Remembering in quadrants: Non-linear representation of mnemonic space in the primate brain

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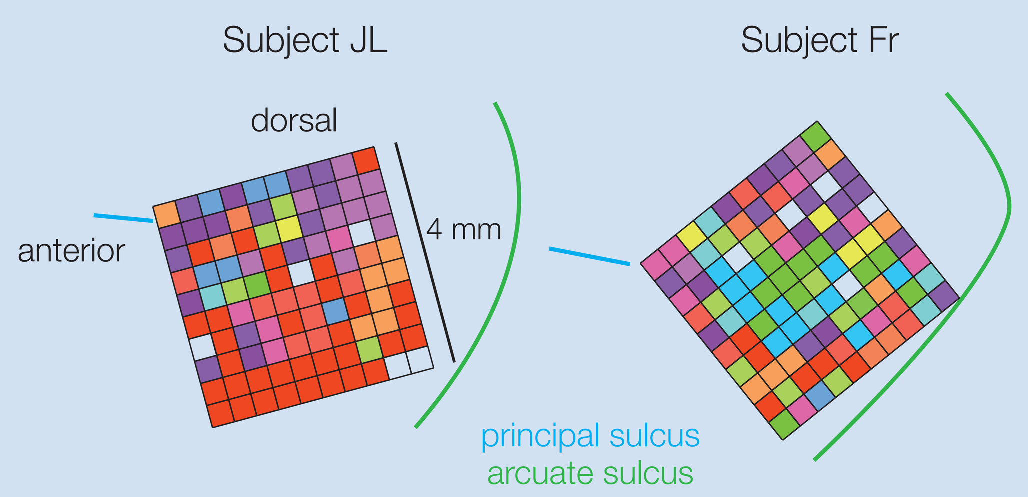
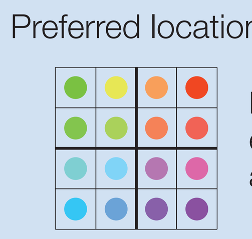
Introduction

Single neurons in the primate prefrontal cortex (PFC) are known to encode working memory (WM) representations of visual space via sustained firing in the absence of external input. Despite the substantial body of research on the neural correlates of WM in the PFC, little is known about whether and how these mnemonic representations vary across the visual field. Previous studies have parameterized visual space as binary (e.g. left/right) or unidimensional (e.g. degrees of angle across the same eccentricity), leading to models of spatial WM that assume a continuous and/or homogenous representation of the visual field. Furthermore, it is unkown whether the information contained within ensembles of simultaneously-recorded neurons is sufficient to encode remembered locations on a single trial basis, and how correlated variability between neurons affects the fidelity of this information.

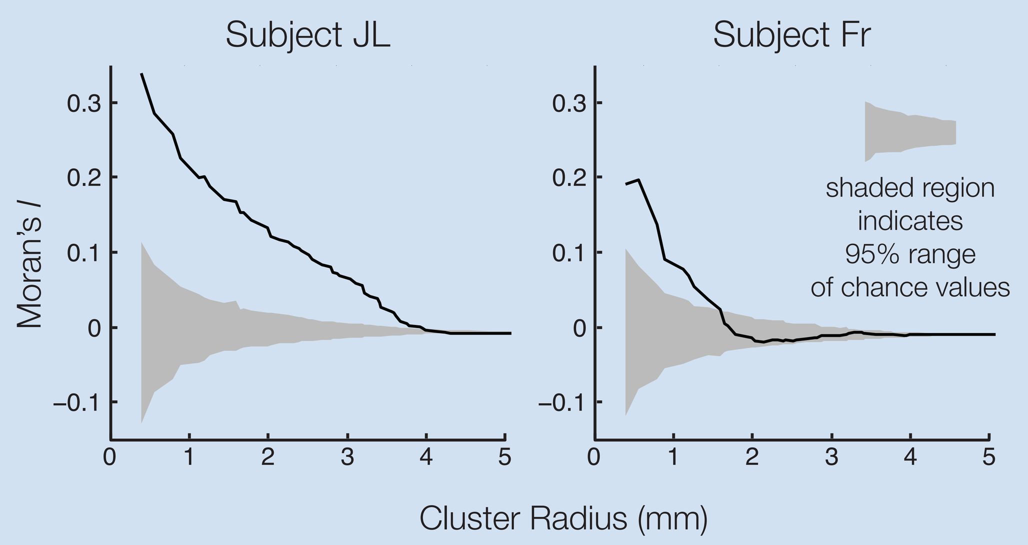
Mnemonic selectivity is anatomically clustered

