



Introduction

Growing evidence suggests that prefrontal cortex (PFC) has predominant number of mixed selectivity neurons and neurons with nonlinear mixed selectivity which enable spanning high dimensional neural space. Conventionally these property was thought to be only applied to higher level brain area, PFC or other brain structures involved in cognition. However, it remains largely unknown whether lower level brain area, such as primary somatosensory (S1) cortex processes information as the same way. S1 is relatively lower level brain area of sensory perception that plays an important role in the perception and discrimination of touch and pain mechanosensations. Here, we examined how population neurons of S1 cortex process information by conducting experiments with diverse features of sensory stimulus of brushing, pressing, and pinching, using in vivo two-photon Ca²⁺ imaging in the layer 2/3 neurons of the mouse S1 cortex (n=4). We investigated the coding principles of S1 neurons at population level with various computational analyses using experimental data.

Coding principles of neural population

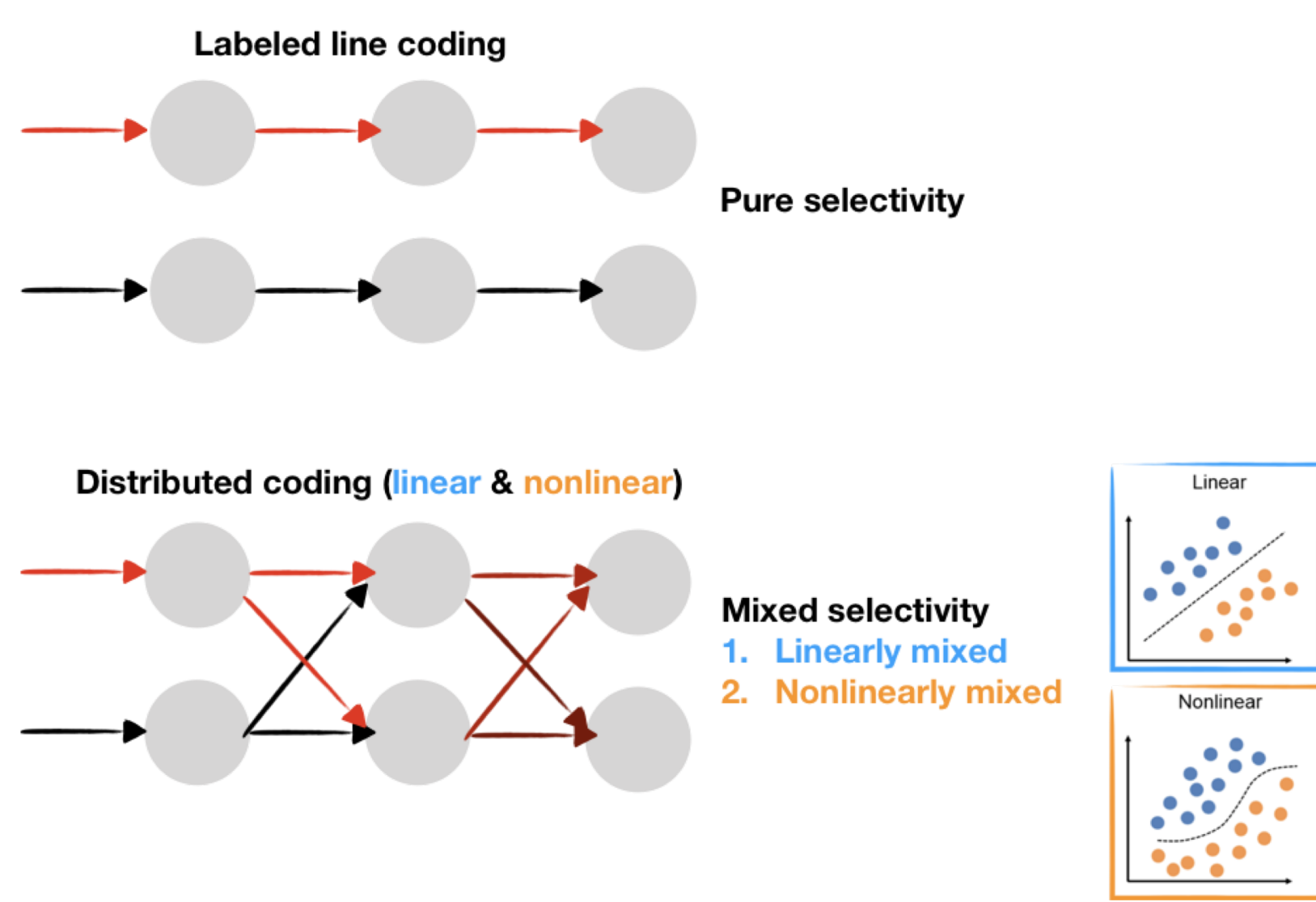


Figure 1. Coding principles of neural population

The neural coding principles at population level can be divided into **labeled line coding** that particular neurons are responsible for coding specific information and **distributed coding** that multiple neurons process information in a distributed and parallel manner. This can be seen as having pure and mixed selectivity, respectively, in terms of individual neurons. Further, according to the way of distribution, distributed coding can be categorized as **linearly distributed** and **non-linearly distributed coding**.

