

Frontal Eye Field Neurons Signal Changes in Decision

Criteria

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SUPPORTING ONLINE MATERIAL

Neuron Classification

The activity of FEF neurons can be classified as visual-, visual-movement-, or movement-related based on whether it is more strongly associated with a visual stimulus or with a saccadic eye movement (Bruce and Goldberg, 1985). To classify cells in this manner, we trained monkeys to perform a delayed, memory-saccade task (MEM). This task was also used to 1) determine if the neuron responded to visual targets and/or prior to saccadic eye movements, and 2) determine the location in the visual field that yielded the strongest response.

In the MEM task, monkeys made saccades to the remembered location of a visual cue. The cue location varied among eight positions, equally spaced (45 deg). Typically, 2 different target eccentricities were used. At the beginning of each trial the monkey fixated a small red square. A peripheral cue was flashed for 250 ms followed by a variable delay (750-1250ms) during which the fixation target remained on and the monkey maintained fixation within a 2 x 2 deg window. At the end of the delay, the fixation target disappeared and the monkey was allowed up to 600 ms to make a saccade to the remembered location of the cue. After the 600 ms saccade interval, and if the monkey's memory-saccade was within a 3 x 3 deg window centered on the cue

location, the cue re-appeared to provide feedback to the monkey and corrective saccades were generally made at this time. More details on this task have been given elsewhere (Cassanello and Ferrera 2007b).

For analysis, each MEM trial was divided in five time intervals including background, visual, delay, pre and peri-saccadic intervals. The intervals were defined as follows: background – 100 msec before the onset of the visual cue; visual – 50-200 msec after onset of visual cue; delay – time between offset of visual cue and “go” signal for saccade; pre-saccade – 150 msec before saccade; peri-saccadic 50 msec before the saccade to 100 msec after.. Average firing rate within each interval is indicated by the variables B, V, D, P and S. We computed a visuomotor index to classify neurons as follows:

$$\text{(Eqn S1)} \quad \text{VMI} = (V - M) / (V + M)$$

This index ranges from –1.0 (pure movement cell) to 1.0 (pure visual cell). In each case, the firing rates were calculated using the trial condition that produced the maximum overall response, i.e. the preferred target location or saccade metric (direction and amplitude). If a cell was recorded with multiple target eccentricities, the VMI was calculated separately for each eccentricity.

The distribution of VMI's across the population of neurons was not significantly biased toward visual or movement (**Fig. S1A**). The average firing rates for the visual, delay, pre-saccade and peri-saccade intervals are shown in **Fig. S1B**. The average firing rates around the time of the saccade were similar for cells with VMI > 0 and those with VMI < 0. The cell classes were better distinguished by activity during the visual interval. Bruce and Goldberg (1985) reported that 60% of FEF neurons were classified

as pure movement or visual-movement neurons, and 40% were purely visual.

However, it is possible that pure movement and pure visual neurons are somewhat under-represented in our sample.

To determine if there was a relationship between cell class and stimulus or boundary speed selectivity, we sorted the neurons into 3 groups: those with $VMI < -0.3$ (“movement” cells), $-0.3 < VMI < 0.3$ (“visual-movement”), and $VMI > 0.3$. We calculated the magnitude of the boundary and stimulus speed parameter estimates for each neuron and compared between groups using a Wilcoxon rank-sum test. None of the between group comparisons were significant ($p < 0.05$). We also computed the correlation between VMI and the magnitude of the boundary and stimulus speed parameter estimates. Neither correlation was significant ($p < 0.05$).

Anatomical location of recording sites

Structural MRI was used to reconstruct electrode penetrations. Monkeys were sedated with ketamine (10 mg/kg), anesthetized with isoflurane (13%), and placed in an MR-compatible stereotaxic frame inside the scanner. An SPGR pulse sequence was used on a GE 1.5T TwinSpeed scanner. **Figure S2A** shows a coronal structural MRI from one monkey (F). The anterior-posterior level of the slice is 26.0 mm anterior to the ear canals. The superior (s) and inferior rami (i) of the arcuate sulcus are indicated. There are two clearly visible electrode tracks in the anterior bank of the arcuate sulcus on the right side. At the site marked with the asterisk, contraversive saccades were evoked at a current of 40 microamps (**Fig. S2B**).

