Encoding By Response Duration in the Basal Ganglia

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Running head: Basal ganglia gating mechanisms
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Abstract
Several models have suggested that information transmission in the basal ganglia (BG) involves gating mechanisms, where neuronal activity modulates the extent of gate aperture and its duration. Here, we demonstrate that BG response duration is informative about a highly abstract stimulus feature, and show that the duration of ‘gate opening’ can indeed be used for information transmission through the BG. We analyzed recordings from three BG locations: the external part of the globus pallidus (GPe), the substantia nigra pars reticulata (SNr), and dopaminergic neurons from the substantia nigra pars compacta (SNc) during performance of a probabilistic visuo-motor task. Most (>85%) of the neurons showed significant rate modulation following the appearance of cues predicting future reward. Trial to Trial mutual information analysis revealed that response duration encoded reward prospects in many (42%) of the responsive SNr neurons, as well as in the SNc (26.9%), and the GPe (29.3%). While the low-frequency discharge SNc neurons only responded with an increase in firing rate, SNr and GPe neurons with high-frequency tonic discharge responded with both increases and decreases. Conversely, many duration-informative neurons in SNr (68%) and GPe (50%) responded with a decreased rather than an increased rate. The response duration was more informative than the extreme (minimal or maximal) amplitude or spike count in responsive bins of duration-informative neurons. Thus, response duration is not simply correlated with the discharge rate and can provide additional information to the target structures of the BG.
Introduction

One of the most important questions in neuroscience is how neuronal activity represents different aspects of the world (Bialek et al. 1991; Averbeck et al. 2006). It is especially interesting to trace how these representations are conveyed along a particular neuronal pathway (Barlow 1959; Las et al. 2005; Chechik et al. 2006). To examine encoding schemes in the basal ganglia (BG), we studied neuronal activity from the GPe and the SNr (central and output nuclei of the BG) and from the dopaminergic neurons of the SNC (which modulate BG responses - Bolam et al. 2000; Bar-Gad et al. 2003; McHaffie et al. 2005) during performance of a probabilistic visuo-motor task (Morris et al. 2004; Nevet et al. 2004; Arkadir et al. 2004). Studying the encoding properties of neurons in these structures can shed light on their interrelated computational roles and how they are implemented.

Most BG models use firing rate for information encoding (Albin et al. 1989; DeLong 1990; Wickens 1997; Berns and Sejnowski 1998; Bar-Gad et al. 2003). These models rely on physiological evidence that BG neurons, as in most areas of the nervous system, change their firing rate in response to behaviorally and emotionally relevant events. However, visual examination of our data suggested that response duration is also modulated by behavioral events (Fig. 1, and see additional example in Fig 3G of reference Morris et al. 2004). This motivated us to study the response duration as an encoding strategy of BG neurons that does not necessarily rely on firing rate alone. Response duration is an attractive encoding candidate since it naturally emerges from models of the basal ganglia that emphasize the role of information gating in BG processing (Deniau and
Chevalier 1985; Hikosaka and Wurtz 1983) and the recent suggestion of duration encoding of reward omission by SNC neurons (Bayer et al. 2007). Unlike rate models, gating models emphasize not only the extent of the gate opening (firing rate amplitude) but also the duration of the opening (e.g., response duration). The required processing of response features such as response duration, may result in a decrease in information (according to the information processing inequality, processing a response feature can only decrease the amount of information that could be provided by the original feature (Cover and Thomas 1991)). However, in gating models, the next neuronal station will not be required to estimate the duration, but to make use of the information passed/blocked through the gate. We therefore used mutual information (MI) to quantify the modulation of response duration and to compare it quantitatively with other carrier of behavioral information in the basal ganglia. The MI is a non-parametric measure of the association between two variables; in our case the visual stimuli (with four different future reward conditions) and the neural responses. We used the MI as a measure of the association, since the MI is able to detect statistical dependence beyond the linear relationships that are detected by the correlation coefficient. When MI=0, the two variables are statistically independent, and the neuronal activity does not encode information regarding the cues. When the MI is equal to the entropy of the stimulus set, in our case about 2 bits (depending on the actual frequency of the four cues, which varied somewhat from session to session), the stimuli can be perfectly distinguished by the response on a single-trial basis. Intermediate values correspond to intermediate resolvability of the stimuli by observation of the neural responses on a single trial basis (Cover and Thomas 1991).
Methods

