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Computational Neuroimaging: Color Signals in the Visual Pathways

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Abstract

This review describes measurements of visual field maps and color signals in human visual cortex. One of the most exciting advances in recent years has been the ability to measure more than a dozen visual field maps in human visual cortex. These maps are grouped into small clusters that share a common eccentricity representation; we speculate that maps within a cluster have shared visual functions. The distribution of color (cone photoreceptor) signals differs strikingly across these clusters. The cluster of maps in ventral occipital cortex responds to all three color dimensions powerfully, and lesions within these maps disturb color appearance. The ventral occipital maps appear to be essential for normal interpretation of colors. Dorsal regions receive input from all three cone classes, but dorsal color coding but the signals are quite unlike human visual perception. Quantitative measurements of the responses in these dorsal and ventral regions promise to clarify the cortical circuitry that is essential for color appearance and related color phenomena.

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INTRODUCTION

From the inception of color science, more than three centuries ago, Newton recognized that color is a biological and psychological phenomenon. As he wrote, 'the rays, to speak properly, are not coloured. In them there is nothing else than a certain power ... to stir up a sensation of this or that colour." Since that time, many scientists have asked what brain structures these rays 'stir up'. The new tools of functional magnetic resonance imaging (fMRI) provide a remarkable technique to trace the effects of Newton's rays as they produce color sensations.

There are several different approaches to studying human color vision. One line of investigation emphasizes our conscious experience of color. This research seeks to identify the 'color center' of the brain whose responses (a) are essential for normal color vision, and (b) predict color experience. The search for a color center has spanned more than a century and is one of the more interesting debates in the neurobiological literature[1, 2]. It is safe to say that the best candidate for a center is within ventral occipital cortex - much more on this later.

A second line of investigation has quantified and explained important aspects of color performance. Perhaps the most important accomplishment in color science is the quantitative understanding of how color matching (trichromacy) can be explained in terms of the photon absorptions in the three types of cones. In this work, careful behavioral measurements are linked in a beautiful series of quantitative experiments to the absorption properties of the cone photoreceptors[3].

A third line of investigation has flowed from introspection concerning color appearance. Surely the most important work is based on Hering's opponent-colors framework[4, 5]. He noted that certain colors never appear in combination (red-green, blue-yellow, and light-dark). This work, rooted in a simple perceptual observation, is at the foundation of nearly all color appearance representations used in industry (textiles, paints). It is also essential in the development of color discrimination metrics; these are formulae that quantify when two lights can be visually distinguished[6, 7]. Opponent-colors theory has been deeply linked to physiological work in the retina and lateral geniculate nucleus[8~11]. Finally, additional behavioral measurements show that color appearance is derived nearly entirely from the low spatial and temporal frequency components in the image[3, 12, 13]. This limitation can be traced to the fact that the red-green and blue-yellow color dimensions have relatively poor spatial and temporal sensitivity. The practical significance of these observations for industry, spanning television transmission standards (NTSC, PAL, SECAM), digital image compression (JPEG), is enormous.

In this article, we provide a selective and somewhat personal review of human functional MRI measurements of color. We argue that this is the right time to undertake a quantitative analysis of the color properties in human visual cortex. In this

way, we believe that cortical physiology will be able to forge strong bonds with behavioral color science, much in the way that industry and physiologists studying the early visual pathways (retina, LGN) already have. We begin by introducing a general framework for the organization of visual cortex, based on visual field map clusters. We then show how it is possible to measure the distribution of color signals from the cones throughout human cortex. These signals differ strikingly between the different visual field map clusters. These differences suggest that the cone signals are used in different ways by multiple cortical systems. In some cases the cone signals appear to be combined to enhance sensitivity of a sub-system, such as motion interpretation. In other cases the cone signals appear to represent the full gamut of color appearance and to be an essential part of the color appearance network.

1. FMRI BACKGROUND AND METHODS

BOLD neuroimaging. Until the early 1990s, scientists had very restricted ability to measure human brain signals directly. Then, Ogawa and colleagues discovered MRI methods that measure blood oxygen level dependent (BOLD) MR signals[14~17]. The BOLD is an indirect measurement of the integrated energy consumption in the brain, and BOLD provides spatially localized information about neural activity. The new ability to measure spatially localized signals within the human brain has transformed visual neuroscience. What does the BOLD signal measure?

Neuronal communication is mediated by transient changes in the voltage potential across cell membranes, in particular at pre- and post-synaptic sites. This signaling requires significant amounts of metabolic energy, much of which is consumed as the ion specific channels restore the charge balance following a signal[16~19]. The energy is obtained mainly by a glycolytic process that requires oxygen. Hence, the neural signaling causes a vascular response that increases the arterial blood flow and volume to active regions and supplies oxygen. By measuring changes in oxygen, the BOLD signal informs us about the energy consumption caused by sensory stimulation or even mental effort. This energy consumption is an indicator of local neuronal signaling. The amount of energy consumed depends on the amount of activity as well as the neural circuitry.

