Responses to Noisy Periodic Stimuli Reveal Properties of a Neural Predictor

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Joiner, Wilsaan M. and Mark Shelhamer. Responses to noisy periodic stimuli reveal properties of a neural predictor. J Neurophysiol 96: 2121–2126, 2006. First published June 21, 2006; doi:10.1152/jn.00490.2006. In programming motor acts, the brain must consider both internal and external noise sources: inherent variation in sensory estimates and changes within the environment. An interesting question in motor control is how reliable responses can be programmed in the face of noise and how these two noise sources interact. We study this by investigating the generation of sequences of predictive saccades to visual targets. First, eight normal subjects tracked targets that alternated at a pacing frequency (0.9 Hz) that promoted predictive behavior, for 300 trials. When tracking this perfectly periodic stimulus, there was variability in the timing of the saccades (intersaccade intervals) that was distributed around the interval of the stimulus (556 ms). We used this inherent variability to set the timing of subsequent stimuli; subjects completed three additional sessions in which the variance of the stimulus timing (the interstimulus intervals) had the same (1.0 SD), less (0.5 SD), or more (2.0 SD) variability than the subject displayed when tracking the perfectly periodic stimulus. Despite changes in stimulus timing variability, variance of the response timing (intersaccade intervals) was equal to the variance of the stimulus plus “inherent variance” (response variance when tracking a perfectly periodic stimulus). Examining the correlations between saccade latency and interstimulus interval, this relationship is interpreted as a tradeoff between reliance on previous saccade performance (intratrial correlations) and reliance on the current stimulus.

I N T R O D U C T I O N

There are two sources of noise when programming a motor act: inherent variability caused by sensory noise (Osborne et al. 2005) and stimulus/environment noise. An interesting problem in motor control is how reliable responses can be programmed in the face of these noise sources (Baddeley et al. 2003; Davidson and Wolpert 2003; Georgopoulos et al. 1981; Körding and Wolpert 2004; Scheidt et al. 2001; Trommershäuser et al. 2005; Witney et al. 2001). This question has been addressed by adding noise to sensory feedback when performing simple motor tasks (Baddeley et al. 2003; Körding and Wolpert 2004; Trommershäuser et al. 2005). The resulting behavior has been generally modeled as a statistically optimal combination of past and present information (Baddeley et al. 2003; Körding and Wolpert 2004; Trommershäuser et al. 2005).

In other tasks, where instead of sensory feedback stimulus variability was systematically altered (adding increasing levels of noise to a sinusoidal pursuit stimulus, Michael and Jones 1967), behavior changed with increasing variability. As stimulus variability increased, prediction of upcoming stimuli was impaired and responses became more reactive and less anticipatory.

In a recent study of anticipatory smooth pursuit eye movements (Badler and Heinen 2006), a fixation target appeared, and a pursuit target started moving after a fixed interval (500–1,000 ms). In blocks of identical trials, the fixation target was extinguished a second fixed interval (0–450 ms) before the pursuit target moved. (The interval values were selected from within their respective ranges, but fixed within a single block of trials, to generate repeatable stimuli.) Thus the timing of pursuit onset could be based on prediction (of the interval between fixation target appearance and pursuit target motion, fixed in a given session) or on the more immediate cue of fixation-target offset. When the interval between fixation target appearance and pursuit target motion was long, and thus the neural estimates of this interval less reliable, pursuit timing was more dependent on the offset time of the fixation target. This shows that the timing of tracking of repetitive motion is adjusted based on the relative reliability of target timing. We take a different approach to this general issue, by directly modifying the timing of a repetitive target to modulate its reliability, with similar results.

In this report we are interested in the process used by a sensorimotor system to adjust its reliance on previous timing performance as the reliability of the stimulus changes. We address this in the context of sequences of predictive saccadic eye movements to periodic targets with different amounts of timing variability. In predictive tracking, feedback of past performance is used to form an internal estimate of target timing and hence to program future saccades in anticipation of target motion and with the proper timing to match that of a periodic stimulus; this feedback is manifest as correlations between the latencies of consecutive saccades (Shelhamer 2005; Shelhamer and Joiner 2003). We examined how this reliance on previous performance is adjusted when the internal timing estimate (neural clock) becomes less useful, by increasing the variability of stimulus timing.