Spatial bias

Most FEF neurons have strong spatial selectivity both for visual target location and/or for saccade direction and amplitude. In the speed categorization task, there were two locations for saccade targets. We generally attempted to place both saccade targets outside the receptive/movement field of the neuron being recorded. However, it was still possible that a neuron could fire somewhat more strongly prior to saccades directed toward one target location than the other, particularly if the targets were near the edges of the RF/MF. **Fig. S3** illustrates a case where one target location might evoke a stronger response than the other. In fact, across the population of neurons recorded, saccades directed toward one target location did tend to evoke a response that averaged 19% stronger than the response at the weaker location. This effect was small, but significant across the population (paired t-test, $p < 10^{-6}$).

Even though the experiment was designed to dissociate categorical from spatial responses (by randomizing the response targets between the two locations), it is possible that subjects could have systematic biases. It is possible that this spatial response bias, if combined with a behavioral bias, could be confounded with categorization effects. This would happen, for example, if the monkey systematically selected the target at the stronger location when one boundary was in effect, and chose the target at the weaker location when the other boundary was in effect. **Fig. S3** illustrates the possibility that the monkey could make more saccades to the “preferred” target location on “slow” boundary trials (**Fig. S3A**), but have the opposite bias on “fast” boundary trials (**Fig. S3B**).

To test this, we calculated the proportion of trials for which the monkey chose the target at the stronger location. This was accomplished by first finding the target location that produced the strongest neuronal response for each cell, and then calculating the percentage of responses directed to that location as opposed to the opposite location. **Fig. S4** shows the spatial response bias of each subject, sorted by stimulus and boundary speed, relative to the preferred spatial location of each neuron. To account for the categorization effects, there would have to be a systematic difference between the distribution of the red and blue data points. **Fig. S4 A,B** shows data for the subset of cells that responded more strongly when the slow boundary was in effect ($n = 51$). If this were due to a spatial bias, then the red data points would show a tendency to lie above the blue points. This is not evident either at the level of individual sessions (small circles) or in the aggregate data (solid lines). **Fig. S4 C,D** shows data for the subset of cells that responded more strongly when the fast boundary was in effect ($n = 45$). In this case, the blue points should lie above the red. These data show that the monkeys had no systematic spatial biases that could account for the effects of boundary speed.

As another test for the robustness of boundary and stimulus speed effects, we performed a 4-way ANOVA with boundary speed, stimulus speed, target position and saccade direction as the explanatory variables. Target position refers to the position of the correct target and hence differs from saccade direction on incorrect trials. At the $p < 0.05$ level, the following numbers of cells showed significant effects: 45 for boundary speed, 37 for stimulus speed, 32 for target position, 43 for saccade direction. None of the interactions were significant for more than 12 cells. A 2-way ANOVA was also performed with only boundary and stimulus speed as the independent variables. In the

2-way analysis, 45 cells were significant for boundary speed ($p < 0.05$) and 36 for stimulus speed (none of the 6 first-order interactions was significant, $p < 0.05$, for more than 10% of the cells, except for the interaction between target position and saccade direction, which was significant for 22% of cells). All of the cells that were significant for boundary speed in the 2-way ANOVA also showed a significant boundary effect in the 4-way ANOVA when target position and saccade direction were included as covariates. Thus, while target position and saccade direction were significant for 33% and 45% of the cells, respectively, these effects did not reduce the significance of boundary and stimulus speed.