We studied recordings from 4 monkeys (Y, E, C and G) engaged in a probabilistic visuo-motor task. In each trial one of a set of 4 visual cues was briefly presented to monkeys in one of two possible locations on a computer screen. After a constant delay of two seconds, a go signal instructed the monkeys to indicate the cue location by pressing one of two keys. Correct performance was rewarded in a probabilistic (p=0.25, 0.5, 0.75 and 1) manner, depending on the preceding visual cue. The inter trial interval was 4-7s. Our database consisted of 61 neurons from the GPe (32 from Y, and 29 from C), 56 neurons from the SNr (10 from Y, 15 from E and 31 from G), and 109 dopaminergic SNc neurons (22 from Y, 71 from E, and 16 from C). The spike waveforms of all neurons were judged to be well isolated during the experiment, and the longest period with discharge rate stability was off-line selected for each neuron. In addition, in this study we only included neurons that were recorded during at least 10 correct trials of each of the possible trial types. The behavioral paradigm, recording methods and data pre-processing are detailed in (Morris et al. 2004; Nevet et al. 2004; Arkadir et al. 2004).

We limited our study to the first 500 ms of the cue epoch to avoid the confounding effects of the limb and the reward licking movements. To study the response on a trial-by-trial basis, we divided the spike trains into 50 ms bins aligned on the onset of the cue signal indicating future reward prospects. We then characterized the type of activity in each bin of each trial as either no response, decrease in firing rate, or increase in firing rate by comparing the number of spikes in that bin to baseline activity. The baseline activity was
calculated as the mean spike count (firing rate) during inter-trial intervals. In more than 43% of the responses, we found that the peak response deviated by more than 2 standard deviations (SD). However, the changes in firing rates could be gradual, and at the response onsets and offsets the changes in firing rates were often substantially smaller. Therefore, decreases/increases in firing rate were detected by changes of at least 1.25 SD with respect to baseline activity. We repeated the same analysis with a criterion at 1.5 SD, with no appreciable difference (data not shown). For each trial, we defined the duration of the negative/positive responses as the number of bins in the longest sequence during the time period between 150 ms to 500 ms after cue onset (allowing single or multiple gaps of no more than one bin) in which the activity was characterized as either a negative or positive response. We denoted this time period as the “firing rate response period”. Figure 1 depicts this process in 5 different neurons from the three BG structures.

We estimated the MI between the cues and the neuronal responses, using explicit bias-information loss tradeoff optimization (Nelken et al. 2005). Four response features were used: (i) response duration (as defined above), (ii) the response spike count - the cumulative spike count during the response period, (iii) the extreme response amplitude (maximal for positive response and minimal for negative response), (iv) the total spike count – the cumulative spike count during the entire tested time period (i.e. the period between 150ms and 500ms after cue onset). Although calculating the total spike count over a shorter epoch could have produced more information in some cases it might have also induced a bias between the different events and the different neural populations.
We therefore preferred the conservative choice of a fixed window that enabled better comparison of the different populations. The 150-500ms time window was chosen since it captures the response in the tested data.

In the SNr and GPe, but not in the SNc, neurons responded to the future direction of movement indicated by the cue as well as to the reward probability (Arkadir et al. 2004; DeLong et al. 1983; Wichmann and Kliem 2004). In these structures the information on the reward probability was calculated for each of the movement directions separately and averaged according to the number of times each direction occurred. Cells were scored as response duration-informative if the information extracted from a cell's positive or negative response duration on future reward probability was significant when compared to 150 surrogate shuffled MI values (The reward probabilities were shuffled between trials, and the significance of the non shuffled vs. shuffled results was calculated according to the Mann-Whitney test, p<0.05). Cells in which less than 20% of the trials from each type had a positive/negative response were not considered as responding by positive/negative responses. For each nucleus, we calculated the mean response duration for duration-informative neurons as a function of reward probability.

In order to check whether the information provided by the other response features was redundant or synergistic with the information provided by response duration, and to evaluate the exclusiveness of the information to one of the different response features (duration, extreme responses or spike count) we used a normalized synergy measure. In synergistic encoding the information


provided by two response features simultaneously is greater than the sum of the information provided by each one of them separately, while in redundant encoding the sum of information is smaller than the information provided by both features together. The normalized synergy between the information provided by a response feature $R_1$ on a stimulus $S$ and the information provided by a response feature $R_2$ on $S$ is given by (Schneidman et al. 2003):

$$\text{Norm Syn}(R_1, R_2) = \frac{\text{MI}(S; R_1, R_2) - \text{MI}(S; R_1) - \text{MI}(S; R_2)}{\text{MI}(S; R_1, R_2)}$$

This measure tests whether the information provided by $R_1$ is redundant or synergistic to the information provided by $R_2$ assuming $\text{MI}(S; R_1, R_2) \neq 0$. It ranges from 1 (total synergy, $\text{MI}(S; R_1) = \text{MI}(S; R_2) = 0$); through 0 (MI independent variables, when $\text{MI}(S; R_1) + \text{MI}(S; R_2) = \text{MI}(S; R_1, R_2)$); to -1 (total redundancy, when $\text{MI}(S; R_1) = \text{MI}(S; R_2) = \text{MI}(S; R_1, R_2)$).

