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Choice (-history) correlations in sensory cortex: cause or consequence?

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One challenge in neuroscience, as in other areas of science, is to make inferences about the underlying causal structure from correlational data. Here, we discuss this challenge in the context of choice correlations in sensory neurons, that is, trial-by-trial correlations, unexplained by the stimulus, between the activity of sensory neurons and an animal's perceptual choice. Do these choice-correlations reflect feedforward, feedback signalling, both, or neither? We highlight recent results of correlational and causal examinations of choice and choice-history signals in sensory, and in part sensorimotor, cortex and address formal statistical frameworks to infer causal interactions from data.

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Introduction

In neuroscience, we want to unravel the brain mechanisms that lead to cognitive behavior. Often, we start out by measuring correlations. For example, to probe how sensory neurons are linked to perceptual choices, one approach is to measure choice-related signals. We repeatedly measure perceptual choices in a challenging perceptual task, and correlate choices with trial-by-trial neural activity. A correlation between choices and fluctuations in neural activity across multiple trials with identical stimuli is then referred to as a choice-related signal. Such choice-related signals (often termed choice-probability or choice-correlation) have been reported for numerous tasks and sensory areas (e.g. Refs. [1–17]). The interpretation of these choice-correlations, that is, whether they reflect feedforward or feedback signaling,

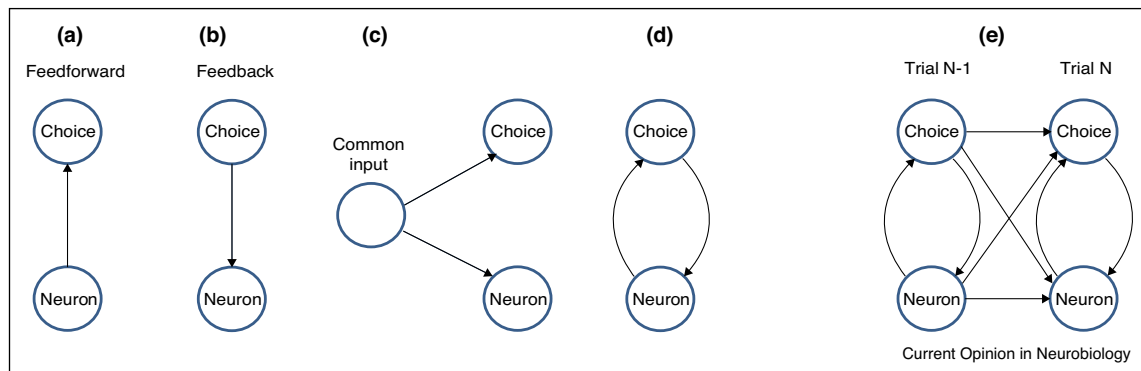
or both, or neither- and their dependence on inter-neuronal co-variability in response to an identical stimulus ('noise correlations' [18–20]) has received substantial attention (e.g. Refs. [21–26]). These questions exemplify the challenge of inferring causal structure from observational data (Figure 1). The conceptual challenges will likely persist with the ability to record from larger and larger neuronal populations [27]. The interpretational challenge increases when additionally considering that a choice is not an isolated event, which is solely determined by the current stimulus and task. Rather, choices are also affected by the behavioral history of the subject: Previous choices and stimuli might influence both the behavior of the animal [28–37], and associated neural activity [38[•],39[•],40[•],41,42], further complicating the search for causal interpretations of choice-related neural activity. Here, we will discuss these challenges, as well as recent empirical results and progress in the context of correlational and causal examinations of choice and choice history signals in sensory and, in part, sensorimotor cortex.

Interpreting choice signals in sensory cortex

Inferring the structure and directionality of the interactions that give rise to choice correlations in sensory neurons is complicated for a number of reasons (Figure 1a–d): Wiring in the brain is highly recurrent, and sensory neurons receive both feedforward, feedback and modulatory inputs. Neuronal responses show slow fluctuations [43–45], which can be unspecific global fluctuations in internal state (e.g. Ref. [46]), such as an animal's motivation [47] that may change over the course of a session. Such fluctuations might affect both neural activity and behavior, leading to choice-correlations even in the absence of a direct causal link in either direction. Even with modern recording technologies, it is only possible to record from a small subset of neurons in any cortical area simultaneously, and it is thus generally impossible to rule out common input between neurons (or a common influence on activity and behavior) from neurons whose activity is not observed directly (indeed, in most experimental settings, the majority of inputs will likely be coming from unobserved neurons [48]).