We also performed a regression analysis by adding target and saccade direction co-variates to the model of Eqn 1. The 6-parameter model provided a significant fit ($p < 0.01$) for all but 6 neurons. The 6-parameter model provided a better fit than the 4-parameter model for 87 neurons, and a worse fit for 9 neurons. On average, the 6-parameter model improved the correlation between predicted and actual firing rate by 23% over the 4-parameter model. This improvement was significant (paired t-test $p < 0.00001$).

The effects of target position and saccade direction were expected and consistent with the small (avg 19%) but significant bias in neuronal responses. However, these effects did not degrade the encoding of boundary and stimulus speed. **Fig. S5** is reproduction of **Fig. 5** from the main body of the paper. The only difference is that the neurons were sorted based on the 6-parameter, rather than 4-parameter model. The results for both models are nearly identical.

Effects of behavioral choice and outcome

To determine if neurons encode both the boundary speed and the stimulus speed even when one controls for the subject's final choice, we ran all combinations of 1-, 2-, 3-, and 4-way ANOVAS with the following explanatory variables: boundary speed, stimulus speed, choice (fast/slow), and outcome (correct/incorrect). The results were highly consistent. In all analyses, 45 cells had a significant effect of boundary speed ($p < 0.05$) and 36 were significant for stimulus speed. These numbers were the same with and without outcome and choice as covariates. The results for the 4-way ANOVA at $p < 0.05$ were as follows: boundary speed: 45 cells; stimulus speed: 36 cells; outcome: 25 cells; choice: 12 cells. These results suggest that more cells were modulated by boundary and stimulus speed than by outcome and choice.

The ANOVA results were consistent with regression analyses. In particular, we compared the 4-parameter model of Eqn 1 with 5- and 6-parameter models that included behavioral outcome and choice as additional regressors. The results were consistent across all models, so we will only discuss the 6-parameter model (explanatory variables = boundary speed, stimulus speed, outcome, choice, trial number). Compared to the 4-parameter model (Eqn 1), adding the additional behavioral variables improved the fit of the model for 64 cells and worsened the fit for 32 cells. The mean difference (6-parameter fit – 4-parameter fit) was +7%. Fit was measured by computing the correlation between predicted and actual firing rate. The improvement was rather small considering the 50% increase in the number of parameters.

As far as the results shown in **Fig. 5**, adding the behavioral variables to the regression model changed things only slightly. The most notable change was that the

negative correlation between the boundary speed and stimulus speed parameters became a bit stronger (-0.41 for the 4-parameter model to -0.44 for the 6-parameter model). This is important because it is this negative relationship that allows one to predict the animal's behavior based on neural activity. The numbers of slow ($n = 24$) and fast ($n = 32$) cells did not change appreciably, nor did the fit between predicted and actual behavior ($r^2 = 0.952$).

Time-dependence of stimulus and category effects

Response times for the speed categorization task were typically about 400 ms (measured as the time from stimulus onset to saccade onset). To gain a sense of the relative timing of boundary and stimulus speed signals, we subdivided this interval into two 200-msec subintervals, one starting at stimulus onset (VIS) and the other ending at saccade onset (SACC). The ANOVA and regression model analyses were performed on activity (average firing rate) in these two intervals. A 4-way ANOVA found significant ($p < 0.05$) effects during the VIS interval for the following numbers of cells: 39 boundary speed; 25 stimulus speed; 9 target direction; 23 saccade direction.

The number of cells showing a significant boundary speed effect was similar to that obtained with a 2-way ANOVA using either the entire decision period ($n = 45$) or just the VIS interval ($n = 39$). The number of cell showing a significant boundary speed effect during the SACC interval was 43 and 42 for the 4- and 2-way ANOVAs, respectively. Hence, the boundary speed effect is stable over time.

The number cells with a significant stimulus speed effect in the VIS interval was the same ($n = 25$) for 2- and 4-way ANOVAs. This number increased 40% (to $n = 42$)

for activity in the SACC interval. This number was also independent of whether target direction and saccade direction were included as covariates. Hence, the effect of stimulus speed was stronger during the SACC interval than the VIS interval.

