Behavioral States, Network States, and Sensory Response Variability

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INTRODUCTION

The primary goal of the sensory neuroscientist is to describe the brain’s reaction to specific environmental stimuli and to relate these characterizations to perceptual function. To this end, neurophysiologists typically present a stimulus multiple times while recording the spiking activity of the subject’s sensory neurons. The fact that these single-neuron responses are affected by the firing of other neurons to which they are connected—that each sensory neuron is extensively connected to others within local and distributed networks, such that activity in the network will affect the probability of firing in others—is not a subject of much debate.

The network activity in question can be summarized in terms of “states” of balanced inhibition and excitation (Brunel 2000; MacLean et al. 2005; Vogels et al. 2005) and monitored in “spontaneous” (i.e., not driven by any specific stimulus) local field potential (LFP) recordings, a measure of the average electrical activity of local networks (see Buzsáki 2006); the term “network state”, then, serves as shorthand for emergent, coherent structure (typically oscillatory) in the activity of multiple interconnected single neurons. Theoretical analyses predict that when these network states change, the changes should have significant, nonrandom impacts on single-neuron processing of inputs (Chance et al. 2002; Jaeger and Bower 1999; Santamaria et al. 2002). Thus it is reasonably clear that sensory responses should be studied in the context of the current states of networks in which the neurons reside.

In this review, we explore the implications of this innocuous-seeming claim. After first reviewing data demonstrating that large-scale state changes in unconscious animals—across levels of anesthesia and sleep—do indeed significantly influence sensory function, we relate these effects to a series of successively more subtle phenomena in awake animals. We discuss well-studied behavioral state changes known to modulate sensory responsiveness—switches from consciousness to unconsciousness and from attentiveness to inattentiveness—and show that they are associated with (and perhaps synonymous with) neural network changes. We then turn to learning-related behavioral modifications, suggesting that the sensory response changes typically linked to learning-related synaptic changes may in fact be more directly related to network reconfigurations. Finally, we extend this analysis to include sensory variability occurring across one to three trials; this extension leads us ultimately to suggest that trial-to-trial variability in sensory responses may not be meaningless noise, as is commonly believed, but may instead be a function of behavioral and network state changes.

If this last point is correct—if network states shift on a moment-to-moment basis, such that sensory responses change from trial to trial—then the nervous system does not act on reliable sensory representations; thus the innocuous-seeming link between network states and sensory responses may in fact represent a challenge to current thinking about sensory processing, which is based on the idea that objects are represented in the brain by stationary (plus random noise) sensory codes.

RESPONSES CHANGE ACROSS LEVELS OF ANESTHESIA AND SLEEP

At first glance, it appears that brain function should be easily described in an unconscious animal. The animal is simply anesthetized, knocked out, dead to the world. A closer look, of course, makes it clear that this description is not strictly correct; physiological and behavioral parameters frequently change during surgery as a function of anesthesia level: reflexes disappear and reappear, muscular tone increases and decreases, and heart rate, respiratory frequency, and core temperature change. With these changes come dramatic shifts in neural network states (Friedberg et al. 1999), measured in terms of shifts in the characteristic frequencies in single LFPs, or in the coupling between multiple LFPs or spike trains. During periods of lighter anesthesia, spontaneous patterns of cortical activity are reminiscent of the “fast oscillations” observed in animals during periods of active waking or rapid eye movement (REM) sleep. Activity patterns of a deeply anesthetized animal, meanwhile, are more reminiscent of “slow-wave sleep” (Adrian 1950; Fontanini and Bower 2005; Friedberg et al. 1999; Murakami et al. 2005). These phenomena have been explicitly linked to changes in thalamocortical network...
functioning (Destexhe and Sejnowski 2001) and to modulations of the balance between intrinsic excitatory and inhibitory conductances (Bazhenov et al. 2002; Hill and Tononi 2005).

