



Preparing and selecting actions with neural populations: toward cortical circuit mechanisms

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How the brain selects one action among multiple alternatives is a central question of neuroscience. An influential model is that action preparation and selection arise from subthreshold activation of the very neurons encoding the action. Recent work, however, shows a much greater diversity of decision-related and action-related signals coexisting with other signals in populations of motor and parietal cortical neurons. We discuss how such distributed signals might be decoded by biologically plausible mechanisms. We also discuss how neurons within cortical circuits might interact with each other during action selection and preparation and how recurrent network models can help to reveal dynamical principles underlying cortical computation.

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Introduction

How the brain decides to select an action among multiple alternatives is a central question of neuroscience. As far as a decision entails the selection of an action, decisions are tightly linked to action preparation. Evidence favors the idea that these processes occur in parallel and might share neural substrates: multiple potential actions are simultaneously ‘prepared’ in motor related areas while an action is being selected. Selection of actions may be performed through competition among neurons preparing for available actions [1–3]. Thus, the study of the action preparation process will help to advance our understanding of decision-making and *vice versa*.

The field has made much progress in understanding single neuron response properties in different behavioral paradigms in different brain areas. But we still lack an understanding of how populations of neurons within and

across circuits act together to perform the computations required for a decision. Recent studies have highlighted the distributed and mixed nature of the representation of decision-related and action-related signals within neural populations. This prompts the question of how interactions between these neurons can perform circuit computations and how the distributed signals can be decoded in downstream areas. Here, we review recent studies addressing these questions and other steps toward elucidating the computations and circuit dynamics underlying decision-making.

Although the processes of decision-making and action preparation are thought to take place at multiple cortical and subcortical levels, including the basal ganglia, and superior colliculus [2,4], here we focus mainly on cortical areas, namely primary motor and higher motor cortices, including the frontal eye fields in the primate prefrontal cortex, and parietal association cortex.

Classical view of action preparation and decision-making

One old and influential hypothesis for the neural mechanism of action preparation is that it simply involves moderate pre-activation of the same neurons that are responsible for execution of the action being considered or prepared. This view is consistent with the observation that the level of activation during preparation is lower than required for actually executing the actions and is positively correlated with how quickly an animal responds to a cue to initiate the action [5,6]. Extending this hypothesis, action selection or decision-making is performed through ‘competition’ between neurons responsible for preparing the available actions [1]. Factors influencing a choice, such as sensory evidence in the case of perceptual decision or the value of options in the case of value-based decision, modulate the subthreshold activity and thereby bias the final choice. The action associated with most active neurons at the time of reporting a choice will be the selected action.

Notably, in a task where a subject is free to choose when ready, ‘pre-activation’ signals can indicate not only what action to be chosen but also when. A neuron preferring the eventually chosen action appears to gradually increase its activity at subthreshold level during decision period and the activity reaches a constant level of activation just before the action [2]. Such ‘ramp-to-threshold’ activity has been seen in several species and contexts, including

timing behavior [7], proactive movement in response to sensory stimuli [8], and giving up waiting in a waiting task [9^{••}].

In some sense, the level of activity of ramp-to-threshold neurons dynamically reflects how ‘close’ the animal is to executing the action. But in a task where the sensory accumulation and movement preparation were dissociated, the activity of many neurons in lateral intraparietal area (LIP) reflected sensory accumulation more so than motor preparation [10]. The interpretation of what exactly these neurons encode (e.g., movement intention/preparation, sensory accumulation or saliency of the stimulus) is still a matter of debate [11,12]. Rather than focusing on the question of ‘what is represented’ by a particular area or set of neurons, it may be more productive to address this issue by understanding the causal role of the activity of these neurons: how the activity is decoded or read out by the downstream areas and eventually used for behavior.

Multiplexed representation of decision-related and action-related signals

More recently, the view that decision-related or movement preparatory activity simply consists of a subthreshold, scaled-down, version of action-related activity has been questioned. That such activity patterns might be a special case of a much broader class of single neuron correlates of decision-making started to become evident once researchers began to sample neurons in a relatively unbiased manner, with fewer constraints in selecting neurons. In the context of action preparation, Churchland *et al.* [13] observed a striking mismatch between preferred movement direction tuning during the preparation versus the movement phases within individual neurons in monkey primary motor and premotor cortex. Similarly, in the context of perceptual decision-making, several groups reported that signals correlated with sensory evidence and predictive of choice in the posterior parietal cortex and frontal eye field are not as simple as might be imagined. First, they occur not only in the form of classically observed ramping activity but also in a variety of different temporal patterns [14[•],15^{••},16,17[•]]. Furthermore, decision signals can be mixed with decision-unrelated signals within individual neurons [14[•],17[•]]. Thus, reading out decision-related signals requires de-mixing them from other signals [18^{••},19,20]. These findings call for taking into account a broader range of neuronal responses and asking more complicated but interesting questions: how do decision-related neurons exhibiting different dynamics, ramping and otherwise, interact with each other, and how are these signals read out in downstream areas to cause an action?

