Perceptual Decision-Making: A Field in the Midst of a Transformation

Farzaneh Najafi[1] and Anne K. Churchland[1,*]
[1]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA
*Correspondence: churchland@cshl.edu
https://doi.org/10.1016/j.neuron.2018.10.017

Major changes are underway in the field of perceptual decision-making. Single-neuron studies have given way to population recordings with identified cell types, traditional analyses have been extended to accommodate these large and diverse collections of neurons, and novel methods of neural disruption have provided insights about causal circuits. Further, the field has expanded to include multiple new species: rodents and invertebrates, for example, have been instrumental in demonstrating the importance of internal state on neural responses. Finally, a renewed interest in ethological stimuli prompted development of new behaviors, frequently analyzed by new, automated movement tracking methods. Taken together, these advances constitute a seismic shift in both our approach and understanding of how incoming sensory signals are used to guide decisions.

Introduction

In recent years, the field of decision-making has begun what will likely be a transformation. Historically, work in the field of decision-making was restricted to a small number of species, relied on a limited set of techniques, and leveraged only a handful of theoretical models. This traditional approach was fruitful in revealing behavioral strategies for decision-making under uncertainty and in providing a theoretical framework for understanding how they might be implemented in the brain (Shadlen and Kiani, 2013). However, many questions were left unanswered because the experimental techniques available to test the neural implementations of the models were limited, and the generality of behaviors across species was not known. Fortunately, the shift in recent years surmounts many of these challenges. This shift includes advances in how neural data are acquired and measured, changes in animals and behaviors that are studied, and major developments in how neural data are analyzed (Figure 1). Here, we will describe how these innovations are being used in the field of decision-making and highlight new discoveries that they have revealed thus far. Finally, we will speculate as to how the field is poised to evolve in the coming years.

The Ability to Target Cell Types May Drive Reconsideration of Neural Models of Decision-Making

For many years, electrophysiologists could only identify putative excitatory and inhibitory cells based on spike waveform shape (Niell and Stryker, 2008; Viswanathan and Nieder, 2015), and target projection-specific excitatory neurons via cumbersome methods (Churchland and Lisberger, 2005). As a result, the yield was low and the different cell types within each population were not known. New advances in experimental techniques, however, allow excitatory and multiple subtypes of inhibitory neurons to be reliably labeled. This has offered new insight into their specific contributions to decision-making, and has made it finally possible to test predictions of long-standing models of decision-making.

For example, some decision-making models are constructed so that inhibitory neurons are targeted broadly by excitatory neurons in pools favoring each of two possible choice alternatives (Deneve et al., 1999; Wang, 2002; Bogacz et al., 2006; Wang, 2008; Rustichini and Padoa-Schioppa, 2015; Mi et al., 2017). However, the predications for neural responses of inhibitory neurons had not been tested *in vivo* because of the challenges in reliably identifying inhibitory neurons and simultaneously measuring the activity of excitatory and inhibitory populations. A recent study investigated choice selectivity in inhibitory versus excitatory neurons in posterior parietal cortex (PPC) during decision-making by taking advantage of transgenic mice in which inhibitory neurons are labeled and can therefore be distinguished from excitatory neurons. The study found that, surprisingly, inhibitory neurons were as selective for choice as excitatory neurons (Najafi et al., 2018). These findings argue against the long-held assumption that inhibitory neurons constitute a broadly targeted pool and are thus weakly selective for choice. The findings are consistent with alternative decision-making architectures, including ones in which inhibitory neurons receive targeted input from excitatory neurons with particular choice preferences (Najafi et al., 2018).

Heterogeneous physiological responses during decision-making (Kim and Shadlen, 1999; Hayden and Platt, 2010; Freedman and Ibos, 2018) point to diversity not just across cell types, but within the excitatory population. Classic experiments have previously demonstrated that response heterogeneity could be partly explained by projection targets (Movshon and Newsome, 1996; Sommer and Wurtz, 2004), but these studies had limited use in the field of decision-making: they relied on a challenging and lower-yield technique and antidromic stimulation, and thus were used only rarely. Recent experimental advances, however, allow neurons projecting to a given target to be tagged by expressing distinct fluorescent proteins so that they can be easily identified and recorded (Li et al., 2015; Itokazu et al., 2018). One recent study (Chen et al., 2013) aimed to understand heterogeneity of neurons in somatosensory cortex in mice

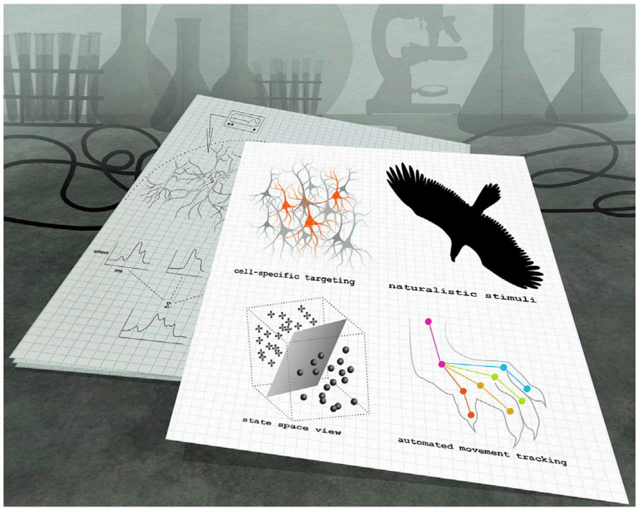

Figure 1. Traditional Techniques for Studying Decision-Making Are Now Augmented by a Host of New Approaches
Back page: drawings schematize traditional techniques including single-cell electrophysiology (top) in which cell identity is often mysterious, and population averaging of neural responses (bottom). Front page: drawings schematize new techniques in the field including cell-specific targeting, the use of naturalistic stimuli, new analyses for population recordings, and automated methods for movement tracking.

making decisions about texture or object location. By separately labeling neurons projecting to higher-level somatosensory areas versus primary motor cortex, they were able to better understand this heterogeneity: neurons projecting to higher somatosensory cortex were more strongly modulated by an object's texture, while neurons projecting to motor cortex were more strongly modulated by an object's location. Without knowledge of projection targets, the collection of neurons altogether might have appeared bewilderingly heterogeneous in terms of their response properties during decision-making. Tagging the neurons based on projection target, by contrast, revealed that distinct populations of neurons selectively transmit decision-relevant information to particular cortical targets.

Long-Term Tracking of Neural Activity Offers Insight into the Flexibility and Stability of Networks

Vast behavioral changes occur as animals learn the structure of a decision-making task, implying parallel changes in neural activity in different brain areas. Existing work has offered key insights into the changes that occur in certain brain areas with training (Freedman and Assad, 2006; Viswanathan and Nieder, 2015). However, many open questions remain: how does learning change the activity of individual neurons and neural ensembles? How do learning-induced changes vary across different cell types? Once animals are experts, does the activity of neurons keep changing even in the absence of behavioral changes, or is it largely static?

