2020).

Here we address the limitations in characterizing the neuronal processes underlying corrective movements using deep learning–based single-trial analytic methods. This allows a novel comparison of neuronal dynamics during not only initial but also corrective movements. We examined neuronal population activity recorded from primary motor cortex during a precision-movement task that elicited a range of initial and corrective movements. We apply a previous approach, AutoLFADS, to uncover representations of neuronal population dynamics that have a stable relationship with behavior across months, which allows aggregation of data from many sessions (Keshtkaran et al., 2022). Importantly, we are able to identify the most neurally similar movements across many sessions and then examine what is shared in their kinematics to better infer how the brain organizes its repertoire of movements.

Materials and Methods

Experimental preparation

All procedures for the care and use of nonhuman primates followed the *Guide for the Care and Use of Laboratory Animals* and were approved by the University Committee on Animal Resources at the University of Rochester, Rochester, New York. Two male rhesus monkeys, P and Q (weights 11 and 10 kg, ages 7 and 6 years old, respectively), performed the task in the study.

Behavioral analysis

The monkeys performed a center-out task using an 18 cm–long cylindrical rod as a joystick to control a cursor on a 24" LCD display. The joystick could move freely with little resistance. The cursor on the screen represented the joystick position which freely moved within a 1000-x-1000-pixel workspace. A small cross symbol served as the cursor to indicate a single point in the workspace. Customized software sampled the joystick data, refreshed the scene, and saved the cursor position and trial event times at 100Hz.

We recorded 12 sessions of neural recordings for monkey P and 12 sessions for monkey Q over a time span of 2 months and analyzed the recorded neural signals using AutoLFADS. One session of monkey Q was excluded due to greater variation in the behavior likely due to reduced motivation by the animal that AutoLFADS could not resolve. The two monkeys successfully completed a total of 10,958 (monkey P) and 8737 (monkey Q) trials across recording sessions. The description of the task and analysis of behavior and condition-invariant neural activity have been described previously (Rouse et al., 2022). Briefly, in the task trials, after obtaining and holding the cursor for 300-500 ms in a center target with a radius of 75 pixels, the monkey would reach from the center to 1 of 8 instructed directions, equally spaced by 45° around the origin as shown in Fig. 1A. Each of those peripheral directions included one of three different sizes defined as large, shallow, and narrow targets. The monkey would receive a liquid reward once he successfully made a complete hold of 500-600 ms with the joystick within the peripheral target. The required initial and final hold times for each trial were randomly and uniformly sampled from within the given range.

The behavioral task schematic and cursor speed profile for a subset of trials are shown in Figure 1. Fig.

1B demonstrates the reach trajectories for the shallow targets. The monkey would acquire the center target and then reach towards 8 peripheral targets (the shallow outer boxes). Movement trajectories of the initial reach submovements are indicated in blue, the speed peaks of each trial are marked as blue squares. Corrective submovement trajectories are shown in red, the speed peaks of each trial are marked red squares. Gray lines connect the rest of a trial before, between, or after submovements with a speed peak. Fig. 1C shows the cursor speed profile over time throughout the trials. The initial peak speeds (blue boxes) and corrective peak speeds (red boxes) are marked as the annotation points across the speed profile plot. We calculated cursor speed offline by filtering cursor position with 10 Hz low-pass first order Butterworth filter (bidirectionally for zero phase lag). We used a peak finding algorithm to identify speed peaks (findpeaks function in Matlab (Mathworks 2020)) to define both initial and corrective submovements. Cursor speed peaks were identified when the following criteria were met: i) the peak speed was greater than 250 pixels/s and ii) the peak had a prominence (the height difference between the peak and the larger of the two adjacent troughs) at least 50% of the absolute height of peak. Submovements within a trial are defined as the surrounding time window of 400 ms before and 200 ms after cursor speed peaks. We defined the initial speed peaks to be first submovements which ended at least 150 pixels from the center, and any small movements before were excluded from further analysis. Speed peaks following the initial speed peak were defined as corrective submovements, and any corrective submovements occurring only within the peripheral target were excluded to focus analysis on submovements made to successfully reach towards the target. Over all characterized submovements, there were 6464 and 3728 corrective submovements identified for monkeys P and Q, respectively. Across all trials, 17.5% (P) and 20.2% (Q) of trials required one additional corrective submovement, and 14.2% (P) and 8.7% (Q) of trials required more than one correction after an initial movement.

Neural Recordings

Floating microelectrode arrays (MicroProbes for Life Science) were implanted in the anterior bank of the central sulcus in each monkey to record signals from primary motor cortex (M1) as described previously (Mollazadeh et al., 2011; Rouse and Schieber, 2016; Rouse et al., 2022). Recordings were collected from six 16-channel arrays implanted in M1 for monkey P and two 32-channel arrays plus one 16-channel array implanted in M1 for monkey Q. Plexon MAP and Blackrock Cerebus data acquisition systems were used to manually threshold the spiking activities and collect spike-snippets and spike times which were then offline sorted using a custom, semi-automated process (Rouse et al., 2022).

AutoLFADS and 'Stitching' process

The deep-learning based technique AutoLFADS was used to identify latent factor representations of neuronal population dynamics (Keshtkaran et al., 2022). We combine the automated hyperparameter optimization of AutoLFADS with LFADS model *stitching*, which has been previously shown to identify latent factors that are consistent with behavior across months, allowing data aggregation from multiple recording sessions (Pandarinath et al., 2018b).

We analyzed all neural and cursor data by time aligning to the identified speed peaks used to define each submovement. We preprocessed the raw neural data by calculating the trial perimovement time histogram (PMTH) in 20 ms sampling bins. We then analyzed the neural data for each submovement from 400 ms before peak speed to 200 ms after peak speed.

After recording and preprocessing across days, multiple sessions of preprocessed neural data were sent to a configured AutoLFADS model using the pre-session 'read-in' matrices. Each read-in matrix is fixed with weights W^{input}, which are learned from a principal component regression (PCR) that maps the trial-averaged firing rates from each individual session to the shared principal components across all sessions. Passing the spiking data through these read-in matrices provides a set of input factors. Then the input factors were fed into a single encoder, generator and factor matrix W^{fac} shared across sessions to get output factors within a common latent state-space across all sessions. We finally concatenated those single session output factors to infer the stitched latent dynamics.

Quantitative analysis on measuring correlation between LFADS factors and kinematics

Ridge Regression

We used ridge regression to quantify the correlation between LFADS factors and the submovement kinematics. We performed the same regression between neural population and submovement kinematics of the smoothed firing rates to allow comparison between decoding using the smoothed neural data or the AutoLFADS latent factors.

Ridge regression was implemented as in Scikit-Learn (Pedregosa et al., 2011), where the regression model solves for some set of weights *W* that minimize the linear least squares loss in the following equation:

$$\|y - XW\|_2^2 + \alpha\|W\|_2^2$$

where *X* is the neural data, *y* is the behavioral data to predict, $\|.\|_2^2$ is the squared L2 norm, and □ is the L2 penalty applied to the weights.

Prior to training the ridge regression model, we applied a lag to the data such that the neural activity preceded movement by 100ms. The ridge regression model was trained using five fold cross-validation with an L2 regularization value of □ = 1.0. Final decoding accuracy was reported as the average velocity R^2 of the held-out folds for within-day decoders, or as the velocity R^2 for held-out data (sessions or trials).

t-SNE

To identify neurally similar movements within the high-dimensional data and visualize the data in a low-dimensional subspace, we used t-distributed stochastic neighbor embedding (t-SNE), a non-linear dimensionality reduction tool. We mapped 30 dimensions of LFADS factors from individual trials into a 2D space using the built-in t-SNE toolbox in Matlab. Data fed into t-SNE consisted of LFADS output with time value from 100ms before and 100ms after peak speed sampled every 20ms. We resized the stitched latent factors by stacking the time and factors dimensions, from [$trial \times time \times Factor$] to [$trial \times (time \times Factor)$] to identify trials with similar factors across time. We performed t-SNE with the Barnes-Hut algorithm using the Euclidean distance metric with perplexity set to 50 and learning rate to 500 (Wattenberg et al., 2016). The t-SNE output was set to two dimensions to introduce a simple and clear view of data structure.