The mesh of fine capillaries in the brain regulates blood flow on a fine spatial scale; the localization of blood flow appears to have a sub-millimeter resolution. The increase in the local blood flow and volume, however, takes 4-6 seconds to evolve. Mosso[20] observed the increase in blood flow in the human brain. The phenomenon was studied in animal models[21] and a particularly interesting human case was described by Fulton[22].

The BOLD signal does not inform us about a unique neural signal, such as the number of action potentials or the amplitude of the sub-threshold synaptic potentials. Both of these signals correlate with the BOLD signal, but experimentally it is possible to dissociate the BOLD signal and action potentials[23]. Also, Logothetis' group

simultaneously measured action potentials, local field potentials, and BOLD activity[24] and found instances in which the local field potential correlates well with the BOLD signal but action potentials do not.

There are several important advantages of the BOLD signal over other human brain measurement techniques. First, the BOLD signal measures the human brain non-invasively. It is possible to make multiple measurements with a single person, either to improve signal-to-noise or to trace changes in the human brain over time. Humans are excellent subjects in general, and they are the only species where we can study language. Second, the BOLD signals measures cortical activity at a much finer spatial scale than any previous non-invasive human brain measurement method. This is because the cortical blood supply forms a very fine mesh, and the oxygen delivery is controlled at a fine spatial scale[25]. It is common to measure activity at a spatial resolution of 3x3x3 mm (1-2 million neurons); several groups have reported good fMRI signals at sub-millimeter resolution in animals and human (50 thousand neurons)[26, 27]. However, the low temporal resolution is a significant disadvantage. It takes the vascular response several seconds to develop over time. The BOLD signal is well-suited to measuring certain types of neural responses but not others, which is true for any measurement methodology.

2. VISUAL FIELD MAPS

Visual field maps. The neurons in primary visual cortex, V1, are organized into a visual field map; stimuli near one another in the visual field are represented by the responses of neurons that are near one another in cortex. This spatial arrangement probably has functional value, allowing dense connectivity between neurons that process neighboring visual field locations. The organization of primary visual cortex has been known for more than 100 years. The discovery and characterization of more than a dozen additional visual field maps in the neocortex of macaque and other mammalian species is one of the great advances in visual neuroscience during the last fifty years[2, 3].

The organization of the human V1 map was inferred first from visual field scotomata in patients with cortical lesions, many of these caused by the wars in the 19th and 20th centuries. Additional information came from human cortical stimulation experiments[28, 29]. Horton and Hoyt summarized these observations and added new results from neurological studies of lesions[30]. They confirmed that (a) the foveal signal occupies a very large portion of the posterior calcarine, wrapping around onto the lateral convexity, (b) the upper visual field is mapped onto the lower bank of the calcarine (lingual gyrus), and (c) the lower visual field is mapped onto the upper bank of the calcarine sulcus.

A major step forward occurred when it became possible to measure human visual field maps using fMRI in the brain of single subjects. This method enables us to make quantitative, non-invasive measurements that identify multiple maps in the human brain.

Several software and computational methods are used, in combination with functional MRI, to measure these maps. A first important step in measuring these maps is processing the anatomical data to identify the white matter. The mass of white matter, which comprises the long axons connecting different parts of cortex, forms the large core of the brain. It can be identified reasonably efficiently from structural MR images (**Fig 1**A). There are many published algorithms for automatically segmenting gray and white matter. While there may be an algorithm that could work well to automate the process, no one has yet found one. In our lab we first use an automatic classification algorithm and then we spend 8-10 hours per hemisphere checking and hand-editing the results. An example of the classification of white matter in a single plane is shown by the purple region on the left side of the image in Fig 1A.

The second step is identifying the gray matter. Because the gray matter forms a thin (2-4mm) sheet of tissue that covers the white matter, it can be derived automatically from the white matter. There are adequate (and freely available) routines for using the white matter to estimate the gray matter sheet; this is a very quick computational step.

There are several reasons this anatomical processing is valuable. Perhaps most important is that knowledge of the gray matter surface guides proper analysis of the signals. The most important consideration can be seen in Figure 1A. Notice that certain locations within the gray matter, on opposite sides of a sulcus, are adjacent to one another in the image but not adjacent in the brain in terms of the sheet of cortical gray matter. By identifying the gray matter surface, we also learn which signals arise from locations adjacent in the cortex, rather than just adjacent in the image.