The regression analysis confirmed these results. Estimates of the boundary speed parameter (k_b) were similar for the VIS and SACC interval. They averaged 1.89 spikes s^{-1} for the VIS interval and 1.96 spikes s^{-1} for the SACC interval (mean absolute value). This result was obtained with the 4-parameter model (Eqn 1), but also held for the 6-parameter models that included outcome and choice or target and saccade direction as additional covariates.

In contrast, the parameter estimate for stimulus speed was much larger during the SACC interval (0.34 spikes/sec per deg s^{-1}) than the VIS interval (0.19 spikes s^{-1} per deg s^{-1}). This result was consistent across all 4- and 6- parameter regression models. Hence, the effect of stimulus speed increased with time during the decision interval.

As the influence of stimulus speed increased, so did the negative correlation between the parameter estimates for stimulus and boundary speed (k_s and k_b in Eqn 1). In the VIS interval, this correlation was -0.26 ($p = 0.012$), and increased to -0.56 ($p < 0.0001$) in the SACC interval.

These results are consistent with the idea that the boundary speed effect is established prior to the appearance of the stimulus. This makes sense because the boundary cue appears 800 msec before the motion stimulus. In some cells, the stimulus speed effect is present early, but in others it takes more time to evolve. In either case, stimulus speed signals can be modulated by a boundary speed signal that is present throughout the decision period. These results further support the idea that

differential modulation of sensory signals may be a mechanism for implementing decision criteria.

