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Amplitude and Direction of Saccadic Eye Movements Depend on the Synchronicity of Collicular Population Activity

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Brecht, Michael, Wolf Singer, and Andreas K. Engel. Amplitude and direction of saccadic eye movements depend on the synchronicity of collicular population activity. *J Neurophysiol* 92: 424–432, 2004. First published February 18, 2004; 10.1152/jn.00639.2003. Synchronization of neuronal discharges has been observed in numerous brain structures, but opinions diverge regarding its significance in neuronal processing. Here we investigate whether the motion vectors of saccadic eye movements evoked by electrical multisite stimulation of the cat superior colliculus (SC) are influenced by varying the degree of synchrony between the stimulus trains. With synchronous activation of SC sites, the vectors of the resulting saccades correspond approximately to the averages of the vectors of saccades evoked from each site alone. In contrast, when the pulses of trains applied to the different sites are temporally offset by as little as 5–10 ms, the vectors of the resulting saccades come close to the sum of the individual vectors. Thus saccade vectors depend not only on the site and amplitude of collicular activation but also on the precise temporal relations among the respective spike trains. These data indicate that networks within or downstream from the SC discriminate with high temporal resolution between synchronous and asynchronous population responses. This supports the hypothesis that information is encoded not only in the rate of neuronal responses but also in the precise temporal relations between discharges.

INTRODUCTION

It is commonly held that neurons convey information by changing discharge rate. Because neurons are usually broadly tuned, precise information about the presence of a particular feature or about the vector of a movement is thought to be encoded in the distribution of graded response amplitudes of a population of conjointly active neurons, the so-called population vector (Georgopoulos 1995). However, conjointly activated neurons often exhibit temporal correlations among their discharges that exceed the correlations expected from the covariance of rate changes. The functional significance of these excess correlations is controversial (Shadlen and Movshon 1999; Singer 1999). Theoretical considerations (Gerstein et al. 1989; von der Malsburg 1981) and experimental evidence from the visual system (Singer 1999; Singer and Gray 1995) suggest that synchronization of discharges with a precision in the millisecond range might serve to selectively and conjointly raise the saliency of the synchronized responses, thereby providing for subsequent processing stages a signature of relatedness. A necessary prerequisite for such a coding strategy is that neurons in target structures can discriminate between synchronous and asynchronous inputs. Here we investigate this question by activating multiple sites in the superior colliculus with synchronous and asynchronous trains of electrical stimuli, using the resulting eye movement as a measure of down stream integration. Because electrical stimulation allows precise control of both the frequency (amplitude) and the exact timing of neuronal population responses and because the vectors of saccadic eye movements can be quantified with great precision, we have chosen electrically evoked saccades as a model to examine whether synchronized and nonsynchronized population responses have different effects on down-stream processes. Although the hypothesis motivating the present experiments was not formulated in the context of oculomotor control, the results are likely to also have some bearing on the question how collicular population activity is translated into oculomotor output. The effects of single-site activation by microstimulation have been characterized in much detail (Stanford et al. 1996), but there are less data on the effects of multi-site stimulation and in particular on the role of precise timing patterns in collicular population activity. However, such data are needed to constrain models of the read out of collicular population activity (Groh 2001) that make specific predictions on how information from multiple collicular sites is integrated.

The amplitude and direction of saccadic eye movements are specified by the population vector of neuronal responses in the superior colliculus (Lee et al. 1988; Sparks 1986), and these population responses can be mimicked in great detail by electrical microstimulation in the deep layers of the superior colliculus. The resulting saccades closely resemble those that would have occurred had the same cell groups been activated with light stimuli (Pare et al. 1994).

The deep collicular layers contain a motor map for orienting responses (Robinson 1972) so that activation of a particular site either by natural or electrical stimuli leads to rapid eye and head movements the vector of which is specific for that site. Evidence indicates further that simultaneous activation of different sites often leads to saccades whose motion vectors correspond to the average of the vectors corresponding to the respective stimulation sites. Experiments involving the partial inactivation of the SC suggest that saccade vectors are derived from averages across the population responses (Lee et al. 1988). When multiple SC sites are synchronously electrically stimulated, the resulting saccade vector corresponds to a vector average (Robinson 1972). We reasoned that synchronously

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active collicular neurons might signal a common saccade target and that synchronous stimulation might thus evoke vector averaging. According to our hypothesis, asynchronous stimulation should signal multiple saccade targets and might thus evoke eye movements different from a vector averaging outcome. To test this possibility, we positioned two or three microelectrodes in the deep layers of the superior colliculus of awake cats and compared the vectors of eye movements elicited by synchronous and asynchronous stimulus trains applied simultaneously through different electrodes.

METHODS

Implantation and recording

We used standard surgical and recording techniques. Three cats were implanted under general anesthesia induced by ketamine and xylazine (10 and 2 mg/kg im, respectively) and maintained by ventilating the animal with a mixture of 70% N_2O, 30% O_2, and 0.8–1.2% halothane. Dental acrylic implants included a recording cylinder over a small trepanation above the SC, a head fixation bolt and, in three animals, a connector to Ag/AgCl electrodes chronically implanted above and below as well as lateral to the eyes for DC electrooculography (EOG). In a fourth animal, a coil of fine insulated wire was secured to the bulb of one eye for magnetic search coil measurement of eye movements (Robinson 1963). Calibration of eye-movement amplitudes was performed in two ways both for DC electrooculography and search-coil measurements. Prior to the recording sessions, two salient targets were presented repeatedly at defined positions of the visual field to evoke saccades of defined direction and amplitude. Additional measurements were performed under anesthesia after implantation and at the end of the experiments. In this case, the eyes were moved passively, and direction and amplitude of the induced eye movements were assessed from the displacement of the optic discs that were traced on a tangent screen with a fundus camera. Quantitatively similar results were obtained when saccade beginnings and endings were defined by a threshold criterion (5 vs. 95%) of the final saccade amplitude or by a velocity criterion (beginning $>20°/s$, ending $<20°/s$); in most cases, the former criterion was used. Experimental sessions began after recovery from the surgery and habituating animals to the experimental procedures. Stiff 200-μm tungsten microelectrodes were advanced through the intact dura to a depth of 1–2.5 mm below the SC surface, which was identified in each session by recording of visually evoked neural activity. The collicular location of stimulation/recording sites was confirmed in all animals by electrolytic lesions in terminal recording tracks and subsequent histological reconstruction.