The synergy measurement does not indicate how the information is distributed between the two variables. For example, norm syn($R_1, R_2$) = -0.5 can occur in a number of scenarios: a) both variables have equal amount of information on $S$, and they share 2/3 of their information ( $\text{MI}(S; R_1) = \text{MI}(S; R_2) = 0.75 \text{MI}(S; R_1, R_2)$ ). b) $R_1$ has twice as much information on $S$ than $R_2$, and all the information $R_2$ has is already provided by $R_1$ ($\text{MI}(S; R_1) = \text{MI}(S; R_1, R_2) = 2 \text{MI}(S; R_2)$). In the similar way, ambiguity exists when norm syn($R_1, R_2$) = 0 (Fig. 2). We therefore also used a different measure, the normalized contribution. The normalized contribution of $R_2$ to the information on $S$ carried by the pair $R_1$ and $R_2$ is the fraction of information that could not have been extracted without $R_2$:
Norm Contrib(S;R₂;R₁) = \frac{MI(S;R₁,R₂) - MI(S;R₁)}{MI(S;R₁,R₂)}.

The normalized contribution ranges between 0 (observing R₂ does not contribute to the information in addition to R₁) and 1 (none of the information could have been extracted without observing R₂). Note that

\text{Norm Contrib}(S;R₁;R₂) + \text{Norm Contrib}(S;R₂;R₁) = 1 + \text{Norm Syn}(R₁,R₂),

i.e. the sum of the norm. contributions is 0 in cases of total redundancy (all the information could be extracted with either one of the parameters alone), and 2 in total synergy (the information is totally dependent on both parameters). In addition, this measurement is not defined when MI(S;R₁,R₂)=0.

In summary, we used three measures of the information encoded in the neuronal responses regarding the prospects of future reward. The MI is a measure of the information encoded on future reward probability by each of the tested reduced response measures (duration, extreme response and response count). The normalized synergy quantifies the overlap between information encoded by two reduced measures of the responses, and the normalized contribution indicates how much each of the reduced measures contributes to the total information.
Results

We reanalyzed recorded data from the GPe, SNr and SNe of four behaving monkeys to assess the encoding of reward probability by response duration. Most neurons in the SNr, SNe, and GPe showed significant spike rate responses (Mann-Whitney test on spike counts of response bins vs. inter-trial-interval bins, p<0.05) to the appearance of at least one of the four possible cues (Table 1, % responding neurons). Hereafter, we refer to the significant decreases in firing rate as "negative responses" and the increases in firing rate as "positive responses".

Raster plots of neural recordings revealed that the duration of the single-trial response often varied with the cue (Fig. 1). We used the MI between cue (indicating reward probability) and neuronal response to measure the amount of information that could be extracted from the response duration and from other response features on the probability of future reward. In all three BG structures, the response duration of many neurons provided a significant amount of information on the reward probabilities (Table 1, % duration informative neurons).

All of the responding SNe neurons exhibited positive responses (increase in discharge rate) to the cue, and therefore all of the duration-informative neurons in the SNe showed a positive response. However, twice as many of the SNr duration-informative neurons (68%) responded with a negative rather than a positive response, whereas in the GPe the duration-informative neurons distributed evenly between positive and negative responses.
The average response duration in SNr and SNe duration informative neurons exhibited monotonic increases/decreases with the probability of future reward (Fig. 3). Such behaviors were not observed in the average response duration of GPe duration informative neurons. The mean duration of the SNe positive responses was longer for high reward probabilities and shorter for low reward probabilities (one-way ANOVA, p<0.01). The mean response duration in SNr neurons presented a different behavior from the SNe responses. Whereas the SNr negative response followed the same monotonic increase as SNe neurons (duration increased for high reward probability one-way ANOVA, p<0.01), the positive response tended (without reaching statistical significance) to be shortened with increased reward probability. In addition, the average durations of the negative GPe responses in duration informative neurons are significantly shorter (one-way ANOVA p<0.01) than the positive responses. We checked whether the negative vs. positive difference seen in response duration of SNr neurons exists also in other response features discussed in the paper. Only the mean total spike count of negative duration informative neurons showed a significant monotonic decrease (one-way ANOVA p<0.01) displaying higher values for low reward probabilities.