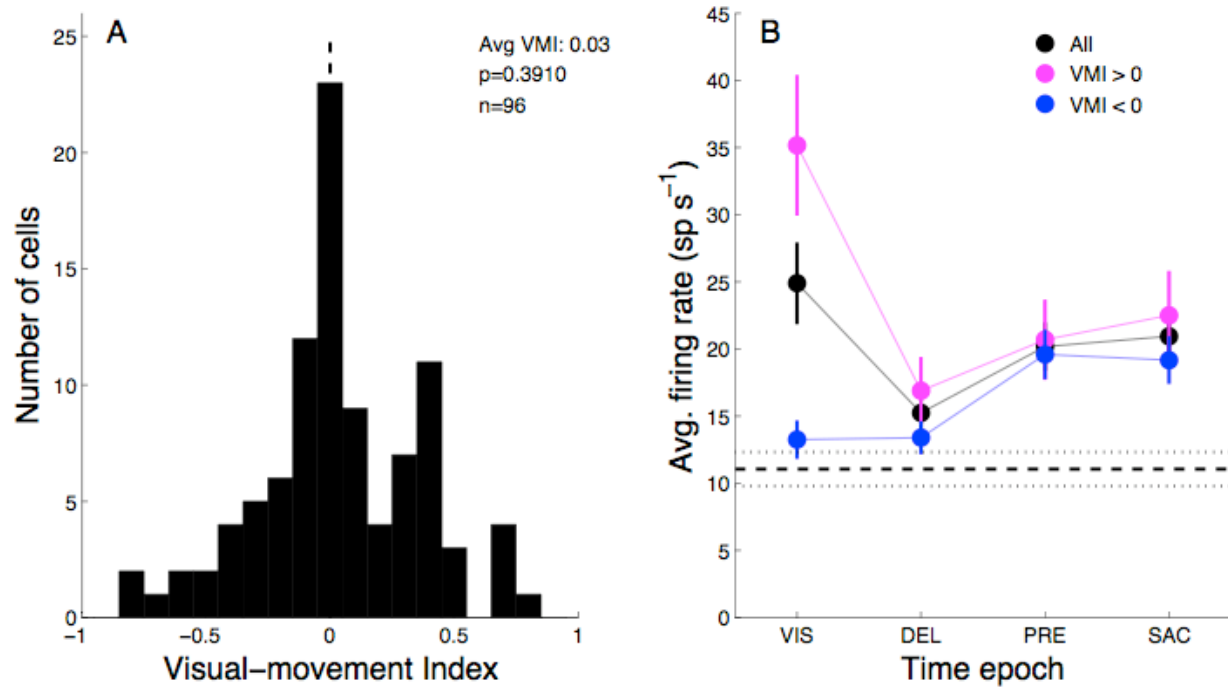


Figure S1. Classification of FEF neurons based on activity during memory-saccade task. **A)** Distribution of visual-motor indices (VMI). Most cells were recording with 2 target eccentricities and a VMI was computed for each eccentricity, hence the y-axis label refers to the number of recordings rather than the number of cells. **B)** Avg. firing rate for visual (VIS), delay (DEL), pre-saccade (PRE) and peri-saccade (SAC) time intervals. Black symbols include all cells, blue includes only cells with VMI < 0, magenta includes cells with VMI > 0.

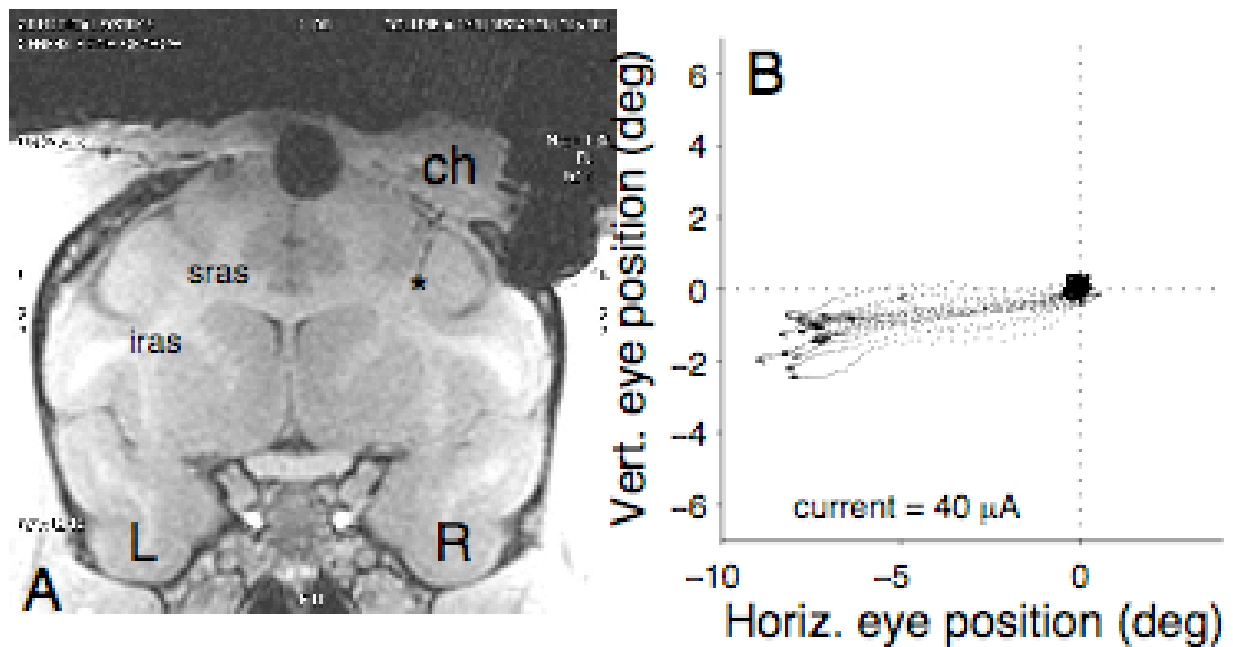


Figure S2. Anatomic localization of recording sites. **A)** Structural MRI of monkey F showing coronal slice at the level of the arcuate sulcus (iras – inferior ramus of arcuate, sras – superior ramus). A recording chamber (ch) and electrode track are shown in the right hemisphere. **B)** Saccades evoked by stimulation of the site labeled with the asterisk in A. The current level was 40 μ A.

