

Dynamics of Neural Population Responses in Prefrontal Cortex Indicate Changes of Mind on Single Trials

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Summary

Decision making is a complex process in which different sources of information are combined into a decision variable (DV) that guides action [1, 2]. Neurophysiological studies have typically sought insight into the dynamics of the decision-making process and its neural mechanisms through statistical analysis of large numbers of trials from sequentially recorded single neurons or small groups of neurons [3–6]. However, detecting and analyzing the DV on individual trials has been challenging [7]. Here we show that by recording simultaneously from hundreds of units in prearcuate gyrus of macaque monkeys performing a direction discrimination task, we can predict the monkey's choices with high accuracy and decode DV dynamically as the decision unfolds on individual trials. This advance enabled us to study changes of mind (CoMs) that occasionally happen before the final commitment to a decision [8–10]. On individual trials, the decoded DV varied significantly over time and occasionally changed its sign, identifying a potential CoM. Interrogating the system by random stopping of the decision-making process during the delay period after stimulus presentation confirmed the validity of identified CoMs. Importantly, the properties of the candidate CoMs also conformed to expectations based on prior theoretical and behavioral studies [8]: they were more likely to go from an incorrect to a correct choice, they were more likely for weak and intermediate stimuli than for strong stimuli, and they were more likely earlier in the trial. We suggest that simultaneous recording of large neural populations provides a good estimate of DV and explains idiosyncratic aspects of the decision-making process that were inaccessible before.

Results

Psychophysical studies of the decision-making process in various contexts suggest an underlying neural mechanism based on integration of evidence toward a decision criterion [11–17]. Supporting evidence for this mechanism has emerged from electrophysiological studies of the parietal cortex, frontal cortex, basal ganglia, and superior colliculus of monkeys performing simple perceptual decisions [3, 5, 18–22]. More

recently, magnetoencephalography, electroencephalography, and functional magnetic resonance imaging studies have revealed homologous mechanisms in the human brain [23–26].

Although these studies have significantly advanced our understanding of the decision-making process, they have mainly relied on statistical analyses across trials because of the stochastic nature of spiking activity at the single-neuron level. Yet tracking the evolution of the decision variable (DV) on single trials and relating fluctuations in the DV to internal cognitive states and overt behavior are critical for incisive tests of current models of decision making. Recent advances in multielectrode recording promise to break this barrier through measurement and analysis of the underlying neural population responses on single trials. So far, this ability has been mainly used in the field of neural prosthetics, where accurate, real-time decoding of neural population responses is necessary for guidance of motor prosthetic devices (e.g., [27, 28]). However, similar techniques can also be used to advance our understanding of cognitive processes, especially decision making [7, 29].

We used 96-channel multielectrode arrays to record from neural populations in area 8Ar of the prearcuate gyrus of two macaque monkeys while they performed a direction discrimination task [30, 31] (Figure 1A). On each trial, the monkey viewed a patch of randomly moving dots for 800 ms. After a delay period of variable length, the monkey received the “go” cue and reported the perceived motion direction by making a saccadic eye movement to one of the two available targets (T1 and T2). The multielectrode array covered 4 mm × 4 mm of the cortical surface (Figure 1B) and enabled us to record simultaneously from hundreds of single- and multi-neuron units in a significant portion of the prearcuate gyrus. Compatible with previous studies, many units showed differential activity for the two choices during the motion viewing and delay periods [20, 32], in addition to the perisaccadic period [33] (Figure 1C).

To explore the efficacy of simultaneous, high-density recording for analyzing dynamics of the decision-making process, we trained a logistic classifier to predict the monkey's upcoming choice based on neural population responses at successive times during individual trials (100 ms sliding window; see the [Supplemental Experimental Procedures](#)). The classifier finds a set of linear weights (\vec{w}) on the population neural responses (\vec{r}) that maximizes the probability of correctly predicting the choice. Although it is possible to improve the prediction accuracy by adopting more-sophisticated nonlinear models, in this report we adhere to the linear model for its simplicity and biological plausibility. Other models yielded qualitatively similar results. Figure 2A shows the cross-validated accuracy (see the [Supplemental Experimental Procedures](#)) of our model, averaged across sessions. Model prediction accuracy is near chance at the beginning of the trial but rises quickly ~200 ms after motion onset, reaching perfection just before the saccade.

