A Division of Light and Dark in the Visual Cortex

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The fate of ON-OFF receptive field segregation in the visual cortex has long eluded scrutiny. In this issue of *Neuron*, Smith et al. (2015) now reveal the intricate relationship between luminance polarity and orientation selectivity in the upper layers of ferret visual cortex.

Long before early civilizations drew up their first maps, the brain had already acquired the ability to represent the outside world in topographically organized internal maps. Indeed, when Hubel and Wiesel (1962) moved an electrode through the cat primary visual cortex (V1), they found neighboring neurons to respond to nearby locations in the visual field. What they observed in addition, however, went beyond the by then long-known retinotopic organization: cells that they encountered when advancing the recording electrode orthogonal to the cortical surface shared preference for the same orientation of bars and edges, while the best orientation changed smoothly with the electrode moving tangentially in the visual cortex. Likewise, they found alternating regions that responded more strongly to visual stimuli presented via one eye or the other. They termed these structures orientation and ocular dominance (OD) columns and later presented a model of V1 in which neurons were orderly arranged in discrete modules that each covered a specific region of the visual field and consisted of a complete set of orientation and OD columns, such that the full range of functional properties was represented for each part of the visual field (Hubel and Wiesel, 1977).

For around two decades, ocular dominance and orientation columns were thought to be the only building blocks of the visual cortex's functional architecture. In part sparked by the advent of new methods like intrinsic signal imaging (Grinvald et al., 1986), other qualities of visual stimuli—for example motion direction (Weliky et al., 1996), binocular disparity (Kara and Boyd, 2009), and spatial frequency (Shoham et al., 1997)—were subsequently found to be mapped in a systematic fashion across the cortical surface.

A paper in this issue of *Neuron* (Smith et al., 2015) now adds a map for luminance selectivity to this list. Assisted by the improved sensitivity of the newest generation of genetically encoded calcium indicators, Smith et al. (2015) used wide-field fluorescence imaging to show that the upper layers of ferret visual cortex contain patchy regions responding to either increasing (ON) or decreasing (OFF) steps in luminance. A spatial organization for polarity selectivity in layer 2/3 was not entirely unexpected, since it was already known that axonal projections from ON and OFF selective layers of the lateral geniculate nucleus (LGN), the thalamic relay station for visual information, terminate in a segregated fashion within layer 4 of the visual cortex (McConnell and LeVay, 1984). In addition, layer 4 itself was recently shown to contain clusters of ON and OFF dominated receptive fields (Wang et al., 2015). The present study, however, directly demonstrates the existence of a map for ON and OFF luminance selectivity in layer 2/3.

Zooming in on single cells with two-photon calcium imaging, Smith et al. (2015) proceeded by showing that uniform polarity selectivity of individual neurons in layer 2/3 varies all the way from strongly ON to exclusively OFF selective. Although the overall majority of layer 2/3 cells were not particularly selective for ON-OFF polarity, combined wide-field and two-photon imaging identified patches that were strongly responsive to luminance polarity. These patches hosted a large subset of highly selective cells, thus confirming that the functional organization for uniform polarity holds down to the level of single cells. It may be too early to speak of uniform luminance-polarity

columns in a strict sense, as their extent throughout all cortical layers has not been demonstrated, but the present study confirms that polarity selectivity is an organizing feature in layer 2/3 of the visual cortex.

The canonical neuron in layer 2/3 of the visual cortex is tuned to the orientation of edges and bars. How does this reconcile with a modular organization for uniform luminance changes? Smith et al. (2015) addressed this question by contrasting response amplitudes in wide-field maps acquired during presentation of luminance steps, with maps containing responses to drifting gratings. This revealed that the visual cortex was tessellated into regions more responsive to uniform polarity changes and regions more responsive to drifting gratings. Cells within uniform polarity-selective domains were less orientation selective and had larger receptive fields compared to cells in grating-responsive regions. The organization of V1 into polarity-selective patches surrounded by regions selective for stimulus orientation suggests that the cortex spatially segregates processing of these qualitatively different visual features.

How are the selectivities for luminance polarity (ON or OFF dominance) and orientation integrated in layer 2/3? Smith et al. (2015) investigated this by presenting visual stimuli combining these two features, namely dark or bright edges of particular orientations moving across the entire visual field. They then compared the resulting edge-polarity maps to maps for uniform changes in luminance or grating orientation. Interestingly, maps for edge polarity could be accurately predicted by intersecting individually acquired maps for uniform polarity and orientation; e.g., the

Figure 1. Organization for Orientation and Luminance Polarity in Ferret Visual Cortex
(A) Example orientation preference map. Color code indicates preferred orientation.
(B) Example luminance polarity map. Polarity preference ranges from OFF (black) to ON (white).
(C) Map of joint polarity and orientation preference. The sphere indicates how both polarity (vertical axis) and orientation (along circumference) can be represented continuously.
(D) Zoomed-in view of a section of the map in (C). Colored lines are iso-orientation contours. Black and white lines indicate uniform polarity patches; gray line marks the boundary between ON and OFF domains. Black and white disks: uniform polarity selective neurons. Edge-arrows: neurons selective for edge orientation and polarity. Gratings: neurons selective for orientation, but not for polarity. Note that all maps shown are schematic illustrations.

OFF-horizontal edge map could be inferred from the individual map for OFF stimuli and another single map for horizontal stimuli. Moreover, the authors could demonstrate that most individual neurons, also those outside the polarity-selective patches, have receptive fields that are selective for luminance polarity as well as orientation. These data strongly suggest that while selectivity for polarity and orientation is partly integrated, the ON and OFF pathways essentially remain segregated within layer 2/3 (Figure 1).

