Discharge characteristics of pontine reticular formation neurons in head-unrestrained primates

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INTRODUCTION

Many studies have investigated the contribution of cells in the pontine reticular formation to head-restrained saccades. Excitatory burst neurons (EBNs) and long-lead burst neurons (LLBNs) are characterized by high frequency bursts of spikes associated with ipsiversive saccades. For both classes of cells, the number of spikes is highly predictive of saccade amplitude. Relatively little is known, however, about the precise role that these cells play in the control of head-unrestrained gaze shifts.

Even when the head is unrestrained, the kinematics and relative contributions of the eyes and head are highly lawful, which can complicate efforts to correlate neural activity with movement parameters. Varying the initial positions of the eyes in the orbits, however, permits a dissociation of the contributions of the eyes and the head and highly variable movement kinematics. For example, when the head is free to move, gaze and eye velocity profiles often have two peaks (Freedman and Sparks 2000). The size of the head's contribution affects the duration of the saccade such that, for gaze shifts of a given vector, eye amplitude and eye duration are negatively correlated (Freedman, 2008).

Currently, the neural basis for these effects is not well understood. According to the Freedman (2001) model, the dual peaks in the velocity profiles are a consequence of inhibition of premotor elements by a signal related to head velocity. This would have the effect of increasing the duration of the eye movement, lowering the peak velocity, and producing velocity profiles with two peaks. If this is correct, EBNs in the paramedian pontine reticular formation (PPRF) should show longer burst durations and lower peak firing rates when the head contribution is large. Additionally, the firing rate profile should show two peaks that reflect the dual peaks in the velocity profiles for gaze and eye.

One can also ask whether and how the complex kinematics of head-unrestrained gaze shifts are represented by LLBNs. To date, very few studies have analyzed LLBN discharge properties in detail, and none have done so with the head unrestrained. If the dual peaks in the velocity profile is due to input to, or upstream from, LLBNs then this should be reflected in the firing rates of these cells. The goal of the present study, therefore, was to test critical predictions of the Freedman (2001) model by recording from PPRF while head-unrestrained monkeys perform gaze shifts from different initial eye positions.

METHODS

One hundred fifteen cells were recorded from PPRF of three monkeys while they performed a delayed gaze shift task. Initial eye-in-head position was controlled with the use of three head-mounted lasers aimed 18deg apart. At the start of a trial, one of these lasers was randomly selected and was turned on at the same time that a fixation target came on. Monkeys then looked to, and aligned the laser spot with, the visual target. After a variable delay, a second target came on. Monkeys were required to continue to align the laser and gaze with the fixation target until it and the laser were switched off. Animals then had to look to the location of the second target.

Target locations were chosen to elicit predominantly ipsiversive gaze shifts of ~4, 10, 20, 30, 40, 50, 60 and 70 degrees. Half of the trials were along the horizontal meridian and half included vertical components ranging from 40 deg up to 40 deg down.

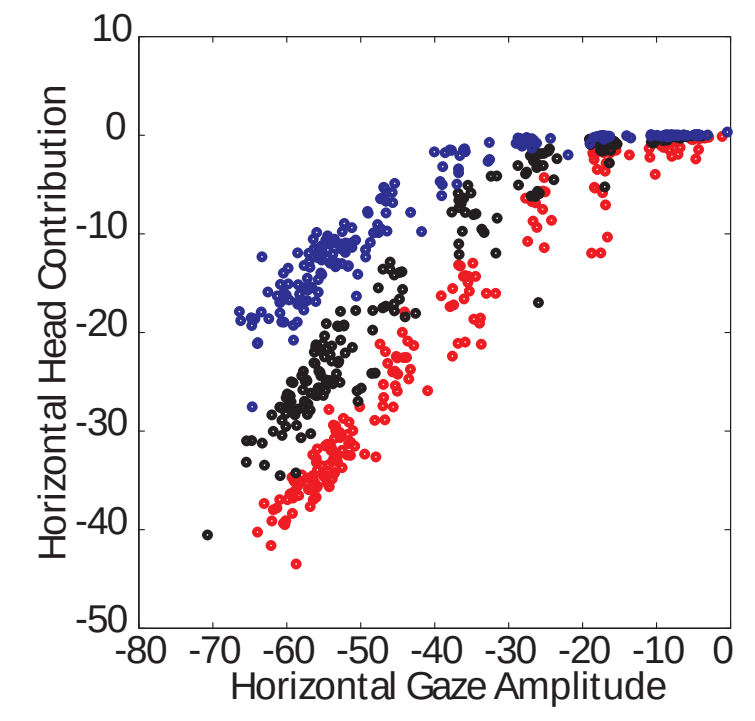


Figure 1. The three different lasers produced different initial eye positions. Although the relationship between head contribution and gaze amplitude is highly lawful, this relationship is highly dependent on the initial positions of the eyes in the orbits. Colors correspond to the three different lasers. Blue: initial eye position was 18 deg right; Black: eyes began centered in the orbits; Red: initial eye position was 18 deg left.

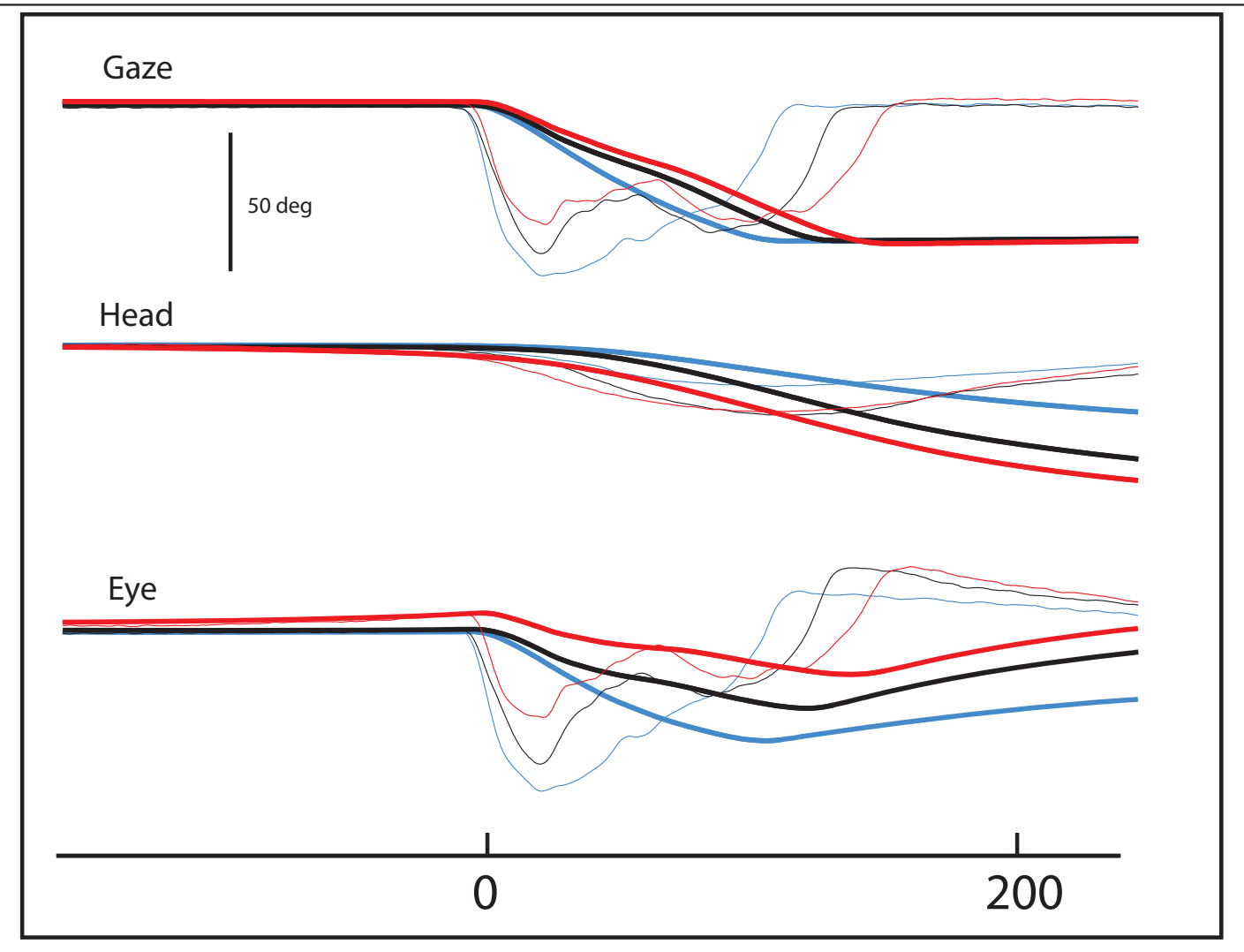


Figure 2. Horizontal position and velocity traces for gaze, head, and eye for three single trial examples from three different initial eye positions. Color conventions are the same as previous figure. For gaze shifts of a given amplitude, larger head contributions are associated with smaller saccades, lower peak velocities, and longer durations. Note also that, as the head contribution increases, the gaze and eye velocity profiles increasingly show two peaks.