While, in general, such inputs pose major challenges for any causal analysis, in practice *unspecific* common input is not likely to drive systematic choice correlations across a population of neurons in feature discrimination tasks (e.g. discriminating upward versus downward direction of motion, as opposed to, e.g. a detection task): choice correlations in feature discrimination tasks are typically

Figure 1



Interactions that can result in choice correlations.

(a) A causal effect of the (sensory) neuron on choice, reflecting feedforward processing. **(b)** A causal effect of the choice on the neural activity, reflecting feedback processing. **(c)** A common input has a causal effect on both, the choice and the neuron, resulting in a correlation between these. Such a common input may not be observable, and is also termed confounder. **(d)** Recurrent connections between the sensory neurons and neurons encoding choices, for example, reflecting the combination of (a) and (b). **(e)** Possible causal interactions when also considering inter-trial dependencies.

signed [1], that is, quantified with respect to a neuron's preferred feature, for example, upward rather than downward motion (cf. Figure 2a). It would thus require the correlation of the common input with choice to change signs depending on the tuning preference of the simultaneously recorded neurons, an unlikely scenario. Moreover, if a balanced population of neurons preferring either feature to be discriminated is simultaneously recorded during such a feature discrimination task, an unspecific common input would result in positive choice correlations for neurons preferring one feature while negative choice correlations in neurons preferring the other feature, such that on average, the population would not be correlated with choice.

Choice signals in sensory cortex: cause and consequence

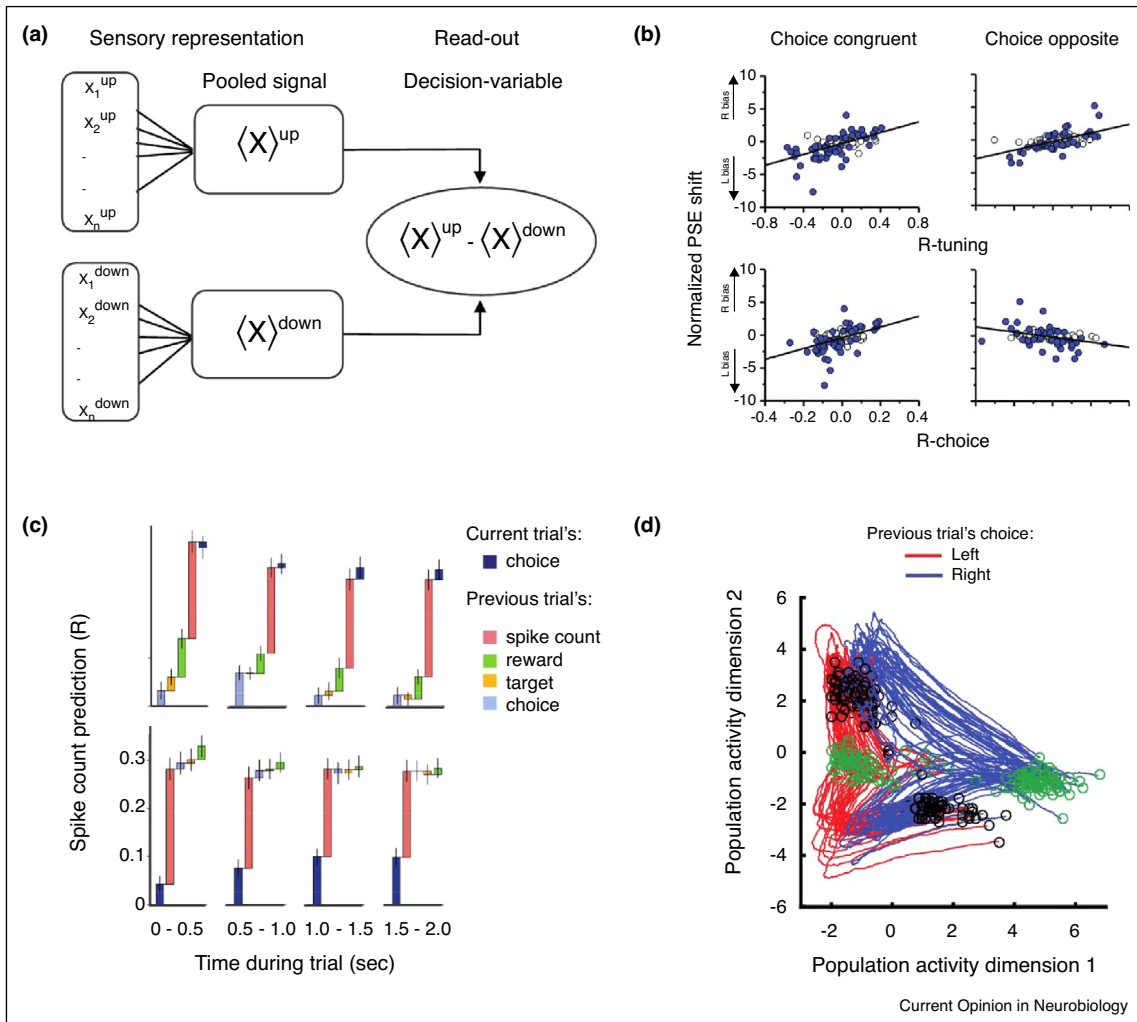
A landmark study discovered choice-correlations in neurons in the middle temporal visual area MT of macaques during a motion discrimination task [1]. It is worth noting that before this study, the same group had established a causal role of this area for motion discrimination [49] using electrical microstimulation. (That is electrically stimulating clusters of MT neurons selective for a particular direction of motion systematically biased the monkeys' choices towards that direction.) The discussion about how to interpret choice signals in MT was therefore less about whether these reflect a causal relationship but rather whether they only reflect the causal effect of (correlated noise between) these neurons [19] on choice (Figure 1a), as opposed to feedback from the choice to the neuron (Figure 1b,d). (We will not discuss the implications of correlated noise for choice correlations, nor the origin of noise correlations and their role for population coding [50,51], as these have been extensively addressed