Microstimulation

Stimulation experiments with microelectrodes were performed in seven colliculi of four awake cats. Because our animals were head-fixed and cats execute larger saccades by combined eye and head movements, we restricted our analysis to the anterior part of the SC where small eye movements are represented (Guitton et al. 1980; Roucoux et al. 1980). Our animals were not required to fixate but, as confirmed by measurements of eye position with the search coil technique, had a pronounced tendency to look straight ahead. Stimulation trains consisted of 5–10 pulse triplets (unipolar cathodal stimulation, pulse duration: 0.3 ms, pulse interval: 1.2 ms) delivered at a rate of 50 Hz. This rhythmic stimulation pattern was chosen to mimic the gamma-oscillations evoked with visual stimuli in the cat SC (Brecht et al. 2001). Relatively long stimulation trains (100–200 ms) were applied to achieve saturation of both large and small evoked saccade amplitudes. The current strength was carefully adjusted for a balanced efficiency of all stimulation sites and equaled two to three times threshold. Current strength was between 15 and 220 μA, whereby the majority of stimulation sites were stimulated with <100 μA. Different timing patterns were applied 20 or 50 times interleaved in a random sequence.

RESULTS

In a first series of experiments, we investigated the effects of varying the synchronicity among stimulus trains applied through two microelectrodes positioned in the deep layers of one hemisphere of the SC (Figs. 1–5). Figure 1 schematically introduces vector averaging and vector summation, two hypothetical ways in that saccade vectors from two stimulation sites might interact. Figure 2, *A* and *B*, illustrates the eye movements evoked from two different sites with 140-ms-long train stimuli consisting of pulse triplets (pulse duration: 0.3 ms, intervals: 1.2 ms) repeated at a frequency of 50 Hz. Synchronous stimulation at both sites (Fig. 2*C*) resulted in eye movements the vector of which corresponded approximately to the average of the vectors of the saccades evoked by stimulation of each site alone. In contrast, when the stimulus trains were made asynchronous by introducing stimulus onset asynchronies (SOAs) of 10 or 5 ms between the triplets of the two trains, the vectors of the resulting saccades were close to the sum of the vectors of the individual saccades (Fig. 2, *F–I*). The saccades had the same direction as those evoked by the synchronous pulse trains, but their amplitude was nearly doubled. For both synchronous and asynchronous stimulation conditions, we generally observed relatively straight saccades and no large-scale changes of saccade direction in midflight. Saccades evoked by synchronous and asynchronous stimulation both terminated before the end of the stimulation train (Fig. 2*A*), suggesting that both stimulation regimes saturated saccade amplitudes and that different saccade amplitudes are not due to truncation of saccades but to changes in synchrony. For SOAs $\leq$2.5 ms, the saccades resembled closely those expected from vector averaging, suggesting that the switch between the different motor responses occurs around SOAs of 3–5 ms (Fig. 2, *D* and *E*). The sequence in which temporally offset trains were presented had no effect on the saccades (compare Fig. 2, *H* and *I*). Both

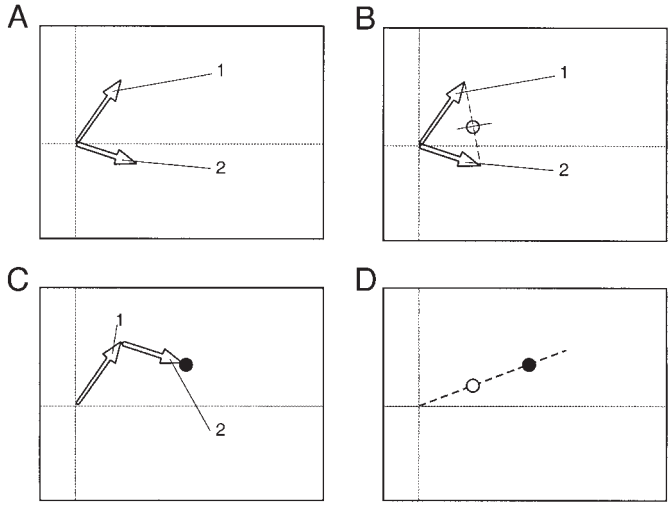

FIG. 1. Computation of vector sum and vector average. *A*: single vectors (the same ones as in the experiment shown in Fig. 2). *B*: computation of the vector average (○). *C*: computation of the vector sum (●). *D*: note that vectors corresponding to average and sum share the same direction.