Methods

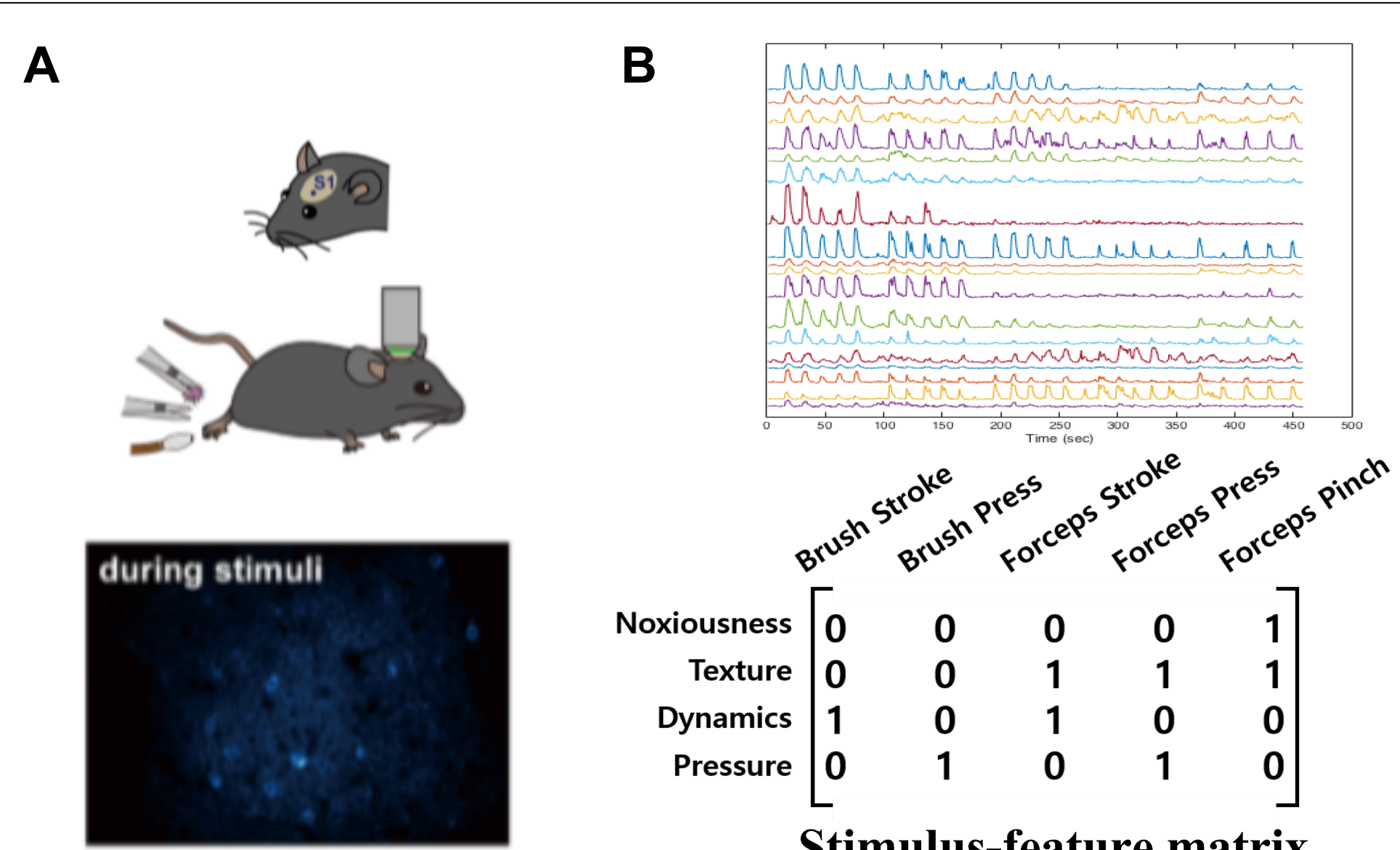


Figure 2. (A; Top) Schematic diagrams of experimental approach: A craniotomy was made over the S1 cortex corresponding to the hind limb in the left hemisphere and five types of sensory stimuli were delivered to the right hind paw of anesthetized head-fixed mice using brush and forceps. **(Bottom)** Representative in vivo two-photon Ca²⁺ fluorescence images of layer 2/3 S1 neurons during stimulation with brushes and forceps. **(B; Top)** Representative data of in vivo two-photon Ca²⁺ imaging in layer 2/3 S1 neurons during stimulation (5 types*5 repetitions) **(Bottom)** Data used in the present study has 5 types of stimulus (each column): brush stroke, brush press, forceps stroke, forceps press, and forceps pinch. According to the stimulus, feature can be derived (each row).

Definition of pure selectivity, linear and nonlinear mixed selectivity

$$P_i = \beta_0 + \sum_{j=1}^4 \beta_j f_{ij}, \quad i = 1, 2, \dots, 25. \quad (1)$$

A neuron is determined to show pure selectivity to the feature j , when the response of the neuron in i th trial are significantly explained by the feature j , but not the other features ($p < 0.05$ only for β_j) in multiple linear regression model, where predictors are features and the the outcome is the peak response value of the neuron in each trial.

$$\sigma^2_{total} \cdot v_{total} = \sigma^2_{lin} \cdot v_{lin} + \sigma^2_{nonlin} \cdot v_{nonlin} + \sigma^2_{error} \cdot v_{error} \quad (2)$$

linear mixed components:

$$\frac{\sigma^2_{lin} \cdot v_{lin}}{\sigma^2_{total} \cdot v_{total} - \sigma^2_{error} \cdot v_{error}} \quad (3)$$

nonlinear mixed components:

$$1 - \frac{\sigma^2_{lin} \cdot v_{lin}}{\sigma^2_{total} \cdot v_{total} - \sigma^2_{error} \cdot v_{error}} \quad (4)$$