M E T H O D S

The eye movements of eight subjects were recorded while they performed four main saccade tasks. Informed consent, according to the local institutional review board, was obtained from each participant. Data were acquired on a PC-compatible Pentium 166-MHz
computer running real-time experiment control software developed in-house. Horizontal movements of the eyes were recorded with a Series 1000 Binocular Infrared Recording System (Microguide), sampled at 1,000 Hz. The system was calibrated before data acquisition by having subjects fixate targets at known locations. Subjects were seated in a stationary chair, and the head was fixed with a chin rest.

Previous experiments (Ross and Ross 1987; Shelhamer and Joiner 2003; Stark et al. 1962; Zambarbieri et al. 1987) have shown that predictive saccades are promoted at pacing frequencies between 0.5 and 1.0 Hz. We based our selection of 0.9-Hz pacing on these previous results.

The eye movements of eight subjects were recorded while they tracked alternating visual targets (±15° horizontal). First, they tracked the targets at 0.9 Hz (interstimulus interval, \(ISI = 556 \text{ ms}\)) for 300 trials. The distribution of intersaccade intervals (\(I\)) for this condition (SD-0.0) was determined and fit with a Gaussian distribution. [The quality of these Gaussian fits was assessed using the MATLAB function NORMPLOT, which is a qualitative graphical means of displaying a cumulative distribution with the ordinate scaled so that Gaussian data appear as a straight line. Data from the subsequent test sessions (SD-0.5, -1.0, -2.0) were not tested for normality. This is because our fitting of a normal distribution was simply a means to measure and manipulate stimulus variability, and the final results hold whether or not the response distributions are in fact normal. This also justifies our use of a qualitative goodness-of-fit test. The mathematical analysis to follow makes no assumptions about normality.] Subjects tracked targets (300 trials) that alternated with intervals drawn randomly (uncorrelated) from the individual fitted distribution (SD-1.0) for that subject and from distributions with 0.5 and 2.0 times the original standard deviation (SD-0.5, SD-2.0). (Stimulus variability is thus based on each subject’s “inherent variability,” so that they experienced the same level of stimulus variability relative to their inherent variability.) Predictive saccades were generated by all subjects in each of these conditions, as evidenced by the latencies of their saccades (SD-0.0: \(-43.6 ± 77.3 \text{ ms}\), SD-0.5: \(-56.3 ± 73.3 \text{ ms}\), SD-1.0: \(-30.9 ± 91.3 \text{ ms}\), SD-2.0: \(-3.2 ± 119.7 \text{ ms}\)), except for two cases as noted below and in Fig. 2A.

Analysis of eye-tracking data was done off-line. First, eye velocity was calculated using a four-point digital differentiator based on a least-squares derivative algorithm (Savitzky and Golay 1964). This is an efficient iterative method of fitting a third-order polynomial to each data point and the preceding and following two values, then finding the derivative of the fitted polynomial, and introduces less noise than conventional differentiators. Saccade onset was found using a velocity threshold (>60°/s). Saccade latency was determined by comparing the onsets of the primary saccade and the target in each trial; intersaccade interval is the time between primary saccades. When subjects missed a target jump (especially during the largest variability condition; see Fig. 1, middle column, bottom row), the resulting intersaccade interval was discarded. That is, only intersaccade intervals between saccades assigned to target jumps were included in the analysis.

![Figure 1](http://jn.physiology.org/)

**FIG. 1.** Saccade timing results for subject A. *Left column:* probability distributions (20-ms bins) of interstimulus intervals, with increasing variance from top to bottom row (SD of 0.0, 0.5, 1.0, and 2.0). *Center column:* large panels are samples (10 s each) of eye tracking (gray) and target position (black) for the corresponding interval distributions. Smaller panels show change in interstimulus interval throughout each specific 10-s sample; each plotted point corresponds to a single interstimulus interval from the graph immediately above, and stimulus timing variability is evident as the variation from point to point. *Right column:* corresponding probability distributions of intersaccade intervals, with increasing variance from top to bottom row.
**RESULTS**

Results from one subject for the four stimulus-variability conditions are presented in Fig. 1. In the **left column** are ISI histograms (20-ms bins) with increasing variability from the **top** to **bottom row** (SD-0.0, -0.5, -1.0, -2.0). The larger panels in the **center column** are 10-s samples of eye and target position (gray and black traces, respectively) for each variability condition. The smaller panels track the change in intersaccade interval throughout the 10-s sample. In the **right column** are the corresponding intersaccade interval histograms for each variability condition. The **top panel** in the right column represents the inherent variance for this subject, the distribution of intersaccade intervals at the perfectly periodic condition (SD-0.0). As shown by the interval distributions (right column), intersaccade interval variability increases as interstimulus interval variability increases.