Converging observations argue that learning shapes the activity and interactions of multiple cell types. Learning studies in mouse V1 have revealed stark functional differences between cell types to support visual discrimination decisions (Khan et al., 2018). Learning increased selectivity for task-relevant stimuli in excitatory (pyramidal), parvalbumin (PV), and somatostatin (SOM), but not vasoactive intestinal peptide (VIP), neurons. Also, SOM activity became strongly decorrelated from the network as a result of learning to make decisions in virtual reality (Khan et al., 2018). Excitatory and inhibitory neurons have also been examined in motor cortex during learning a lever press task (Peters et al., 2014). During training, inhibitory neurons were more stable, while excitatory neurons were more dynamic: they explored different activity patterns and subsequently refined into populations with reproducible activity (Peters et al., 2014).

Learning studies also help with interpreting the nature of signals observed in an area. In PPC, for example, population activity changes dramatically over the course of learning, even though the animal's movements change little (Najafi et al., 2018), suggesting that PPC neurons reflect features of the animal's choice that extend beyond movements. Indeed, numerous studies, in primates (Roitman and Shadlen, 2002; Churchland et al., 2008) as well as rodents (Pho et al., 2018), have suggested that PPC responses are not purely sensory or purely motor, but may mediate computations that intervene between sensation and action.

Long-term population recordings have afforded new insights into how correlations evolve over learning and depend on cell identity. During learning, converging work in rodents and primates has demonstrated that noise correlations decrease as an animal becomes expert at judging sensory stimuli (Najafi et al., 2018; Ni et al., 2018). An appealing possibility is that these changes allow the neural representation within a given area to more effectively drive its downstream targets (Ruff and Cohen, 2018). In mice, cell-specific recording methods reveal that the strongest couplings are between inhibitory neurons, especially those with similar stimulus selectivity (Hofer et al., 2011; Khan et al., 2018; Najafi et al., 2018). Strikingly, this correlation structure is evident both in primary visual cortex (V1) of passively viewing mice (Hofer et al., 2011) and in the PPC of mice making perceptual decisions (Najafi et al., 2018). This similarity was not at all guaranteed: the stimulus-response contingencies in the decision-making task were abstract and only gradually mastered by the animal. The observation that these decisions nonetheless engaged a PPC network with similar properties to that seen in V1 during passive viewing argues that strong inhibitory coupling may implement a canonical computation, critical in multiple brain regions and behavioral contexts.

Finally, repeatedly measuring the same neural population also offers insight into the stability of neural representations of learned task parameters after animals have become experts (Figure 2). For instance, chromic imaging in mice that are experts in navigational decision-making revealed that PPC population activity can be stably decoded to predict the animal's choice, but that individual neurons nevertheless undergo major reorganizations (Driscoll et al., 2017). These changes may reflect dynamic changes in synapse formation and pruning (Peters et al., 2014), and allow for a tradeoff between stability in memory and flexibility in incorporating new information (Driscoll et al., 2017).

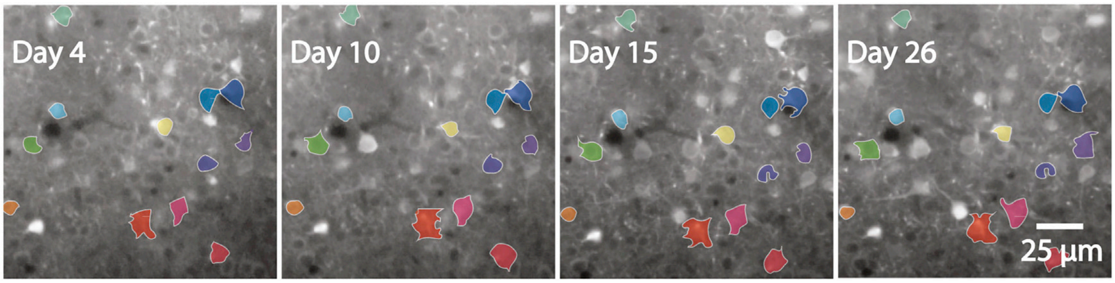

Figure 2. The Same Neural Population Can Be Imaged Over Multiple Days
This allows investigation of flexibility and stability of networks (Driscoll et al., 2017). Colors indicate example neurons that are present in all sessions.

Measurement Methods Spanning Multiple Areas Uncover Large Networks Engaged during Decision-Making

Complex decisions likely engage multiple cortical and subcortical structures as animals perceive sensory inputs, interpret them in favor of decision outcomes, and ultimately plan an action to report the choice. Until recently, however, most decision-making studies in animals were restricted to one or two structures. For example, many traditional electrophysiological studies relied on single electrodes recording over a very limited region, and even conventional two-photon imaging spans only about $\sim$1 mm^2 (Stirman et al., 2016). The emergence of methods to measure neural activity over a much larger area are starting to provide insight into decision-related signals in multiple structures.

High-density electrophysiology techniques, such as Neuropixels probes, have become recently available, allowing simultaneous recording of the activity of hundreds of neurons across multiple cortical layers and subcortical regions (Jun et al., 2017; Stringer et al., 2018). The ability to measure activity from cortical and subcortical regions simultaneously is a boon for decision-making studies because of the importance of subcortical structures such as the striatum (Ding and Gold, 2013; Yartsev et al., 2018). Similarly, recent advances in imaging techniques allow large field-of-view imaging at cellular resolution from multiple areas (Sofroniew et al., 2016; Stirman et al., 2016). The opportunity to probe still larger networks may grow in the coming years as new volumetric imaging methods allow imaging using stereoscopy (Song et al., 2017a), and collecting volumetric data at unprecedented speeds (Hillman et al., 2018).

Widefield imaging likewise offers the opportunity to measure neural activity in multiple regions simultaneously (Wekselblatt et al., 2016). Although this method lacks cellular resolution, it provides a window into brain-wide activity during decision-making. For example, widefield imaging during decision-making has revealed that movements play a far larger role in modulating neural activity than previously appreciated (Musall et al., 2018). The influence of operant movements (e.g., saccades or licking) on neural activity is well established. However, the influence of spontaneous, uninstructed movements is often even larger than operant ones. These observations underscore the need to measure movements more broadly and to use more extensive analysis methods to distinguish movement and decision-related activity (Musall et al., 2018). Finally, wide-field imaging has afforded the opportunity to define visual areas using retinotopic mapping (Garrett et al., 2014; Zhuang et al., 2017). This technique is important as it allows researchers to identify and target functionally defined visual areas with high precision. This is a major advance because multiple areas that are engaged in decision-making might be close together and difficult to confidently distinguish *in vivo*. Multiple decision-making structures are evident within the monkey intraparietal sulcus, for instance (Cook and Maunsell, 2002; de Lafuente et al., 2015). In mice, widefield imaging has revealed multiple retinotopically organized regions surrounding area V1. These are beginning to be evaluated in terms of their unique contributions to visual decision-making (Andermann et al., 2011; Odoemene et al., 2017), and can be examined using well-studied visual stimuli with established theoretical foundations (Juavinett and Callaway, 2015).

The Ability to Perturb Neural Activity with Increased Selectivity Uncovers Causal Structures

Advances in optogenetic and chemogenetic perturbation techniques afford the opportunity to transiently manipulate the activity of specific areas and cell types. Below we discuss example perturbation studies that uncover the causal role and the timing of neural activity underlying decision-making.

Transient inactivation studies have helped identify areas that contribute information during decision-making. Suppressing the anterior lateral motor cortex (ALM) or the thalamus during a tactile delayed-response task has revealed the importance of each area in maintaining choice selectivity and persistent activity in the other area (Guo et al., 2017). These results demonstrated that the reciprocal connection between the thalamus and ALM is essential in motor preparation.

