Investigating the Large-Scale Topographic Organization of the Visual System
in Humans and Macaques

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Abstract

A fundamental question in vision neuroscience is how information from our environment is represented throughout the visual system. Much of visual cortex consists of several orderly representations of our environment along sensory surfaces. These topographic representations, referred to as visual field maps, are thought to facilitate the processing and communication of visual information. Using neuroimaging, we investigated the organization of visual field maps across visual cortex and the connectivity between cortical areas that support visuo-spatial processing. We identified 26 distinct visual field maps in humans and 15 in monkeys. These maps revealed several parallels, and a few dissociations, in the organization of the visual system between species. Many of these maps were within regions of cortex thought to lack organized representations of visual space. At a coarser scale, several visual maps formed distinct clusters with maps within a cluster sharing similar functional response properties. Functional and anatomical connectivity between human visual field maps emphasized local connections that, broadly, distinguished dorsal and ventral cortex and paralleled the well-established organization of the macaque visual system. Functional connectivity analyses also revealed a novel, large-scale organization based on eccentricity representations, in which areas with non-overlapping visual field representations, but matching eccentricity representations, were correlated. This eccentricity-based organization provides a new functional parcellation scheme of the visual cortex, which may be crucial for the integration of information across visual maps. Together, these data provide clear criteria for the comparison of human and macaque visual systems. They demonstrate that the representation of visual space is a major organizational principle of the primate visual system from individual maps to broad pathways consisting of several maps. This organization extends previous hypotheses on the efficient organization of individual topographic
maps and suggests that the primate visual system is organized to efficiently communicate information at multiple spatial scales by broadly minimizing distances between areas involved in similar computational processes.
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1 Introduction

A large portion of cortex, including auditory, motor, somatosensory, and visual cortex, consists of orderly representations of our environment along sensory surfaces. These topographic representations are commonly thought of as a fundamental organizational principle for the processing of sensory information (Mountcastle 1957; Kaas 1997). Within the visual system, a prominent topographic representation is the visual field map, in which the receptive fields of adjacent neurons along the cortical surface typically receive input from adjacent points on the surface of the retina. Visual maps are thought of as functional units that exhibit some degree of specialization; neurons within a map share similar response selectivities (Zeki, 1993). As such, the visual field map provides important information about the location of a particular perceptual process within the brain. The topographic organization and functional response properties have been well established for several visual maps. For example, neurons within area MT are highly selective for motion direction and damage to MT yields impairment in direction discrimination, but does not impair other perceptual processes such as contrast detection thresholds (Newsome & Pare 1988). How these visual field maps relate to one another and what they can inform us about the large-scale organization of the primate visual system is much debated (Kaas 1997; Rosa & Tweedale 2005; Wandell et al. 2007; Huberman et al. 2008). In this dissertation, I will discuss a series of experiments investigating the organization of visual field maps across the visual system, their relation to other functional topographies, and their connectivity. Experiments were conducted in both humans and macaques.

The macaque monkey serves as an important animal model for vision neuroscience. Decades of invasive functional and anatomical work in non-human primates have provided
invaluable insight into the organization of the brain. Though functional imaging enables the exploration of human brain function noninvasively, fMRI only indirectly reflects neuronal activity and is limited in spatial and temporal resolution. The interpretation of fMRI data can greatly benefit from drawing upon the vast knowledge collected from non-human primate studies. Comparisons between humans and macaques can reveal important insights about the nature of commonalities within the primate animal order. The extent to which functional organization differs between species can potentially explain important evolutionary differences. Major differences in the neurobiological nature of single-cell and (fMRI) BOLD signals complicate such comparisons. Monkey fMRI bridges human fMRI and monkey electrophysiology, enabling direct comparisons between species. Even with using similar experimental methodologies between species, objective criteria need to be established as grounds for comparison in order for the macaque model to be relatable to the human visual system. Visual maps provide such objective criteria for systematic comparisons of the organization of the visual system between species.

Early electrophysiological recordings in monkeys and cats identified several topographic representations of the contralateral visual field in and around the calcarine sulcus (Daniel and Whitteridge 1961; Zeki 1969; Allman and Kaas 1971; Van Essen et al. 1984). It was initially assumed that much of extrastriate cortex lacked any organized representation of visual space due to large receptive field size and position scatter. Though many additional visual field maps have since been identified across primate extrastriate cortex (see Gattass et al. 2005 for review), large parts of visually-responsive cortex are still thought to lack any organized representation of space (e.g. Platt & Glimcher 1998; Halgren et al. 1999; Tsao et al. 2003). In particular, human ventral
temporal cortex, which specializes in the identification of object stimuli, is not commonly thought to represent those objects’ location in space. At some point along the processing stream, identification and location information must be integrated. One possibility is that the integration of information occurs in a common higher-order area that both areas project to, such as prefrontal cortex, as suggested by some physiological studies in monkeys (Rao et al., 1997). Another possibility is that there is parallel encoding of object and location information throughout visual cortex (e.g. Konen and Kastner, 2008a,b). We tested the later hypothesis by investigating the topographic organization of human ventral temporal cortex. In chapter 2, I will discuss several visual field maps identified within ventral temporal cortex that support the hypothesis of parallel encoding of object and location information throughout visual cortex.

It is critical to resolve whether the abundance of maps identified in human imaging studies reflects a major difference in the organization of the visual system between species, or different methodologies. Despite data from macaque studies identifying several regions of parietal cortex that represent parts of space in various reference frames (Graziano & Gross 1994; Andersen et al. 1997; Colby & Goldberg 1999; Grefkes & Fink 2005), there has been little evidence for orderly visuotopic representations of visual space (Platt & Glimcher 1998, Blatt et al. 1990; Ben Hamed et al. 2001). In contrast, seven maps of the visual field have been identified within human posterior parietal cortex. These apparent differences may reflect fundamental dissociations in the organization of parietal cortex between species, or may just reflect differences between single-unit and fMRI methodologies. In particular, single-unit studies may not have the broad sampling resolution needed to reveal the organization of visual field maps in areas with large receptive fields, such as parietal cortex. In chapter 3, I will discuss the visuotopic organization of macaque
posterior parietal cortex as revealed by fMRI. We found several parallels in the topographic organization between humans and macaques, but also several differences that may highlight fundamental differences between species.

The experiments discussed in the 2nd and 3rd chapters demonstrate that visual field maps are prevalent throughout much of the primate visual system. Visual field maps provide an important architecture for the communication of information across the visual system at multiple spatial scales (Mountcastle 1957; Kaas 1997; Wandell 2005). Within a visual field map, the spatial structure of a scene is preserved with nearby parts of visual space represented by neighboring neurons. At a coarser scale, visual field maps appear to be arranged in spatial clusters. This cluster organization provides a framework for the coordination of information between individual areas within clusters (Wandell et al. 2005). In chapter 4, I confirm the existence of 26 visual field maps in humans and 15 in macaques that have been reported across various labs, and discuss the large-scale organization of these visual field maps across cortex into distinct clusters. I also propose a broader organization of these clusters into separate topographic streams that extend into parietal, lateral occipital, and ventral temporal cortex.

It is possible that these topographic streams are functionally specialized. Each map within a stream is further specialized such that all maps contribute towards a common perceptual process. It is unclear how these streams, and the visual field maps within, relate to other known functional selectivities in extrastriate cortex. Visual field maps have been identified within a large region of lateral occipital and ventral temporal cortex that contains several regions highly selective for a particular stimulus category (e.g. motion, objects, faces, and places). The relation between these
two functional topographies has not been systematically investigated. In chapter 5, I will discuss the correspondence between category-selective regions and visual field maps in lateral occipital and ventral visual cortex. Several visual maps were highly selective for particular stimulus categories. Category-selective regions generally overlapped with segments of multiple visual field maps at particular spatial locations, particularly along the eccentricity dimension. Our data suggest that the two topographies are not distinct, and that category-selective “areas” may actually be parts of multiple visual maps involved in the similar computational processes.

A fundamental question is how such category selectivities arise within particular maps. Functional response properties of a particular area are, to a large extent, a function of the intricate pattern of connections within and between these visual areas. Much of our understanding of the organization of human visual cortex is inferred from anatomical studies of macaque visual cortex (e.g. Boussaoud et al. 1990; Felleman & Van Essen 1991; Felleman et al. 1997; Lewis & Van Essen 2000). However, the visual system has undergone considerable cortical expansion from macaques to humans, making a detailed account of the anatomical connectivity of the human visual system difficult to infer from macaque data. Visual maps offer a framework for cross species comparisons of connections between visual areas. In chapter 6, I will discuss the large-scale functional and anatomical connectivity between visual field maps in human visual cortex. Both anatomical and functional data reveal large-scale patterns of connectivity that parallel known connections in the macaque.

The topographic organization of individual maps may provide an infrastructure for these large-scale connectivity patterns. The organization of visual space is preserved in the
connections between visual field maps with neurons representing similar regions of visual space interconnected between areas (Cragg 1969; Maunsell and Van Essen 1983; Van Essen and Zeki 1978; Zeki 1969). In addition to such topographically-local connections between neurons with overlapping receptive fields, large-scale connectivity patterns have been observed between foveal and peripheral visual cortex in macaques (Zeki 1969; Colby et al. 1988; Nakamura et al. 1993; Ungerleider et al. 2008; Gattass et al. 2005; Vincent et al. 2007) and in humans (Dougherty et al. 2005; Yeo et al. 2011). While these patterns may be important for the integration of information across the entire visual field, the governing organization principles of such large-scale connectivity patterns are still unknown. In chapter 7, I will discuss potential large-scale functional organization principles of visual cortex. We identified an organization of functional connectivity based on eccentricity, which spanned the entire visual field.
2. The Visuotopic Organization of Human Ventral Visual Cortex

In the human brain, objects are represented in a large swath of ventral temporal and lateral occipital cortex that responds more strongly to object stimuli than to their scrambled counterparts (e.g. Malach et al., 1995; Grill-Spector et al., 1999; Kourtzi and Kanwisher, 2001; see Grill-Spector and Malach, 2004 for review). Initially, it was thought that this substantial part of visual cortex lacked any organization of visual space. This notion was later revised by Malach and colleagues who found evidence for a systematic representation of eccentricity in ventral visual cortex with medial regions such as parahippocampal cortex representing peripheral eccentricities and lateral regions such as lateral occipital cortex representing foveal eccentricities (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002; Hasson et al., 2003). However, no orderly representation of polar angle was found to delineate visual areas by meridian boundaries, an organization that is typical for early visual cortex (Levy et al., 2001). According to the organizing principle of eccentricity, object categories requiring foveal vision such as faces and words are associated with center-biased representations, whereas objects that require the integration of parts over a larger scale such as scenes and buildings are associated with periphery-biased representations (Hasson et al., 2002).

More recently, however, improved imaging techniques at higher resolutions and field strength have revealed an increasing number of retinotopically organized areas containing both an orderly polar angle as well as an eccentricity representation in ventral visual cortex. Anterior to hV4, in ventral occipital (VO) cortex, two visual field maps have been found that share a fovea and each contain a topographic representation of contralateral visual space, termed VO-1 and VO-2 (Brewer et al., 2005). The VO areas are characterized by similar response profiles and
code for stimulus color and object-related information. In lateral occipital (LO) cortex, two areas have been identified that share a fovea with early visual cortex and hV4 and each contain a representation of contralateral space, termed LO-1 and LO-2 (Larsson and Heeger, 2006). As with the VO areas, the LO areas appear to share common functional response properties and code for stimulus shape.

Using attentive wedge and ring tracking paradigms as well as standard phase-encoded retinotopic mapping, we confirm the organization of hV4 and the VO areas, and report here two new visual field maps anterior to VO-2 within posterior parahippocampal cortex (PHC), referred to as PHC-1 and PHC-2. The PHC areas were found to share a fovea, represent contralateral space, and show a strong bias towards the representation of peripheral eccentricities. Our findings lend further support to the notion that retinotopic organization persists well into higher-order visual cortex (Wandell et al., 2007).

2.1 Materials and Methods

Subjects. Eleven subjects (aged 20–36 years, 4 females) participated in the study, which was approved by the Institutional Review Panel of Princeton University. All subjects were in good health with no history of psychiatric or neurological disorders and gave their informed written consent. Subjects had normal or corrected-to-normal visual acuity. All subjects participated in three scanning sessions, during which high-resolution structural images were acquired for cortical surface reconstructions, and polar angle and eccentricity measurements were obtained across visual cortex using attentive wedge and ring tracking paradigms (attentionotopy studies). Three subjects exhibited excessive head motion and were excluded from further analyses. The
remaining eight subjects participated in a fourth scanning session in which various object stimuli were probed, and four of them participated in a fifth and sixth scanning session, in which polar angle and eccentricity maps were measured using standard retinotopic mapping procedures (Sereno et al., 1995; DeYoe et al., 1996; Engel et al., 1997).

**Visual Display.** The stimuli were generated on Macintosh G4 and G5 computers (Apple Computer; Cupertino, CA) using MATLAB software (The MathWorks; Natick, MA) and Psychophysics Toolbox functions (Brainard, 1997; Pelli, 1997). Stimuli were projected from a PowerLite 7250 liquid crystal display projector (Epson; Long Beach, CA) located outside the scanner room onto a translucent screen located at the end of the scanner bore. Subjects viewed the screen at a total path length of 60 cm through a mirror attached to the head coil. The screen subtended 30° of visual angle in both the horizontal and vertical dimensions. A trigger pulse from the scanner synchronized the onset of stimulus presentation to the beginning of the image acquisition.

**Stimuli.** *Polar angle measurements:* In order to measure polar angle representations in visual cortex, visual stimuli consisted of a wedge that rotated either clockwise or counterclockwise around a central fixation point (see Arcaro et al. 2009, Supplementary Fig. 1.1A). The wedge spanned 1-15° in eccentricity with an arc length of 45° and moved at a rate of 9 deg/s. There were two variations of wedge stimuli, one used in the attentionotopy studies and one used in the standard retinotopic mapping studies.
The wedge used in the attentionotopy studies was filled with 1000 white dots (0.1°, 65 cd/m²) that moved either randomly or in a coherent direction at a rate of 7 deg/s. The percentage of coherently moving dots ranged from 30-65% and was determined separately for each subject based on the individual motion coherence threshold to yield behavioral performance of ~75% accuracy in a behavioral testing session prior to scanning. The direction of motion for the coherent dots changed randomly every 3-5 s. Subjects were instructed to maintain fixation while covertly attending to the rotating wedge and to detect a change in the direction of the coherently moving dots by pressing a button with their right index finger. The change in radial direction of the coherently moving dots ranged between 75° and 105°. Each run consisted of six cycles of 40 s each of the rotating wedge and started and ended with a 10 s blank period amounting to an overall run length of 260 s. Runs alternated between clockwise and counterclockwise wedge rotations, with a total of 10 runs per scan session.

The wedge used for the standard retinotopic mapping studies consisted of a colored checkerboard with each check’s chromaticity and luminance alternating at a flicker frequency of 4 Hz (see Arcaro et al. 2009, Supplementary Fig. 2.1A; see Swisher et al., 2007 for details). A transparent wedge within a dark foreground rotated around a central fixation. The underlying checkerboard was only visible through the transparent wedge, giving the appearance of a rotating checkerboard wedge. The size and speed of the rotating wedge was the same as in the attentionotopy experiment. Subjects attended to and performed a luminance detection task at fixation, indicating by button press when a change in luminance occurred. Luminance changes occurred, on average every 4.5 s. Each run consisted of seven cycles of the rotating
checkerboard. Runs alternated between clockwise and counterclockwise wedge rotation, with a total of 10 runs per scan session.

**Eccentricity measurements.** In order to measure eccentricity representations in visual cortex, visual stimuli consisted of an annulus that either expanded or contracted around a central fixation point (see Arcaro et al. 2009, Supplementary Fig. 2.1B). The duty cycle of the annulus was 12.5%, that is, any given point on the screen was within the annulus for only 12.5% of the time. The annulus increased on a logarithmic scale over time in size and rate of expansion to approximately match the human cortical magnification factor of early visual cortex (Horton and Hoyt, 1991; Swisher et al., 2007). The outer part of the ring expanded to a maximum eccentricity of 16.875°, to ensure that the whole visual display (1-15°) was stimulated for an equal amount of time, before returning to the foveal origin (and vice versa for the contracting ring). There were two variations of ring stimuli, one used in the attentionotopy studies and one used in the standard retinotopic mapping studies.

The ring used in the attentionotopy studies was red (9.8 cd/m²) and filled with white balls (65 cd/m²) bouncing randomly within the annulus. The diameter of each ball varied such that the radius was always equal to 1/4 of the ring size throughout the cycle. Additionally, the number of balls varied (15-20) throughout each cycle to maintain full coverage within the annulus. Every 3-5 seconds, one ball, that was randomly chosen, changed in luminance. The presentation length of the luminance change was matched to each subject’s detection threshold to yield behavioral performance of ~75% accuracy, as determined in behavioral testing sessions prior to scanning, and ranged from 0.08 to 0.15 s. During each run, subjects were instructed to maintain fixation while covertly attending to the bouncing balls within the ring and to perform the luminance
detection task. The stimulus was coded to allow the balls to move about freely within the ring. Each run consisted of six cycles of 40 s each and started and ended with a 10 s blank period amounting to an overall run length of 260 s. Runs alternated between annulus expansions and contractions, with a total of 10 runs per scan session.

The ring used for the standard eccentricity mapping consisted of a colored checkerboard with each check’s chromaticity and luminance alternating at a flicker frequency of 4 Hz (see Arcaro et al. 2009, Supplementary Fig. 2.1B; see Swisher et al., 2007 for details). A transparent annulus within a dark foreground layer either expanded or contracted around a central fixation point. The underlying checkerboard was only visible through the transparent annulus, giving the appearance of an expanding or contracting checkerboard ring. Subjects maintained fixation and performed a central luminance detection task at fixation, as described in the last section. The size and rate of expansion for the ring was the same as in the attentionotopy experiment. Each run consisted of 7 cycles of 40 s each, and runs alternated between annulus expansion and contraction, with a total of 10 runs per scan session.

Data acquisition. Data were acquired with a 3T Allegra head-dedicated MRI scanner (Siemens, Erlangen, Germany) using a 4-channel bi-temporal phased array coil (Nova Medical, Wilmington, Massachusetts, Model NMSC-003A). For the attentionotopy and standard retinotopy studies, 20 axial slices were acquired in 10 runs of 130 and 140 volumes, respectively, covering ventral occipital and temporal cortex. For the object category studies, 25 axial slices were acquired in four to six runs of 138 volumes, covering ventral occipital and temporal cortex. All acquisitions used a gradient echo, echo planar sequence with a 128 square matrix (slice
thickness: 2 mm, with a 0.5 mm gap between slices, interleaved acquisition) leading to an in-plane resolution of 2 x 2 mm$^2$ [field of view (FOV), 256 x 256 mm$^2$; repetition time (TR), 2.0-2.5 s; echo time (TE), 40 ms; flip angle 90°]. A partial Fourier factor of 7/8 was used to acquire asymmetric fraction of k-space to reduce the acquisition time. Echo-planar images were compared with a high-resolution anatomical scan taken at the end of each session (MPRAGE sequence, TR = 2.5 s, TE = 4.38 s, flip angle = 8°, 256 x 256 matrix, 1-mm$^3$ resolution). An in-plane magnetic field map image was acquired to perform echo planar imaging undistortion (FOV = 256 x 256 mm, 128 matrix, TR = 345 ms, TE = 5.06/8.06 ms, flip angle = 40°, bandwidth = 260 Hz/pixel). For cortical surface reconstructions, high-resolution structural scans were acquired in a separate session (MPRAGE sequence, same parameters as above, 2 acquisitions).

**Data analysis.** Data were analyzed using AFNI (Cox, 1996) (http://afni.nimh.nih.gov/afni/), SUMA (http://afni.nimh.nih.gov/afni/suma), MATLAB, and FREESURFER (Dale et al., 1999; Fischl et al., 1999) (http://surfer.nmr.mgh.harvard.edu/). Functional images were motion corrected (Cox and Jesmanowicz, 1999) to the image acquired closest in time to the anatomical scan, undistorted using the images from the field map scan, and normalized to percent signal change by dividing the time series by its mean intensity. After normalization, attentionotopy and retinotopy data were projected onto cortical surface reconstructions created with FREESURFER that were aligned to each of the experimental sessions using AFNI/SUMA. All voxels that fell between the gray and white matter boundaries were mapped to the surface. The units of data projected to the surface are referred to as nodes. Given that there is not a one-to-one correspondence between nodes and voxels, the value of each node was calculated by taking a
weighted average of all the voxels that overlapped with each node. All subsequent analysis procedures for attentionotopy and retinotopy datasets (e.g. Fourier analysis) were performed on the surface-mapped data, which favorably restricts analyses to data that are primarily within the gray matter, since white matter voxels do not get mapped onto the surface. No spatial smoothing was used for any of the analyses (i.e. topography and object representations). For display purposes, the attentionotopy and retinotopy data presented in the figures were smoothed with a 2 mm full-width-half-max on the surface (Chung et al., 2005). For each subject, structural images were transformed into Talairach space and linked to the surface reconstructions using AFNI software to obtain Talairach coordinates for the areas investigated (Talairach and Tournoux, 1988). Surface size estimates were measured using SUMA tools that calculate the volume of all nodes that fall in-between the white matter and pial surface layers.

For each attentionotopy data set, the volumes acquired during the blank periods were discarded. For each retinotopy data set, the first 20 volumes corresponding to the first cycle were discarded. A Fourier analysis was used to identify surface nodes activated by the polar angle and eccentricity stimuli (Bandettini et al., 1993; Engel et al., 1994). For each node of the surface, the amplitude and phase—the temporal delay relative to the stimulus onset—of the harmonic at the stimulus frequency was determined by a Fourier transform of the mean time series of the node. To correctly match the phase delay of the time series of each node to the phase of the wedge/ring stimuli, and thereby localize the region of the visual field to which the underlying neurons responded best, the response phases were corrected for the hemodynamic lag (3 s). The counterclockwise/inward runs were then reversed to match the clockwise/outward runs and averaged together for each node. An F-ratio was calculated by comparing the power of
the complex signal at the stimulus frequency to the power of the noise. From the F-ratio, we calculated a \( p \)-value (uncorrected) taking into account degrees of freedom of the signal and noise. To quantify the reliability of phase estimates across runs, the variance of a mean phase across cycles was determined for each node. A jack-knifing method in which phase estimates were calculated from \( n-2 \) cycles (eliminating one clockwise and one counterclockwise cycle per calculation) across all runs was used to determine the standard error of phase estimates (see Hansen et al., 2007 for similar application). A grand mean phase estimate was calculated from the average of each of these phase estimates along with the standard error to account for variance across estimates for each node. The standard error was then converted into seconds per cycle.