Reading out population neural activity

To understand how the variety of responses in cortical populations contribute to behavior, we need to understand

the mechanism of decoding population activity. In turn, to gain insights on the decoding mechanisms, it is important to understand how the signals are distributed across populations of cortical neurons.

When signals are distributed across neurons, it is likely to be useful to look at population activity from a multi-dimensional perspective [19,21[•]]. The population activity of any number of neurons at a given time point can be represented as a single point in a multi-dimensional space, and the population activity pattern over time as a trajectory in this space. Given that the neural trajectories normally do not span the entire space, dimensionality reduction can be used to extract important features of the data [19,20,22]. In other words, population activity can be projected onto certain axes, which may be more interpretable and meaningful. Importantly, such a projection also corresponds to taking a weighted sum of the population of neurons’ activity, an operation that might be considered as an elementary kind of neural readout.

A multi-dimensional approach has proven to be useful in the study of decision-making and action preparation [15^{••},23–25,26[•],27]. Applying a multi-dimensional approach to a study of action preparation, Kaufman *et al.* [26[•]] proposed a simple population decoder of motor cortex activity that produces a readout resembling the activity of downstream areas (e.g., muscle activity) during the movement period. Interestingly, when observed through the same decoder, motor cortex output is suppressed during the preparatory period (i.e., when the action is withheld), even though individual neurons can be as active as during movement period. This happens because population trajectory during the preparatory period lies in a subspace orthogonal to the movement subspace. This constitutes a novel mechanism by which movement is withheld during preparatory period, which does not rely on non-linear thresholding mechanisms.

In a decision-making task, population activity can also be collapsed to a relatively few dimensions that carry information about future choice. Mante *et al.* [15^{••}] applied multi-dimensional analysis to recordings from the frontal eye field of monkeys performing a task in which decisions are made based on either the color or the motion direction of a visual stimulus, depending on the context cue presented at the beginning of each trial. Although individual neurons could display complex mixed selectivity, they found a single effective choice axis that was common to both color and motion contexts. This suggests that the same readout mechanism can be used in two different contexts in order to appropriately choose actions according to the sensory evidence.

In tasks in which a subject can freely choose the timing of actions (e.g., a reaction time task or a waiting task), ramp-to-threshold activity has been repeatedly found in multiple

brain areas (Figure 1a). However, this normally involves selection criteria that might exclude neurons that do not exhibit the classical ramp-to-threshold activity but could be crucially involved in the decision process. If a multi-dimensional population approach is applied to datasets obtained in these tasks, a threshold for decision commitment can be defined as a ‘threshold hyperplane’ in population activity (Figure 1b). By analyzing the activity of individual neurons that strongly contribute to this threshold hyperplane, we might be able to better understand the contribution of each neuron to the decision and how downstream circuits can read out these signals.

Park *et al.* [18**] approached the problem of population representation and readout of population activity with a different technique. Using a generalized linear model-based statistical approach, they proposed a mechanism to decode choice from population of LIP activity, which relied on biologically plausible leaky integrators and competition mechanisms and could approximate the statistically optimal decoding model.

These studies have advanced our understanding of how decision-related and action-related signals are distributed across populations of neurons and how downstream circuits might in principle decode them. To examine readout mechanisms directly, a critical step will be to determine what types of signals are actually transmitted to which downstream areas. For example, in many studies of decision-making, it is proposed or implied that the decision-related signal predictive of a future action is

