

# Examining the Paradoxical Relation between Number of Spikes and Gaze Amplitude in Abducens Neurons

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**ABSTRACT:** During head-unrestrained gaze shifts, the number of spikes in the burst of abducens neurons increases with gaze amplitude, even when corrected for the component of the discharge related to the change in eye position. We examine this paradoxical dissociation between the number of spikes and eye amplitude, which occurs because eye amplitude in the head saturates for larger gaze shifts. First, we show that the extra spikes are unlikely to be due to antagonist muscle loading because the abducens neurons are completely silent during large gaze shifts when the muscle acts as an antagonist. Next, we divide the firing rate profile of abducens neurons into terms that represent signals related to eye position, velocity, and acceleration; a d.c. offset term specifying the firing associated with straight-ahead gaze; and a slide term, which compensates for the zero of the oculomotor plant. Then we examine the contribution of each term to the number of spikes recorded. A comparison of the number of spikes with the integral of the fitted function, combining all of the terms, for the duration of the burst reveals that the simulation captures much of the actual data. However, even a model with a slide term cannot reproduce the nonlinear relationship of the number of spikes with amplitude that characterizes large gaze shifts.

**KEYWORDS:** motoneuron; burst discharge; saccades

## INTRODUCTION

The first recordings of the activity in the motor nuclei of the extraocular muscles with the head restrained revealed a characteristic burst-tonic discharge pattern in association with saccades.<sup>1-3</sup> During fixation, the tonic firing rate is linearly related to orbital eye position. During a saccade that requires the innervated muscle to shorten, there is a burst of spikes that lasts the duration of the saccade and reaches a rate in excess of that associated with the final eye position. For saccades in the opposite (off) direction when the muscle lengthens, motoneurons exhibit a pause in activity. The number of spikes in the saccadic burst of abducens neurons show a linear increase with saccade amplitude when the spikes associated with the change in eye position due to the rate-position relationship are subtracted.<sup>4,5</sup>

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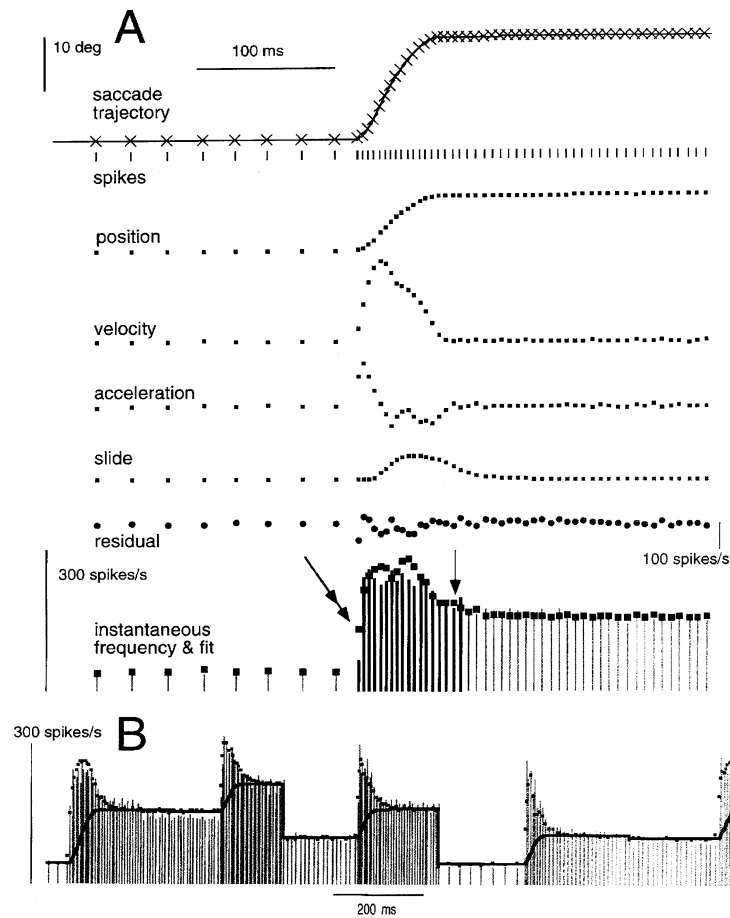
With the head free to rotate and contribute to the gaze shift, the number of spikes still increases, but with the amplitude of the gaze movement rather than the amplitude of the eye movement.<sup>6</sup> As gaze amplitudes grow larger, the eye movement contribution to gaze amplitude gradually saturates even as the number of spikes continues to increase. Therefore, for larger gaze shifts it appears that more spikes than those associated with the eye movement alone are necessary.

