et al. (2017) using Ca^{2+} reporters has shown how astrocytes and SCN neurons are active during the night and day, respectively. Furthermore the astrocytes inhibit the dorsal SCN neurons via releasing glutamate into the extracellular space, and, remarkably, molecular manipulation of the astrocytes significantly alters the mouse free-running locomotor period. This antiphasic functional relationship between astrocytes and neurons in the SCN echoes the E and M cell groups in the fly circuit. Similar logic with different cellular actors...

REFERENCES

Brancaccio, M., Patton, A.P., Chesham, J.E., Maywood, E.S., and Hastings, M.H. (2017). Neuron *93*, 1420–1435.e5.

Holekamp, T.F., Turaga, D., and Holy, T.E. (2008). Neuron *57*, 661–672.

Liang, X., Holy, T.E., and Taghert, P.H. (2016). Science *351*, 976–981.

Liang, X., Holy, T.E., and Taghert, P.H. (2017). Neuron *94*, this issue, 1173–1189.

Ni, J.D., Baik, L.S., Holmes, T.C., and Montell, C. (2017). Nature *545*, 340–344.

Roberts, L., Leise, T.L., Noguchi, T., Galschiodt, A.M., Houl, J.H., Welsh, D.K., and Holmes, T.C. (2015). Curr. Biol. *25*, 858–867.

Constructing the External World

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In this issue of *Neuron*, Pluta et al. (2017) find a novel map of external space in primary somatosensory cortex, generated by multi-whisker interactions during active touch.

The analysis of neuronal receptive fields has been a powerful organizing principle to understand how the brain generates a representation of the external world. For tactile sensation, stimuli delivered through cutaneous receptors have provided evidence for precisely organized topographic receptive fields that map the body surface onto neural assemblies throughout the neuraxis, serving as a powerful conceptual framework for understanding neural response properties and brain function.

Touch—to the skin or to sensory hairs or vibrissae in the rodent whisker system—has been long appreciated as the best way to drive neurons in primary somatosensory cortex. However, it has long been clear that tactile sensation involves much more than the sequential activation of receptors for stimulus detection, as touch can assemble complex features into well-differentiated object representations. In the visual system, stimulus detection is an initial step in the emergence of complex feature representations that reflect real and complex objects in the external world, and both rodents and primates show position-invariant object identification (Zoccolan, 2015; Hung et al., 2005). In the visual system, complex feature assembly from receptor activation is thought to occur in higher-order visual areas that receive and transform simple receptor-coupled activity into a sensitivity to specific objects or faces. In contrast, how tactile features of the external world emerge with hierarchical processing in the rodent somatosensory system has been poorly studied (Sathian, 2016).

Using two-photon Ca imaging in awake mouse somatosensory cortex, Pluta et al. (2017) compared how neocortical neurons were activated by simple receptor activation (single whisker touch) versus active, multi-whisker sensation of variations in *external* stimulus location—a bar that could be placed in multiple positions, some of which lay outside of the single-whisker topographic area (barrel column) imaged. The assay itself is refreshing, as the vast majority of studies in the rodent barrel cortex have used isolated, single-whisker deflections as a way to understand neocortical response properties in S1. In contrast, neural activity evoked by naturalistic activation of multiple whiskers has been less comprehensively investigated. Analysis of neural firing with multi-whisker activation is critical to understand somatosensory processing in barrel cortex. It is hard to conceive of naturalistic conditions under which a single whisker would be deflected in the absence of input from adjacent whiskers; during active sensation, animals deploy their whiskers as a group, sweeping them together where object contact is not restricted to a single hair.

Surprisingly, unlike the discrete, whisker-specific preferences of barrel cortex neurons that have been well characterized in previous studies, Pluta et al. (2017) found that neuronal activity in superficial layers was markedly different when animals scanned space with multiple whiskers, even when the topographic "best" whisker for the imaged region did not contact the stimulus. Their analysis revealed a continuous map of external space generated by the activation of distant (surround) whiskers. This map reflected rostro-caudal "space" scanned by the whiskers and was disrupted in both superficial and deep layers when adjacent whiskers were removed, suggesting that it was not a fixed feature of the map. Thus, Pluta et al. (2017) provide