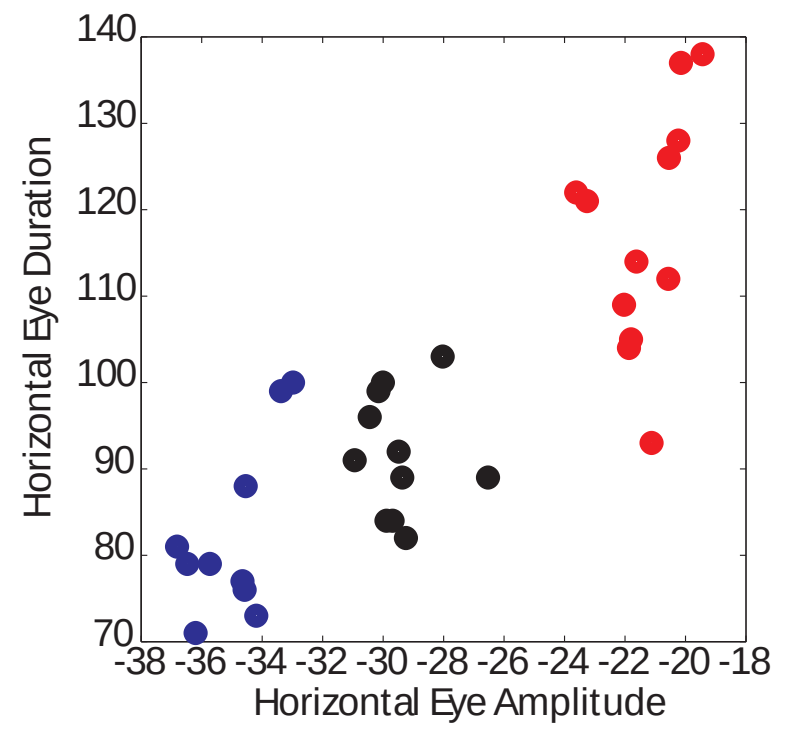
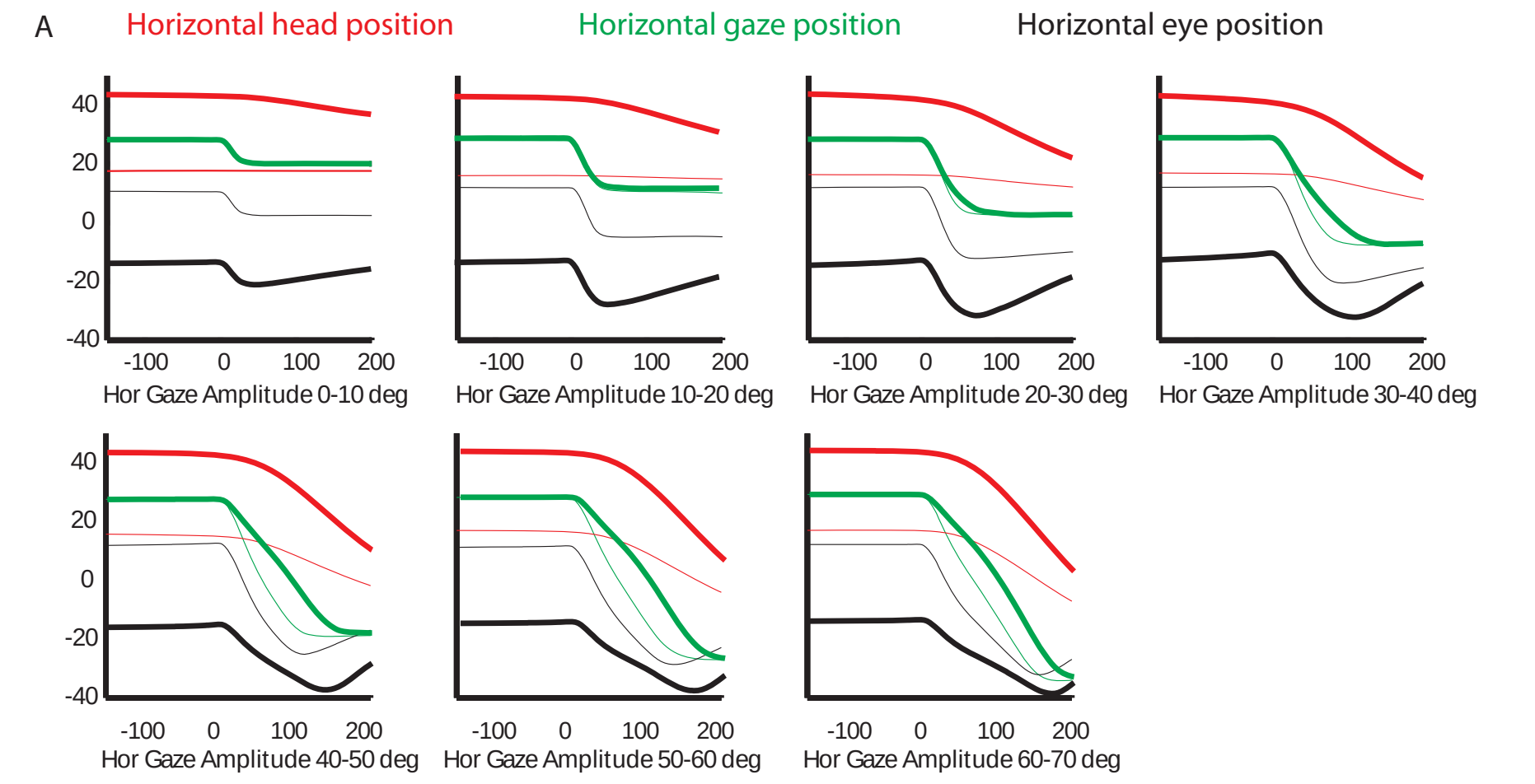


Figure 3. Eye amplitude-duration relationship for gaze shifts with horizontal gaze amplitudes between 52 and 57 degrees.

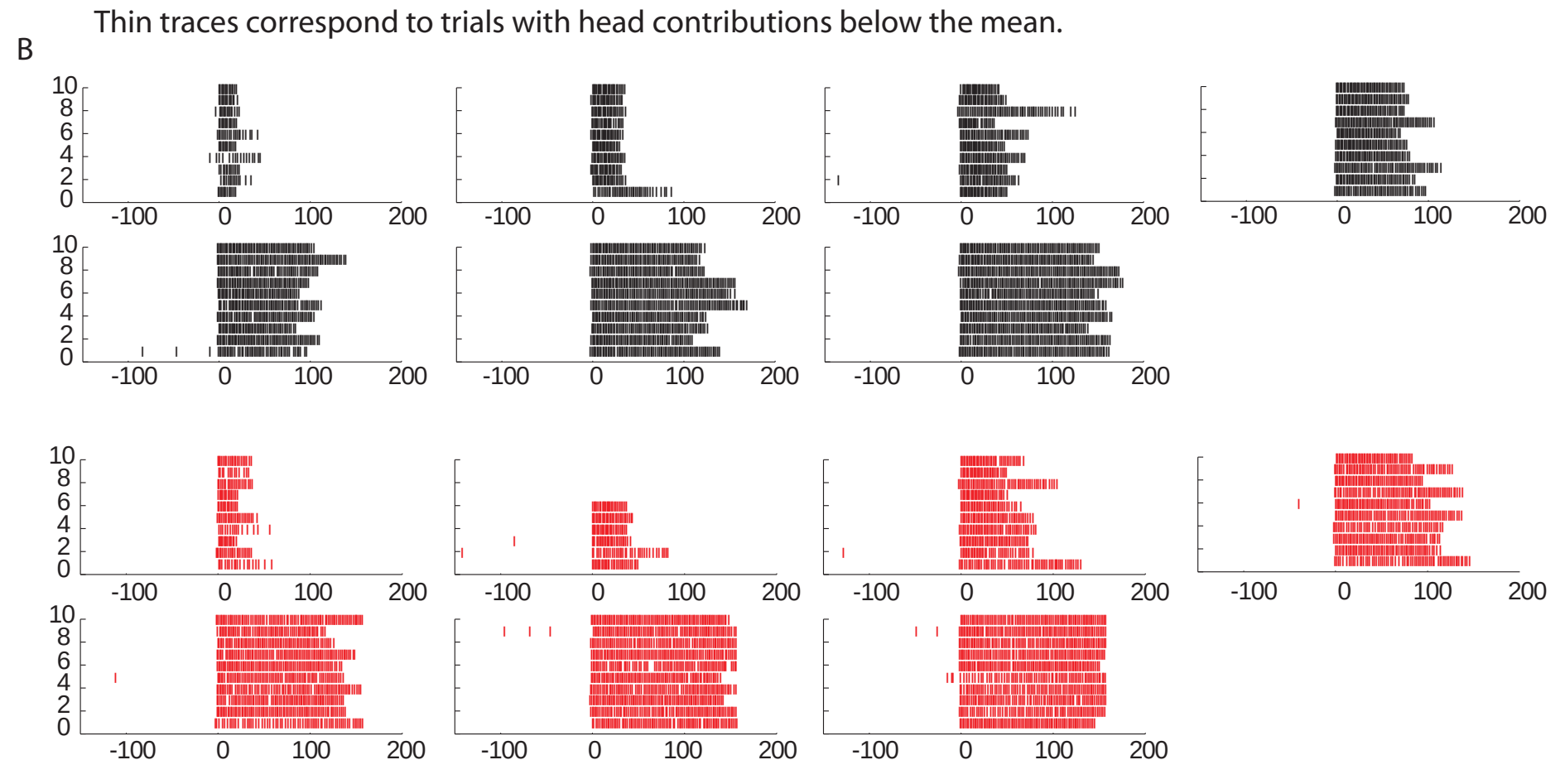
For these trials, smaller eye amplitudes are associated with longer durations.