The paradoxical dissociation between the number of spikes and eye amplitude in abducens neurons remains unexplained. Cullen and colleagues<sup>4</sup> have described the net discharge profile of abducens units in terms of eye movement attributes, such as position and velocity, and have demonstrated that a model based on gaze movement trajectories does not provide a satisfactory fit. They failed, however, to explain how their fit accounts for the extra spikes during head-unrestrained gaze shifts. We also examined the neural activity and decomposed the firing pattern into signals whose contribution to the number of spikes in the burst can be evaluated separately. In particular, we investigate whether the addition of a “slide” term, which compensates for the zero of the peripheral eye movement apparatus (the plant) and is manifest late in the saccade, provides the extra spikes: this term may exhibit a nonlinear relationship with eye amplitudes because its contribution to the number of spikes in the burst is cut off during head-fixed saccades of short duration.

## METHODS

We recorded neurons in the abducens nucleus of rhesus monkeys trained to follow spots of light by fixating sequentially illuminated LEDs. The abducens nucleus was identified by the characteristic discharge of its units and that of nearby cells such as inhibitory burst neurons. All units paused in the off direction, a feature that distinguishes abducens neurons from those in the nearby nucleus prepositus hypoglossi. Eye position in space was recorded by a search coil in a magnetic field.<sup>7</sup> Head position was measured with a precision potentiometer in line with a post that restricted the animal's head movements to the horizontal plane. Both signals were digitized at 1 kHz. The associated unit activity was recorded as interspike-intervals at a resolution of 10  $\mu$ s. For details of the behavioral controls and the recording techniques, the reader is referred to our previous reports.<sup>8,9</sup>

We decomposed the discharge profile of abducens neurons into five separate components, consisting of terms proportional to eye position, velocity, and acceleration; a d.c. offset term and a slide term (FIG. 1A). The slide term was produced by passing eye velocity through a first-order filter.<sup>10</sup> The time constant of this filter is estimated for each unit by fitting a single exponential through the sagging discharge following the end of head-restrained saccades (see single arrow, FIG. 1A). The d.c. offset term represents the firing rate associated with straight-ahead gaze. The movement trajectories are sampled at the time of each action potential, then delayed to optimize the fit (that is, to produce the largest variance accounted for). This delay is larger than the average latency of the neural response by 2 to 3 ms and tends to align the time of peak velocity with the occurrence of the peak burst rate. The five coefficients of the three eye movement terms, the d.c. offset, and the slide term are then determined using a least-squares minimization procedure.



**FIGURE 1.** Analysis of the discharge profile of an abducens neuron during gaze shifts. **(A)** The top two traces show the time course of a saccade with the accompanying discharge of an abducens neuron. Each action potential is marked by a tic. Crosses in the eye movement trace indicate when samples are taken for the analysis. Samples of the position, velocity, acceleration, and slide terms are then displayed. Linear combinations of these terms are summed to fit the neural discharge. The results are superimposed (*filled squares*) on the instantaneous discharge frequency, which is indicated by the height of the vertical bars aligned on the occurrence of each spike. The difference between the neural data and the fit (*residual*) is shown at the time of each spike. **(B)** Data from several saccade trials is concatenated. The discharge profile (*vertical bars*) for a number of trials, providing an excerpt of the full dataset for one unit, is displayed with the saccadic eye movement (*black line*) and the resulting fits (*dots*).

An example of the fitting procedure is shown in FIGURE 1B. We anchor the fit by including the steady discharge preceding (about 200 ms, starting from the target step time) and following the saccade (about 180 ms unless a correction saccade occurs earlier). Nearly all trials exhibit preburst tonic activity. Data from several trials were concatenated and fit simultaneously (between 40 and 100 gaze shifts per unit). We attempt to describe the neural discharge strictly in terms of a linear system; therefore, the model does not include hysteresis, which probably is the reason for the offset of the fit during the steady firing preceding the second saccade shown in FIGURE 1B.