In PPC, transient perturbations have led to conflicting results on whether PPC is causal for decision-making: while PPC perturbations alter some visual decisions (Harvey et al., 2012; Raposo et al., 2014; Driscoll et al., 2017; Licata et al., 2017), tactile (Guo et al., 2014) and auditory decisions (Raposo et al., 2014; Erlich et al., 2015; Zhong et al., 2018) remain intact following PPC inactivation. Importantly, the effects of PPC perturbations may depend on the animal's level of expertise, at least for some modalities. A recent study of auditory decision-making showed that PPC was essential during category learning (when mice were learning to incorporate new sensory stimuli into previous categories) but no longer required once categories were mastered (Zhong et al., 2018). These results suggest that PPC

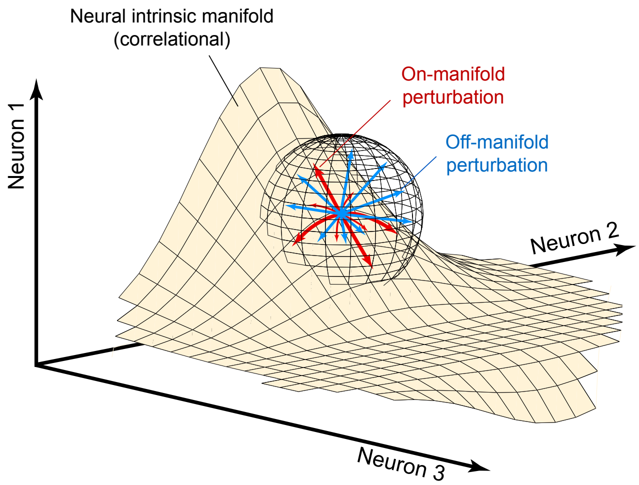

Figure 3. A Graphical Framework for Considering Neural Perturbations
From Jazayeri and Afraz (2017). Each axis represents the response of a single neuron. The surface depicts the subspace of activity patterns of the three example neurons during a behavioral task. This surface is the intrinsic manifold. On-manifold perturbations (red arrows) are those that respect the intrinsic manifold, while off-manifold perturbations (blue arrows) do not because they push the network into activity patterns that it would not ordinarily visit.

may perform essential computations while the animals are learning to make associations and update their predictions, but not after the learning process is complete. The role of PPC in decision-making is yet more complicated, as some studies suggest that the nature of the task may matter as well: a rat study found PPC important in an internally guided visual task (Erlich et al., 2015). Also, while motion discrimination in monkeys does not require the lateral intra-parietal area (LIP), this area is required for memory-guided saccades (Katz et al., 2016).

The temporal precision of optogenetic perturbations makes it possible to examine the exact moments when putative decision-making structures are causal for behavior. This enables testing of a leading hypothesis, that decisions involve sequential activation of a hierarchy of cortical areas (Hernández et al., 2010). Serial information flow from sensory to motor areas has been suggested based on systematic photo-silencing of multiple cortical regions during a delayed object-location discrimination task in mice (Guo et al., 2014). In agreement with this hypothesis, V1 activity is required initially during the stimulus in a visual discrimination task (Resulaj et al., 2018); in contrast, prefrontal cortex activity at the end of the stimulus is essential for performing an auditory rate-discrimination task (Hanks et al., 2015). Follow-up studies will reveal the temporal windows that sensory, motor, and decision areas contribute to decision-making, and will help reveal how information is routed across areas as evidence is transformed to a choice. Finally, transient perturbations can reveal compensatory changes in the animal's behavioral strategy, sometimes spanning multiple timescales (Fetsch et al., 2018).

Although advances in neural perturbations have been fruitful in defining necessary circuits for decision-making, it is crucial to be cautious when interpreting their effects. One concern is that transient manipulations within a given area may have "off-target" effects: i.e., a manipulation influences behavior by activating areas downstream of that being perturbed (Otchy et al., 2015). For instance, permanent lesions to motor cortex in rats and the nucleus interface (Nif) in songbirds do not disrupt skilled motor behaviors in rats and birds: lever press and courtship songs, respectively. Nevertheless, the transient inactivation of these areas alters the animals' behavior. This behavioral change does not arise because the perturbed areas are causal for behavior, but because transient inactivation of the areas changes the baseline excitation level of the downstream areas that are causal for behavior (Otchy et al., 2015).

Off-target effects are not the only concern: the effect of perturbations within an area must also be carefully considered. A framework was recently proposed to help interpret how activating and inactivating perturbations affect activity within an area (Figure 3; Jazayeri and Afraz, 2017). According to this framework, the most informative perturbations are those that produce activity patterns normally experienced by the networks of neurons in the structure being perturbed ("on-manifold" perturbations). Activity patterns that are never experienced by the network ("off-manifold" perturbations) can be less informative. An example of an off-manifold perturbation is stimulation that drives all excitatory neurons to fire at a low rate. This would be off-manifold if normal population activity consisted of both high-firing and low-firing excitatory neurons. The effects of off-manifold perturbations are hard to interpret: for instance, off-manifold perturbations might give rise to a behavioral outcome that would never normally be produced, or might lead to no behavioral outcome at all, even though an area is causal for behavior. On-manifold perturbations are preferable, when possible. These need not necessarily rely on optogenetics. For instance, electrical stimulation within a cortical column in which neurons share the same preferred direction (Murasugi et al., 1993) and the cooling of birdsong premotor nucleus (Long and Fee, 2008) are examples of perturbations that are on-manifold, at least within a moment in time. Overall, this new framework argues that the most interpretable perturbations in decision-making experiments will take place in areas for which both the baseline and perturbed activity are well-characterized.

Studying Multisensory Integration Is Critical for a Full Understanding of Decision-Making

Although stimuli in decision-making studies have historically been unisensory, real-world decisions often center on stimuli that activate multiple sensory systems. Food, predators, and potential mates, for instance, all provide multisensory information that can be integrated across modalities to make better decisions. Studies on multisensory integration in human and nonhuman primates have already furnished key insights into how sensory stimuli are weighted and combined to guide behavior (Landy et al., 1995; Knill and Saunders, 2003; Fetsch et al., 2011). Studies in rodents and invertebrates have recently begun to enhance this approach, bolstered by the fact that multisensory integration strategies are often conserved across species (Raposo et al., 2012; Sheppard et al., 2013).

Much of the work in rodents has built directly on the insights gained from human and non-human primates. For example, rats, like humans, integrate visual and tactile cues in a near-optimal fashion for object recognition (Nikbakht et al., 2018). This was an important extension of traditional multisensory principles: somatosensory information from whisking differs from vision considerably in its temporal dynamics, making integration potentially challenging. Other rodent work has employed conflict stimuli in which two sensory modalities provide conflicting instructions about what to do. Conflict stimuli have historically been used to demonstrate that sensory systems can optimally combine cues based on their certainty (Landy et al., 1995; Knill and Saunders, 2003). The outcome of one recent study, by contrast, demonstrated near-dominance of auditory cues over visual cues in a go-no task in mice (Song et al., 2017b). The features of the task that led to this auditory dominance are mysterious given other observations: one study found that auditory and visual cues in rats were weighted according to their uncertainty (Sheppard et al., 2013). Another study found that mice could attend to either auditory or visual stimuli, depending on instructions, using a circuit that consists of the visual thalamic reticular nucleus and the prefrontal cortex (Wimmer et al., 2015). A deeper understanding of the environmental cues that encourage reliance on one modality over another is greatly needed, especially because the above studies demonstrate that animals can idiosyncratically favor one modality over the other depending on the context.