Moran's *I* is a measure of spatial correlation that ranges between -1 and 1. Positive values indicate that similar feature values (in this case preferred locations) are spatially clustered; a given location in space (in this case the area around an electrode) is more likely to be in a local neighborhood with other similar values. Negative values of Moran's *I* indicate that similar feature values are spatially repellant. Moran's *I* is computed across the range of all distances between electrodes on the array, allowing us to determine how preferred location similarity clusters across different spatial scales.





Preferred memory location is defined as location that elicits maximum response of all thresholded activity on an electrode.



Moran's *I* is defined as:

$$I = \frac{N}{\sum_i \sum_j w_{ij}} \frac{\sum_i \sum_j w_{ij}(X_i - \bar{X})(X_j - \bar{X})}{\sum_i (X_i - \bar{X})^2}$$

where *N* is the number spatial units indexed by *i* and *j*; *X* is the the variable of interest; $\bar{X}$ is the mean *X*; and w_{ij} is an element of a matrix of spatial weights.

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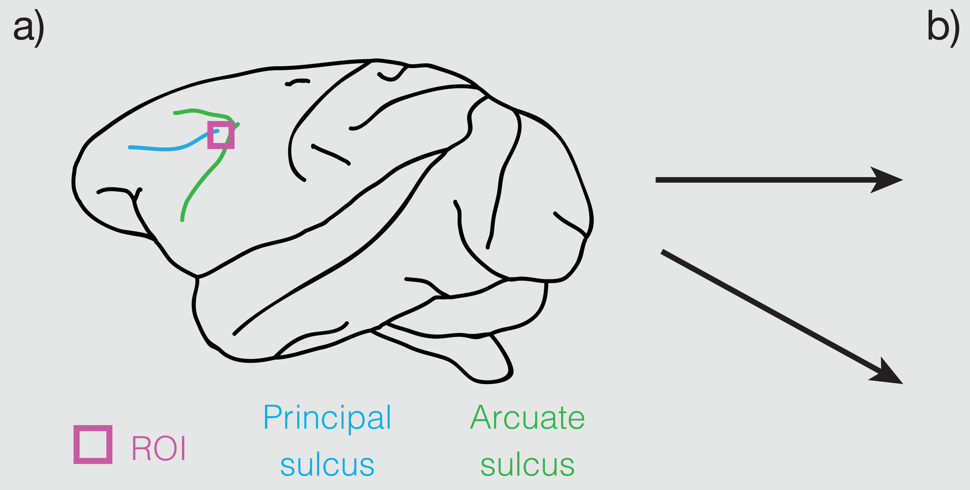
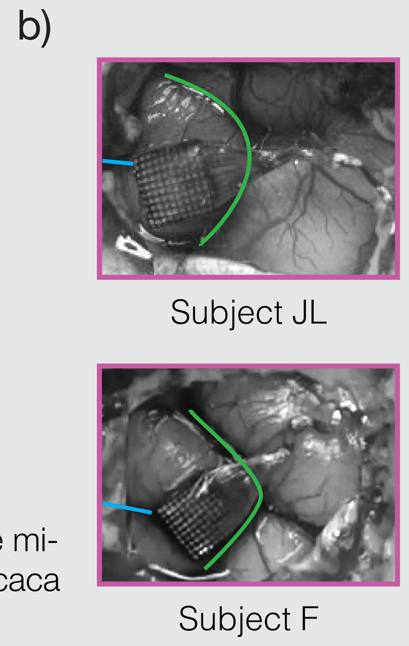
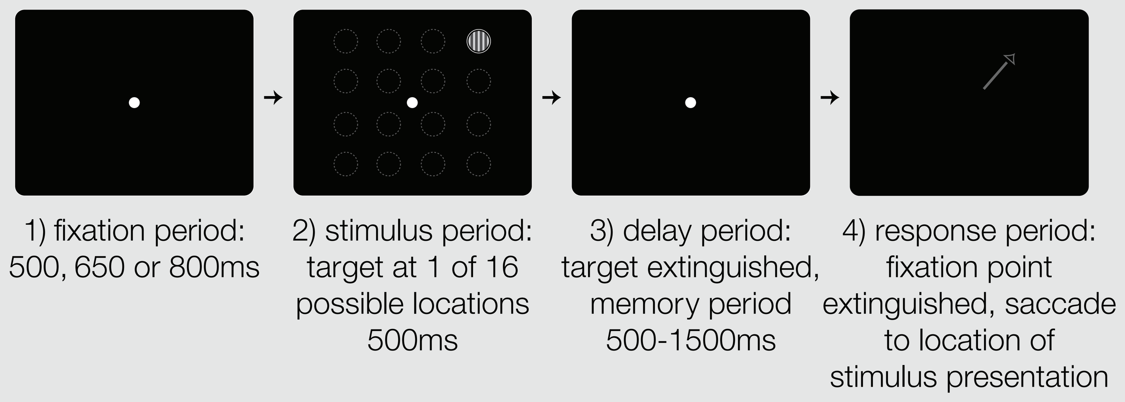
Methods