Figure 4 compares the MI between response duration and reward probability to the information provided by other response features. Since extracting response duration required classifying each time bin in each single trial, we also derived the more standard responses (extreme response and response spike count) of each single trial, using only those bins that were classified as having a
significant response. Table 2 compares the average MI values of the different response features of duration informative neurons. In both figure 4 and table 2 the results are displayed separately for each of the three structures and for positive vs. negative responses. For neurons with negative responses, duration was more informative than either extreme (maximal or minimal) response or response spike count. For neurons with positive responses, extreme response and response spike count were as informative as response duration.

We therefore further tested whether combining response features could increase information about reward probability (Table 2). As expected, in almost all cases, there was clear redundancy between the response features (negative normalized synergy). Thus, on average the information provided by the extreme amplitude or by the response spike count was highly redundant with the information provided by the response duration. Unexpectedly, we found that the additional information supplied by extreme response and by response spike count when used in association with response duration was close to zero (see 'Methods' and average "norm contribution" in Table 2). Thus, the information that can be decoded from response duration encompasses essentially all the information that can be decoded from response spike count or extreme amplitude.

Extracting response duration from single trials is rather complex (Fig. 1), since it involves classifying each time bin in the responses of each single trial. Different ways of decoding the neuronal responses may be more informative. The standard way of quantifying responses is by counting the total spike count in a fixed, long window. Whereas total spike count encompasses time bins that
may not be really important, possibly diluting the information it carries through
the addition of noise, it also may take into account the responses during time
bins that were wrongly classified as non-responsive. In practice, the second
effect probably dominated since we found that total spike count carried as much
or more information than the response duration. This can be seen in Fig. 4 where
the MI extracted from the total spike count over the fixed 350 ms window for
both positive and negative responses was typically higher than the MI carried by
response duration (as also reflected in Table 2). Nevertheless, since the duration
did not add significantly to the information provided by the total spike count, the
information provided by both the total spike count and the duration is actually
provided by the total spike count alone. Therefore the amount of information
given by both features exclusive to the total spike count (see 'norm contribution'
in Table 2 - 32%, range 20-50%) is the amount of information given by the total
spike count and not by the response duration, i.e. most (68%, range 50-80%) of
the information provided by the total spike count was encoded by the response
duration as well. Thus, the difference between response duration and total spike
count as a carrier of information was not substantial. In addition, we tested more
detailed temporal representations of the response (such as analyzing the activity
as a sequence of responsive and non-responsive bins). However, the bias-
corrected amount of information did not significantly increase with greater
detail, suggesting that there is no easily decoded additional information in the
temporal pattern of the 50 ms bins of the BG responses (data not shown).
Discussion

Our results confirm previous reports of future reward probability encoding in basal ganglia neurons (Arkadir et al. 2004; Morris et al. 2004). However, previous studies tested duration encoding directly only for the negative dopaminergic responses (Bayer et al. 2007). The main results of this study is the demonstration that response duration carries much of the information available in responses of BG neurons about future reward probability, and that there is a difference between encoding processes of positive and negative responses. Note that in this manuscript, we only tested the responses to cue predicting rewards, and therefore evoked only positive SNc responses. However, another study of our group failed to reveal duration encoding in the responses of SNc neurons to omission of predicted rewards (Joshua et al. 2008).

Evidence for the importance of response duration in the nervous system (DeBusk et al. 1997; Christensen-Dalsgaard et al. 1998; Rogers and Newland 2002; Nagata et al. 2003; Zhang et al. 2004; Kanold and Manis 2005) and even specifically in the responses of striatal cholinergic neurons (Ravel et al. 2003; Aosaki et al. 1995) and in responses of pallidal neurons (Anderson and Turner 1991) have been reported. Recently, Steuber et al. (Steuber et al. 2007) found that the best criterion to distinguish between different patterns of the cerebellar parallel fibers was the duration of the pause. O'Donnell et al. have showed that a known psychotic modulator (phencyclididine) acts by reducing the frequency and duration of the spontaneously occurring depolarized plateaus observed in the membrane potential of accumbens neurons (O'Donnell and Grace 1998). In addition, Kepecs et al. have presented a model that can account for the
generation of different duration up-state activity in striatal neurons (Kepecs and Raghavachari 2007). By simulating a bursting neuron model, Kepecs et al. showed that bursts of different durations can code for different stimulus features (Kepecs et al. 2002; Kepecs and Lisman 2003). Moreover, they found that synapses can be tuned to preferentially respond to specific burst durations, and demonstrated the decodability of a neural code based on burst duration (Kepecs and Lisman 2004). In addition, a study of dopaminergic neurons suggested that these neurons overcome the limited dynamic range available for encoding of negative values by modification of the duration of their negative responses (Bayer et al. 2007). Finally, a recent study (Person and Perkel 2005) have revealed in zebra finch songbirds that high-frequency trains of pallidal spikes can drive activity in thalamic relay neurons by rebound excitation. The latency of this rebound is strongly affected by the duration of the pallidal spike train (their figure 4). Thus, positive SNr responses will yield different thalamic rebound excitation as a function of the response duration, and perhaps longer SNr pauses will cause longer and probably stronger thalamic disinhibitory effects.