Invertebrate studies have furnished insights on the molecular and cellular basis of multisensory decision-making. Invertebrates offer unprecedented neuronal access and control, and like mammals, they combine information from multiple senses to select the best course of action. For instance, *C. elegans* integrate multiple sensory cues to balance the reward of food with the threat of dangers like hyper-osmosis (Ghosh et al., 2016). The underlying decision circuitry involves neurons that receive converging reward and threat sensory signals, and project to premotor neurons directing locomotion. This multisensory pathway is modulated by the worm's hunger state (Ghosh et al., 2016). Action selection via multisensory cues has also been studied in fruit flies (Ohyama et al., 2015). Flies selected the fastest escape mode when synergistic mechanosensory and nociceptive cues were presented. Electron microscopy reconstruction of the multisensory circuit revealed a multimodal convergence architecture, which may be a general feature of multisensory circuits.

New Decision-Making Paradigms Incorporate Ethologically Relevant Stimuli

The approaches described above have mainly been used to study decisions between two alternatives. These two-choice decisions are useful in that they are well studied and sometimes can be trained using automated methods (Aoki et al., 2017). A downside is that two-choice decisions represent only a single class of decision and they are less complex than many realistic decisions. One way to circumvent this challenge is to study decisions among more than two alternatives (Churchland et al., 2008; Schmitt et al., 2017). A second approach is to rely on ethological behaviors that are innate to the animals (Juavinett et al., 2018). Ethological behaviors can afford the opportunity to study decisions among a continuously varying array of choices (such as where and how fast to move) and often have the additional benefit of not requiring training.

Looming stimuli are thought to simulate predators and have been recently used to investigate the circuitry underlying threat detection and escape behavior in mice (Yilmaz and Meister, 2013; De Franceschi et al., 2016). A monosynaptic pathway from the medial superior colliculus (mSC) to the dorsal periaqueductal gray (dPAG) has been suggested as a putative pathway for encoding threat signals that govern the decision to stay or to flee (Evans et al., 2018): mSC neurons represent and integrate the threat evidence, while dPAG neurons threshold the threat information provided by the mSC, and reflect the animal's decision. Another looming study (Salay et al., 2018) considered how internal state affects the animal's decision to freeze versus flee. The stimulation of ventral midline thalamus (vMT) enhanced arousal and promoted escape behavior, perhaps through its connection with medial prefrontal cortex. On the other hand, stimulation of another nucleus within vMT, which targets the basolateral amygdala, promoted freezing decisions. These observations argue that vMT acts as a hub for integrating sensory inputs with internal state to determine the proper threat response.

The ability to use freely moving animals in more ethological paradigms will likely be supported by new developments to characterize animal movements with precision. These approaches, pioneered in invertebrates (Kabra et al., 2013), use machine learning techniques to quantify behavior of diverse species in an automated fashion. These tools allow researchers to circumvent many of the challenges inherent to characterizing the diverse and complex movements made by unrestrained animals (Wiltschko et al., 2015; Robie et al., 2017; Mathis et al., 2018; Pereira et al., 2018). One such automated tracking method is DeepLabCut, a tool that tracks and labels multiple parts of the animal's body simultaneously so that movements can be monitored continuously and with precision (Mathis et al., 2018). A second method, LEAP, likewise uses deep learning for pose estimation in *Drosophila* and circumvents many of the traditional problems with the dimensionality reduction that is needed to quantify postural dynamics from video (Pereira et al., 2018). These approaches bolster existing automated software for tracking movements that was developed a few years back in *Drosophila* (Kabra et al., 2013). Automated tracking is likely to change decision-making studies by making the process of connecting neural activity to diverse movements feasible. This is critical for decision-making studies in which movement-related signals can resemble decision-making signals (Musall et al., 2018). Further, automated tracking will greatly extend the number of experimental setups that are available to researchers. In the past, restraining the animals was essential in part because it eliminated a large class of movements that could muddle potential decision-making signals. Now, experimenters may elect to use freely moving preparations, which have the advantage of reducing animal anxiety and are also closer to the animal's ethological niche (Juavinett et al., 2018). The ability to make neural measurements will be bolstered by new technology that allows for recordings in freely moving animals (Cai et al., 2016), such as miniature fluorescent microscopes (Ghosh et al., 2011).

New Methods for Assessing Internal State Reveal Its Impact on Neural Activity and Behavior

A major change in the field of decision-making is the growing realization that both neural responses and behavior depend critically on the animal's internal state. The importance of internal state on network activity has been known for some time in other fields (Csicsvari et al., 1999; Buzsáki and Draguhn, 2004), and more recently, two classes of internal state are becoming widely appreciated within the field of decision-making.

First, the importance of the animal's overall level of arousal is becoming abundantly clear. For example, the effect of locomotion on visual inputs is now well established (Niell and Stryker, 2010; Polack et al., 2013; Vinck et al., 2015; Mineault et al., 2016; Dipoppa et al., 2018; Socha et al., 2018), and has been shown to influence decision-related computations such as the integration of visual motion (Ayaz et al., 2013; Saleem et al., 2013) and predictive coding (Keller et al., 2012). Locomotion likely indicates a brain state change, characterized by global desynchronization of cortical activity and increased engagement in the task (Jacobs et al., 2018). In V1, the variance in neural activity explained by global fluctuations exceeds that explained by sensory stimuli (Schölvinck et al., 2015; Stringer et al., 2018). There is a temptation to think that movement-induced state changes are more frequent in rodents because in most primate experiments the animals are not running. Nevertheless, the impact of small, idiosyncratic movements, including those of facial movements, argues that movements need to be carefully accounted for even in restrained animals (Pachitariu et al., 2015; Musall et al., 2018). Both operant and uninstructed, spontaneous movements must be tracked and accounted for.

Second, the importance of animals' internal estimates of task-relevant variables is being considered. These internal estimates must be inferred by experimenters because they are not immediately evident. For example, when animals base decisions on fluctuating sensory evidence, experimenters can use a model to infer the subject's internal estimate of the evidence (Brunton et al., 2013). These estimates are useful in understanding neural activity because they are based on the animal's internal estimate of task variables, which may differ from the presented evidence (Hanks et al., 2015; Katz et al., 2016). For instance, an animal might more heavily weigh stimuli late versus early in the trial, or might not accumulate each of two samples if they are presented too closely in time. These latent behavioral variables affect behavior and neural activity in posterior parietal cortex in rats, monkeys, and mice (Morcos and Harvey, 2016; Purcell and Kiani, 2016; Hwang et al., 2017; Akrami et al., 2018).

Novel Analyses for Interpreting Neural Activity Have Led to New Hypotheses about Network Mechanisms Underlying Decisions

New analyses of neural data have been transformative, leading to novel ideas about how networks support decisions. These analyses largely leverage the ability of researchers to record neural populations while animals make decisions (Churchland and Abbott, 2016).