Results

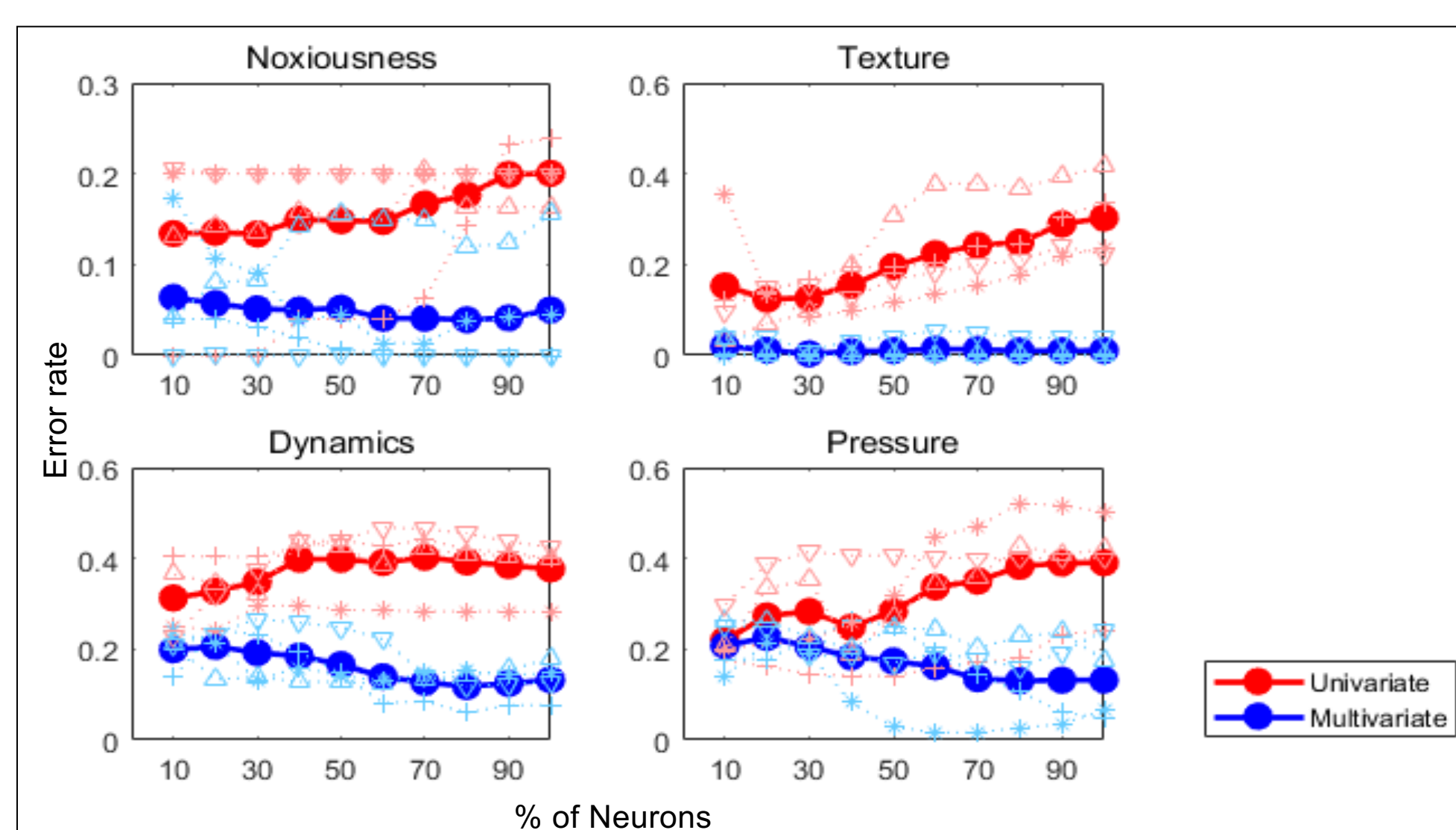
