Responses to Noisy Periodic Stimuli Reveal Properties of a Neural Predictor

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Abstract

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 (inter-saccade intervals) that was distributed around the interval of the stimulus (556 ms). We utilized this inherent variability to set the timing of subsequent stimuli; subjects completed three additional sessions in which the variance of the stimulus timing (the inter-stimulus 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 (inter-saccade 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 inter-stimulus interval, this relationship is interpreted as a tradeoff between reliance on previous saccade performance (inter-trial correlations) and reliance on the current stimulus.
**Introduction**

There are two sources of noise when programming a motor act: inherent variability due to 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 (Georgopoulos et al. 1981; Scheidt et al. 2001; Witney et al. 2001; Baddeley et al. 2003; Davidson and Wolpert 2003; Körding and Wolpert 2004; Trommershauser et al. 2005). This question has been addressed by adding noise to sensory feedback when performing simple motor tasks (Baddeley et al. 2003; Körding and Wolpert 2004; Trommershauser 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; Trommershauser et al. 2005).

In others tasks, where instead of sensory feedback stimulus variability was systematically altered (adding increasing levels of noise to a sinusoidal pursuit stimulus- Michael and Jones 1966; changing the probability of stimulus occurrence - Gordon 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 (500-1000 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, in order 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 utilized 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 and Joiner 2003; Shelhamer 2005). We
examined how this reliance on previous performance is adjusted when the
internal timing estimate (neural clock) become less useful, by increasing the
variability of stimulus timing.
Methods

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 1000 Hz. The system was calibrated prior to 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 (Stark et al. 1962; Ross and Ross 1987; Zambarbieri et al. 1987; Shelhamer and Joiner 2003) have shown that predictive saccades are promoted at pacing frequency ranges 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 deg horizontal). First, they tracked the targets at 0.9 Hz (inter-stimulus interval, ISI=556 ms) for 300 trials. The distribution of inter-saccade 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 then 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 ms, SD-0.5: -56.3±73.3 ms, SD-1.0: -30.9±91.3 ms, SD-2.0: -3.2±119.7 ms), except for two cases as noted below and in Figure 2A.

Analysis of eye-tracking data was done off-line. First, eye velocity was calculated using a four-point digital differentiator based upon a least-squares derivative algorithm (Savizky 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 deg/s). Saccade latency was determined by comparing the onsets of the primary saccade and the target in each trial; intersaccade interval was the time between each primary saccade. When subjects
missed a target jump (especially during the largest variability condition; see for example Figure 1, middle column, bottom row) the resulting inter-saccade interval was discarded. That is, only inter-saccade intervals between saccades assigned to target jumps were included in the analysis.
Results

Results from one subject for the four stimulus-variability conditions are presented in Figure 1. In the left column are ISI histograms (20 ms bins) with increasing variability from 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 (black and gray traces respectively) for each variability condition. The smaller panels track the change in inter-stimulus interval throughout the 10 s sample. In the right column are the corresponding inter-saccade interval histograms for each variability condition. The top panel in the right column represents the inherent variance for this subject, the distribution of inter-saccade intervals at the perfectly periodic condition (SD-0.0). As demonstrated by the interval distributions (right column), inter-saccade interval variability increases as inter-stimulus interval variability increases.

Results for all subjects are summarized in Figure 2A, which shows for each subject the variance of the inter-saccade intervals (for example, the histograms in the bottom three rows in the right column of Figure 1) as a function of the sum of stimulus variance (the histograms in the bottom three rows in the left column of Figure 1) and “inherent variance” (the top panel in the right column of Figure 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 two 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 variance and a constant “inherent timing variance.” Inter-saccade 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 then:

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

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: $Var[L(i)] \approx Var[L(i + 1)]$. 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 $L(i + 1)$:

$$Cov(L(i), L(i + 1)) = R_{LL}(1),$$

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 inter-stimulus interval series $ISI(i)$ with no relative time shift as $Cov(ISI(i), L(i)) = R_{ISI,L}(0)$, and with a relative shift of 1 trial as
\[ \text{Cov}(ISI(i), L(i+1)) = R_{ISI,L}(1). \] These identities are now used to express the previous equation for \( \text{Var}[I(i)] \) in these terms:

\[
\text{Var}[I(i)] = \text{Var}[ISI(i)] + [2[1 - R_{LL}(1)]\text{Var}[L(i)] + 2[R_{ISI,L}(1) - R_{ISI,L}(0)]\sigma_{ISI}\sigma_{L}]\cdot
\]

Since our results indicate that inter-saccade 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:

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

An increase in stimulus variability leads to an increase in latency variability \( \text{Var}[L(i)] \), 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 \( \text{Var}[ISI(i)] \) increases.