Sequential sampling models, which explain accumulation of evidence during decision-making, continue to be important for understanding behavior. Therefore, uncovering how they are mechanistically implemented in the brain is critical (O'Connell et al., 2018). New evidence suggests that in some cases, populations of neurons might implement sequential sampling via sequential firing of multiple neurons within a structure, without any individual neuron firing persistently (Harvey et al., 2012; Morcos and Harvey, 2016; Rajan et al., 2016). New methods for model discovery (Zhao and Park, 2016) may reveal still other ways to characterize complex neural activity. New models may be essential, especially as the timescale of sustained activity grows from hundreds of milliseconds to tens of seconds (Waskom and Kiani, 2018) and the size of population recordings is growing fast (Pillow and Aoi, 2017).

A second new direction for analysis was likewise prompted by population-level neural recordings. One traditional way to handle population data is to tailor the stimulus (i.e., the spatiotemporal frequency of a visual stimulus) for each individual neuron under study. The responses of many such neurons can then be summarized by averaging their responses (Figure 1, bottom sheet). This simple method of dimensionality reduction is a convenient way to summarize the activity of many neurons, but has the disadvantage of being ill-suited to the heterogeneous neural activity that is observed when many neurons are recorded simultaneously. Fortunately, a host of new approaches have emerged to extend the electrophysiologist's analysis toolbox (Cunningham and Yu, 2014). These new methods for visualizing data and pooling neural activity across a population have revealed surprising implementations of decision-related computations. For instance, a now-classic study demonstrated that late selection through recurrent dynamics underlies an animal's ability to alternate between color or motion as the sensory features that guide decisions (Mante et al., 2013). This mechanism is an alternative to sensory gating, a long-held candidate for how context can guide decision-making. Other work demonstrated that neurons, while they might be strongly tuned for a particular decision-making parameter, need not constitute a distinct category specialized in supporting a specific computation (Raposo et al., 2014). This approach is gaining a foothold in value-based decisions as well (Blanchard et al., 2018), suggesting a reconsideration of the often implicit assumption that neurons strongly tuned for a particular stimulus constitute a distinct category, specialized for computations related to that stimulus.

A Look Ahead

How will the field of decision-making evolve in coming years? Certainly, new technologies will enhance our ability to understand decision circuits. For example, a more precise understanding of connectivity patterns will be critical. At the moment, the field's knowledge of how areas connect to one another is largely based on anatomical tracing studies. Although tracing studies are a critical first step, they often miss subtleties of connectivity that are critical for understanding circuits. For instance, recent work using high-throughput DNA sequencing of genetically barcoded neurons (MAP-seq) reveals that in V1, most neurons project not just to a single downstream target, but to multiple targets (Han et al., 2018). Further, when single neurons bifurcate and project to two downstream areas, the pattern is non-random. For example, in V1, a bifurcation to the posteromedial (PM) and anterolateral (AL) areas is greatly under-represented, while bifurcations to lateromedial (LM) and laterointermediate (LI) areas are over-represented (Han et al., 2018). Traditional decision-making circuit schematics, such as the projections from V1 to MT (middle temporal area) and MT to LIP (lateral intraparietal area), may need to be reconsidered in light of newly discovered projections. Further, the assumption that motor structures are the only output of a decision area might need to be reconsidered in favor of an alternative hypothesis, i.e., a given neuron could influence multiple downstream targets. How would the activity and behavioral representations vary in such a neuron compared to its neighbors that innervate only a single target? This remains to be seen.

Beyond technology, a very different force may shape the field of decision-making in years to come: the growing opportunity for scientists to team up and work collaboratively. Inspired by other fields such as physics and genomics, these collaborations leverage the collective power of groups that exceed the size of a traditional laboratory and thus are well positioned to tackle big problems in the field. The Allen Institute for Brain Sciences (AIBS), while not working exclusively on decision-making, will impact the field tremendously by virtue of the tools it has made available and its discoveries about visual areas. The International Brain Laboratory (IBL) will focus its efforts exclusively on decision-making, and in particular the neural computations supporting mouse decisions that combine internal and external variables (Abbott et al., 2017). Both the AIBS and the IBL will need to surmount challenges related to data storage and sharing, and have the opportunity to generate pipelines that the entire community can share.

Conclusions

Recent years have seen major advances in the field of perceptual decision-making. Features of neural activity that were long mysterious are beginning to be well understood, and widely accepted mechanisms are being updated based on new evidence. The combined approaches outlined here pave the way for a strong future, and emerging techniques can further fuel our understanding of decision-making mechanisms. This new understanding will be a critical part of our understanding of brain function, and may inform clinical conditions in which the ability to use sensory inputs to guide actions is disrupted.

ACKNOWLEDGMENTS

We wish to acknowledge Anne Urai, Sashank Pisupati, and Kanaka Rajan for helpful suggestions for an early version of the manuscript, and Julia Kuhl and Ashley Juavinett for the artwork. This work was supported by the ONR MURI, the Simons Collaboration on the Global Brain, and the NEI (R01EY022979).

REFERENCES

Abbott, L.F., et al.; International Brain Laboratory. Electronic address: churchland@cshl.edu; International Brain Laboratory (2017). An International Laboratory for Systems and Computational Neuroscience. Neuron *96*, 1213–1218.

Akrami, A., Kopec, C.D., Diamond, M.E., and Brody, C.D. (2018). Posterior parietal cortex represents sensory history and mediates its effects on behaviour. Nature *554*, 368–372.

Andermann, M.L., Kerlin, A.M., Roumis, D.K., Glickfeld, L.L., and Reid, R.C. (2011). Functional specialization of mouse higher visual cortical areas. Neuron *72*, 1025–1039.

Aoki, R., Tsubota, T., Goya, Y., and Benucci, A. (2017). An automated platform for high-throughput mouse behavior and physiology with voluntary head-fixation. Nat. Commun. *8*, 1196.

Ayaz, A., Saleem, A.B., Schölvinck, M.L., and Carandini, M. (2013). Locomotion controls spatial integration in mouse visual cortex. Curr. Biol. *23*, 890–894.

Blanchard, T.C., Piantadosi, S.T., and Hayden, B.Y. (2018). Robust mixture modeling reveals category-free selectivity in reward region neuronal ensembles. J. Neurophysiol. *119*, 1305–1318.

Bogacz, R., Brown, E., Moehlis, J., Holmes, P., and Cohen, J.D. (2006). The physics of optimal decision making: a formal analysis of models of performance in two-alternative forced-choice tasks. Psychol. Rev. *113*, 700–765.

Brunton, B.W., Botvinick, M.M., and Brody, C.D. (2013). Rats and humans can optimally accumulate evidence for decision-making. Science *340*, 95–98.

Buzsáki, G., and Draguhn, A. (2004). Neuronal oscillations in cortical networks. Science *304*, 1926–1929.

Cai, D.J., Aharoni, D., Shuman, T., Shobe, J., Biane, J., Song, W., Wei, B., Veshkini, M., La-Vu, M., Lou, J., et al. (2016). A shared neural ensemble links distinct contextual memories encoded close in time. Nature *534*, 115–118.

Chen, J.L., Carta, S., Soldado-Magraner, J., Schneider, B.L., and Helmchen, F. (2013). Behaviour-dependent recruitment of long-range projection neurons in somatosensory cortex. Nature *499*, 336–340.

Churchland, A.K., and Abbott, L.F. (2016). Conceptual and technical advances define a key moment for theoretical neuroscience. Nat. Neurosci. *19*, 348–349.