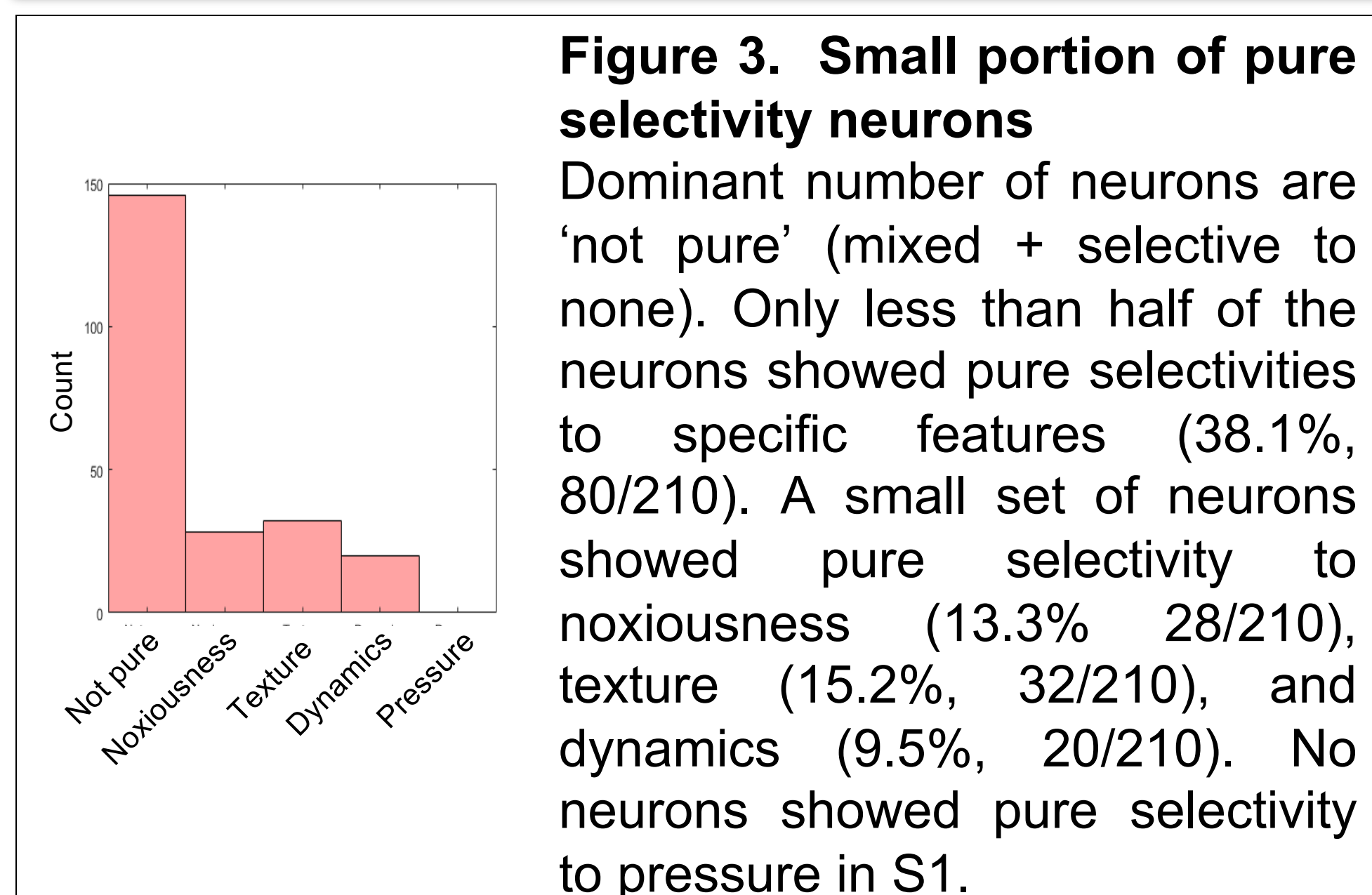