Statistical maps were thresholded at a variance of 1.5 s of the 40 s cycle and overlaid on cortical surface reconstructions. The pattern and significance of activation approximately compares to a statistical threshold of \( p < .01 \) (uncorrected for multiple comparisons, derived from the F-ratio that was calculated from the fourier transform). When displaying phase estimates, a 12 point color scale was assigned to the polar angle datasets with each color representing 18° visual angle and a 10 point color scale was assigned to the eccentricity data sets with each color representing 1.5° eccentricity. For the purpose of this report, we focused our analysis on ventral temporal cortex, i.e., to brain regions located along the collateral sulcus and adjacent cortex. Contiguous clusters of activated nodes within this anatomical region that showed a systematic representation of visual space in polar or eccentricity coordinates were defined as regions of interest (ROIs). Borders between adjacent visual areas were defined as reversals in polar phase progression of the contralateral visual field. Surface analyses of these ROIs were performed using AFNI and MATLAB. To estimate the representation of the visual field for each ROI, the
polar angle and eccentricity phases for each surface node were plotted including only nodes that had both significant values for polar angle and eccentricity measures. Nodes that only had a significant polar angle representation, but no significant eccentricity measurement (or vice versa) were not included in the plots. To compute the representation of the visual field for each visual area as a function of polar angle and eccentricity, the visual field was divided into several sectors: contra- and ipsilateral, upper and lower, and foveal (0°-7.5°) and peripheral (7.5°-15°). The number of nodes within each sector was tallied and divided by the total number of nodes in each area to derive a mean representation for each subject. Data were collapsed across hemispheres and averaged across subjects to derive a group mean average. T-tests were used to assess statistical significance.

To quantitatively compare the alignment between the attentionotopy and retinotopy data sets for each subject, we calculated alignment indices and correlation coefficients for each visual area. The alignment index (AI) was defined as

\[ \text{Alignment Index} = 1 - \frac{|\Delta \phi|}{\pi} \]

where \( \Delta \phi \) is the difference between the polar angle (or eccentricity) phase for the two experiments (see Sereno and Huang, 2006 for further details). Only nodes that had phase values for both data sets thresholded at 1.5 s variance were included in the analysis. AIs were calculated for both polar angle and eccentricity measurements within each ROI on a node-by-node basis. The distribution of AI values within an ROI were plotted for single subjects in a histogram (Fig. 2.7a). AI distributions peaking at or near 1 indicate that the two data sets were in good
alignment (indicating that the polar angle at a vertex is identical in the two data sets). In contrast, for two uncorrelated data sets the distribution of AIs is a shallow linear ramp starting at a count of zero at an AI of zero and ending at a small value \((2v/n, \text{where } v \text{ is the number of vertices and } n \text{ is the number of bins})\) at an AI of 1 (red line, Fig. 2.7a; see Sereno and Huang, 2006). In order to perform statistical comparisons on the AIs, single subject mean index values were derived by averaging across all index values obtained for individual nodes within an ROI. One sample t-tests were conducted for each ROI between the mean index values and an index alignment value of .5 (representing chance). To derive a group index value, single subject mean index values were averaged within each ROI. To further evaluate the strength of alignment between both data sets for a given ROI, the correlation between phase estimates was calculated on a node-by-node basis for each subject.

**Eye-movement recordings.** For the attentionotopy experiments, eye movements were monitored for each subject in behavioral testing sessions outside the scanner. Subjects placed their heads on a chinrest located 60 cm in front of a monitor (Mitsubishi Electronics America, Irvine, CA), while performing the same task as used during the scanning sessions. Eye position was measured at a sampling rate of 60 Hz and was displayed in real-time on a video monitor, superimposed on the stimulus image using a telephoto lens (Model 5000 control unit and standard Model 504 remote optics, Applied Science Laboratories, Bedford, MA). The experimenter observed the eye-position display to ensure that the subjects were alert and maintained central fixation. Eye-position data were recorded for four subjects on the stimulus computer through a serial interface with the eye-tracker control module. The eye-tracking system had a resolution of 0.14° and the ability to resolve differences in relative eye position of
0.25° or less. Ilab software (Gitelman, 2002) was used to analyze the eye-movement data. Data were processed to automatically detect and remove eye blinks. Subjects maintained fixation within a 2.5° window for 97% (±.01, standard error of the mean) of the time in the polar angle experiment and 97% (±.03) in the eccentricity experiment, indicating an excellent ability to maintain fixation while covertly directing attention to the peripheral target stimuli.

2.2 Results

**Polar angle and eccentricity maps in ventral visual cortex**

The polar angle component of retinotopic maps in ventral visual cortex was measured for the central 15 degrees of the visual field using a smoothly rotating wedge stimulus that was filled with moving dots (see Arcaro et al. 2009, Supplementary Fig. 2.1A). Subjects were instructed to maintain fixation while covertly attending to the rotating wedge stimulus and to detect a change in the direction of the coherently moving dots. Subjects performed at an accuracy of 73 % (± 0.03 S.E.M.) on average during the scan sessions. The behavioral data were further evaluated relative to the location of the wedge stimulus in the visual field. There were no significant performance differences across the visual field (see Arcaro et al. 2009, Supplementary Fig. 2.2A, (F(19,38) = .442, p > .05). In addition, there were no significant differences in performance for runs with clockwise as compared to counterclockwise wedge rotation (F(1,2) = .494, p > .05).

The eccentricity component of the topographic maps in ventral visual cortex was measured for the central 15 degrees of the visual field using an annulus, filled with bouncing balls that either expanded or contracted around a central fixation point (see Arcaro et al. 2009 see
Arcaro et al. 2009, Supplementary Fig. 2.1B). Subjects were instructed to maintain fixation while covertly attending to the annulus and to detect a luminance change that occurred randomly in one of the balls. Subjects performed at an accuracy of 80% (± .01) on average. Performance was similar across the visual field (see Arcaro et al. 2009, Supplementary Figure 2.2B), and an analysis of variance showed no significant differences in performance as a function of eccentricity (F(12,84) = .639, p > .05).

Bilateral activations within visual cortex extending from the calcarine sulcus, across the collateral sulcus into the posterior PHC were found in all eight subjects in the polar angle and eccentricity mapping studies. For the polar angle measurements, activations within each hemisphere were mainly confined to the contralateral hemifield. Individual activation maps of polar angle and eccentricity in ventral
visual cortex are shown overlaid on flattened surface reconstructions for two representative subjects (S1 and S2) in Figures 2.1 (right hemisphere, RH) and 2.2 (left hemisphere, LH). Additional activation maps are shown in Figure 2.7a for subject S3 and see Arcaro et al. 2009, Supplementary Figures 2.3, 2.4, & 2.5 for subjects (S3-S8). For each surface node, the variance of the phase estimates across runs was calculated using a jack-knifing method (see Methods), and the threshold was chosen to only include data with a variance of less than 1.5 s per 40 s cycle. The color of each surface node was determined by the phase of its response and indicates the region of the visual field to which the surface node was most responsive. For the polar angle component, the upper visual field (UVF) is denoted in red-yellow, the horizontal meridian (HM) in green, and the lower visual field (LVF) in blue. Area boundaries that are formed by phase angles at or close to either the upper or lower vertical meridian (VM) are indicated with dotted and dashed lines, respectively. For the eccentricity measurements, the fovea is denoted in red and the periphery in blue.

Five criteria were used to identify individual visual areas: (1) an area contains continuous polar angle and eccentricity phase progressions with adjacent voxels.

Figure 2.2: Polar angle and eccentricity maps in human ventral visual cortex obtained in attentionotopy studies – left hemisphere. Flattened surface reconstructions of early and ventral visual cortex of the same subjects (S1 and S2) shown in Figure 1. All conventions as in Figure 1.
representing adjacent parts of contralateral visual space, (2) polar angle and eccentricity phase progressions were at (approximately) orthogonal angles, (3) the borders between areas were defined at reversals in phase progression (4) the pattern of polar angle and eccentricity phase progression was consistent in the majority of subjects and, when tested, replicable in individual subjects, (5) the anatomical location an area was relatively consistent across subjects. We consistently found eight distinct topographically organized cortical areas within ventral occipital and temporal cortex in each subject. Six of these areas have been previously reported: V1v, V2v, V3v, hV4, VO-1, and VO-2 (Sereno et al., 1995; DeYoe et al., 1996; Engel et al., 1997; Tootell et al., 1997; Brewer et al., 2005). Anterior to VO-2 we identified two additional areas in the posterior portion of the PHC, which we will refer to as PHC-1 and PHC-2 in keeping with a labeling scheme that emphasizes anatomical landmarks rather than function or presumed homology to the macaque cortex (for similar approaches, see Brewer et al., 2005; Larsson and Heeger, 2006; Wandell et al., 2007). All eight areas are described in greater detail below.

*Areas V1v, V2v, and V3v:* Consistent with numerous previous studies (e.g. Sereno et al., 1995; DeYoe et al., 1996; Engel et al., 1997) ventral areas V1, V2, and V3 were identified in all subjects (N=8) from a phase progression starting in the calcarine sulcus from a HM representation (green, not marked) to an upper vertical meridian (UVM) representation (red, dotted) that forms the border to area V2, and then reversing back to a HM that corresponds to the border of ventral V2 and V3 (Figs. 2.1 & 2.2, lefthand panels). The anterior border of ventral V3 was formed by a representation of the UVM. These three areas represent the upper quadrant of the contralateral visual field. Ventral V1, V2, and V3 share a foveal confluence; the
peripheral representations extend towards the collateral sulcus (Figs. 2.1 & 2.2, righthand panels).

*Area hV4:* Adjacent and anterior to ventral V3, a representation of contralateral space was identified that extended along the ventral surface and shared its posterior border, an UVM, with ventral V3 (red, dotted line; Figs. 2.1 & 2.2, lefthand panels), while its anterior border was formed by LVF angles (blue, dashed line). All subjects showed the same general topographic organization of hV4 in both hemispheres. For additional examples see Arcaro et al. 2009, Supplementary Figures 3, 4, & 5. The fovea of hV4 was found to be continuous with the foveal confluence shared by ventral V1, V2, and V3 (Figs. 2.1 & 2.2, righthand panels), and the peripheral representation extended towards the collateral sulcus, parallel with the eccentricity map of ventral V1, V2, and V3. As observed previously (Hansen et al., 2007), the anterior border of hV4 was often formed by a continuous representation of LVF angles such as the one seen in the RH of S1 (Fig. 2.1, lefthand panel, 7 of 16 hemispheres), but was sometimes formed by a discontinuous representation of LVF angles intermixed with those closer to the HM representation as seen in the RH of S2 (Fig. 2.1, lefthand panel, 9 of 16 hemispheres). The medial part of this border was drawn in the region of the most peripheral representations found in hV4 (purple line) that reversed from there towards the foveal representations of VO-1. Taken together, our data suggest a representation of contralateral space anterior to ventral V3 that is consistent with the hV4 model, proposed by Wandell and colleagues (Wade et al., 2002; see also Kastner et al., 1998; Kastner et al., 2001). This mapping scheme has been termed human V4, or hV4, to distinguish it from the topography observed in macaque V4 that is different and
represents only a quarterfield (Gattass et al., 1988; Wade et al., 2002; Brewer et al., 2005; see also Kastner et al., 1998; Kastner et al., 2001).

In a complimentary approach to investigate the topographic organization of hV4, its polar phase progression was quantitatively evaluated. Small line segments were successively drawn parallel to the polar angle progression and perpendicular to the eccentricity progression from the posterior border of hV4 to the anterior border of PHC-2, as indicated by the schematic outlines in Figure 2.3a. The blue dots indicate the phase values for individual nodes located along the line segments, and the red line indicates the average phase values as a function of distance on the surface. Individual subject polar phase progressions between area borders were interpolated into a common space, which allowed for intersubject averaging (Fig. 2.3b). As seen in the LH of subject S1 (Fig. 2.3a) as well as the group polar phase plots for both hemispheres (Fig. 2.3b), the anterior

Figure 2.3: Analysis of topographic organization within areas hV4, VO-1, VO-2, PHC-1, and PHC-2. (a) Polar angle maps of early and ventral visual cortex for the LH are shown for subject S1 (obtained in attentionotopy studies). Response phase was analyzed as a function of distance on the surface by drawing small line segments, as indicated in A, that run in parallel to the polar angle progression and perpendicular to the eccentricity progression. The line segments were successively drawn from the posterior border of hV4 to the anterior border of PHC-2. The blue dots indicate the phase values for individual nodes located along the line segments. The red line indicates the average phase values as a function of distance on the surface. The smooth progression of phase values as a function of distance on the map is apparent. Importantly, the response phase reverses at the shared boundaries between adjacent areas (red arrows). (b) Group polar phase plots are shown for both RH and LH (N=8). Response phases in-between identified area borders were interpolated into a common space, which allowed for intersubject averaging. The blue dots indicate phase values for individual subjects after interpolation. The red line indicates the group average. The smooth progression of phase values in-between identified area borders is apparent in the group averages as well as in the individual subjects.
and posterior borders of hV4 corresponded to the peaks of phase angles near the lower vertical meridian (LVM) and UVM, respectively, with a smooth progression of phase values in-between. The mean Talairach coordinates for left and right hV4 were -23 -75 -11 and +26 -77 -11 (Table 2.1). The mean activation sizes of hV4, for the RHs and LHs, were 1410 (± 329) and 1152 (± 289) mm³ respectively, which is 50% and 46% of the surface area for V1’s RH and LH (Table 2.2; Fig. 2.4).

**VO-1 and VO-2:** In accordance with Brewer et al. (2005), two representations of contralateral space, VO-1 and VO-2, were identified anterior to hV4 in all subjects. These two areas were located along the posterior medial fusiform gyrus and within the posterior portion of the collateral sulcus. The posterior extent of VO-1 shared a border with hV4 that was constituted by a polar angle phase reversal within the LVF near the LVM (blue, dashed line; Figs. 2.1 & 2.2, lefthand panels). VO-1 and VO-2 shared a border that constituted UVF angles close to the UVM (red, dotted line), and the anterior border of VO-2 was formed by LVF angles towards the LVM.
Similar to the anterior border of hV4, the border shared by VO-1 and VO-2 was often formed by a continuous representation of visual field angles near the UVM such as in the LH of subjects S1 & S2 (Fig. 2.2, lefthand panel, 10 of 16 hemispheres), but was sometimes formed by phase angle representations near the UVM intermixed with those closer to the HM representation as seen in the RH of subject S3 (Fig. 2.1a, 6 of 16 hemispheres). Likewise, the anterior border of VO-2 was sometimes formed by a continuous representation of phase angles close to the LVM (5 of 16 hemispheres), but was often intermixed with those closer to the HM representation as seen in the RH of subject S2 (Fig. 2.1, lefthand panel, 11 of 16 hemispheres). The mirror reversal in phase angle representations within VO-1 and VO-2 is further illustrated by the pattern of phase progressions (Fig. 2.3). A foveal representation separate from the large foveal confluence shared by V1, V2, V3, and hV4 (asterisk; Figs. 2.1 & 2.2, righthand panels) was identified that was typically shared by VO-1 and VO-2 and located near the border between VO-1 and VO-2 along the posterior part of the medial fusiform gyrus. The periphery of the visual field was represented posterior from the foveal representation abutting the peripheral representations of hV4 and ventral V3. The lateral border of VO-1 was identified as extending from the VO fovea to the peripheral extent abutting hV4 (purple line). In 12 of the 16 hemispheres, the foveal representation was evenly split between the two areas, as is the case for the LH of subjects S2 (asterisk, Fig. 2.2, righthand panel). In the remaining cases, the foveal representations were largely located within VO-2 with only a small part extending into VO-1, as in the RH of subject S1 (asterisk, Fig. 2.1, righthand panel).

Mean Talairach coordinates for left and right VO-1 were -27 -69 -8 and +27 -67 -8, respectively, and for left and right VO-2 were -26 -60 -7 and +25 -60 -7, respectively (Table
2.1). The mean activation sizes of VO-1 and VO-2 were 1145 and 1452 mm³ respectively, which is 22% and 27% the size of V1 and 45% and 57% the size of hV4 (Table 2.2, Fig. 2.4).

**PHC-1 and PHC-2:** Two cortical areas, each containing a representation of contralateral space, were identified anterior to VO-2. These two areas were found to be located within the posterior PHC extending along the collateral sulcus and flanked by the lingual gyrus and the posterior portion of the parahippocampal gyrus on one side and the medial fusiform gyrus on the other side. Following a naming convention based on approximate anatomical landmarks, we will refer to these two areas as parahippocampal cortical areas PHC-1 and PHC-2. The posterior border of PHC-1 was formed by LVF angles (blue, dashed; Figs. 2.1 & 2.2, lefthand panels), forming the shared border with VO-2. The polar phase map of PHC-1 progressed within posterior collateral sulcus from angles within the LVF to those within the UVF close to the UVM (red, dotted), constituting the shared border with PHC-2, with a systematic polar angle representation of the contralateral hemifield (Fig. 2.3a,b). A mirror reversal of the polar angle representation extending from the upper to the LVF was found in PHC-2 (Fig. 2.3a,b); the anterior border of PHC-2 was formed by LVF angles (blue, dashed; Figs. 2.1 & 2.2, lefthand panels). For additional examples see Arcaro et al. 2009, Supplementary Figures 2.3, 2.4, & 2.5. For PHC-1, hemifield representations of contralateral visual space were identified in all 16 hemispheres as seen in the RH of subjects S1 and S2.

![Figure 2.4: Estimated surface volume for V1, hV4, VO-1, VO-2, PHC-1, and PHC-2. (a) Surface volumes in mm³ for right (light gray) and left (dark gray) hemispheres of V1, hV4, VO-1, VO-2, PHC-1, and PHC-2 (N=16). (b) Surface volumes for hV4, VO-1, VO-2, PHC-1, and PHC-2 for RH and LH calculated as a percentage of V1 (same data as in a). Vertical bars indicate S.E.M. On average, hV4 was about half the size of V1 and visual areas VO-1 to PHC-2 were between a quarter and a third the size of V1.](image-url)
(Fig. 2.1, lefthand panels). Similar to the observations for hV4 and VO-1/2, the border shared by PHC-1 and PHC-2 was often formed by a continuous representation of UVF angles such as the one seen in the RH of subject S2 (Fig. 2.1, lefthand panel, 13 of 16 hemispheres), but was sometimes formed by UVF angles intermixed with those near the HM as seen in the LH of subject S2 (Fig. 2.2, lefthand panel, 3 of 16 hemispheres). For PHC-2, all subjects showed a consistent pattern of phase angles within the UVF progressing anterior and medial to a representation of the HM as seen in the LH of subjects S1 and S2 (Fig. 2.2, lefthand panel). A further progression to a LVF representation was found in PHC-2 for most subjects, as seen in the LH of subjects S1 and S2 (Fig. 2.2, lefthand panel, 11 of 16 hemispheres).

We identified a progression of eccentricity within PHC-1/2, with the foveal representation located on the medial fusiform gyrus. This foveal representation was typically separated from the foveal representation of VO-1 and VO-2 (12 of 16 hemispheres, e.g. RHs of subjects S1 and S2, asterisk, Fig. 2.1, righthand panel), but was found to be continuous with the fovea of VO-1 and VO-2 in some cases (4 of 16 hemispheres). The foveal representation was typically located on the anterior/inferior border of PHC-1 and PHC-2 with the peripheral representations of PHC-1 and PHC-2 bordering the presumed far peripheral representation of ventral V3 (not measured in the current experiment). Both areas exhibited a sudden transition from foveal to peripheral representations, which has previously been reported for other topographically organized higher-order visual areas (Larsson and Heeger, 2006; Swisher et al., 2007). Mean Talairach coordinates for left and right PHC-1 were -27 -54 -5 and +31 -52 -5, respectively, and for PHC-2 -28 -46 -5 and +32 -44 -5 (Table 2.1). The mean activation sizes of PHC-1 and PHC-2 were 1378 and 1642 mm³, which is 26% and 31% the size of V1; 54% and
64% the size of hV4; 120% and 143% the size of VO-1; and 95% and 113% the size of VO-2 (Table 2.2, Fig. 2.4).

In order to evaluate the strength of the stimulus-evoked signal relative to noise in PHC-1 and PHC-2, the response amplitudes were plotted as a function of temporal frequency for the polar angle and eccentricity measurements (Fig. 2.5). The temporal frequency histograms were derived for each subject and each hemisphere and then averaged across subjects to yield group data. For each subject, the response at the stimulus frequency (SF) of six cycles was several standard errors greater than the mean response across all other frequencies, demonstrating a strong link between the measured neural response and stimulus location. For the polar angle component, the average % signal changes at the SF for right and left PHC-1 were 1.70 (±.30) and 1.53 (±.35), and for right and left PHC-2 were 0.33 (±.06) and 0.32(±.09). For the eccentricity component, the average % signal changes at the SF for right and left PHC-1 were 1.20 (±.15) and 1.0 (±.2), and for right and left PHC-2 were 0.47 (±.10) and 0.30 (±.06). For both the polar angle and eccentricity components, the response at the SF (6) was significantly greater than noise (all ts(7) > 4.4, ps < .01).

Visual field representations of ventral visual areas

The visual field representations for V1, hV4, VO-1, VO-2, PHC-1 and PHC-2 were
computed by aligning the eccentricity and polar angle maps for each subject on the surface and extracting all surface nodes that had a significant phase value for both measurements. The location of each surface node with respect to eccentricity and polar angle was then plotted for each area and subject to yield an estimate of the visual field representation, as shown for the group of subjects and for each individual subject in Figure 2.6. The inner sector represents the foveal 5°, the mid-sector eccentricities between 5 and 10°, and the outer sector eccentricities between 10 and 15°. Blue dots denote data from the LH, and red dots those from the RH. All areas represented almost exclusively the contralateral visual field: 91% (±1) of nodes in area V1, 96% (±1) in hV4, 97% (±1) in VO-1, 98% (±1) in VO-2, 95% (±2) in PHC-1 and 87% (±4) in

Figure 6: Visual field representation in areas V1, hV4, VO-1, VO-2, PHC-1, and PHC-2. Vertex plots from each individual subject and group analysis (N = 8) based on polar and eccentricity maps thresholded at 1.5 s of the cycle S.E.M. variance (see Methods) obtained in the attentionotopy studies. Surface nodes that had significant phase estimates for both polar angle and eccentricity were plotted such that each point represents the corresponding preferred visual field location for a given node. Red and blue points indicate data from the RH and LH, respectively. All areas showed strong contralateral preference. hV4, VO-1, VO-2, PHC-2 and to some degree PHC-1 showed a smaller representation of the LVF relative to the UVF. hV4 and VO-1 demonstrated an almost exclusive activation of the visual field representation within 0°-7.5° eccentricity. In contrast, PHC-1 and PHC-2 represented the fovea and eccentricities ranging from 7.5° to 15° better than other eccentricities.
PHC-2 (contralateral vs. ipsilateral visual field: all ts(7) > 8.5, ps < .0001). Data were further evaluated for UVF versus LVF representations. There was a significantly greater number of nodes preferring the UVF over the LVF in hV4 (UVF: 65% ±4), VO-1 (UVF: 61% ±3), VO-2 (UVF: 72% ±4), and PHC-2 (UVF: 76% ±3; all ts(7) > 3.277, ps < .05), with a non-significant trend in PHC-1 (UVF: 62% ±6; t(7) = 1.9, p = .097). In contrast, cortical area V1 did not show such an upper field bias (UVF: 48% ±2, t(7) = -0.681, p > .518). Consistent with the cortical magnification of foveal representations, area V1 showed a relatively larger representation of eccentricities up to 7.5° (68% ±2 of nodes, t(7) = 5.97, p < .001). Areas hV4 and VO-1 also showed a strong bias towards foveal and parafoveal eccentricities up to 7.5° (hV4: 95% ±2 of nodes; VO-1: 86% ±4; both ts(7) > 5.141, ps < .001). PHC-1 and PHC-2 showed a significantly larger number of nodes preferring eccentricities ranging between 7.5° and 15° (83% ±2 of nodes in each area) as compared to eccentricities up to 7.5° (both ts(7) > 9.75, ps < .0001), suggesting that these areas have large RFs, thereby making it difficult to attain reliable estimates of detailed eccentricity maps using a traveling wave paradigm (Larsson and Heeger, 2006; Wandell et al., 2007).