The t-SNE map that identified submovements with similar neural activity could then be divided into subgroups to evaluate what movement trajectories in the physical two-dimensional workspace. For

identifying and visualizing similar individual trials into clusters, we utilized k-means nearest neighbors (KNN) clustering on the t-SNE space of LFADS factors for initial and corrective submovements separately. For comparing the identified neural features with the behavior, we used the cursor movement within the time window from 100 ms before until 100 ms after speed peak to define direction and magnitude of each submovement as a single straight-line vector.

Neural Trajectories Analysis

Principal Component Analysis (PCA, pca function in Matlab (Mathworks 2021)) was used to reduce the dimensionality of the LFADS factors for visualization while maintaining the most variance in the neural data. PCA imposes a minimum number of assumptions about the underlying structure of data and reveals the dimensions that explain most of the variance. We projected the LFADS factors into a single PCA subspace across all sessions as a function of time to create neural trajectories and reveal the neural dynamics for given submovements.

State-dependent decoder

A discrete state-dependent linear decoder was used to measure the decoding performance within corrective submovements when classified by different states based on their initial neural state. Different states were defined by k-means clustering of the t-SNE space of LFADS factors at a timepoint before the corrective submovements (340 ms before peak speed). The number of clustered states was varied from 1 to 14 in the analysis. After performing k-means clustering on the test data, a separate ridge regression was then trained on each k-means cluster. For decoding, each test trial was assigned to its nearest cluster centroid by its neural activity 340 ms before peak speed. The ridge regression coefficients for the given assigned cluster were then use to transform the neural activity into predicted movement.

The regression was performed using 5-fold cross-validation. All trials were divided into 5 equal testing groups with the remaining 80% of data used for training the prediction for each test group. Global sum of squares residuals and total sum of squares total were manually calculated and summed across the states to return the variance predicted in the kinematic dataset and the total variance. The coefficient of determination (R^2) for the state-dependent decoders was then calculated with the variance values.

Bootstrap testing by selecting trials with replacement for 1000 iterations was used to estimate 95% confidence intervals.

Results

Stitched AutoLFADS infers consistent neural dynamics across sessions

To address the limitation of combining trials across sessions, AutoLFADS with stitching was used to consistently obtain neural representations of submovements across sessions despite the inherent constraint of a limited number of submovement trials available per recording session. We first evaluated AutoLFADS for its ability to extract these single submovement neural population dynamics. Since there are smaller numbers of submovements for individual recording sessions, especially for idiosyncratic corrective submovements, stitching allowed us to compare neural dynamics across sessions and identify when the neural representation of a submovement was similar. In Fig. 2A, we visualized the stitched AutoLFADS latent factors corresponding to initial submovements from 6 representative sessions by projecting them to a 3D PCA subspace and color coding by the 8 reach directions. All subplots showed a similar neural pattern in the PCA subspace, indicating that AutoLFADS successfully identified shared latent structure across all sessions. We then used t-SNE on the neural latent factors to also show the eight reach directions could be consistently identified and stitched by their latent factors across sessions. In Fig. 2C, t-SNE of all sessions of initial submovements are color coded by reach velocity vectors between 100 ms before and 100 ms after peak speed in the left subplot. In the middle and right subplot, two representative sessions were selected for visualization (colored by reach velocity vectors); all other sessions of submovements were colored as gray. Together, Figs. 2A and 2C show AutoLFADS generates consistent latent factors for the initial reaching submovements and stitching creates a common neural space across days corresponding to the 8 reach directions.

We further assessed how well the latent factors can capture single-trial movement variability by utilizing ridge regression. We fit the regression model from latent factors to movement direction of initial and corrective submovements in Figs. 2B and 2D, respectively. For each set of submovements, we fit a single ridge regression model on all but one session and evaluated how well that model could decode velocity on the held-out session. For reference, we also fit a separate ridge-regression model on the smoothed spiking data from the same held-out session. The red bar on each session shows the variance explained

(R^2) of the behavioral predictions from LFADS factors when a regression model is trained on only that session. The blue bar on each session shows the R^2 of behavioral predictions from a held-out day when a regression model is trained on the LFADS factors of all other datasets. The gray bar on each session shows the R^2 of behavioral predictions when a regression model is trained using smoothed firing rates from the same day. For both monkeys we analyzed, there was a small drop in performance from held-in to held-out R^2 as expected. The average drop in R^2 was 0.02 (monkey P) and 0.13 (monkey Q) for initial submovements and 0.06 (P) and 0.15 (Q) for corrective submovements. Even with the small decrease in R^2 for the held-out LFADS factors, the held-out regression was favorable compared to regression with smoothed firing rates performed on a given session. For initial submovements, both monkey P and monkey Q had significantly better R^2 ($p<1e-8$ and $p=0.02$, respectively, paired t-test) for held-out LFADS factors compared to smoothed spikes. For corrective submovements, LFADS factors were significantly better for monkey P ($p<1e-2$, paired t-test) and there was no statistical difference for monkey Q ($p=0.675$, paired t-test). Overall, these results indicate a significant improvement in initial decoding performance and a slight improvement or similar performance for corrective movements using AutoLFADS in both monkeys compared to smoothed firing rates. Additionally, AutoLFADS has the added benefit of stitching the sessions into a common neural space. We also note that the predictions for corrective submovements yielded worse decoding performance than those for initial submovements. This indicates that there is likely more diversity in the neural encoding of corrective submovements and a single linear velocity tuning model does not fit as well as initial submovements.

Corrective submovements are encoded using a combination of reach direction and location

Given the result that corrective submovement latent factors cannot predict movement direction as well as initial, we next wanted to examine how the neural activity for the corrective submovements related to the position and velocity of individual submovements. We defined the position of each submovement as the starting position at 100 ms before peak speed. A velocity vector of the submovement from 100 ms before to 100 ms after peak speed defined the direction and magnitude of each reach. We performed t-SNE to project the high-dimensional neural data into a 2-dimensional subspace as shown in Fig. 3, with each scatter point representing a submovement. We applied t-SNE on corrective submovements of a single session of smoothed firing rates and projected to the t-SNE space, color coded on position (Fig. 3A) and velocity vector (Fig. 3B). For the smoothed firing rates t-SNE subplots, only a weak and noisy relationship with both the position and velocity vector was observed.

Next, we projected LFADS factors of a single session from the stitched model into t-SNE space and also color coded on position (Fig. 3C) and velocity vector (Fig. 3D). Some distinct grouping based on both the velocity vector or position is revealed but the overall grouping remains noisy and unclear. Finally, when all sessions of LFADS factors were stitched together and visualized in the t-SNE space, clearer groups and gradients based on a combination of position (Fig. 3E) and velocity vector (Fig. 3F) are observed. Interestingly, the different clusters of corrective submovements are not dominated by velocity vector or position alone but are a combined interaction between the two. For some clusters, all submovements within a dense area appear to be related to reach direction while other groups of submovements appear to be more related to a distinct location in the workspace. This provides evidence for a combined neural representation of the corrective submovements that depends on both where the submovement originates as well as the direction of the movement. The better organized stitched LFADS factors t-SNE plot vs single session t-SNE plots indicates the importance of being able to stitch corrective submovements LFADS factors. Stitching gathered enough submovements with high similarity and pulled out an informative structure in the corrective neural data.

Distinct neural patterns associated with kinematics revealed within neural state-space

We then explored the distinct neural patterns between various submovements by examining the neural trajectories and movement trajectories for groupings identified using the t-SNE representation of neural data. In Fig. 4A, the same t-SNE plot of initial submovement LFADS factors as shown in Fig. 2C was classified by KNN into 8 groups. In this case, the KNN classification was based only on the Euclidean distance in t-SNE neural space, not kinematic information. Fig. 4B shows the neural trajectories of initial submovements in the plane of the first two principal components. The average initial neural trajectories originate from a similar point and show 8 distinct curved trajectories in the PC plane. For these initial submovements, 6 of the 8 trajectories move towards a similar end point while the trajectories for 2 of the groups (purple and dark yellow) move to a different location in the neural space. Furthermore, we plotted the 8 KNN groups of submovement trials separately in the kinematic space to show the corresponding movements of this neural data (Fig. 4C). The movement trajectories show good alignment with the 8 directions of the instructed targets, highlighting the strong discriminability of initial reach direction from the neural data processed with AutoLFADS.