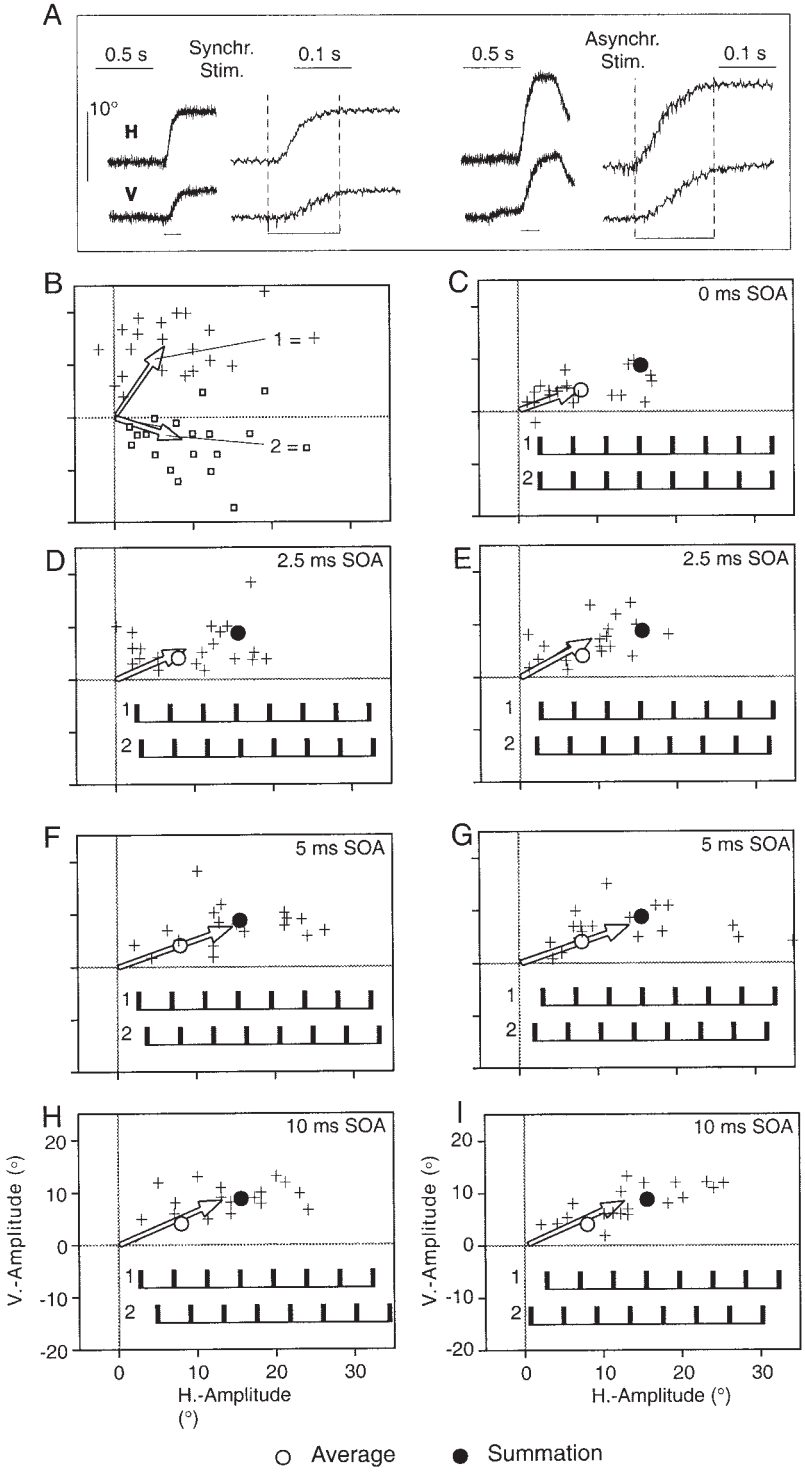

FIG. 2. Effects of varying stimulus synchrony on the vectors of saccades evoked from 2 sites where stimulation which led to saccades with different directions. Sites 1 and 2 were stimulated with currents of 60 and 70 μA, respectively. *A*: horizontal and vertical electrooculographic (EOG) traces of saccades evoked by synchronous stimulation at low (*left*) and high (*right*) temporal resolution and asynchronous stimulation at low (*left*) and high (*right*) temporal resolution. The saccades selected for illustration have vectors close to the mean vectors obtained in the 2 conditions. Part of the stimulation artifact was clipped. *B*: saccade vectors evoked by single site stimulation. crosses, saccades from site 1; squares, saccades from site 2; thick arrow: respective mean vectors. *C–I*: saccade vectors obtained with dual-site stimulation and different timing protocols. Crosses, end points of individual saccades; thick arrow, mean vector. Dots, calculated end points of the vectors that would have resulted from summation (black dot) or averaging (white dot) of the saccades evoked from the 2 sites by single site stimulation. The temporal pattern of the stimuli is schematically indicated below each set of saccades, the vertical lines corresponding to a pulse triplet. *C*: saccade vectors evoked by synchronous stimulation. *D* and *E* saccade vectors evoked by asynchronous stimulation with 2.5 ms stimulus onset asynchrony (SOA). Site 1 leads in *D* and lags in *E*. *F* and *G* saccade vectors evoked by asynchronous stimulation with 5 ms SOA. Site 1 leads in *F* and lags in *G*. *H* and *I*: saccade vectors evoked by asynchronous antiphasic stimulation (10 ms SOA). Note that site 1 leads in *H*, whereas it lags in *I*. Note that the average saccade vectors in *C–I* are very similar in direction. The amplitude differences between saccades evoked by synchronous (in *C*) and asynchronous stimulation (in *H*) were significant at the level of $P < 0.0001$ (paired *t*-test).

for single (Fig. 2*B*) and multi-site (Fig. 2, *C–I*) stimulation, we observed a large scatter in end points of saccades.

Figure 3 shows an example in which the two individual saccades were of very different amplitudes (Fig. 3*A*). Synchronous stimulation led again to saccades close to those predicted by vector averaging (Fig. 3*B*). In contrast, asynchronous microstimulation evoked again much larger saccades close to those expected from vector summation (Fig. 3*C*). With asynchronous stimulation, coactivation of the site representing the small saccade contributed only little, the resulting saccades resembling those evoked by stimulation of the site representing the large saccade. In contrast, with synchronous stimulation, coactivation of the site representing the small saccade led to a drastic reduction of saccade amplitude. Thus the extent to which coactivation of a second site affected saccades evoked from the first depended not only on the specific vector configuration but also and to a critical extent on the degree of synchronicity of the stimuli.