Comparison of attentionotopy and retinotopic maps

In a subset of subjects (N=4), we performed an additional study that used standard retinotopic mapping with rotating wedge and expanding or contracting ring stimuli that were presented while subjects performed a luminance detection task at fixation. The same amount of data as in the attentionotopy studies were collected in these subjects. The data obtained in the retinotopic mapping studies were then qualitatively and quantitatively compared in the four subjects to address two major issues. First, we asked whether directed attention to the mapping
stimuli was a requirement in order to reveal orderly maps in anterior parts of ventral visual
cortex, because this part of cortex may not activate well under passive viewing conditions.
Second, we were concerned that the visual field representation yielded with the attentionotopy
paradigm may be distorted due to the attentional manipulation. As is evident from the
retinotopic maps in the right hemisphere of subject S3 (Fig. 2.7a), qualitatively similar visual
field maps were identified in ventral visual cortex using standard retinotopic mapping
techniques. Importantly, the area borders identified with standard retinotopy matched the
borders identified with attentionotopy. Also, individual variations of visual area representations
remained consistent between paradigms within a given subject (Fig. 2.7a, additional examples:
see Arcaro et al. 2009, Supplementary Fig. 2.6). For example, discontinuous representations of
the border between VO-2 and PHC-1 were identified in two of the eight hemispheres in the
attentionotopy studies, which were also present in the same subjects and hemispheres in the
retinotopy studies. Further, the foveal representation of PHC-1 and PHC-2 could be clearly
identified in all subjects with both mapping approaches with the same typical separation from the
foveal representation of VO-1/2 (Fig. 2.7a). Although there were significantly fewer nodes
activated in the retinotopic mapping study in PHC-1 and PHC-2 (ranging from 14-17% fewer
nodes on average, t(3) > 5.7, p < .05), indicating a main effect of attention in terms of response
enhancement, the relative representations of the visual field for both areas were almost identical
between the two paradigms (Fig. 2.7c). All four subjects had dominant representations of the
contralateral visual field in PHC-1 and PHC-2 for both retinotopy and attentionotopy datasets
(contralateral vs. ipsilateral; all ts(3) > 4.77, ps < .05; Fig. 7b) with 89% (±6) as compared to
93% (±4) in PHC-1 in the attentionotopy and retinotopy studies, respectively and with 78% (±5)
as compared to 78% (±6) in PHC-2 (both ts(3) < 1.4, ps > .05). All four subjects had
significantly greater peripheral representations between 7.5°-15° in PHC-1 and PHC-2 for both retinotopy and attentionotopy datasets (7.5°-15° vs. 0° - 7.5°; all ts(3) = 8.7, ps < .05; Fig. 2.7c). The peripheral representations of the retinotopy data did not significantly differ from the attentionotopy data in PHC-1 with 85% (±2) as compared to 83% (±3), nor in PHC-2 with 77% (±8) as compared to 78% (±4; both ts(3) < .51, ps > .05). All four subjects also had a significantly greater UVF representations in PHC-2 for both retinotopy and attentionotopy datasets (UVF vs. LVF; both ts(3) > 5.19, ps < .05; Fig. 7b) with 78% (±4) as compared to 74% (±9) for the attentionotopy and retinotopy experiments, respectively (t(3) = .27, p > .05). Together, these results suggest first, that the
visual field maps in the posterior PHC can be activated under passive viewing conditions using standard retinotopy techniques and second, that the visual field representations within the PHC areas were not distorted due to the allocation of spatial attention to the mapping stimuli.

To further evaluate the similarity of phase estimates between the attentionotopy and retinotopy data on a node-by-node basis, alignment indexes (AI) were calculated for both hemispheres in each of the four subjects (see Methods, Fig. 2.7b, Supplementary Fig. 2.6; see Arcaro et al. 2009). The AI values range from 1, which indicates perfect phase alignment between retinotopy and attentionotopy, to 0, which indicates that the values obtained in the two data sets were completely out of phase by 180°. Histograms of AIs are shown for the PHC areas from subject S3 in Figure 2.7b (also see Supplementary Fig. 2.6; see Arcaro et al. 2009). The mean index values for the RH of PHC-1 and PHC-2 were .92 (± 6) and .92 (± 8), illustrating the strong alignment between attentionotopy and retinotopy measurements in this subject (Fig. 2.7a). Mean AI values were averaged across subjects to yield group data. For polar angle phase estimates, the group AI was .96 (±.01) in the RH and LH for VO-1, .94 (±.01) in the RH and .95 (±.01) in the LH for VO-2, .93 (±.01) in the RH and .91(±.02) in the LH for PHC-1, and .91(±.01) in the RH and .91(±.01) in the LH for PHC-2. For eccentricity phase estimates, the group AI was .90 (±.01) in the RH and .88 (±.02) in the LH for VO-1, .86 (±.01) in the RH and .86 (±.01) in the LH for VO-2, .90 (±.01) in the RH and .89 (±.01) in the LH for PHC-1, and .88 (±.01) in the RH and .88 (±.02) in the LH for PHC-2. AI values were significantly above chance (see methods; polar angle: all ts(3) > 16.62, ps < .001; eccentricity: all ts(3) > 19.10, ps < .001). Additionally, the calculated correlation coefficients of each ROI were highly significant for each subject’s polar angle and eccentricity measurements (all rs > .33, ps < 10^-10; median polar r = .60, p < 10^-15; median eccentricity r = .83, p < 10^-15; see Methods), demonstrating that there
was good alignment throughout each ROI for every subject. These analyses indicate that both paradigms yielded highly consistent results for both polar angle and eccentricity measurements for individual subjects.

**Reproducibility of attentionotopy maps**

In an additional experiment, we established the reliability of the polar angle and eccentricity measurements within ventral visual cortex by re-scanning two subjects using an identical experimental paradigm (i.e. the attentionotopy study design). The resulting maps were highly reproducible within subjects, as indicated qualitatively by the similarities in characteristics of polar phase and eccentricity progressions discussed above and quantitatively by the virtually identical visual field representations in PHC-1 and PHC-2 (see Arcaro et al. 2009, Supplementary Fig. 2.7). AI indices were calculated between the two attentionotopy experiments for both polar angle and eccentricity phase estimates (see Arcaro et al. 2009, Supplementary Fig. 2.7, righthand column). Strong correlations ranging between .89 and .95 were found within PHC areas for each subject. For comparison, AI values for V1 ranged between .94 and .96 for these subjects. Together with the retinotopy experiments, these studies provide important test-retest verification for the newly described retinotopic maps in PHC-1 and PHC-2.

**2.3 Discussion**

We investigated the topographic organization of human ventral visual cortex using attentional wedge and ring tracking paradigms as well as standard phase-encoded retinotopic mapping in combination with high-resolution fMRI. Two previously not described retinotopic
areas were identified within posterior PHC and anterior to the VO-cluster, referred to as PHC-1 and PHC-2. In each subject, both PHC areas exhibited BOLD modulations specifically in phase with polar angle and eccentricity stimuli in both hemispheres. Cortex that lacks spatially specific representations would not show such specific phase-dependent modulations. When defining the borders of PHC, polar angle and eccentricity phase estimates were considered together. These areas shared a fovea and represented predominantly the contralateral visual field with a systematic progression of polar angle from the LVF to UVF in PHC-1 that was mirror-reversed in PHC-2. Both areas showed a strong bias towards peripheral visual field locations, indicative of large RFs and similar to observations in other higher-order topographic areas (Larsson and Heeger, 2006; Swisher et al., 2007). The topographic organization within ventral visual cortex and the presented framework for identifying borders was consistent across all 16 hemispheres, despite some individual variability, as has been previously noted in higher-order cortex of both human and macaque (Gattass et al., 1988; Boussaoud et al., 1991; Brewer et al., 2005; Larsson and Heeger, 2006; Kastner et al., 2007; Konen and Kastner, 2008a).

In addition to identifying two new retinotopic areas in human ventral visual cortex, we also confirmed the topographic organization of areas hV4, VO-1 and VO-2, as previously described by Wandell and colleagues (Wade et al., 2002; Brewer et al., 2005; see also Tyler et al., 2005). Consistent with previous reports of hV4, we found that while this area represented predominantly the contralateral hemifield in each hemisphere, coverage was particularly sparse at mid to far-eccentricities for the LVF (Larsson and Heeger, 2006; Hansen et al., 2007). To account for this asymmetry in V4’s UVF and LVF representations, Hansen et al. (2007) have proposed an alternative mapping scheme for this region. They propose a region labeled dorsal
V4, located adjacent to parafoveal dorsal V3 and representing the ‘missing’ part of the LVF; an interpretation that has been controversial (see Wandell et al., 2007 for discussion). Our data cannot speak to this debate, since the coverage of the acquisition volume within dorsal visual cortex was limited due to the high-resolution fMRI protocol that we used. Two areas were located anterior to, and contiguous with hV4, VO-1 and VO-2, that form together the VO-cluster. Consistent with previous studies (Brewer et al., 2005; Wandell et al., 2005) we found that both VO-areas represented predominantly the contralateral visual field with a preference for foveal and parafoveal eccentricities. The VO-areas also exhibited a preference for the UVF, consistent with an UVF ‘hypertrophy’ that has been previously observed within this part of cortex (Tyler et al. 2005).

In the current study, functional response properties of hV4, VO-1, and VO-2 were probed using a greater number of stimulus categories than in previous investigations (Brewer et al., 2005). We found no preference for objects versus face stimuli nor objects versus scrambled stimuli in hV4 in contrast to previous reports of object-selective responses in this region of cortex (Grill-Spector et al., 1998). Consistent with Brewer and colleagues (2005), we observed a preference for object relative to face stimuli in both VO areas. However, we observed no preference for objects versus scrambled images in hV4, VO-1, nor VO-2, suggesting that the two VO areas are not part of the object-selective lateral occipital complex (LOC). This region of cortex has also been shown to be involved in texture segregation and modulated by selective attention (Kastner et al., 1998, 2000, 2001; Pinsk et al., 2004). Taken together, these results suggest that the VO areas are an intermediate visual processing stage between early visual cortex processing and higher-order object-selective cortex. It should be noted that a preference for
scenes versus object and scrambled stimuli was observed in VO-2, suggesting that VO-2 may be involved in scene recognition. However, the preference for scene stimuli in VO-2 appeared to be driven by peripheral representations as no such selectivity was observed within the fovea of VO-2.

Anterior to VO-2, two new retinotopic areas, PHC-1 and PHC-2, were identified. These areas may have been missed in previous investigations due to the smaller amount of data typically acquired in retinotopic mapping studies. We acquired about 2-3 times more data and utilized a phased array coil targeting ventral cortex to obtain polar angle maps. The unusually large amount of data necessary to reveal polar angle representation in this part of cortex may be due to neurons with large RFs, as suggested by the strong bias towards peripheral representations in the PHC areas. This bias towards peripheral eccentricities is also consistent with previous studies describing a systematic representation of eccentricity across ventral visual cortex with preference for peripheral visual field locations in PHC and preference for foveal locations in lateral occipital cortex (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002). However, our and others’ (Brewer et al., 2005; Larsson and Heeger, 2006) findings of discrete foveal clusters in addition to mirror-reversing polar angle representations in ventral visual cortex are not compatible with an organizing principle based on eccentricity biases alone (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002).

Our findings do lend support to the hypothesis that visual cortex is organized at a large scale into a number of clusters that share common functional response properties (Wandell et al., 2005; Wandell et al., 2007; see Kaas and Catania, 2002 for related concepts). According to this
account, a cluster is comprised of several maps with parallel eccentricity representations that share a fovea. Within a cluster, maps can be delineated on the basis of reversals in polar angle representation. Importantly, maps that belong to a cluster are characterized by similar functional computations to mediate common perceptual processes. As summarized above, the PHC areas fulfill all of these criteria, and therefore we suggest that PHC-1 and PHC-2 form a cluster that processes object information related to processing of scene stimuli. The PHC cluster adds to a growing list of functional clusters that have been identified in visual cortex: a posterior cluster comprised of early visual areas V1-V3, the LO cluster comprised of LO-1, LO-2 and possibly hV4 (on the basis of common response properties related to shape information), the VO-cluster comprised of VO-1 and VO-2 (involved with color processing), and the MT cluster (involved with motion processing). Other clusters such as the V3A/B cluster and the posterior IPS cluster (IPS-0/1) need to be better defined in terms of their functional characteristics before determining whether they are consistent with the cluster hypothesis. Determining whether regions within a cluster share response properties can be difficult given that many of these clusters and areas are involved in multiple visual functions that we have only begun to define. For example, IPS-0/1 share a common fovea as well as common response properties with respect to motion and object selectivity, but deviate with respect to the representation of high-level object information that is present in IPS-1, but not in V7/IPS-0 (Konen and Kastner, 2008a; b). However, the cluster hypothesis provides an overall useful and straightforward framework to characterize the large-scale organization of the visual system further.

PHC-1 and PHC-2 were found to heavily overlap with the functionally defined PPA (Epstein and Kanwisher, 1998). The PPA has been shown to respond strongly to spatial layouts
such as buildings, landmarks, rooms, tabletop scenes, and even ‘scenes’ made out of LEGO blocks (Aguirre et al., 1998; Epstein and Kanwisher, 1998; Epstein et al., 1999; see Epstein, 2008 for review). The PPA has been shown to respond more strongly to contra- than to ipsilateral stimuli (MacEvoy and Epstein, 2007), consistent with our findings of visual field maps in the PHC areas that represent mainly contralateral space. Further, the PPA has been shown to respond more strongly to scene stimuli in the UVF as compared to foveal and LVF locations (Schwarzlose et al., 2008), again consistent with our findings of an UVF bias within the PHC areas.

Whatever the implications of having topographic information in ventral temporal cortex might be, the existence of spatial maps in this region of cortex complicates the traditional view of two distinct visual pathways that segregate along the dimensions of object and space representations (Ungerleider and Mishkin, 1982). At some point of neural processing, identification and location information must be integrated. One possibility is that the integration of information occurs in a common higher-order area that both areas project to, such as prefrontal cortex, as suggested by physiological studies in monkeys (Rao et al., 1997). Another possibility is that there is parallel encoding of object and location information in both pathways, suggested by the present and recent studies (e.g. Konen and Kastner, 2008a,b). Future studies will be needed to reveal the nature of this information integration within ventral temporal cortex.
3. The Visuotopic Organization of Macaque Posterior Parietal Cortex

Multiple visual areas within and adjacent to the intraparietal sulcus have been identified in posterior parietal cortex (PPC) of macaque monkeys (Pandya & Seltzer, 1982; Andersen et al., 1990; see Van Essen, 2004 for review). Visual areas within PPC have been distinguished based on their cyto- and myeloarchitecture as well as their connectivity patterns, including the ventral and dorsal lateral intraparietal areas (LIPv/d), and two cortical zones, dorsal prelunate (DP) and lateral occipital parietal (LOP), also referred to as caudal intraparietal (CIP). Identifying basic functional properties of these regions, such as topographic large-scale organization, may prove useful in further parcellating PPC into functional units, as it has been for other parts of the macaque visual system (Van Essen & Zeki, 1978; Maguire & Baizer, 1984; Desimone & Ungerleider, 1986; see Gattass et al., 2005 for review).

Physiology and functional brain imaging studies have provided some evidence in support of topographic large-scale organization within PPC. Specifically, dorsal portions of area DP have been shown to exhibit spatially specific representations of the visual field (Fize et al., 2003; Heider et al., 2005), though no systematic map of visual space has been demonstrated thus far. A topographic map of visual space has been reported within LIP with both physiology (Blatt et al., 1990; Ben Hamed et al., 2001) and more recently functional magnetic resonance imaging (fMRI; Patel et al., 2010). However, there were notable differences in the pattern of topographic organization described in these studies that remain unresolved. Furthermore, previous studies of visual topography within PPC have typically focused on one particular area without investigating the relations of topographic organization to neighboring cortical areas within PPC or dorsal extrastriate cortex. Therefore, it is unclear whether macaque PPC indeed lacks organized
representations of the visual field outside of LIP, as recently proposed (Patel et al., 2010). Here, we sought to investigate the visual topography across PPC and dorsal extrastriate cortex using fMRI and phase-encoded retinotopic mapping to clarify its large-scale organization.

Phase-encoded retinotopic mapping along the polar angle and eccentricity dimensions with fMRI has been widely used to reveal topographic organization within the human (Sereno et al., 1995; Engel et al., 1997; Schneider et al., 2004; Brewer et al., 2005; Hagler & Sereno, 2006; Larsson & Heeger, 2006; Swisher et al., 2007; Kastner et al., 2007; Konen & Kastner, 2008; Arcaro et al., 2009) and also the macaque visual system (Brewer et al., 2002; Kolster et al., 2009). Specifically, such topographic mapping enables the simultaneous investigation of visuotopic organization across a large region of cortex, thereby allowing the visuospatial map of an individual area to be anchored in the framework of the topographic organization across multiple surrounding areas. We investigated the representation of visual space across PPC and dorsal extrastriate cortex in awake macaque monkeys trained to maintain fixation for extended periods of time, and identified multiple topographically organized areas. Our results confirm the visuotopic organization within area V3a and the adjacent DP zone. Importantly, we report two new visuotopically organized areas within the caudal PPC which we refer to as CIP-1 and CIP-2 and clarify the visuotopic organization within LIP. Lastly, we compare the visuotopic organization within PPC between macaque monkeys and humans.

3.1 Materials and Methods

Subjects. Two adult male macaque monkeys (Macaca fascicularis) weighing 4 – 6 kg
participated in the study. All procedures were approved by the Princeton University Animal Care and Use Committee and conformed with National Institutes of Health guidelines for the humane care and use of laboratory animals. For more details, see attached Arcaro et al. 2011.

**Surgical and training procedures.** Each animal was surgically implanted with a plastic head bolt for restraining the head by using ceramic screws and dental acrylic. All surgical procedures were performed under strictly aseptic conditions and under general anesthesia with isoflurane (induction 2–4%, maintenance 0.5–2%) following preanesthetic medication with atropine (0.08 mg/kg, i.m.), ketamine (2–10 mg/kg, i.m.), and acepromazine (1 mg/kg, i.m.). The animals were treated postsurgically with antibiotics (e.g., Baytril, 2.5 mg/kg, i.m.) and analgesics (e.g., buprenorphine, 0.01 mg/kg, i.m.), and wound margins of skin surrounding the implant were cleaned regularly. Monkeys were placed prone in an MR-compatible primate chair in a sphinx-like position, with their heads erect and fixed in a head-holding apparatus (Pinsk et al., 2005). The animals were acclimated to the scanner environment through the use of a mock training environment. Monkeys were trained to fixate on a small dot (0.5° diameter) at the center of a display screen by using an infrared eye tracking system sampling at a 60 Hz refresh rate (Model 504, Applied Science Laboratories). The nominal accuracy of the ASL LRO model is 0.5°. By providing the animals with regular juice rewards (PHD 2000, Harvard Apparatus) while they maintained fixation within a 4° x 4° (2° to each side of the fixation point) square window and systematically increasing the frequency of their juice reward (2.5 to 1 s in 500 ms steps), the animals were trained to maintain fixation for several minutes. Further details regarding surgery and training procedures have been given by Pinsk et al. (2005).
Data acquisition. Data were acquired in both species with a 3T head-dedicated scanner (Magnetom Allegra; Siemens, Erlangen, Germany). A 12 cm transmit/receive surface coil (Model NMSC-023; Nova Medical, Wakefield, MA) was used for the scanning sessions during which functional images were acquired, and a 16 cm transmit/receive quadrature volume coil (Model NM-016; Nova Medical) was used for a scanning session, during which high-resolution anatomical images were acquired. A whole-brain structural volume was acquired with the volume coil while the animals were anesthetized with Telazol (tiletamine/zolazepam, 10 mg/kg, im) in a magnetization-prepared rapid gradient echo (MPRAGE) sequence (i.e. extra-session structural: 0.5 X 0.5 X 0.5 mm resolution; field of view (FOV) = 128 mm; 256 X 256 matrix; repetition [TR] = 2,500 ms; echo time [TE] = 4.4 ms; inversion time [TI] = 1,100 ms; flip angle = 8°; 20 acquisitions). In addition, a second whole-brain structural volume was acquired with the surface coil and the animal placed in the primate chair under anesthesia (i.e. within-session structural: MPRAGE sequence; 0.5 X 0.5 X 1.0 mm resolution; FOV =128 mm; 256 X 256 matrix; TR = 2,500 ms; TE = 4.4 ms; TI = 1,100 ms; flip angle = 8°; 1 acquisition). This second structural volume was acquired with the head in the same location as during the awake experimental sessions and served as an alignment reference for the higher-quality structural volume acquired with the volume coil. All other scan sessions, each lasting about 1.0 h, were performed with the animals awake.

For awake scanning sessions, an optimized multiecho gradient echo sequence was used (ME-EPI sequence; 1.5 X 1.5 mm in-plane resolution; 26 axial slices; 1.5 mm slice thickness, no interslice gap; FOV = 120 mm; matrix = 80 X 80; TR = 2,500 ms; TE = 26 ms; flip angle = 80°; bandwidth = 2,500 Hz per pixel). This sequence permits the acquisition of data at several echo
times, under reversed gradient readouts, thereby allowing for simultaneous estimation of the magnetic field, resulting in reduced image distortions with partial recovery of susceptibility-induced signal loss (Pinsk et al., 2008; Pinsk et al., 2009). The slice prescription covered the entire brain.

**Visual Stimuli.** *Polar angle measurements:* In order to obtain polar angle representations, visual stimuli consisted of a wedge that rotated either clockwise or counterclockwise around a central fixation point. The wedge spanned 1-15° in eccentricity with an arc length of 45° and moved at a rate of 9 deg/s. The wedge consisted of a colored checkerboard with each check’s chromaticity and luminance alternating at a flicker frequency of 4 Hz (see Swisher et al., 2007; Arcaro et al., 2009 for details). A transparent wedge within a dark foreground rotated around a central fixation. The underlying checkerboard was only visible through the transparent wedge, giving the appearance of a rotating checkerboard wedge. Each run consisted of four cycles of 40 s each, and runs alternated between clockwise and counterclockwise wedge rotation. 20 runs were collected for monkey M1 and 30 runs were collected for monkey M2, in 8 and 14 scanning sessions, respectively. For both monkeys, half of the runs were in the clockwise direction and the other half were in the counterclockwise direction.