When the head is free to move, therefore, the kinematics of saccadic eye movements are influenced by the contribution of the head to the gaze shift. The increased saccade duration associated with larger head contributions likely reflects a strategy that ensures an optimal balance between speed and accuracy. Note that large gaze shifts may require head contributions of 40 degrees or more. Because the head is a slow-moving, high-inertia system, large gaze shifts appear to be accomplished by prolonging the saccade to allow sufficient time for the head to move 40 degrees or more.

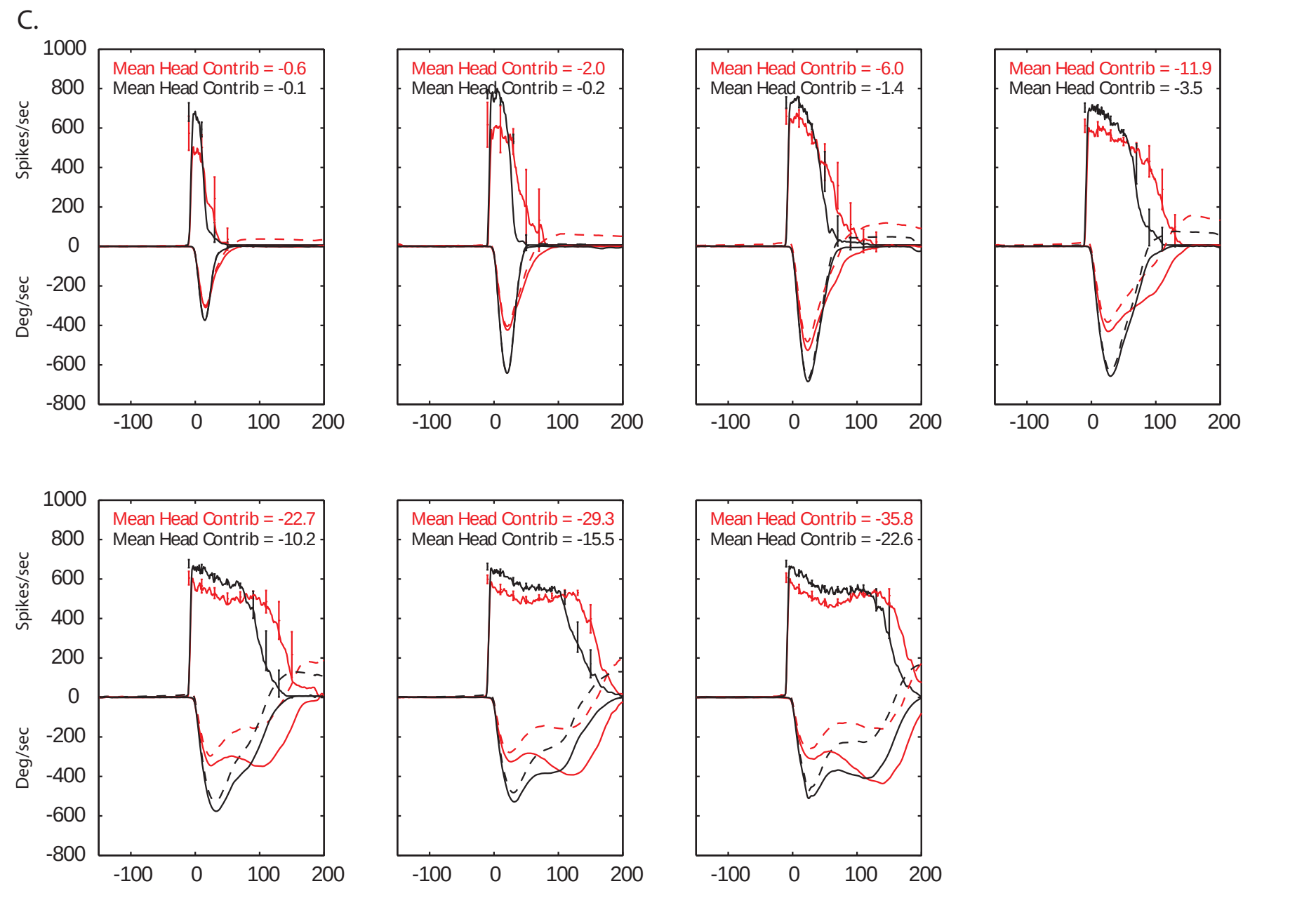
If this is true, then premotor elements in the saccadic system should show firing rate modulations that are correlated with these kinematic complexities.



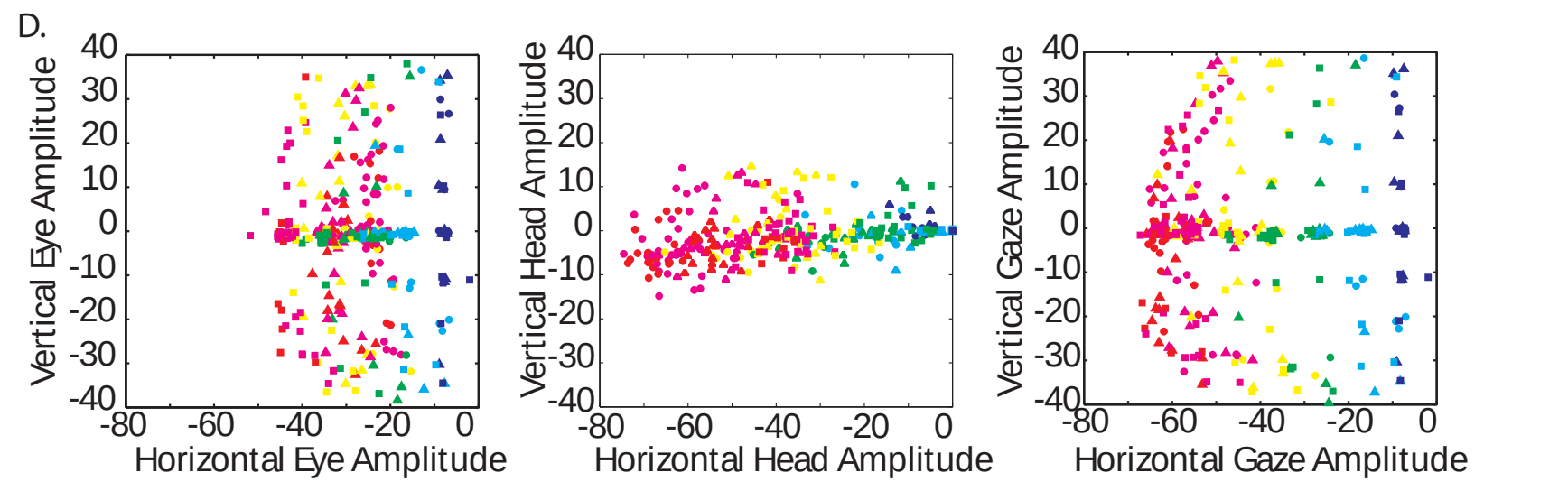
A. Data were grouped into 10deg bins according to horizontal gaze amplitude. Note that, for the same size gaze shift, when the head makes a large contribution, the movement is of longer duration. Horizontal head position is shown in red, horizontal gaze position in green, and horizontal eye position in black. Thick lines correspond to trials with head contributions above the mean for the bin. Thin traces correspond to trials with head contributions below the mean.



B. Rasters for one example EBN. Data for trials with head contributions above the mean for the bin are shown in red; data for trials with head contributions below the mean for the bin are shown in black. For both black and red rasters, panels correspond to the gaze amplitude bins shown in A.