Sensory responses change with these sudden, anesthesia-linked transitions from one LFP regime to another. In the olfactory cortex of rats, for example, odors evoke smaller and shorter-lasting responses when the animal is in sleep-like states than when it is in waking-like states (Murakami et al. 2005; Fig. 1A). Similar results have been noted in auditory cortex (Kisley and Gerstein 1999) and in somatosensory thalamus and cortex (Aguilar and Castro-Alamancos 2005; Castro-Alamancos 2004). A series of analogous results from visual cortex—coupled changes in spontaneous patterns of background activity and receptive field shapes—have been successfully modeled in terms of specific shifts in the balance between excitation and inhibition in simulated networks (Worgotter et al. 1998).

Given these results from studies of anesthesia (Steriade 2000), it is natural to ask whether sensory responses change across different sleep stages—each of which is associated with distinctive patterns of LFP, physiology, and behavior—they themselves. In fact, responses to a particular stimulus are different in each of the different network states that distinguish stages of sleep. In auditory thalamus (Edeline et al. 2000), for instance, sensory responses recorded during slow-wave sleep differ in several ways from those recorded during REM sleep: neurons recorded during REM sleep typically respond to larger frequency ranges, in a less homogeneous fashion, than do neurons recorded during slow-wave sleep.

In summary, even under apparently monolithic conditions (i.e., situations in which the animal is immobile and not producing any obviously visible movement), sensory responses depend on subtle distinctions in the animal’s physiology, distinctions that are synonymous with local and distributed neural network states.

**RESPONSES CHANGE ACROSS THE BOUNDARY OF CONSCIOUSNESS**

Given that coupled plasticity in network activity and sensory responses is observed within periods of time in which an animal remains still and unconscious, it comes as no surprise that the transition between consciousness and unconsciousness is associated with large differences in both network states and sensory function. The spectral character of LFPs in the olfactory bulb changes as an animal falls under (or climbs out of) the sway of anesthetic (Adrian 1950). Furthermore, odor responses in olfactory bulb neurons are much sparser in awake animals than in anesthetized animals. Approximately three fourths of the neurons that can be identified as odor responsive

![Figure 1](http://jn.physiology.org/)

**FIG. 1.** Macroscopic states modulate neural responsiveness. A: responses to odors in the olfactory cortex of rats are larger during periods dominated by fast electroencephalographic (EEG) waves (right) than during periods of slow waves (left). From top to bottom: EEG recorded from neocortex; a single-trial, single-neuron olfactory cortical response histogram and associated spike train (SU); simultaneously recorded record of artificial inhalation (AI); and, finally, an across-trial peristimulus time histogram (PSTH). B: average firing rate (y-axis) across time (x-axis) of a murine olfactory bulb mitral cell in response to amyl acetate (red) and citral (blue) during anesthesia and wakefulness. Note that the excitatory response to amyl acetate turns inhibitory during wakefulness. Gray shadow: period of odor presentation. Colored bars: average response amplitude across the last half of the stimulus period. Black line in the prestimulus period: average spontaneous firing frequency. C: spread of activity following magnetic stimulation of the cortex in human subjects during nonrapid eye movement (NREM) sleep (left) and wakefulness (right). Traces on the left of each panel are global mean field powers (yellow line: significance level). On the right of each panel, brain diagrams showing the location of current sources, color coded according to the latency of activation (blue = 0 ms; red = 300 ms). The yellow cross marks the location of the stimulus. Panels modified with permission from Murakami et al. (2005) (A), Rinberg et al. (2006) (B), and Massimini et al. (2005) (C).
in the anesthetized state become less responsive as the animal wakes and some of the remaining responses change from excitatory to inhibitory (Rinberg et al. 2006; Fig. 1B). These network and sensory phenomena are likely related to the fact that, in awake animals, olfactory bulb responses are involved more in task-related functions than in olfactory coding itself (Kay and Laurent 1999), via strong feedback connectivity from piriform cortex (Martin et al. 2007).