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

\[ 2[R_{ISI,L}(1) - R_{ISI,L}(0)]\sigma_{ISI}\sigma_{L}. \]

Both \( \sigma_{ISI} \) and \( \sigma_{L} \) increase with \( \text{Var}[ISI(i)] \); the first by definition since \( \text{Var}[ISI(i)] = \sigma_{ISI}^2 \), and the second since we know from the experimental results that the latency variability \( \sigma_L \) increases with stimulus variability \( \text{Var}[ISI(i)] \).

Therefore, the term in square brackets must decrease, as it does (Fig. 2C). This
means that although the individual values may change, their difference must decrease. In fact, $R_{ISI,L}(1)$ becomes increasingly negative (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 then is that, as stimulus variability increases, there is less reliance on previous saccades (reduced $R_{LL}(1)$) and more reliance on current stimulus timing (increased $R_{ISI,L}(0)$). 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, since a sequence is perfectly correlated with itself when there is no relative time shift, $R_{LL}(0) = 1$:

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

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

The results plotted in Figures 2B and C represent both means across subjects (thick lines) and results from individual subjects. But 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 (open circles in Figure 2A) are not included in these plots.
A more direct analysis of the inter-trial correlations during steady-state tracking, via 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 Figure 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 $R_{LL}=0.2$, and determine when the latency autocorrelation $R_{LL}$ 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): $3.1 \pm 2.1$, $2.5 \pm 1.4$, $1.5 \pm 0.6$, $1.3 \pm 0.4$ (for SD-0.0, 0.5, 1.0, 2.0). This can be seen clearly in Figure 3B, where the means as well as data from individual subjects are plotted. (Small inconsistencies between subjects are due to individual differences as well as 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 have 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 find 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 inter-stimulus interval. Since 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 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 inter-saccade intervals. This could be accomplished if the subjects establish an internal clock with a fixed
interval (Treisman 1963; Buhusi and Meck 2005; Joiner and Shelhamer 2006) within the first few saccades, and maintain this interval throughout subsequent tracking. This is not a practical approach, since 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 (Mätes et al. 1994; Shelhamer 2005). The decrease in inter-trial 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 (Mätes et al. 1994; Buhusi and Meck 2005); this is true because inter-trial 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 inter-saccade 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 (since it occurs with zero 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. In order 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 appear 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 (e.g., Joiner and Shelhamer 2006). In trying to predict something that is unpredictable, as in the present 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 (Figure 2A, open circles), 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 non-predictive cases of 183.6±148.4 ms, versus -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 appear to be predominantly distributed between the cerebellum and the basal ganglia (for review see Buonomano and Karmarkar 2002; Buhusi and Meck 2005). A recent fMRI 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 inter-trial 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).

**Acknowledgements:** Supported by NIH T32-MH 20069 and EY015193. We appreciate the technical assistance of Dale Roberts and Adrian Lasker, helpful discussions with Drs. Richard Krauzlis and Grace Peng, and the comments of three anonymous reviewers.
References


Figure Legends

**Figure 1:** Saccade timing results for subject A. (*left column*) Probability distributions (20 ms bins) of inter-stimulus 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 (black) and target position (gray) for the corresponding interval distributions. Smaller panels show change in inter-stimulus interval throughout each specific 10 s sample; each plotted point corresponds to a single inter-stimulus 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 inter-saccade intervals, with increasing variance from top to bottom row.

**Figure 2:** Timing variance and correlation results for all subjects. (*A*) Variance of inter-saccade interval distributions (SD 0.5, 1.0, and 2.0) vs. variance of corresponding inter-stimulus interval plus variance of “inherent variability” (intersaccade interval distribution with no variability in stimulus timing). Dashed gray line represents best-fit line (slope=0.97, $r=0.89$). Non-filled circles represent data from two subjects who made reactive rather than predictive saccades in the SD-2.0 condition. (*B*) Correlations between saccade latencies, $R_{LL}(1)$, as stimulus variability increases. (*C*) Difference between the correlation between the latency of a given trial and the previous ISI, $R_{ISI,L}(1)$, and the correlation between the latency of a given trial and the current ISI, $R_{ISI,L}(0)$. Black lines in B and C are
means across subjects, gray lines are from individual subjects. Data from conditions where the subjects did not predict, corresponding to the open circles in panel A, are omitted from panels B and C.

**Figure 3:** Inter-trial correlations. (A) Autocorrelation functions of the series of latency values, for one subject, at the four stimulus conditions. Horizontal bars at approximately $R_{LL} = 0.2$ indicate the width of the autocorrelation functions at that point. This is the threshold for defining a “correlation window” over which previous trials are correlated. The bars are offset vertically for clarity. (B) Width of the correlation window (size of the horizontal bars in panel 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.
Figure 1
Figure 2

(A) Sum of Inherent Inter-saccade Interval Variance and Inter-stimulus Variance ($10^4$ ms$^2$)

(B) $R_{UL}(1)$ vs SD

(C) $R_{UL}(1)-R_{UL}(0)$ vs SD
Figure 3