A similar analysis was then performed on the corrective submovements. Fig. 4D shows a t-SNE plot of the corrective submovement LFADS factors. Although the corrective submovements had less distinct groups than initial in the t-SNE space, we again used KNN to subdivide the neural data for display. We chose to label 9 groups for visualization of the kinematics and neural trajectories of submovements with similar neural features. Fig. 4E shows the neural trajectory plot of corrective data in the same two principal components of the global LFADS factors space. For the corrective submovements, the average neural trajectories show smaller amplitude relative to initial trajectories. Additionally, the starting points of each cluster in corrective trajectories were relative to the ending point of initial trials in the LFADS factors space. Therefore, the smaller, corrective submovements do not begin at the same origin as the initial submovements and thus represent a different neural pattern than would be expected if a corrective submovement was encoded as just a smaller initial movement in a given direction. Similarly, we plotted the 9 KNN groups of submovements separately in the kinematic space to show the corresponding movement trajectories of this neural data (Fig. 4F). Seven out of nine groups showed similar kinematic patterns covering many different starting positions in the upper portion of the workspace and were primarily grouped by reach direction. Two out of nine groups showed patterns covering only those movements occurring in the bottom positions of the workspace. In particular, the 6th and 7th group marked in the left yellow box and 8th and 9th group marked in the right blue box demonstrate good examples of 2 separate groups, each pair of groups with their own portion of the workspace and each group within the pair associated with different reach directions. A separate neural trajectory plot for those 4 groups highlighted were presented in Fig. 4G and Fig. 4H to show how the starting position in neural space could define the workspace when looking in the movement trajectory. Overall, the results suggest distinct domains or types of corrective submovements rather than a single direction- or position-based organization and demonstrate the encoding complexity of corrective submovements.

Decoding performance

Finally, we trained ridge regression decoders on the initial and corrective neural data to assess how well the brain activity could be decoded to predict movement and how well the decoders generalized between the two types of submovements. We trained decoders on LFADS factors of the two different types of submovements and applied the trained model to the other submovements. Fig. 5A and 5C shows decoders trained and tested on either the initial or corrective submovements alone and then also tested on the other type of submovement. Blue and red bars show R^2 of initial prediction and corrective prediction on the trained neural data, correspondingly. For the decoder trained on initial data, the predictions were

poor for corrective submovements. Interestingly, the decoder for corrective submovements provided a reasonable prediction of initial movements. The decoding performance on the two submovements showed that although AutoLFADS improved the R^2 of velocity predictions over smooth firing rates (Fig. 2), there was little generalizability between the two movement state decoders. This indicates distinct patterns of corrective neural activity with unique features compared to initial submovements.

Finally, we trained discrete-state linear decoders on the corrective movements as shown in Fig. 5B and 5D. This two-stage decoder i) divided the neural data into discrete states and then ii) fit and evaluated a linear decoder only within that state. As the number of states increased, the decoding performance R^2 improved. For both animals, the performance plateaus around 7-10 states, similar to the 9 groups we labeled in Fig. 4D. The improved performance with more decoder states indicates that the corrective submovement neural activity is more diverse and cannot be described well using a single, linear decoder. Rather, identifying submovements with similar starting neural features provides a better prediction even with using a smaller training dataset available within only a single state. Again demonstrating that distinct neural patterns may underlie individual subtypes of corrective movements that cannot be well-represented by a global encoding space defined by velocity or other kinematic features.

Discussion

Our results highlight that the encoding process of movement planning and execution in the brain contains significantly higher dimensions of neural dynamics and is recruiting neurons in a more diverse way than projecting neural dynamics into a single linear plane or hyperplane for each movement feature such as velocity, force, or position. Previous studies have built linear models with time invariant instructed movements with a common origin in the workspace and produced reasonably accurate predictions (Moran and Schwartz, 1999; Serruya et al., 2002; Taylor et al., 2002; Santhanam et al., 2006; Wang et al., 2010; Gilja et al., 2012). These datasets are most similar to the initial movements in this study. However, the decoding performance of similar models was much worse for our self-generated corrective movements explored here. While some have previously reported the importance of neural fragments (Hatsopoulos et al., 2007), trajectories (Yu et al., 2007), or sequential reaches (Shanechi et al., 2012) for accurately representing neural encoding of reaching, the ability to organize this neural activity into the neural space on a single trial basis such as individually unique, corrective movements has remained

challenging.

AutoLFADS provides a method to analyze consistent single-trial neural features across sessions

We have demonstrated that AutoLFADS is a useful tool in extracting generalized neural features across many recording sessions and identifying distinct neural features between the initial and corrective phase of precise reaching movements. Although classic trial-averaging approaches provide important insights about neural encoding despite variability in the neural population on individual trials, it is limited when used on behaviors with more complexity. AutoLFADS utilized an auto-encoder deep-learning framework to infer latent dynamics from single-trial spike data (Keshtkaran et al., 2022). The algorithm also allows for fitting multiple sessions of latent dynamics into the same latent factor space, referred to as stitching. The stitching process along with AutoLFADS showed a consistent neural pattern (Fig. 2A) and good correlation between latent dynamics and kinematics (Fig. 2B) of initial submovements across different recording sessions. The generalized latent dynamics helped denoise the neural data for individual trials and provide a better representation of kinematics compared to smooth firing rates (Fig. 2B, D). Additionally, by utilizing t-SNE and subgrouping the neural latent factors, we could analyze the neural features of reaching relatively agnostic to any underlying model of reach kinematics. Rather than searching for neural firing rates representing experimenter-defined kinematic features with tools such as linear regression, we could examine trials when motor cortex activity was similar and then identify the commonalities and differences with regards to the corresponding kinematics of this similar appearing brain activity. These results demonstrate that AutoLFADS is a powerful tool in evaluating high-dimensional neural populations across different sessions.

Distinct neural features for initial and corrective phases of precise reaching

A previous study has shown uninstructed movements can dominate single-cell and population activity throughout the brain, outpacing task-related activity (Musall et al., 2019). Other recent analysis of our dataset showed a similar condition-independent cyclic neural trajectory pattern between initial and corrective submovements (Rouse et al., 2022). We now show here that when projected to the same latent factor plane, while the neural trajectory contains the cyclic structure, the neural trajectories for corrective movements also lie in an entirely different portion of the neural space for some neural dimensions (Fig. 4B). Unlike initial movements (Fig. 4A), latent factors of corrective movements cannot be clearly

classified under a single 2D plane when multiple kinematic features define the movements being encoded (Fig. 4B). Notably, this difference in corrective movements could not be explained by differences in starting position in the workspace as would be expected in a linear velocity plus position model (Moran and Schwartz, 1999). Rather, the dominant neural feature was a small number of neural origins for most corrective submovements.

Corrective submovements cannot be generalized in a single decoder

When applying a single linear decoder, initial and corrective movements cannot be decoded well across both types of movements. The corrective movements were especially poorly decoded by the initial movement decoder (Fig. 5A, 5C). We observed that the neural latent factors had large shifts for initial versus corrective movements, and corrective neural features were diverse. Therefore, we built multiple state-dependent decoders on clusters of the neural data to examine whether neural features distinct for subtypes of movements helped better describe the neural encoding of corrective movements.