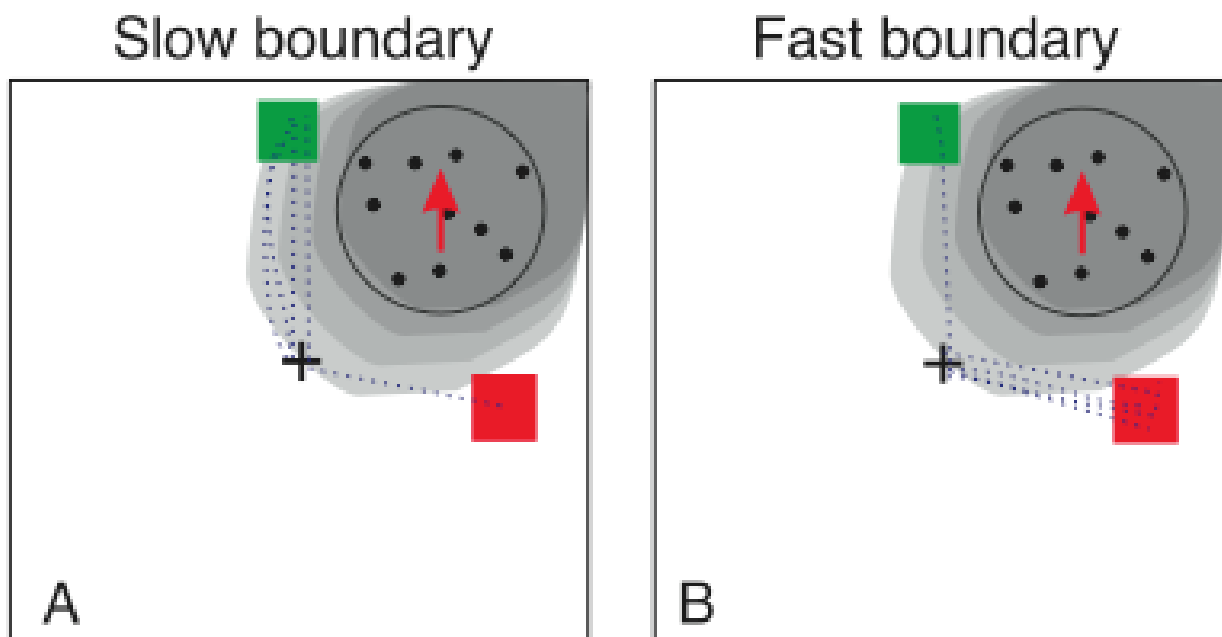


Figure S3. Worst-case scenario for spatial bias confound. **A)** One response target (green) has greater overlap with the RF/MF (gray shaded region) than the other target (red), and the monkey's saccades (dotted blue lines) are biased toward the "preferred" target location. **B)** Same target configuration, but monkey's saccades are biased toward the "non-preferred" location.