Our results are in line with models of the basal ganglia in which information transmission is carried through gating mechanisms - where the neuronal activity determines the extent of gate aperture and its duration (Deniau and Chevalier 1985; Mink 1996). GPe is probably involved in gating the inputs to the subthalamic nucleus, striatum and the output structures of the BG, whereas the SNr gates the reciprocal thalamo-cortical neuronal loops. Contrary to other models (Mink 1996), gating models suggest that the basal ganglia output
enables, rather than selects or initiates (Mink 1996; McHaffie et al. 2005) movements or other voluntary behaviors. We suggest that the duration of the gate aperture might take part in the competition between possible actions (giving advantage to those BG-thalmic channels with longer opened gate duration). In addition, reward expectation has been shown to influence response latency (Lauwereyns et al. 2002), therefore it is possible that response duration is part of the mechanism that modulates or affects the action's vigor through the multiple channels of the basal ganglia output to the reciprocal thalamo-cortical networks. The significant fraction of duration informative SNr neurons with negative responses is compatible with this suggested role of the SNr. The SNr has GABAergic projections to the thalamus and to the superior colliculus (Hikosaka and Wurtz 1983; Redgrave et al. 1992), Thus when SNr neurons decrease their activity, they disinhibit their targets. This may be the mechanistic implementation of the gating mechanism, where the background tonic activity and positive responses of SNr neurons close the gate, while negative SNr responses open the gate (Hikosaka and Wurtz 1983; Deniau and Chevalier 1985). Our finding that the mean negative response durations of duration informative neurons monotonically increases (long durations for high probability, and short durations for low probability – Fig. 3) is also compatible with the gating model. Negative SNr responses open the gate, and we expect the gate to be opened for longer durations (and enable a movement) for the higher reward prospects. The positive responses show (non-significant) an opposite trend. This could also be explained by the gating model. Since closing the gate does not determine the movement, its' duration is less significant. The monotonic decrease seen in the mean total spike count of negative duration
informative neurons, displaying higher values for low reward probabilities, is in line with the monotonic increase found in the mean response duration of those neurons. The total spike count consists of responsive and non responsive bins, therefore long negative responses which have less bins with normal activity and more bins with low activity, will have a low total spike count and vice versa. In addition, it has been shown that dopamine (D1- receptors) inhibits SNr activity (Kliem et al. 2007). Therefore, in line with SNr negative responses, the mean response duration in SNc (positive) responses is long for high reward probabilities and short for low probabilities.

A negative response, i.e., response with a decrease in firing rate has the advantage of being detectable faster than an increase of the same magnitude (appendix a). However, in negative responses, when the neurons decrease their firing rate to close to zero for different time lengths, the minimal firing rate and the response spike count do not differ between different probabilities and therefore provide little information on the reward probability. In this situation, the response duration remains informative (consequently, the total spike count that includes time bins in which short responses return to normal activity will also be informative). On the other hand, in positive responses, when the neurons respond with an increase in firing rate for different time lengths, the response spike count varies between reward probabilities. Hence for neurons with positive responses, duration did not have a major advantage over maximal firing rate or response spike count.
Spike train analyses usually have focused on two extreme schemes of neuronal encoding. Most studies have dealt with the highly information-reduced measure of spike count or rate (Georgopoulos et al. 1986; Shadlen and Newsome 1998; Gershon et al. 1998; Ahissar et al. 2000). Other studies have focused on information in spike patterns (Victor and Purpura 1996; Prut et al. 1998; Panzeri et al. 2001; Ikegaya et al. 2004; Friedrich et al. 2004; Jones et al. 2004; Arabzadeh et al. 2006). However, even when spike timing carries information, the use of simple reduced measures of the timing of the responses may be sufficient (Nelken et al. 2005). Our observations demonstrate that coding schemes based on response duration are viable, and that they use much of the information available in the responses of BG neurons. Furthermore, we show that response duration encodes reward probability not only in positive (increase in firing rate, bursts) responses, but also (in the GABAergic BG nuclei) in negative (decrease in firing rate) responses, and that duration encoding is not a simple epiphenomenon of rate encoding. Finally, we argued that response duration may be highly relevant to the effects of BG neurons on their target structures. The significant amount of information encoded in response duration makes response duration a prominent coding element that can mechanistically control the influence of the basal ganglia on its target structures.
Appendix A