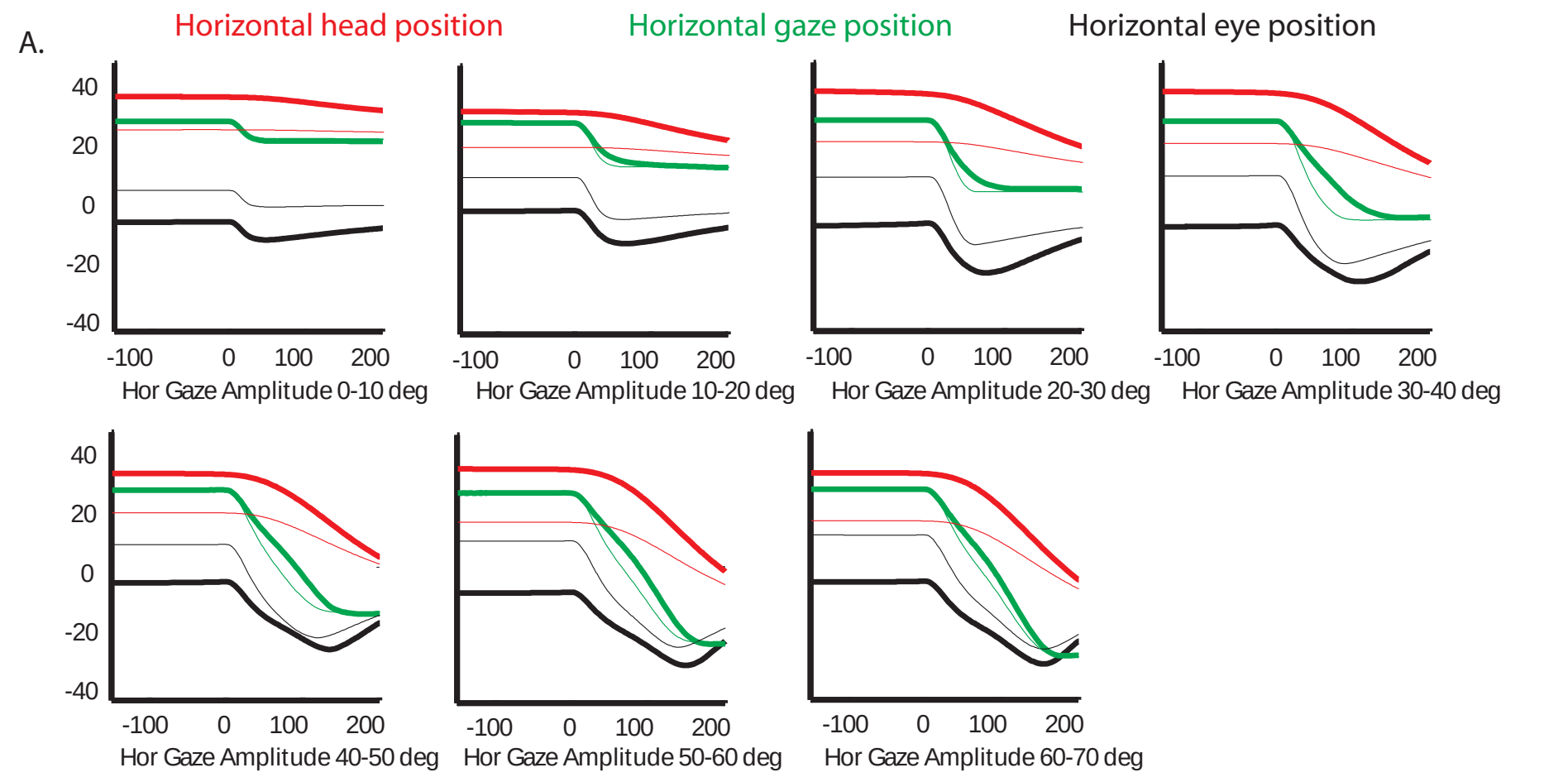


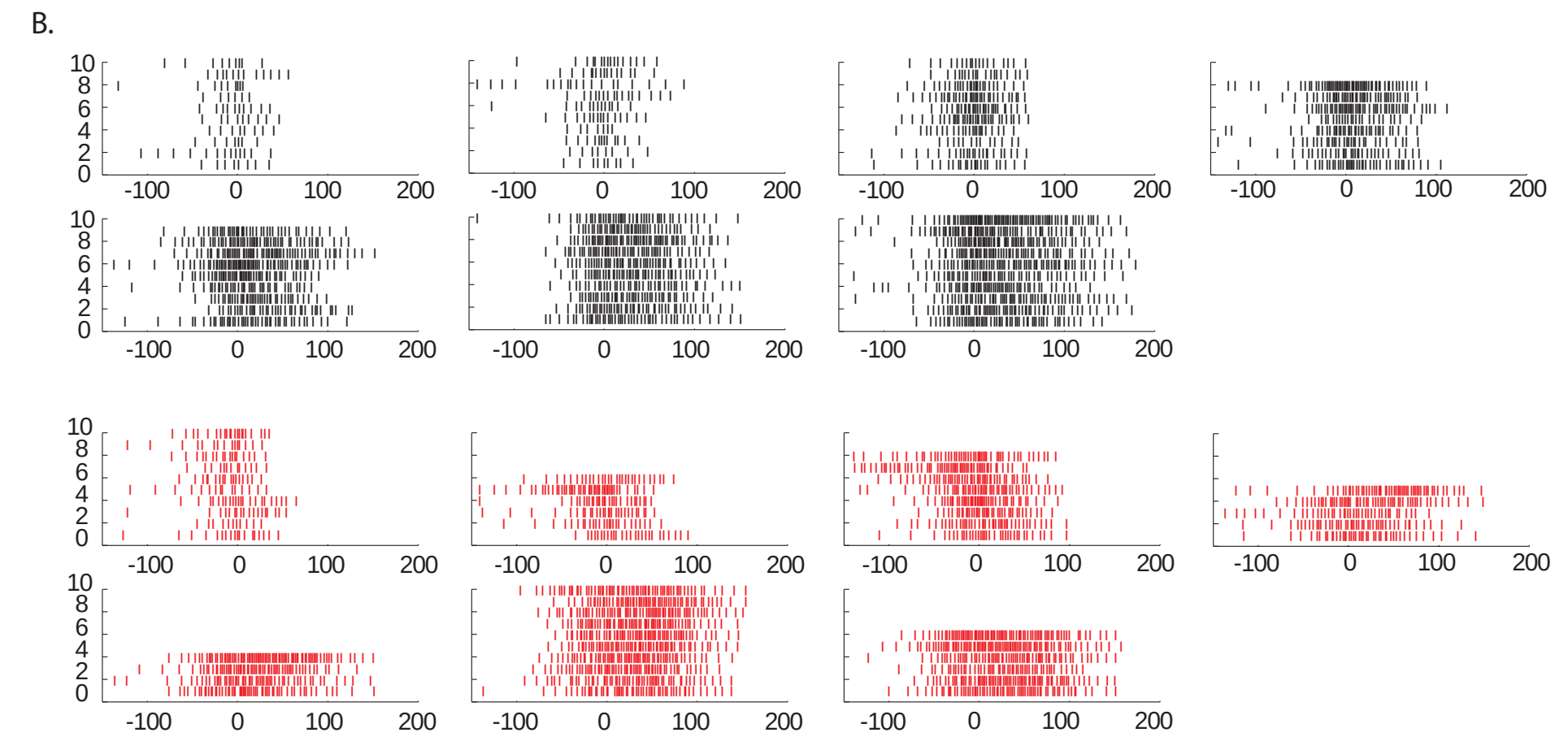
C. Averaged firing rates (upward traces), horizontal gaze velocity (downward solid traces), and horizontal eye velocity (dashed traces). Note that, when there are two peaks in the velocity profiles, this is reflected in the firing rate of the cell. Note also that the peak firing rate is lower when the head makes a larger contribution. Note also that the peak firing rate is actually lower for 60-70 deg gaze shifts than for 10-20 deg gaze shifts.