a) region of implantation. b) implantation site of the 96-electrode microarray (Blackrock Microsystems, Utah) in each of the two Macaca fascicularis (subjects JL and F).

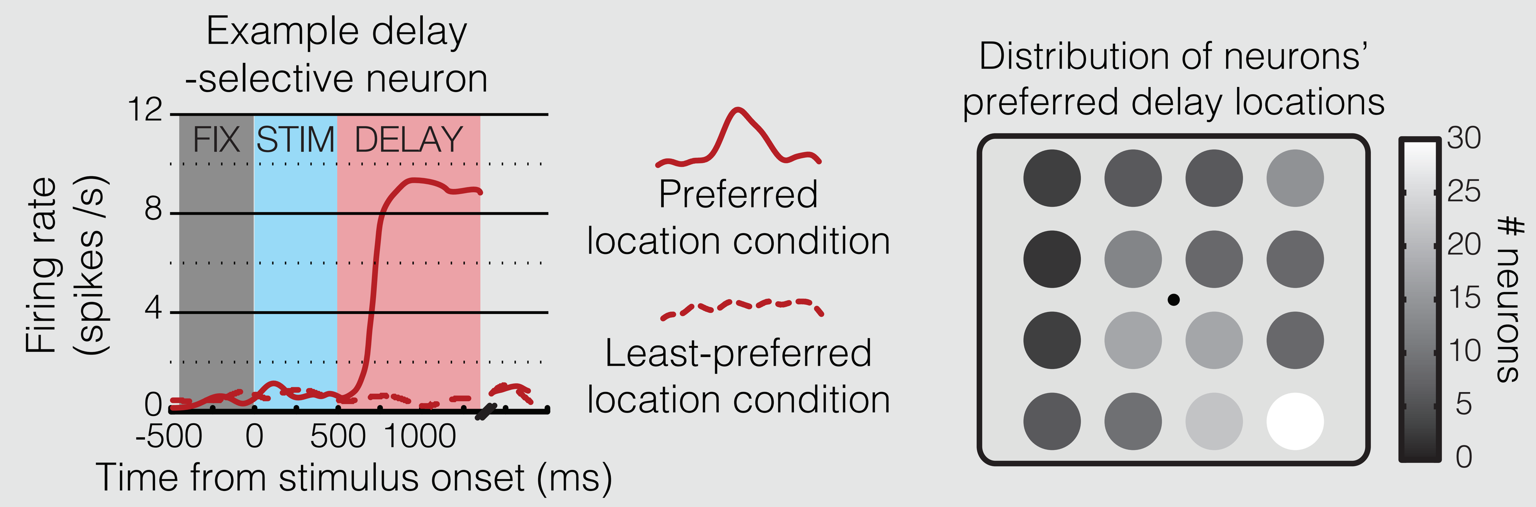
Task



Subjects initiated a trial by fixating on a dot in the center of a back-projection screen and depressing a lever. Dashed circles indicate potential target locations. Only successfully completed trails were analyzed.

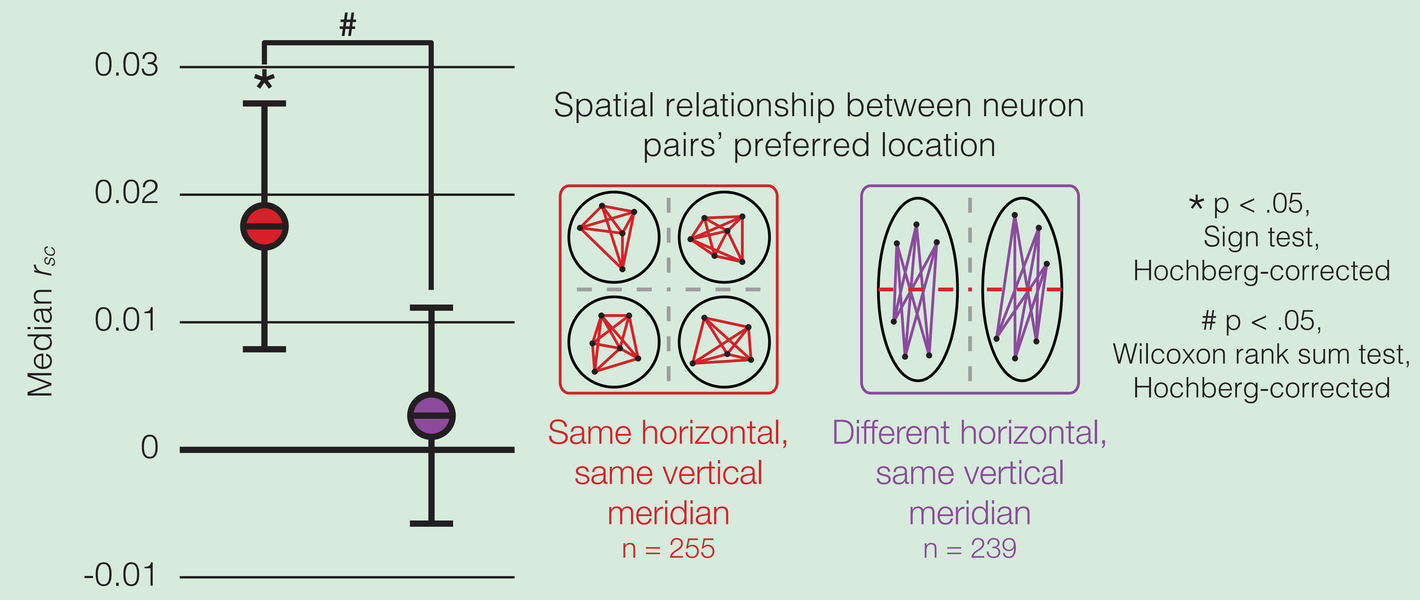
Single neuron statistics

Selectivity was determined by calculating spike rates during the delay epoch of all successful trials and performing a Kruskal-Wallis with location as the factor. Selective neurons showed a significantly different firing rate (P < .05) for at least one location. A neuron's preferred location was defined as the location that elicited the largest response averaged over the delay epoch. We identified 157 of the 201 recorded neurons as delay-selective.