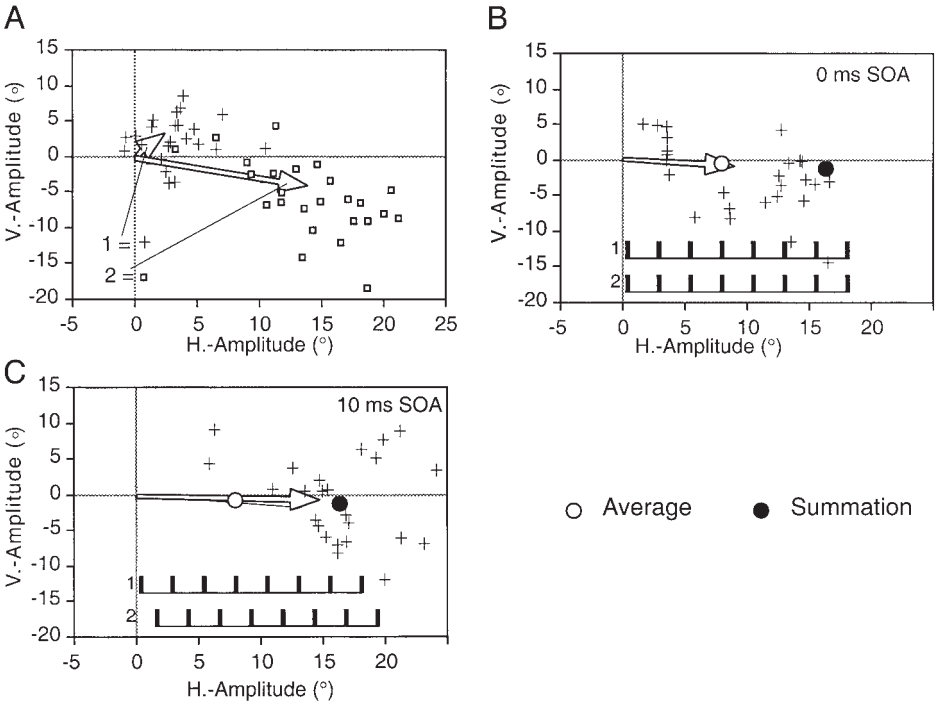

FIG. 3. Effects of stimulus timing on the vectors of saccades evoked with dual stimulation of sites leading to saccades with very different amplitudes. Conventions as in Fig. 1. For the sake of clarity, only every 2nd evoked saccade is shown. Sites 1 and 2 were stimulated with currents of 80 and 50 μA, respectively. *A*: saccades evoked by single site stimulation. +, site 1; □, site 2. *B*: vectors of saccades evoked by synchronous stimulation. *C*: saccades evoked by asynchronous antiphasic stimulation (10 ms SOA). Amplitudes of saccades evoked by stimulating site 2 alone did not differ significantly from those of saccades evoked by stimulating the two sites asynchronously. For all other stimulation conditions, saccade amplitudes differed significantly at the level of $P < 0.0001$ (paired *t*-test).

In the experiments described so far, we had measured eye position with EOG electrodes that prevented precise determination of absolute eye position at stimulation onset because of possible DC drifts. As initial eye position affects saccade amplitude in head-fixed cats (Guitton et al. 1980; Roucoux et al. 1980), variations in initial position could have increased the variance of our data. Therefore we performed experiments with dual site microstimulation ($n = 5$) in which we quantified eye

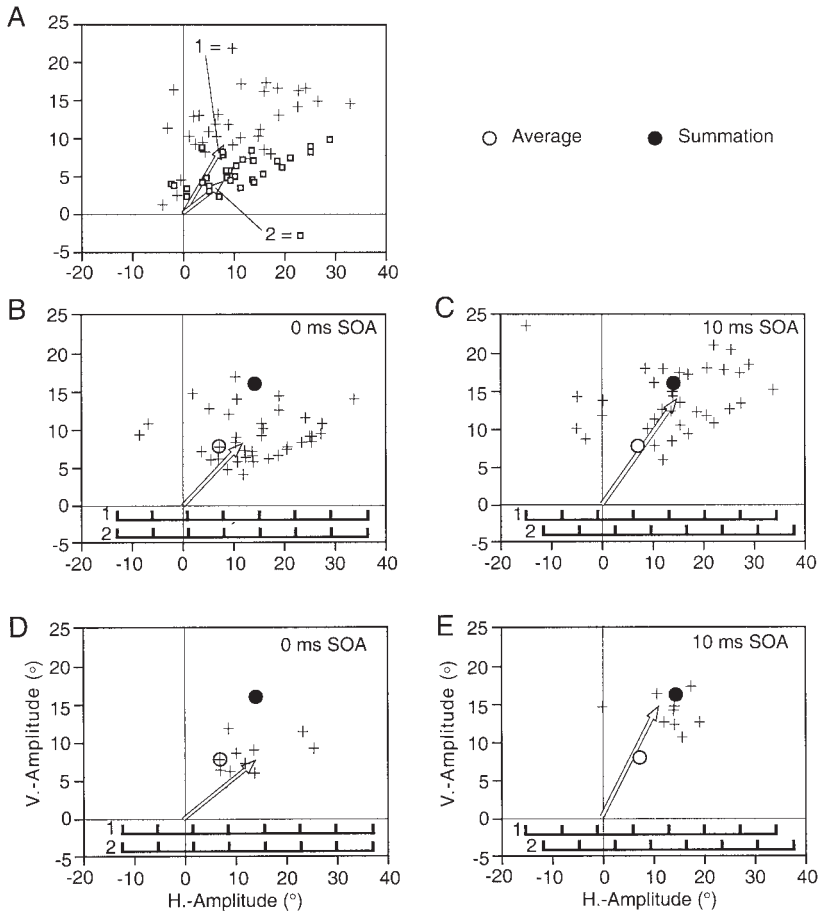

FIG. 4. Effects of stimulus timing and initial eye position on vectors of saccades measured with the search-coil technique. Conventions as in Fig. 1. Sites 1 and 2 were stimulated with currents of 40 and 60 μA, respectively. *A*: saccades evoked by single-site stimulation. +, site 1; □, site 2. *B*: vectors of 40 saccades evoked by synchronous stimulation. *C*: vectors of 40 saccades evoked by asynchronous antiphasic stimulation (10 ms SOA). The amplitude differences between saccades evoked by synchronous (*B*) and asynchronous stimulation (*C*) were significant at the level of $P < 0.001$ (paired *t*-test). *D* and *E*: vectors of 10 saccades evoked by synchronous (*D*) and asynchronous (*E*) stimulation, respectively, that were evoked from similar initial eye positions. Those 10 saccades were selected that were initiated from eye positions that were closest to the animal's average direction of gaze in nonstimulation epochs, i.e., close to the eyes' preferred resting position. The amplitude differences between saccades evoked by synchronous (*D*) and asynchronous stimulation (*E*) were significant at the level of $P < 0.001$ (paired *t*-test).

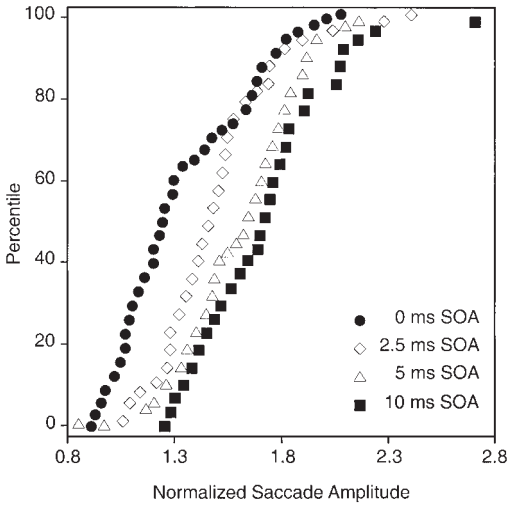

FIG. 5. Cumulative distribution of normalized (see text) saccade amplitudes from 34 dual site stimulation experiments. For clarity of presentation, half of the data points in the asynchronous stimulation conditions were omitted. For each experiment, saccade amplitudes were normalized by dividing them by the amplitude of the predicted vector average. Differences between the various stimulation conditions (0 ms SOA: mean = 1.32, median = 1.24; 2.5 ms SOA: mean = 1.48, median = 1.45; 5 ms SOA: mean = 1.58, median = 1.59; 10 ms SOA: mean = 1.70, median = 1.71) were all significant at a level of $P < 0.0012$ or lower (*t*-test, unequal sample sizes 34/68).