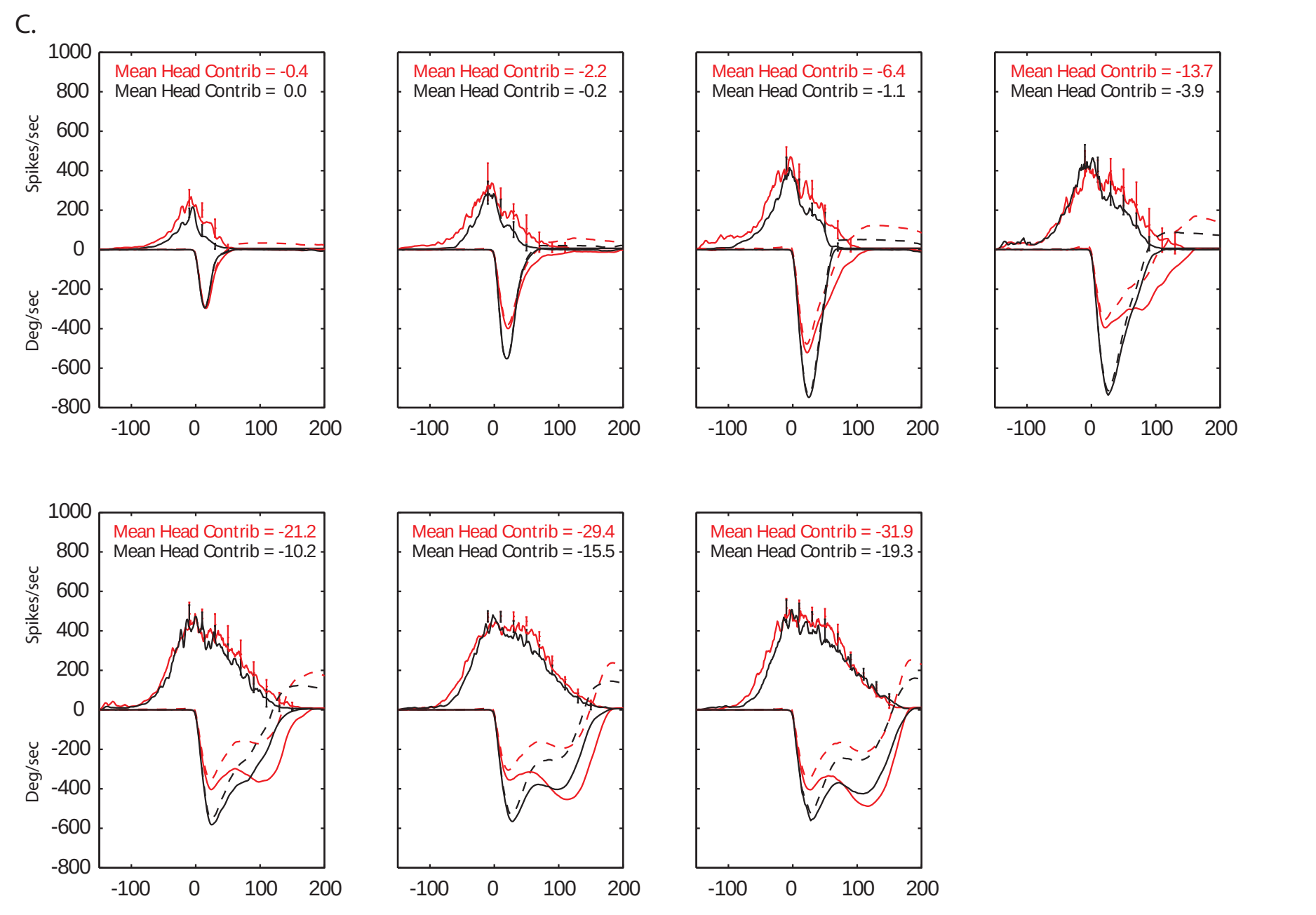
D. Number of spikes in the burst as a function of horizontal and vertical eye, head, and gaze amplitudes. Squares indicate trials with initial eye positions 18 deg to the right in the orbits. Triangles indicate trials in which the eyes began centered in the orbits; circles show trials in which the initial eye position was 18 deg left. Note that the number of spikes is more predictive of gaze amplitude than head or eye amplitude.

Figure 4. Position traces, rasters, averaged firing rates and movement field plots for one example EBN. The firing rate profile clearly shows two peaks when the gaze and eye velocity profiles do. Additionally, the peak and average firing rates are reduced when the head contribution is large. The cell's firing rate, therefore, clearly reflects the kinematic complexities of the movement.