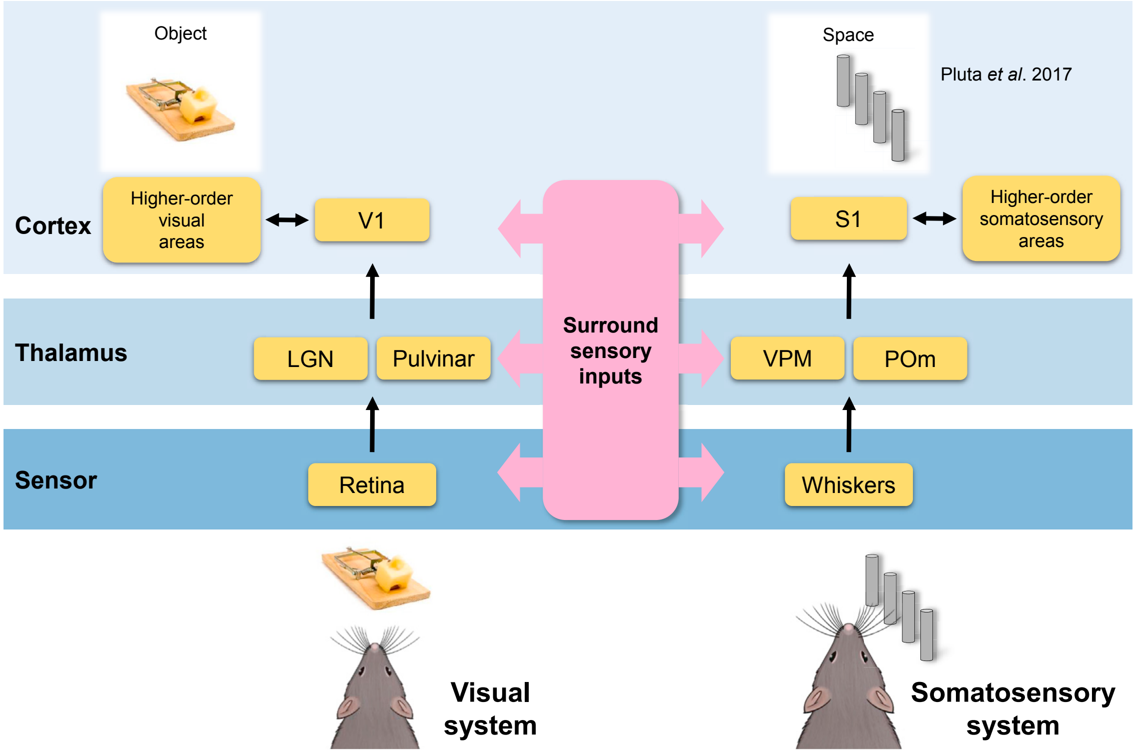

Figure 1. Construction of the External World in the Mammalian Brain from Visual and Tactile Inputs

evidence that the transition from simple, receptor-driven spiking responses—tied to sensor activation in the periphery—to more complex responses that assemble these inputs into a schema of the external world can occur directly in primary sensory cortex S1 (Figure 1). In doing so, they could observe sensory representations shift from sensor dominated (referenced to the cutaneous receptors themselves) to external space dominated.

How do these emergent properties arise from the simple sequence of receptor activation that occurs during tactile sensation? It is well known that a representation of external space is reflected by the activity of place cells in the hippocampus that fire briskly when the animal is in a certain location, irrespective of how the animal arrived at the location. We accept that place cues are derived from multiple streams of information that are somehow combined to yield a specific location in the external world. In this case, sensor activation can vary according to different features from the environment that are detected based upon animal orientation or direction. Perhaps one of the most surprising aspects of this study was that a map of the scanned space from the external world could be observed in a primary sensory area (Figure 1). Previously, more complex stimulus features—invariant object recognition, for example—that are well displaced from the identity of the specific peripheral photoreceptors activated are thought to be generated in higher-order visual areas, not V1.

Pluta et al. (2017) examine the possibility that this continuous map of space is inherited from upstream structures such as the thalamus by investigating changes in response properties of neurons from the ventroposterior-medial nucleus (VPM). Removal of adjacent whiskers did not significantly alter the VPM neurons' spatial preference for the remaining single whisker. Thus, they hypothesize that the continuous space map observed in superficial layers was generated through intracortical processing by asymmetric excitation generated in a rostral-caudal gradient when adjacent whiskers touch the object.