Results for all subjects are summarized in Fig. 2A, which shows for each subject the variance of the intersaccade intervals (e.g., the histograms in the **bottom 3 rows** in the **right column** of Fig. 1) as a function of the sum of stimulus variance (the histograms in the **bottom 3 rows** in the **left column** of Fig. 1), and “inherent variance” (the **top panel** in the **right column** of Fig. 1). A linear regression line (dashed gray line) is shown (slope = 0.97, \( r = 0.89 \)). To a remarkable degree, response variance (ordinate) is the sum of stimulus and inherent variances. This is true even at SD-0.5, where stimulus variance is less than inherent response variance; one might expect the smaller stimulus variance to be overwhelmed by the inherent variance, but they add directly even at this level. (The open circles represent 2 cases in which predictive tracking was not attained; these do not follow the same pattern of variability as the other cases.)

These results suggest that response timing variability when tracking a noisy stimulus is the combination of stimulus timing variability and a constant “inherent timing variance.” Intersaccade intervals \( I \) can be represented in terms of ISI and saccade latency \( L \)

\[
I(i) = ISI(i) - L(i) + L(i + 1)
\]

The variance of the response intervals is

\[
Var[I(i)] = Var[ISI(i)] + Var[L(i)] + Var[L(i + 1)] - 2Cov[ISI(i), L(i)] + 2Cov[ISI(i), L(i) + 1] - 2Cov[L(i), L(i + 1)]
\]

We make use of the following facts. First, the latency series is statistically stationary, at least over the short term, so that its variance does not change appreciably from one trial to the next: \( Var[L(i)] = Var[L(i + 1)] \). Also, we know from probability theory that \( Cov(x, y) = R_{xy}(\tau)\sigma_x\sigma_y \), where \( R_{xy}(\tau) \) is the cross-correlation function. This can be used to express the correlations between the latency series \( L(i) \) and a version of the same series shifted in time by one trial \( L(i + 1) = R_{LL}(1) \), where the index of 1 indicates the relative shift between the two series. Similarly, we can express the correlations between the latency series \( L(i) \) and the intersaccade interval series \( ISI(i) \) with no relative time shift as \( Cov[ISI(i), L(i)] = R_{ISIL}(0) \), and with a relative shift of one trial as \( Cov[ISI(i), L(i + 1)] = R_{ISIL}(1) \). These identities are now used to express the previous equation for \( Var[I(i)] \) in these terms

\[
Var[I(i)] = Var[ISI(i)] + 2[1 - R_{LL}(1)]Var[L(i)] + 2[R_{ISIL}(1) - R_{ISIL}(0)]\sigma_x\sigma_L
\]

Because our results indicate that intersaccade interval variance is the sum of ISI variance and a constant inherent variability, the expression in braces must be constant, for a given subject, across stimulus conditions (and also, incidentally, equal to that subject’s inherent variability).

The first term in braces is

\[
2[1 - R_{LL}(1)]Var[L(i)]
\]

An increase in stimulus variability leads to an increase in latency variability, \( Var[L(i)] \), and also to a decrease in the correlations between trials \( R_{LL}(1) \) (Fig. 2B). As latency variability increases, there is less reliance on previous trials, which is why \( R_{LL}(1) \) decreases. The net result is that this overall term increases as \( Var[ISI(i)] \) increases.

