The needle in the haystack

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Spike-based approaches to feature selectivity in sensory pathways can bias toward only the most active neurons. A subthreshold method identifies feature selectivity in the rodent vibrissal system regardless of spiking activity.

We live in a complex sensory environment and are constantly being bombarded by signals that activate each of our sensory pathways. The basic premise of sensory neuroscience is that, as we move through the pathway from the periphery to deeper in the brain, individual neurons become increasingly selective for particular features in the sensory world. It is this feature selectivity on which we form our perceptions of the outside world. Since the seminal work of Hubel and Wiesel in the visual pathway[1], the race has been on to identify complex feature selectivity in a range of sensory pathways so that we may unlock the mysteries behind what the pathway is actually doing, how the synaptic architecture of the circuitry creates the selectivity, and how the selectivity feeds computations that ultimately give rise to inferences and decision-making. In this issue, Ramirez et al.[2] use a multi-whisker stimulator and in vivo whole-cell recording in the cortical region associated with the facial vibrissae of the rat in the search for feature selectivity and the synaptic inputs that shape the selectivity in this well-studied pathway.

Identifying complex feature selectivity of sensory neurons is difficult, to say the least. This is certainly what made the discovery of orientation selectivity in the visual pathway all the more remarkable. The range of possible features in the visual environment that could in principle have elicited activity in V1 neurons is enormous, making the process feel like searching for a needle in a haystack. More systematic approaches that did not rely solely on the intuition of the experimenters were later developed to characterize the spatiotemporal receptive fields of cortical visual neurons, and these approaches uncovered receptive field structure revealing the orientation selectivity commonly observed in V1. Specifically, using complex, random spatiotemporal patterns of visual input and correlating the inputs with evoked spiking activity revealed structure in the visual input associated with neuronal firing[3]. This so-called spike-triggered

averaging technique (or reverse correlation, and a range of variants) has become a common means by which to characterize receptive field properties of neurons throughout sensory pathways (**Fig. 1a**). Although this has become a mainstay in vision and audition, it has been less widely explored in somatosensation[4], owing in no small part to the difficulty of delivering complex tactile inputs[5,6]. Ramirez et al.[2] used a systematic approach to deliver complex, random spatiotemporal patterns of whisker stimulation across the whisker pad to probe the feature selectivity of the pathway without restrictions on the relevant stimulus dimensions.

Although delivering complex stimuli is critical to characterizing feature selectivity, it will not necessarily solve all issues with spike-based approaches. The catch with spike-based approaches for characterization of coding properties of sensory neurons is that you need spikes, and lots of them. Neurons in sensory cortex are known to be sparse, both in the sense that small numbers of neurons are active at any given time and in the sense that an individual neuron can

fire relatively few action potentials over time. In an elegant study of multi-whisker interactions in barrel cortex, Estebanez et al.[5] explored the effect of spatiotemporal correlations on cortical coding, finding complementary coding schemes in the presence and absence of correlations in the input, consistent with a context-dependent code. However, in this study, feature selectivity was based on observed extracellular action potentials, and approximately 70% of more than 1,500 recorded neurons could not be characterized because of the lack of spiking over the experimental period. The implications of this are profound: most of what we know about sensory coding has been derived from observations of only the most active neurons in the circuit, undoubtedly introducing a bias into our understanding of neocortex[7]. This issue is especially important in the case of the comparatively quiet cortical layer 2/3, making the characterization of feature selectivity for this layer in the vibrissal pathway nearly impossible given present analytical techniques. Ramirez et al.[2] introduce a new computational approach
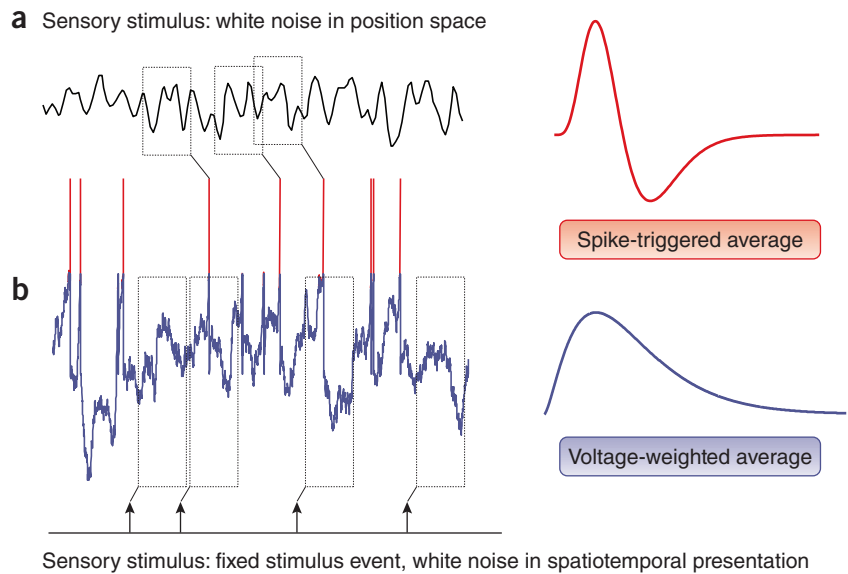
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a Sensory stimulus: white noise in position space

Spike-triggered average

Voltage-weighted average

Sensory stimulus: fixed stimulus event, white noise in spatiotemporal presentation