*Eccentricity measurements:* In order to obtain eccentricity representations, visual stimuli consisted of an annulus that expanded around a central fixation point. The duty cycle of the annulus was 12.5%, that is, any given point on the screen was within the annulus for only 12.5% of the time. The annulus increased on a logarithmic scale over time in size and rate of expansion to approximately match the cortical magnification factor (Horton and Hoyt, 1991). The outer
part of the ring expanded to a maximum eccentricity of 16.875°, to ensure that the whole visual display (1-15°) was stimulated for an equal amount of time, before returning to the foveal origin. The ring consisted of a colored checkerboard with each check’s chromaticity and luminance alternating at a flicker frequency of 4 Hz (see Swisher et al., 2007; Arcaro et al., 2009 for details). A transparent annulus within a dark foreground layer expanded around a central fixation point. The underlying checkerboard was only visible through the transparent annulus, giving the appearance of an expanding checkerboard ring. 20 runs were collected for monkey M1 and 30 runs were collected for monkey M2, in 5 and 14 scanning sessions, respectively.

Data analysis. Data were analyzed using AFNI (Cox, 1996) (http://afni.nimh.nih.gov/afni/), SUMA (http://afni.nimh.nih.gov/afni/suma/), Matlab (The Mathworks Inc., Natick, MA), and FreeSurfer (Dale et al., 1999; Fischl et al., 1999) (http://surfer.nmr.mgh.harvard.edu/). Scanning runs during which the animal refused to fixate or moved its body were easily discernible in the eye traces and EPI images. Deviations several orders of magnitude greater than the mean variance were apparent in EPI volumes where the animal moved. Due to the nature of the analyses, these runs were discarded. A rigid motion-correction procedure (Cox and Jesmanowicz, 1999) was performed to a reference EPI volume that was acquired during the anesthetized structural scanning session when the animal was in the primate chair. The motion-corrected data were projected onto cortical surface reconstructions created with FreeSurfer from the extra-session structural scans that were aligned to each monkeys’ within-session structural. All voxels that fell between the gray and white matter boundaries were mapped to the surface. The units of data that were projected to the surface are referred to as nodes. Given that there is
not a one-to-one correspondence between nodes and voxels, the value of each node was calculated by taking a weighted average of all the voxels based on the spatial overlap within each node. All subsequent analysis procedures for the visuotopy datasets (e.g. Fourier analysis) were performed on the surface-mapped data, which favorably restricts analyses to data that are primarily within the gray matter, since white matter voxels do not get mapped onto the surface. Surface projections introduce a small degree of spatial smoothing to the data. Since the degree of smoothness from surface projections can vary across cortex, the data were spatially filtered using a Gaussian filter to a maximum smoothness of 2 mm FWHM (by estimating the FWHM prior to spatial filtering), ensuring uniformity across the surface and maintaining spatial specificity while increasing the signal-to-noise ratio (SNR; Chung et al., 2005). Surface-based spatial filtering has been shown to increase both sensitivity and spatial accuracy of BOLD signal sources (Jo et al., 2007; 2008). Surface size estimates were measured using SUMA tools that calculate the volume of all nodes that fall in between the white matter and pial surface layers.

Volumes acquired during the blank periods at the start and end of each run were discarded. A Fourier analysis was used to identify spatially selective surface nodes by the polar angle and eccentricity stimuli (Bandettini et al., 1993; Engel et al., 1994). For each node of the surface, the amplitude and phase—the temporal delay relative to the stimulus onset—of the harmonic at the stimulus frequency was determined by a Fourier transform of the mean time series of the node. To correctly match the phase delay of the time series of each node to the phase of the wedge/ring stimuli, and thereby localize the region of the visual field to which the underlying neurons responded best, the response phases were corrected for the hemodynamic lag (5 s). The counterclockwise runs were then reversed to match the clockwise runs and averaged
together for each node. To quantify the reliability of phase estimates across runs, the variance of a mean phase across cycles was determined for each node. A jack-knifing method in which phase estimates were calculated from n-2 cycles (eliminating one clockwise and one counterclockwise cycle per calculation for polar angle runs) across all runs was used to determine the standard error of phase estimates (see Hansen et al., 2007; Arcaro et al., 2009 for similar application). A grand mean phase estimate was calculated from the average of each of these phase estimates along with the standard error to account for variance across estimates for each node. The standard error was then converted into seconds per cycle.

Statistical maps were thresholded at a variance of ±2 s of the 40 s cycle and overlaid on cortical surface reconstructions. The pattern and significance of activation approximately compares to a statistical threshold of p < 0.01 (uncorrected for multiple comparisons, derived from the F-ratio that was calculated from the Fourier transform). When displaying phase estimates, a 20 point color scale was assigned to the polar angle datasets with each color representing 18° visual angle, and a 10 point color scale was assigned to the eccentricity data sets with each color representing 1.5° eccentricity. While activations were found in both ventral and dorsal striate and extrastriate cortex, ventral regions are outside the scope of this report, and we will focus our analysis on dorsal extrastriate cortex, i.e., brain regions located along the lunate sulcus and in PPC. Contiguous clusters of spatially selective nodes within this anatomical region that showed a systematic representation of visual space in polar or eccentricity coordinates were defined as regions of interest (ROIs). Borders between ROIs were manually identified by the primary author based on reversals in the systematic representation of visual space, particularly with respect to polar angle. Eccentricity representations were evaluated to ensure that phase
progressions were essentially orthogonal (non-parallel) to the polar angle phase progression. Prior physiology and fMRI reports were used to guide the identification of borders for previously established visuotopically organized areas. All three authors subsequently assessed the borders between ROIs independently. Surface analyses of these ROIs were performed using AFNI and MATLAB. To evaluate the progression of phase values within each visual area and across PPC, response phase was analyzed as a function of distance on the surface by drawing small line segments that run parallel to the polar angle progression and perpendicular to the eccentricity progression. Phase values within a given area were then interpolated into a common space, which allowed for inter-subject averaging. To estimate the representation of the visual field for each ROI, the polar angle phases for each surface node were binned into 20 different segments of the visual field and plotted in a polar graph as a function of percentage of the visual field coverage. To compute the representation of the visual field for each visual area as a function of polar angle, the visual field was divided into four sectors: contra- and ipsilateral, as well as upper and lower quadrants. The number of nodes within each sector was tallied and divided by the total number of nodes in each area to derive a mean representation for each subject. Data were collapsed across hemispheres and averaged across monkeys to derive a group mean average. T-tests were used to assess statistical significance.

To quantitatively compare the phase alignment between clockwise and counterclockwise polar angle datasets for each monkey, we calculated alignment indices and correlation coefficients for each visual area. The alignment index (AI) was defined as

\[
\text{Alignment\_Index} = 1 - \frac{|\Delta \phi|}{\pi}
\]
where $\Delta \phi$ is the difference between the polar angle phase for the clockwise and counterclockwise runs (see Sereno & Huang, 2006 for further details). Only nodes that had phase values for both data sets thresholded at $\pm 3$ s variance were included in the analysis. AIs were calculated for both polar angle measurements within each ROI on a node-by-node basis. The distribution of AI values within an ROI were plotted for single subjects in a histogram. AI distributions peaking at or near 1 indicate that the two data sets were in good alignment (i.e. when the polar angle at a vertex is identical in the two datasets). In contrast, for two uncorrelated datasets the distribution of AIs is a shallow linear ramp starting at a count of zero at an AI of zero and ending at a small value ($2v/n$, where $v$ is the number of vertices and $n$ is the number of bins) at an alignment of 1 (see Sereno & Huang, 2006). In order to perform statistical comparisons on the AIs, single subject mean index values were derived by averaging across all index values obtained for individual nodes within an ROI. One sample $t$-tests were conducted for each ROI between the mean index values and an index alignment value of 0.5 (representing chance). To derive a group index value, single subject mean index values were averaged within each ROI. To further evaluate the strength of alignment between both data sets for a given ROI, the correlation between phase estimates was calculated on a node-by-node basis for each subject.

To directly compare visuotopic maps in the two monkeys, standard-mesh cortical surfaces were created. Briefly, each monkey’s surface was inflated and transformed into a sphere in a manner that minimized metric distortion (Fischl et al., 1999). The individual spheres were used to create a template sphere for each hemisphere, where the curvature pattern consisted of the average pattern across both monkeys. The individual spheres were non-rigidly aligned to the
templates so that the curvature patterns of each monkey matched those of the template. To avoid interpolation of the fMRI data to match the warped spheres, the SUMA software package was used to create standard-mesh surfaces from the warped spheres using icosahedral tessellation and projection (Saad et al., 2004; Argall et al., 2006). The geometry of the resulting standard-mesh surfaces is identical to the individual monkey’s original surface geometry, but the topology is common across both monkeys. The use of standard-mesh surfaces allowed for node-to-node correspondence across surfaces of both monkeys, so that functional data mapped onto one monkey’s surface could be directly compared with data mapped on the other monkey’s surface. Datasets for polar angle and eccentricity experiments were normalized for each monkey using a Fisher’s z-score transformation. Average polar angle and eccentricity maps were derived by performing a Fourier analysis on the combined data from both monkeys. To further quantify the similarity in topography between the two monkeys, each monkey’s data were also analyzed separately on their standard mesh surfaces and AI indices were calculated for both polar angle and eccentricity between them.

Cortical surfaces containing borders of the Lewis & Van Essen macaque F99 atlas (Lewis & Van Essen, 2000a,b; Van Essen, 2002) were converted from Caret (Van Essen et al., 2001) into FreeSurfer and aligned with the standard-mesh surface of the two monkeys. Both the borders and the cortical surface areas of regions defined by the atlas were compared to the corresponding regions defined by the averaged topography data.

Eye-movement recordings. Several analyses of the eye-tracking data acquired in each monkey during the scanning sessions were performed to confirm that the animals maintained fixation for
the majority of the time during the scanning runs, and that there were no systematic differences in the eye position, in the amount of eye movement, or in the frequency of saccades, while different portions of the visual field were stimulated. In each monkey, eye positions, amounts of eye movement, and frequency of saccades were compared using repeated-measures ANOVAs to test for main effects of stimulus location on these measures. Individual comparisons between the stimulus locations were performed using matched paired t tests. Significant pairwise comparisons (p < 0.05) are reported before correction for multiple comparisons, and comparisons that remained significant after Bonferroni correction (alpha level of 0.01) are also reported. Effect sizes for significant pairwise comparisons are reported using Cohen’s $d$ (for further details, see Arcaro et al. 2009, supplemental Methods and Supplemental Fig. 8, available at www.jneurosci.org as supplemental material).

3.2 Results

The same five criteria used to delineate human visual areas were used to delineate macaque visual areas. We found consistent and distinct visuotopically organized cortical areas within striate and extrastriate cortices in both monkeys (Fig. 3.1). Several of these areas have been previously reported in monkey fMRI studies (Brewer et al., 2002; Fize et al., 2003; Kolster et al., 2009): V1, V2, V3, V3a, V4d, V4t, MT, MST, and FST. Anterior and lateral to V3a, we identified an additional visuotopic area along the dorsal prelunate gyrus, DP (Andersen et al., 1990; Heider et al., 2005). Anterior and adjacent to V3a and DP, we identified two previously not described visuotopic areas within the caudal, lateral PPC, which we refer to as CIP-1 and CIP-2. Anterior and adjacent to CIP-2, we found another visuotopic area within LIP, referred to as LIPvt. We identified two visual field maps, V4ta & PITd, along the inferior bank of the STS
We also observed significant phase activity in neighboring ventral temporal cortex; however, the topography was more variable, therefore no consistent visuotopic organization could be identified across the four hemispheres. The topographic organization of each area will be described below. The organization of the DP, CIP-1, CIP-2, and LIP will be described in greater detail since this is the first report of visual field maps for these areas.

The polar angle and eccentricity components of visuotopic maps were measured for the central 15° of the visual field using a smoothly rotating wedge stimulus and an expanding annulus stimulus, respectively, in monkeys trained to maintain fixation for

Figure 3.1: Polar angle and eccentricity maps in dorsal visual cortex for left and right hemispheres of M1. Inflated surface reconstructions of dorsal occipital and parietal cortex for M1. The left-hand panel shows the topography for the left hemisphere (LH) and the right-hand panel shows the topography for the right hemisphere (RH). (a) Polar angle maps for M1. The color code depicts the phase of the fMRI response and indicates the region of the visual field to which the surface node responds best. White lines denote area boundaries formed by phase angles at or close to the upper (dotted) or lower (dashed) vertical meridian. The gray dashed lines denote the discontinuity in the anterior border of area V3d. Asterisks indicate representations of central space. Maps were thresholded at ±2s per cycle S.E.M. variance (see Methods). (b) Eccentricity maps for M1. The color code indicates phase of the fMRI response and the region of the visual field to which the surface node responds best. (c) Schematic borders of defined topographic regions overlaid on inflated surfaces to relate the functionally defined areas and the underlying anatomy. Abbreviations: A- anterior; P- posterior; M- medial; L- lateral; RH – right hemisphere; LH – left hemisphere; ls – lunate sulcus; pos – parieto-occipital sulcus; sts – superior temporal sulcus; ips- intra-parietal sulcus.
several minutes (Pinsk et al., 2005). Bilateral activations within striate and extrastriate cortex were found in both hemispheres of both monkeys for polar angle and eccentricity mapping studies. For the polar angle measurements, activations within each hemisphere were mainly confined to the contralateral hemifield. Individual activation maps of polar angle and eccentricity are shown overlaid on inflated surface reconstructions for the left (LH) and right (RH) hemispheres for monkey M1 (Fig. 8) and monkey M2 (Fig. 9). For each surface node, the variance of the phase estimates across runs was calculated using a jack-knifing method (see Methods), and the threshold was chosen to only include data with a variance of \( \pm 2 \) s per 40 s cycle. The color of each surface node was determined by the phase of its response and indicates the region of the visual field to which the surface node was most responsive. For the polar angle component (Figs. 3.1A, 3.2A, 3.4A, 3.6A, 3.8 & see Arcaro et al. 2009, Supplementary Fig. 3.5), the upper visual field (UVF) is denoted in red-yellow, the horizontal meridian (HM) in green, and the lower visual field (LVF) in blue. Area boundaries
that are formed by reversals in polar angle phase progression at either the UVF or LVF near the vertical meridian (VM) are indicated with dotted and dashed lines, respectively. For the eccentricity measurements (Figs. 3.1B, 3.2B, 3.6B), the central space (foveal and parafoveal) is denoted in red/orange and the periphery in blue.

We found consistent and distinct visuotopically organized cortical areas within striate and extrastriate cortices in both monkeys. Several of these areas have been previously reported in monkey fMRI studies (Brewer et al., 2002; Fize et al., 2003; Kolster et al., 2009): V1, V2, V3, V3a, V4d, V4t, MT, MST, and FST. Anterior and lateral to V3a, we identified an additional visuotopic area along the dorsal prelunate gyrus, DP (Andersen et al., 1990; Heider et al., 2005). Anterior and adjacent to V3a and DP, we identified two previously not described visuotopic areas within the caudal, lateral PPC, which we refer to as CIP-1 and CIP-2. Anterior and adjacent to CIP-2, we found another visuotopic area within LIP. We also observed significant phase activity in neighboring cortex; however, the topography was more variable and therefore no consistent visuotopic organization could be identified across the four hemispheres. Below, we provide a brief description of the previously reported areas and a more detailed one of the newly found areas.

Analysis of eye position indicated that both monkeys maintained gaze within the specified fixation window during both polar angle and eccentricity mapping, and that there were no significant shifts in gaze with the stimulus position during the experiments. Furthermore, analyses of eye movements and saccade frequency indicated that neither monkey had a tendency
to make significantly more eye movements for any particular stimulus position (See Arcaro et al. 2009 Supplementary Methods & Supplementary Fig. 3.1 for further details).

Areas V1d, V2d, V3d: In agreement with previous reports (Daniel & Whitteridge, 1961; Zeki, 1969; Van Essen et al., 1984; Brewer et al., 2002; Fize et al., 2003), visual areas V1, V2, and V3 were identified in each hemisphere of both monkeys by a phase progression starting within the calcarine sulcus from a HM representation to a VM representation (Figs. 3.1A & 3.2A; blue color-coded phase, dashed line) that forms the border to area V2, and then reversing back to a HM that corresponds to the border of V2 and V3 (Figs. 3.1A & 3.2A; green, boundary not drawn). Within dorsal extrastriate cortex, a phase progression was identified from the HM border of V2d/V3d to a LVM representation (Figs. 3.1A & 3.2A, blue color-coded phase, dashed line) corresponding to the anterior border of V3d. In two hemispheres, the anterior LVM border of V3d was discontinuous within the lunate sulcus with a representation near the HM in between LVM representations, as seen in the LH of M1 (Fig. 3.1A; left-hand column), but continuous in the other hemispheres as seen in the RH of M1 (Fig. 3.1A; right-hand column). These results are in agreement with previous physiology studies that have reported two variants of the anterior V3d border, one forming a continuous representation of the LVM, and the other forming a discontinuous representation of the LVM with HM representations intermixed (see Figs. 5 and 22 in Gattass et al., 1988 for examples of the two variants). All three areas share a representation of central space within the anterior extent of the calcarine sulcus with representations of the periphery extending both dorsally and ventrally approximately perpendicular to the polar angle phase progressions (Figs. 3.1B & 3.2B).
Areas V3a and DP: A representation of the contralateral visual field including both the LVF and UVF was identified within the lunate sulcus and parieto-occipital sulcus (POS) of each hemisphere, consistent with known topography of area V3a (Van Essen & Zeki, 1978; Gattass et al., 1988; Brewer et al. 2002; Fize et al., 2003). The posterior, lateral border of V3a was identified by a LVF representation within the dorsal, anterior bank of the lunate sulcus and along the cortex separating the lunate sulcus from the POS (Figs. 3.1A & 3.2A; blue color-coded phase, dashed line). In all hemispheres, the posterior portion of the LVF representation was continuous with the LVM border of V3d, but separated from the V3d border, as it extended in an
anterior direction to the prelunate gyrus. A polar angle phase progression of contralateral space was identified extending from this LVF representation in a caudal/lateral – rostral/medial direction to an UVF representation within the POS (Figs. 3.1A & 3.2A; red color-coded phase, dotted line). A representation of the central space was found within the prelunate gyrus, anterior and lateral to portions of cortex that split the lunate sulcus and POS (Figs. 3.1B & 3.2B; asterisk). The peripheral representations of the eccentricity map extended ventrally into both the posterior and anterior POS (Figs. 3.1B & 3.2B). The anatomical extent of V3a was consistent between hemispheres and monkeys as is shown on the surface (Figs. 8C & 9C) as well as within the volume (Fig. 3.3 & see Arcaro et al. 2009, Supplementary Figs. 3.2 & 3.3). The mean surface area of V3a was 45.6 ±3.0 mm². The borders for V3a, in Horsley Clarke stereotaxic coordinates, extended from -6.0:-12.5 (A-P), +19.5:+25.5 (I-S), +7.0:+16.0 (M-L ) (Table 3.1).

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<th>Table 1. Range of Horsley Clarke coordinates for right and left hemispheres of V3a, DP, CIP-1, CIP-2, and LIPmt</th>
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A LVF representation of contralateral space was identified anterior to V3a along the dorsal portion of the prelunate gyrus in each hemisphere, which we tentatively label area DP (May & Andersen, 1986; Gattass et al., 1988; Fize et al., 2003; Heider et al., 2005; but also see
Maguire & Baizer, 1984). A representation of the HM was identified within the POS, adjacent and medial to this LVF representation with an UVF representation extending into area V3a located further medially within the POS (Figs. 3.1A & 3.2A). This region was largely encompassed by a representation of central space abutting representations of central space within V3a, but also included cortex along the prelunate gyrus, located anterior and medial to the central space, that appeared to be distinguished from the topography of V3a (Figs. 3.1B & 3.2B). The anterior portion of V3a roughly encompassed the posterior half of the central space and the posterior portion of DP encompasses the anterior half of the central space. No clear eccentricity progression was apparent, though consistent representations of the periphery were observed in this region anterior and medial to the central space (e.g. Fig. 3.2B; LH of M2, left-hand column). The anatomical extent of DP was consistent between hemispheres and monkeys as is shown on the surface (Figs. 3.1C & 3.2C) as well as within the volume (Fig. 3.3 & see Arcaro et al. 2009, Supplementary Figs. 3.2 & 3.2). The mean surface area of DP was 35.1 ± 3.0 mm². The borders for DP extended from -6.5:-10.5 (A-P), +22.0:+28.0 (I-S), +6.0:+14.0 (M-L) (Table 3.1). The mean surface volume estimates (measured between pial and white matter) for DP was 35.1 ± 3.0 mm³ (Table 3.2).

To further investigate the topographic organization of V3a, the polar angle phase progression was quantified and evaluated. Small line segments were successively drawn parallel to the polar angle progression and perpendicular to the eccentricity progression (see Methods) from the posterior border of V3a to the shared anterior border, as indicated by the schematic lines in Figure 4A. As shown in Figure 4B, the polar angle phase values from these line segments were plotted as a function of distance (in mm) from the rostral border of V3a. The blue
dots indicate the phase values for individual nodes located along the line segments, and the red line indicates the average phase values as a function of the distance on the surface. Polar angle phase progressions between area borders for individual monkeys were interpolated into a common space, which allowed for group averaging (Fig. 3.4C). As seen in the LH of M1 and M2 (Fig. 3.4B), as well as in the group polar phase plot (Fig. 3.4C), the posterior and anterior borders of V3a corresponded to the peaks of phase angles near the LVF and UVF, respectively, with a smooth progression of phase values in-between.

**Areas CIP-1 and CIP-2:** Anterior to area V3A, two polar angle phase representations of contralateral space were found in each hemisphere, spanning across the POS, posterior
portions of the intraparietal sulcus (IPS), and posterior portions of the inferior parietal gyrus (at the junction of the prelunate gyrus and the inferior parietal gyrus), which we refer to as CIP-1 & CIP-2. In each hemisphere, CIP-1 was defined by a polar angle phase progression extending from the UVF representation of V3a / DP (red color-coded phase / dotted line) anterior to a phase reversal in posterior IPS (Figs. 3.1A & 3.2A). In two of the four hemispheres, a small strip of LVF representation (blue color-coded phase, dashed) within a HM representation defined the phase reversal as seen in the RH of M2 (Fig. 3.2A). In the other two hemispheres, the phase progression reversed within a HM representation (also indicated with dashed line). In all hemispheres, CIP-2 was defined by polar angle phase progressions extending further anterior to an UVF representation (red color-coded phase, dotted line) within the posterior portion of the IPS (Figs. 3.1A & 3.2A). The UVF representation spanned across the inferior parietal gyrus medially and into the fundus of the IPS. This region of cortex within the lateral bank of caudal IPS likely corresponds to a region of cortex that has been previously referred to as cIPS (Sakata et al., 1998), LOP (Lewis & Van Essen, 2000a,b), CIP (Taira et al., 2000), CIPS (Tsao et al. 2003), and pLIP (Kagan et al., 2010). In the RH hemisphere of M1, the UVF representation of CIP-1 appeared fragmented from medial portions of the UVF representation of V3a (Fig. 3.1A), though the remaining polar angle phase progression was consistent with the other hemispheres. The mirror reversal in phase angle representations within CIP-1 and CIP-2 is further illustrated by the pattern of phase progressions (Fig. 3.4).