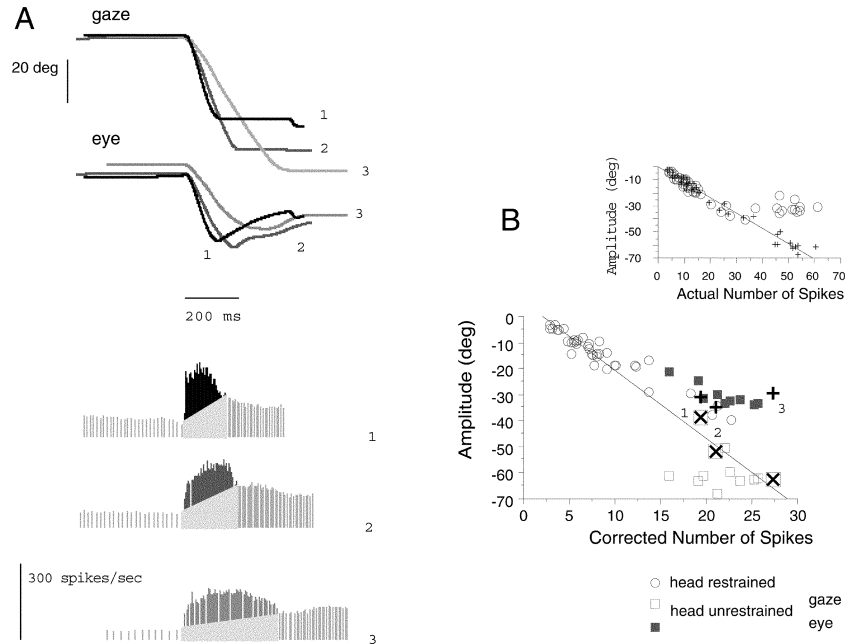
## RESULTS

Typically, our fitting procedure utilizing functions proportional to eye position, velocity, acceleration and a slide term and a d.c. term (FIG. 1A) accounts for more than 85% of the variance of the neural data (six neurons). The variation of residuals (difference between fit and actual data) during the time course of the burst-tonic discharge indicates where the problematic parts of the fit occur. The mean absolute residual error during a period of fixation is approximately 2–5 spikes/s. The residual error increases during a burst, reaching values of 15–20 spikes/s. In particular, the fitting procedure cannot simulate the rapid rising edge of the bursts. Thus, the fit rises earlier (FIG. 1A, double arrow), causing a large negative error. However, the actual burst rates quickly surpass the fitted values, resulting in positive errors. This pattern of swing from positive to negative errors is often observed at the beginning of the burst (FIG. 1B).

When the head is unrestrained, the magnitude of the eye excursions in the orbit remains roughly constant as the size of the gaze shift increases and the head makes a growing contribution to gaze amplitude. For example, for the monkey illustrated in FIGURE 2, eye movements have a nearly constant amplitude of 30° to 35° although gaze amplitude varies between 40° and 70°. The discharge patterns associated with three gaze shifts of increasing gaze movement amplitudes but with rather similar eye movement amplitudes are shown in FIGURE 2A. As the gaze shift increases in amplitude, the number of spikes in the burst (the number of dark bars) increases. To quantify the magnitude of this transient response, we count the number of spikes occurring in the burst after subtracting the number of spikes associated with the tonic eye position sensitivity. The eye position contribution to the burst is estimated as the number of spikes represented by the gray shaded area of the burst shown in the discharge profiles in FIGURE 2A.

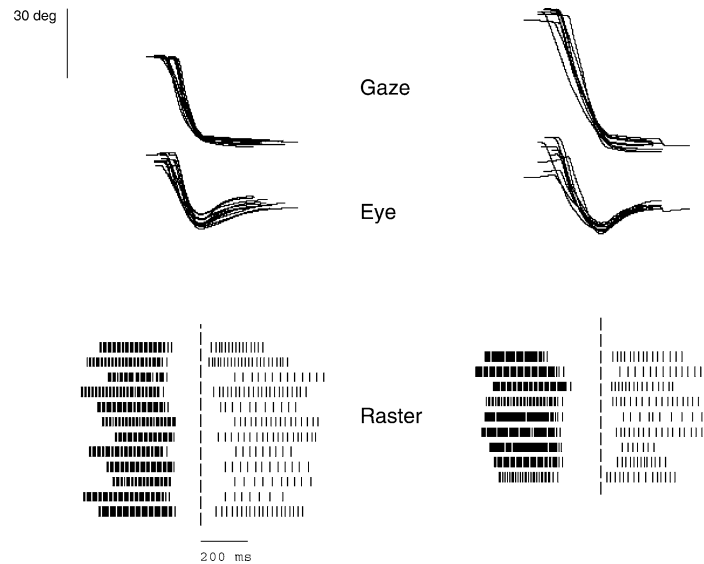
FIGURE 2B (inset) shows that the uncorrected number of spikes in the burst is linearly related to gaze (plus signs), not eye (open circles) amplitude. In addition, FIGURE 2B (main) shows that this pattern remains for the corrected number of spikes, which is also linearly related to the amplitudes of head-restrained saccades (open circles) and continues to increase for gaze shifts of larger amplitude during head-unrestrained movements (open squares). In contrast, the relation between the eye movement amplitude of head-unrestrained gaze shifts and the corrected number of spikes in the burst veers off from the relation obtained for head-restrained saccades as the eye amplitude saturates (filled squares).