Indeed, the corrective movements were not well organized into a single, linear encoding model in the neural space. When neural activity was decoded with only the most similar neural patterns in the neural space rather than fitting the neural features to a global space, decoding performance increased (Fig. 5B). The improvement continued to increase for up to at least 10 local subgroups. This suggests that the manifold for encoding corrective submovements is highly local with neural features not mapping neatly in a single, linear velocity space. Rather, idiosyncratic patterns of neural activity for subtypes of corrective movements appear to better define and predict the direction of a corrective movement. We hypothesize the motor cortex relies on a variety of corrective motor plans to generate a wide variety of corrective movements. The much higher-dimensional neural space of motor cortex would allow for a diverse set of patterns, all with convergent synaptic connections to the common lower-dimensional output of motor units.

Future implications

Understanding the range of neural features that arise across submovements is important for optimizing brain-computer interfaces (BCIs). Historically, most BCI decoders for continuous control have assumed

simple (e.g., linear, time-invariant) relationships between neural activity and intended movements (reviewed in (Pandarinath and Bensmaia, 2022)). More flexible decoding approaches, such as multi-state decoders (Williams et al., 2013; Sachs et al., 2016) and neural networks (Sussillo et al., 2012, 2016; Willsey et al., 2022; Deo et al., 2023) have introduced the ability to capture both nonlinear relationships between neural features and intended movements, and potentially any state-dependence in this relationship. Here we demonstrated that linear decoders that are localized to different regions of state space can improve decoding of single-trial movements, which helps elucidate the mechanisms that allow flexible decoding strategies to improve BCI performance, and can guide data collection and data augmentation strategies when training flexible decoders. These insights are also important when considering how to train and incorporate latent variable models, which have the potential to achieve complementary improvements in BCI stability (Pandarinath et al., 2018a; Farshchian et al., 2019; Karpowicz et al., 2022; Ma et al., 2022).

With the help of AutoLFADS, we were able to better reveal the neural dynamics between initial and corrective submovements across sessions. Even with stitching, our dataset is still limited since the motor errors were self-generated by the animal and resulted in impromptu corrective submovements on each single trial. The sample size for each corrective movement phase including correction start position and correction velocity vector is thus still unbalanced even after data aggregation. More tasks that likely include not just user-generated errors but multiple instructions and online visual or mechanical perturbations are needed to further quantify all types of corrective movements. Future work is also likely needed to identify features that best separate the corrective submovements to build state-dependent decoders that can transition kinematics under different movement states to best predict the kinematics.

Figures:

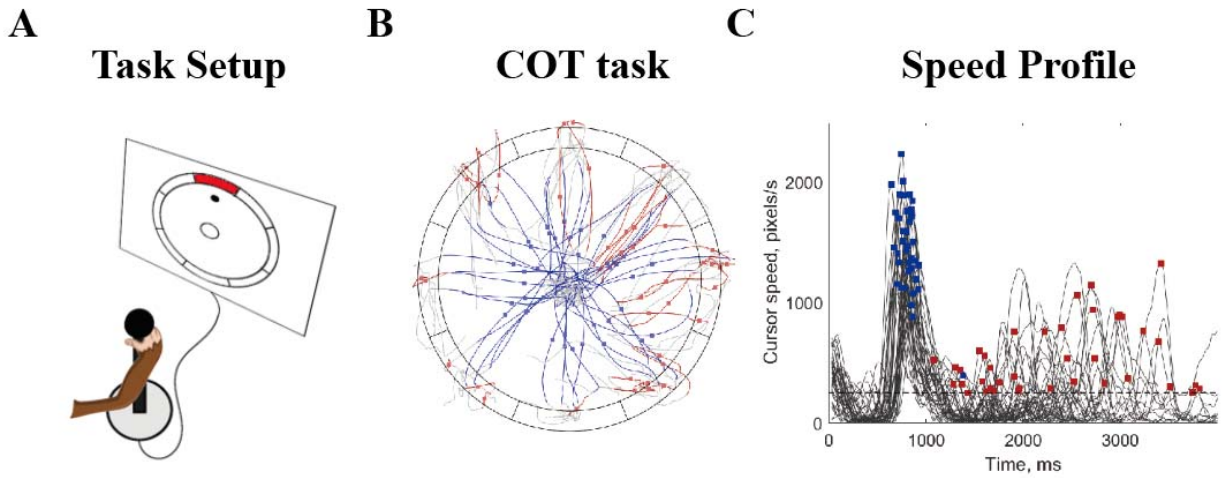

Fig1. Behavior task schematic

A) Behavior task scheme showing the control and display of cursor. B) The schematic for the center-out task displays the targets arranged in eight uniformly distributed outer blocks, with the initial reaching movements illustrated in blue and the corrective reaching movements in red. C) Cursor speed profile of the movement trials over time, Initial (blue) and corrective (red) submovement speed peaks are identified with squares.

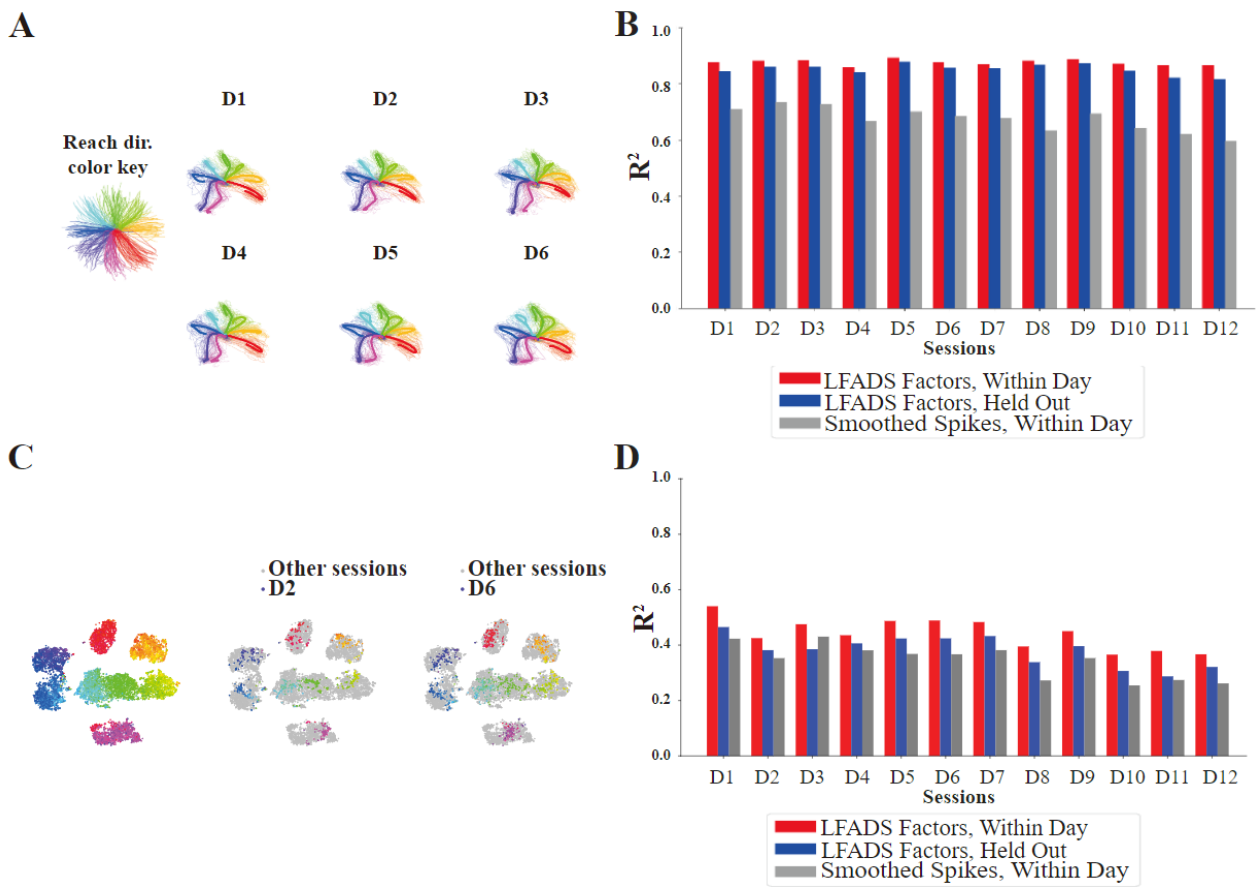

Fig2. AutoLFADS and stitching enables analysis of cross-session neural data

A) Neural trajectories for each single session are shown in the subplots in the first three PC space of LFADS factors. The single trials in each session are presented as thin lines in the subplot and average trajectories for 8 different directions are presented in bold colored lines the color key for each reaching direction is shown on the left. C) t-SNE plot of initial submovements across all sessions and 2 of the single sessions, color coded by movement direction. B,D) Correlations between kinematic and latent factors of both hold-in/hold-out dates for LFADS factors and hold-in dates for smoothed spikes, showing separately for initial submovements (B) and corrective submovements (D) . Indicating inferred neural dynamics after ‘stitching’ process can generalize to single sessions not in the original training set and also better correlates to the kinematic data than smoothed firing rates.

