Encoding by Response Duration in the Basal Ganglia

Naama Parush,1,2,3 David Arkadir,2 Alon Nevet,2 Genela Morris,1,2 Naftali Tishby,1,3 Israel Nelken,1,4 and Hagai Bergman1,2

1The Interdisciplinary Center for Neural Computation; 2Department of Physiology, Hadassah Medical School; 3The School of Engineering and Computer Science; and 4Department of Neurobiology, Life Science Institute, Faculty of Sciences, The Hebrew University, Jerusalem, Israel

Submitted 25 March 2008; accepted in final form 6 October 2008

Parush N, Arkadir D, Nevet A, Morris G, Tishby N, Nelken I, Bergman H. Encoding by response duration in the basal ganglia. J Neurophysiol 100: 3244–3252, 2008. First published October 8, 2008; doi:10.1152/jn.90400.2008. 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 visuomotor 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%). Whereas the low-frequency discharge SNc neurons responded with only 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 rate 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 (Averbeck et al. 2006; Bialek et al. 1991). It is especially interesting to trace how these representations are conveyed along a particular neuronal pathway (Barlow 1959; Chechik et al. 2006; Las et al. 2005). To examine encoding schemes in the basal ganglia (BG), we studied neuronal activity from the external part of the globus pallidus (GPe) and the substantia nigra pars reticulata (SNr) (central and output nuclei of the BG) and from the dopaminergic neurons of the substantia nigra pars compacta (SNc) (which modulate BG responses; Bar-Gad et al. 2003; Bolam et al. 2000; McHaffie et al. 2005) during performance of a probabilistic visuomotor task (Arkadir et al. 2004; Morris et al. 2004; Nevet 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; Bar-Gad et al. 2003; Berns and Sejnowski 1998; DeLong 1990; Wickens 1997). 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; also see additional example in Fig. 3G of 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 decrease only 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 carriers of behavioral information in the basal ganglia. The MI is a nonparametric 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
We studied recordings from four monkeys (Y, E, C, and G) engaged in a probabilistic visuomotor task. In each trial one of a set of four visual cues was briefly presented to monkeys in one of two possible locations on a computer screen. After a constant delay of 2 s, correct performance was rewarded in a possible locations on a computer screen. After a constant delay of 2 s, 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- to 500-ms period. The rows show: A: substantia nigra pars reticulata (SNr) neuron: encoding by positive response duration (112 trials). B: SNr neuron: encoding by negative (decreased) response duration (383 trials). C: substantia nigra pars compacta (SNc) neuron: encoding by positive response duration (135 trials). D: external part of globus pallidus (GPe) neuron: encoding by negative response duration (229 trials). E: GPe neuron: encoding by positive response duration (229 trials).

Methods

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 intertrial intervals. In >43% of the responses, we found that the peak response deviated by >2SDs. 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 ≥1.25SD with respect to baseline activity. We repeated the same analysis with a criterion at 1.5SD, 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 and 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 five different neurons from the three BG structures.

We estimated the MI between the cues and the neuronal responses using explicit bias-information loss trade-off optimization (Nelken et al. 2005). Four response features were used: 1) response duration (as defined earlier), 2) the response spike count (the cumulative spike count during the response period), 3) the extreme response amplitude (maximal for positive response and minimal for negative response), and 4) the total spike count (the cumulative spike count during the entire tested time period; i.e., the period between 150 and 500 ms after cue onset). Although calculating the total spike count over a shorter epoch could have produced more information in some cases it might...

FIG. 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- to 500-ms period. The rows show: A: substantia nigra pars reticulata (SNr) neuron: encoding by positive response duration (112 trials). B: SNr neuron: encoding by negative (decreased) response duration (383 trials). C: substantia nigra pars compacta (SNc) neuron: encoding by positive response duration (135 trials). D: external part of globus pallidus (GPe) neuron: encoding by negative response duration (229 trials). E: GPe neuron: encoding by positive response duration (229 trials).
also have 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- to 500-ms 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 with 150 surrogate shuffled MI values. (The reward probabilities were shuffled between trials and the significance of the nonshuffled vs. shuffled results was calculated according to the Mann–Whitney test, \( P < 0.05 \).) Cells in which <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.