These data seem to show that the number of spikes in the burst of large gaze shifts exceeds that needed to achieve the observed eye amplitude. Such an increase in mo-



**FIGURE 2.** Number of spikes in burst of an abducens neuron during head-unrestrained gaze shift. (A) Three gaze shifts of increasing amplitude (gaze) and the accompanying eye saccades (eye) are shown together with the corresponding discharge of an abducens motoneuron. The height of the spikes in the unit raster corresponds to instantaneous frequency. The corresponding traces are labeled with numbers (1–3). The *gray portion* of the burst discharge denotes the discharge removed through the correction procedure. (B) The inset shows original uncorrected number of spikes re amplitude relationships for eye (*open circles*) and gaze (*plus signs*) movements. The main image displays the number of spikes corrected for the position term (that is, following removal of the gray portion of the burst discharge in A) plotted against amplitude for a variety of movement amplitudes. Data is displayed for head-restrained saccades (*open circles* with corresponding regression line), for gaze amplitudes during head-unrestrained gaze shifts (*open squares*), and for the amplitude of eye saccades during the same large gaze shifts (*filled squares*). The three example trials in A are identified (*crosses*: gaze; *plus signs*: eye) and labeled with numbers (1–3).

toneuron drive might be expected if the antagonist created an additional load during large gaze shifts. Unfortunately, no direct recordings are available from the motoneurons that innervate the antagonist medial rectus muscle during head-unrestrained gaze shifts. When the lateral rectus acts as an antagonist during head-unrestrained gaze shifts, however, abducens neurons exhibit a prominent pause, which lasts for the entire duration of the gaze movement. In fact, the pause typically continues beyond the end of the eye saccade. In FIGURE 3, two sets of gaze shifts are displayed with different mean amplitudes ( $36.0^\circ$  vs.  $56.3^\circ$ ) but similar eye components ( $27.8^\circ$  vs.  $33.2^\circ$ ). These data, which are similar for all abducens neurons we have studied, indicate that extra spikes are not needed to overcome an additional load imposed by antagonist contraction, because the antagonist is silent.