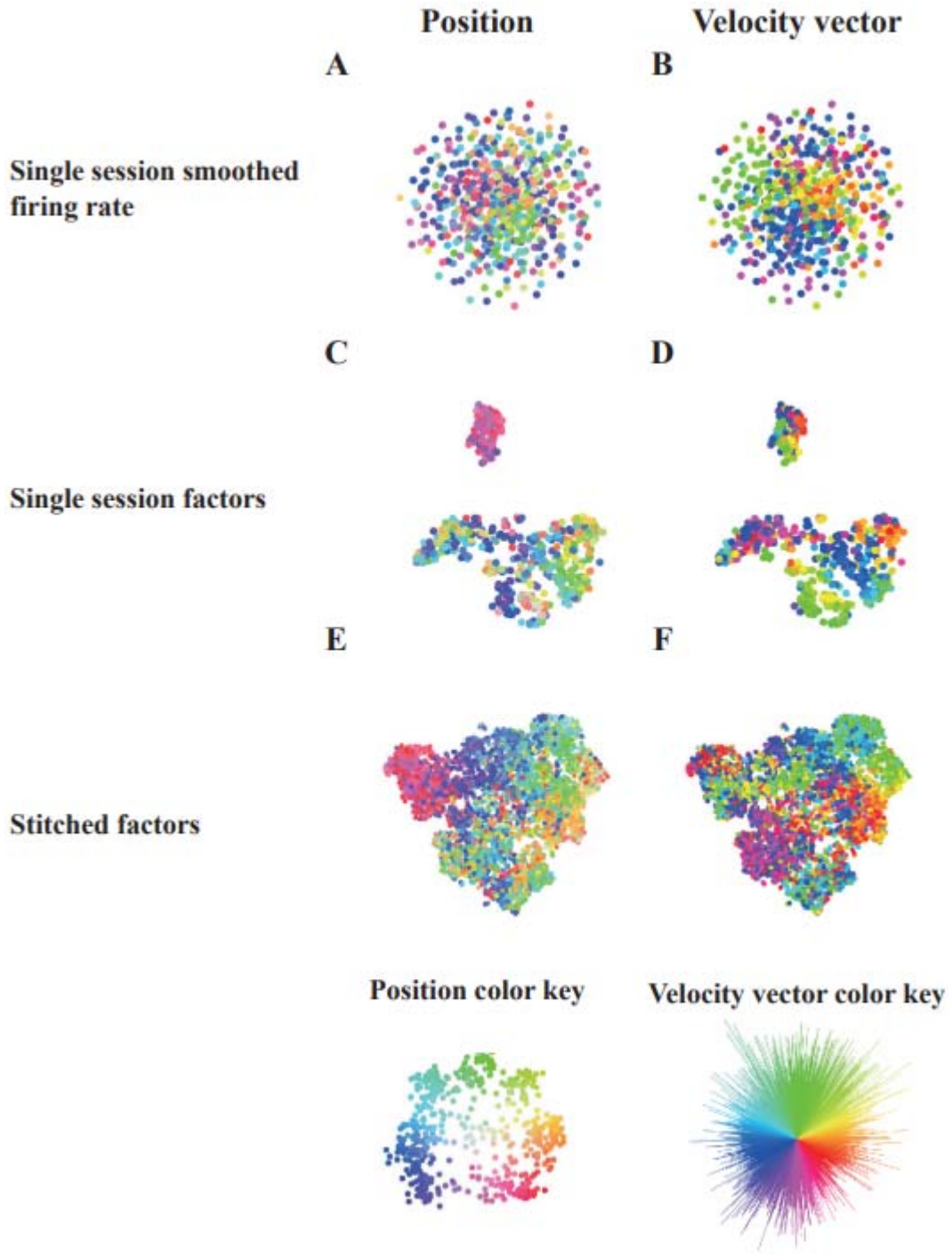

Fig3. t-SNE cluster plots of corrective submovements in A/B) smoothed firing rates space C/D) latent factors space for a single session and E/F) latent factors space across all sessions.

A/B) Single session t-SNE plots of corrective submovement color coded by position and velocity vector projected in smoothed firing state space. C/D) Single session t-SNE plots of corrective submovement color coded by position and velocity vector projected in latent factor space. E/F) 'Stitched' session t-SNE plots of corrective submovement color coded by position and velocity vector projected in latent factor space. Bottom row shows the color key for position and velocity vector color coding.

Left panels are color coded for position at the onset of each submovement 100 ms before peak speed using the direction from the center for color hue and the distance from the center for saturation. Right panels are colored by reach direction using the straight-line reach direction from 100 ms before until 100 ms after peak speed. Showing AutoLFADS factors can better identify and separate the neural patterns related to the corrective kinematics, and stitching across sessions is necessary to have a large enough sample of the diverse movements diverse to better identify structure in corrective movements.

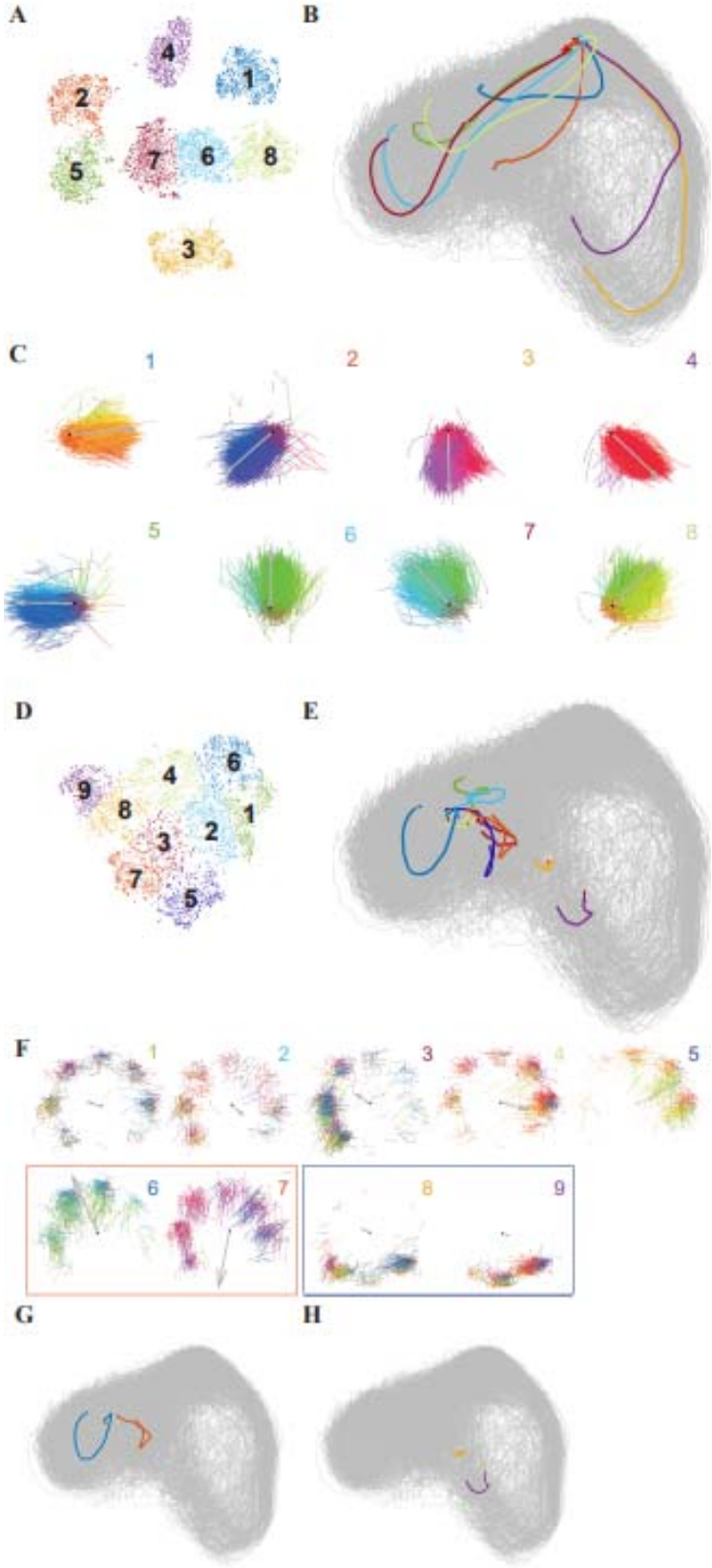
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Fig 4. The identified organization of submovements in the neural space and their corresponding kinematics for initial and corrective submovements