Although such studies are scarce, data from other sensory systems match those observed in the olfactory bulb. The auditory cortical tonotopy, for instance, also changes across the consciousness boundary. Primary auditory cortex (AI) tone responses increase in latency, decrease in number and amplitude, and even change in best frequency under equithesin anesthesia (Gaese and Ostwald 2001). Between waking to slow-wave sleep the changes are more variable but no less striking (Edeline et al. 2001). Network function changes across the slow–wake divide and this change has major implications for single-neuron processing.

Research from Tononi and colleagues (Massimini et al. 2005) puts these findings in a larger systems context and provides additional evidence for the link between network organization and response changes seen during the transition from wakefulness to slow-wave sleep. These researchers used high-density scalp electrodes to record the spread of transcranial stimulation in human subjects during sleep (specifically during periods of nonrapid eye movement sleep characterized by slow oscillations) and wakefulness. The initial stimulus-induced activity was stronger, but the spread of activation was greatly reduced in both temporal and spatial extent, in sleeping compared with waking subjects (Fig. 1C). The processing of activity (in this case, electrically induced) was greatly curtailed during sleep because of greatly increased damping of the effective network.

**NEURAL RESPONSES CHANGE WITH ATTENTION**

The value of working with awake animals lies in the fact that the researcher has the opportunity to explore the interaction between cognitive variables, typically thought of as top-down influences on sensory processing, and the bottom-up sensory neural responses themselves. The most obvious and well studied of these cognitive state shifts is the one between attentiveness and inattentiveness. Here we suggest that shifts in attention are analogous to the variations in anesthesia and sleep levels described earlier. In each case, reconfigurations of the network underlie changes in sensory responsiveness.

Sizable, meaningful changes in animal behavior accompany sudden shifts of an animal’s focus toward particular features or modalities of its stimulus environment. Attention affects performance on stimulus detection and discrimination tasks and, in general, is a central variable controlling sensory processing (for review, see Posner 1980). Furthermore, evidence tightly links changes in attention to modulations of neural response magnitudes, both in higher-order (Mitchell et al. 2007; Reynolds and Chelazzi 2004) and primary sensory cortices—including visual (Li et al. 2006) and auditory (Fritz et al. 2005, 2007) cortices—and even in sensory thalamus (Kastner et al. 2006; Wunderlich et al. 2005).

More recently, it has become apparent that attention is, like sleep and anesthesia level, intimately related to specific network states (Buschman and Miller 2007; Saalmann et al. 2007; Womelsdorf and Fries 2007; Womelsdorf et al. 2006). Specifically, attention acutely changes the spectral content of LFPs, enhancing activity in multiple frequency ranges, most notably $\theta$ (4–7 Hz) and $\gamma$ ($\sim 30–80$ Hz; Ekstrom et al. 2005; Engel et al. 2001; Fan et al. 2007; Womelsdorf and Fries 2007). Such enhancements are positively correlated with performance on attention-intensive behavioral tasks (Womelsdorf et al. 2006; Fig. 2A).

Whereas $\theta$ and $\gamma$ rhythms become enhanced in the LFP of an attentive animal, intermediate rhythms—7–12 Hz ($\alpha$ or $\mu$)—become enhanced specifically when an animal stops attending (Fig. 2B); in the extreme, enhancement of neural activity in this frequency range evidences itself as complete attentional withdrawal and the onset of “absence seizures” (Shaw 2004, 2007). The sudden withdrawal of attention and the attendant enhancement of $\mu$ and $\alpha$ rhythms can happen spontaneously and transiently and, when it happens, performance on behavioral tasks suffers (Fontanini and Katz 2005; Molle et al. 2002; Slobounov et al. 2000). In essence, the prominence of $\theta$ and $\gamma$ (or of $\alpha$ and $\mu$)—that is, specific measures of network state—can serve as a continuous measure of an animal’s level of attention (or inattention).