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, whereas 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 \( R_i \) on a stimulus \( S \) and the information provided by a response feature \( R_j \) on \( S \) is given by (Schneidman et al. 2003)

\[
\text{Norm Syn}(R_i, R_j) = \frac{\text{MI}(S; R_i, R_j) - \text{MI}(S; R_i) - \text{MI}(S; R_j)}{\text{MI}(S; R_i, R_j)}
\]

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

The synergy measurement does not indicate how the information is distributed between the two variables. For example, \( \text{norm syn}(R_i, R_j) = -0.5 \) can occur in a number of scenarios: 1) both variables have equal amount of information on \( S \) and they share two thirds of their information \( \{\text{MI}(S; R_1) = \text{MI}(S; R_2) = 0.75\text{MI}(S; R_1, R_2)\} \), 2) \( R_j \) has twice as much information on \( S \) than \( R_i \) and all the information \( R_j \) has is already provided by \( R_i \) \( \{\text{MI}(S; R_1) = \text{MI}(S; R_1, R_2) = 2\text{MI}(S; R_2)\} \). In a similar way, ambiguity exists when \( \text{norm syn}(R_i, R_j) = 0 \) (Fig. 2). We therefore also used a different measure: the normalized contribution. The normalized contribution of \( R_j \) to the information on \( S \) carried by the pair \( R_i \) and \( R_j \), is the fraction of information that could not have been extracted without \( R_j \)

\[
\text{Norm Contrib}(R_j, R_i) = \frac{\text{MI}(S; R_j, R_i) - \text{MI}(S; R_j)}{\text{MI}(S; R_i, R_j)}
\]

The normalized contribution ranges between 0 (observing \( R_j \) does not contribute to the information in addition to \( R_i \)) and 1 (none of the information could have been extracted without observing \( R_j \)). Note that \( \text{Norm Contrib}(S; R_i; R_j) + \text{Norm Contrib}(S; R_j; R_i) = 1 + \text{Norm Syn}(R_i, R_j) \), 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 \( \text{MI}(S; R_i, R_j) = 0 \).

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 SNc of four behaving monkeys to assess the encoding of reward probability by response duration.

Most neurons in the SNr, SNc, and GPe showed significant spike rate responses (Mann–Whitney test on spike counts of response bins vs. intertrial-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 SNc neurons exhibited positive responses (increase in discharge rate) to the cue and thus all of the duration-informative neurons in the SNc 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 SNc 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 SNc 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 SNc responses. Whereas the SNr negative response followed the same monotonic increase as SNc 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 versus positive difference seen in response duration of SNr neurons also exists in other response features discussed herein. 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 Fig. 4 and Table 2 the results are displayed separately for each of the three structures and for positive versus 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.

| Table 1. Quantitative analysis of neural responses in different basal ganglia nuclei |
|---------------------------------|----------|----------|----------|
| Total number of cells           | 56       | 109      | 61       |
| Number of responsive cells (% of total cells) | 50       | 93       | 54       |
| Number of duration-informative cells (% of responsive cells) | 21       | 25       | 16       |
| Number of duration-informative cells with positive or negative responses (% of responsive cells) | 7        | 14       | 25       |
| Positive Response               | (33.3%)  | (66.7%)  | (100%)   |
| Negative Response               | (50%)    | (50%)    | (50%)    |

Responsive and duration-informative neurons in the SNr, SNc, and GPe.
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 may also take into account the responses during time bins that were wrongly classified as nonresponsive. In practice, the second effect probably dominated since we found that total spike count carried as much information as, 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 nonresponsive 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 are 1) the demonstration that response duration carries much of the information available in responses of BG neurons about future reward probability and 2) that there is a difference between encoding processes of positive and negative responses. Note that in this study, we tested the responses only to cue-predicting rewards and thus 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 (M Joshua, A Adler, R Mitelnan, E Vaadia, and H Bergman, unpublished observations).

Evidence for the importance of response duration in the nervous system (Christensen-Dalsgaard et al. 1998; DeBusk et al. 1997; Kanold and Manis 2005; Nagata et al. 2003; Rogers and Newland 2002; Zhang et al. 2004) and even specifically in
different response features. Other models (Mink 1996), gating models suggest that the basal gates the reciprocal thalamocortical neuronal loops. Contrary to the striatum, and the output structures of the BG, whereas the SNr probably involved in gating the inputs to the subthalamic nucleus, where the neuronal activity determines the extent of gate aperture longer and probably stronger thalamic disinhibitory effects. Different thalamic rebound excitation as a function of the train (their Fig. 4). Thus positive SNr responses will yield relay neurons by rebound excitation. The latency of this re-