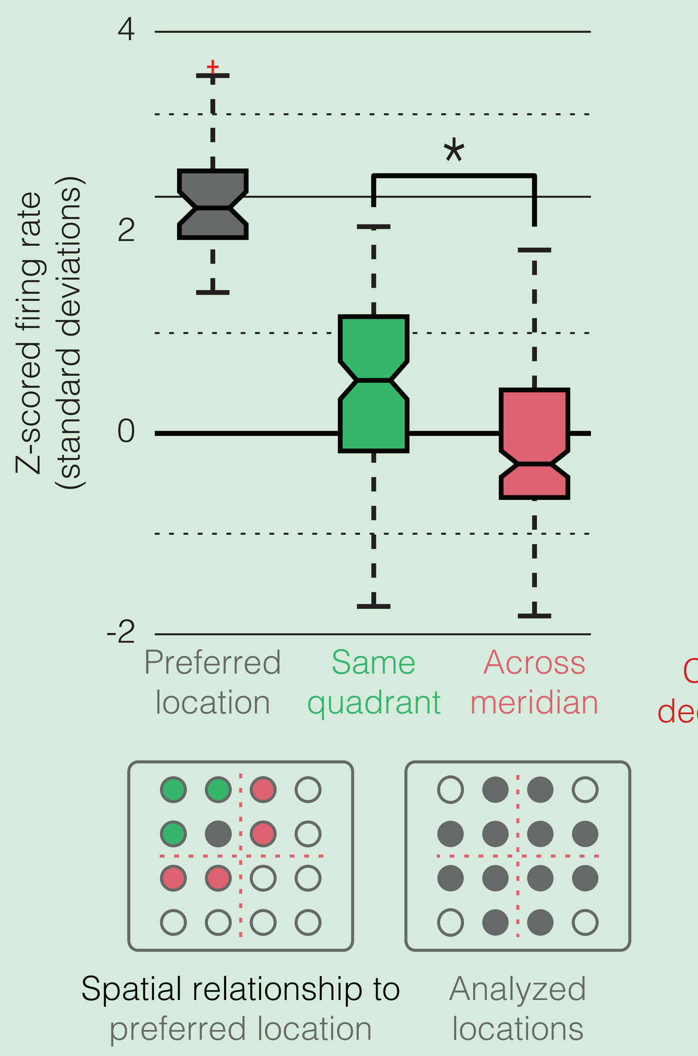
Quadrantic bias in correlation structure

It is thought that the sustained activity encoding visuo-spatial WM is maintained at a neural circuit level by a recurrent excitatory + lateral inhibitory connection scheme, which results in shared fluctuations, or correlated variability, in firing rate between pairs of PFC neurons during WM tasks (Goldman-Rakic, 1995; Wimmer et al., 2014). If pairs of neurons encoding visuo-spatial WM representations in the same quadrant (intraquadrant pairs) are more coupled than pairs of neurons encoding representations in different quadrants (extraquadrant pairs), we should see higher correlated variability between the intraquadrant neuron pairs relative to the extraquadrant pairs. We found that r_{sc}, a measure of correlated variability, during the delay epoch between intraquadrant neuron pairs was significantly larger than r_{sc} between neurons with preferred locations on the same side of the vertical meridian but opposite sides of the horizontal meridian (*P* = 0.012, Wilcoxon rank sum test, Hochberg-corrected).