elsewhere [52–54]). Choice signals are often measured over the duration of a trial, thus allowing time for feedback to modulate an initial feedforward sensory response (cf. Figure 1d). Indeed, a comparison of the temporal profile of the choice signals with that of the correlation between the stimulus and choices suggests that choice signals at least later in the trial are primarily driven by feedback [55,56], and can be well accounted for by models that incorporate feedback from the decision variable to the sensory neurons. In these models, the activity of the sensory neurons maintains a causal role on the decision despite the feedback, unless the subject commits to a decision before the end of the trial and the feedback to the sensory neurons persists (post-decision feedback). In such a scenario choice signals early in the trial would reflect the causal effect of the sensory activity on choice, while after the subject committed to a choice towards the end of the trial choice signals would reflect the consequence of the decision. Self-reinforcing feedback [56,57] can result in a mixture of both, and the trial averaged choice signal then reflects both cause and consequence [55,56].

Choice signals and the decoding of sensory information

A related general question is what we can learn from choice signals about the sensory read-out. That is, how is the activity from the sensory neurons is decoded [13,58–60]? For a number of areas and tasks both perturbation experiments have been performed and choice signals have been measured [4,7,61–69], and a pattern is emerging. For earlier, predominantly sensory, areas, perturbation experiments result in effects, which are consistent with a causal role, largely in line with their choice correlations. For sensorimotor areas for which neural activity showed

Figure 2



Findings highlighting the difficulties interpreting choice correlations.

(a) Schematic of the original pooling model (after Shadlen *et al.* [19]). It consists of a sensory stage of neurons whose activity is pooled and a read-out stage. It was devised to aid the interpretation of choice correlations (exemplified for an up/down direction discrimination task), and on how choice correlations depend on noise correlations between sensory neurons within and across the two pools (here ignored). **(b)** During a heading discrimination task (Yu and Gu [68^{*}]) performed by macaques, the partial correlation of the neuronal responses in MST with the stimulus when accounting for the correlation with choice, ('R-tuning') or the partial correlation of the responses with the choice when accounting for the correlation with the stimulus ('R-choice', each x-axis) was measured. R-tuning and R-choice were compared to the size of the behavioral bias induced by electrical microstimulation (shift of the point of subjective equality, PSE-shift, y-axis). R-tuning was correlated with the size of the behavioral bias across the population. In contrast, R-choice was positively correlated with PSE-shift for units whose choice correlation was consistent with the tuning ('choice congruent' units), but negatively correlated for units whose choice correlation was opposite to the tuning ('choice opposite' units). It exemplifies the difficulties to infer the decoding of the units from choice correlations (modified from Yu and Gu [68^{*}], with permission). **(c)** During a disparity discrimination task the spike counts of neurons in visual area V2 of macaques were predicted from experimental covariates. Model parameters (color coded) were included cumulatively such that the height of each bar quantifies the predictive effect attributable to individual parameters. Note that behavioral history (previous choice and target, light blue and yellow) had a sizeable predictive effect when included as initial parameters (top) but not when conditioned on, that is, included after, the current choice (blue) or the preceding spike count (pink) (bottom, modified after Lueckmann *et al.* [39^{*}], with permission). **(d)** During a navigation-based discrimination task in mice, the trajectories of the population activity in the posterior parietal cortex (PPC) differed as a function of the choice of the previous trial (green and black circles mark the beginning and end of a trial, respectively; modified after Morcos and Harvey [40^{*}], with permission).