Perkel (2005) revealed in zebra finch songbirds that high-
sponses (Bayer et al. 2007). Finally, a recent study (Person and O’Donnell and Grace (1998) showed that a known psychotic modulator (phenycyclidine) acts by reducing the frequency and duration of the spontaneously occurring depolarized plateaus observed in the membrane potential of accumbens neurons. In addition, Kepecs and Ragha-
vachari (2007) presented a model that can account for the generation of different duration up-state activity in striatal neurons. By simulating a bursting neuron model, Kepecs and colleagues showed that bursts of different durations can code for different stimulus features (Kepecs and Lisman 2003; Kepecs et al. 2002). Moreover, they found that synapses can be tuned to preferentially respond to specific burst durations and demonstrated the decorrelation 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) 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 re-bound is strongly affected by the duration of the pallidal spike train (their Fig. 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 thalamocortical neuronal loops. Contrary to other models (Mink 1996), gating models suggest that the basal ganglia output enables, rather than selects or initiates (McHaffie et al. 2005; Mink 1996), 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–thalamic channels with longer opened gate duration). In addition, reward expectation has been shown to influence response latency (Lauwereyns et al. 2002); it is thus 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 thalamocortical 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, whereas negative SNr responses open the gate (Deniau and Chevalier 1985; Hikosaka and Wurtz 1983). 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 (nonsignificant) 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 nonresponsive bins; thus long negative responses that have fewer 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).

### Table 2. Comparison of information contents of the neuronal responses of duration-informative cells in different basal ganglia nuclei

<table>
<thead>
<tr>
<th>Information Content</th>
<th>SNr (Positive Response)</th>
<th>SNr (Negative Response)</th>
<th>SNc (Positive Response)</th>
<th>SNc (Negative Response)</th>
<th>GPe (Positive Response)</th>
<th>GPe (Negative Response)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI(reward probability; duration)</td>
<td>0.35</td>
<td>0.38</td>
<td>0.22</td>
<td>0.17</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>MI(reward probability; max amplitude)</td>
<td>0.29</td>
<td>0.18</td>
<td>0.16</td>
<td>0.12</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>MI(reward probability; response spike count)</td>
<td>0.38</td>
<td>0.19</td>
<td>0.24</td>
<td>0.20</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>MI(reward probability; total spike count)</td>
<td>0.43</td>
<td>0.50</td>
<td>0.28</td>
<td>0.24</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>MI(reward probability; (duration, max amplitude))</td>
<td>0.38</td>
<td>0.34</td>
<td>0.26</td>
<td>0.20</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>MI(reward probability; (duration, response spike count))</td>
<td>0.38</td>
<td>0.38</td>
<td>0.27</td>
<td>0.20</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>MI(reward probability; (duration, total spike count))</td>
<td>0.44</td>
<td>0.52</td>
<td>0.33</td>
<td>0.27</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>Norm Synergy(max amplitude; duration)</td>
<td>-0.63</td>
<td>-0.44</td>
<td>-0.54</td>
<td>-0.43</td>
<td>-0.57</td>
<td></td>
</tr>
<tr>
<td>Norm Contrib(reward prob.; duration; max amplitude)</td>
<td>0.32</td>
<td>0.56</td>
<td>0.34</td>
<td>0.47</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>Norm Synergy(reward spike count; duration)</td>
<td>0.05</td>
<td>0.00</td>
<td>0.12</td>
<td>0.10</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Norm Contrib(reward prob.; duration; max amplitude)</td>
<td>-0.91</td>
<td>-0.49</td>
<td>-0.81</td>
<td>-0.91</td>
<td>-0.16</td>
<td></td>
</tr>
<tr>
<td>Norm Contrib(res spike count; duration)</td>
<td>0.00</td>
<td>0.51</td>
<td>0.09</td>
<td>0.00</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>Norm Contrib(reward prob.; res spike count; duration)</td>
<td>0.09</td>
<td>0.00</td>
<td>0.10</td>
<td>0.09</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Norm Synergy (total spike count; duration)</td>
<td>-0.76</td>
<td>-0.65</td>
<td>-0.50</td>
<td>-0.49</td>
<td>-0.37</td>
<td></td>
</tr>
<tr>
<td>Norm Contrib(reward prob.; total spike count; duration)</td>
<td>0.04</td>
<td>0.08</td>
<td>0.19</td>
<td>0.15</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Norm Contrib(reward prob.; total spike count; duration)</td>
<td>0.20</td>
<td>0.27</td>
<td>0.31</td>
<td>0.36</td>
<td>0.50</td>
<td></td>
</tr>
</tbody>
</table>

Mean over positive and negative response duration-informative cells of MI, normalized synergy, and contribution between the reward probability and the different response features.
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). 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 thus 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 (Ahissar et al. 2000; Georgopoulos et al. 1986; Gershon et al. 1998; Shadlen and Newsome 1998). Other studies have focused on information in spike patterns (Arabzadeh et al. 2006; Friedrich et al. 2004; Ikegaya et al. 2004; Jones et al. 2004; Panzeri et al. 2001; Prut et al. 1998; Victor and Purpura 1996). 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 encodes reward probability not only 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.