This appendix proves that a decrease in firing rate response can be detected faster than an increase of the same magnitude in neurons with Poisson-like firing pattern.

The sequential probability ratio test (SPRT) (Wald A 1947) is a serial Bayesian test designed to determine which of two hypothesized distributions is used to generate data samples. In this test we obtain data samples, and examine the log likelihood (the probability of a given distribution to generate these data points) ratio of the two distributions. The test sequentially inputs data samples until the ratio is above an acceptance or below a rejection threshold. At that time the test can determine (with a reliability that depends solely on the thresholds) which of the two distributions generated the data.

We assume that the spike trains are generated by a Poisson distribution and that an external/internal event can cause the neuron to switch from one firing rate ($\lambda_1$) to a different firing rate ($\lambda_2$). We wish to evaluate how many samples (spike counts/rates) are needed (using SPRT) in order to determine the neuron's firing rate after the switch has occurred.

The likelihood ratio for the two hypotheses is: $s = \log \frac{L(x^n | \lambda_1)}{L(x^n | \lambda_2)}$, where $x^n = (x_1, \ldots, x_n)$ are $n$ i.i.d data samples, $p(x_i | \lambda) = \frac{\lambda^x e^{-\lambda}}{x!}$.
\[
s = \log \frac{L(x^n | \hat{\lambda}_1)}{L(x^n | \hat{\lambda}_2)} = \log \prod_i p(x_i | \hat{\lambda}_1) ^ {p(x_i | \hat{\lambda}_1)} = \log\left( \prod_i p(x_i | \hat{\lambda}_1) \right)
\]

\[
= \sum_i \log \left( \frac{p(x_i | \hat{\lambda}_1)}{p(x_i | \hat{\lambda}_2)} \right) = n \sum_i \log \left( \frac{p(x_i | \hat{\lambda}_1)}{p(x_i | \hat{\lambda}_2)} \right) = nE(\log \frac{p(x | \hat{\lambda}_1)}{p(x | \hat{\lambda}_2)})
\]

\[
E(\log \frac{p(x | \hat{\lambda}_1)}{p(x | \hat{\lambda}_2)}) = \sum_x p(x | \hat{\lambda}_1) \log \left( \frac{p(x | \hat{\lambda}_1)}{p(x | \hat{\lambda}_2)} \right), \text{ which is also denoted as the Kullback-Leibler distance (Cover and Thomas 1991): } D_{KL}[p(x | \hat{\lambda}_1) \parallel p(X | \hat{\lambda}_2)]
\]

\[
= \sum_x p(x | \hat{\lambda}_1) \log \left( \frac{\hat{\lambda}_1 x e^{-\hat{\lambda}_1}}{\hat{\lambda}_2 x e^{-\hat{\lambda}_2}} \right) = \sum_x p(x | \hat{\lambda}_1) [x \log(\frac{\hat{\lambda}_1}{\hat{\lambda}_2}) + (\hat{\lambda}_2 - \hat{\lambda}_1)] = \log(\frac{\hat{\lambda}_1}{\hat{\lambda}_2}) E(x | \hat{\lambda}_1) + (\hat{\lambda}_2 - \hat{\lambda}_1) = \log(\frac{\hat{\lambda}_1}{\hat{\lambda}_2}) \hat{\lambda}_1 + (\hat{\lambda}_2 - \hat{\lambda}_1)
\]