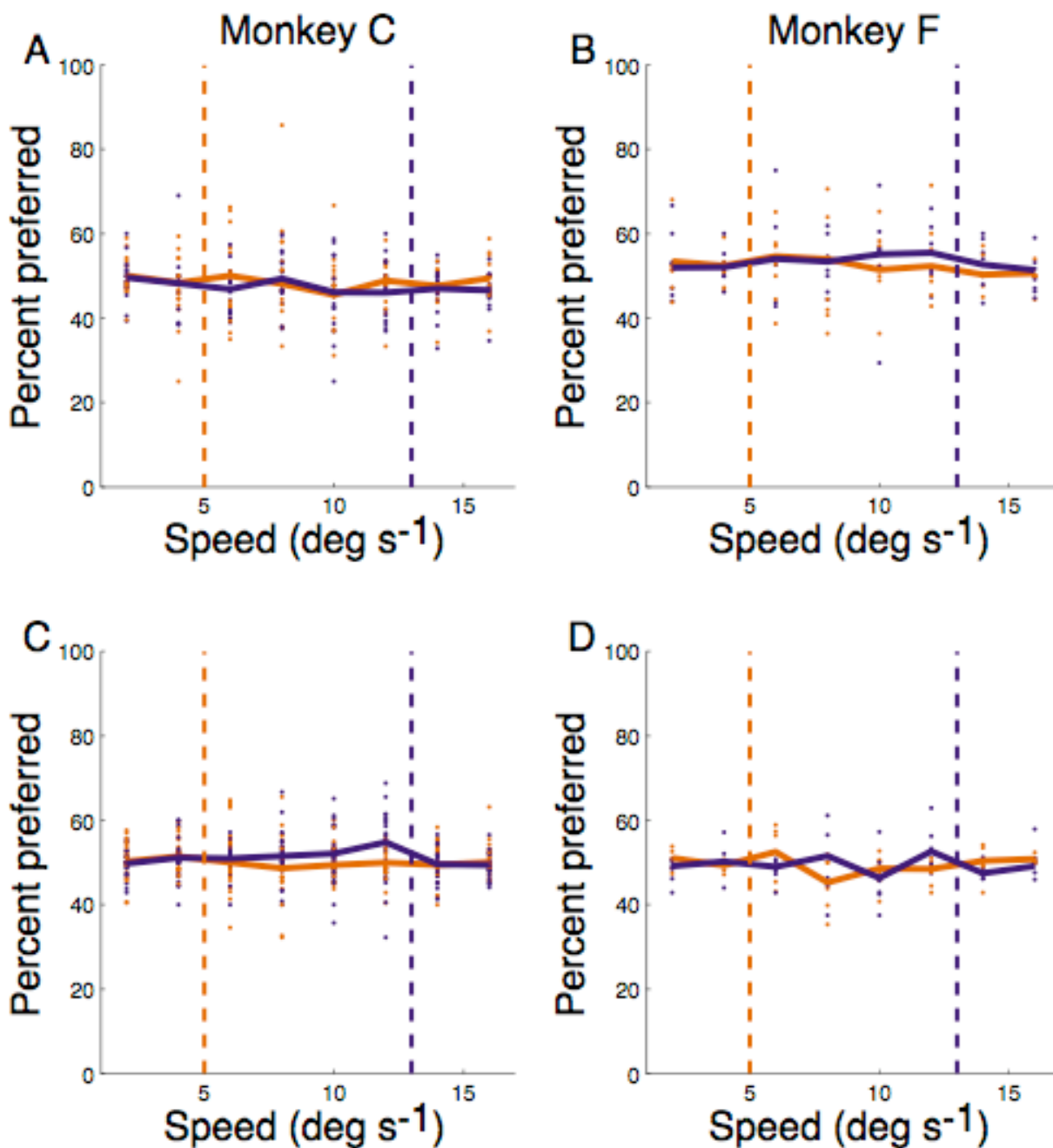


Figure S4. Control for spatial bias. **A)** Percentage of saccades directed toward the target at the "preferred" location of the cell. Red and blue dots are within session averages sorted by stimulus and boundary speed. Solid lines are across-session averages. Dashed vertical lines indicate the two boundary speeds. The data in this panel represent fast-preferring neurons in monkey C. **B)** Same format as A, showing fast-preferring cells in monkey F. **C)** Slow-preferring cells in monkey C. **D)** Slow-preferring cells from monkey F.