APPENDIX

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 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 seek to evaluate how many samples (spike counts/rates) are needed (using SPRT) to determine the neuron’s firing rate after the switch has occurred. The likelihood ratio for the two hypotheses is

$$ s = \log \frac{L(x'|\lambda_1)}{L(x'|\lambda_2)} $$

where $x' = (x_1, \ldots, x_n)$ are $n$ independent and identically distributed data samples

$$ p(x|\lambda) = \lambda^e^x = \lambda^e \frac{x!}{x!} $$

$$ s = \log \frac{L(x'|\lambda_1)}{L(x'|\lambda_2)} = \log \frac{\prod_i p(x_i|\lambda_1)}{\prod_i p(x_i|\lambda_2)} = \log \frac{\prod_i p(x_i|\lambda_1)}{\prod_i p(x_i|\lambda_2)} $$

$$ = \sum_i \log \frac{p(x_i|\lambda_1)}{p(x_i|\lambda_2)} = \frac{1}{n} \sum_i \log \frac{p(x_i|\lambda_1)}{p(x_i|\lambda_2)} $$

$$ = nE[\log p(x|\lambda_1)p(x|\lambda_2)] $$

which is also denoted as the Kullback–Leibler distance (Cover and Thomas 1991)

$$ D_k[p(x|\lambda_1)||p(x|\lambda_2)] = \sum p(x|\lambda_1) \log \left( \frac{\lambda_1 e^{-\lambda_1/t_1}}{\lambda_2 e^{-\lambda_2/t_2}} \right) $$

$$ = \sum p(x|\lambda_1) \left[ \log \left( \frac{\lambda_1}{\lambda_2} \right) + (\lambda_2 - \lambda_1) \right] $$

$$ = \log \left( \frac{\lambda_1}{\lambda_2} \right) E(x|\lambda_1) + (\lambda_2 - \lambda_1) $$

$$ = \log \left( \frac{\lambda_1}{\lambda_2} \right) x_1 + (\lambda_2 - \lambda_1) $$

Let $n_{R|R1+\Delta}$ denote the number of samples needed to detect a distribution switch from $\lambda = R$ to $\lambda = R(1 + \Delta)$, $n_{R|R1-\Delta}$ denote the number of samples needed to detect a distribution switch from $\lambda = R$ to $\lambda = R(1 - \Delta)$, and $S_{th}$ denote the ratio acceptance threshold (the threshold to detect the distribution change). We can express the required sample sizes as

$$ n_{R|R1+\Delta} = \frac{S_{th}}{E \left[ \log \frac{p(x|\lambda_1)}{p(x|\lambda_2)} \right]} $$

$$ = \frac{S_{th}}{\log \left( \frac{R(1 + \Delta)}{R} \right) R(1 + \Delta) - R\Delta} $$

$$ n_{R|R1-\Delta} = \frac{S_{th}}{E \left[ \log \frac{p(x|\lambda_1)}{p(x|\lambda_2)} \right]} $$

$$ = \frac{S_{th}}{\log \left( \frac{R(1 - \Delta)}{R} \right) R(1 - \Delta) + R\Delta} $$

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 $>1$ 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.

**Acknowledgments**

We acknowledge the authors’ specific contributions: N. Parush initiated and designed the study of response duration, developed the information theoretic tools, performed the data analysis, and wrote the manuscript; D. Arkadir, A. Nevet, and G. Morris trained the monkeys for the behavioral tasks and recorded Neuralg activity during the performance of the task; H. Bergman contributed to training of the monkeys, recording, and the writing of the manuscript; and N. Tishby and I. Nelken contributed to the development of the information analysis tools and writing of the manuscript.

**Grants**

This study was partly supported by Netherlands Friends of the Hebrew University “Fighting against Parkinson” grant to H. Bergman. I. Nelken was supported by the German–Israel Foundation and by the VolkswagenStiftung. N. Parush and G. Morris were supported by a Horowitz fellowship and D. Arkadir and A. Nevet were supported by the MD–PhD program of the Hebrew University–Hadassah Medical School.

**References**