A representation of central space was identified anterior to that of V3a, and overlapped with lateral portions of CIP-1 and CIP-2 along the lateral IPS and onto the inferior parietal lobule (Figs. 3.1B & 3.2B; asterisk). The central space representations of CIP-1/2 appeared continuous
with the central space representations of V3a in two hemispheres as seen in the RH of M1 (Fig. 3.1B), but were clearly separate in the LH of M2 (Fig. 3.2B). The eccentricity maps lacked detail in this region of cortex. In M1, representations of the periphery extended medially into the fundus of the parieto-occipital confluence and IPS (Fig. 3.1B). However, eccentricity representations were mostly central space and parafoveal in M2 (Fig. 3.1B). The anatomical extent of CIP-1 and CIP-2 was consistent between hemispheres and monkeys, as is shown on the surface (Figs. 3.1C & 93.2) as well as within the volume (Fig. 3.3 & see Arcaro et al. 2009, Supplementary Figs. 3.2 & 3.3). The mean surface area of CIP-1 and CIP-2 were 32.1 ±4.8 mm² and 34.2 ±4.5 mm² respectively (Table 3.2). The borders for CIP-1 extended from -3.5:-9.5 (A-P), +20.0:+28.5 (I-S), +5.5:+10.0 (M-L) and for CIP-2 from -1.0:-7.5 (A-P), +20.0:+28.5 (I-S), +5.5:+8.5 (M-L) (Table 3.1).

*Area LIP* vt: A representation of the contralateral visual field was observed within the lateral portion of the IPS anterior to CIP-2 in all four hemispheres, referred to as visuotopic LIP, or LIP vt. A polar angle phase progression extended in a caudal-rostral direction from the UVF representation shared by CIP-2 to a LVF representation that spanned across the lateral bank and fundus of the IPS (Figs. 3.1A & 3.2A). In agreement with prior reports, this phase progression within lateral IPS (Blatt et al., 1990; Ben Hamed et al., 2001) encompassed both ventral and dorsal portions of LIP with the UVF located slightly more lateral to the LVF. The mirror reversal in phase angle representations within LIP vt is further illustrated by the pattern of phase progressions (Fig. 3.4).
In all four hemispheres, a representation of central space was identified anterior to CIP-1 and CIP-2 along the lateral bank of the IPS (Figs. 3.1B & 3.2B; asterisk). The central space appeared continuous with the representations of central space within dorsolateral portions of CIP in two hemispheres, as seen in the RH of M1 (Fig. 3.1B), but was separate in the other two hemispheres as seen in the LH of M1 (Fig. 3.1B). In agreement with prior reports (Blatt et al., 1990; Ben Hamed et al., 2001), no clear progression of eccentricity was observed, though peripheral representations were generally observed ventromedially, along the fundus of the IPS, as seen in the RH and LH of M1 (Fig. 3.1B). Aside from a dorsolateral-central and ventromedial Peripheral distinction, the eccentricity maps within this region of cortex were quite coarse. The anatomical extent of LIP<sub>vt</sub> was consistent between hemispheres and monkeys as is shown on the surface (Figs. 3.1C & 3.2C) as well as within the volume (Fig. 3.3 & see Arcaro et al. 2009, Supplementary Figs. 3.2 & 3.3). The mean surface area of LIP<sub>vt</sub> was 38.6 ±4.6 mm<sup>2</sup>. The borders for LIP<sub>vt</sub> extended from +1.5:-5.0 (A-P), +22.0:+29.0 (I-S), +6.0:+13.0 (M-L) (Table 3.1).

To evaluate the strength of the stimulus-evoked signal relative to noise in LIP<sub>vt</sub>, as well as V3a, DP, CIP-1 and CIP-2, response amplitudes were calculated as a function of temporal frequency for the polar angle and eccentricity measurements. For each monkey, the response at the stimulus frequency (SF) of four cycles was at least 2 standard errors (SEs) greater than the mean response across all other frequencies, demonstrating a strong link between the measured neural response and stimulus location. Temporal frequency histograms were derived for each monkey and each hemisphere and then averaged to yield group data. For both the polar angle and eccentricity data, the response at the SF (4 cycles) was significantly greater than noise for V3a, DP, CIP-1, CIP-2, and LIP<sub>vt</sub> (Table 3.3; for polar angle, all t values > 4.30, p values < 0.05; for
eccentricity, all t values $> 3.40$, $p$ values $< 0.05$). In a complimentary analysis, the time series of fMRI signals within line segments from the polar angle phase progression analysis corresponding to the UVF and LVF reversal points were averaged to derive a mean time series for each border between visuotopic areas in PPC. Consistent with the power analysis, the stimulus-evoked signal in V3a, DP, CIP-1, CIP-2, and LIPvt was apparent in the time series, as demonstrated in monkey M1 (see Arcaro et al. 2009, Supplementary Figure 3.4A). The phase offsets between UVF and LVF time series were estimated by calculating the correlations between the two time series across 10 timepoint offsets for each ROI and measuring the distance between the original time series and the offset time series with the highest correlation. The time series between UVF and LVF borders were out of phase with each other on average by $17 \pm 0.5s$ for M1 and $17.5 \pm 0.79s$ for M2. To evaluate the relation of phase between UVF and LVF borders with polar angle phase estimates, the time series were averaged between monkeys and collapsed across cycles. The modulation in fMRI signal for each area corresponded to the estimated phases from the Fourier analysis (see Arcaro et al. 2009, Supplementary Figure 3.4B). The cycles of UVF borders (V3a/CIP-1 & CIP-2/LIPvt) were in phase with each other and $17.5s$ out of phase with the cycle of LVF anterior border of LIPvt. The cycle of the LVF border between CIP-1 and CIP-2 was $5s$ out of phase from the cycle of the anterior LVF border of LIPvt, consistent with the phase progression analysis that demonstrated the phase progression reversal point to be closer to the HM.

Area 7a: Along the inferior parietal gyrus, lateral and adjacent to the central space representations of CIP-1, CIP-2, and LIPvt, a representation of the contralateral LVF was evident in all hemispheres, though no clear topographic organization could be identified beyond these
representations (Figs. 3.1 & 3.2). This region of cortex likely corresponds to area 7a (Andersen et al., 1990). This part of cortex appears to have mainly peripheral representations, but also overlaps with central space regions shared by CIP-1 and CIP-2 (Figs. 8B & 9B). Notably, Heider and colleagues (2005) have found coarse retinotopic organization within area 7a using optical imaging techniques. However, the specific details of the topographic organization appeared to vary from day-to-day. Though our results suggest the existence of some spatial topography within this region of cortex, no clearly organized map of the visual field could be identified; consistent with the interpretation that area 7a forgoes a static retinotopic organization for a spatial topography capable of adapting to alternating environments (Heider et al. 2005).

**Visual field representations**

As seen in Table 3.3, areas V3a, DP, CIP-1, CIP-2, and LIP_vt represented almost exclusively the contralateral visual field (contralateral vs ipsilateral visual field: all t(3) values > 25, p values < 0.0001). For comparison, 97 ±1% of nodes represented contralateral visual space in area V1. The strong laterality is further demonstrated in the polar plots of V1, V3a, DP, CIP-1,
CIP-2, and LIP_{vt} (Fig. 3.5). As is evident in the polar plots as well as the polar angle maps, V3a and LIP_{vt} contained roughly equivalent representations of the upper and lower quadrants of the contralateral visual space (Table 3.3). The caudal IPS areas, CIP-1/2, contained a larger representation of the upper quadrant. Conversely, area DP contained a larger representation of the lower quadrant. For comparison, 47 ±1% of nodes represented the upper quadrant and 50 ±2% of nodes represented the lower quadrant in V1. Due to the limited number of samples (n = 4), more data will be necessary to conclusively assume any asymmetries in visual field for the CIP areas or DP.

**Reproducibility of polar angle phase maps**

To further evaluate the consistency and reproducibility of the topography, polar angle phase estimates were determined for clockwise and counterclockwise runs separately. The resulting phase maps were highly consistent between clockwise and counterclockwise runs, as indicated qualitatively by the similarities in characteristics of polar angle phase progressions described above (see Arcaro et al. 2009, Supplementary Fig. 3.5). To quantify the similarity of phase estimates between clockwise and counterclockwise data on a node-by-node basis, alignment indices (AI) were calculated for both hemispheres in both monkeys (see Methods). The AI values range from 0, which indicates that the values obtained in the two data sets were completely out of phase by 180°, to 1, which indicates perfect phase alignment. Mean AI values were averaged across monkeys for V3a, DP, CIP-1, CIP-2, and LIP_{vt} (Table 3.4). In comparison, AI values for V1 ranged between 0.97 and 0.92. Histograms of mean AIs are shown for V1, V3a, DP, CIP-1, CIP-2, and LIP_{vt} (see Arcaro et al. 2009, Supplementary Fig. 3.6). Additionally, the calculated correlation coefficients of each ROI were significant for each monkey’s polar phase.
measurements (all $r$ values $> 0.67$, all $p$ values $< 10^{-10}$ uncorrected; median $r = 0.78$), demonstrating that there was good alignment throughout each ROI for each monkey. These analyses provide a quantitative measure for the consistency of the topographic organization across runs regardless of the direction of stimulus rotation.

**Group average map**

To evaluate the consistency of the large-scale topographic organization across the individual animals, polar angle and eccentricity data from both monkeys were mapped onto a standard-mesh surface (see Methods), and average topography maps were calculated for each hemisphere. The topographic organization throughout V3a, DP, CIP-1, CIP-2, and LIPvn was remarkably similar in visual field representation as compared to that seen in individual monkeys (Figs. 3.1, 3.2, 3.5 & 3.6A/B). Though the sample size is limited, this consistency across all 4 hemispheres of the 2 monkeys suggests that the organization is not much influenced by inter-individual
variability in the higher – order areas in the macaque brain, which is in contrast to the known individual variability of human PPC (Silver et al., 2005; Schluppeck et al., 2005; Swisher et al., 2007).

To further evaluate the similarity of phase estimates between the data sets of the two monkeys on a node-by-node basis, AI values were calculated between M1 and M2. Histograms of mean polar angle AIs are shown for V1, V3a, DP, CIP-1, CIP-2, and LIPvt (see Arcaro et al. 2009, Supplementary Fig. 3.7A). The mean AI values for polar angle are listed in Table 3.4. Additionally, the calculated correlation coefficients of each ROI were significant for each monkey’s polar phase measurements (all $r$ values $> 0.51$, all $p$ values $< 10^{-10}$ uncorrected; median $r = 0.64$), indicating that there was good alignment throughout each ROI between monkey datasets. This analysis provides quantitative measures for the consistency of the topographic organization between individual monkeys.

The mean AI values for eccentricity are listed in Table 4. Histograms of mean eccentricity AIs are shown for V1, V3a, DP, CIP-1, CIP-2, and LIPvt (see Arcaro et al. 2009 Supplementary Fig. 3.7B). The calculated correlation coefficients of each ROI, though smaller than those for the polar angle data, were significant for each monkey’s eccentricity phase measurements (all $r$ values $> 0.28$, all $p$ values $< 10^{-5}$ uncorrected; median $r = 0.37$). For comparison, AI values were also calculated for polar angle (RH 0.93, $r = 0.72$, $p < 10^{-10}$ uncorrected; LH 0.92, $r = 0.65$, $p < 10^{-10}$ uncorrected) and eccentricity data (RH 0.92, $r = 0.84$, $p < 10^{-10}$ uncorrected; LH 0.90, $r = 0.74$, $p < 10^{-10}$ uncorrected) for V1.
**Comparison to anatomical parcellation of PPC**

To compare our results to an anatomical and histological parcellation of PPC, area borders (Lewis & Van Essen, 2000a,b) from the F99 macaque atlas (F99; Van Essen, 2002) were mapped onto the standard-mesh surface and compared to the boundaries determined from the average topography data of V3a, DP, CIP-1, CIP-2, and LIPvt (see Methods). Overall, there was good agreement between the atlas and topography data, particularly for early visual areas V1, V2, and V3 as well as V3a. However, there were a few notable differences between the functional mapping and the atlas data (Fig. 3.6C). Visuotopically - defined DP overlapped with posterior portions of the F99 - defined DP, but also included anterior portions of the F99 - defined V3a. There was no direct correspondence of CIP-1 and CIP-2 to individual areas in the atlas. Both areas fell largely within area LOP, thereby subdividing area LOP into posterior and anterior portions, though CIP-1 also overlapped with anterior portions of the F99 - defined V3a. Though CIP-2 did not overlap with F99 - defined LIP, CIP-2 may also overlap with other anatomical and functional definitions of LIP (Andersen et al., 1990; Blatt et al., 1990).

Visuotopically - defined LIPvt overlapped with both LIPd and LIPv of the atlas with representations of central space falling largely within LIPd, and more peripheral representations falling within LIPv. In both hemispheres, visuotopically - defined LIPvt comprised only the posterior half of LIP defined by the atlas. Even though the comparison to anatomically and histologically-defined areas and zones of an atlas relative to functional topography in individual animals can only reveal approximate correspondences, the comparison of our data to the F99 parcellation scheme may prove useful for investigators performing recordings in these regions, taking the atlas as a guide for electrode placement.
Comparison to functional organization of human PPC

Recent fMRI studies including from our laboratory and others have identified several visuotopically-organized areas within dorsal visual cortex extending into the posterior parietal cortex in humans using a variety of different mapping methods including phase-encoded retinotopic mapping similar to that used here (Sereno et al., 2001; Silver et al., 2005; Schluppeck et al., 2005; Swisher et al., 2007; Konen & Kastner, 2008; see Silver & Kastner, 2009 for review). In Figure 3.7, we compare the topographic organization of PPC in the macaque and human based on polar angle (Konen & Kastner, 2008) and representations of central space (Konen & Kastner 2008, unpublished observations; also see Swisher et al., 2007). In both species, polar angle and eccentricity phase progressions were apparent throughout the lunate sulcus and into PPC. As has been noted previously, the topographic organization of V3a in the macaque is similar to area V3a in the human (Van Essen et al., 2001; Brewer et al., 2002; Fize et al., 2003; Tsao et al., 2003). In both species, there is a posterior-anterior polar angle phase progression from LVM to UVM representations with a representation of central space on its lateral border. The topographic organization observed for DP appears similar to the topography of human area V3b. In both species, there is a posterior-anterior polar angle phase progression from LVM to UVM.
representations with a representation of the central space on its medial border shared with V3a. The topographic organization and location in relation to surrounding topographic regions of CIP-1 and CIP-2 in the macaque is similar to areas V7 (IPS-0) and IPS-1 in the human. In both species, there is a posterior - anterior polar angle phase progression starting and ending with an UVF representation. However, in the human, the border of IPS-0 and IPS-1 is defined by a reversal in polar phase in the LVF, whereas in the monkey, the border between CIP-1 and CIP-2 is largely within the HM (though a sparse LVF representation was identified along the border in two of four hemispheres). For both monkey and human topographies, the representations of central space are located on the lateral border, with more peripheral representations located medially. LIP\textsubscript{vt} in the macaque appears similar to IPS-2 in the human. In both species, there is a posterior - anterior polar angle phase progression from UVM to LVM representations with a representation of central space on the lateral border.

Topographic organization within the IPS in humans consists of additional areas, IPS-3/4/5, extending further anterior. The IPS also extends anterior from LIP\textsubscript{vt} in the macaque. However, consistent topographic organization was not identified beyond LIP\textsubscript{vt} in all hemispheres. It is important to note that our comparison of the topographic organization of the dorsal pathway in humans and monkeys is not aimed at establishing homology between areas, but instead, it is aimed at revealing similarities and differences in large-scale brain topography that may aid future investigations with a simple starting point to find regions that have analogous functions or regions that show similar functional organization.
3.3 Discussion

We investigated the topographic organization of dorsal extrastriate cortex and PPC using fMRI and phase-encoded retinotopic mapping in monkeys trained to maintain fixation. By considering both the polar angle and eccentricity phase estimates, we identified four visuotopically-organized areas representing contralateral visual space within PPC. A representation of the visual field adjacent and lateral to area V3a was found within dorsal portions of the prelunate gyrus, referred to as DP. Adjacent and anterior to V3a within the caudal, lateral portions of the IPS, two previously not described visuotopic areas were found, referred to as CIP-1 and CIP-2. Adjacent and anterior to CIP-2, we identified a representation of the visual field within the lateral bank of the IPS, referred to as LIP_vt. The visuotopic organization within dorsal extrastriate cortex and PPC and the presented framework for outlining area borders was highly consistent in all four hemispheres.

Macaque dorsal extrastriate cortex and PPC have been subdivided based on results from anatomy and physiology studies, and several different parcellation schemes have been derived (Pandya & Seltzer, 1982; Seltzer & Pandya, 1986; Colby et al., 1998; Andersen et al., 1990; Felleman & Van Essen, 1991; Preuss & Goldman-Rakic, 1991; Lewis & Van Essen, 2000a,b). We compared our data to the areas delineated in the F99 macaque atlas (Lewis & Van Essen, 2000a,b; Van Essen, 2002) since it proposes subregions within caudal IPS, dorsal prelunate, and the lateral IPS, and has been applied to both physiology (Stoet & Snyder, 2004; Huk & Shadlen, 2005; Janssen et al., 2008; Chen et al., 2010) and fMRI studies (Tsao et al., 2003; Denys et al., 2004; Durand et al., 2007; Kagan et al., 2010; Patel et al., 2010).
Within dorsal portions of the prelunate gyrus, we identified a visual field map, DP, that predominantly contained representations of the LVF with adjacent cortex within POS representing the horizontal and upper vertical meridians. Our results are consistent with physiology recordings that have found the receptive fields within DP to be concentrated within the contralateral LVF (Andersen et al., 1990), and with fMRI studies that have found representations of the LVF within the dorsal prelunate gyrus (Fize et al., 2003). Using optical imaging, Heider and colleagues (2005) found representations of both the UVF and LVF within DP, though the topography varied between monkeys with no apparent systematic progression of visual field locations. Thus, our results extend these prior findings by identifying a systematic visual field map within the dorsal prelunate gyrus and its relation to neighboring topographic cortex.

Within the caudal PPC, we found, to our knowledge for the first time, spatial topography suggesting that this region of cortex may be functionally subdivided into two separate areas, referred to as CIP-1 and CIP-2. CIP-1/2 were located within caudal PPC, including anterior portions of the POS and lateral IPS. CIP-2 extended into lateral portions of posterior IPS that may correspond to cortex defined as part of LIP (Blatt et al., 1990; Kagan et al., 2010). The posterior border of CIP-1 abutted the borders of V3a and DP with the anterior border of CIP-2 extending into the lateral bank of the IPS. This region of cortex has been shown to represent 3-dimensional (3D) shape and texture information (see Katsuyama et al., 2010 for review). Future investigations are required to define a functional role of topographic organization in the processing of 3D stimulus features, and to characterize whether the response properties of CIP-2
more closely reflect previously defined CIP (Sakata et al., 1998; Taira et al., 2000) relative to LIP (Bushnell et al., 1981; Gnadt & Andersen, 1988; Shadlen & Newsome, 2001).

Within the lateral IPS, we identified a visual field map, LIP\textsubscript{vt}, that shared its posterior border with the anterior border of CIP-2 and encompassed both dorsal and ventral portions of lateral IPS. Based on results from previous physiology studies, the topographic organization within LIP has been rather unclear (Blatt et al., 1990; Platt & Glimcher, 1998; Ben Hamed et al., 2001). Blatt and colleagues (1990) reported a posterior-anterior gradient from LVF to UVF representations of the contralateral visual field, whereas Ben Hamed and colleagues (2001) reported the opposite pattern, a posterior-anterior gradient from UVF to LVF representations. Both studies agreed regarding a central space representation within LIPd. However, a third report was unable to find any systematic organization of contralateral space within LIP (Platt & Glimcher, 1998). The polar angle phase progression of LIP\textsubscript{vt} appears in agreement with the topographic organization suggested by Ben Hamed and colleagues (2001), as

![Figure 3.8: Comparison of LIP topography based on physiology and fMRI data. (top) Schema of LIP topography adapted from Ben Hamed et al. (Fig 8C in 2001). The fundus of the IPS and crown of the inferior parietal lobule are denoted by black lines. A representation of the upper visual field was found in posterior LIP, and the lower visual field representation was found anterior. A representation of central space was identified on the lateral border of LIP. The schema of LIP topography defined by physiology data overlaid upon the topography of LIP\textsubscript{vt} from the LH of monkey M1 (middle) and the group map (bottom) revealed by fMRI. There is strong correspondence of LIP topography between the physiology and fMRI data with the upper visual field progressing anterior and medial to a lower visual field representation, and a representation of central space on the lateral border (white asterisk).]
shown in Figure 3.8, where we adapted the scheme of LIP topography based on their single-unit data (Fig. 8C in Ben Hamed et al., 2001) and projected it onto the LH of M1. However, the polar angle phase progression of CIP-2 just posterior to LIPvt is in good agreement with the topographic organization and anatomical coordinates reported by Blatt and colleagues (1990), suggesting that the discrepancies between these two physiology studies are due to differences in the recording site location and the existence of multiple organized visuotopic maps within lateral IPS. Thus, our data is in good agreement with physiology and offers an interpretation regarding discrepancies observed in previous studies.

Our results of visuotopic organization within LIP partially confirm, but more importantly extend recent findings of topographic organization within PPC using fMRI (Patel et al., 2010; see also Fize et al., 2003). Using a covert attention task on visual stimuli presented at only few different polar angle and eccentricity locations within the visual field, a topographic representation of the contralateral hemifield was found that appeared to be confined to LIPv (Patel et al., 2010). It was concluded that PPC contains a single topographic representation that can only be revealed in a complex cognitive task, suggesting a specific role of LIPv in higher cognition. While our results concur with the posterior-anterior progression of an UVF to LVF representation, there are several notable differences between our findings and those of Patel and colleagues (2010). First and foremost, we demonstrate a systematic and continuous progression of phase angle representations within LIP, which is an important criterion in establishing a visual field map (see Wandell et al., 2007). This requires identifying the most effective visual field position for each location within a map and can be best achieved with a continuous mapping approach such as phase-encoded mapping, rather than by stimulating a few discrete locations.
within the visual field. It is also noteworthy that the visuotopic map within LIP was revealed using standard mapping procedures under passive viewing conditions without requirement of a cognitive task. Second, the visuotopic map within LIP is not isolated, but is embedded in a rich topographic organization of PPC with several visuotopically organized areas adjacent to LIP, which were differentiated on the basis of their systematic representation of visual space and reversals in polar angle phase progression at or near the vertical meridians. Third, given the posterior-anterior direction of polar angle phase progression, the dorsolateral representation of central space that was identified in our and prior physiology studies appears to be a better candidate for LIP than an anterior fovea reported within LIPv (Patel et al., 2010). Throughout the visual system, the progressions of polar angle and eccentricity are typically represented orthogonal (and not parallel) to each other. It is possible that the anterior representation of central space that was also found in the present study corresponds to additional topographic representations within anterior LIPv.