Across 15 data sets, the prediction accuracy of the population responses was much higher than that of the average single unit (Figure 2B). In the 100 ms window immediately before the “go” cue, the cross-validated accuracy of

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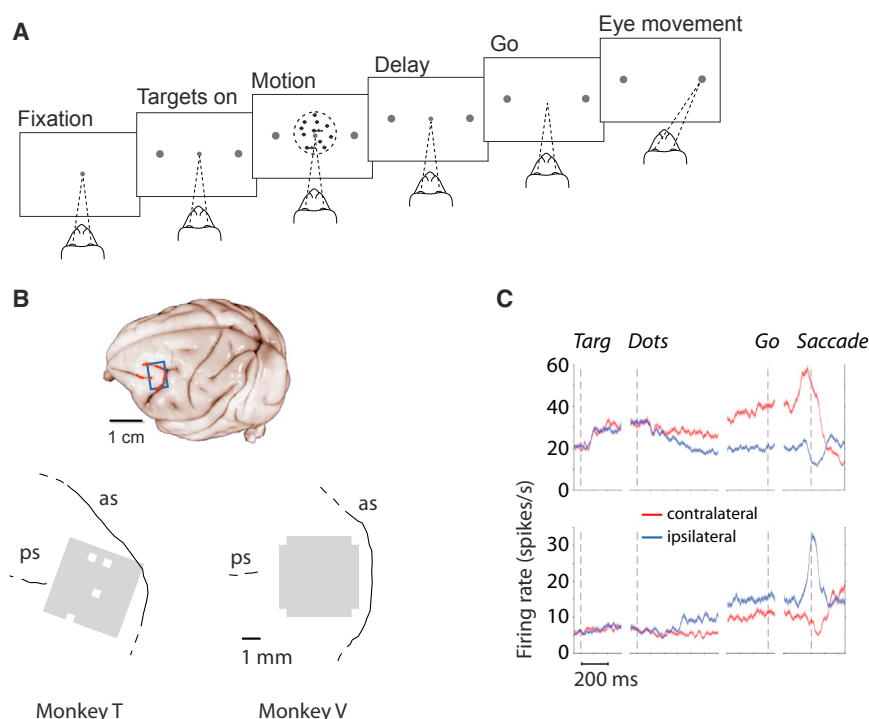


Figure 1. Multielectrode Recording from the Prearcuate Gyrus during a Direction Discrimination Task

(A) Behavioral task. The monkey views 800 ms of random dot motion while maintaining its gaze on a central fixation point. The strength and direction of motion varied randomly from trial to trial. After a variable delay period, the monkey received the “go” signal (fixation point disappeared) and reported the perceived motion direction with a saccadic eye movement to one of two visual targets. Correct responses were rewarded with juice after a short hold period.

(B) Two macaque monkeys were implanted with multichannel electrode arrays in the prearcuate gyrus, which is marked with a blue box on the lateral surface of a typical macaque brain (top; University of Wisconsin Brain Collection). The exact location of each array with respect to the arcuate (as) and principal (ps) sulci is shown for each monkey (bottom). The white squares on the array show the locations of the ground pins. The portions of the principal and arcuate sulci that were visible in the craniotomy are indicated with black lines. Dashed segments at the end of a sulcus indicate that the sulcus extended in that direction beyond our window of visibility.

(C) Average responses of two example prearcuate units for correct ipsilateral and contralateral choices. The units were recorded from the same electrode in the same session but had different motion and saccade selectivities. Shading indicates mean \pm SEM.

the population prediction was close to 0.9 on average (mean \pm SEM: 0.86 ± 0.01), whereas the average accuracy of individual units was barely above chance (mean \pm SEM: 0.557 ± 0.001) and was significantly smaller than that of the population (*t* test, $p < 10^{-8}$). More importantly, not only was population performance better than the average single unit, but it was consistently superior to the best unit recorded in each session (Figure 2C; *t* test, $p = 3 \times 10^{-5}$). The population was superior to individual units in other time epochs as well (data not shown).