Neural sensory responses in awake animals prove sensitive to such changes in concurrently recorded LFPs, even when those changes appear to happen “spontaneously” in relation to general levels of attention and arousal. Investigations on the visual, auditory, and somatosensory systems demonstrate that response magnitudes rise as a function of $\gamma$ power and fall as a function of $\alpha$ and $\mu$ power (Bezdudnaya et al. 2006; Cano et al. 2006; Fanselow and Nicolelis 1999; Womelsdorf et al. 2006). Although this phenomenon has been explicitly referred to as an active “gate” that prevents stimuli from activating the forebrain of inattentive animals (Shepherd 2005), responses to stimuli with emotional valence (such as taste stimuli) are not “gated out” during $\mu$-related inattention; rather, inattention alters responses to these stimuli, emphasizing hedonics and palatability (the emotional content of the stimulus) over actual stimulus identity (Fontanini and Katz 2006).

Regardless of the specifics, it is clear that the sensory impact of attentional changes can be directly related to network function, which changes across a session, sometimes as the intended result of an experimenter’s task manipulations and sometimes despite (or even because of) an experimenter’s lack of manipulation. Attention can in fact be reconceptualized in terms of network function, which shapes the way stimuli are processed in meaningful and reasonable ways, enhancing or suppressing particular aspects of the neural responses. Thus it is important to track changes in network states, to avoid treating data collected under different conditions as differing only in random ways.

**NEURAL RESPONSES CHANGE WITH LEARNING**

As described earlier, attention pertains to an animal’s focus on a sensory modality that has particular relevance at that point in time. Of course, in natural conditions, and in most laboratory tasks, stimulus relevance is a learned quality. It is thus reasonable to suspect that learning and learning-related response changes might themselves be explainable in terms of network states (Gilbert and Sigman 2007). Indeed, when an animal
learns the relationships between stimuli and particular rewards (Maunsell 2004; Schoenbaum et al. 1998), this learning is accompanied by modifications in network states: not only does the spectral content of spontaneous (i.e., prestimulus) activity in primary sensory areas vary in ways that are similar to those caused by attention; the within- and between-region functional connectivities change over the course of learning as well (Bressler 2004; Kay and Freeman 1998; Schoenbaum et al. 2000; see Fig. 3A). Learning is in fact a network change.

Of course, learning has long been known to modulate neural responses to task-related stimuli. In studies on human subjects, stimuli are perceived more according to expectation than reality and these perceptions are tracked by neural activity (functional magnetic resonance imaging [fMRI] blood oxygenation level–dependent signals) in sensory areas (de Araujo et al. 2005; Nitschke et al. 2006). It is not only the coding of expected stimuli that is changed by learning; however: at least in the task context, the neural response to the cue stimulus itself changes, as well, according to its learned predictive value (Schoenbaum and Roesch 2005). In the olfactory cortex, for instance, neurons alter their responsiveness to two different odors as the animal learns within an experimental session the predicted outcome of each of them; furthermore, responses reverse if and when the odor cue-outcome association is reversed (Calu et al. 2007; Roesch et al. 2007). A similar phenomenon has also been observed in the olfactory bulb, where spiking responses of neurons can be ascribed as much to the predictive value of a stimulus as to its sensory quality (Kay and Laurent 1999). It is reasonable to suggest that these changes in responding to stimuli with learned relevance are a direct function of the spontaneous and driven network state changes described in the preceding paragraph—a possibility for which direct evidence has recently been collected, in a study showing that taste learning is accompanied by changes in amygdalo–cortical interactions (Grossman et al. 2008).