Churchland, A.K., and Lisberger, S.G. (2005). Discharge properties of MST neurons that project to the frontal pursuit area in macaque monkeys. J. Neurophysiol. *94*, 1084–1090.

Churchland, A.K., Kiani, R., and Shadlen, M.N. (2008). Decision-making with multiple alternatives. Nat. Neurosci. *11*, 693–702.

Cook, E.P., and Maunsell, J.H. (2002). Dynamics of neuronal responses in macaque MT and VIP during motion detection. Nat. Neurosci. *5*, 985–994.

Csicsvari, J., Hirase, H., Czurkó, A., Mamiya, A., and Buzsáki, G. (1999). Oscillatory coupling of hippocampal pyramidal cells and interneurons in the behaving Rat. J. Neurosci. *19*, 274–287.

Cunningham, J.P., and Yu, B.M. (2014). Dimensionality reduction for large-scale neural recordings. Nat. Neurosci. *17*, 1500–1509.

De Franceschi, G., Vivattanasarn, T., Saleem, A.B., and Solomon, S.G. (2016). Vision guides selection of freeze or flight defense strategies in mice. Curr. Biol. *26*, 2150–2154.

de Lafuente, V., Jazayeri, M., and Shadlen, M.N. (2015). Representation of accumulating evidence for a decision in two parietal areas. J. Neurosci. *35*, 4306–4318.

Deneve, S., Latham, P.E., and Pouget, A. (1999). Reading population codes: a neural implementation of ideal observers. Nat. Neurosci. *2*, 740–745.

Ding, L., and Gold, J.I. (2013). The basal ganglia's contributions to perceptual decision making. Neuron *79*, 640–649.

Dipoppa, M., Ranson, A., Krumin, M., Pachitariu, M., Carandini, M., and Harris, K.D. (2018). Vision and locomotion shape the interactions between neuron types in mouse visual cortex. Neuron *98*, 602–615.e8.

Driscoll, L.N., Pettit, N.L., Minderer, M., Chettih, S.N., and Harvey, C.D. (2017). Dynamic reorganization of neuronal activity patterns in parietal cortex. Cell *170*, 986–999.e16.

Erlich, J.C., Brunton, B.W., Duan, C.A., Hanks, T.D., and Brody, C.D. (2015). Distinct effects of prefrontal and parietal cortex inactivations on an accumulation of evidence task in the rat. eLife *4*, https://doi.org/10.7554/eLife.05457.

Evans, D.A., Stempel, A.V., Vale, R., Ruehle, S., Lefler, Y., and Branco, T. (2018). A synaptic threshold mechanism for computing escape decisions. Nature *558*, 590–594.

Fetsch, C.R., Pouget, A., DeAngelis, G.C., and Angelaki, D.E. (2011). Neural correlates of reliability-based cue weighting during multisensory integration. Nat. Neurosci. *15*, 146–154.

Fetsch, C.R., Odean, N.N., Jeurissen, D., El-Shamayleh, Y., Horwitz, G.D., and Shadlen, M.N. (2018). Focal optogenetic suppression in macaque area MT biases direction discrimination and decision confidence, but only transiently. eLife *7*, https://doi.org/10.7554/eLife.36523.

Freedman, D.J., and Assad, J.A. (2006). Experience-dependent representation of visual categories in parietal cortex. Nature *443*, 85–88.

Freedman, D.J., and Ibos, G. (2018). An integrative framework for sensory, motor, and cognitive functions of the posterior parietal cortex. Neuron *97*, 1219–1234.

Garrett, M.E., Nauhaus, I., Marshel, J.H., and Callaway, E.M. (2014). Topography and areal organization of mouse visual cortex. J. Neurosci. *34*, 12587–12600.

Ghosh, K.K., Burns, L.D., Cocker, E.D., Nimmerjahn, A., Ziv, Y., Gamal, A.E., and Schnitzer, M.J. (2011). Miniaturized integration of a fluorescence microscope. Nat. Methods *8*, 871–878.

Ghosh, D.D., Sanders, T., Hong, S., McCurdy, L.Y., Chase, D.L., Cohen, N., Koelle, M.R., and Nitabach, M.N. (2016). Neural architecture of hunger-dependent multisensory decision making in C. elegans. Neuron *92*, 1049–1062.

Guo, Z.V., Li, N., Huber, D., Ophir, E., Gutnisky, D., Ting, J.T., Feng, G., and Svoboda, K. (2014). Flow of cortical activity underlying a tactile decision in mice. Neuron *81*, 179–194.

Guo, Z.V., Inagaki, H.K., Daie, K., Druckmann, S., Gerfen, C.R., and Svoboda, K. (2017). Maintenance of persistent activity in a frontal thalamocortical loop. Nature *545*, 181–186.

Han, Y., Kebschull, J.M., Campbell, R.A.A., Cowan, D., Imhof, F., Zador, A.M., and Mrsic-Flogel, T.D. (2018). The logic of single-cell projections from visual cortex. Nature *556*, 51–56.

Hanks, T.D., Kopec, C.D., Brunton, B.W., Duan, C.A., Erlich, J.C., and Brody, C.D. (2015). Distinct relationships of parietal and prefrontal cortices to evidence accumulation. Nature *520*, 220–223.

Harvey, C.D., Coen, P., and Tank, D.W. (2012). Choice-specific sequences in parietal cortex during a virtual-navigation decision task. Nature *484*, 62–68.

Hayden, B.Y., and Platt, M.L. (2010). Neurons in anterior cingulate cortex multiplex information about reward and action. J. Neurosci. *30*, 3339–3346.

Hernández, A., Nácher, V., Luna, R., Zainos, A., Lemus, L., Alvarez, M., Vázquez, Y., Camarillo, L., and Romo, R. (2010). Decoding a perceptual decision process across cortex. Neuron *66*, 300–314.

Hillman, E.M., Voleti, V., Patel, K., Li, W., Yu, H., Perez-Campos, C., Benezra, S.E., Bruno, R.M., and Galwaduge, P.T. (2018). High-speed 3D imaging of cellular activity in the brain using axially-extended beams and light sheets. Curr. Opin. Neurobiol. *50*, 190–200.

Hofer, S.B., Ko, H., Pichler, B., Vogelstein, J., Ros, H., Zeng, H., Lein, E., Lesica, N.A., and Mrsic-Flogel, T.D. (2011). Differential connectivity and response dynamics of excitatory and inhibitory neurons in visual cortex. Nat. Neurosci. *14*, 1045–1052.

Hwang, E.J., Dahlen, J.E., Mukundan, M., and Komiyama, T. (2017). History-based action selection bias in posterior parietal cortex. Nat. Commun. *8*, 1242.

Itokazu, T., Hasegawa, M., Kimura, R., Osaki, H., Albrecht, U.R., Sohya, K., Chakrabarti, S., Itoh, H., Ito, T., Sato, T.K., and Sato, T.R. (2018). Streamlined sensory motor communication through cortical reciprocal connectivity in a visually guided eye movement task. Nat. Commun. *9*, 338.

Jacobs, E., Steinmetz, N., Carandini, M., and Harris, K. (2018). Cortical state fluctuations during sensory decision making. bioRxiv. https://doi.org/10.1101/348193.

Jazayeri, M., and Afraz, A. (2017). Navigating the neural space in search of the neural code. Neuron *93*, 1003–1014.

Juavinett, A.L., and Callaway, E.M. (2015). Pattern and component motion responses in mouse visual cortical areas. Curr. Biol. *25*, 1759–1764.