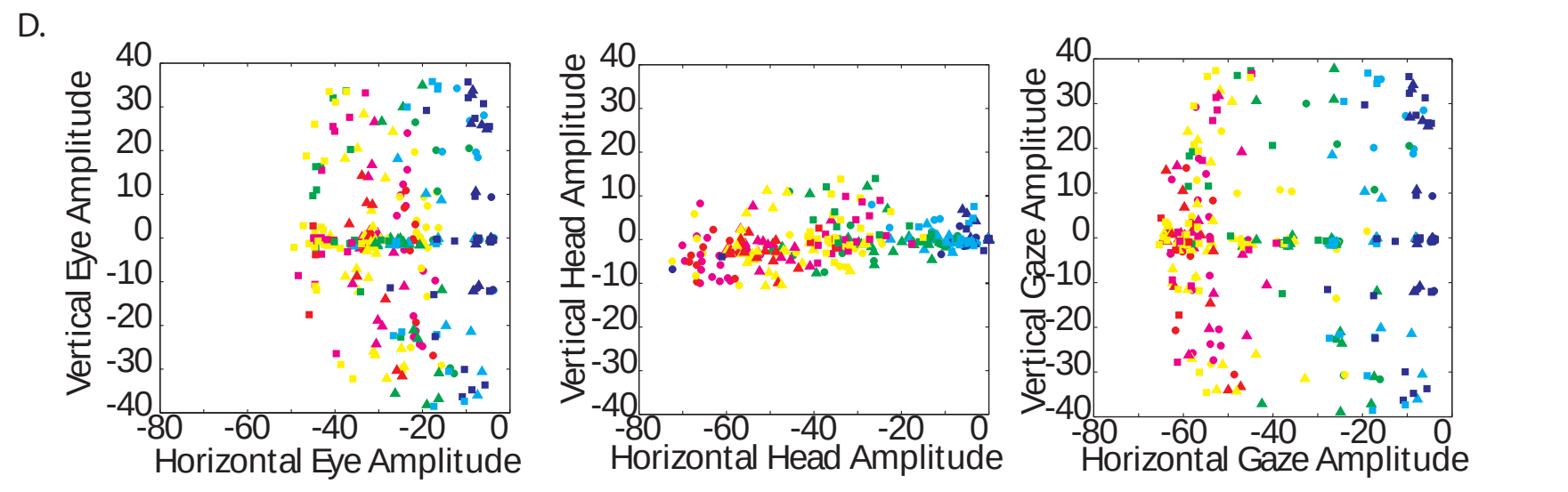




B. Rasters for an example long-lead burst neuron. Same color conventions used for the EBN.

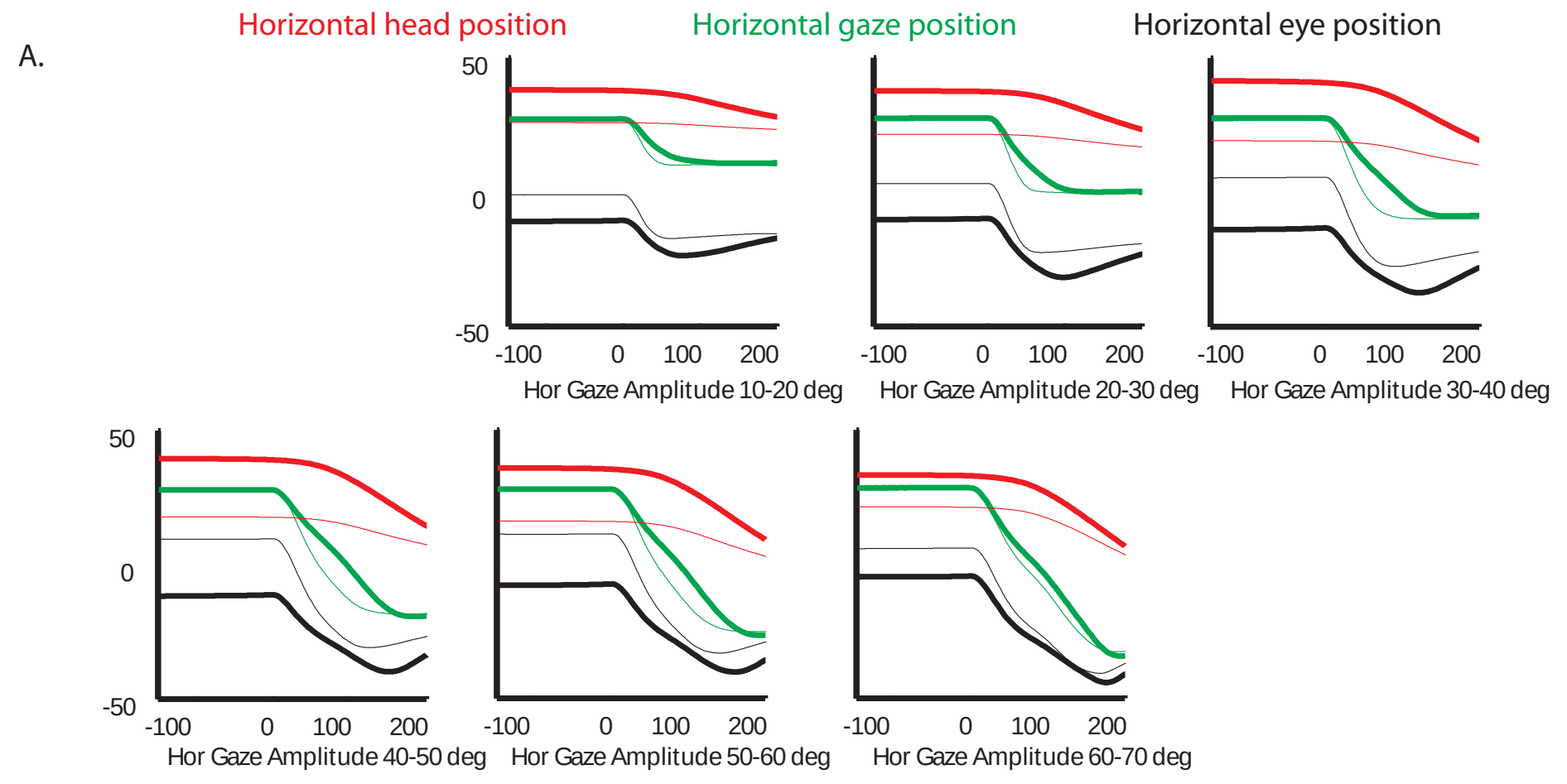


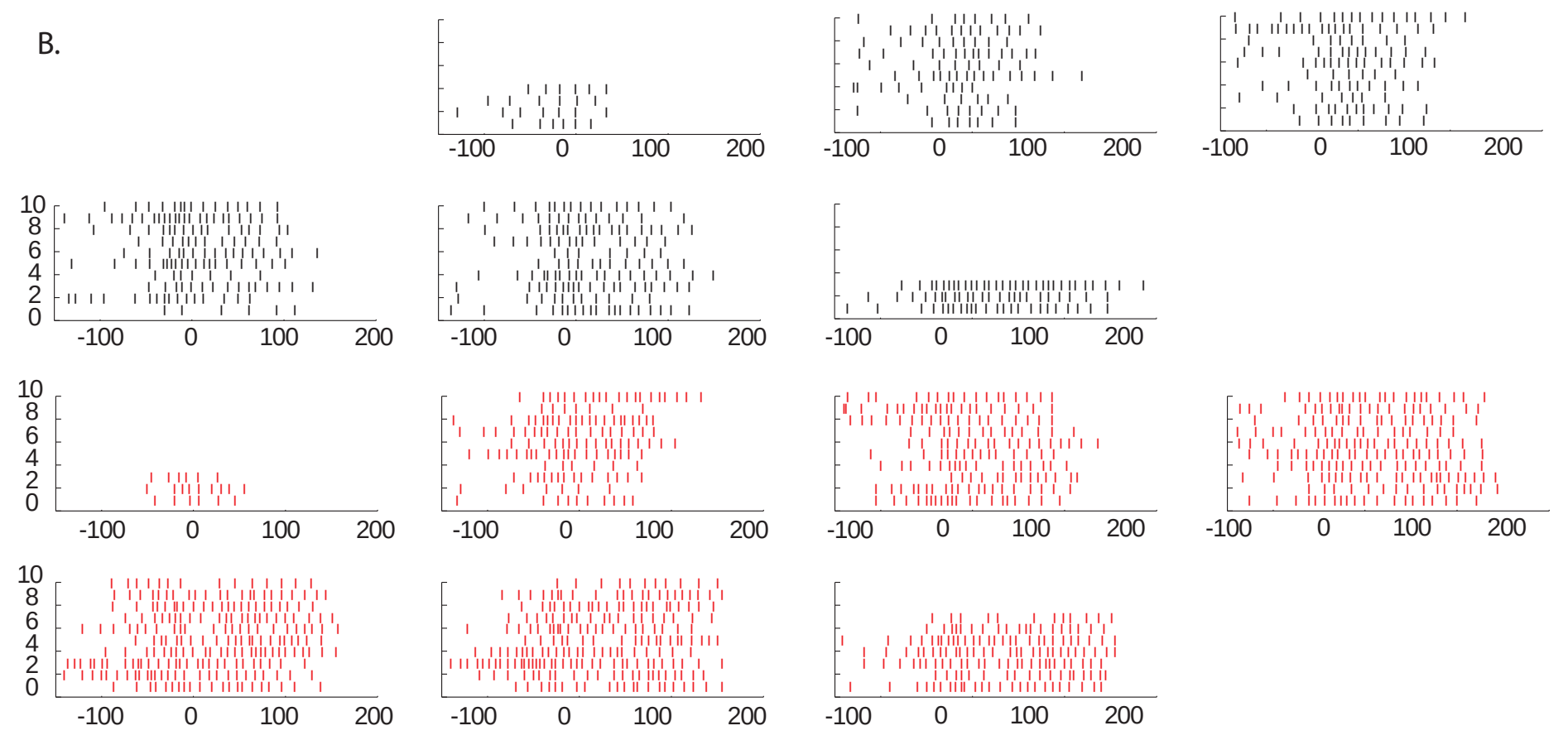
C. Averaged firing rates, horizontal gaze velocity, and horizontal eye velocity traces. Same conventions used for the EBN. Although the burst duration increases as gaze duration increases, the dual peaks in the velocity traces are NOT reflected in the firing rate of the cell.



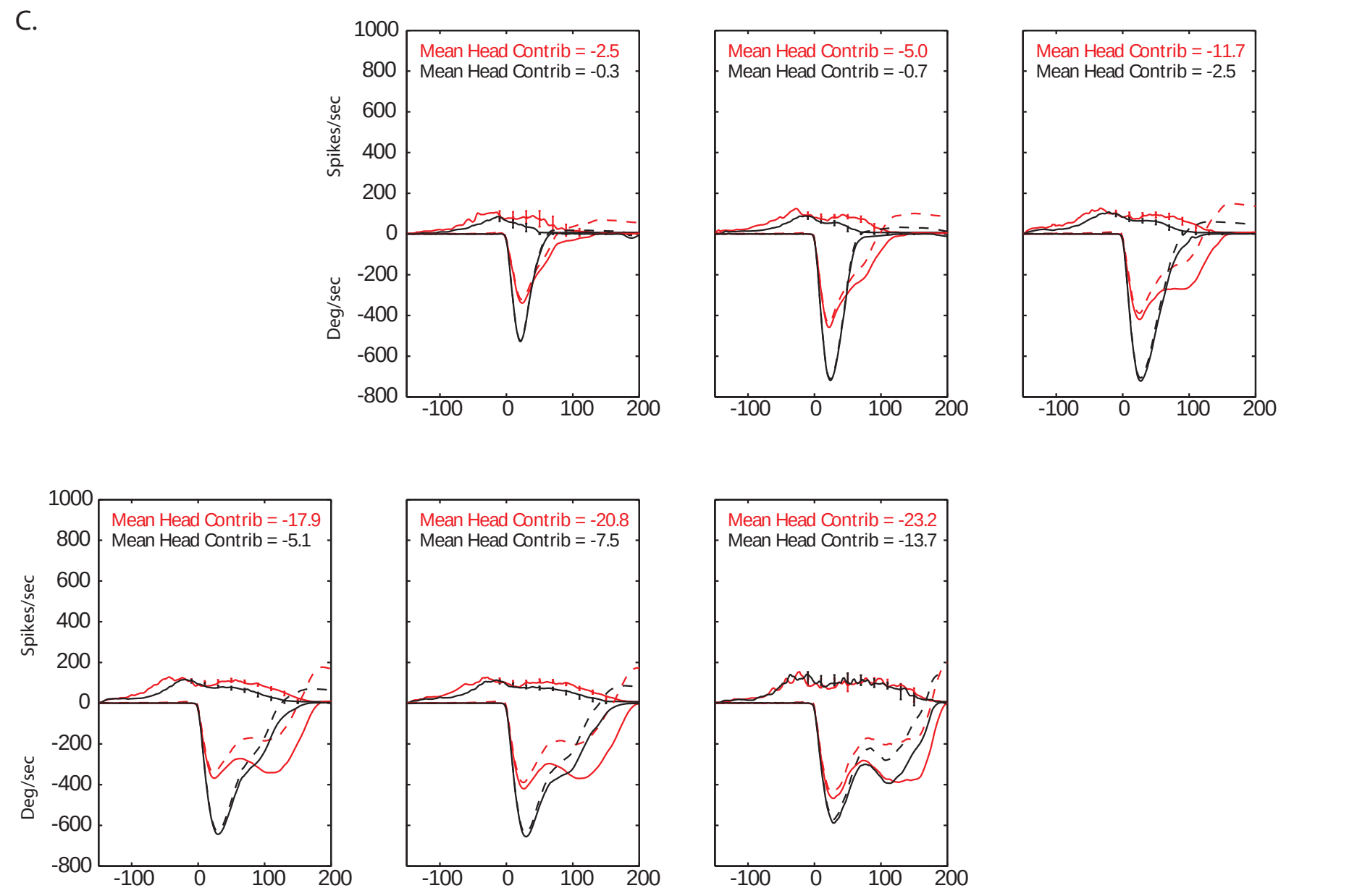
D. Although long lead burst neurons were, in general, more variable in many respects than EBNs, one similarity between the two cell classes was that the number of spikes in the burst was consistently more predictive of gaze amplitude than eye or head amplitude.

Figure 5. Position traces, rasters, averaged firing rates and movement field plots for one example LLBN. Unlike the EBN, the dual peaks in the velocity profiles are not reflected in the averaged firing rates of the cell. The peak and average firing rates are not clearly different for the large and small head contribution groups.