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Figure 1 Identifying feature selectivity. (**a**) Spike-triggered average (red) correlates the sensory white noise stimulus (black) with the action potential events. The stimulus segments immediately before an action potential (measured in stimulus units; for example, degrees of whisker deflection) are averaged to represent spatiotemporal features of the stimulus associated with spiking. (**b**) Voltage-weighted average probes the spatiotemporal feature selectivity through the use of stimulus events that are presented randomly in time and space across the whisker pad (black). The subthreshold membrane potential (measured in millivolts) immediately following a discrete stimulus is averaged across trials to develop a spatiotemporal filter of the subthreshold response.

using intracellular recordings: instead of performing spike-triggered averaging from the whisker stimulus, they performed a voltage-weighted averaging from the continuously varying intracellular voltage signal (**Fig. 1b**). The result is an approach that can provide a robust characterization of the spatiotemporal receptive field properties, and thus feature selectivity, with substantially less observation time and without any required spiking activity. The authors go on to show the explicit relationship between the voltage-weighted average and the classical spike-triggered characterization. Furthermore, they achieved layer specificity using histological analysis to quantify cell morphology and cortical depth.

Beyond the technical advance, however, Ramirez et al.[2] have made several scientific advances that will certainly prompt many further investigations. Although often not described as such, the receptive field of a sensory neuron is not an invariant property of the neuron and the circuit in which it is embedded but instead reflects a complex interplay between the circuitry and the way the circuit is engaged by the sensory input. Ramirez et al.[2] found that the complex, spatiotemporal tactile patterns that they presented led to sharpened receptive fields, in contrast with the broad, diffuse receptive fields that they observed for simple, single-whisker stimuli that have been classically used. Counterintuitively, this complex sensory stimulation corresponded to a facilitative surround influence, in contrast with the findings in a range of previous studies. The authors suggest that the sharpening of the receptive fields that they observed for complex stimuli reflects an adaptation that may shift the pathway from a

regime in which inputs are encoded for detection to a regime in which enhanced acuity might facilitate sensory discrimination, as shown in recent studies[8,9]. They further found distinct receptive field properties from layer 2/3 neurons that have not been well described from this functional perspective, owing in large part to the sparse firing activity in these layers. This begs the question, as asserted by Barth and Poulet[7], as to whether the lack of functional characterization of layer 2/3 neurons might perhaps be a result of experimentally impoverished inputs. In contrast, however, Ramirez et al.[2] provide evidence that even rich spatiotemporal tactile inputs are often insufficient to drive spiking activity in layer 2/3. The implications for these findings are that superficial layers may not be purely responsive to sensory input in a simple way but are instead part of a more integrative, cross-laminar computation. These findings are consistent with recent behavioral studies in rodent primary visual cortex that show an increase in layer 2/3 activation during locomotion[10,11], potentially as part of a sensorimotor integration framework.

What remains, in this pathway and other sensory pathways, is connecting the dots between feature selectivity and the natural world that we live in. For example, we presume that, because the visual world is made up of objects that have boundaries, the complex natural scene must be comprised of oriented edges that engage this ubiquitous feature selectivity in visual cortex. However, the relationship between simple feature selectivity and the natural world is very poorly understood, especially in the context of a dynamically varying environment. So what is the needle in the

haystack for the vibrissal system? Ramirez et al.[2] have provided a layer-by-layer analysis of the encoding of somatosensory information in the rodent vibrissal pathway using complex sensory inputs that identify nontrivial multi-whisker interactions that directly affect feature selectivity. This work begins to identify the processing roles of each cortical layer, even those with little to no spiking activity, in response to complex sensory inputs. Although our understanding of how feature selectivity gives rise to perception is still limited, the work from Ramirez et al.[2] sets the stage for a range of investigations that may help us to more fully understand the complex coding of the sensory world across cortical laminae that forms the substrate of basic computations.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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The (gamma) power to control our dreams

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Stimulating the brain in the gamma frequency range, which is the frequency band most often associated with conscious awareness in the awake state, boosts the ability to engage in lucid dreaming during REM sleep.

I have long been fascinated by dreams, both personally and scientifically. Early in graduate school, I tried to keep this interest hidden for fear of being perceived as 'far out' or lacking in scientific credibility. But what was this state of consciousness that allowed us to defy the laws of physics, to connect fragments of

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our experience in creative, even preposterous ways and to sometimes become aware of these experiences as they unfolded in our sleeping minds? In spite of my long-held interest in dreams, however, even I was shocked to learn that lucid dreaming—the phenomenon in which a dreamer becomes aware that he or she is dreaming and can potentially exert control over the dream—was a distinct cognitive state whose existence has quite a bit of scientific support[1,2]. Lucid dreaming finds its strongest support yet in a study published in this issue of *Nature Neuroscience*, in which

Voss et al.[3] demonstrate that lucid dreaming can be experimentally triggered by stimulating the brain at a frequency associated with conscious awareness.

Lucid dreams are believed to occur exclusively during rapid eye movement (REM) sleep, which is an active brain state that is similar in some respects to wakefulness. Usually, the REM-sleep dreamer uncritically accepts the bizarre and disjointed themes of dreams as normal. As protagonist Dom Cobb explains in the science fiction heist thriller film *Inception*, which was inspired by lucid dreaming,