Juavinett, A.L., Erlich, J.C., and Churchland, A.K. (2018). Decision-making behaviors: weighing ethology, complexity, and sensorimotor compatibility. Curr. Opin. Neurobiol. *49*, 42–50.

Jun, J.J., Steinmetz, N.A., Siegle, J.H., Denman, D.J., Bauza, M., Barbarits, B., Lee, A.K., Anastassiou, C.A., Andrei, A., Aydın, Ç., et al. (2017). Fully integrated silicon probes for high-density recording of neural activity. Nature *551*, 232–236.

Kabra, M., Robie, A.A., Rivera-Alba, M., Branson, S., and Branson, K. (2013). JAABA: interactive machine learning for automatic annotation of animal behavior. Nat. Methods *10*, 64–67.

Katz, L.N., Yates, J.L., Pillow, J.W., and Huk, A.C. (2016). Dissociated functional significance of decision-related activity in the primate dorsal stream. Nature *535*, 285–288.

Keller, G.B., Bonhoeffer, T., and Hübener, M. (2012). Sensorimotor mismatch signals in primary visual cortex of the behaving mouse. Neuron *74*, 809–815.

Khan, A.G., Poort, J., Chadwick, A., Blot, A., Sahani, M., Mrsic-Flogel, T.D., and Hofer, S.B. (2018). Distinct learning-induced changes in stimulus selectivity and interactions of GABAergic interneuron classes in visual cortex. Nat. Neurosci. *21*, 851–859.

Kim, J.N., and Shadlen, M.N. (1999). Neural correlates of a decision in the dorsolateral prefrontal cortex of the macaque. Nat. Neurosci. *2*, 176–185.

Knill, D.C., and Saunders, J.A. (2003). Do humans optimally integrate stereo and texture information for judgments of surface slant? Vision Res. *43*, 2539–2558.

Landy, M.S., Maloney, L.T., Johnston, E.B., and Young, M. (1995). Measurement and modeling of depth cue combination: in defense of weak fusion. Vision Res. *35*, 389–412.

Li, N., Chen, T.W., Guo, Z.V., Gerfen, C.R., and Svoboda, K. (2015). A motor cortex circuit for motor planning and movement. Nature *519*, 51–56.

Licata, A.M., Kaufman, M.T., Raposo, D., Ryan, M.B., Sheppard, J.P., and Churchland, A.K. (2017). Posterior parietal cortex guides visual decisions in rats. J. Neurosci. *37*, 4954–4966.

Long, M.A., and Fee, M.S. (2008). Using temperature to analyse temporal dynamics in the songbird motor pathway. Nature *456*, 189–194.

Mante, V., Sussillo, D., Shenoy, K.V., and Newsome, W.T. (2013). Context-dependent computation by recurrent dynamics in prefrontal cortex. Nature *503*, 78–84.

Mathis, A., Mamidanna, P., Abe, T., Cury, K.M., Murthy, V.N., Mathis, M.W., and Bethge, M. (2018) Markerless tracking of user-defined features with deep learning. arXiv, arXiv:1804.03142, https://arxiv.org/abs/1804.03142.

Mi, Y., Katkov, M., and Tsodyks, M. (2017). Synaptic correlates of working memory capacity. Neuron *93*, 323–330.

Mineault, P.J., Tring, E., Trachtenberg, J.T., and Ringach, D.L. (2016). Enhanced spatial resolution during locomotion and heightened attention in mouse primary visual cortex. J. Neurosci. *36*, 6382–6392.

Morcos, A.S., and Harvey, C.D. (2016). History-dependent variability in population dynamics during evidence accumulation in cortex. Nat. Neurosci. *19*, 1672–1681.

Movshon, J.A., and Newsome, W.T. (1996). Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. J. Neurosci. *16*, 7733–7741.

Murasugi, C.M., Salzman, C.D., and Newsome, W.T. (1993). Microstimulation in visual area MT: effects of varying pulse amplitude and frequency. J. Neurosci. *13*, 1719–1729.

Musall, S., Kaufman, M.T., Gluf, S., and Churchland, A.K. (2018). Movement-related activity dominates cortex during sensory-guided decision making. bioRxiv. https://doi.org/10.1101/308288.

Najafi, F., Elsayed, G.F., Cao, R., Pnevmatikakis, E., Latham, P.E., Cunningham, J.P., and Churchland, A.K. (2018). Excitatory and inhibitory subnetworks are equally selective during decision-making and emerge simultaneously during learning. bioRxiv. https://doi.org/10.1101/354340.

Ni, A.M., Ruff, D.A., Alberts, J.J., Symmonds, J., and Cohen, M.R. (2018). Learning and attention reveal a general relationship between population activity and behavior. Science *359*, 463–465.

Niell, C.M., and Stryker, M.P. (2008). Highly selective receptive fields in mouse visual cortex. J. Neurosci. *28*, 7520–7536.

Niell, C.M., and Stryker, M.P. (2010). Modulation of visual responses by behavioral state in mouse visual cortex. Neuron *65*, 472–479.

Nikbakht, N., Tafreshiha, A., Zoccolan, D., and Diamond, M.E. (2018). Supralinear and supramodal integration of visual and tactile signals in rats: psychophysics and neuronal mechanisms. Neuron *97*, 626–639.e8.

O'Connell, R.G., Shadlen, M.N., Wong-Lin, K., and Kelly, S.P. (2018). Bridging neural and computational viewpoints on perceptual decision-making. Trends Neurosci. Published online July 11, 2018. https://doi.org/10.1016/j.tins.2018.06.005.

Odoemene, O., Pisupati, S., Nguyen, H., and Churchland, A.K. (2017). Visual evidence accumulation guides decision-making in unrestrained mice. bioRxiv. https://doi.org/10.1101/195792.

Ohyama, T., Schneider-Mizell, C.M., Fetter, R.D., Aleman, J.V., Franconville, R., Rivera-Alba, M., Mensh, B.D., Branson, K.M., Simpson, J.H., Truman, J.W., et al. (2015). A multilevel multimodal circuit enhances action selection in Drosophila. Nature *520*, 633–639.

Otchy, T.M., Wolff, S.B., Rhee, J.Y., Pehlevan, C., Kawai, R., Kempf, A., Gobes, S.M., and Ölveczky, B.P. (2015). Acute off-target effects of neural circuit manipulations. Nature *528*, 358–363.

Pachitariu, M., Lyamzin, D.R., Sahani, M., and Lesica, N.A. (2015). State-dependent population coding in primary auditory cortex. J. Neurosci. *35*, 2058–2073.

Pereira, T., Aldarondo, D., Willmore, L., Kislin, M., Wang, S.S., Murthy, M., and Shaevitz, J.W. (2018). Fast animal pose estimation using deep neural networks. bioRxiv. https://doi.org/10.1101/331181.

Peters, A.J., Chen, S.X., and Komiyama, T. (2014). Emergence of reproducible spatiotemporal activity during motor learning. Nature *510*, 263–267.

Pho, G.N., Goard, M.J., Woodson, J., Crawford, B., and Sur, M. (2018). Task-dependent representations of stimulus and choice in mouse parietal cortex. Nat. Commun. *9*, 2596.

Pillow, J.W., and Aoi, M.C. (2017). Is population activity more than the sum of its parts? Nat. Neurosci. *20*, 1196–1198.