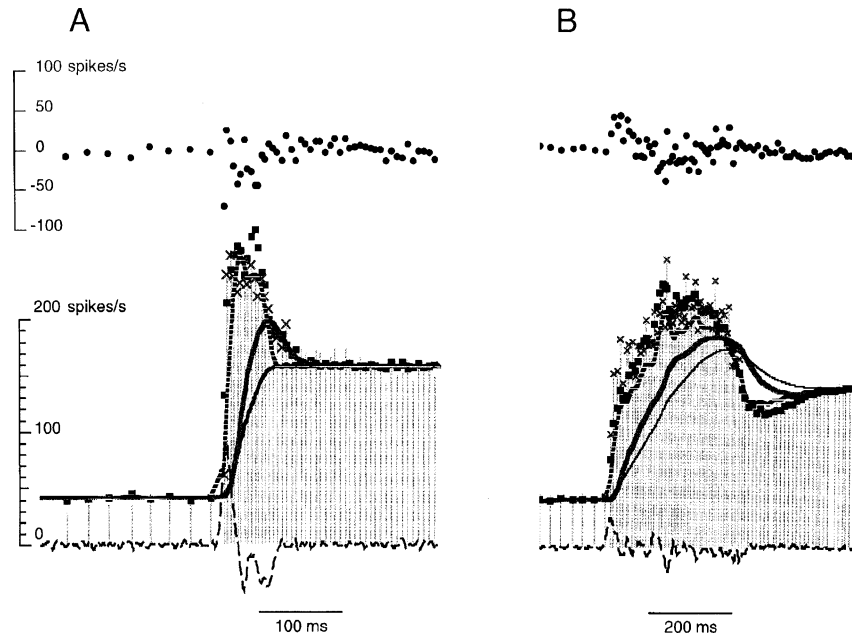


**FIGURE 3.** Off-direction responses of an abducens neuron during head-unrestrained gaze shifts. Gaze and eye in head are displayed for two amplitudes of gaze shift with comparable eye movement amplitudes. The accompanying neural activity is presented in the form of a raster display (raster). All traces are aligned on eye end. Each trial demonstrates a pause in tonic activity, which clearly extends beyond the end of the movement.

If not the antagonist activity, what is the explanation for the extra spikes? To address this issue we decomposed the discharge in abducens neurons during head-restrained and head-unrestrained gaze shifts in terms of components related to a d.c. offset, eye position, velocity, acceleration, and a slide term by fitting the discharge profile to a linear sum of these signals. From the fit, we can predict the actual number of spikes and ascertain the contribution of each term. This procedure allows us to locate the source of the extra spikes during head-unrestrained gaze shifts.

Our results show that the fit to the instantaneous firing rate nicely captures much of the discharge pattern associated with head restrained (FIG. 4A) and unrestrained (FIG. 4B) saccades. The position term (solid black line) follows the steady firing while the animal fixates before and after the saccade. When the velocity term is added during the head-restrained saccade in FIGURE 4A, the sum of eye position and velocity (dotted black line) describes much of the burst itself, especially when helped at the start by the acceleration term (dashed line at bottom) to produce the rapid onset of the burst. However, the sum of the position and velocity terms returns to the post-saccadic firing rate well before the actual firing rate does. To keep the firing somewhat elevated after the contributions related to parameters of the movement have dissipated, a slide term must be added.

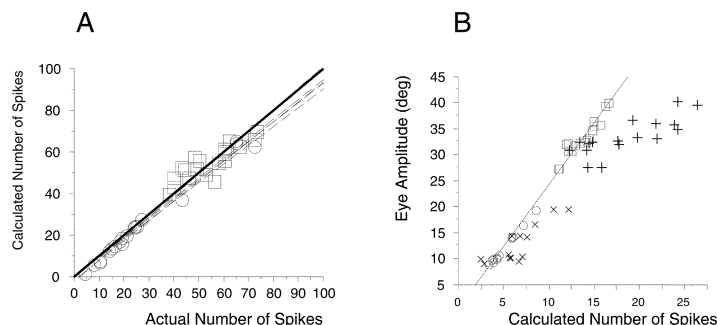
The results of the fit provide a d.c. term, which is equal to the intercept of the relationship between steady firing rate and eye position during fixation, and a position



**FIGURE 4.** Decomposing the discharge profile of abducens neurons. (A) Resulting components for a head-restrained saccade exemplified in a single trial (same trial as in FIG. 1). *Top trace* displays the residual between fit and neural data. *Bottom traces* display a raster of the neural activity with the instantaneous discharge frequency represented by the height of the corresponding vertical bars. Also shown are the linear sums of the offset plus position terms (*solid black line*); the velocity plus position plus offset terms (*dotted black line*); the offset plus position plus slide terms (*solid gray line*), and the acceleration term (*dashed line* at bottom). *Filled squares* correspond to the sum of all terms in the fit. The instantaneous firing rates for spikes during the burst are denoted with *crosses*. (B) Resulting components for an eye movement during a head-unrestrained gaze shift. The trace definitions follow the description in A above.

coefficient, which corresponds to the slope of that relationship. The values are within the range of identified motoneurons<sup>11</sup> and confirm the numbers determined experimentally during steady fixation. Furthermore, when such data were available, the magnitude of the velocity coefficient is equal to the velocity sensitivity of the unit at 1 or 1.4 Hz, as estimated during sinusoidal pursuit or sinusoidal passive vestibular stimulation while fixating a target stationary in space.