The increased prediction accuracy afforded by multielectrode recording enabled more accurate tracking of the decision variable over time. In essence, our logistic regression finds the best hyperplane that separates the population response patterns associated with the two choices. The population response pattern at each moment can be envisioned as a point in a high-dimensional space whose axes are the firing rates of individual units. The distance of this point from the discriminant hyperplane ($\vec{w}^T \vec{r}$) represents the strength of model’s prediction: a small distance corresponds to low certainty about the monkey’s upcoming choice, and a large distance corresponds to high certainty. We call this distance “model decision variable.” The model DV provides an estimate of the monkey’s internal DV, especially when the model prediction accuracy is high. Averaged across trials, the model DV gradually increased from zero to large values (positive and negative values corresponded to T1 and T2 predictions, respectively; Figure 3A). The rate of this rise depended on the strength of motion, especially during the motion-viewing period (Figure 3A, inset): DV increased more rapidly for stronger stimuli, compatible with previous observations in parietal and prefrontal neurons, where the rate of change of neural responses depends on the strength of sensory evidence [3, 6, 20, 34, 35].

Similarly, on individual trials, the DV fluctuated around the discriminant hyperplane at the beginning of the motion-viewing period but gradually moved farther from the hyperplane over time. After gaining an initial distance, the population-based DV typically stayed on one side of the hyperplane during the late motion-viewing period and the ensuing delay (Figure 3B, two example trials). On a minority of trials, however, the population response crossed from one side of the hyperplane to the other side during the trial, signaling a shift in the predicted choice from one target to the other (Figure 3C, two example trials).

An intriguing possibility is that these changes in DV sign, calculated from the neural population response, identify changes of mind (CoMs) that occur in human and animal observers as they make choices on the basis of variable evidence [7–10]. Alternatively, however, changes in sign of the DV might simply reflect noise from any number of sources that are irrelevant to performance on the task.

We conducted four analyses to test whether observed variations in the DV reflect, at least in part, genuine changes of mind. The first analysis concerns the reliability of DV fluctuations for monitoring the momentary “decision state” of the system as time passes during long-duration trials. The remaining three analyses assess whether intratrial DV sign changes conform to change-of-mind properties that are predicted by decision-making models and empirically observed in humans and monkeys performing a similar decision-making task.

Prediction of Choice Is Reliable throughout Long Delay Periods

The initial important question is whether intratrial sign changes in the DV, like those illustrated in Figure 3C, are simply noise or whether they accurately reflect moment-to-moment variation in the decision state of the system—the decision that would

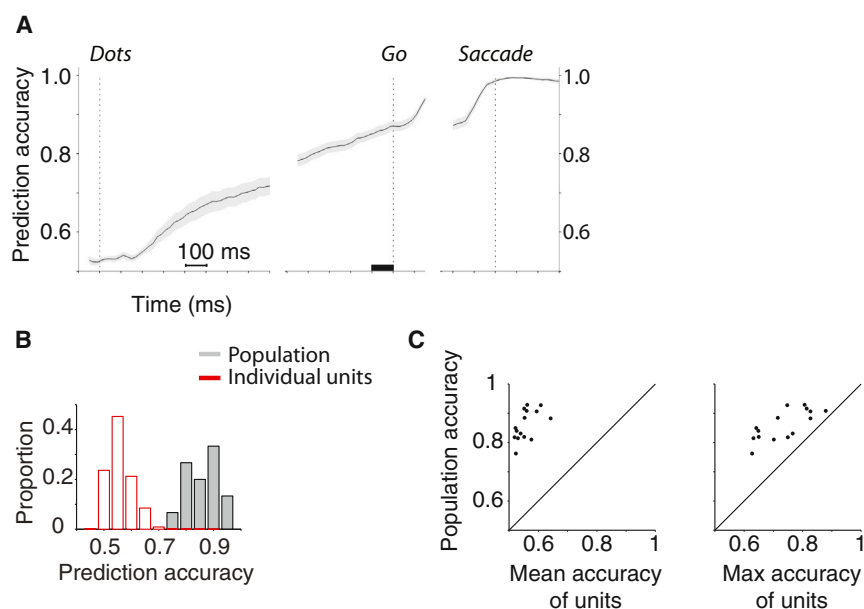


Figure 2. The Recorded Neural Populations Afford High Accuracy Prediction of the Monkeys' Choices

(A) Prediction accuracy of the recorded population for the monkey's choice. A logistic model was fit to 90% of the trials in each session and was used to predict the choice in the remaining 10%, in sliding 100 ms bins. The dark trace and shading indicate mean \pm SEM across the sessions. The horizontal black bar indicates the time window that was used in the analyses in (B) and (C).