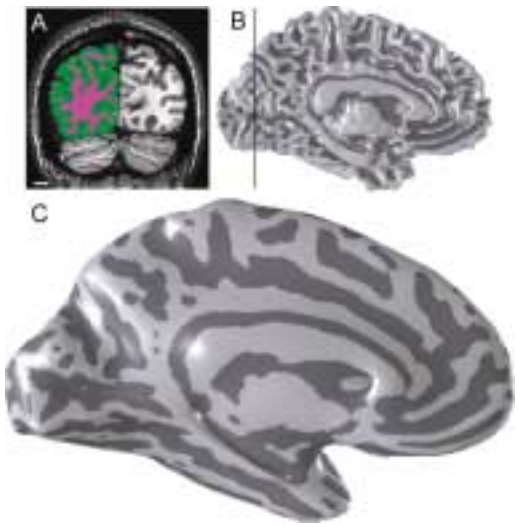

Figure 1 (A) FMRI data are analyzed by identifying the white matter of the brain. The segmentation of gray and white matter is done by a combination of automated estimates and then manual correction of these estimates. The gray matter is estimated by creating a thin (2-3 mm) sheet surrounding the white matter. (B) It is common to visualize the boundary between white and gray matter as a surface. In this rendering the sulci are shown with slightly darker shading and the gyri with slightly lighter shading. (C) Because it is difficult to see activations within the sulci, it is common to smooth the surface of the brain. Such a smoothed (sometimes called inflated) image of the surface is a very convenient visualization of fMRI activations.

With this knowledge, we can restrict signal processing so that we combine only MR signals from adjacent locations in the gray matter.

A second value of the anatomical processing is that it helps in data visualization. Specifically, it is possible to use the segmentation to define a surface between the gray and white matter. This surface can then be rendered as a 3D object (Fig 1B). Such surface rendering methods are part of both commercial products (http://www.brainvoyager.com/) and freely available (http://surfer.nmr.mgh.harvard.edu/; http://afni.nimh.nih.gov/afni/) software packages. The images in this paper were created using our software (http://white.stanford.edu/newlm/index.php/Main_Page).

Commonly the surface is shaded using the local curvature of the gray matter: sulci are shaded dark and gyri are shaded light. Notice that for any given view of the brain, visualization of the bottom of the sulci is limited. Hence, for communicating the locations of activation in scientific papers and talks, it is common to smooth the brain surface (Fig 1C). In this smoothed view, the relative spatial relationships between all of the major landmarks are maintained. When the brain is smoothed, it is easy to see activity at the bottom of a sulcus.

Another advantage of identifying the gray-white surface boundary is that algorithms are available for measuring surface area and gray matter volume of the gray matter sheet. These measurements permit specification of the surface area of different cortical regions. For example, it has been possible to measure the surface area of V1, V2 and V3 in human subjects. The same approach can also be used to quantify the size and shape of other brain structures.

To identify visual field maps, the fMRI data are aligned with the anatomical data. The principal method used to measure visual field maps is called the *phase-encoding or traveling wave method*. These methods are described in detail in many publications[31~36]. In this method, the subject fixates at a point while a series of stimuli are presented that sequentially stimulate each point in the visual field. In most experiments to date, two types of stimuli are presented. To measure the eccentricity component of the map, the subject views a series of rings at increasing eccentricity from the fovea. The ring measurements provide an estimate of the most effective visual field eccentricity for each voxel. The angular component is estimated by measuring the BOLD to a rotating wedge contrast pattern that rotates slowly around fixation. The wedge measurements estimate the most effective angular direction for each voxel. Combining these two measurements yields a complete measurement of the cortical representation of the visual field. This method reconstructs the entire visual field map representation and does not assume a layout (in contrast with mapping of the horizontal and vertical meridians: Fox et al., 1987; Shipp et al., 1995; Hasnain et al., 1998; Fize et al).

Borders between visual field maps can be identified in several ways from phase-

encoded mapping data. In many cases, simple visual inspection of the raw phase data reveals the borders between the maps. These borders typically fall on either the horizontal or vertical meridians and are associated with a reversal of the direction of the visual field map representation[33, 34]. Automatic algorithms aim to establish these borders in a more objective fashion either by an explicit fit of visual field map models to the phase data[41], or by calculating the field sign of the visual field map, where neighboring visual field maps can be distinguished due to opposite field signs[32, 42, 43].

These traveling-wave methods using ring and wedge stimuli have been used widely and are quite reliable. We think there are many opportunities for improving the methods. Some of these are being developed for clinical applications (A. Furuta and S. Nakadomari, personal communication). Our group is developing new methods to provide a more specific model of the neuronal signals that mediate the BOLD response[44].