movements with the search-coil technique (Robinson 1963). The result of one of these experiments is shown in Fig. 4. As in the previous experiment, synchronous stimulation at both sites (Fig. 4*B*) resulted in eye movements the vector of which was close to the average of the vectors resulting from single site stimulation. Asynchronous stimulation with 10 ms SOA led to saccades whose vectors were close to the sum of the individual vectors (Fig. 4*C*). Figure 4, *D* and *E*, shows a selection of 10 saccades, which were evoked from similar initial eye positions. The average vectors of this selected subgroup of saccades were very similar to those of the whole sample both for synchronous and asynchronous stimuli, but the variance of individual saccades was markedly reduced (compare Fig. 4, *B* and *C*, with *D* and *E*). Thus the larger variability of the data obtained with EOG recordings is most likely due to greater variability in initial eye position. However, because stimulation trials were randomly interleaved and our evaluation of saccade vectors is based on averages, this variability cancels out and does not invalidate our conclusions.

The results of 34 experiments with dual site stimulation are summarized by cumulative plots of saccade amplitudes induced by synchronous and asynchronous stimulation, respectively (Fig. 5). Saccade amplitudes are expressed as ratios of measured values over values expected from vector averaging. Thus ratios of 1 and 2 correspond to vector averaging and summation, respectively. The average amplitude ratio of saccades evoked by synchronous stimulation (SOA: 0 ms) was 1.3 and that of saccades evoked by asynchronous stimuli (SOA: 10.0 ms) was 1.7. The saccade amplitudes differed significantly between all stimulation conditions (SOA: 0, 2.5, 5, and 10.0 ms), but more than two-thirds of the amplitude increase occurred for the switch from 0 to 5 ms SOA. No differences were noted in the dynamics of saccades evoked at various SOAs, but saccades evoked by synchronous stimuli exhibited a smaller variance both with respect to amplitude and direction.

With two stimulation sites, differences between vector averaging and summation are solely reflected by amplitude changes but not by changes in saccade direction (Fig. 1). Therefore we extended the experiment to three stimulation sites, where a vector averaging/summation scenario predicts saccades of different directions (Fig. 6). Figure 7*A* illustrates the mean vectors of the saccades evoked from the three sites in one of the experiments with triple-site stimulation. Saccades were smallest when all three sites were stimulated synchronously (Fig. 7*B*) and largest when stimuli at all three sites were asynchronous (Fig. 7*C*) and the respective saccades were of different directions. This agrees qualitatively with a switch from vector averaging to vector summation. Similarly, when two sites were activated synchronously and the third asynchronously in different constellations, both saccade amplitudes and directions changed (Fig. 7, *D–F*). In other experiments with triple-site stimulation, we made similar observations. In particular, we observed in most of them significant direction differences between saccades as they were predicted by an averaging/summation scenario outlined in Fig. 6 (data not shown, $n = 10$).

There was an important quantitative difference between the results of the two- and the triple-site stimulation experiments. In all triple-site experiments, the largest saccades were evoked when all sites were stimulated asynchronously but evoked saccade vectors fell substantially short of the vector predicted by summation. Thus the relative difference between synchronous and asynchronous stimulation was smaller than predicted by a vector averaging/summation scenario.

In another series of experiments, we studied intercollicular interactions by inserting the electrodes into the left and right colliculi, respectively, and applying the same stimulation patterns as in the first experiment. In contrast to intracollicular stimulation, there was only little or no evidence of vector summation for asynchronous stimulation of vertical saccades. Figure 8 shows the case with the strongest vector summation effect. It can be seen that even in this case saccades evoked by asynchronous stimulation fall short of the vector summation prediction (Fig. 8*C*). Overall there was only a weak systematic dependence of saccade vectors on SOA (Fig. 9). Only in 4 of 16 experiments we observed significant differences between saccades evoked by synchronous and asynchronous microstimulation.

DISCUSSION

The effects observed with intracollicular multisite stimulation indicate clearly that small changes (<5 ms) in the relative timing of otherwise unchanged, temporally overlapping stimulus trains lead to remarkably different saccades. Because the saccades evoked with asynchronous stimuli were the same irrespective of which site received the first pulse, the critical variable determining the saccade vectors must have been the degree of synchronicity of the applied stimulus trains. Changes in synchronicity could have affected saccade vectors through two rather different mechanisms. One possibility is that the switch from synchronous to asynchronous stimulation changed the size and the spatial distribution of the directly activated cell populations and/or the amplitude of their responses, leading to a different composition of the rate coded population vector. Another possibility is that the activated cell populations re-