A,D) t-SNE plots of initial and corrective submovements AutoLFADS factors, color coded by subgroup identified with Kmeans. We selected the number of KNN groups to be 8 for initial and 9 for corrective submovements based on visual inspection. B,E) Neural trajectories of initial and corrective submovements factors. Average neural trajectories are color coded based on the t-SNE subgroups. All neural trajectories are colored gray in the trajectory plot. C,F) Movement trajectories for each subgroup identified based on the neural activity. The colored number for each subgroup corresponds to the subgroups shown in panels A&B and D&E. The movement trajectories are color coded based on velocity vector (same color key as Fig. 4). Within each subplot, the center target position was marked with a black dot, start position of each submovement was marked with red dot, and average velocity vector and relative amplitude are annotated in gray arrow.

Distinct neural dynamics between initial and corrective submovements were observed with corrective submovements occurring in a different location of the neural space. Also, the corrective submovements form subgroupings of movement that depend both on the current hand location following the initial reach and the subsequent movement direction.

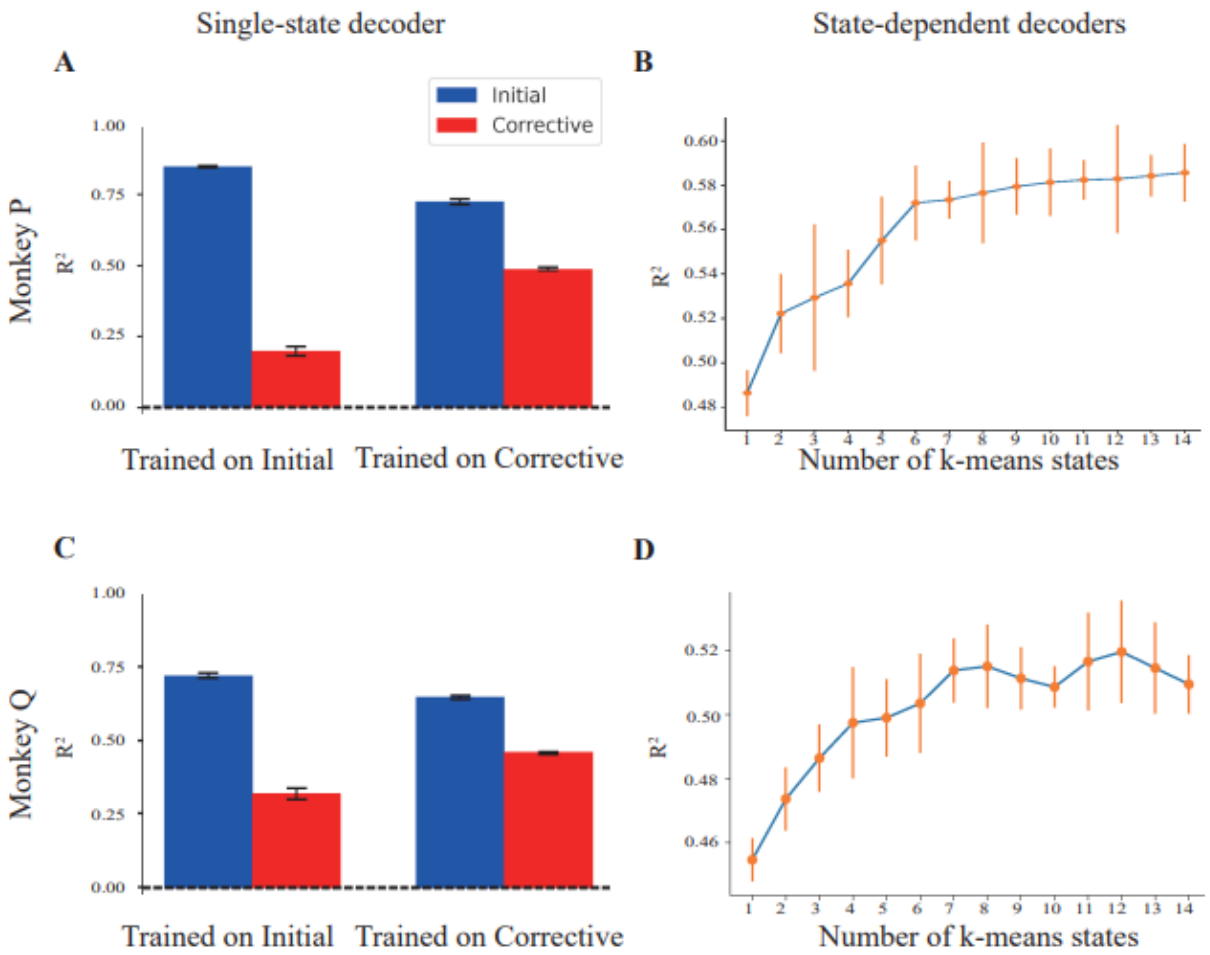

Fig 5.

A,C) Decoding performance and generalizability for initial and corrective movements. Prediction/ accuracy of initial/corrective velocity from latent factors as measured with R^2. The velocity of neural data is predicted for initial submovements in blue bars and corrective submovements in red bars using a ridge-regression linear neural decoder that was trained on initial(left) or corrective(right) data. Showing poor generalization from initial to corrective submovements. B,D) Decoding performance on velocity and discrete state corrective movement decoders. Regression analysis using sub groups decoders. Discrete state linear regression decoders were trained utilizing 1 (a single global decoder) to 14 separate states. For the discrete state linear decoder, each trial would be classified based on its neural state at the onset of the corrective submovement and then a linear prediction from a regression model specific to that subgroup was used to predict velocity. Error bars represent 95% confidence intervals for 1000 bootstrapped iterations. Showing subgrouping of corrective submovements improves predictions significantly compared to a single decoder over all corrective submovements.