Even when reward and punishment do not drive explicit learning—when features of the environment naturally co-occur, for instance—sensory responses change in tight conjunction with alterations of network states. Primates and rodents are in fact exquisitely sensitive to the coherent statistics of the environment, even when the interstimulus relationships are unrelated to the attainment of reward (and even when the subjects cannot consciously identify these relationships; see Arcediano and Miller 2002; Orban et al. 2008; Saffran et al. 1996). Particularly clear examples of this phenomenon can be found in studies of multimodal stimuli, which occur together by virtue of being part of the same real-world event. Human infants quickly learn the importance of multimodal coherence (Bahrick et al. 2004); such multimodal interactions appear to modulate single-unit responses in such a way that responses to each unimodal stimulus are altered by the presence of the other (Ghazanfar and Schroeder 2006; Ghazanfar et al. 2005). Although no network changes were specifically observed in the background activity preceding the presentation of multimodal stimuli in these studies, a more recent paper demonstrates that the spectral signature of LFP responses in A1 is

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**FIG. 2.** Relationship between behavioral and network states. A, top and middle panels: time course of average relative power in the gamma band of a visual cortex local field potential (LFP, y-axis) across trials (x-axis) in which a monkey showed fast and slow reactions to a sudden visual change taking place within the receptive field of neurons simultaneously recorded from the same electrode. The 0 time point in the x-axis shows when the stimulus change occurred. The top panel shows the relative LFP power when the changing stimulus was the focus of the monkey’s attention, whereas the middle panel represents the power induced when it was meant to be ignored. In each, the solid line shows LFP power for trials with fast reaction times (i.e., when attention was allocated most effectively) and the dashed line shows power for trials with slow reaction times (those when attention was less effective); the gray-shaded area shows significant differences between those two trial types. Gamma power predicts faster reactions to attended stimuli and slower reactions to unattended stimuli. Bottom: Z-score of correlation coefficients across monkeys and recording sites for LFP power vs. reaction times, showing that higher gamma power predicts faster performance (i.e., smaller reaction times). B: correlation between μ oscillations and reaction times in rat engaged in a tasting session. Top trace: session-long recording trace of a single cortical LFP, showing a general change at 71 min into the session; below, two 2-s-long traces, one from early in the session and one from late, showing in detail the emergence of μ rhythms late in the session. Bottom: the 2 bars show the amount of μ rhythms in and after the 1st h; the points overlaid on the bars show the reaction times of the first purposeful orofacial movement in response to a taste stimulus. Note the correlation with μ rhythms. A modified with permission from Womelsdorf et al. (2006); B from Fontanini and Katz (2005).
modified by the simultaneous presentation of the visual stimulus with the auditory stimulus (Ghazanfar et al. 2008; Fig. 3B).

In summary, learning-related response changes that are usually discussed as a function of plasticity at discrete and specific synapses may in fact be better thought of as secondary to distributed changes in network and neural function (Maffei and Turrigiano 2008; Maffei et al. 2004)—modifications that are themselves a function of more spatially diffuse patterns of plasticity at multiple levels of the circuit or (in the case of attention) of more transient phenomena such as phasic activation of neuromodulatory nuclei (Bouret and Sara 2005). Learning is just another example of network function driving sensory function, with synaptic plasticity serving to shift the network into new states such that handling of incoming stimuli is consistently updated by experience.

Sensory Responses Change from Moment to Moment

The work described in previous sections demonstrates that experience and context—even subtle experience and ephemeral and/or internal context—can have a powerful impact on the states of sensory networks and thus on the processing of specific sensory stimuli. Carried to their logical extreme, these findings have implications that are both exciting and worrying. Since experience accrues gradually and since internal and external contexts can effectively change from moment to moment, the possibility arises that nonrandom network state shifts may develop quickly and capriciously and that sensory function may therefore be subject to trial-by-trial variations that are not appropriately described as random noise. An ideal paradigm in which to look for such effects would be one in which the impact of experience accrues gradually across a session. The ongoing sensory experience during feeding is just such a paradigm because an animal’s internal homeostasis gradually changes as the animal approaches satiety (de Araujo et al. 2006). With decreasing appetite comes changes in the animal’s behavioral and neural responses to the specific food on which it is being fed (Corbit et al. 2007; Rolls et al. 1989), which relate to profound modifications of spontaneous ensemble activity across the many areas involved in feeding behaviors (orbitofrontal cortex, amygdala, lateral hypothalamus, and gustatory cortex; de Araujo et al. 2006).