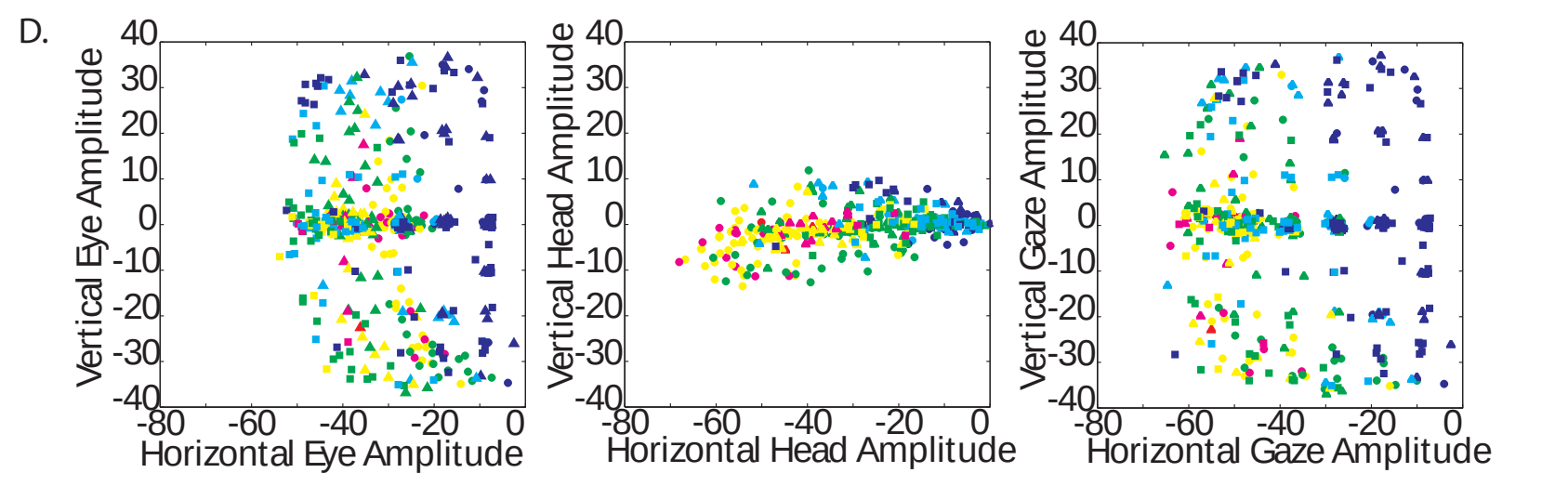




B. Many neurons were isolated that have firing rates much lower than have been commonly reported for EBNs or LLBNs. Like previously described LLBNs, these cells begin firing 50-100 msec before the onset of the gaze shift. For large target eccentricities, the first gaze shift was often hypometric, requiring a corrective saccade. In these cases, the neuron continued to discharge at a lower rate after the end of the first gaze shift until a corrective saccade brought the eyes to the target.



C. Same format used for the EBN and LLBN. Unlike most EBNs and some LLBNs, the firing rates were generally similar for gaze shifts of a particular amplitude, regardless of the size of the head contribution.



D. Movement fields for low frequency cells were similar to those for EBNs and hfLLBNs. Of 31 low frequency cells recorded, one was selective for gaze shifts of a particular vector, having an SC-like movement field. For all others, the number of spikes increased monotonically with horizontal gaze amplitude. These cells showed little modulation associated with the vertical component.

Figure 6. Position traces, rasters, averaged firing rates and movement field plots for a neuron that discharged at low frequency in association with gaze shifts. Thirty-one such cells have been recorded from three monkeys. These neurons were found in close association with EBNs, often on the same electrode track. In some cases, low frequency cells were recorded within 100 µm of an EBN.

These cells will be referred to as "Low frequency LLBNs" (lfLLBNs). They had the following characteristics:

1. Low peak firing rate – the peak firing did not exceed 400 spikes/sec for gaze shifts of any amplitude up to 70 degrees. For all but three of these cells, the firing rate never exceeded 300 spikes/sec.
2. Began firing up to 50-150 ms before gaze onset.
3. Gradual increase in FR, with no clearly defined burst.
4. For most (70%), the number of spikes, burst duration, and peak firing rate all increased as gaze amplitude increased.
5. For gaze shifts of a given amplitude, no clear sign of a decrement in firing rate associated with large head contributions.
6. Most continued firing at a lower rate after the end of the gaze shift until a corrective saccade is made or until the head stopped moving.
7. Some fire during head-only movements and some don't.

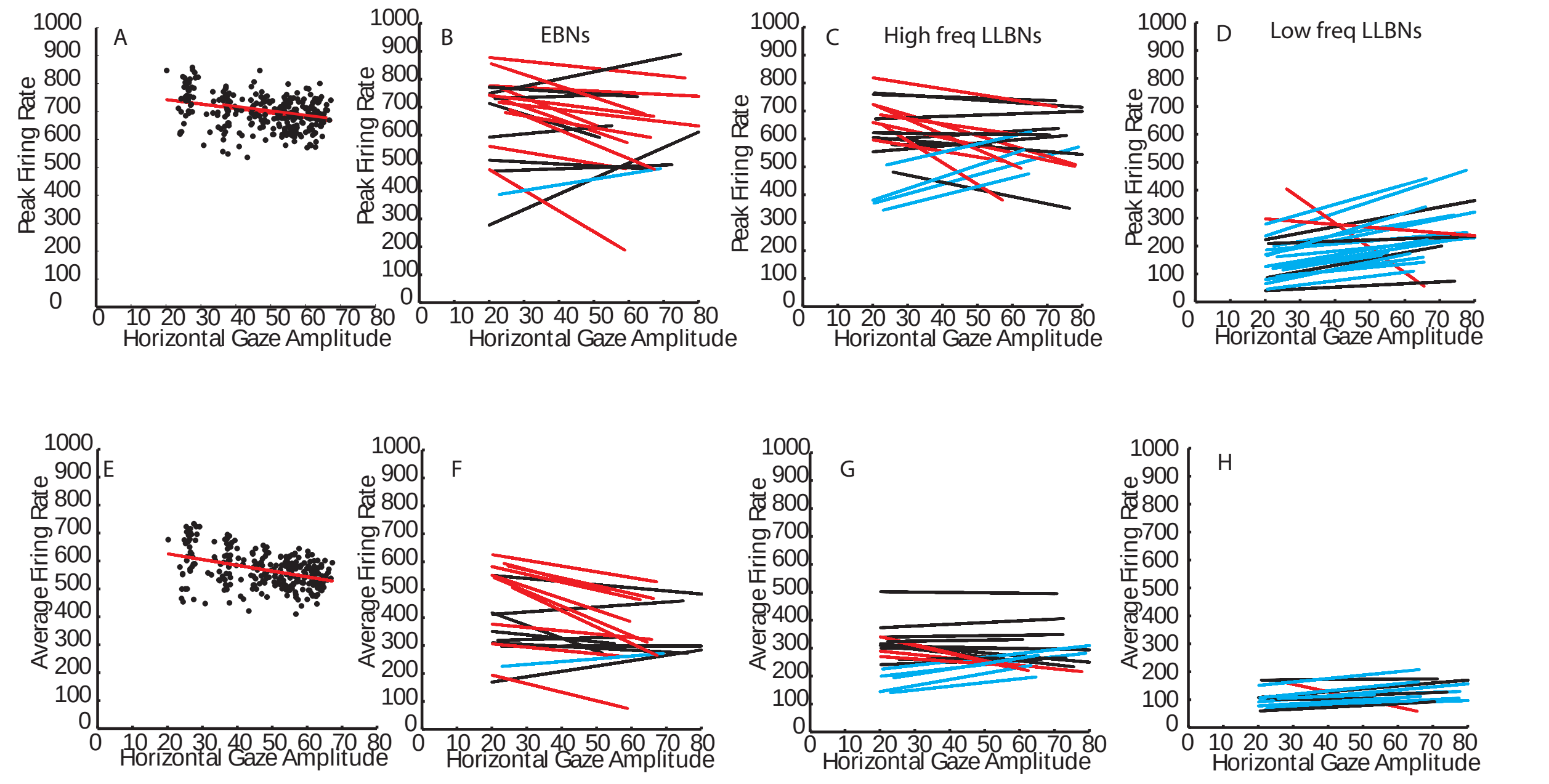


Figure 7. Peak (top row) and average (bottom row) firing rates were plotted as a function of the horizontal component of gaze amplitude and a linear regression analysis was performed on trials with horizontal gaze amplitudes of at least 20 degrees. The left column shows examples of these analyses for the same EBN shown to the left. The next three columns show the regression lines for EBNs, high frequency LLBNs, and low frequency LLBNs. Red and blue lines indicate significant negative and positive slopes, respectively.