A spatial map of saccade trajectories was recently found within anatomically - defined LIPv (Savaki et al., 2010). It is not entirely clear how this map of oculomotor space relates to the visuotopic map identified in our data and prior studies due to the differences in criteria used for parcellating LIPd and LIPv (Medalla & Barbas, 2006). However, the apparent close proximity of the oculomotor map to the anterior intraparietal area (AIP; see Figs. 3b, 9 & 10a in Savaki et al., 2010) suggests that the oculomotor map lies anterior to the visuotopic map observed within the posterior half of the anatomical extent of LIP. Consistent with this interpretation, Kagan and colleagues (2010) reported stronger BOLD modulation for saccades towards the contralateral visual field within an anterior portion of LIP (aLIP), which appears to be anterior to LIP (see
Interestingly, Savaki and colleagues (2010) reported representations for small saccade trajectories within LIPv, which may correspond to the representations of central visual space observed in the current data anterior to LIPv, but within the anatomical extent of LIP. The findings of oculomotor and visuotopic maps, possibly in different parts of LIP, suggest the existence of topographic organization along multiple functional reference frames in macaque PPC.

Several visuotopically-organized areas within dorsal extrastriate cortex and PPC have recently been reported using fMRI in humans (Sereno et al., 2001; Silver et al., 2005; Schluppeck et al., 2005; Swisher et al., 2007; Konen & Kastner, 2008; reviewed in Silver & Kastner, 2009). In our comparison of macaque and human large-scale PPC topography, several parallels in polar angle and eccentricity representations were identified based on the topography within individual areas and their relation to the surrounding large-scale topography. In addition to the previously noted correspondence of V3a topography, macaque CIP-1 and human IPS-0, CIP-2 and IPS-1, as well as LIPv and IPS-2 showed striking similarities in topographic organization. Similarities in large-scale topographic organization between species do not necessitate or imply homology, nor do they preclude functional dissociations between species. Rather, large-scale cortical organization can be used to systematically investigate functional properties between species. Our results provide a framework for detailed comparisons of parietal cortical areas between humans and monkeys that should prove useful in relating the functional similarities and dissociations between species.
4 The Large-scale Organization of Visual Field Maps in Humans and Macaques

The visual field map is a fundamental organizational principle for the processing of sensory information across visual cortex. Much of the visual system appears to contain visual field maps. Early electrophysiological recordings in monkeys and cats identified several visual field maps in posterior occipital cortex (Daniel and Whitteridge 1961; Zeki 1969; Allman and Kaas 1971; Van Essen et al. 1984). As shown in the chapters 2 and 3, many additional visual maps have been identified throughout the visual system in humans and macaques using fMRI, including lateral occipital, posterior parietal, and ventral temporal cortices (DeYoe et al. 1996; Tootell et al. 1997; Silver et al. 2005; Schluppeck et al. 2005; Swisher et al. 2007; Konen & Kastner 2008; Larsson and Heeger 2006; Amano et al. 2009; Hagler and Sereno 2006; Kastner et al. 2007; Brewer et al. 2005; Hansen et al. 2007; Arcaro et al. 2009; Kolster et al. 2009; Kolster et al. 2010; Arcaro et al. 2011). As such, visual field mapping enables the systematic parcellation and investigation of brain function across most of the visual system.

Visual maps provide an important architecture for the efficient communication of information across cortex at multiple scales (Mountcastle 1957; Kaas 1997; Wandell 2005). The spatial structure of a scene is preserved in a visual map with adjacent neurons representing nearby parts of visual space. As such, visual field maps facilitate the local processing of a scene in a metabolically efficient manor by minimizing the distance of connections (Kaas 1997). This efficiency in the representation and local processing of a scene is preserved across visual field maps in connections between neurons that represent overlapping parts of visual space (Cragg 1969; Maunsell and Van Essen 1983; Van Essen and Zeki 1978; Zeki 1969), and may be
preserved at a coarser scale through the clustering of visual field maps (Wandell et al. 2005). Visual field maps appear to be arranged in spatial clusters, anchored to a common foveal representation. These clusters minimize the distance of connections between individual maps within clusters. The topographic organization of clusters on the cortical surface forms a complex network of visual maps across the visual system.

The identification of visual field maps in both humans and macaques provides an important template for cross-species comparisons. Though the functional and anatomical properties of early visual cortex appear to be largely similar between species, the relations between higher order visual areas are less clear (Van Essen 2003; Orban et al. 2004; Wandel 2007). Difficulty in establishing grounds for making such cross-species comparisons has proven to be a major limiting factor. Structure-to-function correspondence differs greatly between species, and both inter-species and inter-individual variability across extrastriate cortex overshadow the distinction of individual cortical areas based on cytoarchitectonic features (de Sousa et al. 2010). Comparisons based on visual field map organization overcome both of these limitations, and provide objective criteria for cross-individual and cross-species comparisons.

We investigated the visuotopic organization of human and macaque visual systems and identified 26 visuotopic areas in the human and 15 in the macaque. The large-scale organization of these visuotopic areas was compared between species. Our findings provide a framework for detailed comparisons of visual cortex between humans and monkeys that should prove useful in relating the functional similarities and dissociations between species.
4.1 Materials and Methods

**Subjects.** Thirty-two human subjects (19 male, 18-35 years of age) gave informed written consent for participation in this study. All subjects reported that they were right-handed except one subject who was left-handed, had normal or corrected-to-normal vision, and were in good health with no history of neurological disorders. All subjects participated in retinotopic mapping and/or memory-guided saccade task. All procedures were approved by the Institutional Review Board of Princeton University.

**Visual Display.** Stimuli were presented using a Macintosh G4, G5 or Pro computer (Apple Computers, Cupertino, CA) running MATLAB (The MathWorks, Natick, MA) and the Psychophysics Toolbox (Version 3, Brainard, 1997, Pelli, 1997). Visual stimuli were projected from a Powerlite 7250 liquid crystal display projector (Epson, Long Beach, CA; Allegra setup) or a Hyperion MRI Digital Projection System (Psychology Software Tools, Sharpsburg, PA; Skyra setup) onto a translucent screen located at the end of the scanner bore, which subjects viewed through a mirror attached to the head coil. The projection covered a circular region of 30° of visual angle (Allegra setup) or a rectangular region of 28 x 48° of visual angle (Skyra setup). In all experiments, stimulus presentation was time-locked to fMRI acquisition via a trigger from the scanner at the start of image acquisition.

**Stimuli.** *Travelling-wave paradigm:* In order to measure polar angle representations in ventral visual cortex and subcortical structures, visual stimuli consisted of a wedge that rotated either clockwise or counterclockwise around a central fixation point. In order to measure eccentricity representations, visual stimuli consisted of an annulus that either expanded or contracted around
a central fixation point. Both stimuli subtended 15° of the visual field. Subjects performed a change detection task either at fixation or at the stimulus. For visual cortex scanning, each run consisted of eight 40s stimulus cycles, with a total of 3-6 runs per scan session. For subcortical scans, each run consisted of 8 cycles of 40s each, with a total of 8-12 runs per scan session. For more details, see Arcaro et al. 2009.

Memory-guided saccade task: A memory-guided saccade task was used to localize topographically organized areas within posterior parietal cortex (Kastner et al. 2007; Konen & Kastner, 2008). The task consists of covert shifts of attention, working memory and saccadic eye movements in a traveling wave paradigm. Subjects had to remember and attend to the location of a peripheral cue (~8° from fixation) over a delay period while maintaining a central fixation. After the delay period, each subject had to execute a saccade to the remembered location and then return to a central fixation. Peripheral cues rotated clockwise around a central fixation point. Each run consisted of 8 cycles of 40s stimulus cycles, with a total of 8 runs per scan session. See Kastner and colleagues (2007) and Konen and Kastner (2008) for details.

Data acquisition. Data were acquired with a Siemens 3T Allegra scanner using a standard head coil and a Siemens 3T Skyra scanner using 16-channel phased-array head coil (Siemens, Erlangen, Germany). Functional images were acquired with a gradient echo, echo planar sequence using an interleaved acquisition. The specific parameters for each scan session were outlined below.
Visual Cortex Scans: Twenty-five coronal slices covering occipital, posterior parietal and temporal cortex were acquired using a partial Fourier factor of 7/8 to sample an asymmetric fraction of $k$-space to reduce acquisition time (128 square matrix, $256 \times 256$ mm$^2$, field of view [FOV], $2 \times 2$ mm$^2$, in-plane resolution, 2 mm slice thickness, 1 mm gap, 2.5 s repetition time [TR], 40 ms echo time [TE], 75 or 90° flip angle [FA]).

Posterior Parietal Scans: The scanning parameters were the same as for the retinotopic mapping, except we acquired oblique axial slices covering parietal, frontal and dorsal occipital cortex (90° FA).

In addition, an in-plane magnetic field map image ($2 \times 2$ mm$^2$ in-plane resolution, 2 mm slice thickness, same gap as functional scans, 0.5 s TR, 5.23 or 7.69 ms TE, 55° FA) was acquired to perform echo planar image undistortion (Jezzard and Balaban, 1995, Jenkinson, 2001). In each session, a high-resolution anatomical scan (magnetization-prepared rapid-acquisition gradient echo sequence, MPRAGE; Allegra: 256 square matrix; $256 \times 256$ mm$^2$ FOV; 1 mm isotropic resolution; 2.5 s TR, 4.38 ms TE; 8° FA; Skyra: 256 square matrix; $240 \times 240$ mm$^2$ FOV; 0.9375 $\times$ 0.9375 mm in-plane resolution; 0.9 mm slice thickness; 1.9 s TR, 2.1 ms TE; 9° FA; GRAPPA acceleration factor of 2) was acquired to facilitate alignment of functional data with the cortical surface. Two high-resolution structural scans (MPRAGE, same parameters as above) were acquired in a separate session, averaged, and used for cortical surface reconstruction.

Data analysis. Data were analyzed using the AFNI software package (Cox & Hyde 1996), FreeSurfer (Dale et al. 1999; Fischl et al. 1999), SUMA (http://afni.nimh.nih.gov/afni/suma),
MATLAB (The MathWorks, Natick, MA), and FSL (Smith et al. 2004). Functional images were motion corrected (Cox and Jesmanowicz, 1999) to the image acquired closest in time to the anatomical scan, undistorted using the images from the field map scan, and normalized to percentage signal change by dividing the time series by its mean intensity. After normalization, the data were projected cortical data onto surface reconstructions created with FreeSurfer that were aligned to each of the experimental sessions using AFNI/ SUMA. A Fourier analysis was used to identify surface nodes for cortical scans and voxels for subcortical scans activated by the stimuli (Bandettini et al., 1993; Engel et al., 1994). For each node (or voxel), the amplitude and phase—the temporal delay relative to the stimulus onset—of the harmonic at the stimulus frequency (SF) was determined by a Fourier transform of the mean time series of the node. To correctly match the phase delay of the time series of each node to the phase of the stimulus, and thereby localize the region of the visual field to which the underlying neurons responded best, the response phases were corrected for the hemodynamic lag (4 s). The counterclockwise/inward runs were then reversed to match the clockwise/ outward runs and averaged together for each node (or voxel). An F ratio was calculated by comparing the power of the complex signal at the stimulus frequency with the power of the noise. From the F ratio, we calculated a p value (uncorrected) taking into account degrees of freedom of the signal and noise. To quantify the reliability of phase estimates across runs, the variance of a mean phase across cycles was determined for each node. A jackknifing method in which phase estimates were calculated from n-2 cycles (eliminating one clockwise and one counterclockwise cycle per calculation) across all runs was used to determine the SE of phase estimates (for similar application, see Hansen et al., 2007). A grand mean phase estimate was calculated from the average of each of these phase estimates along with the SE to account for variance across estimates for each node. The SE was
then converted into seconds per cycle. Statistical maps were thresholded at a variance of 2 s of the 40 s cycle and overlaid on cortical surface reconstructions (or viewed in the volume for subcortex). The pattern and significance of activation approximately compares with a statistical threshold of \( p < 0.01 \) (uncorrected for multiple comparisons, derived from the F ratio that was calculated from the Fourier transform). For more details on analyses, see attached Arcaro et al. 2009.

To directly compare visual field maps across subjects (both species separately), standard-mesh cortical surfaces were created. Briefly, each subject’s surface was inflated and transformed into a sphere in a manner that minimized metric distortion (Fischl et al., 1999). The individual spheres were used to create a template sphere for each hemisphere, where the curvature pattern consisted of the average pattern across subjects. The individual spheres were non-rigidly aligned to the templates so that the curvature patterns of each subject matched those of the template. To avoid interpolation of the fMRI data to match the warped spheres, the SUMA software package was used to create standard-mesh surfaces from the warped spheres using icosahedral tessellation and projection (Saad et al., 2004; Argall et al., 2006). The geometry of the resulting standard-mesh surfaces is identical to the individual subject’s original surface geometry, but the topology is common across subjects. The use of standard-mesh surfaces allowed for node-to-node correspondence across surfaces, so that the visual maps could be compared across subjects.

After normalization to a standard space, each node was coded based on their inclusion in an ROI. That is, nodes belonging to one of the visual areas were coded a unique number for each
area, whereas the nodes outside visual areas were set zero. The corresponding areas (i.e., the same nodal index) of the different subjects were superimposed within standard surface space. For each human area, a probabilistic map of a ROI was generated by dividing, at each particular stereotaxic location (i.e., node), the number of times a node belonged to that ROI by the number of subjects examined. Hence, the probability values represent the likelihood that any node in the SBA will be classified as part of that visual area. Next, a maximum probability map (MPM) was calculated for each node by comparing the probabilities of all areas at that node and assigning the node to the area with the highest probability.

The average human cortical surface and both macaques’ cortical surfaces were converted to Caret (Van Essen et al., 2001) and aligned with the PALS-B12 and F99 atlases, respectively. Both macaques’ surfaces and visual maps were registered to the human PALS surface using a multi-point anatomical landmark deformation (Van Essen 2001). The percent overlap of each monkey’s visual field maps and the human probabilistic atlas was calculated for both hemispheres. These data were then averaged to derive group averages of percent overlap for each visual field map.

4.2 Results

Five criteria were used to identify individual visual areas: (1) an area contained continuous polar angle and eccentricity phase progressions with adjacent voxels representing adjacent parts of contralateral visual space, (2) polar angle and eccentricity phase progressions were at (approximately) orthogonal angles, (3) the borders between areas were defined at reversals in phase progression; (4) the anatomical location of an area was relatively consistent across subjects (5) the pattern of polar angle and eccentricity phase progression was consistent in the majority of
subjects and, when tested, replicable in individual subjects. Using these criteria, we identified 23 distinct human visual field maps and 15 macaque field maps across occipital, temporal, and parietal cortex and 3 human visual field maps within the thalamus. The topographic organization of each area will be described below, grouped by regional anatomy.

**Occipital Cortex**

*Human V1, V2, V3:* Consistent with prior studies (Sereno et al., 1995; DeYoe et al., 1996; Engel et al., 1997), visual areas V1, V2, and V3 were identified in all subjects (Fig. 15). The horizontal meridian (HM) representation of V1 was identified in the fundus of the calcarine sulcus. A ventral phase progression was observed from this HM representation (green, not marked) to an upper vertical meridian (UVM) representation (red, dotted) that forms the border to area V2 on the ventral gyrus of the calcarine, and then reversing back to a HM that corresponds to the border of ventral V2 and V3 further anterior (Fig. 4.1). The anterior border of ventral V3 was formed by a representation of the UVM. These three areas each represent the upper quadrant of the contralateral visual field. A dorsal phase progression was observed from the HM representation of V1 (green, not marked) to a lower vertical meridian (LVM) representation (red, dotted) that forms the border to area V2 on the dorsal gyrus of the calcarine, and then reversing back to a HM that corresponds to the border of dorsal V2 and V3 further anterior (Fig. 15, left panels). The anterior border of dorsal V3 was formed by a representation of the LVM. These three areas each represent the lower quadrant of the contralateral visual field. The eccentricity representations are confluent across these areas. Ventral V1, V2, and V3 share a foveal confluence that splits dorsal and ventral portions with peripheral representations extending both towards the collateral sulcus as well as towards the cuneus and superior occipital lobe (Fig. 15, right panels).
Macaque V1, V2, V3: In agreement with previous reports (Daniel & Whitteridge, 1961; Zeki, 1969; Van Essen et al., 1984; Brewer et al., 2002; Fize et al., 2003), visual areas V1, V2, and V3 were identified in each hemisphere of both monkeys by a phase progression starting within the calcarine sulcus from a HM representation to a VM representation (Figs 4.2; blue color-coded).
phase, dashed line) that forms the border to area V2, and then reversing back to a HM that corresponds to the border of V2 and V3 (Fig. 4.2; green, boundary not drawn). Within dorsal extrastriate cortex, a phase progression was identified from the HM border of V2d/V3d to a LVM representation (Fig. 4.2, blue color-coded phase, dashed line) corresponding to the anterior border of V3d. Within ventral extrastriate cortex, a phase progression was identified from the HM border of V2v/V3v to a UVM representation (Fig. 4.2, blue color-coded phase, dashed line) corresponding to the anterior border of V3v. All three areas share a representation of central space within the anterior extent of the calcarine sulcus with representations of the periphery.

Figure 4.2: Polar angle and eccentricity maps in macaque visual cortex. Flattened surface reconstructions of early visual cortex of two representative subjects (M1 and M2). The lefthand panel shows the polar angle maps; the middle panel shows the eccentricity maps; the righthand panel shows outlines of the areas in relation to anatomy. See Figure 4.1 for conventions.
extending both dorsally and ventrally approximately perpendicular to the polar angle phase progressions (Fig. 4.2).

Dorsal Extrastriate Cortex

*Human V3a & V3b:* Consistent with prior studies (DeYoe et al. 1996; Tootell et al. 1997; Press et al. 2001; Swisher et al. 2007), two representations of contralateral space, V3a and V3b, were identified adjacent to dorsal V3, near the transverse occipital sulcus (TOS) and dorsal to lateral occipital areas: LO-1 and LO-2 (Fig. 4.3). Unlike dorsal V3, V3a and V3b each contain a full representation of contralateral visual space. V3a shares a LVM representation with the peripheral, but not foveal, representation of dorsal V3 with angular representations progressing anterior and dorsal to a HM representation and then to a representation of the UVF near posterior parietal cortex. V3b shares a LVM representation with part of LO-1 that is anterior to dorsal V3 with angular representations progressing dorsal and medially to a HM representation and then to a representation of the UVM adjacent and lateral to V3a’s UVM. The LVM and UVM borders of V3a and V3b form an “elbow.” A representation of central visual space separates V3a and V3b. Across subjects, this central representation was mainly of parafoveal space (< 3°), and rarely within foveal space (< 1°). The lateral border of V3a is defined by this parafoveal representation with peripheral representations extending medially. The medial border of V3b is defined by this parafoveal representation with peripheral representations extending laterally.
Macaque V3a & DP: A representation of the contralateral visual field including both the LVF and UVF was identified within the lunate sulcus and parieto-occipital sulcus (POS) of each hemisphere, consistent with known topography of area V3a (Van Essen & Zeki, 1978; Gattass et al., 1988; Brewer et al. 2002; Fize et al., 2003). The posterior, lateral border of V3a was identified by a LVF representation within the dorsal, anterior bank of the lunate sulcus and along the cortex separating the lunate sulcus from the POS (Fig. 4.4; blue color-coded phase, dashed line). In all hemispheres, the posterior portion of the LVF representation was continuous with the LVM border of V3d, but separated from the V3d border, as it extended anterior towards the
prelunate gyrus. A polar angle phase progression of contralateral space was identified extending from this LVF representation in a caudal/lateral – rostral/medial direction to an UVF representation within the POS (Fig. 4.4; red color-coded phase, dotted line). A LVF representation of contralateral space was identified anterior to V3a along the dorsal portion of the prelunate gyrus in each hemisphere, which label area DP (May & Andersen, 1986; Gattass et al., 1988; Fize et al., 2003; Heider et al., 2005; but also see Maguire & Baizer, 1984). A representation of the HM was identified within the POS, adjacent and medial to this LVF representation with an UVF representation extending into area V3a located further medially within the POS (Fig. 4.4). This region bordered V3a, but also included cortex along the prelunate gyrus, located anterior and medial to the topography of V3a (Fig. 4.4). A representation of the central space was found within the prelunate gyrus, anterior and lateral to portions of cortex that

Figure 4.4: Polar angle and eccentricity maps in macaque dorsal extrastriate and posterior parietal cortex. Inflated surface reconstructions of dorsal extrastriate visual cortex of two representative subjects (M1 and M2). The lefthand panel shows the polar angle maps; the middle panel shows the eccentricity maps; the righthand panel shows outlines of the areas in relation to anatomy. See Figure 4.1 for conventions.
split the lunate sulcus and POS (Fig. 4.4; asterisk). The peripheral representations of the eccentricity map extended ventrally into both the posterior and anterior POS (Fig. 4.4). The anterior portion of V3a roughly encompassed the posterior half of the central space and the posterior portion of DP encompasses the anterior half of the central space.

**Posterior Parietal Cortex (PPC)**

*Human IPS-1/2/3/4/5 & SPL-1:* From the delayed-saccade experiment, six topographically organized areas in human PPC were identified: V7 (IPS-0), IPS-1, IPS-2, IPS-3, IPS-4, IPS-5 (Figure 4.5). An additional visual field map within superior parietal cortex, SPL-1, was also identified in several subjects. These representations were generally oriented in a posterior - anterior direction, though conforming to the anatomical curvature of the IPS. The posterior most area, IPS-0 (V7) is adjacent and anterior to V3a and V3b and shares a UVM border. A phase progression extended anterior to a LVF representation that forms the border between IPS-0 and IPS-1. The phase progression reversed back to a UVF representation that forms the border between IPS-1 and IPS-2. The phase progression reversed again to a LVF representation that forms the border between IPS-2 and IPS-3. In most subjects, the medial part of this LVF forms a border of SPL-1. The phase progression forks at this LVF representation: one dorsal-medially and the other ventrolaterally. The dorsomedially phase progression extends into the superior parietal lobe back to a UVF representation that forms the medial border of SPL-1. The ventral-lateral phase progression curves with the anatomy of the IPS back to a UVF representation that forms the border between IPS-3 and IPS-4. The phase progressions reverses twice more: back to a LVF that forms the border between IPS-4 and IPS-5 and then to a UVF that forms the anterior border of IPS-5 and the anterior most part of the IPS. Similar topographic organization was
observed in human PPC using the traveling-wave paradigm with covert attention (Fig XXC).

Eccentricity representations were measured across the IPS in a subset of these subjects.

Consistent with Swisher and colleagues (2007), lateral portions of these IPS areas represented central, foveal space with peripheral representations located medially. Though the foveal
representations were contiguous in some subjects, a few subjects showed discrete foveal representations. In these subjects, a representation of central space was identified anterior to V3a, and overlapped with IPS-0 and IPS-1. A second foveal representation was identified anterior to this, and overlapped with IPS-2 & IPS-3. No clear, consistent eccentricity representations were observed within IPS-4 & IPS-5.