pronounced correlation with choice the effects of perturbative manipulations were often weak [63] or absent (e.g. Refs [62,64,68^{*},69]), but see also recent findings which identified a causal role of parietal cortex under certain

conditions [70]). These results call into question influential accounts of the decision process based on, in part, choice signals in sensorimotor areas [66]. However, note that a weak effect on choice is expected for an area that integrates

sensory evidence [63], and the interpretation of perturbative manipulations themselves can be problematic [71]. For example, given the redundancies in the brain it is possible that even if an area is causally involved in a task, such redundant mechanism might compensate and no loss of function is apparent when this area is silenced.

Perhaps the most detailed insights into the what can be learned from choice correlations about the decoding of sensory neurons come from an elegant series of studies using a cue-combination task in a virtual reality environment [72]. Macaque monkeys were trained to discriminate heading direction using vestibular, visual or both cues [72]. The researchers then recorded neurons in several areas, including the dorsal portion of the medial superior temporal area (MSTd) and discovered that some cells had incongruent tuning across sensory conditions: for example they would prefer rightward heading in the visual condition and leftward heading in the vestibular condition. Interestingly, these ‘opposite’ cells, were, on average, negatively correlated with choice in the visual condition but positively correlated with choice in the vestibular condition. A variant of the original pooling model [19] (Figure 2a) with appropriate noise correlations could account for these findings when assuming that signals from opposite cells are decoded according to their vestibular tuning preference (‘selective decoder model’ [73]). Since MSTd is a predominantly visual area, such decoding according to the vestibular preferences seems surprising, and a valuable prediction. A recent study could test this by comparing the choice correlations and perturbation effects using microstimulation [68^{*}] directly on a site-by-site basis. These experiments were restricted to the visual condition and congruency between the visual and vestibular condition could therefore not be evaluated directly. But the authors identified a subset of units in MST that were negatively correlated with choice, which suggests that these were largely ‘opposite’ units. And even for these putative ‘opposite’ units the causal effects were consistent with their visual tuning, and opposite to their choice signals (Figure 2b). This contradicts the above model predictions of selective decoding according to the units’ vestibular tuning. Note that this conclusion assumes that these neurons were indeed ‘opposite’ cells as previously characterized [74], that the electrical perturbation was sufficiently similar to the physiological neural response subspace [71] to be interpretable, and that the perturbed [75] and recorded units were roughly equivalent. But under these assumptions, these results show that it can be misleading to infer decoding rules from choice signals, even when the neurons are causally linked to the decision process.

Interpreting choice-history signals in sensory cortex

A further complication arises from the fact that both choices and neural activity are not determined by the current trial

alone, but can be influenced by experimental history. Psychophysics in humans and animals has long revealed that choices are often biased both by previous stimuli, as well as by a subject’s preceding choices [28–34,36,37]. Recent studies have characterized how such choice history leads to loss in performance (e.g. Refs. [29,31,33^{*}]), how it adapts to the statistics of the task [33^{*}], or how it depends on motor commands [34,36]. Evidence for a sensory involvement of such effects comes, for example, from the observation of choice-history signals in sensory cortex [42]. Thus, both choices and neural activity are correlated with each other, as well as with previous choices and previous neural activity (Figure 1e); this can make it complicated to disentangle the statistical structure that gives rise to choice-history signal in sensory neurons, let alone gain insights into the underlying causal mechanisms.

A recent study [39^{*}] addressed this question and found that choice history was predictive both of the spiking activity and the choice on the current trial (Figure 2c, top). But when asking whether this effect was statistically independent of the effect of the preceding spike count and the current choice (by conditioning on the preceding spike count and the choice of the current trial) the study found that the previous predictive effect of choice history largely disappeared (Figure 2c, bottom), arguing against an effect of choice history on spiking activity independent of the inter-trial fluctuations in the neural activity. In addition, the *partial* correlation between neural activity and choice (i.e. when taking out the effect predicted by trial-history, not shown in Figure 2c) was comparable to the total correlation, suggesting that choice-correlations are dominated by within, rather than across-trial (cf. diagonal arrows in Figure 1e) effects in this task.