Thus to maintain the braced expression constant, the second term in braces must decrease as \( Var[ISI(i)] \) increases

\[
2[R_{ISIL}(1) - R_{ISIL}(0)]\sigma_x\sigma_L
\]

Both \( \sigma_{ISI} \) and \( \sigma_L \) increase with \( Var[ISI(i)] \); the first by definition because \( Var[ISI(i)] = \sigma_{ISI}^2 \), and the second because we know from the experimental results that the latency variability \( \sigma_L \) increases with stimulus variability \( Var[ISI(i)] \). Therefore the term in square brackets must decrease, as it does (Fig. 2C). This means that, although the individual values may change, the sum is constant.
their difference must decrease. In fact, $R_{\text{ISI,L}}(1)$ becomes increasingly negative (data not shown), which indicates how strongly the latency of a given trial is related to the previous ISI; that is, how strongly the timing of a saccade is tied to the timing of the stimulus. The overall effect is that, as stimulus variability increases, there is less reliance on previous saccades [reduced $R_{\text{ISI,L}}(1)$] and more reliance on current stimulus timing [increased $R_{\text{ISI,L}}(0)$]. The balance of these two effects is adjusted in a way that keeps their combined effect just equal to the variability that is attained when tracking a periodic stimulus with no variability.

We can further explore the two terms in braces by recalling that, because a sequence is perfectly correlated with itself when there is no relative time shift, $R_{\text{ISI,L}}(0) = 1$

$$[R_{\text{ISI,L}}(0) - R_{\text{ISI,L}}(1)]\sigma_{\text{ISI,L}} = \text{constant}$$

This shows even more clearly a tradeoff between the weighting of previous saccades ($R_{\text{ISI,L}}$) and reliance on incoming stimulus timing ($R_{\text{ISI,L}}(0)$) and that the weights are based on the rate of decrease in correlations.

The results plotted in Fig. 2, B and C, represent both means across subjects (thick lines) and results from individual subjects. Except for one or two small anomalies in each plot, the mean data represent the trends followed by the individual subjects. Data from the two cases in which subjects did not make predictive saccades (Fig. 2A, open circles) are not included in these plots.

A more direct analysis of the intertrial correlations during steady-state tracking, through autocorrelation functions, shows that they decrease more rapidly, in a given subject, as stimulus variability increases. Autocorrelation functions for the series of latency values for one subject are shown in Fig. 3A. As stimulus variability increases, the width of the central peak decreases, which quantifies this decrease in correlation extent. We define a “correlation window” over which the latencies of past saccades are “significantly” correlated; as in our previous work we set the threshold for significant correlation at $R_{\text{ISI,L}} = 0.2$ and determined when the latency autocorrelation $R_{\text{ISI,L}}$ crosses this threshold; this is indicated as the set of horizontal bars in the figure. There is a consistent decrease in the correlation window as stimulus variability increases (expressed in terms of number of trials in the correlation window); $3.1 \pm 2.1$, $2.5 \pm 1.4$, $1.5 \pm 0.6$, and $1.3 \pm 0.4$ for SD-0.0, -0.5, -1.0, and -2.0, respectively. This can be seen clearly in Fig. 3B, where the means and data from individual subjects are plotted. [Small inconsistencies between subjects are caused by individual differences and the fact that autocorrelation functions were estimated on relatively small numbers of trials over which tracking was in steady state (no missed trials).]

In addition, although prevailing behavior remains predictive, there is an increase in the proportion of reactive saccades with increasing stimulus variability: 0.05, 0.06, 0.15, and 0.38. The presence of some reactive saccades during these high-SD sessions actually strengthens our results: the decrease in the correlation window and increased reliance on stimulus timing (with increasing stimulus variability) should make reactive responses relatively more common as prediction deteriorates.

**DISCUSSION**

We examined the behavior of predictive tracking in the face of increasing stimulus uncertainty. This is manifest as a balancing of the weighting of previous experience and incoming sensory information. We found that, as the stimulus becomes less reliable (the variance of its timing increases), there is less reliance on previous trials relative to the current trial—weaker correlations with latencies of past saccades and stronger correlations with the timing of the present stimulus. (By “timing of the present stimulus” we mean the system’s short-term and immediate estimate of target timing based on the most recent interstimulus interval. Because it requires little processing or storage, we attribute to it a high accuracy.) These correlations are adjusted so that, as stimulus timing variability is increased, stimulus variability adds directly to inherent response variability.