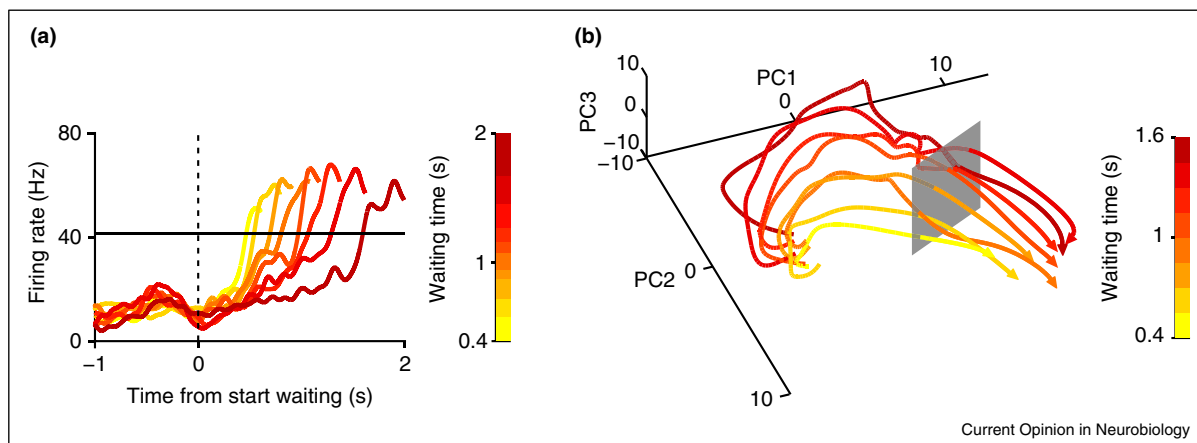
enriched in the signal transmitted out of the cortical decision circuit (e.g., from layer 5 neurons). Although experimentally challenging, attempts to record activity transmitted through a specific projection pathway have been made previously, for example for pathways from the frontal eye fields to the superior colliculus [28,29]. But, these two studies were controversial in terms of whether there is [29] or is not [28] a selective enrichment of certain types of signals sent from the cortex to superior colliculus. With recently developed genetic approaches to record and manipulate activity in specific pathways, we can anticipate that data relevant to this point will become more readily available [30,31,32*,33*,34*].

Computation within a cortical circuit

Understanding the computations performed through interactions amongst cortical neurons is one of the most challenging problems of neuroscience. Cortical circuits consist of different neuronal cell types (e.g., glutamatergic versus GABAergic, parvalbumin-positive versus somatostatin-positive versus vasoactive intestinal polypeptide-positive) distributed across several distinct layers. Each neuron’s input and output connection patterns are systematically organized according to cell identity determined by, for example, cell types and layer [35,36].

An influential idea for the circuit architecture underlying perceptual decision-making is that sensory signals are fed into integration circuits whose activity crossing a threshold level serves as commitment to a decision [37]. More

Figure 1



Levels of approach to study decision-making and action preparation. **(a)** Single-neuron correlates of decision commitment. An example of ramp-to-threshold type activity of a neuron recorded from the rat secondary motor cortex during spontaneous termination of waiting. Trials are grouped according to the time taken to give up waiting, and spike density functions are calculated for each group. Different trials are aligned on the start of waiting. Spike density function traces end at the end of waiting. Note that the activity of this neuron crosses a hypothetical threshold just before giving up waiting (adapted from Murakami *et al.* [9**]). **(b)** Population perspective of decision commitment. Population data (188 neurons) recorded from the rat secondary motor cortex [9**] was projected onto the first three principal components. Principal component analysis was applied to spike density functions during the waiting period of eight different sets of trials, grouped according to waiting times as indicated by the color bar. Note that population activity crosses a hypothetical threshold plane just before giving up waiting.

recently, a similar circuit model was proposed for spontaneous action generation in which actions are generated without explicit sensory inputs [9[•],38]. Furthermore, mutual inhibition between neurons responsible for potential actions is thought to play an important role in competition between different possible actions [39]. But these ideas have not been directly tested and how these models could map onto actual cortical circuits is unknown. To build and test cortical circuit models, a first important step is to correlate the response properties of neurons with their identified cell-types and layers. A second, even more demanding, step is to establish the functional connectivity between neurons and to understand the patterns of signal propagation within the cortical circuit [40,41,42[•]].

Such an attempt has been made in pioneering work by Isomura *et al.* [41], who correlated the response properties of neurons during action preparation and execution with their cell-types and functional connectivity between neurons. They found that most of the inhibitory interneurons, some of which were identified with juxtacellular labeling and immunohistochemistry, were active during movement periods, slightly after movement-related activity of pyramidal neurons. Furthermore, when they examined functional connectivity among neurons with different types of response properties, a few instances of recurrent excitation between pairs of pre-movement type neurons were found, suggestive that they might constitute elements of an integrator circuit.