Polack, P.O., Friedman, J., and Golshani, P. (2013). Cellular mechanisms of brain state-dependent gain modulation in visual cortex. Nat. Neurosci. *16*, 1331–1339.

Purcell, B.A., and Kiani, R. (2016). Neural mechanisms of post-error adjustments of decision policy in parietal cortex. Neuron *89*, 658–671.

Rajan, K., Harvey, C.D., and Tank, D.W. (2016). Recurrent network models of sequence generation and memory. Neuron *90*, 128–142.

Raposo, D., Sheppard, J.P., Schrater, P.R., and Churchland, A.K. (2012). Multisensory decision-making in rats and humans. J. Neurosci. *32*, 3726–3735.

Raposo, D., Kaufman, M.T., and Churchland, A.K. (2014). A category-free neural population supports evolving demands during decision-making. Nat. Neurosci. *17*, 1784–1792.

Resulaj, A., Ruediger, S., Olsen, S.R., and Scanziani, M. (2018). First spikes in visual cortex enable perceptual discrimination. eLife *7*, https://doi.org/10.7554/eLife.34044.

Robie, A.A., Hirokawa, J., Edwards, A.W., Umayam, L.A., Lee, A., Phillips, M.L., Card, G.M., Korff, W., Rubin, G.M., Simpson, J.H., et al. (2017). Mapping the neural substrates of behavior. Cell *170*, 393–406.e28.

Roitman, J.D., and Shadlen, M.N. (2002). Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task. J. Neurosci. *22*, 9475–9489.

Ruff, D.A., and Cohen, M.R. (2018). Simultaneous multi-area recordings suggest a novel hypothesis about how attention improves performance. bioRxiv. https://doi.org/10.1101/372888.

Rustichini, A., and Padoa-Schioppa, C. (2015). A neuro-computational model of economic decisions. J. Neurophysiol. *114*, 1382–1398.

Salay, L.D., Ishiko, N., and Huberman, A.D. (2018). A midline thalamic circuit determines reactions to visual threat. Nature *557*, 183–189.

Saleem, A.B., Ayaz, A., Jeffery, K.J., Harris, K.D., and Carandini, M. (2013). Integration of visual motion and locomotion in mouse visual cortex. Nat. Neurosci. *16*, 1864–1869.

Schmitt, L.I., Wimmer, R.D., Nakajima, M., Happ, M., Mofakham, S., and Halassa, M.M. (2017). Thalamic amplification of cortical connectivity sustains attentional control. Nature *545*, 219–223.

Schölvinck, M.L., Saleem, A.B., Benucci, A., Harris, K.D., and Carandini, M. (2015). Cortical state determines global variability and correlations in visual cortex. J. Neurosci. *35*, 170–178.

Shadlen, M.N., and Kiani, R. (2013). Decision making as a window on cognition. Neuron *80*, 791–806.

Sheppard, J.P., Raposo, D., and Churchland, A.K. (2013). Dynamic weighting of multisensory stimuli shapes decision-making in rats and humans. J. Vis. *13*, https://doi.org/10.1167/13.6.4.

Socha, K., Whiteway, M., Butts, D., and Bonin, V. (2018). Behavioral response to visual motion impacts population coding in the mouse visual thalamus. bioRxiv. https://doi.org/10.1101/382671.

Sofroniew, N.J., Flickinger, D., King, J., and Svoboda, K. (2016). A large field of view two-photon mesoscope with subcellular resolution for in vivo imaging. eLife *5*, https://doi.org/10.7554/eLife.14472.

Sommer, M.A., and Wurtz, R.H. (2004). What the brain stem tells the frontal cortex. I. Oculomotor signals sent from superior colliculus to frontal eye field via mediodorsal thalamus. J. Neurophysiol. *91*, 1381–1402.

Song, A., Charles, A.S., Koay, S.A., Gauthier, J.L., Thiberge, S.Y., Pillow, J.W., and Tank, D.W. (2017a). Volumetric two-photon imaging of neurons using stereoscopy (vTwINS). Nat. Methods *14*, 420–426.

Song, Y.H., Kim, J.H., Jeong, H.W., Choi, I., Jeong, D., Kim, K., and Lee, S.H. (2017b). A neural circuit for auditory dominance over visual perception. Neuron *93*, 940–954.e6.

Stirman, J.N., Smith, I.T., Kudenov, M.W., and Smith, S.L. (2016). Wide field-of-view, multi-region, two-photon imaging of neuronal activity in the mammalian brain. Nat. Biotechnol. *34*, 857–862.

Stringer, C., Pachitariu, M., Steinmetz, N., Reddy, C., Carandini, M., and Harris, K.D. (2018). Spontaneous behaviors drive multidimensional, brain-wide neural activity. bioRxiv. https://doi.org/10.1101/306019.

Vinck, M., Batista-Brito, R., Knoblich, U., and Cardin, J.A. (2015). Arousal and locomotion make distinct contributions to cortical activity patterns and visual encoding. Neuron *86*, 740–754.

Viswanathan, P., and Nieder, A. (2015). Differential impact of behavioral relevance on quantity coding in primate frontal and parietal neurons. Curr. Biol. *25*, 1259–1269.

Wang, X.J. (2002). Probabilistic decision making by slow reverberation in cortical circuits. Neuron *36*, 955–968.

Wang, X.J. (2008). Decision making in recurrent neuronal circuits. Neuron *60*, 215–234.

Waskom, M.L., and Kiani, R. (2018). Decision-making through integration of sensory evidence at prolonged timescales. bioRxiv. https://doi.org/10.1101/385989.

Wekselblatt, J.B., Flister, E.D., Piscopo, D.M., and Niell, C.M. (2016). Large-scale imaging of cortical dynamics during sensory perception and behavior. J. Neurophysiol. *115*, 2852–2866.

Wiltschko, A.B., Johnson, M.J., Iurilli, G., Peterson, R.E., Katon, J.M., Pashkovski, S.L., Abraira, V.E., Adams, R.P., and Datta, S.R. (2015). Mapping sub-second structure in mouse behavior. Neuron *88*, 1121–1135.

Wimmer, R.D., Schmitt, L.I., Davidson, T.J., Nakajima, M., Deisseroth, K., and Halassa, M.M. (2015). Thalamic control of sensory selection in divided attention. Nature *526*, 705–709.

Yartsev, M.M., Hanks, T.D., Yoon, A.M., and Brody, C.D. (2018). Causal contribution and dynamical encoding in the striatum during evidence accumulation. eLife *7*, https://doi.org/10.7554/eLife.34929.

Yilmaz, M., and Meister, M. (2013). Rapid innate defensive responses of mice to looming visual stimuli. Curr. Biol. *23*, 2011–2015.

Zhao, Y., and Park, I.M. (2016). Interpretable nonlinear dynamic modeling of neural trajectories. In NIPS.

Zhong, L., Zhang, Y., Duan, C.A., Pan, J., and Xu, N.-l. (2018). Dynamic and causal contribution of parietal circuits to perceptual decisions during category learning. bioRxiv. https://doi.org/10.1101/304071.

Zhuang, J., Ng, L., Williams, D., Valley, M., Li, Y., Garrett, M., and Waters, J. (2017). An extended retinotopic map of mouse cortex. eLife *6*, https://doi.org/10.7554/eLife.18372.