(B) The neural population classifier is a better predictor of the monkey's choice than the average of the individual units recorded in a session. The probability densities of population and individual unit choice prediction accuracies are highly distinct. Prediction accuracies were calculated for a 100 ms window immediately before the "go" cue.

(C) Comparison of population choice prediction accuracy with the mean (left) and best (right) individual units. Each point represents one data collection session. Even the best individual units are inferior to the population.

be made if the trial were to end *now*. We addressed this question by separately analyzing predictive accuracy of the population activity for trials of different delay period duration. During each experiment, the duration of the delay period was varied randomly among several preset values (see the [Supplemental Experimental Procedures](#)). We grouped the trials into quintiles based on the length of the delay period. For each quintile, we then calculated the hyperplane that best separated the T1 and T2 choice trials from the pattern of neural population response in the 100 ms immediately *before* the "go" cue. For all quintiles, the model achieved high cross-validated accuracies for predicting the monkey's choice on individual trials ([Figure 4A](#); 0.76 ± 0.02 for the shortest delays to 0.87 ± 0.02 for the longest delay). The results were not critically dependent on using a separate model for each quintile; similar results were obtained when a single model was used for all quintiles ([Figure S1](#) available online). Although predictive accuracy improved modestly for longer delay periods, it was far above chance even for the shortest delays. Thus, the sign of the DV during the delay period is a good predictor of choice, even for the shortest-duration trials.

Importantly, there is no distinction between long- and short-duration trials prior to the first possible "go" signal—the temporal structures of the trials are identical until that point. Thus, predictive accuracy of the DV sign measured prior to the "go" signal on shorter-duration trials provides an objective estimate of predictive accuracy on longer-duration trials *had those trials ended at an earlier point in time*. We therefore conclude that DV sign changes on longer-duration trials (e.g., [Figure 3C](#)) provide insight into the momentary decision state of the system, reflecting in part choices that would have been made had we terminated the trial earlier.

DV Sign Changes Reflect Expected Properties of Behavioral Changes of Mind

After identifying candidate CoMs using DV sign changes, we performed three analyses to determine whether candidate CoMs exhibit properties that are associated with actual CoMs in behavioral studies and are expected from current models of the decision process [7, 8].

First, CoMs should happen more frequently for weak- and intermediate-strength motion stimuli than for strong motion stimuli because counterevidence that elicits a CoM will occur less frequently for stronger stimuli [8]. [Figure 4B](#) shows that the predicted trend is indeed present in our data (Equation S3 in the [Supplemental Experimental Procedures](#), $\beta_1 = -0.23 \pm 0.04$, $p = 1.6 \times 10^{-8}$).

Second, CoMs are more likely to steer the decision from an incorrect to a correct option than vice versa because they are based on evidence that is not yet processed during the initial stages of choice formation [8, 9]. On average, incorporation of additional evidence should improve the decision maker's accuracy. Consistent with this prediction, we observed that candidate CoMs derived from our neural population data were more likely to shift the predicted choices from the incorrect target to the correct target ([Figure 4C](#)). The difference in CoM toward correct versus wrong choices was significantly larger than zero (sign test, $p < 10^{-8}$) and grew as a function of motion strength (Equation S4 in the [Supplemental Experimental Procedures](#), $\beta_1 = 0.19 \pm 0.07$, $p = 0.009$). Thus, CoMs increased the monkey's overall reward intake. We also tested whether the monkey's final choices after CoMs were more likely to be correct compared to the trials in which CoMs were not detected. Controlling for motion strength and delay duration, we found no significant difference between the two trial types (Equation S5 in the [Supplemental Experimental Procedures](#), $\beta_2 = -0.004 \pm 0.043$, $p = 0.92$). Since CoMs improved the probability of a correct response, they must have occurred selectively on trials for which the initial decision state was likely to be incorrect, perhaps due to lapses of attention earlier in the trial.