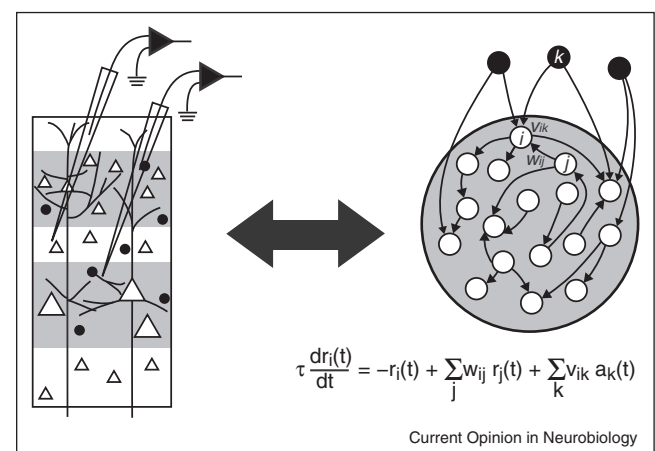
In the context of decision-making, it is proposed that different pools of recurrently-connected excitatory neurons compete with each other through mutual inhibition [39,43], which provides neural substrate of decision-making. Consistent with this model, although not a direct proof, it has been observed that neuron pairs from the 'same pool' exhibit positive correlations and neuron pairs from the 'different pools' exhibit negative correlations in their activity fluctuations across trials [9[•],19,44]. Examining further the sources of correlations will be crucial in pursuing this hypothesis.

Recent advances in optogenetic and pharmacogenetic approaches provide more powerful means to record and manipulate specific elements of neural circuits [45,46]. These approaches have already proven to be powerful in understanding circuit computations in sensory and other systems [34[•],47,48[•]]. Kvistiani *et al.* applied this approach to a study of foraging decision and found cell-type specific functional differentiation of inhibitory interneurons in anterior cingulate cortex of mice [48[•]]. While parvalbumin-positive interneurons were activated upon leaving reward sites, narrow-spiking somatostatin-positive interneurons were active during reward approach. These studies strongly suggest that the diversity of response profiles seen in 'blind' recordings may in part be dictated

by an underlying circuit logic related to the computations being performed. It will no doubt be extremely revealing, albeit painstaking, to systematically map this logic for tasks involving decision-making and action preparation.

As mentioned in the previous sections, recent studies have suggested that multiple signals are often mixed within individual neurons. Meaningful and potentially simple neural dynamics can be hidden in interactions among populations of these neurons in a manner that is not intuitively obvious. In such scenarios, it may be useful, if not necessary, to use model-based approaches to help to analyze dynamics of population activity and relate it to possible circuit computations. While this approach may be still in its infancy, it has been shown that recurrent network models can reproduce important features of population neural activity and animal behavior [15^{••},19,49,50^{••}]. Recurrent networks can be built in a number of different ways. They can be built by explicitly designing a computation [39], but they can also be constructed without explicitly specifying computation, either by fitting dynamics of population neural data compressed in low dimensions [19,25], by constraining what the network should do but not how to do it [15^{••}], or even

Figure 2



Two complementary approaches to circuit-level understanding of decision-making and action preparation. (Left) Schematic illustration of recordings of cortical neuron activity. Recording the activity of neurons together with identification of cell-types of recorded neurons from awake, behaving animals will characterize response properties of different neuron types. (Right) Schematic illustration of a recurrent network model and an example recurrent model equation. In the equation, $r_i(t)$ denotes activity of a model unit i , $a_k(t)$ denotes activity of an external input unit k , w_{ij} denotes connection strength from a unit j to a unit i , v_{ik} denotes connection strength from an external input unit k to a unit i , and τ denotes decay time constant of model unit. Recurrent network models are useful in simulating large number of neurons and analyzing the dynamics of population activity. Detailed information gained from experimental approaches helps to constrain cortical network models. In turn, network models help to explain variable neuronal responses observed in cortex.

by using an independent principle [50^{••}]. By analyzing these models, one can extract the dynamical structure in the network that is critical for performing a given task by analyzing locally linear dynamical system [51]. For example, in the recurrent network model of Mante *et al.* [15^{••}], different continuous attractors appear for different contexts, enabling integration of sensory stimuli in a context-dependent manner. Local dynamics near the attractor select the task-relevant sensory features to be integrated, while ignoring the irrelevant features.