Quadrantic bias in single neuron firing rates

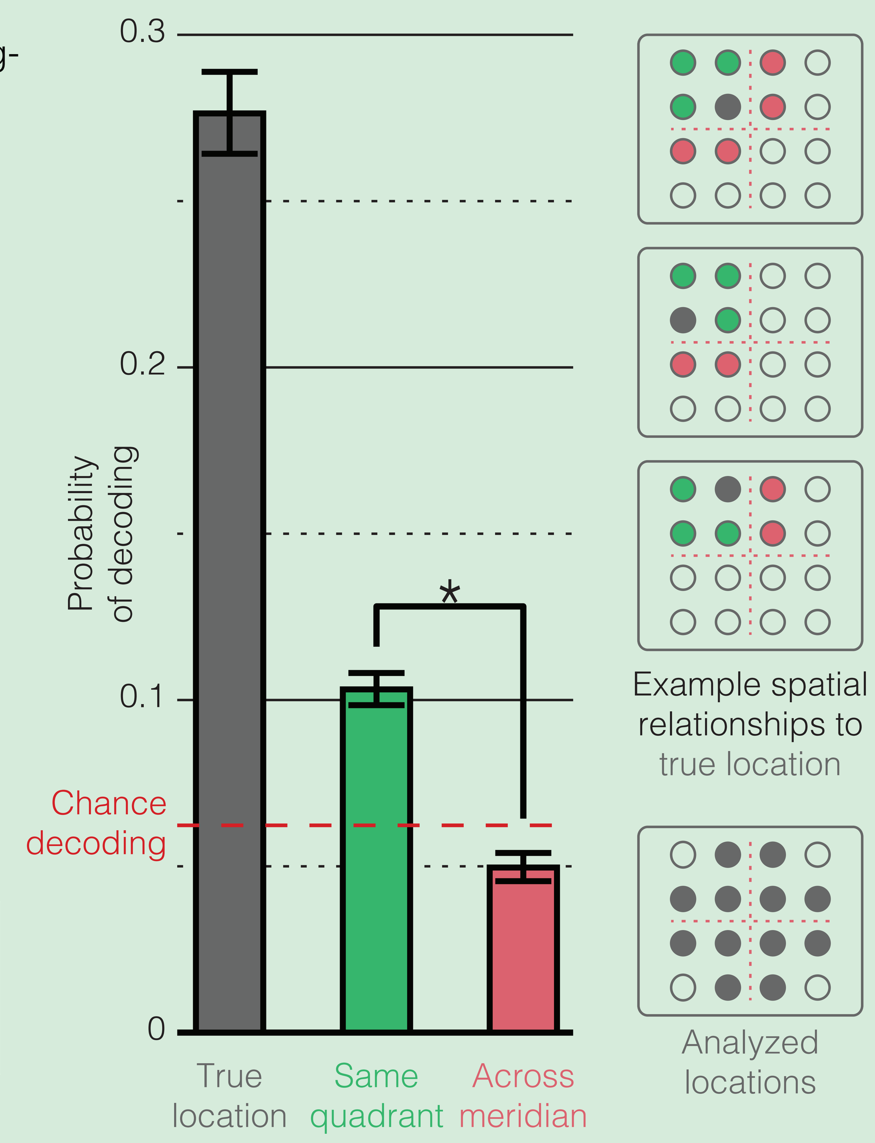
To determine whether PFC neurons represent visual space homogenously we first examined how delay activity changed *across* versus *within* quadrants of the visual field. For neurons with preferred locations adjacent to both a horizontal and vertical meridian (grey circle), we examined delay activity in trials in which stimuli were remembered at locations equidistant to the neurons' preferred locations, within the same quadrant (intraquadrant, green circles) versus across a meridian (extraquadrant, red circles). We found that delay epoch activity was significantly lower for remembered stimuli in different quadrants as compared to equidistant remembered stimuli in the same quadrant (*P* = 3.1×10^{-8}, Mann-Whitney U, Hochberg-corrected).