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Contributions:

	WL	BK	CP	AR
Designed research	v	v	v	v
Performed research	v	v		
Contributed unpublished reagents/analytic tools				
Analyzed data	v	v	v	v
Wrote the first draft of the paper	v	v		
Edited the paper	v	v	v	v
Wrote the paper	v	v	v	v

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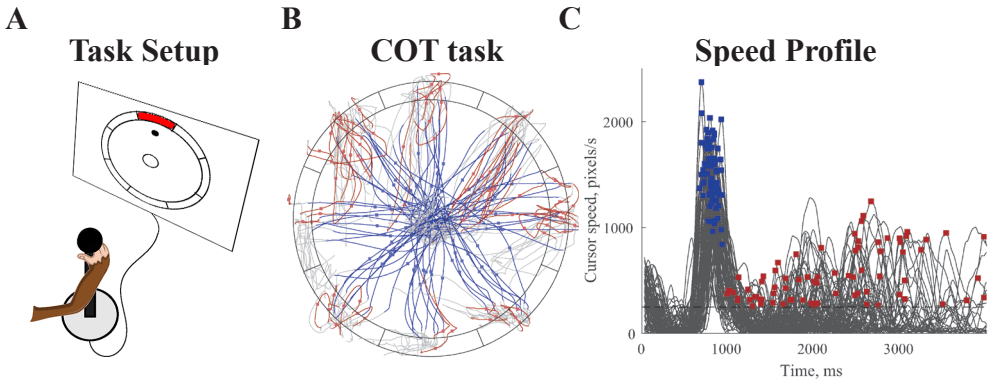
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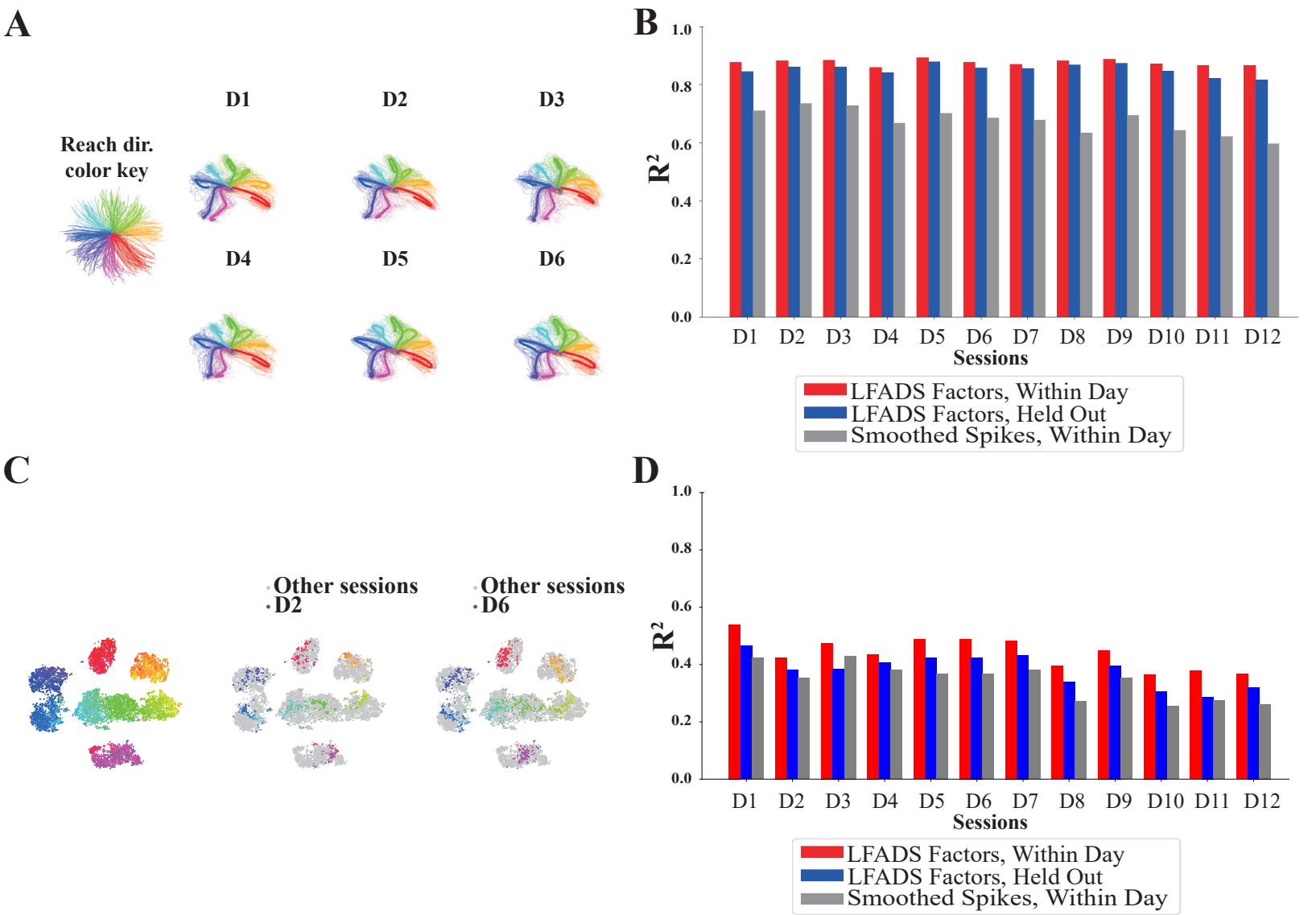
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Sessions
LFADS Factors, Within Day
LFADS Factors, Held Out
Smoothed Spikes, Within Day
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Other sessions
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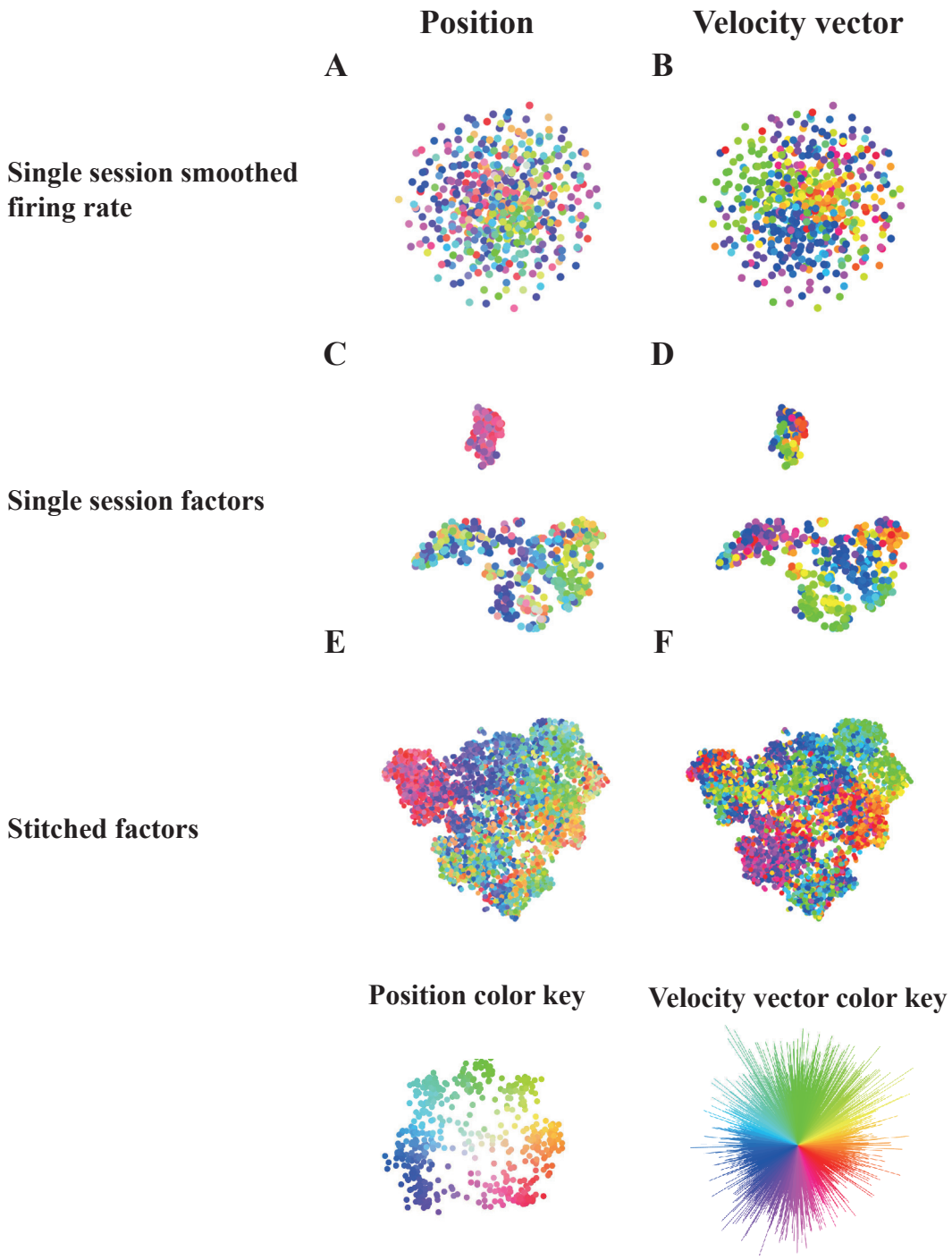