*Macaque CIP-1/2 & LIP<sub>vt</sub>:* In macaque PPC, three topographically organized areas were identified: CIP-1, CIP-2, and LIP<sub>vt</sub>. These representations were generally oriented in a posterior–anterior direction, though conforming to the anatomical curvature of the IPS. The posterior most part of CIP-1 is anterior and adjacent to V3a and DP and shares an UVF representation. A polar angle phase progression extended anterior to a LVF in posterior IPS that forms the border between CIP-1 & CIP-2 (Fig. 4.4). The phase progression reverses back to an UVF representation (red color-coded phase, dotted line) that forms the border between CIP-2 and LIP<sub>vt</sub> within the posterior portion of the IPS (Fig. 4.4). The UVF representation spanned across the inferior parietal gyrus medially and into the fundus of the IPS to a LVF representation that forms the anterior border of LIP<sub>vt</sub>. A representation of central space was identified anterior to that of V3a, and overlapped with lateral portions of CIP-1 and CIP-2 along the lateral IPS and onto the inferior parietal lobule (Fig. 4.4; asterisk). The eccentricity maps lacked detail in this region of cortex though representations of the periphery extended medially into the fundus of the parieto-occipital confluence and IPS. A second representation of central space was identified anterior to CIP-1 and CIP-2 along the lateral bank of the IPS (Figs. 4.4; asterisk) with peripheral representations were generally observed ventromedially, along the fundus of the IPS.
Lateral Occipital Cortex

*Human LO-1 & LO-2:* Consistent with prior studies (Larsson & Heeger 2005), two representations of contralateral space, LO-1 and LO-2, were identified adjacent to dorsal V3 along the lateral and inferior occipital sulci in anterior lateral occipital cortex (Fig. 4.6). Unlike dorsal V3, LO-1 and LO-2 each contain a full representation of contralateral visual space. The posterior border of LO-1 shares a LVM representation with foveal, but not peripheral, dorsal V3. The LVM of LO-1 forms an “elbow,” branching off the parafoveal representations (~5-7°) of V3 and extending anterior, just below the transverse occipital sulcus. A phase progression was observed anterior from this LVM representation to representations within the upper visual field (UVF). Consistent with prior observations (Hansen et al. 2007), the phase progression in several subjects reversed close to the horizontal meridian, suggesting only a quarterfield representation.

![Figure 4.6](image)

*Figure 4.6: Polar angle and eccentricity maps in human lateral occipital. Inflated surface reconstructions of lateral occipital visual cortex of two representative subjects (S4 and S5). The lefthand panel shows the polar angle maps; the middle panel shows the eccentricity maps; the righthand panel shows outlines of the areas in relation to anatomy. See Figure 4.1 for conventions.*
However, the phase progression in most subjects reversed well within the upper visual field, consistent with an interpretation that LO-1 represents a full hemifield. Anterior to this border, the phase progression of LO-2 reversed back to a HM representation and then to a LVM representation. The foveal representation of LO-1 and LO-2 is confluent with the foveal representation of early visual cortex (at least at the resolution of fMRI) with peripheral representations extending dorsally towards the transverse occipital cortex.

*Macaque V4 complex - Areas V4d, V4t, V4ta:* In agreement with previous studies (Zeki, 1969; Zeki, 1980; Maguire & Baizer, 1984; Desimone & Ungerleider, 1986; Gattass et al., 1988; also see Fize et al., 2003), visual areas V4d and V4t were identified in each hemisphere of both monkeys. A phase progression was identified from the LVM representation corresponding to the border between V3d and V4d to a HM representation corresponding to the border between V4d and V4t (Figs. 4.7A & 4.7A). The phase progression reversed further anterior into the ventral bank of the posterior superior temporal sulcus (STS) to a LVM representation corresponding to the border between V4t and MT/V5 dorsally and V4ta ventrally. Anterior to V4t, along the inferior bank of the STS, the phase progression reversed to a UVM representation corresponding to the anterior border of V4ta (also referred to as posterior PITd). The foveal representation of V4d appears to be continuous with the foveal representation shared by early visual areas V1, V2, and V3 (Figs. 4.7B & 4.7B). The foveal representation of V4t is located more laterally along the ventral surface of the STS and within the fundus of posterior STS. It appeared continuous with the representation of foveal space in early visual cortex, though may be distinct from the central space representations of early visual areas (see Kolster et al., 2009). The foveal representation of
V4ta is located on the ventral surface of STS, and appeared continuous with the fovea of early visual cortex.

Figure 4.7: Polar angle and eccentricity maps in macaque lateral occipital and the superior temporal sulcus. Inflated surface reconstructions of lateral occipital visual cortex of two representative subjects (M1 and M2). The lefthand panel shows the polar angle maps; the middle panel shows the eccentricity maps; the righthand panel shows outlines of the areas in relation to anatomy. See Figure 4.1 for conventions.

Medial Temporal Cortex

*Human TO-1 (phMT) & TO-2 (phMST):* Consistent with prior studies (Amano et al. 2009; Kolster et al. 2010), two representations of contralateral space, TO-1 and TO-2, were identified anterior to LO-2 within posterior inferior temporal sulcus (Fig. 4.6). The posterior border of TO-1 shares a LVM representation with the anterior border of LO-2. In most subjects, there was a clear reversal in phase progression between LO-2 and TO-2, consistent with Amano and colleagues’ (2009) interpretation that these areas directly border one another. In about a quarter of our data, there was no clear single phase reversal, but instead a prolonged extension of LVM representations with two peaks (one posterior and one anterior) at or near the vertical meridian. These data could support the interpretation of a break in phase progression between LO and TO, suggesting that TO-1 and TO-2 (phMT & phMST) form their own distinct cluster and do not
directly border each other (Kolster et al. 2010). A phase progression was observed anterior from
the LVM to a representation of the UVF that forms the border between TO-1 and TO-2 and
continued anterior to another representation of the LVF, forming the anterior border of TO-2.

Macaque MT, MSTv, and FST: Polar angle phase progressions of contralateral space were
observed within posterior STS, consistent with previous studies delineating MT, MSTv, and FST
(Kolster et al., 2009; also see Gattass & Gross, 1981; Van Essen et al., 1981; Desimone &
Ungerleider, 1986). A phase progression was identified from the LVM representation (Figs. 4.7A
& 4.7A) corresponding to the border between V4t and MT to an UVF representation within the
lower bank of posterior STS corresponding to the border between MT and MSTv. The phase
progression reversed back towards a LVF representation further anterior and within the fundus of
the STS corresponding to the border between MSTv and FST. Within the dorsal portion of the
posterior STS, superior to MT and MST, a peripheral representation of the LVF and HM was
observed in all four hemispheres (Figs. 4.7 & 4.7). As suggested by Kolster and colleagues
(2009), this anatomical area may correspond to MTp or other neighboring motion sensitive areas
(Desimone and Ungerleider, 1986). No apparent representations central space could be
identified.

Occipital Temporal Cortex

Human OT-1 & OT-2 (phPIT): Consistent with a prior study (Kolster et al. 2010), we identified
spatially specific responses within the inferior occipital sulcus (IOS) and the posterior portion of
the occipital temporal sulcus (OTS) in a subset of our subjects (18/31) (Fig. 4.8). These patterns
of spatial representations were more variable than neighboring cortex, which could be due to
transverse sinus imaging artifacts (see Winawer et al. 2010). In this subset of subjects, two representations of the visual field, OT-1 and OT-2, were identified. A phase progression was identified from LVF representation located on the posterior bank of the IOS that forms the border of OT-1 to an UVF representation on the anterior bank of the IOS, which forms the border between OT-1 and OT-2. The phase progression reverses back to a LVF representation within the posterior portion of the OTS that forms the anterior border of OT-2. Both areas contained mainly representations of the central visual space (< 3°) with no clear phase progression. Across subjects, there were clear LVF (vs. UVF) and foveal (vs. periphery) biases, consistent with prior studies (Hasson et al. 2002; Schwarzlose et al. 2008). Based on anatomical location, these areas correspond to the phPITd and phPITv areas identified by Kolser and colleagues (2010), though the orientation of phase progression appears to differ. Kolster and colleagues identified a circular polar angle phase progression around a central foveal representation. A posterior to anterior polar angle phase progression was more prominent in our data that continued further along the lateral fusiform gyrus.

Figure 4.8: Polar angle and eccentricity maps in human lateral occipital and the occipital temporal sulcus. Inflated surface reconstructions of inferior lateral occipital visual cortex of two representative subjects (S8 and S9). The lefthand panel shows the polar angle maps; the middle panel shows the eccentricity maps; the righthand panel shows outlines of the areas in relation to anatomy. See Figure 4.1 for conventions.
Macaque PITd: Consistent with a prior study (Kolster et al. 2009), visual area PITd was identified on the ventral surface of the STS in each hemisphere of both monkeys (Fig. 4.7). A polar angle phase progression of contralateral space was identified from the UVM representation corresponding to the border between V4ta and PITd to a LVM representation corresponding to the anterior border of PITd. A representation of foveal space was observed on the inferior bank of the STS with peripheral representations extending into the STS.

Ventral Temporal Cortex

Human hV4, VO-1, VO-2, PHC-1, PHC-2: Five representations of contralateral space were identified along the ventral surface and anterior to V3. The posterior border of hV4 shares an UVM representation with ventral V3 (Fig. 4.9, red, dotted line). A phase progression was identified from the UVM anterior and ventral to a representation of the LVF (blue, dashed line). The fovea of hV4 was found to be continuous with the foveal confluence shared by ventral V1, V2, and V3 (Fig. 4.9), and the peripheral representation extended toward the collateral sulcus, parallel with the eccentricity map of ventral V1, V2, and V3. The medial part of hV4’s border was drawn in the region of the most peripheral representations found in hV4 (purple line) that reversed from there towards a foveal representation along the posterior medial fusiform, separate from early visual cortex, and overlapping with VO-1 & VO-2. VO-1 and VO-2 were located along the posterior medial fusiform gyrus and within the posterior portion of the collateral sulcus. The posterior extent of VO-1 shares a LVF representation with hV4 (Fig. 4.9, left panels, blue, dashed line). A phase progression was observed anterior and medial to a representation of the UVF that formed the border between VO-1 and VO-2. The phase progression reversed back
towards a LVF that forms the border between VO-2 and PHC-1. VO-1 and VO-2 share a foveal representation along the posterior part of the medial fusiform gyrus. The periphery of the visual field was represented posterior from the foveal representation abutting the peripheral representations of hV4 and ventral V3. PHC-1 and PHC-2 were located within the posterior PHC extending along the collateral sulcus and flanked by the lingual gyrus and the posterior portion of the parahippocampal gyrus on one side and the medial fusiform gyrus on the other side. The posterior border of PHC-1 shares a LVF representation with VO-2 (Figs. 4.9, blue, dashed). A phase progression continues anterior along the collateral sulcus to a UVF representation that forms the border between PHC-1 and PHC-2. The phase progression reversed back to a representation of the LVF that forms the anterior border of PHC-2. The eccentricity organization was very coarse within the collateral sulcus. A small foveal representation was identified anterior to VO-1 and VO-2 along the medial fusiform gyrus, overlapping with PHC-1 and PHC-2. Peripheral representations were identified medial to the foveal representation throughout the collateral sulcus.
Thalamus

*Human LGN & Pulvinar:* Three topographically organized areas were identified within the thalamus: the lateral geniculate nucleus (LGN), lateral pulvinar, and inferior pulvinar (Figs. 4.10 & 4.11). The anatomical location of these visual field maps was verified using the Morel (2007) human thalamic atlas. The polar angle phase progression within the lateral and inferior pulvinar is consistent with electrophysiological recordings in monkeys (Fig. 4.12, adapted from Bender et al. 1981). Within the anatomically-defined LGN, a phase progression was identified from a LVM representation located anterior and dorsomedially to a UVM representation located posterior and ventrolaterally. A large representation of foveal space was found in anterior portions of the LGN with peripheral representations located more posterior and dorsal. Posterior to the LGN, two maps of the visual field, PuL and PuI, were identified within the ventral pulvinar. A LVM representation shared by PuL and PuI was identified within the dorsal anterior border of the thalamus.

Figure 4.10: *Polar angle maps in human thalamus.* Sagittal views of four representative subjects (S1, S2, S3, and S4). See Figure 4.1 for conventions.
ventral pulvinar. A phase progression extended posterior to a UVM representation that split laterally and ventrally, forming the posterior borders of PuL and PuI, respectively. A foveal representation was identified within posterior portions of the pulvinar, splitting PuL and PuI. No visual field maps were identified in the macaques thalamus, likely due to poor signal from the surface coil.

**Figure 4.11:** Group Average polar angle maps in human thalamus. Coronal views of group average maps for pulvinar, superior colliculus, and LGN. See Figure 4.1 for conventions.

**Figure 4.12:** Comparison of pulvinar visual field maps in humans and macaques. Coronal views of group average for pulvinar. Single-unit recording studies (lefthand side in both columns) were color coded based on polar angle (left) and eccentricity (right) representations and compared to human maps measured using fMRI (righthand side in both columns). See Figure 4.1 for conventions.

**Parallels between species**

Each human subject’s cortical surface was aligned to a common surface space for cross-
subject alignment of visual field maps (See Methods). A probabilistic atlas was calculated for all visual field maps and aligned to the Caret PALS B12 atlas. Both macaques’ cortical surfaces were converted to a common surface space and then to the Caret F99 atlas. Surface-based registration guided by a set of anatomical landmarks common between humans and macaques was performed between on the species (Van Essen 2001) to align each macaque’s visual field maps with the human probabilistic atlas. The macaque maps heavily overlapped with the human group average maps (Fig 4.13). The human group average maps extended into ventral temporal and anterior parietal cortex, where visual maps have not yet been identified in macaques. The percent overlap with the human probabilistic atlas was calculated for each monkey’s visual fields. The pattern of visual map overlap between species reflected the gross anatomical groupings listed above. Many visual maps overlapped the most with their proposed species parallel. For example, 70% (±2) of macaque V1 overlapped with human V1, 59% (±2) of macaque V3a overlapped with human V3a, 71% (±4) of macaque LIPvt overlapped with human IPS-2. A few visual maps overlapped greatest with a neighbor of their proposed species parallel. The majority of macaque V2 overlapped with human V1, not human V2 (47% vs. 37%) and the

Figure 4.13: Comparison of cortical visual field maps in humans and macaques. Flattened surface reconstructions of human atlas (PALS-B12). Human and macaque surfaces were registered to each other using Caret’s PALS surface warping. The human topographic probabilistic atlas (left) and visual field maps from two macaque hemispheres were projected onto the aligned surface for comparison.
majority of macaque V3 overlapped with human V2, not human V3 (67% vs. 15%). Macaque DP overlapped with human V3a, but not V3b (59% vs. 0%). Overall, there was good correspondence in topographic organization between species with visual maps either overlapping the predicted species parallel map or one of the adjacent maps.

**Visual Clusters**

In both species, the large-scale organization of these areas supports the hypothesis that visual cortex is organized into a number of clusters that share common functional response properties (Wandell et al. 2005, 2007; Kaas & Catania 2002). Eight distinct clusters were identified within human visual system (7 cortical and 1 subcortical) and four clusters within macaque visual cortex, though we found evidence for additional clusters in both species. Each cluster was comprised of several maps with parallel eccentricity representations that share a fovea (Fig 4.14). As a general principle, maps are delineated on the basis of reversals in polar angle representation within clusters where both polar angle and eccentricity reversals define borders between clusters. In both species, one cluster was identified within occipital cortex. In humans, this cluster consisted of visual areas V1, V2, V3, hV4, LO-1, and LO-2. In macaques, this cluster consisted of visual areas V1, V2, V3, V4, V4t, V4ta. It has been proposed that human lateral occipital cortex containing LO-1 and LO-2 is a separate cluster from visual areas V1-hV4 (Wandell et al. 2005), though the critical evidence of a separation in foveal representation is largely lacking (Larsson & Heeger 2006; Sayres & Grill-Spector 2008). Within ventral temporal cortex, two clusters were identified only in humans. Anterior to hV4, a cluster was identified containing VO-1 and VO-2. Anterior to the VO cluster, a second cluster was identified consisting of PHC-1 and PHC-2. The relatively poor signal from the surface coil made it difficult
to identify visuotopic areas within macaque ventral temporal cortex. In both species, two maps were identified within lateral occipital cortex: OT-1 & OT-2 in humans and V4ta & PITd in macaques. These maps may represent complete clusters for each species, though the foveal representation was difficult to distinguish across subjects from the fovea of early visual cortex.

In both species, a single cluster was identified within medial temporal cortex. In humans, one cluster was identified anterior to LO-2 consisting of TO-1 and TO-2. In macaques, one cluster was identified anterior to V4t, consisting of MT, MST, and FST. In both species, a single cluster was identified within dorsal extrastriate cortex. The cluster was identified anterior to dorsal V3 consisting of V3a and V3b (humans) or DP (macaques). In both species, a single cluster was
identified within posterior parietal cortex. In humans, a cluster was identified anterior to V3a consisting of IPS-0 and IPS-1. In macaques, a cluster was identified anterior to V3a consisting of CIP-1 and CIP-2. In both humans and macaques, additional areas and foveal representations were identified further anterior within posterior parietal cortex. However, the relation of individual maps to foveal representations was less distinct. Our data suggest at least one more foveal representation within posterior parietal cortex in both species. This foveal representation appears to span several areas in humans, but only one area in macaques. This may indicate a fundamental difference in the organization of posterior parietal cortex between species, though it is difficult to rule out technical constraints limiting our ability to resolve additional topographic organization anterior to LIPin the macaque that would parallel the human. Though visual field maps clusters are proposed to be an organizational principle for visual cortex, the two maps within the human pulvinar satisfy the criteria to be considered a cluster. Both maps are anchored to a common fovea and have similar functional response properties and connectivity (Shipp 2002). We propose that visual clusters are not unique to cortex and can be an organizational principle for subcortex as well.

A larger topographic structure emerged across the visual system when considering the location of clusters relative to one another. Clusters abutted each other with borders between clusters defined a combination of polar angle and eccentricity phase reversals between individual areas (e.g. LVM and far periphery between hV4 and VO-1 as well as LO-2 and TO-1). For most clusters, the large scale topographic structure observed in humans paralleled that in macaques. In humans, the V3a/b cluster bordered the occipital cortex cluster antero-dorsally at the polar angle phase reversal between dorsal V3 and V3a. Similarly, in macaques, the V3a/DP cluster bordered
the occipital cortex cluster antero-dorsally at the polar angle reversal between dorsal V3 and V3a. In humans, the TO cluster bordered the occipital cortex antero-laterally at the polar angle phase reversal between LO-2 and TO-1. Similarly, in macaques, the MT cluster bordered the occipital cortex antero-laterally at the polar angle reversal between V4t and MT. In humans, the VO cluster bordered the occipital cortex cluster antero-ventrally at the eccentricity phase reversal between hV4 and VO-1. In humans, the PHC cluster bordered the VO cluster antero-ventrally at the polar angle phase reversal between VO-2 and PHC-1. In humans, the posterior parietal cluster (IPS-0/IPS-1) bordered the V3a/b cluster antero-dorsally at the polar angle phase reversal between V3a/b and IPS-0. Similarly, in macaques, the posterior parietal cluster (CIP-1/2) bordered the V3a/DP cluster antero-dorsally at the polar angle phase reversal between V3a/DP and CIP-1.

4.3 Discussion

Spatially specific activity was observed throughout occipital, temporal, and parietal cortex in both humans and macaques. Based on the topographic patterns of these activations, 26 visual field maps (23 cortical & 3 subcortical) were identified in the human visual system and 15 maps were identified in the macaque visual cortex. These visual field maps extended beyond occipital cortex, into regions of the visual system commonly thought of as lacking any organized representation of space (e.g. Platt & Glimcher 1998; Halgren et al. 1999; Tsao et al. 2003). When compared to the activation maps from visual stimulation (vs. blank fixation), these maps cover most of visually-responsive cortex (Fig. 4.15). Further, most of visually-responsive cortex that did not overlap with any of the defined visuotopic areas (e.g. ventral temporal and lateral occipital cortex) still contained spatially specific modulations. It may be that these areas contain
additional topographic organization that has yet to be classified. These data demonstrate that the topographic organization of space is not just a major organizing principle for early visual cortex, but for most, if not all, of the visual system.

Based on the pattern of spatial topography within individual areas and each area’s location relative to surrounding areas, many of the visual field maps identified in human visual cortex appeared to have a parallel in macaque visual cortex. Our cross-species surface alignment also supports this interpretation. The underlying anatomy of early visual cortex, located within and around the calcarine sulcus, appeared to correspond between species. Though, there was a great degree of variability in the underlying anatomy between species for most areas. For example, the
topographic organization of area TO-1 in the human appears to parallel that of area MT in the macaque, though TO-1 is located in the medial temporal sulcus and MT is located in the superior temporal sulcus. The correspondence in topographic organization between species does not necessitate other functional parallels. Though the functional response properties of early visual areas appear to be similar between species, functional differences have been observed for other potentially parallel areas, such as V3a (Tootell et al. 1997; Vanduffel et al. 2001; Orban et al. 2004). Our results provide a framework for detailed comparisons of visual cortex between humans and monkeys that should prove useful in relating the functional similarities and dissociations of individual areas between species.

We also found differences in the topographic organization of visual cortex between species. Several visuotopic areas in human posterior parietal and ventral temporal cortices had no apparent parallel in the macaque. These differences may reflect fundamental dissociations in the topographic organization of visual cortex between species. However, such differences are not overly conclusive as it is difficult to rule out stimulus and imaging factors that could limit the ability to identify visual field maps in particular regions of cortex. The apparent lack of visual field maps ventral to macaque V4v in our data could be due to relatively poor signal in this region from using a surface coil placed on the top of each monkey’s head. Also, spatial attention tasks such as the delayed saccade task are generally utilized for mapping the topographic organization of human posterior parietal cortex. Our stimulus may have been insufficient for revealing topographic organization of macaque posterior parietal cortex anterior to macaque LIPvt.
Our data support the hypothesis that visual cortex contains clusters comprised of several visual field maps with parallel eccentricity representations that share a fovea (Wandell et al. 2005). We identified eight different visual field map clusters in the human and four in the macaque. Our data suggest that additional clusters may exist in parietal and temporal cortex, though additional studies on the organization of eccentricity within these regions is needed to clarify such organization. Our data also show that visual field map clusters are not unique to cortex, but can also be found in subcortex. The four clusters in macaque visual cortex paralleled four of the clusters identified in human visual cortex. A critical component to the visual field cluster hypothesis is that areas within a cluster share resources such as circuitry and serve similar computational goals (Wandell et al. 2005). As such, the organization of anatomical connections and functional response properties should be similar within a cluster and (relatively) distinct from surrounding cortex.

Given the consistent topographic relation of these clusters to each other across subjects, it is possible that these visual clusters are anchored to one another in a meaningful way, potentially forming distinct topographic pathways for the efficient processing and communication of information across the visual system. As such, the organization of anatomical connections and functional response properties should be similar within a pathway and (relatively) distinct from surrounding cortex.
5 Relating Spatial and Categorical Information in Ventral Temporal Cortex

In the human brain, ventral temporal and lateral occipital cortex is involved in the processing and representation of object information (e.g. Malach et al., 1995; Grill-Spector et al., 1999; Kourtzi and Kanwisher, 2001; see Grill-Spector and Malach, 2004 for review). Initially, it was thought that this substantial part of visual cortex had no further functional organization other than containing a small number of modules that appear to preferentially process information regarding specific biologically relevant object categories such as faces (the fusiform face area, FFA; Kanwisher et al., 1997), places (the parahippocampal place area, PPA; Epstein and Kanwisher, 1998), and bodies (the extrastriate body area, EBA; Downing et al., 2001, the fusiform body area, FBA; Peelen and Downing, 2005). Contrary to this view, our lab and others have demonstrated the existence of several visuotopic areas across ventral temporal and lateral occipital cortex based on both polar angle and eccentricity representations, using fMRI paradigms optimized for measuring the spatial selectivity in cortex containing large receptive fields (Larsson & Heeger 2005; Brewer et al. 2006; Arcaro et al. 2009; Amano et al. 2009; Kolster et al. 2010). The existence of numerous visual field maps provides a novel framework for the organization of ventral temporal cortex. The relationship between these spatial maps and object selectivity remains to be tested and should prove informative as to how such systematic representations of space are utilized for object recognition.