Figure 2 summarizes the visual field maps identified to date in the human brain. The first maps identified using fMRI were V1/2/3[33, 34, 45]. There is consensus on these maps and their positions. Primary visual cortex has a visual field coverage that generally matches the cone sampling density in the retina. Neighboring maps (V2, V3) have similar coverage[41]. There is also agreement about the arrangement of other maps, such as V3A[33, 46～48], V3B[47, 48], V7[48, 49], MT[50] and LO1, LO2[51]. Certain details about the maps continue to be discussed[36, 52].

New maps will continue to be discovered. Several visual field maps were recently reported in parietal[42, 53, 54] and frontal[55] cortex. Most of these maps can be reconstructed by sections of a moving or flickering circular checkerboard. It may be that selecting stimuli[50], or including directed actions[42, 53, 54], may elicit stronger responses in some of the maps and reveal them more clearly.

Several of the fMRI derived visual field maps, measured in healthy subjects, are in excellent agreement with the maps inferred from the neurological data in patients with lesions[34, 35]. There is also good agreement between the maps measured in human and macaque using fMRI[56]. The basic positions of the foveal representation (*) and the upper (+) and lower (-) visual field representations within each of the maps is shown in Figure 2.

The visual field maps serve as an important coordinate frame for identifying corresponding locations within the brain of different individuals, especially since their location can vary considerably between subjects both in stereotaxic (Talairach) space[59, 60] and/or with respect to gross anatomical structures[61]. By measuring the maps in an observer's brain first, it is possible to describe subsequent measurements, say of stimulus responsivity, with respect to these maps. These measurements can be compared with similar measurements in other subjects whose brains may differ in

size and folding pattern.

Finally, there is an ongoing discussion about the overall organization of the maps themselves[36, 62, 63]. It has been proposed that there is only a 'weak' retinotopic organization beyond V1/2/3. According to this view, cortex is organized in terms of a general eccentricity bias that extends the V1/2/3 map. An opposing view, that we support, argues that there are several independent clusters of maps. Each cluster is defined as a set of maps that share a common eccentricity representation. The maps within the cluster are distinguished by the reversals in the angular representation.

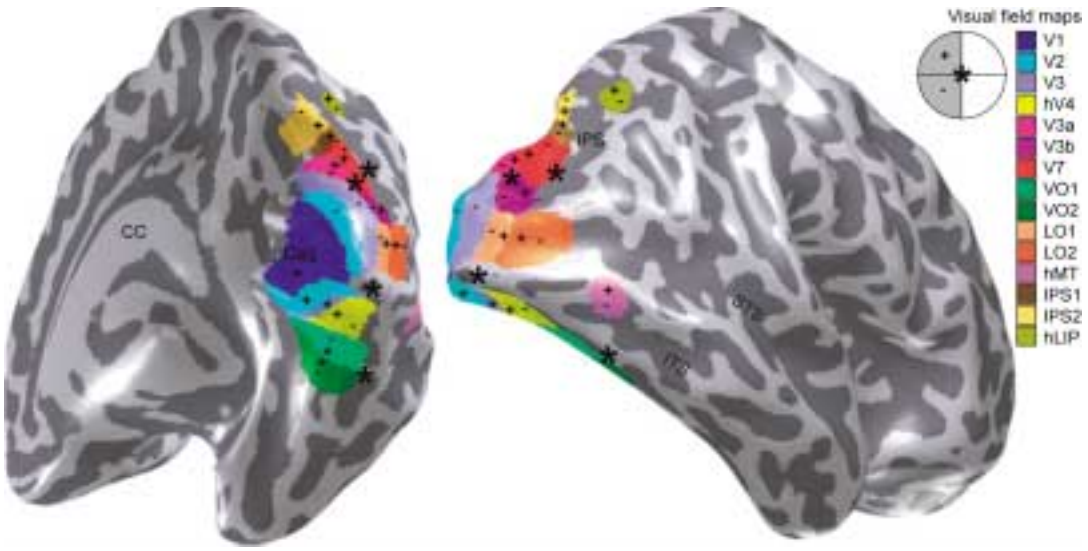

Figure 2 Visual field maps. Visual field maps. More than ten individual visual field maps are identified in human visual cortex. The maps V1 to LO-2 are based upon this subject's data (YM), whereas hMT to hLIP are drawn according to descriptions of the literature. To facilitate orientation on the cortical surfaces gross morphological structures have been labeled, including the corpus callosum (CC), Calcarine sulcus (CaS), superior temporal sulcus (STS), inferior temporal sulcus (ITS) and the intra-parietal sulcus (IPS). These maps form clusters that share a confluent fovea with semicircular eccentricity bands, minimizing the length of the synaptic connections required to compare signals originating at common eccentricities. The posterior cluster, including the maps V1, V2, V3 and hV4, is centered on the occipital pole. Clusters were identified on the ventral occipital (VO) portion of the brain, containing at least two maps[56]. An additional cluster appears to be located on lateral occipital (LO)[57]. This cluster extends towards motion-selective cortex (hMT+) on the anterior-lateral portion of the occipital lobe. Additional maps comprising clusters with their own confluent foveal representations exist on the dorsal surface running along the intra-parietal sulcus[54, 58]. Results are reviewed and the cluster hypothesis introduced in Wandell et al.[36].