Figure 4. Better performance with distributed coding
Univariate and multivariate SVM classifiers were used to decode each feature from neural responses. We investigated the trend of information processing of S1 by analyzing the performance with incremental number of neurons, adding from neurons with high selectivity to feature (absolute t statistic of neurons were calculated), Mean error rate of univariate and multivariate SVM classifiers are shown as filled red circle and filled blue circle, respectively. Individual values are displayed as pink and sky blue symbols (n=4).

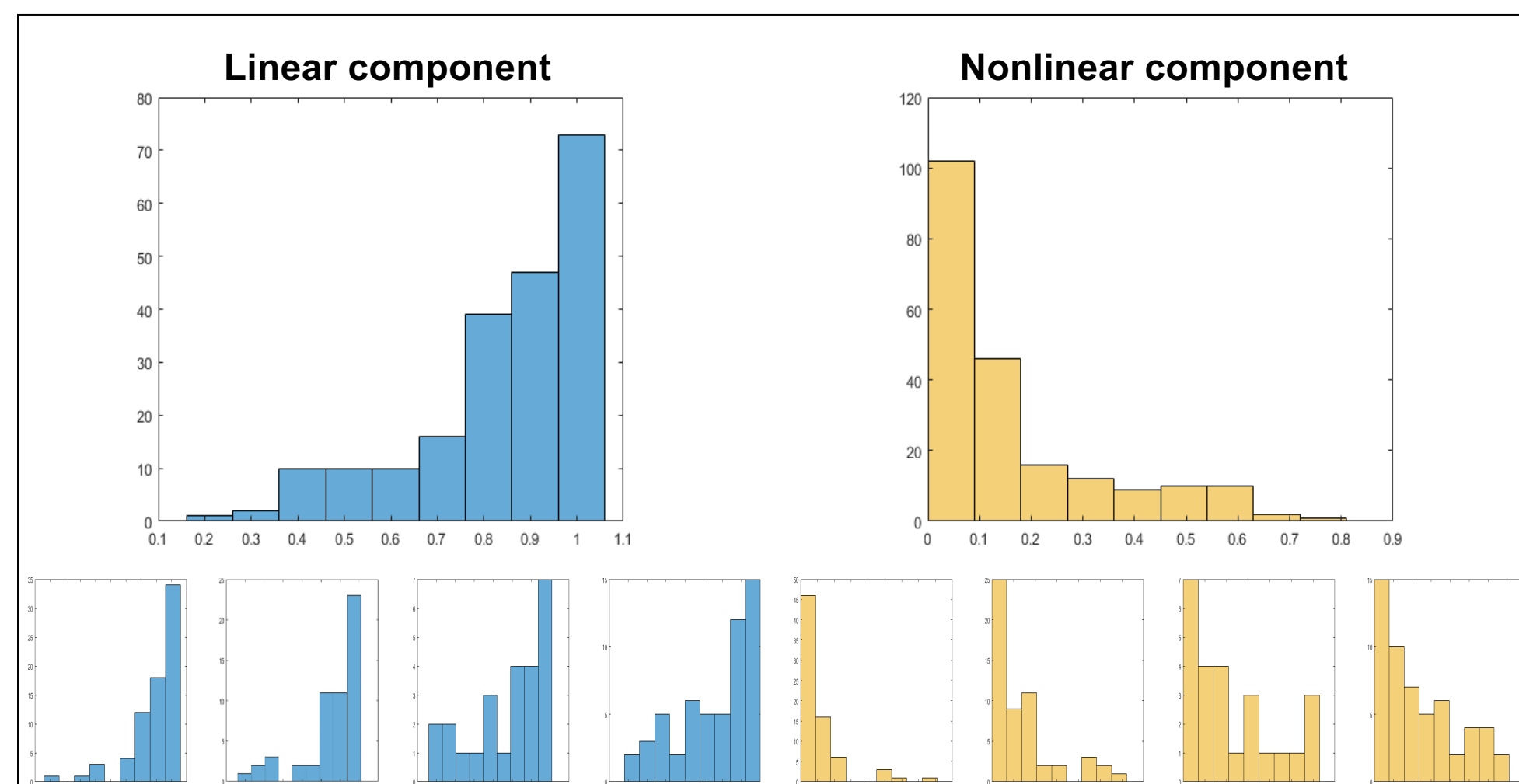


Figure 5. Linear and nonlinear mixed selectivity components of S1 neurons (n=4). While almost all variability of most neurons could be explained by linear mixed selectivity, several neurons showed relatively high proportion of the nonlinear mixed selectivity