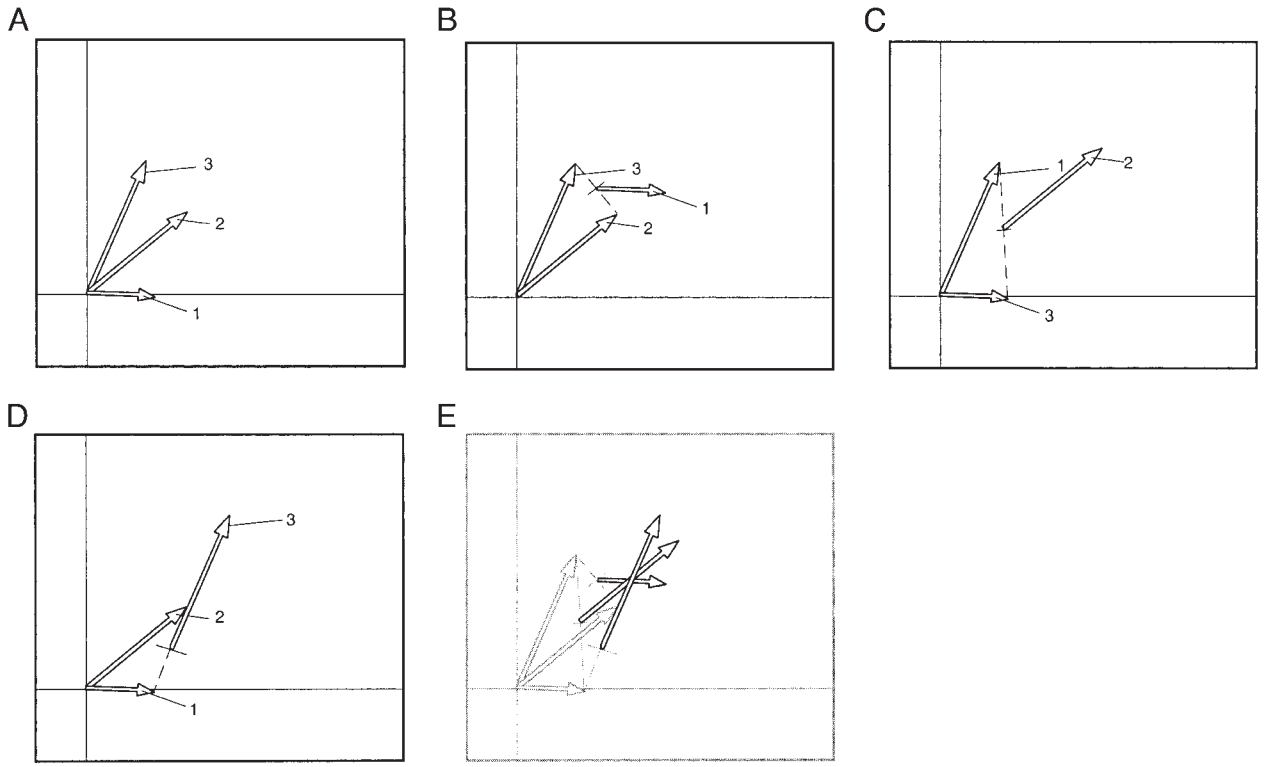

FIG. 6. With 3 vectors, vector averaging and summation can lead to different directions. *A*: single vectors (the same ones as in the experiment shown in Fig. 6). *B–D*: averaging of two vectors and adding a 3rd one. *E*: superposition of the vector configurations shown *B–D*. Note the difference in direction.

mained the same but the neuronal network responsible for the conversion of collicular population responses into saccade vectors is phase sensitive, treating vectors defined by synchronously and asynchronously discharging cells in different ways. The following arguments render the first possibility unlikely. Differences in the composition of the activated cell populations could have resulted from variable recruitment of cells located between the respective stimulation sites, synchronous stimulation leading to more effective summation of currents than asynchronous stimulation. We consider this unlikely because the observed effects were independent of factors influencing recruitment such as electrode distance or strength and polarity of stimulation currents. Timing-effects were similar for a wide range of electrode separations (0.75–3.25 mm) and for a wide range of absolute as well as relative stimulation intensities (15–220 μA, ranging from threshold to high supra-threshold levels). Furthermore, results remained unchanged when stimulus polarity was reversed at one of the electrodes and current strength adjusted to produce control saccades of the same amplitude as before reversal ($n = 3$, data not shown).

Changes in the discharge frequency of otherwise unchanged population responses could have resulted if the cell populations activated by the two electrodes overlap. In this case, asynchronous stimulation would have doubled the discharge rate of cells influenced by the fields of both electrodes. This scenario is unlikely for the following reasons: First, also in this case, effects should be influenced by electrode separation and stimulation strength as these parameters determine the potential overlap of populations. Second, frequency doubling should have increased the saliency of the responses mediated by the population of neurons driven from both electrodes. The population vector of these intermediate neurons should be the same as the average of the vectors of the two stimulation sites. Hence, frequency doubling should have led to saccades resembling those expected from vector averaging. This, however, was never the case. Saccades evoked by asynchronous stimulation were never smaller than those evoked from the site producing the larger of the two saccades, whereas such reductions were frequent with synchronous stimulation. Frequency doubling could have produced larger saccades only if the stimulated populations overlapped and if the frequency of the individual trains would have been too low and their duration too short to saturate the saccade-generating mechanism. In this case, the saccades would have been smaller than predicted from the site of stimulation, and frequency doubling could have increased the amplitudes of these abortive saccades (Stanford et al. 1996). We consider this possibility as unlikely because the duration of our trains was long and stimulation intensity adjusted to saturate saccade amplitudes at the respective stimulation sites. These controls let it appear unlikely that the different effects of synchronous and asynchronous stimulation are due to recruitment of additional cells or frequency doubling in cells activated from more than one stimulation site. Therefore we propose as the most likely interpretation of our results that the mechanism that translates collicular population responses into saccade vectors does not rely solely on the spatial composition and average discharge rate of the activated collicular cells (Moschovakis 1997; Sparks 1986) but, in addition, on the precise temporal relations between the discharges of the activated cell populations.

Asynchronous stimulation appears to bias saccade vectors toward summation, whereas synchronous stimulation biases