The map for ON-OFF responses described by Smith et al. (2015) adds to several other systematic representations known to reside in the visual cortex, raising the question of how the ON-OFF map is spatially related to these other maps. The underlying issue here is that the cortical machinery devoted to the processing of any part of the visual field should ideally contain representations for all combinations of mapped stimulus properties (a concept referred to as coverage). Optimal coverage can be achieved by map gradients that run orthogonally to each other, as Hubel and Wiesel (1977) had already suggested in the original ice cube model and as was later demonstrated directly (Swindale et al., 2000). However, by increasing the number of mapped features, uniform coverage might eventually degrade (Swindale, 2000). An alternative solution

for maintaining uniform coverage results from systematic mismatches in the spatial scale or shape of the different domains.

The study of Smith et al. (2015) now provides evidence for the existence of this second coverage strategy. They show that polarity domains are not arranged orthogonally to orientation columns. Rather, uniform coverage is achieved by slight differences in the size and shape of the hypercolumns of both systems. It will be interesting to map all functional organizations in the same visual cortex in order to determine whether there is any logic to which maps run orthogonal to each other and which ones differ in hypercolumn size and shape.

The observation of a spatial organization for luminance polarity in layer 2/3 may have implications for our understanding of how the cortical map for orientation preference is generated. The local arrangement of ON- and OFF-dominated LGN inputs can be combined into a population-wide ON-OFF receptive field that accurately predicts the preferred orientation of individual neurons within orientation columns of layer 4 in cat visual cortex (Jin et al., 2011). Considering that axons from ON- and OFF-selective LGN layers terminate in a segregated fashion in ON-OFF-dominated regions in layer 4, a systematic spatial relationship between orientation and polarity maps may be expected here, as has also been suggested

by some models (e.g., Nakagama et al., 2000). However, the study of Smith et al. (2015) does not report a specific arrangement in layer 2/3 and rather suggests that in the upper layers the organizations for polarity and orientation are independent of each other. This implies that either the orientation or the ON-OFF map in layer 2/3 is not in register with its counterpart in layer 4. As it is very unlikely that this is the case for the orientation map, we are left with the alternative that the map for polarity preference in layer 2/3 does not match that in layer 4. Layer 2/3 cells could recombine inputs from layer 4 in such a way that the relationship between polarity and orientation maps is lost across layers. It would thus be very important to test whether the layout of ON-OFF domains is continuous across layers 2/3 and 4, which should ideally be done at single-cell resolution using two-photon calcium imaging. Alternatively, the assumption of a fixed spatial relationship between these maps within layer 4 is incorrect, which this experiment would also reveal.

Finally, we are left with the question of whether the spatially segregated processing of luminance polarity in separate ON and OFF pathways in the visual cortex bears any relevance for visual perception. Smith et al. (2015) make a strong case for this. They argue that such segregation may strengthen feature selectivity, assist stereoscopic vision, and maintain useful

ON-OFF asymmetries like higher spatial acuity in the OFF pathway. While these are very valid points, they don't necessarily require that the ON and OFF pathways be spatially segregated in the visual cortex.

The potential functional relevance of a columnar organization for ON-OFF responses then comes down to the more fundamental question of what the function of cortical columns is in general (Horton and Adams, 2005). A straightforward way to tackle this question would be to specifically disrupt the columnar organization and assess the resulting deficits in perception. However, any experiments perturbing map-like organizations are fundamentally difficult to interpret because disrupting the map will almost inevitably also interfere with the tuning properties of the individual cells constituting it. A potential approach to address this conundrum, albeit in a different type of column, is exploiting nature's experiment in squirrel monkeys, where in some individuals the visual cortex features clear OD columns, while in others it does not

(Adams and Horton, 2003). Testing, for instance, depth vision in this species, which in part relies on binocular disparity cues and thus may benefit from a clustered organization of ocular dominance, could indicate potential advantages of a clustered organization for OD. While at present it is unclear as to whether there is any diversity in the degree of ON-OFF segregation within a given species, the discovery of a functional organization for ON-OFF polarity in layer 2/3 might nonetheless provide another potential testing ground for assessing the function of cortical columns for visual processing.

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The What and Where of Visual Attention

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The selective processing of sensory input during attention is known to take many forms, and different forms of attention likely reflect varying underlying neural mechanisms. Bichot and colleagues (2015) identify neurons that appear specialized for the control of feature-based visual attention.

The guidance of behavior by sensory stimuli naturally depends upon the relative tendency of different stimuli to evoke a behavioral response. For any particular organism there exists an inequality in the degree to which different sensory stimuli are able to evoke neural activity and to drive behavior. Different organisms of course exhibit dramatically different relative sensitivities across stimulus modalities (i.e., vision, olfaction, etc.). In addition, even within a particular sensory

modality, different classes of stimuli (e.g., auditory frequencies) exert differing capacities to drive behavior. Naturally, all of this is a direct result of critical differences and varying degrees of specialization in sensory systems across species, particularly at the level of the peripheral sense organs. However, there is yet another source of variation in the degree to which a given stimulus is likely to drive behavior, namely the relevance of that stimulus to a particular organism's behav-

ioral goals. In such a case, sensory processing is filtered accordingly by attention, a basic cognitive function exhibited by many organisms to some extent. Although the broad significance of attention to behavior has prompted extensive study as to its underlying neural circuitry, remarkably little is yet understood, particularly about the neural mechanisms contributing to the various ways in which attention is used to select relevant stimuli. In this issue of *Neuron*, Bichot