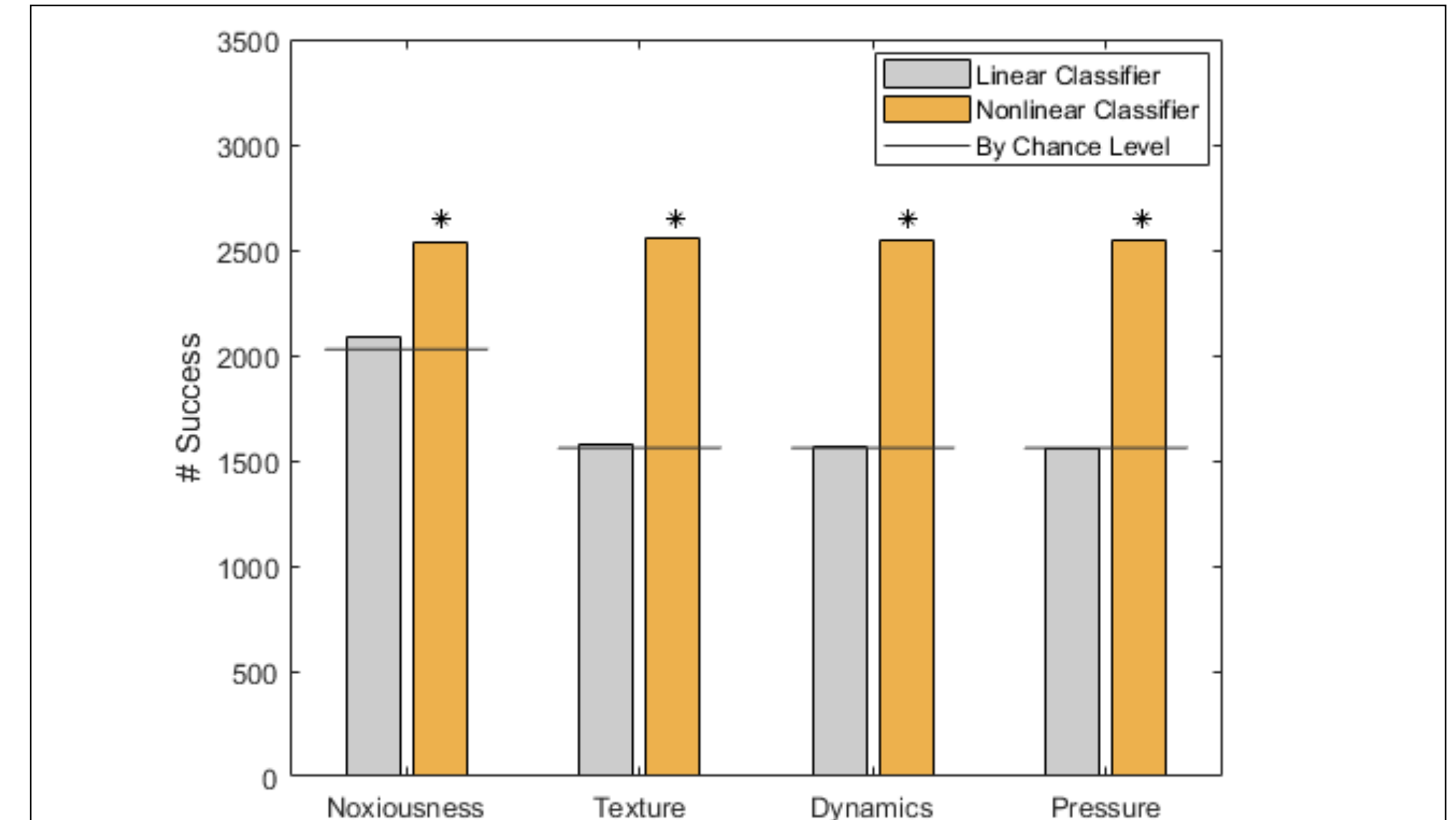


Figure 6. Information coding of S1 neurons with nonlinear mixed selectivity

Linear SVM and polynomial SVM (nonlinear) were used to decode each feature from nonlinear component of neural responses to measure how much feature-related information neurons encode nonlinearly. Note that the prediction performance are significantly higher than by chance level when using nonlinear classifier. On the contrary, the performance of linear classifier is no better than by chance level.