Third, the probability of a CoM should decrease as the monkey waits during the delay period. Due to the finite latency of visual signals, processing the last sensory evidence necessarily occurs during the delay period, and memory processes related to the visual stimulus may influence the final decision as well. As the delay period proceeds, however, a final commitment to a choice is increasingly likely. Consistent with this hypothesis, we observed a monotonic decline in the probability of a CoM with delay period duration ([Figure 4D](#);

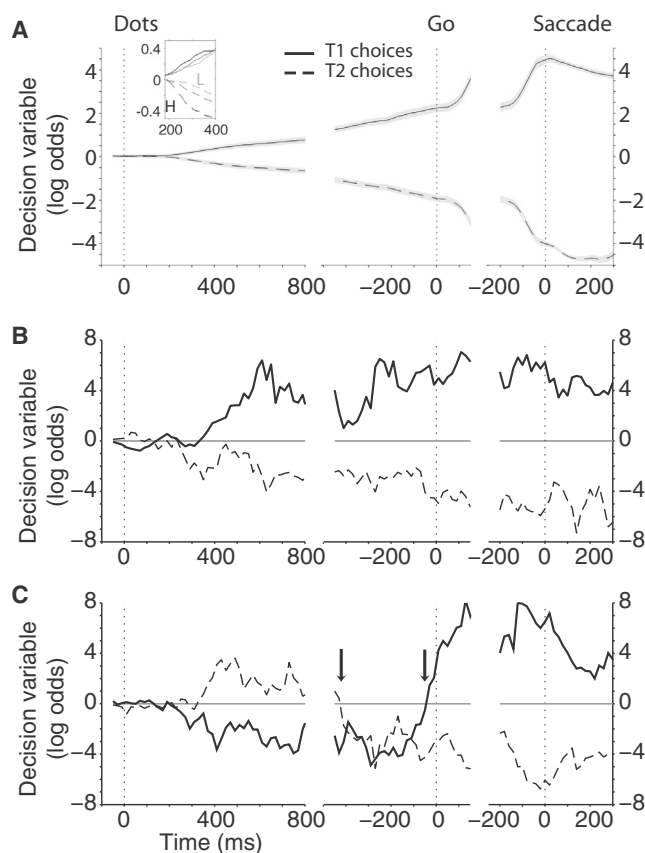


Figure 3. The Model Decision Variable Indicates Accumulation of Evidence over Time, and Intratrial Changes in the Sign of the DV Identify Candidate Changes of Mind

A logistic regression (Equation S1 in the [Supplemental Experimental Procedures](#)) was used to find the best hyperplane that separates the population response patterns corresponding to the two choices. The distance of the population response pattern from this discriminant hyperplane represents the model belief about the upcoming choice. We call this distance the model decision variable, or DV.

(A) Average decision variable across the sessions. The inset shows that the buildup of the decision variable during the motion-viewing period depends on stimulus strength (H, motion strength $\geq 20\%$; L, motion strength $\leq 6\%$). The dark traces and shading represent the mean \pm SEM.

(B) Two sample trials in which the model DV built up to a positive (solid) or negative (dashed) value and maintained its sign throughout the trial. The trials ended with T1 and T2 choices, respectively.

(C) Two sample trials in which the sign of the model DV flipped during the delay period, indicating a change of predicted choice based on the model. Arrows indicate the time of flip.

Equation S6 in the [Supplemental Experimental Procedures](#), $\beta_2 = -0.21 \pm 0.01$, $p < 10^{-8}$).

The success of the model for the delay period encouraged us to investigate the properties of candidate CoMs during the motion-viewing interval as well, even though success was less certain for two reasons. First, because we used a constant stimulus duration in all experiments, we were unable to validate candidate CoMs during motion viewing using short-duration trials as described above for the delay period. Second, candidate CoMs were less reliable during motion viewing as reflected in the lower predictive power of the model during this interval ([Figure 2A](#)). Nevertheless, the properties of candidate CoMs during the motion-viewing interval were similar to those during the delay period. CoMs were less frequent for