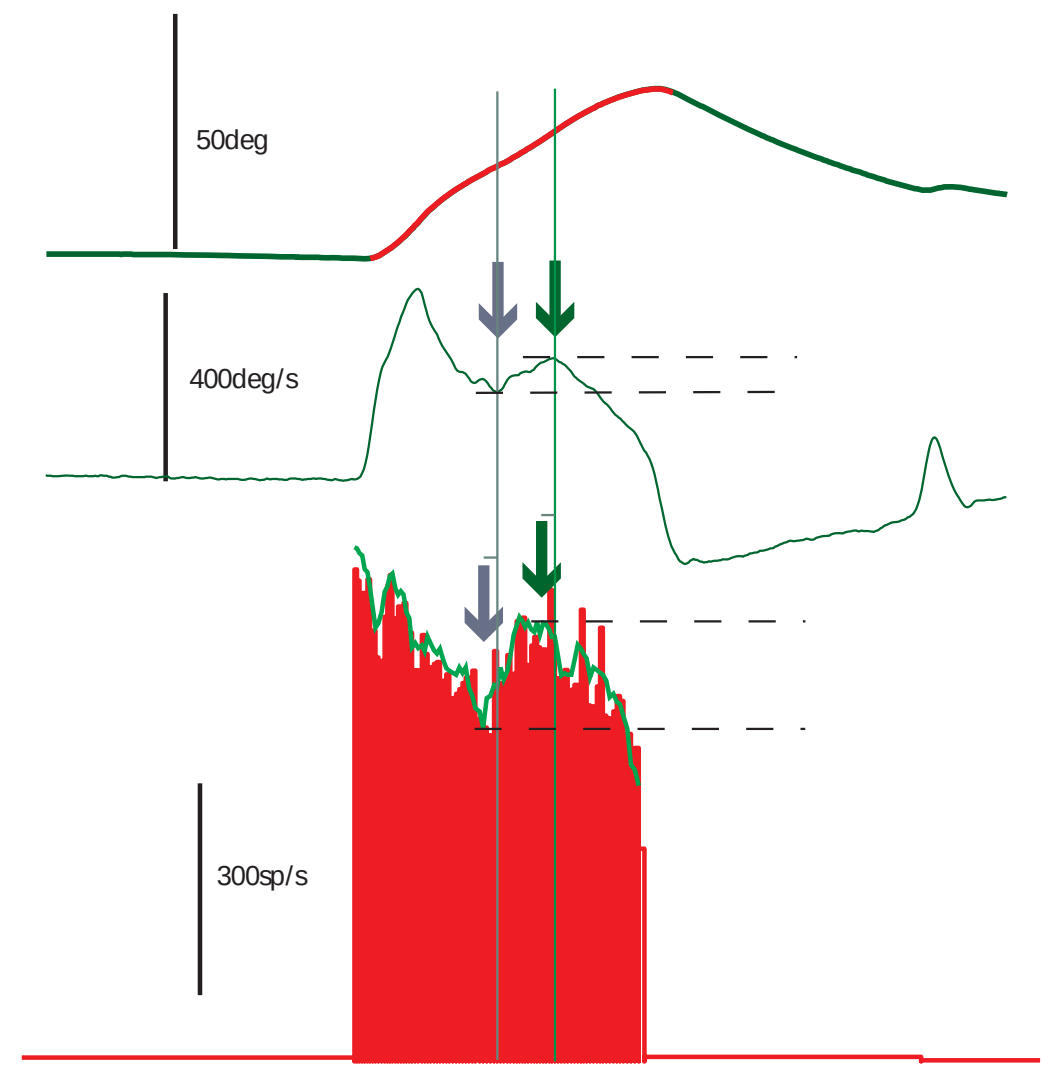


Figure 8. To quantitatively assess the relationship between firing rate and dual peaks in the velocity profile, an algorithm was devised that identifies trials with dual velocity peaks. Briefly, the algorithm identifies periods of sustained acceleration and deceleration and identifies a trial as having two velocity peaks if the eye-in-head velocity profile has the characteristic acceleration-deceleration-reacceleration-deceleration pattern.

The eye velocity before the reacceleration (upper gray arrow) was then subtracted from the eye velocity at the time of the second peak (upper green arrow). The firing rates (time shifted to account for neural delays) corresponding to these time points were also measured (lower arrows).

The differences and ratios (data not shown) for velocity were then compared to those for firing rate. Significant positive correlations were found for 54% of EBNs, 14% of high frequency LLBNs, and 19% of low frequency LLBNs.

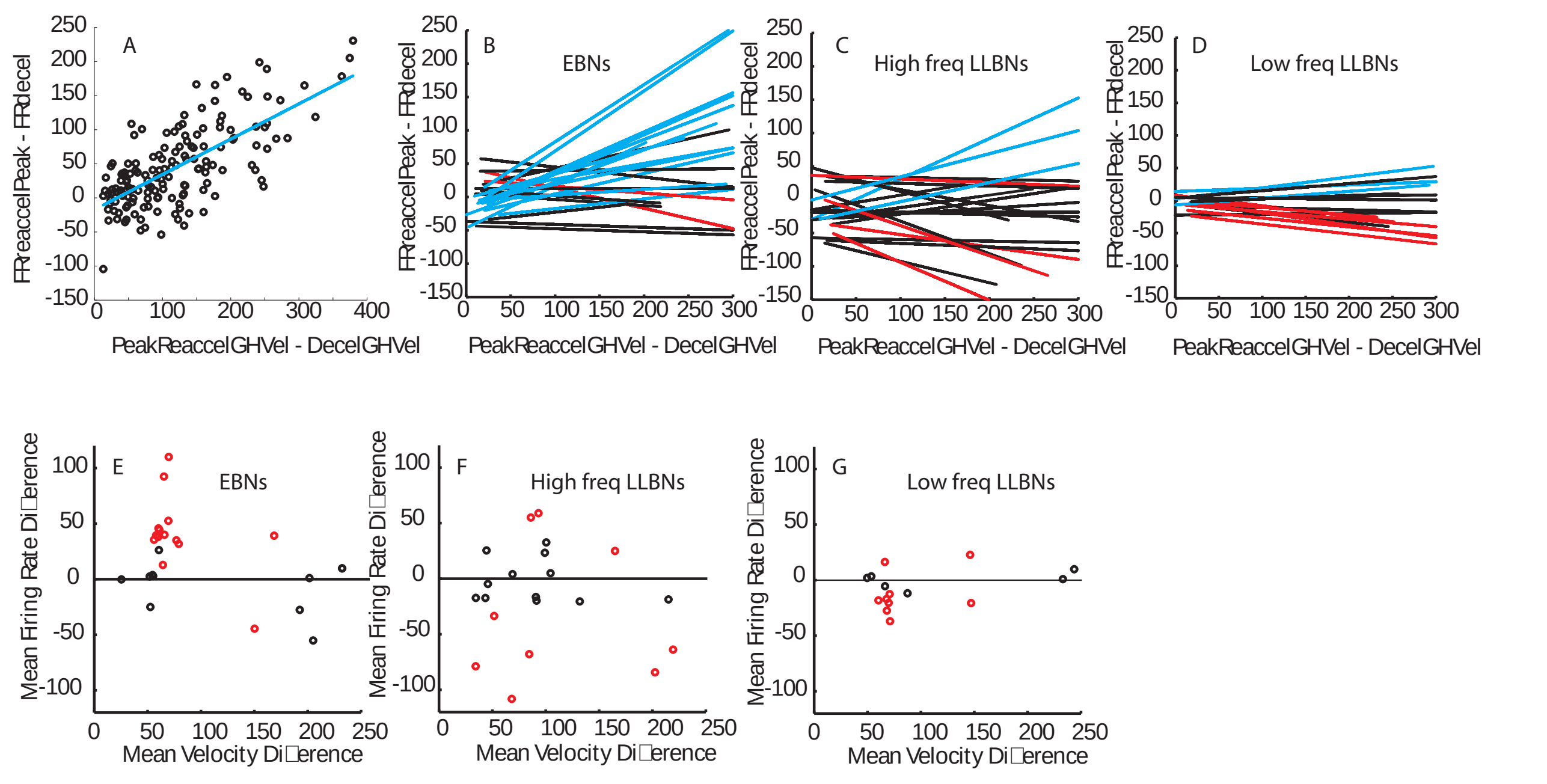


Figure 9. Increases in firing rate associated with dual velocity peaks. A) For each trial, the change in firing rate was plotted as a function of the change in velocity associated with the second peak in the velocity profile and a linear regression analysis was performed on the data for all cells for which there were at least 20 trials with dual peaks in the eye velocity profile. B-D) Resulting regression lines for EBNs, hfLLBNs, and lfLLBNs, respectively. Significant positive correlations are shown in blue. Significant negative correlations are shown in red. E-G) Mean differences in firing rate plotted as a function of mean difference in velocity for EBNs, hfLLBNs, and lfLLBNs.

For the majority of EBNs (13/23 for both analyses), the firing rate significantly increased in association with a reacceleration of the eye. This was not the case for most hfLLBNs or lfLLBNs.

CONCLUSIONS

When the head makes a large contribution to a gaze shift, eye and gaze velocity profiles often have two peaks. The present data show that this is reflected in the firing rates of excitatory burst neurons in paramedian pontine reticular formation. In contrast, no evidence for a similar modulation was found for long-lead burst neurons. Behavioral studies have also shown that the average eye velocity decreases as gaze amplitude increases. This effect also appears to be represented by EBNs, as the peak and average firing rates for many of these cells decreases as gaze amplitude increases. The fact that these effects could not be demonstrated for LLBNs suggests that the firing rate profiles of EBNs -- but not LLBNs -- may be shaped, in part, by inputs from elements related to head movement.

A population of neurons was found in paramedian pontine reticular formation that discharge at low frequency in association with coordinated eye-head movements. The low firing rate, the fact that many continue to fire after the end of the gaze shift and the fact that some fire during head only movements suggest the possibility that these cells may be related to head movement. In support of this possibility, for some of these cells, the onset of discharge is more closely correlated with the time of head onset than the time of gaze onset. On the other hand, one of the most consistent properties of these cells is that the firing rate drops sharply after each corrective saccade is made. Additionally, all of these cells discharge in association with saccades, even when there is no accompanying head movement and some do not fire during head-only movements. Taken together, these data may suggest the possibility that these cells carry varying combinations of eye/gaze related and head movement related activity.

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