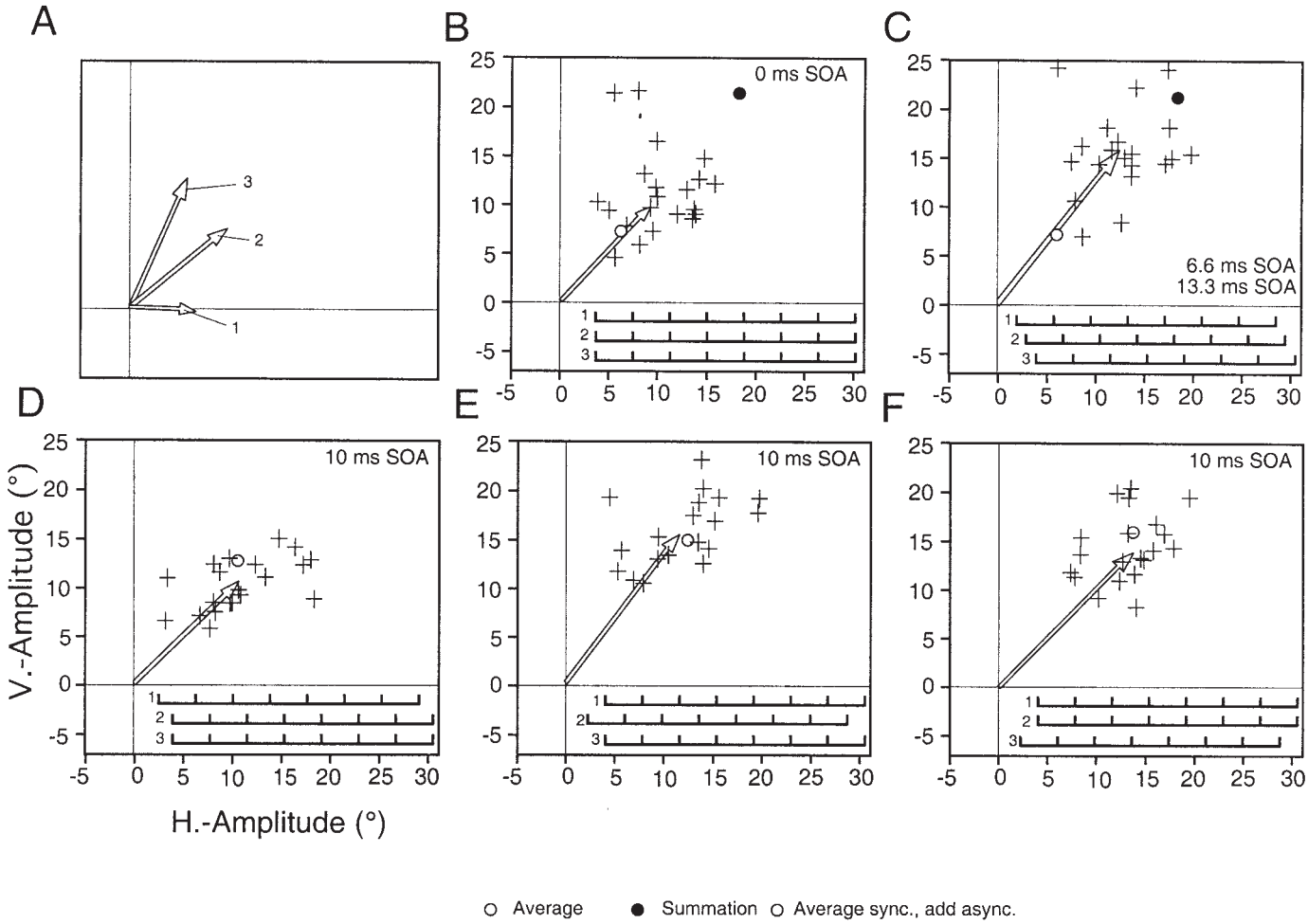

FIG. 7. Effects of stimulus timing on the vectors of saccades evoked with triple-site stimulation. Conventions as in Fig. 2. Sites 1–3 were stimulated with currents of 55, 90, and 40 μA, respectively. *A*: vectors of saccades evoked by single site stimulation. Only mean vectors are shown. *B* and *C*: vectors of saccades evoked by synchronous (*B*) and asynchronous (*C*) stimulation of all 3 sites (with 6.6 and 3.3 ms SOA, respectively). *D–F*: saccades evoked by stimulating 2 sites synchronously and the 3rd site asynchronously with a time lead of 10 ms. The various combinations of synchronously and asynchronously stimulated sites are indicated by the stimulation patterns in each panel. The direction differences between saccades evoked in conditions *D–F* were consistent with a vector averaging at synchronously stimulated sites and a vector summation of asynchronously stimulated sites; the direction differences were significant at the level of $P < 0.001$ or lower (paired *t*-test). Note that the mean saccade vectors in *D–F* have different directions. Amplitude differences between saccades evoked with synchronous (*B*) and asynchronous (*C*) stimulation are significant at the level of $P < 0.01$ (paired *t*-test).

saccade vectors toward averaging. It must be noted, however, that saccades evoked by asynchronous stimuli had on average smaller amplitudes than those expected from exact vector summation and those evoked by synchronous stimuli were larger than expected from simple vector averaging.

The stimulation parameters we have used were very different from those of previous microstimulation experiments, and it is therefore difficult to directly compare our results to those studies. Compared with other microstimulation studies (Pare et al. 1994), the saccades we observed were relatively slow and exhibited a relatively large scatter. These differences probably reflect our specific stimulation parameters, in particular the low repetition rate of our pulse triples. Similarly, we used slightly higher levels of stimulation currents than previous studies in some of our experiments, again suggesting that our pulse triplet stimulation trains were driving saccades less efficiently than the usually applied high-frequency pulse trains. The parameters of stimulation used in our study are quite different from the burst discharge of saccade-related collicular activity associated with a simple saccade to a single flashed visual target in a trained cat. However, the temporal fine structure of collicular activity under conditions where multiple conflicting targets are present has not been studied, and it is therefore difficult to judge how natural our stimulation paradigm actually is. It is important to note that the few studies that dealt with the temporal fine structure of collicular responses to more complex stimuli observed a temporal, often oscillatory, patterning and correlations among discharges that were stronger than expected from simple locking of collicular activity to sensory stimuli or saccades (Brecht et al. 2001; Istvan and Munoz 1998).

Cortical and collicular neurons tend to synchronize their discharges when responding to contours of the same object but not when driven by contours of different objects (Brecht et al. 1999, 2001; Castelo-Branco et al. 2000; Engel et al. 1991; Freiwald et al. 1995; Gray et al. 1989; Kreiter and Singer 1996). Evaluating the synchrony of collicular discharges could