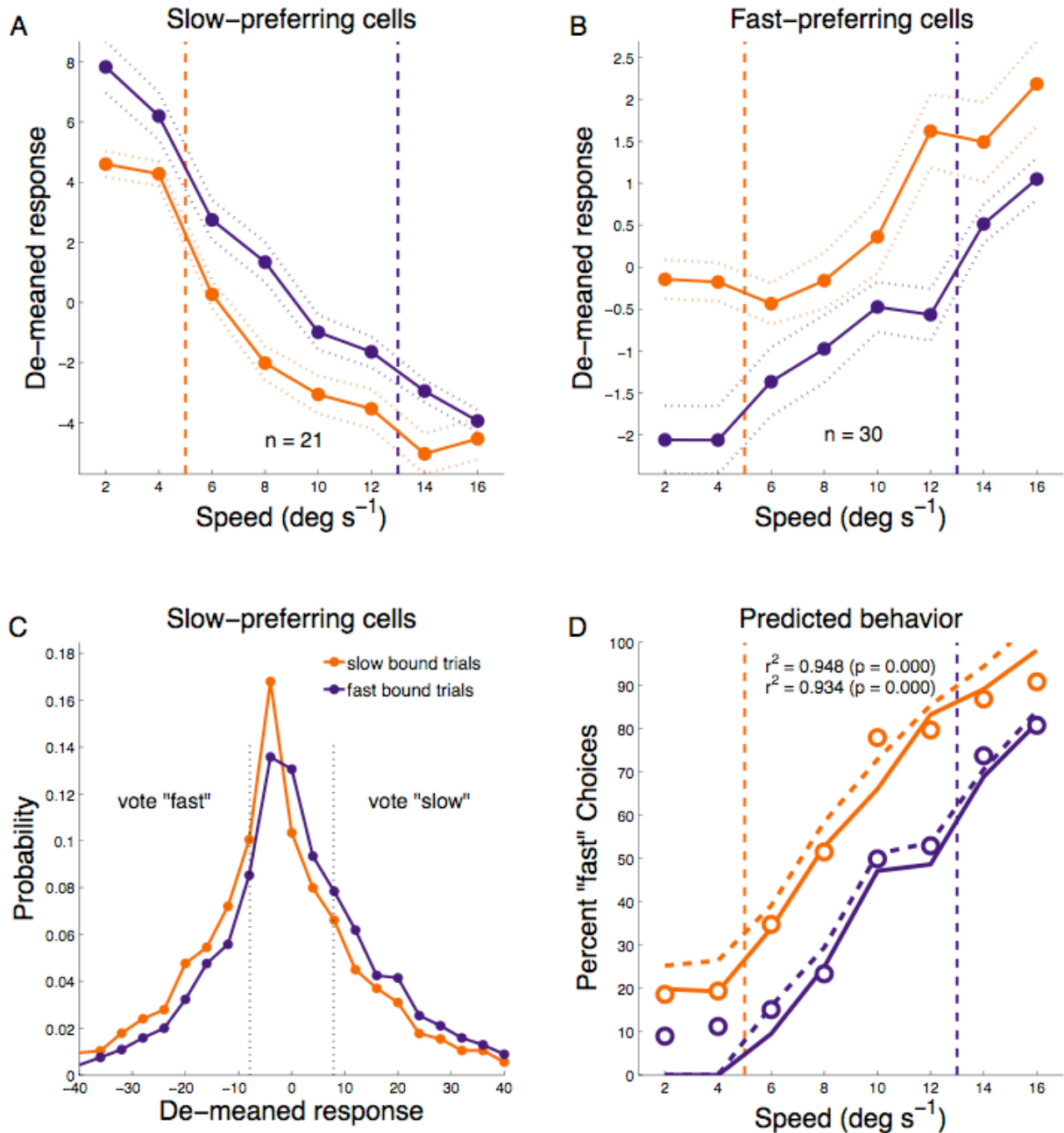


Figure S5. Population data for **A)** “fast” and **B)** “slow” preferring neurons. “n” is the number of cells in each class is given. **C)** De-meaned firing rate distributions for all slow-prefering neurons sorted by boundary speed. All stimulus speeds are included. Vertical dotted black lines represent the typical threshold used for considering activity as a vote for “slow” or “fast.” **D)** Actual behavioral choices (circles) and choices predicted based on FEF activity (lines). Solid lines are predictions of the “threshold” model, dashed lines are predictions of the “proportional” model.