Figure 3 shows further evidence that cortex is not organized into one unified eccentricity map. The image shows the location of regions that are driven predominantly by signals originating within 0.4 deg of the central fovea. Notice that these locations are widely separated, by several centimeters. These distinct foveal representations form the central representations of several visual field map clusters. The largest foveal representation falls at the confluence of a large group of maps including V1/V2/V3/hV4/LO1/LO2. There appear to be two distinct foveal representations on the ventral surface. One is within the VO-1 and VO-2 maps and a second is further anterior in a region that has not yet been described. We noted this region in an earlier publication[48], and we continue to see it in these new data. Another foveal representation can be found in motion-selective cortex (MT+). Our data also show at least two additional and distinct foveal representations on the dorsal surface along the intraparietal sulcus, near V3A/B and V7.

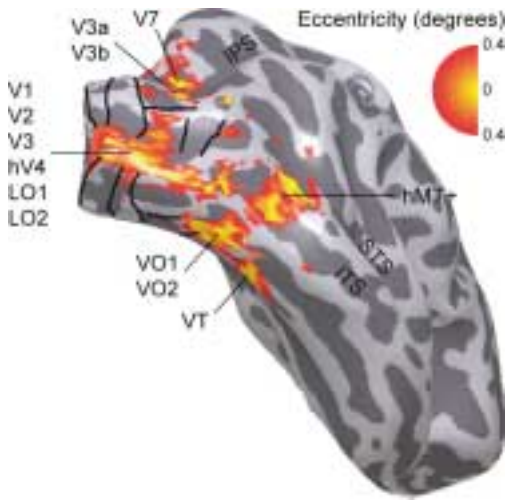

Figure 3 Locations within cortex driven predominantly by signals originating within 0.4 deg from the central fovea.

We note here that these measurements were not made using the conventional ring and wedge stimuli. Rather, we have developed new experimental and computational methods that identify these foveal representations and probe additional features of the responses in these maps[44]. We believe that these methods will come to replace our original phase-encoding (traveling wave) approach.

3. COLOR SIGNALS IN HUMAN CORTEX

The visual field map organization provides an excellent framework, well-grounded in the functional properties of cortex itself, for studying the distribution of color signals. But what approach should we take to measuring the distribution of color signals? In the Introduction, we described two approaches to color that represent different traditions: the search for cortex responsible for the experience of color, and the quantification of cone signals. In the next sections we review examples of each type of measurement.

3.1 Cerebral achromatopsia. A cortical specialization for color experience was first suggested by neurologists who described patients with a disturbance of color vision following cortical damage (achromatopsia). As Zeki describes, this syndrome did not become incorporated into mainstream color science until J.C. Meadows provided a systematic and thoughtful study of the relation-

ship between cortical damage and cerebral achromatopsia[64]. Specifically, Meadows observed that patients with this color appearance disturbance have cortical damage in a common region, located on the ventral occipital surface. Bouvier and Engel[65] confirmed and extended this analysis.

Cerebral achromatopsia frequently presents in association with proposagnosia (distubance in face recognition) and other visual disorders. But, there have been a few cases that have come to clinical attention, roughly 11 according to Bouvier and Engel, which are not associated with proposagnosia. They analyzed the intersection between 8 of the 11 cases, and found its position in ventral occipital cortex, using Talairach coordinates. This position marked with an 'X' in **Figure 4**. The location is shown on the ventral surface of two individuals for whom we have measured visual field maps (also shown). The key position associated with pure cerebral achromatopsia is very close to the foveal representations of the VO-1/VO-2 field maps and also to the hV4 field map.

Roughly at the same time as Meadows was reporting on his work, Semir Zeki was undertaking his pioneering work on visual field maps and primate color vision. Meadows was aware that Zeki believed macaque area V4 is specialized for color vision, and he considered whether human cerebral achromatopsia might be explained by damage to a human homologue of macaque V4. He wrote cautiously in his paper:

"It is natural to speculate upon whether Zeki's colour coded area V4 might represent the same region that is damaged in the present cases. ... there is still a problem in relating these 2 areas, for the human evidence is compatible with a colour-coded area close to the striate cortical representation of only the upper part of the vertical meridian of the visual field, whereas in the