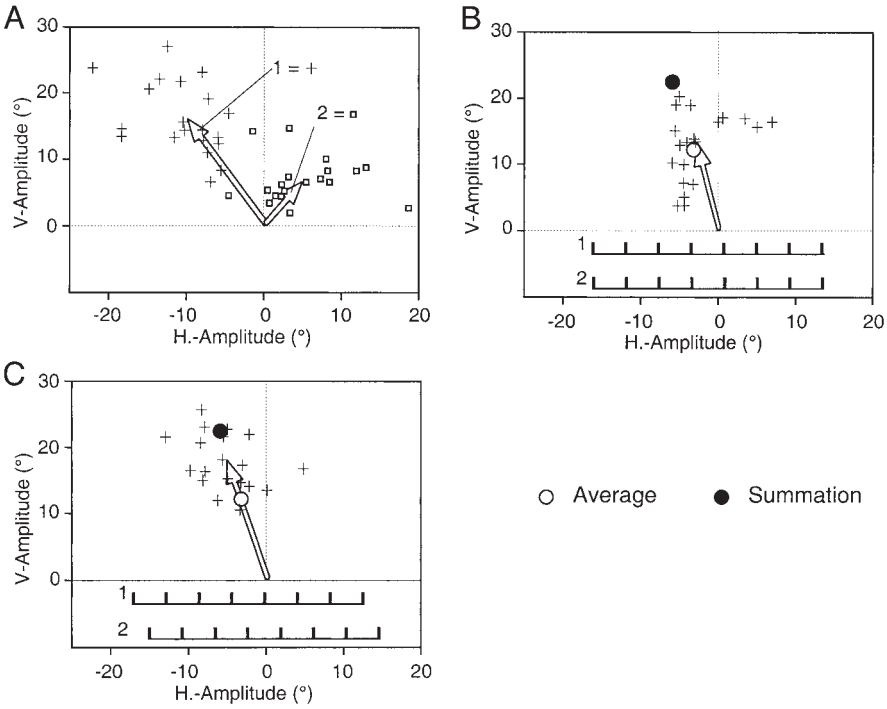

FIG. 8. Effects of paired time-varied intercollicular microstimulation on saccade vectors. All conventions as in Fig. 2. *A*: saccade vectors evoked by stimulating the 2 sites individually. *B*: saccade vectors evoked by synchronous stimulation. *C*: saccade vectors evoked by asynchronous antiphasic stimulation (10 ms SOA). Saccades in *B* and *C* were of very similar directions. The amplitude differences between saccades evoked by synchronous (in *B*) and asynchronous stimulation (in *C*) were small, but in this case significant, $P < 0.0001$ (paired *t*-test).

thus serve to distinguish whether multifocal population responses result from a single object or from different objects. Synchronized responses should direct saccades to the center of contours belonging to the same object. It is less clear, however, what one should expect for asynchronously active populations. Most likely this should lead to competition and to saccades targeted toward only one of the population foci. Our result that synchronized multifocal stimulation led to vector averaging agrees with the first prediction. However, asynchronous stimulation produced saccades similar to those expected from vector summation rather than competition. One reason could be the artificial activation conditions. Direct electrical stimulation of collicular neurons close to the output level could have overridden the complex and attention-dependent mechanisms that normally contribute to competition and target selection (Glimcher and Sparks 1992; Goldberg and Wurtz 1972). In particular, one must consider the possibility that the cat SC is slaved by cortical target-selection mechanisms. Thus our results motivate investigation of the effects of synchronous and asynchronous stimulation at earlier stages of the oculomotor pathway. At present it is unclear why asynchronous stimulation should have caused vector summation because it does not take the eyes to a target position. One possibility is that the simultaneous imposition of different saccade commands that would normally compete and be mutually exclusive led to abnormal summation of the different vectors. A paradigm were such summation has been observed are double-step saccade experiments (Becker and Jürgens 1979). In such experiments, two saccade targets are presented briefly and sequentially. If the first target is presented for a sufficiently long time, two spatially precise sequential saccades are executed; if the first target is presented very briefly, a single spatially precise saccade will be performed only to the second target. At intermediate presentation times of the first target, subjects often perform a saccade to the second target; surprisingly, this saccade is not biased toward the first target but is excessively large as if the two saccade vectors are added rather than averaged. It is likely that the asynchronous presentation of targets induces temporally overlapping but nonsychronized activity at two collicular sites and hence a condition that resembles our asynchronous stimulation.

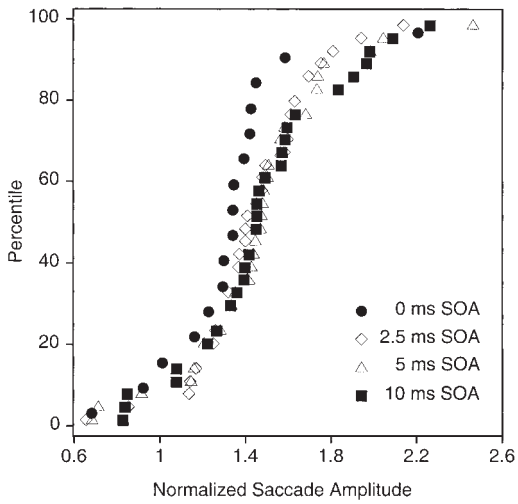

FIG. 9. Cumulative distribution of normalized saccade amplitudes evoked in 16 intercollicular experiments. Saccade amplitudes evoked with small temporal offsets were only slightly smaller than asynchronously evoked saccades. The differences between synchronous stimulation and the 2.5, 5, 10 ms SOA conditions were significant at a level of $P < 0.035$ (paired *t*-test).

A different perspective on our microstimulation results is provided by the modeling efforts of Groh (2001). The summation-saturation-model accurately reproduces not only single-site stimulation data (Stanford et al. 1996) but also predicts that weak stimulation at two sites should lead to vector summation, whereas strong stimulation at two sites should result in vector averaging. Assuming timing dependent (synchronous/asynchronous) changes in the efficacies of stimuli, this model explains the general trend of our data including the differences

between two- and triple-site stimulation. It seems plausible that the amplitude of the largest saccades evoked by triple-site stimulation saturated, reducing the difference between differently timed stimulation conditions in line with the predictions of the summation-saturation-model of Groh (2001).

Incorporating the precise timing of discharges as additional variable in the model might yield even better fits and perhaps account also for the differences between intra- and intercollicular stimulation. Another, nonexclusive explanation of our data is that the collicular activation patterns (as they are imposed by synchronous and asynchronous microstimulation) interact in turn in a time critical fashion with the assumed resettable feedback integrator for saccade signals (Kustov and Robinson 1995; Nichols and Sparks 1995). Such interactions between microstimulation pulses and the assumed integrator can have complex dynamics (Breznen et al. 1997; Gnadt et al. 2001). Although there are detailed models for such interactions with single stimulation sites (Breznen and Gnadt 1997), it is not yet clear how changes in population synchrony would affect the output of such a mechanisms.

Irrespective of the mechanism that translated the electrically activated population responses into saccades our data warrant the conclusion that small variations in the synchronicity of population responses lead to large changes in saccade vectors. Our data provide evidence that neuronal networks in the CNS can be exquisitely sensitive to the relative timing of individual discharges, suggesting that precise timing relations are exploited to encode information.

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