Let \( n_{\Delta R[R(1+\Delta)\lambda]} \) - denote the number of samples needed to detect a distribution switch from \( \lambda=R \) to \( \lambda=R(1+\Delta) \), \( n_{\Delta R[R(1-\Delta)\lambda]} \) - the number of samples needed to detect a distribution switch from \( \lambda=R \) to \( \lambda=R(1-\Delta) \), and \( S_{th} \) is the ratio acceptance threshold (the threshold to detect the distribution change). We can express the required sample sizes as:

\[
n_{th} = \frac{S_{th}}{E(\frac{p(x | \hat{\lambda}_1)}{p(x | \hat{\lambda}_2)}) \log(\frac{\hat{\lambda}_1}{\hat{\lambda}_2}) \hat{\lambda}_1 + (\hat{\lambda}_2 - \hat{\lambda}_1)} = \frac{S_{th}}{\log(\frac{R(1+\Delta)}{R})R(1+\Delta) - R\Delta}, \quad n_{\Delta R[R(1-\Delta)\lambda]} = \frac{S_{th}}{\log(\frac{R(1-\Delta)}{R})R(1-\Delta) + R\Delta}
\]

\[
n_{\Delta R[R(1+\Delta)\lambda]} = \frac{\log(\frac{R(1+\Delta)}{R})R(1+\Delta) + R\Delta}{\log(\frac{R(1-\Delta)}{R})R(1-\Delta) + R\Delta} = (1-\Delta)\log(1-\Delta) + \Delta \quad \text{and} \quad n_{\Delta R[R(1-\Delta)\lambda]} = \frac{\log(\frac{R(1+\Delta)}{R})R(1+\Delta) - R\Delta}{\log(\frac{R(1-\Delta)}{R})R(1-\Delta) - R\Delta} = (1+\Delta)\log(1+\Delta) - \Delta
\]

The ratio between the number of samples needed to detect a distribution switch from \( \lambda=R \) to \( \lambda=R(1+\Delta) \) and the number of samples needed to detect a
distribution switch from \( \lambda = R \) to \( \lambda = R(1-\Delta) \) is always greater than 1, and reaches 2.6 as \( \Delta \) reaches 1. Thus, detecting a decrease in firing rate will require fewer data samples, i.e. less time than detecting an increase of the same magnitude.
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Specific contribution:

NP – initiated and designed the study of response duration, developed the information theoretic tools, performed the data analysis and wrote the manuscript; DA, AN, GM – trained the monkeys for the behavioral tasks and record the single unit activity during the performance of the task; HB – contributed to the monkeys training, recording and the writing of the manuscript; TS, EN – contributed to the development of the information analysis tools and the writing of the manuscript.
Reference List


Ref Type: In Press


41. **Nevet A, Morris G, Saban G, Fainstein N and Bergman H.** Discharge rate of substantia nigra pars reticulata neurons is reduced in non-


Figure and table legends:

**Figure 1 Neural encoding of reward prospects by response duration in the basal ganglia: examples from recordings of 5 neurons.** The visual cue was presented at time 0. For each example we present the neural recording raster plot in which the trials are sorted by the reward probability (first column from the left); the binned responses, colored as either average response (white), negative response (gray), or positive response (black) (second column); and the response duration of each trial (third column from the left). Response durations were calculated for the 150-500 ms period. The rows show:

- **a.** SNr neuron – encoding by positive response duration (112 trials).
- **b.** SNr neuron – encoding by negative (decreased) response duration (383 trials).
- **c.** SNc neuron – encoding by positive response duration (135 trials).
- **d.** GPe neuron – encoding by negative response duration (229 trials).
- **e.** GPe neuron – encoding by positive response duration (229 trials).
Figure 2 MI normalized contribution vs. normalized synergy. Two examples in which the normalized synergy measure can describe multiple distributions of MI between two variables and the normalized contribution measure discriminates between them:

a. Norm. synergy = 0, can describe the case in which the information distributes evenly (left), and the case in which the information provided by one variable is greater than the other (right).

b. Norm. synergy = -0.5, can describe the case in which each variable has the same amount of information, and 2/3 is shared by both variables (left), and the case in which the information provided by one variable is twice as great as the information provided by the other variable, and the latter variable does not add information that is not already provided by the former (right).
Figure 3 Mean response duration. Mean negative and positive response durations of duration informative cells in the SNr, SNC, and GPe. The error bars indicate one standard deviation. Square – positive response, triangle – negative response.
Figure 4 Comparing the MI between reward probability and other response features to the MI between the reward probability and the response duration. For each of the structures, we illustrate the MI between the reward probability and two response features (the extreme response and the response spike count) as a function of the MI between the reward probability and the response duration.
Table 1 Quantitative analysis of neural responses in different basal ganglia nuclei. Responsive and duration informative neurons in the GPe, SNC and SNr.