Although recurrent network models are proving to be a powerful tool to analyze cortical computation, they remain to be validated and refined by more detailed experimental data. Recurrent network models do not yet normally take into account cortical circuit architecture (e.g., layer and cell types) or correlation structure among neurons (but see [52]). As mentioned above, these types of information are becoming more readily available. We expect that a combination of experimental approaches to provide information about response properties and interactions of cortical circuit elements and theoretical approaches to build models incorporating these data and understand principles for cortical computation will be fruitful (Figure 2).

Conclusion

Decision-related and action-related signals appear to be distributed in neural populations with various temporal profiles and mixed with unrelated signals, indicating the necessity of studies of population decoding and interactions among populations of neurons. Dimensionality reduction techniques and other statistical approaches provide important tools to extract relevant information from populations of neurons and can even suggest possible mechanisms for decoding by downstream circuits. Optogenetic approaches allow recording and manipulation of neural activity transmitted to specific downstream areas, experiments that can help to test putative decoding strategies and link decision-related information to animal behavior.

Understanding how populations of neurons interact within a cortical circuit is even more challenging. For this purpose, recurrent network models are made to reproduce important features of neural population data and behavior. Analysis of these network models can be used to extract simple dynamical structures in apparently diverse population dynamics. To further understand the computations performed in cortical circuits, existing cortical circuit architecture must be integrated into models of cortical networks. For this purpose, it is crucial to continue experimental efforts to provide details of neuronal activity together with cell-identity and functional connectivity, and to incorporate such information into cortical network models.

Conflict of interest statement

Nothing declared.

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While a monkey performed a random dot motion direction discrimination task, the authors recorded from neurons in LIP neurons, including ones conventionally excluded from many previous studies. The study reports various temporal dynamics of signals carrying decision-related information to be much more variable than previously described. Furthermore,

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Monkeys discriminated either the motion direction or the color of the random dots depending on the context cue. Analysis of PFC recordings from monkeys performing the task was combined with the analysis of a recurrent network model trained to solve the same task, leading to a proposed mechanism to link sensory stimuli to motor output in a context-dependent manner. This study provides a nice example of how a recurrent network model and analysis of fixed points and linear dynamics around them can be used to make sense of population neural activity.

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The authors analyzed the activity of posterior parietal cortex neurons from rats performing a visual and/or auditory discrimination task, in which subjects reported whether the rate of stimulus pulses were higher or lower than a predetermined threshold. The neurons were selective for both the sensory modality of the stimulus and for the upcoming choice. Importantly, these two types of selectivity were intermixed within individual neurons and no clusters of neurons in terms of how the signals are intermixed were found.

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The authors analyzed neural data recorded from the prefrontal cortex in monkeys performing a task in which the subject is required to remember the identity and order of two sequentially presented objects. The memory was tested after a delay period with either a recognition task or a recall task. The prefrontal cortex neurons recorded in this task showed linear and non-linear mixed selectivity to the task-related feature, such as the task type, first cue, and second cue. Animal performance could be predicted by the effective dimensionality of the data, because it was reduced in error trials. The dimensionality gained by non-linear selectivity components of neuronal responses was crucial in predicting animal performance. This indicates the importance of non-linearly mixed representation of task variables in solving a complex task.

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The study proposes a novel mechanism for controlling whether or not neural signals are transmitted to downstream target areas, without relying on a threshold or gating mechanism. The authors define 'output-potent' readouts as weighted sums of population activity that resembles most the activity of a downstream area during the movement period. Although neurons are active during preparatory period, such output-potent readouts of population activity are strongly reduced because the population dynamics is constrained to an orthogonal subspace.

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This study used a combination of quantitative behavioral tasks and pathway specific neural manipulation to demonstrate a role of locus coeruleus (LC) noradrenergic input to anterior cingulate cortex (ACC) in controlling behavioral choice strategy. In this study, rats performed two-choice tasks against computer-simulated competitors. While rats used history-dependent strategies when faced with weak competitors or when explicitly trained to generate a pattern of choice sequence, they could switch to 'stochastic' choice mode when challenged with a strong competitor. Manipulating LC noradrenergic inputs to ACC, the authors showed that while activation of this pathway suppressed history-dependent strategies and enhanced a stochastic behavioral mode, inactivation caused an opposite effect.

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