★ *P* < .05, Mann-Whitney U, Hochberg-corrected

Quadrantic bias in population representation

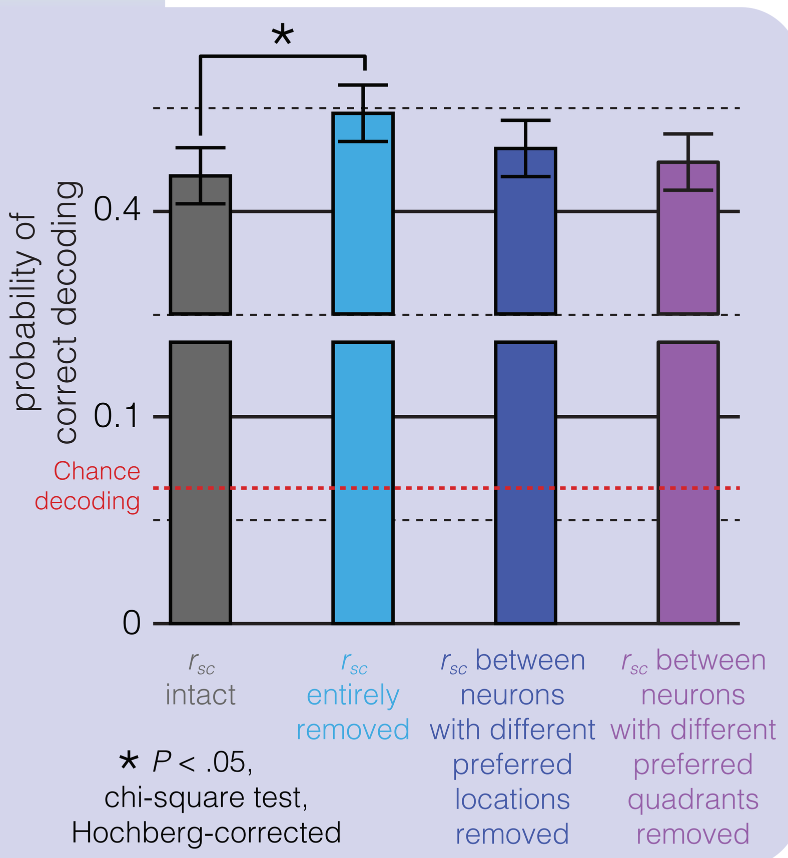
Given that firing rates for locations within a quadrant were more similar than equidistant locations in different quadrants, it follows that it should be easier for a PFC neuronal population to discriminate between two across-quadrants representations than between two within-quadrant representations. To test this hypothesis, we decoded the remembered stimulus location from ensembles of simultaneously recorded neurons on a single-trial basis using a linear classifier (support vector machine, or SVM). Indeed, the decoder commited intraquadrant classification errors with greater probability than extraquadrant classification errors (*P* ≈ 0, test, X^2 test, Hochberg-corrected).



★ *P* < .05, chi-square test, Hochberg-corrected

Correlated variability impairs WM fidelity

Tuning-dependent changes in r_{sc} can significantly impact the fidelity of neural representations. This phenomenon has been widely examined in the field of attention but minimally in WM. Thus, we tested whether the presence of r_{sc} significantly affects the fidelity of WM representations by removing correlated variability from simultaneously-recorded neurons. Removing r_{sc} increased decoding performance by a modest but significant amount (P = 4.4x10-3, chi-square test, Hochberg-corrected), indicating that correlated variability negatively impacts WM signal fidelity.



★ *P* < .05, chi-square test, Hochberg-corrected

Conclusions

Mnemonic selectivity in area dlPFC clustered; a region of cortex around an electrode is likely to be surrounded by other regions of cortex that have similar delay epoch selectivity.

Working memory representations of visual space are biased by both the vertical and horizontal meridians of the visual field, resulting in a non-linear, quadrantic division of mnemonic space.

Ensembles of simultaneously-recorded neurons in dlPFC contain sufficient information to decode the contents of WM on a single trial basis, but correlated variability between neurons impairs WM fidelity.