Sessions
LFADS Factors, Within Day
LFADS Factors, Held Out
Smoothed Spikes, Within Day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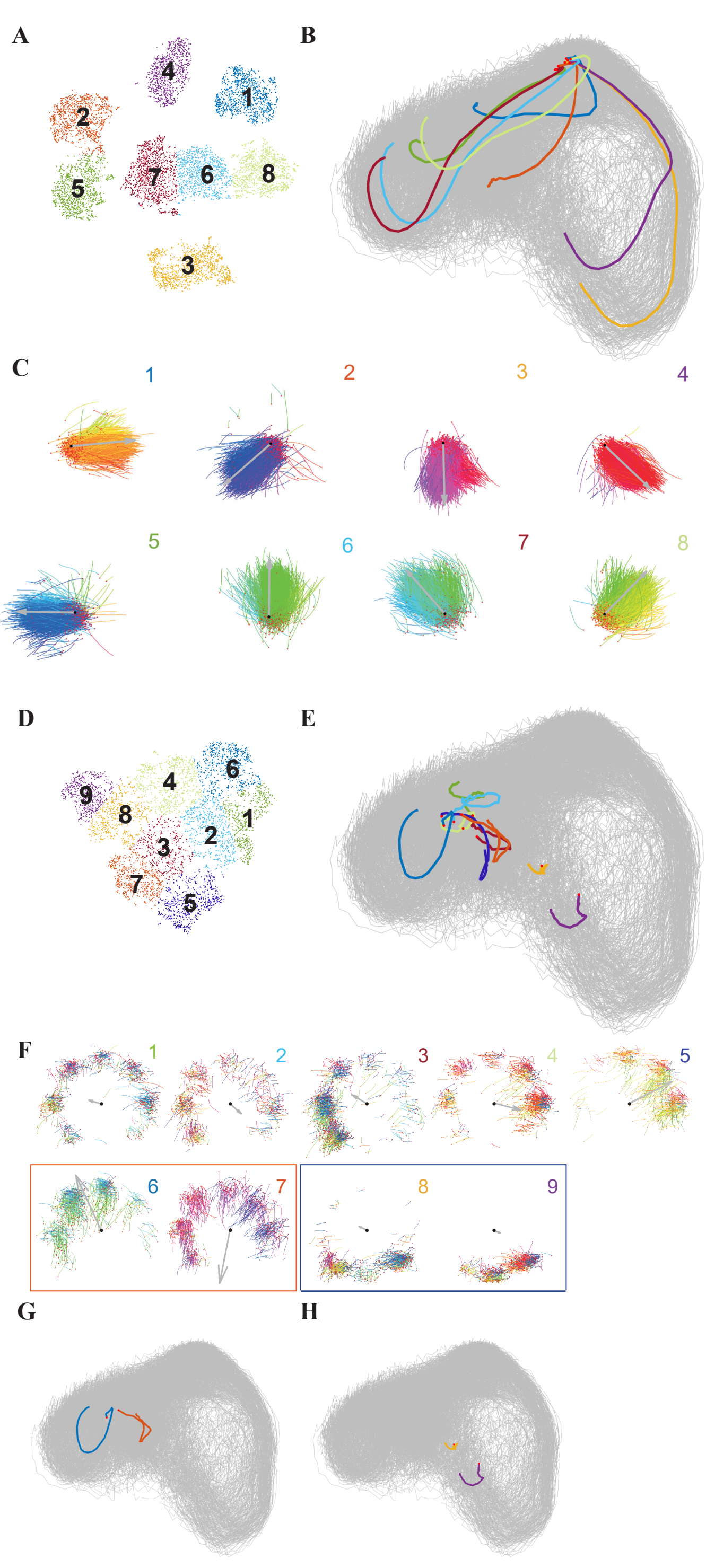
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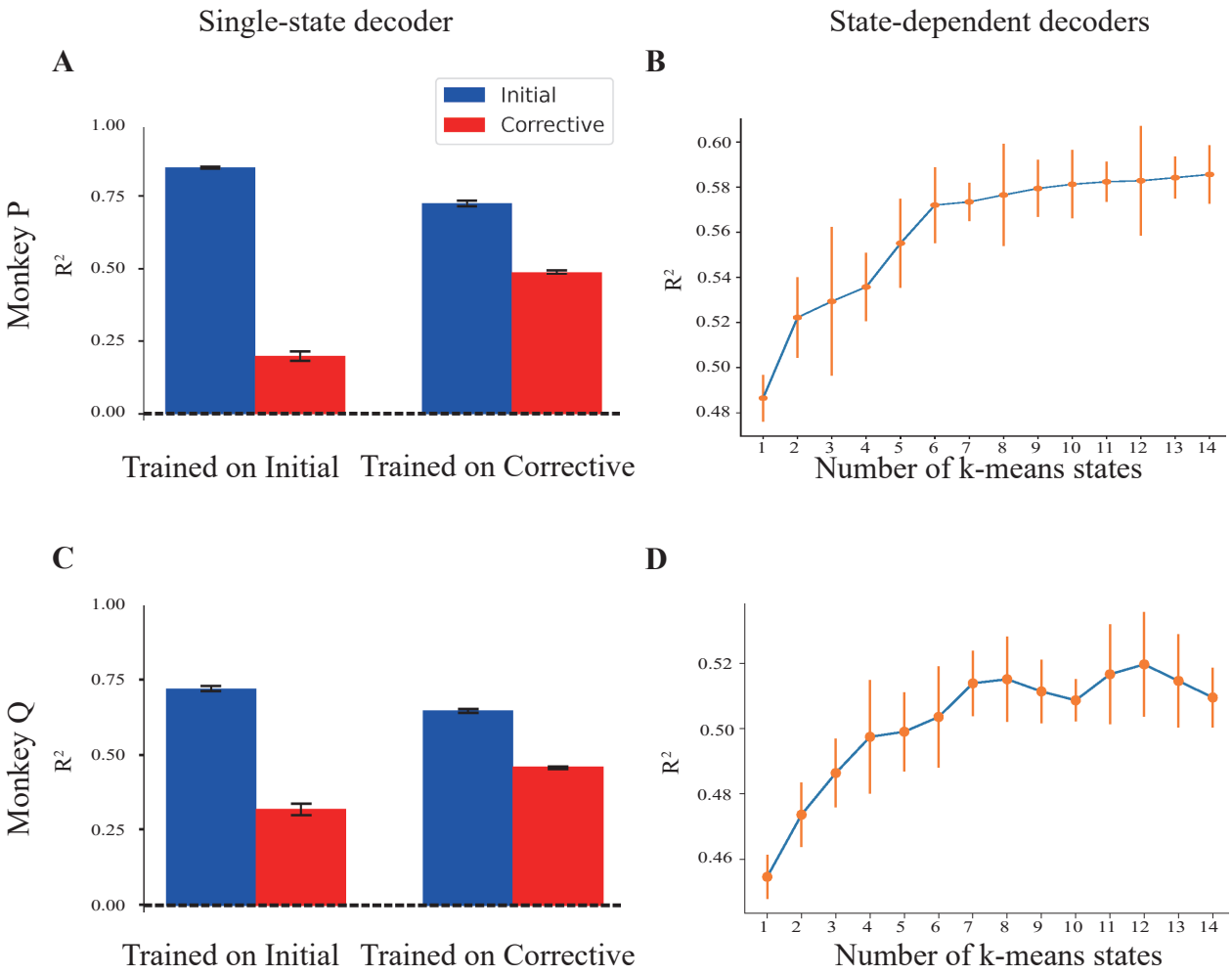
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State-dependent decoders
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C
D
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Corrective
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Monkey Q
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0.50
0.25
0.00
Trained on Initial
Trained on Corrective
0.60
0.58
0.56
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0.52
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Number of k-means states