Even if they cannot provide conclusive evidence for causal relations, correlations may be guidance for causal exploration: For example, a signature of such choice-history signals has been observed in the posterior parietal cortex (PPC) in mice (Ref. [40^{*}], Figure 2d), and inactivating the PPC optogenetically reduced the choice-history induced bias [76] in support of a causal involvement. Since choices typically co-vary with the stimulus it can be difficult to dissociate the effect of choice history from that of stimulus history, which also have been shown to have a pronounced influence on current choices. When disentangling these, a recent study in rats [38^{**}] observed a more pronounced effect of stimulus history rather than choice history, on current choices. This study also found evidence for a causal involvement of the PPC, consistent with a role of working memory inferred from psychophysical studies [35,37].

Formal statistical frameworks for inferring causal interactions from data

What – if any – inferences can we draw from correlations about underlying mechanisms? Extensive work in diverse fields such as epidemiology, econometrics [77], statistics

and machine learning (e.g. Refs. [77,78,79**]) has studied when and how one can make statements about underlying causal interactions from observational data. Many of these approaches are based on the notion of ‘directed causal graphical models’ (or causal Bayesian Networks [78]): In these causal diagrams (cf. Figure 1a–c), each ‘node’ represents a component of the system of interest (e.g. neural activity in a brain region, the current choice, previous choices), and directed edges (‘arrows’) represent assumptions about the presence (or absence), as well as about the directionality of interactions between these components. These models can be used to mathematically reason about the effect of perturbing some nodes on other nodes, via a mathematical framework known as ‘do-calculus’ [78]. Importantly, each such a causal diagram implies a set of conditional independencies. For example, in Figure 1c, the choice and neuron are independent, when conditioning on the common input. These conditional independencies can be thought of as a generalization of partial correlations—therefore, by characterizing partial correlations, one could rule out underlying causal graphs.

However, while *some* graphs can be distinguished from each other based on such conditional independence tests, there are many graphs, which give rise to the same conditional independencies. These therefore cannot be distinguished from observational data alone (the most simple, and worrisome, example being $X \rightarrow Y$ and $Y \rightarrow X$, i.e. the fact that the direction of causal interactions between two observables cannot generally be determined from data alone). To distinguish any two such graphs, either interventions (i.e. targeted perturbations), additional assumptions [80] or specific task-properties (e.g. in regression discontinuity designs [81]) need to be exploited.

However, even beyond these fundamental limitations, there are also many practical ones which make direct application of these formal approaches to identify causes underlying choices challenging: First, choices might be influenced by ‘confounders’ (cf. the common input in Figure 1c) which cannot be measured directly, and for which it is difficult to make reasonable assumptions about how they interact with observable components. In these cases (and in particular if confounders dominate the interactions, likely a common scenario in some neuroscience settings), it can be impossible to make any causal statements [48]. Second, recurrent connections are ubiquitous in the brain, which can be challenging to capture in directed graphical models. Third, conditional independence tests typically require large amounts of data, and this can make it difficult to detect weak, or highly nonlinear, interactions (or provide evidence for its absence). Because of these limitations, formal approaches to causal inference are still rarely used explicitly in neuroscience, but see Refs. [82,83].

Conclusion

Focusing on correlations between perceptual choices and the activity of sensory neurons, we here highlighted challenges to infer causal structure from correlations, both from a formal statistical perspective and by addressing recent experimental studies. In general, it is problematic to infer causal structure, functional significance or decoding strategies from choice correlations of sensory neurons: The fact that one can decode choices from the activity of certain neurons does not imply that the brain, too, decodes these neurons to guide the choice. However, neither does a lack of a causal role imply that these signals are merely the result of confounders, or that they are meaningless for the brain. An illustrative analogy might be the concept of an efference copy in the motor system: it provides a signal that is correlated with the current motor command but is not causally involved, and yet important for subsequent motor control. Moreover, choice signals or other correlations can be informative to identify relevant population subspaces for further exploration [71]. They are also useful for testing predictions of algorithmic models of perceptual decision making (cf [57,84]) and linking these two elements of neural computation [60].

Conflict of interest statement

Nothing declared.

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