Is there a role for thalamic neurons in generating surround responses that help create this continuous map? It is important to remember that primary sensory areas typically receive input from a second thalamic area whose terminals directly target neurons in superficial and deep layers of the cortex (Audette et al., 2017). In the somatosensory system, these inputs arise from the posterior-medial nucleus (POm). Because POm neurons display broad, multi-whisker response properties (Diamond et al., 1992; Jouhanneau et al., 2014), they may be key contributors to integrate space and object representations in S1, an alternate possibility that might contribute to the continuous maps observed by Pluta et al. (2017) (Figure 1).

In addition, primary sensory areas typically receive dense feedback information from higher-order areas, such as S2, that could facilitate the appearance of space maps in S1. Indeed, visual object identification is thought to emerge from neuronal processing that occurs in higher-order sensory areas, such as V2, V4, and inferotemporal cortex (IT), although this information may feedback to primary areas (Gilbert and Li, 2013; Figure 1). The role of more distant cortical areas in generating complex responses that reflect not just receptor activation, but integrative properties of the external world may be a fruitful area for investigation.

Unlike place cells, the spatial preference of S1 neurons observed in this study was not a fixed aspect of their responses; it could be modified or eliminated by removing other whisker inputs. In addition, the maps observed were centered on the detector array (self-centered space), not on distant and multisensory external cues (position-invariant place). This is strong evidence that the continuous map observed was generated by activity driven from adjacent whiskers, whose cortical column was centered in an area outside the imaging window. In fact, modulation by surrounding sensors, with an important contribution of neocortical inhibition, has been observed for multiple sensory systems, particularly in the visual system (Haider et al., 2010; Adesnik et al., 2012).

Data presented in Pluta et al. (2017) support the notion that the whisker-barrel system in rodents can be used to study the generation of more complex tactile features of the external world. This is part of a continuing shift toward the use of rodents for cognitive and perceptual neuroscience, which provides significant advantages for precise cell and molecular interventions to study brain function in complex behavior. Use of Ca imaging in awake mice will enable analysis of how different classes of interneurons are activated during these conditions, as well as testing hypotheses for a role for other up- and downstream areas. Pluta et al. (2017)'s work opens up additional areas for investigation of the limits of rodent sensation and perception. If we can find evidence for representations of the external world that can be generated in S1, can we also find evidence for position-invariant object identification in primary somatosensory cortex? Does the hippocampus rely upon object position representations generated in S1 for generating place codes? Are these space maps relative or absolute? Can they stretch or contract with stimulus location (i.e., bars that are close to, or far from, the whisker array, or bars that are distant from each other)? Results from this new work open multiple paths to determine how sensors assemble information from the external world into complex percepts.

REFERENCES

Adesnik, H., Bruns, W., Taniguchi, H., Huang, Z.J., and Scanziani, M. (2012). Nature *490*, 226–231.

Audette, N.J., Urban-Ciecko, J., Matsushita, M., and Barth, A.L. (2017). Cereb. Cortex. Published online March 10, 2017. http://dx.doi.org/10.1093/cercor/bhx044.

Diamond, M.E., Armstrong-James, M., and Ebner, F.F. (1992). J. Comp. Neurol. *318*, 462–476.

Gilbert, C.D., and Li, W. (2013). Nat. Rev. Neurosci. *14*, 350–363.

Haider, B., Krause, M.R., Duque, A., Yu, Y., Touryan, J., Mazer, J.A., and McCormick, D.A. (2010). Neuron *65*, 107–121.

Hung, C.P., Kreiman, G., Poggio, T., and DiCarlo, J.J. (2005). Science *310*, 863–866.

Jouhanneau, J.S., Ferrarese, L., Estebanez, L., Audette, N.J., Brecht, M., Barth, A.L., and Poulet, J.F. (2014). Neuron *84*, 1065–1078.

Pluta, S.R., Lyall, E.H., Telian, G.I., Ryapolova-Webb, E., and Adesnik, H. (2017). Neuron *94*, this issue, 1220–1233.

Sathian, K. (2016). J. Neurophysiol. *116*, 1795–1806.

Zoccolan, D. (2015). Behav. Brain Res. *285*, 10–33.