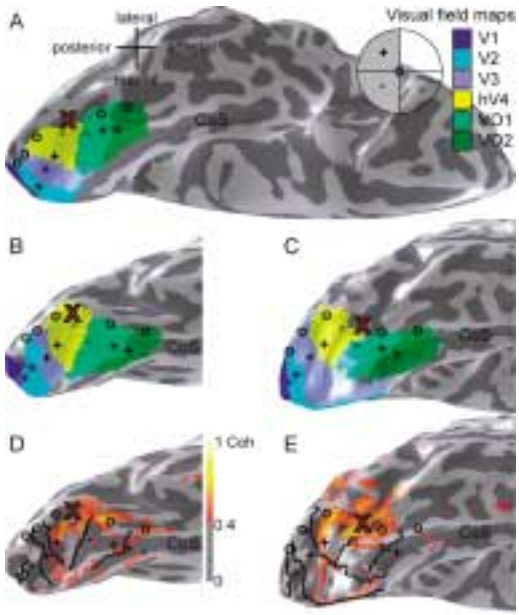

Figure 4 Ventral views of visual field maps and color activations in the right hemisphere. (A-C) The visual field maps in three subjects are shown. The X indicates the projected average center of mass of lesions leading to cerebral achromatopsia[65]. The inset at the upper right describes the visual field representation. (D,E) The color overlay shows the activation during a color-exchange experiment for the same subjects as in A-C. The solid lines mark the boundaries between the visual field maps. The color bar shows the signal coherence level; only responses with a coherence greater than 0.4 are shown.

monkey area V4 appears to extend along the entire vertical meridian. Whether these 2 areas are comparable must therefore await further studies (p. 627-8)."

3.2 Functional imaging. Neurological cases can be immensely informative, but the method is notoriously difficult for scientists to apply. First, appropriate patients are hard to find. Second, the cortical damage is uncontrolled and every case can be different; hence, the scientist cannot be confident about the generality of the findings. Thus, it was a very significant advance when Zeki, in collaboration with others in London, achieved the first controlled demonstration that human ventral occipital cortex is particularly sensitive to color[66, 67]. Zeki and his colleagues had subjects view a simple pattern of rectangular shapes that alternated between monochrome (light-dark) and full color. The luminance of the monochromatic and color rectangles was equated, so that as the pattern changed between achromatic and colorful luminance remained constant. Using positron emission tomography (PET), Zeki and his collaborators measured cortical responses to the introduction and removal of color. The largest activation is centered on the ventral occipital surface.

The papers by Zeki and his collaborators are widely cited and justifiably so. These are the first functional measurements showing singularly large responses to color in ventral occipital cortex. The measurements have been repeated by multiple laboratories. The implications of these measurements for theories of human color vision, and the relationship between human and monkey measurements, has been intensely debated.

Zeki's papers were written as a vindication of a theory called "functional specialization"; indeed, one of the two papers is titled: "A direct demonstration of functional specialization in human visual cortex." To explain the meaning of functional specialization, the authors write: "While we refer to human V4 and V5 as the color and motion centers, respectively, we do not wish to imply that the processing of color or motion is necessarily their only function, or that these are the only areas involved with those submodalities of vision. We state only that color and motion are among their chief functions (p.645)." The conceptual force of "functional specialization" is weak, and such theories are often subjected to misinterpretation and mischief.

As the quoted passage shows, Zeki and his colleagues believed immediately that the human ventral occipital responses to color are homologous macaque V4 signals. Meadows had noted the connection between this location in human and monkey V4 was uncertain, and the new work adduced no new evidence of homology. In fact, the only reason for suspecting a correspondence between the regions was Zeki's hypothesis that V4 and human ventral occipital cortex were both a "functional specialization" for color. Given the weakness of the definition of functional specialization, this argument could hardly be compelling to the conservative scientific community. Where Meadows had been cautious, Zeki was bold.

Following the original PET experiments on color, functional MRI was developed and most neuroimaging work shifted to that methodology. As described above, our lab and others developed methods to identify visual field maps[48]. Also, our lab and others used fMRI to measure responses to color stimuli. We approached the question as a type of engineering measurement, asking for example, how large a response was produced in primary visual cortex by signals initiated in the different types of cones? Or how large a signal was produced by red-green stimulus (L-M cone difference)? How did this depend on the temporal frequency of the stimulus, and so forth? For example, our group and Andreas Kleinschmidt independently observed that under a wide range of conditions human primary visual cortex responds more powerfully (per unit cone contrast) to chromatic signals (the difference of L and M cones) than to luminance signals (the sum of L and M cones)[68, 69]. This result was somewhat surprising as many single unit physiologists reported finding only very few 'color-coded' single units. But of course, new measurement technologies often bring new surprises and open us up to thinking about systems in different ways. And this type of work surely was only a background for the disagreement that was about to erupt.