It is not obvious that the predictive mechanism would deal with stimulus variability in this way. For example, one might expect to see more rather than less averaging over previous trials as stimulus variability increases, in an attempt to average out the increased noise (performance variability). If the predictive tracking system realizes that performance is poor, it might blindly attempt to gather more information in this way. Although this is not the strategy that is implemented, it is clear that the system recognizes that there is a decrement in performance with increasing stimulus variability and alters its processing as a consequence. Another possible approach to the increasing stimulus variability could have as its goal the minimization of variance in the intersaccade intervals. This could be accom-

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**FIG. 3.** Intertial correlations. A: autocorrelation functions of the series of latency values, for 1 subject, at the 4 stimulus conditions. Horizontal bars at approximately $R_{\text{ISI,L}} = 0.2$ indicate width of autocorrelation functions at that point. This is the threshold for defining a “correlation window” over which previous trials are correlated. Bars are offset vertically for clarity. B: width of correlation window (size of horizontal bars in A) for all subjects (gray lines) and means (black line). Window size, a measure of how far in the past saccade latencies are correlated with each other, decreases with increasing stimulus variability.
plished if the subjects establish an internal clock with a fixed interval (Buhusi and Meck 2005; Joiner and Shelhamer 2006; Treisman 1963) within the first few saccades, and maintain this interval throughout subsequent tracking. This is not a practical approach, because predictions of future timing depend on the monitoring of past trials.

Our results suggest a combination of these two strategies. Subjects establish an internal estimate of stimulus timing based on a window of previous trials (Mátes et al. 1994; Shelhamer 2005). The decrease in intertrial latency correlations, as stimulus variability increases, also reflects a decrease in the time over which past performance is monitored for the programming of future behavior (Buhusi and Meck 2005; Mátes et al. 1994); this is true because intertrial correlations decay gradually and only those correlations above a threshold value are considered to be significant, so that smaller correlations imply a shorter time window (Shelhamer 2005). However, as noted, this strategy does not lead to minimum variance in the intersaccade intervals. This means that any optimization strategy—if it exists in this task—must have as its goal more than just minimization of the variance of saccade timing. If we view inherent variability as a lower bound (because it occurs with 0 stimulus variability), it is likely that simply adding stimulus variability to it represents the best possible performance, given the needs of a predictive mechanism to adjust to changing conditions. While simply minimizing the variance of the saccade latencies or intervals is a form of optimization, this would not yield the best performance in terms of minimizing saccade latency itself, which is what the system ideally should do. To minimize saccade latencies in the presence of a variable stimulus, the system can’t simply minimize variability. (Of course this leaves open the question of the meaning of “best possible performance.” We think of it as minimization of response delay: latency close to zero for all trials. This would seem to be the aspect of performance that would have the greatest impact on the ability to get the eyes on target for the longest possible time.)

Previous studies suggest that the predictive state is a preferred behavior: the brain wants to predictively program future motor responses, if the stimulus allows for it (Joiner and Shelhamer 2006). In trying to predict something that is unpredictable, as in this study, the system does not surrender completely, but rather modifies its weighting of information on past performance versus the current stimulus. It is not clear if it does so in any “optimal” way. In trying to continue its predictive behavior, the system must continue to monitor the performance of previous trials. In so doing, noisy (variable) information is unavoidably incorporated into the predictions. Accurate predictions require a predictable stimulus sequence, and one might wonder if performance in our variable-stimulus conditions could be improved if the system gave up trying to predict at all. Examination of two SD-2.0 cases in which subjects stopped predicting in our experiment suggests an answer. For these cases (Fig. 2A, C), the measured variability is less than the sum of inherent variability and stimulus variability (not equal as in the other cases). Thus in terms of minimizing response variability, abandoning prediction is a good strategy. However, latency suffers in this case (mean latency in the nonpredictive cases of 183.6 ± 148.4 vs. −3.2 ± 119.7 ms for predictive tracking at SD-2.0), suggesting that this is not such a good strategy if the goal is to get the eyes to the target with minimum delay.

Recent timing studies give some insight as to where these types of neural predictive mechanisms may be taking place. For example, the neural structures responsible for motor event timing seem to be predominantly distributed between the cerebellum and the basal ganglia (for review, see Buhusi and Meck 2005; Buonomano and Karmarkar 2002). A recent functional MRI study (Simó et al. 2005) has shown that predictive saccadic tracking significantly activated the basal ganglia (striatum, caudate, putamen, and substantia nigra pars reticulata) rather than reactive tracking. Based on these findings, the changes in intertrial correlations with increasing stimulus timing variance (less dependence on prior trials and more dependence on the stimulus timing) might involve the interplay between neural systems supporting sensory-guided behavior and internally generated predictive behavior (Simó et al. 2005).

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