Even the development of familiarity is associated with modulations in the spontaneous activity of brain networks (Bouret and Sara 2005; Harley 2007), with neural plasticity (Berman and Dudai 2001), and with modified responses to stimuli: work on olfaction demonstrates that one to two odor presentations suffice to change a rat’s behavioral responses to formerly novel tastes or odors (Verhagen et al. 2007); early neural responses change on the same timescales (Bazhenov et al. 2005; Stopfer and Laurent 1999; Verhagen et al. 2007). Similar findings have recently been reported in visual cortex (Yao et al. 2008).

Most surprisingly, the motivated processing of familiar stimuli may be modulated from trial to trial. It has long been assumed that sensory responses are “noisy” (Shadlen and Newsome 1998), but recent evidence suggests that this seemingly random variability may in fact reflect meaningful variation in stimulus processing: in many parts of the brain, there appear to be multiple possible responses to stimulation, one member of which is evoked in each individual trial (Fellous et al. 2004; Fig. 4A). Put another way, the difference between one response to a particular stimulus and the next may not be
caused by noise, but instead may be related to some real aspect of brain function.

The evidence suggests that, like the response modulations discussed in previous sections, the source of this trial-to-trial variability of sensory responses may be spontaneously generated network states. fMRI imaging of human subjects demonstrates that large, distributed neural systems fluctuate in coherent fashion from moment to moment during periods between stimulus presentations (Fox et al. 2006, 2007; Raichle et al. 2001). Similar fluctuations, observed in intrinsic signal images of cortex in anesthetized primates (Kenet et al. 2003; Vincent et al. 2007), account for a great deal of the variability in ensemble responses themselves (Arieli et al. 1996) and, in fact, spontaneously attain states that look remarkably similar to

FIG. 4. Trial-to-trial variability in neuronal responses. A, top: raster plot of a neuron in monkey’s middle temporal area (MT) responding to multiple presentations of a moving Gabor stimulus. Each tick mark is an action potential. The middle panels show in detail the spikes occurring in the dotted boxes. The bottom panels are representations of the same trials as in the middle panels, but reordered according to a clustering algorithm. Note that trials are now grouped into subtypes according to similarity of responses. B: population responses to tastes in the rat gustatory cortex go through stimulus-specific sequences of coherent network states. Top: raster plots showing the responses of 4 gustatory cortical neurons to multiple presentations of citric acid (9 trials). y-axis: trials; x-axis: time. Bottom: 4 representative citric acid trials showing the taste- and trial-specific coherent activity of the ensemble of simultaneously recorded neurons (the neurons represented in the top are the first 4 starting from the bottom). The overlaid shadowing represents network states characterized in terms of specific patterns of network activity. A adapted from Fellous et al. (2004); B adapted from Jones et al. (2007).

FIG. 5. Dependence of sensory responses on anatomical and functional connectivity. A: schematic representing evoked activity as depending only on anatomical connectivity: the stimulus activates the cells directly connected to the periphery that, in turn, activate those to which they are more strongly connected. In this case repeated presentations of sensory stimuli always evoke the same responses. B: cartoon summarizing the view emerging from this review: the state of the network varies in parallel with the behavioral state of the animal. Functional connectivity and background activity of the neurons composing the network determine the shape of the evoked response.
stimulus responses themselves (Kenet et al. 2003). Individual sensory responses appear to have as much to do with the coherent activity of the active networks as with the stimulus itself (see also Fiser et al. 2004).

Recent data from our lab demonstrate that the trial-to-trial fluctuations in sensory responses are not simply a by-product of network activity—they in fact represent the very essence of network dynamics in action (Fig. 4B). We have shown that trial-to-trial differences in single-neuron taste responses in cortex—differences that appear at first blush to be noise—are actually coupled across neurons in simultaneously recorded ensembles. When the activity of each neuron is related to that of each other neuron in the ensemble, rather than to trial onset, this network activity relays more information about the stimulus above and beyond that available in across-trial averages, even for the entire ensemble (Jones et al. 2007).