stronger stimuli ([Figure S2A](#); Equation S3 in the [Supplemental Experimental Procedures](#), $\beta_1 = -0.064 \pm 0.021$, $p = 0.003$) and were more likely to change the DV in the direction of a correct judgment ([Figure S2B](#); Equation S4 in the [Supplemental Experimental Procedures](#), $\beta_1 = 0.71 \pm 0.18$, $p = 0.001$). The frequency of candidate CoMs at the beginning of the motion-viewing period was low because the DV is initially near chance and must first build up toward one of the choices before a CoM can be detected reliably (see the [Supplemental Experimental Procedures](#)). Thus, CoM frequency increased initially but declined after 300 ms of motion viewing ([Figure S2C](#)) due to increased likelihood of commitment to a choice, consistent with the delay period results ([Figure 4D](#)). These results from the motion-viewing period are encouraging but should be interpreted cautiously because of sensitivity of some results ([Figure S2C](#)) to time window sizes (see the [Supplemental Experimental Procedures](#)).

Overall, candidate CoMs identified from high-density recordings of prefrontal cortex conform to all three predictions based on behavioral analysis of changes of mind.

Discussion

Neurophysiological studies have typically sought insight into the dynamics of decision making and its neural mechanisms through statistical analysis of large numbers of trials from sequentially recorded single neurons or small groups of neurons. Measurement and analysis of the DV on individual trials has been challenging due to technical and conceptual limitations. We sought to overcome these limitations by (1) recording simultaneously from hundreds of units in cortical areas hypothesized to contribute to the decision-making process, (2) developing simple, efficient algorithms for estimation of the covert DV from neural population responses, and (3) implementing a new analytic approach to verify the accuracy of the estimated DV fluctuations during the delay period.

The ability to track moment-to-moment variation of the DV enables the study of important aspects of the decision-making process that have been largely inaccessible thus far. As a proof of concept, we focused on changes of mind during perithreshold judgments of motion direction. Our behavioral task created fertile conditions for CoMs due to the noisy, temporally extended nature of the visual motion stimulus. Our first new finding is that the covert DV can be accurately tracked during single behavioral trials using the methods introduced in this paper. Crucially, trials with short delay periods verify the accuracy of estimates of the covert DV on longer trials; in essence, short-delay trials act as “probes” of ongoing DV estimates on longer trials [[34](#), [36](#), [37](#)]. Our second new finding is that changes in the sign of the DV identify candidate CoMs and that candidate CoMs conform to three different predictions based on prior behavioral and modeling studies. Together, these results demonstrate the power of high-density neural recordings for single-trial estimates of the fluctuating DV and for detection of covert changes in decision state commonly referred to as changes of mind.

CoMs can arise from various sources: changing sensory evidence [[8](#)], correction of an initial confusion about stimulus-response association [[9](#)], incorporation of a new decision policy, or retrieval of new information from memory [[8](#)]. Our monkeys’ CoMs may stem from any of these sources or others, such as simple lapses in attention or effort. Accumulated over time, CoMs tend to be self-corrections, often benefitting the decision maker by improving accuracy. By characterizing