<table>
<thead>
<tr>
<th></th>
<th>SNr</th>
<th>SNc</th>
<th>GPe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cells:</td>
<td>56</td>
<td>109</td>
<td>61</td>
</tr>
<tr>
<td>Number of responsive cells</td>
<td>50</td>
<td>93</td>
<td>54</td>
</tr>
<tr>
<td>(% of total cells)</td>
<td>(89.3%)</td>
<td>(85.3%)</td>
<td>(88.5%)</td>
</tr>
<tr>
<td>Number of duration informative cells</td>
<td>21</td>
<td>25</td>
<td>16</td>
</tr>
<tr>
<td>(% of responsive cells)</td>
<td>(42%)</td>
<td>(26.88%)</td>
<td>(29.3%)</td>
</tr>
<tr>
<td>Number of duration informative cells with positive or negative responses</td>
<td>7</td>
<td>14</td>
<td>25</td>
</tr>
<tr>
<td>(% of duration informative cells)</td>
<td>(33.3%)</td>
<td>(66.7%)</td>
<td>(100%)</td>
</tr>
</tbody>
</table>
Table 2 Comparison of information contents of the neuronal responses of duration informative cells in different basal ganglia nuclei. Mean over positive and negative response duration informative cells of MI, normalized synergy and contribution between the reward probability and the different response features.

<table>
<thead>
<tr>
<th></th>
<th>SNr</th>
<th>SNe</th>
<th>GPe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive response</td>
<td>Negative response</td>
<td>Positive response</td>
</tr>
<tr>
<td>&lt;MI(reward probability; duration)&gt;</td>
<td>0.35</td>
<td>0.38</td>
<td>0.22</td>
</tr>
<tr>
<td>&lt;MI(reward probability; max amplitude)&gt;</td>
<td>0.29</td>
<td>0.18</td>
<td>0.16</td>
</tr>
<tr>
<td>&lt;MI(reward probability; response spike count)&gt;</td>
<td>0.38</td>
<td>0.19</td>
<td>0.24</td>
</tr>
<tr>
<td>&lt;MI(reward probability; total spike count)&gt;</td>
<td>0.43</td>
<td>0.50</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td>Positive response</td>
<td>Negative response</td>
<td>Positive response</td>
</tr>
<tr>
<td>&lt;MI(reward probability; {duration, max amplitude})&gt;</td>
<td>0.38</td>
<td>0.34</td>
<td>0.26</td>
</tr>
<tr>
<td>&lt;MI(reward probability; {duration, response spike count})&gt;</td>
<td>0.38</td>
<td>0.38</td>
<td>0.27</td>
</tr>
<tr>
<td>&lt;MI(reward probability; {duration, total spike count})&gt;</td>
<td>0.44</td>
<td>0.52</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Synergy(max amplitude; duration)&gt;</td>
<td>-0.63</td>
<td>-0.44</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Contrib(reward prob.; duration; max amplitude)&gt;</td>
<td>0.32</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Contrib (reward prob.; max amplitude; duration)&gt;</td>
<td>0.05</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Synergy (res spike count; duration)&gt;</td>
<td>-0.91</td>
<td>-0.49</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Contrib (reward prob.; duration; res spike count)&gt;</td>
<td>0</td>
<td>0.51</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Contrib (reward prob.; res spike count; duration)&gt;</td>
<td>0.09</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Synergy (total spike count; duration)&gt;</td>
<td>-0.76</td>
<td>-0.65</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Contrib (reward prob.; duration; total spike count)&gt;</td>
<td>0.04</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>&lt;Norm Contrib (reward prob.; total spike count; duration)&gt;</td>
<td>0.2</td>
<td>0.27</td>
</tr>
</tbody>
</table>
\(- \text{MI}(R_1; S) - \text{MI}(R_2; S) - \text{MI}([R_1, R_2]; S) - \text{MI}([R_1, R_2]; S)\)

<table>
<thead>
<tr>
<th>a</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>norm. synergy = 0</td>
<td>norm. synergy = -0.5</td>
</tr>
<tr>
<td>norm. contribution ((R_1; R_1, R_2)) = 0.5</td>
<td>norm. contribution ((R_1; R_1, R_2)) = 0.5</td>
</tr>
<tr>
<td>norm. contribution ((R_2; R_1, R_2)) = 0.5</td>
<td>norm. contribution ((R_2; R_1, R_2)) = 0.75</td>
</tr>
<tr>
<td>norm. contribution ((R_1; R_1, R_2)) = 0.0</td>
<td>norm. contribution ((R_2; R_1, R_2)) = 0.0</td>
</tr>
<tr>
<td>norm. contribution ((R_2; R_1, R_2)) = 0.5</td>
<td>norm. contribution ((R_2; R_1, R_2)) = 0.5</td>
</tr>
</tbody>
</table>
MI(reward probability; response feature) <bits>

- x - positive responses
- o - negative responses

MI(reward probability; response duration) <bits>