These ensemble data “close the loop” between network and sensory activity, directly arguing for network characterizations of sensory responses. Furthermore, they point the way out of the conundrum that develops when changes in network state are recognized to be a moment-to-moment phenomenon: by explicitly considering networks as a formative factor in sensory responses, information need not be lost in across-trial averages; when the importance of network processing is recognized and accounted for, the observed variance in sensory responses decreases. This work takes account of the fact that response variability is related to variability in network function, by quantifying sensory activity in terms of explicit network measures, rather than in terms of across-trial averages of single-neuron activity.

**CONCLUDING COMMENTS: WHY VARIABILITY?**

In the preceding, we suggest that a wide range of phenomena typically considered in isolation from each other—depth of anesthesia, phases of sleep, trial-to-trial variations in levels of consciousness, attention, expectation, and learning—can be reconceptualized as examples of a single overarching process whereby network preconfiguration shapes neural processing (Fig. 5). An essential component of this view is the reconceptualization of synaptic plasticity as not an end in and of itself (e.g., as a “neural trace”) but rather as a tool in the service of network configuration; the functionally active synaptic circuitry of a sensory area, which ultimately manifests itself in specific patterns of spontaneous activity and promotes a particular responsiveness to sensory stimuli, is the result of sensory context, environmental contingencies, and experience.

If it is true that sensory responsiveness is exquisitely sensitive to network fluctuations at work on the moment-to-moment timescale, however, an obvious question arises: How are we to interpret these results from an organismal perspective? Could it be that sensory variability is an epiphenomenon, a useless (in fact, a seemingly counterproductive) result of networks fluctuating for no specific reason other than its organization?

A more satisfying explanation emerges within an ecological framework (Gibson 1986), from which an animal’s brain is studied specifically in relation to the natural environment that surrounds the organism. In that natural environment of odors that ebb and flow, foods that vary in texture and flavor, and moving stimuli that cause ever-changing acoustic and visual experiences, stimulus variability is the name of the game. Just as it is impossible, as Heraclitus pointed out, to step into the same river twice, it is also highly unlikely that an unrestrained perceiver will apprehend exactly the same stimulus more than once. Even if the very same stimulus is presented multiple times to immobile subjects, however, there is no reason to believe that each presentation will be experienced in the same way (Lutz and Thompson 2003; Lutz et al. 2002).

The same sensory stimulus has multiple dimensions and meanings, each of which will be differentially evoked dependent on the internal milieu—where the subject’s “head is at.” The experience of stimulus invariance is simply not something that brains have evolved to handle; capturing stimulus variability, on the other hand, has survival value because it maximizes the experiential content of repeated sensory presentations.

Immersed in this dynamic environment, the subject itself adds variability by engaging in complex and time-varying motor behaviors (see examples from the realm of searching, foraging, and feeding; Edwards et al. 2007; Garcia et al. 2007; Lum et al. 2005), a tendency that is adaptively advantageous in situations of environmental unpredictability (Belanger and Willis 1996) and that in fact matches the variability of motor output to the variability of sensory input (Bernstein 1967; Churchland et al. 2007).

Irrespective of the value of this speculation, however, one thing is clear: the fact that single-neuron responses are a function of network states is not merely a “footnote” or “wrinkle” on sensory processing. It is, instead, an important determinant of sensory processing and of the matching of that sensory processing to the specifics of context. It is, quite possibly, the most important aspect of the nature of sensory processing, equal in importance to the sensory input itself.

**ACKNOWLEDGMENTS**

We thank Drs. Arianna Maffeii, Asif Ghanzanfar, and Benjamin Rubin for helpful comments.

**GRANTS**

This work was supported by National Institute on Deafness and Other Communication Disorders Grants DC-006666 and DC-007102 to D. B. Katz and DC-008885 to A. Fontanini. A. Fontanini was also supported by the Sloan–Swartz Center for Theoretical Neuroscience at Brandeis.

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Review

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