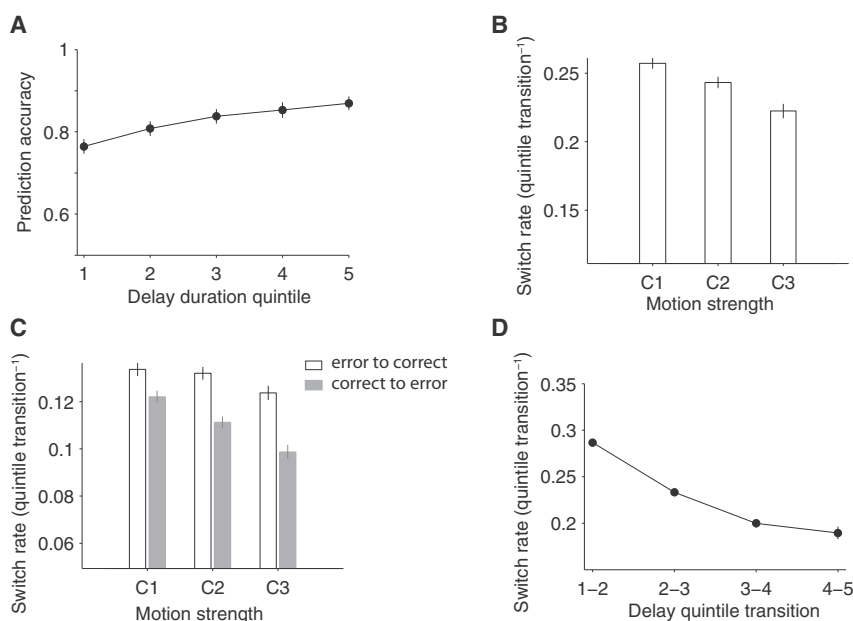


Figure 4. The Sign of the Model DV Reliably Reflects the Incipient Decision throughout the Delay Period

Intratrial changes in the sign of the DV conform to CoM properties expected from theoretical and behavioral studies.

(A) Cross-validated prediction accuracy of the monkey's choice for different delay durations. Trials were grouped into quintiles based on delay period duration. Accurate choice prediction on short-duration trials confirms that variation in DV reflects the monkey's decision state at early points in long-duration trials. Thus, intratrial changes in DV sign are consistent with CoM as opposed to extraneous noise (see the Results).

(B) Probability of switching from one predicted choice to another in consecutive delay quintiles declines for stronger motion (C₁, motion strength ≤ 6%; C₂, 6% < motion strength ≤ 20%; C₃, motion strength > 20%).

(C) Switches in the predicted choice were more likely to rectify an erroneous choice, especially for stronger motion stimuli.

(D) Switches were more frequent early during delay.

Error bars indicate the SEM. See also Figures S1 and S2.

the neural DV and identifying CoMs on individual trials, we show that monkeys, like humans, exhibit self-correcting behavior.

Past studies have documented cortical and subcortical fluctuations in neural activity that might correspond to changes of mind [7, 29, 38]. Those studies focused on the detection of discrete hidden states in the responses of single neurons [38] or small numbers of simultaneously recorded neurons [7, 29]. The discrete states are defined as specific patterns of spiking across the recorded population. Transitions from one state to another—often formalized by a hidden Markov model—can occasionally signal changes of mind. Here we extend those studies by extracting a continuous measure of the DV, characterizing its dynamics, and confirming the inferred CoMs by interrogating the monkey's choice at variable times.

The probabilistic characterization of the choice provides an analog estimation of the DV, compatible with the quantitative models of the decision-making process [12, 17, 35, 39]. In those models, sources of information are integrated into an analog variable [31] that explains both the choice and reaction time. However, it remains to be seen whether various factors, such as priors and value information, that bear on the decision in those models also modify our estimated DV.

Our model incorporates the responses of all neurons recorded on the array in a given experiment. Unlike in many classic single-neuron studies, we did not focus on merely the units that were highly selective for the motion directions or target locations used in the task [20, 40, 41]. We do not know whether all of the recorded neurons contributed to the decision-making process. Nor do we know the exact role that they may play in the process. However, the recorded neurons are informative about the monkey's upcoming action as indicated by the model's high prediction accuracy. We simply exploit this information to provide a probabilistic glimpse into the DV that supports choice and CoM. Our model is not a mechanistic account of how the DV is constructed or how commitment to a choice is made. Addressing those questions requires further experiments and selective recording and

manipulation of neurons based on their response selectivity (e.g., [18, 34, 42–44]).

The advent of techniques for routine, simultaneous recording of tens to hundreds of neurons offers unique opportunities for cognitive neuroscience, particularly for the detection and tracking of cognitive states and processes that occur unpredictably in time and have no overt behavioral correlate. Covert cognitive processes are difficult to monitor in classical neurophysiological studies that require time-locking and across-trial signal averaging, but they are potentially detectable in real time from neural population activity. Even when covert neural processes are detectable, however, their interpretation will depend on creative strategies for behavioral verification. Our study of CoM offers a first step in that direction.

Supplemental Information

Supplemental Information includes Supplemental Experimental Procedures and two figures and can be found with this article online at <http://dx.doi.org/10.1016/j.cub.2014.05.049>.

Author Contributions

R.K. and W.T.N. developed the concept. J.B.R. collected the data. R.K. designed the analyses. R.K. and C.J.C. implemented the analyses. R.K. and W.T.N. wrote the paper.

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