The fit to the discharge during head-restrained saccades accounts for the total number of spikes in the burst. The integral of the actual spike density function over the burst obtained during such saccades yields the number of spikes in that burst. Because the profile of instantaneous firing rates provides a good estimate of the spike density function, a good fit to the discharge profile should also approximate the spike density function. Therefore, integrating the fitted function over the burst should re-



**FIGURE 5.** (A) Plot of the integral of the fit function over the duration of the burst against recorded number of spikes. Data from fits to head-restrained saccades (*open circles*) are combined with that to head-unrestrained gaze shifts (*open squares*) in a single regression (*solid line*). Regression lines from other units are also shown (*dotted lines*). (B) The calculated number of spikes remaining after the position component and d.c. offset have been removed, that is, the sum of the velocity, acceleration, and slide components is plotted against eye amplitude for head-restrained saccades (*open circles*) and head-unrestrained gaze shifts (*open squares*). The slide term does not make the relationship nonlinear. The number of spikes corrected by the position component and d.c. term (*crosses* for head-restrained data; *plus signs* for head-unrestrained data), however, retain a nonlinear relationship with eye amplitude.

sult in values close to the actual number of spikes. FIGURE 5A (open symbols) shows that this is indeed the case for a representative abducens unit. Each point represents the result from a single gaze shift with data for head-restrained saccades in open circles and those for head-unrestrained gaze shifts in open squares. The data is nicely fit by a straight line with a slope of nearly one and an intercept close to the origin, indicating that the observed and the calculated number of spikes are in close agreement. Similar linear fits (dashed lines) pertain to five other units (mean slope:  $0.96 \pm 0.05$  (SD); intercept:  $-0.40 \pm 1.03$ ;  $r^2$ :  $0.977 \pm 0.014$ ). The mean absolute error for the unit selected in FIGURE 5A is 3.2 spikes; however, a larger error may occasionally arise. The error tends to be less pronounced for the fit to head-restrained saccades than for that to the larger head-unrestrained gaze shifts (for example, the mean absolute errors were as follows: 1.5 vs. 4.4 spikes).

We divided the number of spikes calculated from the fit into two groups. First, we combined the velocity, acceleration, and slide components and plotted the spikes of a fit with the position term removed against the eye amplitude of head-restrained saccades (open circles) and head-unrestrained gaze shifts (open squares). The resulting data points fall on a straight line indicating that the neither of these terms gives rise to the nonlinearity of the number of spikes re the amplitude relationship. Second, we subtract the part of the fit that derives from the position component plus the d.c. term from the actual number of spikes to establish a corrected number of spikes. In FIGURE 5B, we plot the corrected number of spikes against eye amplitude. For large gaze shifts, when the eye amplitudes are saturated, the corrected number of spikes still increases. The model has in fact failed to account for the spikes that cause the nonlinearity. Similar patterns were obtained for four other units.

## DISCUSSION

This study shows that during head-unrestrained gaze shifts the relationship between the number of spikes and amplitude does not have much predictive value in discerning what variables the discharge encodes (FIG. 1), in agreement with previous studies.<sup>4,6</sup> For the data set in FIGURE 2, we observe a dissociation between the number of spikes and eye amplitude. The subsequent analysis of fitting the entire discharge profile does provide a more complete description of the unit's behavior. However, our more comprehensive model still fails to account for the excess spikes. A full explanation may require a nonlinear model.

For head-restrained saccades, abducens neurons consistently exhibit a robust linear relationship between the number of spikes in the saccadic burst and the amplitude of the movement. The integral of the spike density function over the duration of the burst furnishes the number of spikes accumulated during the burst. Several factors conspire to result in a linear relationship. To a first approximation, the spike density function consists of the sum of a d.c. offset plus terms that are proportional to eye position and velocity. The integral of the d.c. term is equal to a constant times the duration of the burst, which is proportional to the amplitude of the saccade for main sequence movements. The integral of the position component is linearly related to amplitude as long as the rate-position curve of the unit is linear and, critically, the movement durations do not vary over a wide range. Finally, the velocity component obviously integrates to be proportional to eye amplitude. The sum total of the individual integrals is thus linearly related to eye amplitude as each component in turn is proportional to eye amplitude. With the removal of the position term, the sum of the d.c. and the position components, the linearity of the relationship is even more robustly determined.