3.3 Maps and color. Where is the ventral response to color located with respect to the visual field maps? Until recently, there was considerable uncertainty concerning the organization of ventral occipital maps. These maps are difficult to measure using the conventional rings and wedges used in traveling wave methods. Moreover, the human maps adjacent to V3-ventral differ from maps in macaque. For reasons described in detail elsewhere we believe the organization in human is now well understood[36, 56]. The newly discovered organization is quite pleasing and was foreshadowed by the work from Meadows and Zeki.

In macaque V4 is organized in a band that nearly parallels V3. The V4 vertical representation abuts the V3 vertical representation. Similar to macaque V1/2/3, the V4 map is divided into dorsal and ventral regions that represent mainly the lower and upper visual fields[48]. This arrangement has been measured in macaque with both single unit physiology and fMRI [70, 71]. But in human there is no corresponding map that parallels most of the length of V3. Instead, there is a compact map, adjacent to the ventral portion of V3 that represents the entire hemifield. There are at least two additional visual field maps adjacent and anterior within ventral occipital cortex. The organization of these maps is shown for three subjects in Fig 4ABC. The subject described in (A) represents new data collected using new methods[44]; the subjects in B and C were described by Brewer et al.[56].

We proposed the name hV4, rather than V4, for the map adjacent to V3[36, 72]. Appending the 'h' for 'human' seems important based on the historical considerations outlined above. The spatial arrangement of the V1/2/3 maps is shared between species and there appears to be no need to append an 'h'. But the next map, while fourth in the series, may not be homologous and we

think reminding ourselves in the name is appropriate. Some colleagues suggest that keeping the V4 part of hV4 is a misnomer; but we think eliminating any reference to V4 for this map is too extreme. HV4 is the fourth map along the ventral surface; it has no competition for this number because the fourth map along the dorsal surface is named V3A.

We proposed naming the two additional maps clustered around the ventral occipital (VO) fovea VO-1 and VO-2. We think it is too risky to use the name of a macaque area that one might guess to be homologous to these, such as TEO or VTF[73]. The data in Figure 3 show yet another foveal representation, anterior to VO. We have seen this repeatedly[56, 72]. We presume a cluster will be defined near this representation in the future; we propose the name ventral-temporal (VT) with corresponding maps VT-1, and so forth.

The relationship between these maps and ventral color activation is shown in Figure 4DE. The color overlay shows the spatial distribution of BOLD responses during a color-exchange experiment. In both observers the activation contains within it the center-of-mass of cortical damage measured from subjects with cerebral achromatopsia[65]. The activation includes the foveal representations within hV4 and VO-1. We suspect that the specific coverage of the color-exchange activation must depend on a variety of stimulus properties, including the spatial structure of the pattern and the location of the target within the visual field. Given the achromatopsia results, the color activations from several labs[56, 72, 74～78] and the measurements shown here, there can be little doubt that (a) ventral occipital cortex contains a region that is very responsive to color, (b) the most highly activated portion of the response falls overlaps with visual field maps hV4, VO-1 and VO-2, and (c) damage in this region disturbs normal color vision.

3.4 Quantitative measurements of color signals. The color localization and mapping results together, carefully built up over a century of medical and scientific work, convince us that a quantitative study of the signals from this region will inform us about an essential component of the cortical basis of human color experience.

It is widely understood that the color appearance of a stimulus depends in significant measure on the ratio of cone absorptions caused by that stimulus. Too often, one finds the assumption that other perceptual functions do not depend on stimulus color. Over the last twenty years, however, scientists have found many examples to demonstrate the contrary: perceptual grouping, depth and motion all depend on target color. For example, the apparent speed of a moving object depends on the target contrast and color. Low contrast stimuli generally appear to move more slowly than high contrast stimuli; stimuli initiated by photon absorptions in the S-cones generally appear to move more slowly than stimuli with equal contrast but initiated in the L- or M-cones[80]. The ratio of cone absorptions from a stimulus influences the performance of various human percepts beyond color appearance.

A specific perceptual example that illustrates this interaction comes from studies of the interaction between motion, flicker and color. A fundamental characteristic of color appearance is a slow temporal sensitivity of the chromatic version (red-green and blue-yellow). This can be demonstrated behaviorally by alternating two different colors at, say, 10-15 Hz: the color appears stable and unchanging. These behavioral measurements demonstrate that the color appearance signals are temporally sluggish[81].