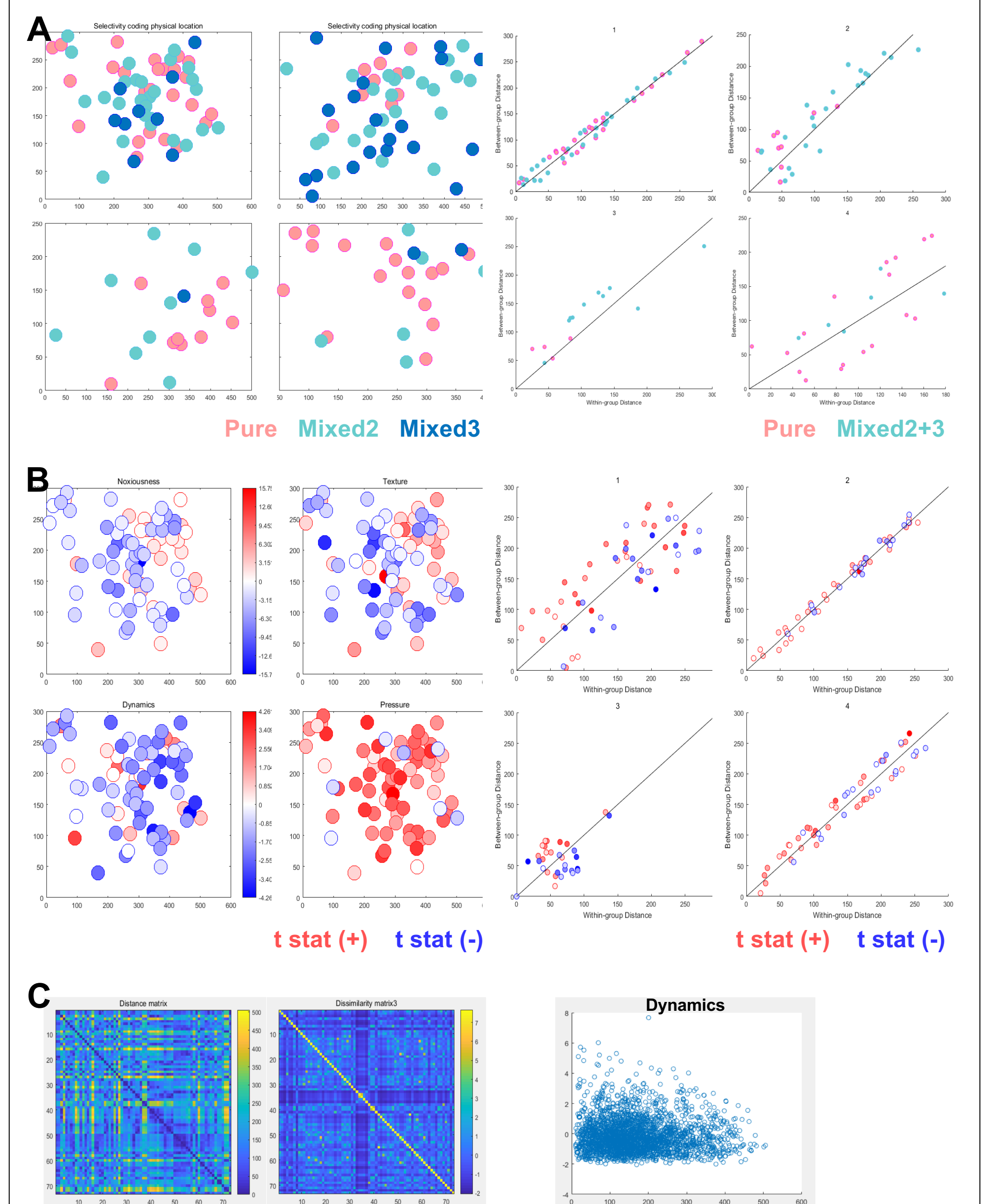


Figure 7. Correlation of physical location and feature coding principles (exploratory analysis)

(A) Color coded map with pure and mixed selectivity neurons (n=4). (Right) Within-group and between-group distance were calculated using centroids. In our data, we could find the trend that both groups have shorter within-group distance, suggesting clustering according to pure and mixed selectivity. **(B)** Color coded map with the degree of selectivity to the specific feature (n=1). (Right) Within-group and between-group distance were calculated using centroids. Neurons with activated response show shorter within-group distance, when coding noxiousness and dynamics feature. However, variability between mouse was high. **(C)** We calculated distance and dissimilarity between all neurons using physical location and t statistic. We could find slight minus correlation between distance and dissimilarity when coding dynamics ($r = -0.04$, $p = 0.03$).

Conclusion

1. Dominant number of S1 neurons show mixed selectivity rather than pure selectivity.
2. S1 neurons showed better decoding performance for all features with distributed coding (multivariate) than labeled line coding (univariate).
3. S1 neurons have nonlinear mixed selectivity components, as well as linear components.
4. S1 neurons encode multiple features of mechanosensation using nonlinear mixed selectivity.