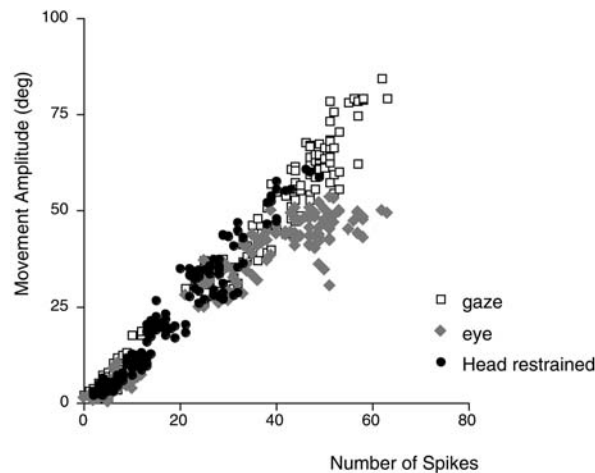
The function of a saccade, the realignment of the line of sight, would be optimally served by a trajectory that approximates a step function as closely as possible. A step change in firing rate in the motoneuron will be distorted by the ocular plant. The discharge of abducens units reflects a control strategy that attempts to compensate for the plant dynamics. From this point of view, the signal decomposition of the discharge profile into terms related to parameters of the movement trajectory describe how the activity accounts for different components of the plant. For instance, the position, velocity, and acceleration terms deal with the poles of the system. Should the plant actually be more complex, containing also zeros, additional signals such as the slide term would be required.

If the discharge of abducens neurons is related to the eye movement, as one would expect, why then does a parametric description of the such units fail during head-unrestrained gaze shifts? A simple first-order system would require only signals proportional to eye position and velocity. As the duration of gaze shifts increases, the contribution of the position component will be nonlinear and will grow with gaze amplitude. But, after the position term has been removed, the relationships between number of burst spikes and eye amplitude can only be linear.

However, the dynamics of head-unrestrained gaze shifts may reveal the complexities of the oculomotor plant and require signals in the neural activity that compensate for such complexities. In particular, a slide term needs to be added to deal with the zero of the system. After removing the position term, the integral of all the other terms cannot add spikes beyond those proportional to the eye amplitude. During

head-restrained saccades, the slide term can be neglected during the burst as it affects the discharge predominantly after the end of the movement. However, as head-unrestrained gaze shifts have much longer durations, the slide term could theoretically make a substantial contribution during the burst, providing the surplus spikes that are observed during such movements. However, the slide term is also linearly related to eye amplitude for large gaze shifts. Furthermore, the nonlinear effect brought about by the truncation of the slide term during head-restrained saccades is not large enough to create the nonlinearity observed in the number of spikes re amplitude relationship.

In the vicinity of the abducens nucleus in the brainstem, one encounters several units that display a robust burst in association with saccades. Some of these project directly to abducens neurons. Such prenuclear elements provide one of the sources of the burst observed in motoneurons during saccades. They also provide the pause in the antagonist motoneurons. These burst units exhibit a linear relationship between the number of spikes in the burst and the amplitude of head-restrained saccades in their on-direction.<sup>12,13</sup> FIGURE 6 plots the response of one such burst neuron, an excitatory burst neuron, during gaze shifts of varying magnitude when the head is restrained and when the head is allowed to contribute. The relationship between number of spikes and the amplitude of head-unrestrained gaze shifts follows the head-restrained data and extends it to larger amplitudes. On the other hand, the relationship for the accompanying eye amplitude deviates from the progression of head-restrained data as the eye amplitudes saturate with increasing gaze shift ampli-



**FIGURE 6.** Response of an excitatory burst neuron (EBN) in the paramedian pontine reticular formation during head-restrained saccades and head-unrestrained gaze shifts. The number of spikes in the burst recorded during gaze shifts is plotted against the amplitude of the head-restrained saccade (*filled circles*), the gaze amplitude of head-unrestrained gaze shifts (*open squares*), and the amplitude of the associated eye movement (*filled diamonds*). The relationship for head-unrestrained gaze amplitudes is linear and superimposes on the head-restrained data points, whereas head-unrestrained eye amplitudes show a nonlinear relationship.

tude. This pattern is reminiscent of the behavior of abducens cells (cf. FIG. 2). The fact that the signals in excitatory burst neurons and abducens neurons are separated by only a single synapse suggests that a common rationale should be applied to both phenomena. We propose that to compensate for the complexities of the oculomotor plant, the pre-nuclear burst neurons and the abducens motoneurons carry more than just a simple velocity command. The additional component becomes apparent only during head-unrestrained gaze shifts when the longer durations require more spikes to produce the same change in eye amplitude.

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