Neural responses in the retina and lateral geniculate nucleus are not temporally sluggish, so that this reduced sensitivity has a cortical basis[10, 82, 83]. An important clue about the cortical basis for the reduced temporal sensitivity can be obtained by comparing the response to flickering stimuli in different cortical regions. The data in **Fig. 5** measure a very large difference in temporal sensitivity when comparing BOLD signals in human motion-selective cortex (MT+) and VO-1. The three graphs in the top row show measurements in VO-1. Each panel shows the contrast response function to a different stimulus color. The two curves within each graph show measurements to that color at two different temporal frequencies. The solid curves show measurements to a 1.5 Hz flicker and the dashed curves show measurements to a 7.5 Hz flicker. In human

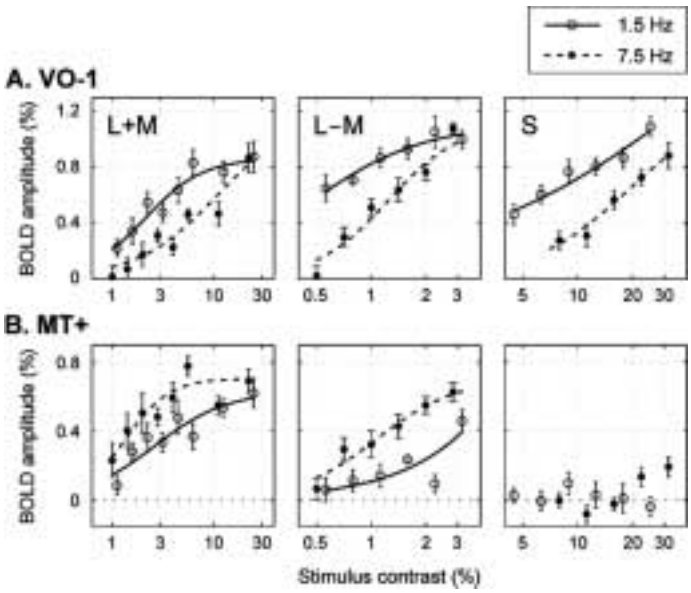

Figure 5 Contrast response functions VO-1 and MT+ to flickering stimuli. ***A***, The three panels show VO-1 contrast response functions to L+M (luminance), L-M (red green), and S-cone initiated signals. The symbols indicate measured BOLD response amplitudes. Open and filled symbols are responses to stimuli at 1.5 Hz and 7.5 Hz, respectively. The fitted contrast response functions are shown as the solid and dashed curves. ***B***, Same as ***A*** but for the MT+ region of interest. The data are replotted from Figs 5 and 6 in Liu[79].

VO-1, there is a significant response to all three colors. In each case the slow temporal flicker produces a stronger response.

The responses to precisely the same signals, this time in MT+, are shown in the bottom three panels. Notice two very significant differences between the VO-1 and MT+ responses. First, there is only a weak response in MT+ to the signals initiated in the S-cones. Weak MT+ responses to S-cone initiated motion were documented previously. These measurements show that the color responses in MT+ do not match the normal color experience. Two color dimensions (light/dark) and (red/green) evoke powerful responses, but the third (blue/yellow) does not. This differs from VO-1 which responds powerfully to all three color dimensions.

Second, the temporal frequency response in MT+ is just the reverse of that in VO-1. In MT+ high temporal frequency responses exceed low temporal frequency responses. While VO-1 is specialized for responding powerfully to all three color dimensions and slow temporal modulations, MT+ has poor color responses in one dimension and responds more powerfully to rapid temporal modulations. Note these quantitative measurements results do not imply that MT+ is color blind: MT+ responds to signals from all three cone types. They do show, however, that the quantitative properties of the MT+ responses do not match the quantitative characteristics of color appearance. As we have explained elsewhere, the MT+ responses do match several aspects of the observed behavioral measurements combining color and motion[80, 84, 85].

4. DISCUSSION

BOLD measurements are transforming our understanding of human visual cortex. We can now measure the organization of visual cortex into many different visual field maps. These maps are grouped into small clusters, with each cluster sharing a common eccentricity representation. The maps themselves provide a general structure for understanding the location of responses to different types of visual signals, or the responses during different types of visual tasks. The organization of the maps in small clusters suggests many hypotheses concerning visual function and development.

The quantitative analysis of cone signals across cortex expands our understanding of visual behavior. The search for a color center is one way in which quantifying the distribution of cone signals informs us about the brain. By measuring responses quantitatively in other parts of cortex, we learn more about the interactions between stimulus color properties and other types of visual performance. The BOLD measurements should serve as an important tool in developing quantitative models of the neural circuits distributing color information and ultimately understanding visual computations.

Current BOLD measurements generally are made at roughly 3 mm isotropic resolution. In this case, each voxel represents several million neurons. In the next few years, it will be common to measure at 1

mm isotropic resolution, and then even smaller. These smaller voxel sizes should reflect the signals in neural circuits comprising only tens of thousands of neurons. These resolutions should reveal the organization of much finer cortical structures, such columnar architectures that have been hidden until recently. It will also be possible to build quantitative models of these cortical circuits and to couple the BOLD measurements with precise models of neural circuits. We expect that quantitative work on visual field maps and color signals will offer a good foundation for these new advances.

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