We investigated the relationship between category sensitivity and two visuotopic areas, PHC-1 & PHC-2. Both the foveal and peripheral representations of PHC-1 and PHC-2 responded more strongly to scenes than to objects or faces and heavily overlapped with the functionally defined PPA. We also demonstrate that visuotopic areas within ventral temporal and lateral
occipital cortex overlap with category-selective areas. We did not find a 1:1 correspondence between visuotopic areas and category-selective areas, but instead, found that category-selective areas typically overlapped with at least two, adjacent visuotopic areas. Our findings lend support to the notion that object-sensitive ventral cortex is organized into multiple topographic representations of visual space (Wandell et al. 2007).

5.1 Materials and Methods

Subjects. Eleven subjects (aged 20–36 years, 4 females) participated in the study, which was approved by the Institutional Review Panel of Princeton University. All subjects were in good health with no history of psychiatric or neurological disorders and gave their informed written consent. Subjects had normal or corrected-to-normal visual acuity. All subjects participated in three scanning sessions, during which high-resolution structural images were acquired for cortical surface reconstructions, and polar angle and eccentricity measurements were obtained across visual cortex using attentive wedge and ring tracking paradigms (see Chapter 2). Three subjects exhibited excessive head motion and were excluded from further analyses. The remaining eight subjects participated in a fourth scanning session in which various object stimuli were probed, and four of them participated in a fifth and sixth scanning session, in which polar angle and eccentricity maps were measured using standard retinotopic mapping procedures (Sereno et al., 1995; DeYoe et al., 1996; Engel et al., 1997).

Visual Display. The stimuli were generated on Macintosh G4 and G5 computers (Apple Computer; Cupertino, CA) using MATLAB software (The MathWorks; Natick, MA) and Psychophysics Toolbox functions (Brainard, 1997; Pelli, 1997). Stimuli were projected from a
PowerLite 7250 liquid crystal display projector (Epson; Long Beach, CA) located outside the scanner room onto a translucent screen located at the end of the scanner bore. Subjects viewed the screen at a total path length of 60 cm through a mirror attached to the head coil. The screen subtended 30° of visual angle in both the horizontal and vertical dimensions. A trigger pulse from the scanner synchronized the onset of stimulus presentation to the beginning of the image acquisition.

**Stimuli.** To determine functional response properties with respect to object-related information across ventral visual and lateral occipital cortex object stimuli from the following categories were used: faces, scenes, inanimate objects, headless bodies, houses, flowers, chairs, tools, and scrambled stimuli (Downing et al., 2006). For the current study, analyses were limited to face, body, inanimate object, scene, and scrambled stimuli. For each category, the stimulus pool contained 40 different grayscale images (Supplementary Fig. 1C). Each object stimulus subtended 12° horizontally by 12° vertically and was presented behind a central fixation point (0.3°, 0.9 cd/m^2^) for 350 ms followed by a 400 ms blank period. Twenty images from a given category were shown in a block that lasted for 15 s. Subjects performed a one-back task indicating the repeated appearance of a stimulus, which occurred randomly three times within each block. During a given run, two blocks from each category were shown in pseudo-randomized order amounting to a total of 18 presentation blocks per condition. A fixation block of 15 s without stimulus presentations was interleaved after every four blocks of object stimuli presentations, resulting in an overall run length of 345 s. Four to six runs were tested during a scan session.
To determine functional response properties with respect to visual motion across lateral occipital and medial temporal cortex, moving and static dot stimuli were used (Konen & Kastner 2008). One thousand dots were presented within a 15° diameter circular aperture sparing the central .75° of the visual field. Each dot (0.15°) moved with an average velocity of 8°/s and had a maximum lifetime of 500ms, after which it was assigned to a new random location within the aperture. If a moving dot traveled outside the aperture, it was relocated to a new random location within the aperture. Subjects performed a luminance detection task at fixation. During a given run, eight epochs of moving dots lasting for 16s alternated with equally long presentations of stationary dots. During motion epochs, dots alternated between planar, circular, and radial motion every 2s. Each run started with 16s fixation block. Two runs were tested during a scan session.

Data acquisition. Data were acquired with a 3T Allegra head-dedicated MRI scanner (Siemens, Erlangen, Germany) using a 4-channel bi-temporal phased array coil (Nova Medical, Wilmington, Massachussettes, Model NMSC-003A). 25 axial slices were acquired in four to six runs of 138 volumes, covering ventral occipital and temporal cortex. All acquisitions used a gradient echo, echo planar sequence with a 128 square matrix (slice thickness: 2 mm, with a 0.5 mm gap between slices, interleaved acquisition) leading to an in-plane resolution of 2 x 2 mm² [field of view (FOV), 256 x 256 mm²; repetition time (TR), 2.0-2.5 s; echo time (TE), 40 ms; flip angle 90°]. A partial Fourier factor of 7/8 was used to acquire asymmetric fraction of k-space to reduce the acquisition time. Echo-planar images were compared with a high-resolution anatomical scan taken at the end of each session (MPRAGE sequence, TR = 2.5 s, TE = 4.38 s, flip angle = 8°, 256 x 256 matrix, 1-mm³ resolution). An in-plane magnetic field map image was
acquired to perform echo planar imaging undistortion (FOV = 256 x 256 mm, 128 matrix, TR = 345 ms, TE = 5.06/8.06 ms, flip angle = 40°, bandwidth = 260 Hz/pixel). For cortical surface reconstructions, high-resolution structural scans were acquired in a separate session (MPRAGE sequence, same parameters as above, 2 acquisitions).

**Data analysis.** Data were analyzed using AFNI (Cox, 1996) ([http://afni.nimh.nih.gov/afni/](http://afni.nimh.nih.gov/afni/)), SUMA ([http://afni.nimh.nih.gov/afni.suma](http://afni.nimh.nih.gov/afni.suma)), MATLAB, and FREESURFER (Dale et al., 1999; Fischl et al., 1999) ([http://surfer.nmr.mgh.harvard.edu/](http://surfer.nmr.mgh.harvard.edu/)). Functional images were motion corrected (Cox and Jesmanowicz, 1999) to the image acquired closest in time to the anatomical scan, undistorted using the images from the field map scan, and normalized to percent signal change by dividing the time series by its mean intensity. Data analysis was performed within the volume. Square-wave functions matching the time course of the experimental design were convolved with a gamma-variate function (Cohen, 1997) and used as regressors of interest in a multiple regression model (Friston et al., 1995). Additional regressors were included in the regression model to account for variance due to baseline shifts between time series, linear drifts within time series, and head motion. Beta-weights corresponding to the amplitude of the gamma function were extracted for each condition and for each node, and were scaled to mean % signal change values. Activations were projected onto each subject’s cortical surface, and the ROIs defined for each hemisphere on the basis of topographic criteria were overlaid. To evaluate the selectivity within individual visuotopic areas, the mean % signal change for each condition was averaged across all nodes within a given area that were activated by the current stimuli as defined by the contrast of all visual presentation blocks vs. fixation, thresholded at p < .0001, uncorrected for multiple comparisons. These data were further quantified by defining a scene
preference index (SPI). The scene preference index quantifies an area’s response preference evoked by scene stimuli relative to those evoked by inanimate object stimuli ($SPI = (R_{scene} - R_{object}) / (R_{scene} + R_{object})$, $R =$ average % signal change within a ROI). Positive index values indicate preference for scene stimuli, values around 0 indicate no preference, and negative values indicate preference for inanimate object stimuli. ANOVAs were used to assess statistical significance of percent signal change within and across cortical areas hV4, VO-1, VO-2, PHC-1, and PHC-2. Data were collapsed across hemispheres for further analysis, since no hemispheric differences were found for any of the ROIs for the different object conditions. Two-tailed t-tests were used to assess statistical significance of object responses for both index values and mean % signal change within each cortical area and for the behavioral data. Brain regions responding preferentially to scenes were identified by contrasting presentation blocks of scenes with inanimate objects ($p < .0001$, uncorrected for multiple comparisons). This yielded a contiguous cluster of bilateral activations within the collateral sulcus in posterior parahippocampal cortex and the transverse occipital sulcus in dorsal extrastriate cortex (Epstein et al., 1999). Brain regions responding preferentially to faces than to other objects were identified by contrasting presentation blocks of faces with inanimate objects ($p < .0001$, uncorrected for multiple comparisons; Kanwisher et al., 1997; Haxby et al., 1999). Brain regions responding preferentially to intact objects were identified by contrasting presentation blocks of inanimate objects with scrambled versions of the objects ($p < .0001$, uncorrected for multiple comparisons). Brain regions responding preferentially to motion were identified by contrasting presentation blocks of motion dots with static dots ($p < .0001$, uncorrected for multiple comparisons).
5.2 Results

Responses to object stimuli

We probed the response properties of ventral visuotopic areas to various object categories. The visuotopic areas within medial ventral visual cortex (see Chapters 2 & 4), were used as ROIs to examine the response properties evoked by scenes, faces, inanimate objects, and scrambled images. Percent signal changes of fMRI signals were calculated for each object category in areas hV4, VO-1, VO-2, PHC-1, and PHC-2 (Fig. 5.1b). In all areas, there was a main effect of object category (all Fs(3,21) = 4.83, ps < .01). Pairwise comparisons revealed significantly stronger responses evoked by scene stimuli than by face stimuli in all areas (all ts(7) > 2.51, ps < .05). However, neural responses in areas hV4 and VO-1 did not discriminate between scene, object or scrambled stimuli (all ts(7) < 2.14, ps > .05; Fig. 5.1b). Scene stimuli exhibited significantly stronger responses than all other categories (inanimate object, scrambled, and face stimuli) in VO-2, PHC-1 and PHC-2 (all ts(7) > 3.66, ps < .05; Fig. 5.1b).

To examine neural responses in different parts of the visual field as well as the specificity of the responses within visuotopically organized ventral visual areas, fifteen ROIs within hV4, VO-1, VO-2, PHC-1, and PHC-2 as well as adjacent (and lateral) to each area were sampled (Fig. 5.2a). Each ROI represented a 3 mm radius disc on the surface that was placed on the horizontal meridian of either foveal (denoted by red circles) or peripheral representations (denoted by blue circles). In addition, a control ROI adjacent, but lateral to each foveal ROI was defined (denoted by yellow circles). Percent signal changes of fMRI signals evoked by scenes, faces, inanimate objects, and scrambled pictures were calculated for each of these ROIs. As shown in Figure 5.2b, a main effect of object category was observed in all foveal and peripheral
ROIs (all Fs(3,21) = 5.40, ps < .01), except for the foveal representation of hV4, which was similarly activated by all object categories (F(3,21) = 1.19, p > .05). Pairwise comparisons were computed for all foveal and peripheral ROIs (except for hV4’s fovea). Scene stimuli evoked significantly stronger responses than all other stimulus categories in the foveal ROIs of PHC-1 and PHC-2 and in the peripheral ROIs of VO-2, PHC-1, and PHC-2 (scene vs. each other individual category per ROI, all ts(7) > 4.69, ps < .05; Fig. 5.2b). The remaining ROIs (foveal VO-1 and VO-2, peripheral hV4 and VO-1) responded more strongly to place, object, and scrambled pictures than to face stimuli (all ts(7) > 3.14, ps < .05), but did not discriminate between the three former categories (all ts(7) < 1.95, ps > .05; Fig. 5.2b), except for the peripheral representation of VO-1 that responded more strongly to places than to scrambled images (t(7) = 2.78, p < .05; Fig. 9b). There were no significant differences in responses evoked by stimuli of any category in the ROIs adjacent to the defined topographic regions (all Fs(3,21) < 2.54, ps > .05; Fig. 5.2b), except for the ROI lateral to VO-2 (F(3,21) = 3.04, p < .05), which

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**Figure 5.1: Responses to object stimuli in ventral visual cortex.** (a) Overlap of the parahippocampal place area (PPA), as defined based on the contrast scenes versus objects, with polar angle maps obtained in attentionotopy studies. The PPA heavily overlaps with PHC-1 and PHC-2. Face-selective activations, as defined by contrasting faces and objects, are shown for further reference. Outlines of the PPA defined at p < .001 (yellow) and p < 10^{-10} (magenta) are shown. (b) FMRI signals in mean % signal change evoked by various category stimuli in areas hV4, VO-1, VO-2, PHC-1, and PHC-2. Both PHC-1 and PHC-2 showed significantly greater responses to scenes than to other object categories. Vertical bars denote significant differences between categories for paired t-tests (p < .05, uncorrected).
showed significantly stronger responses for faces than scrambled pictures ($t(7) = 2.55, p < .05$; Fig. 5.2b), demonstrating the specificity of the response profiles within visuotopic areas. Taken together, these results suggest that PHC-1 and PHC-2 respond more strongly to places and scenes than to any other of the object categories tested here in both their peripheral and foveal representations.

To further quantify the stimulus category response profiles of each area and to compare preferred responses for scenes across areas, a scene preference index was calculated that evaluates preferential responses for scenes relative to inanimate objects (scene preference index, SPI, Fig. 5.3). This analysis confirmed the strong scene preference of PHC-1 and PHC 2. For the SPI, the foveal ROIs of PHC-1 and PHC-2 and the peripheral ROIs of VO-1, VO-2, PHC-1, and PHC-2 showed significant preference for scenes (all $t$s(7) > 2.54, $p_s < .05$; Fig. 5.3). HV4, foveal VO-1, foveal VO-2 and the ROIs adjacent and lateral to PHC-1 and PHC-2 showed no
such preference. Scene preference increased from more posterior to anterior areas. Both PHC-1 and PHC-2 showed significantly stronger scene preference than VO-1, and VO-2 for both foveal and peripheral ROIs (all ts(7) > 5.3, ps < .001), and PHC-2 showed significantly stronger scene preference than PHC-1 in both foveal and peripheral ROIs (both ts(7) > 3.686, ps < .01).

We also probed the response properties of three dorsal extrastriate areas and six lateral occipital areas areas to various object categories. The visuotopic areas described in Chapter 4 were used as ROIs to examine the response properties evoked by scenes, faces, bodies, inanimate objects, and scrambled images. Percent signal changes of fMRI signals were calculated for each object category in areas V3a, V3b, IPS-0, LO-1/2, TO-1/2, OT-1/2 (Fig. 5.4). Overall, stimulus selectivity was a bit more heterogeneous than in ventral visual cortex. Pairwise comparisons revealed significantly stronger responses evoked by scene stimuli than by face stimuli in V3a and V3b (ps < .05). Body stimuli exhibited significantly stronger responses than face stimuli in LO-2 (ps < .05). Body stimuli exhibited significantly stronger responses than any other stimuli in

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Image 324x189 to 540x720
TO-1/2 (ps < .05). Face and body stimuli exhibited significantly stronger responses than scenes and scrambled images in OT-1/2 (ps < .05; Fig. 5.4b). Object stimuli exhibited significantly stronger responses than scrambled in OT-1/2 and stronger response than scenes in OT-1 (ps < .05).

**Overlap of PHC areas with functionally defined PPA**

Given that the foveal and peripheral representations of PHC-1 and PHC-2, as well as the areas as a whole, preferentially responded to pictures of scenes, we compared the location and extent of the functionally defined parahippocampal place area (PPA; Epstein et al., 1999) in relation to these visuotopic areas. The PPA was defined as a contiguous cluster of activation within the collateral sulcus that responded more strongly to scenes than inanimate objects (thresholded at $p < .0001$, uncorrected). Outlines of the extent of PPA in individual subjects as well as those of face-selective activations (faces > object, thresholded at $p < .0001$, uncorrected) are illustrated in Supplementary Figures 2.3, 2.4, & 2.5 from chapter 2 (righthand panel). In all subjects, the PPA overlapped heavily with both PHC-1 and PHC-2 (Fig. 5.1a). The percentage of overlap was calculated for each hemisphere and then averaged across hemispheres to yield
group data. At a statistical threshold of \( p < .0001 \), 70.9% (±3) of the PPA overlapped with PHC-1 and PHC-2 in the RH and 67% (±7) in the LH. In 12 hemispheres of 6 subjects, a small portion of the PPA, 10.4% (±2) in the RH and 15.6% (±2) in the LH, extended into the peripheral representation of VO-2. In 10 of 16 hemispheres, a small portion of the PPA, 18.8% (±3), extended further anterior from PHC-2 into parahippocampal cortex. Conversely, 53.8% (±5) of PHC-1 and PHC-2 overlapped with the PPA in the RH and 47.7% (±8) in the LH. The extent of the PPA activation, and therefore the percentage overlap between PHC and PPA, was greatly affected by the statistical significance at which the activation maps were thresholded. When adjusting the statistical threshold, the overlap of PPA with PHC for the RH and LH spanned from 63% (±4) and 56% (±5) at a more lenient threshold of \( p < .001 \) to 79% (±4) and 76% (±6) at a more stringent threshold of \( p < 10^{-10} \), as illustrated in Figure 5.1. The overlap of PPA with PHC significantly differed between the three thresholds for both hemispheres (both \( F(2,14) > 11.53, ps < .05 \)). Both hemispheres showed significant linear trends with percentage overlap between PPA and PHC increasing at more stringent thresholds (both \( F(1,7) > 25.26, ps < .05 \)). At more liberal thresholds, the extent of the PPA activation spread further posterior to PHC within VO-2 as well as anterior to PHC and beyond retinotopically-defined cortex. However, all subject’s peak activations fell within the PHC areas and the average group Talairach coordinates for the peak activation of the PPA fell within PHC-2 for the RH and near the border of PHC-1 and PHC-2 for the LH (Table 2.1 from chapter 2).

**Overlap of visuotopically-defined areas with other functionally-defined areas**

Spatial overlap between visuotopically organized areas and areas defined by sensitivity to particular stimulus categories was observed throughout extrastriate visual cortex. The transverse
occipital sulcus area (TOS) was defined as a contiguous cluster of activation within dorsal extrastriate cortex that responded more strongly to scenes than to inanimate objects (thresholded at $p < 0.0001$, uncorrected). In each subject, the TOS heavily overlapped with visual areas V3b and IPS-0. Across subjects, 36.0% (±5) of TOS overlapped with V3b and 10.1% (±4) overlapped with IPS-0. The occipital face area (OFA) was defined as a contiguous cluster of activation within the occipital temporal sulcus that responded more strongly to faces than to inanimate objects (thresholded at $p < .0001$, uncorrected). In each subject, the OFA overlapped with phPIT. Across subjects, 60.3% (±6) of the OFA overlapped with OT-1/2. A portion of the OFA extended outside phPIT, around neighboring cortex. The lateral occipital complex (LOC) was defined as a dorsal cluster of activation within lateral occipital cortex and a ventral cluster of activation within ventral occipital cortex that responded more strongly to intact objects than scrambled versions (threshold at $p < .0001$, uncorrected). Across subjects, 16.6% (±3) of the dorsal portion of LOC overlapped with LO-2 and 40 (±2)% overlapped with OT-1/2 extending into adjacent cortex ventral to LO-2. The extrastriate body area (EBA) was defined as a cluster of activation within lateral occipital and medial temporal cortex that responded more strongly to intact objects than to inanimate objects (thresholded at $p < 0.0001$, uncorrected). Across subjects, 22.9% (±3) of the EBA overlapped with TO-1, 8.3% (±3) overlapped with TO-2, and 7.9% (±2) overlapped with LO-2. The motion-selective region (MT) was defined as a cluster of activation within medial temporal cortex that responded more strongly to moving dots than to static dots (thresholded at $p < 0.0001$, uncorrected). In each subject, MT overlapped heavily with TO-1 and TO-2. Across subjects, 55.8% (±3) of MT overlapped with TO-1 and TO-2.
5.3 Discussion

Within ventral temporal cortex, we found several visuotopic areas that preferentially responded to particular stimulus categories. In a complementary analysis, category-selective regions generally overlapped with at least two visual field maps. Visuotopic areas PHC-1 and PHC-2 responded more strongly to places and scenes than to any other of the object categories tested here in both their peripheral and foveal representations. V3b also showed a high degree of stimulus selectivity and responded more strongly to places and scene than to any other of the object categories. Lateral occipital areas, however, showed a broader response profile with sensitivity to multiple stimulus categories. TO-1 responded more strongly to both body and intact objects than to scrambled objects, faces or scenes. OT-1 responded more strongly to both faces and intact objects than to scrambled objects and scenes. In a complementary analysis, PHC-1 and PHC-2 were found to heavily overlap with the functionally defined PPA (Epstein and Kanwisher, 1998). The PPA has been shown to respond strongly to spatial layouts such as buildings, landmarks, rooms, tabletop scenes, and even ‘scenes’ made out of LEGO blocks (Aguirre et al., 1998; Epstein and Kanwisher, 1998; Epstein et al., 1999; see Epstein, 2008 for review). The PPA has also been shown to respond more strongly to contra- than to ipsilateral stimuli (MacEvoy and Epstein, 2007), consistent with our findings of visual field maps in the PHC areas that represent mainly contralateral space. Further, the PPA has been shown to respond more strongly to scene stimuli in the UVF as compared to foveal and LVF locations (Schwarzlose et al., 2008), again consistent with our findings of UVF and peripheral biases within the PHC areas. General object (LOC), face (OFA), body (EBA), and motion-selective (MT) areas also heavily overlapped with visuotopic cortex. Similar to the PPA, most of these stimulus-selective areas heavily overlapped with two visual field maps. Overall, these data
demonstrate that category-selective and visuotopic cortex are not distinct parts of the visual system.

Category-selective regions generally overlapped visual field maps at particular eccentricity ranges. Scene-selective cortex (PPA / TOS) largely overlapped with peripheral representations and face-selective cortex (OFA) largely overlapped with foveal eccentricities. Though consistent with previous observations of large-scale eccentricity biases across lateral occipital and ventral visual cortex (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002; Hasson et al., 2003), our data suggest that these eccentricity biases are part of separate clusters of visual field maps, and not one unified eccentricity organization (Malach et al. 2004). Our data highlight the prominence of eccentricity biases in both the category-selectivity and the visuotopic organization of ventral temporal cortex.

Adhering to the definition that an individual cortical area can only contain a single representation of the visual field (Allman & Kaas, 1971; Van Essen 1985), our data suggest that category-selective regions, such as PPA, OFA, EBA, and MT, are not individual cortical areas as each of these category-selective regions spanned multiple visual field maps. It is possible that visual cortex has multiple, distinct topographies that overlap at the scale of a voxel such that overlapping visuotopic and category-selective regions would be separate, complete cortical areas. Such an interpretation is difficult to evaluate with fMRI. However, fMRI studies in humans (Hemond et al. 2007; Schwarzlose et al. 2008) have shown visual field biases in the degree of selectivity for category-sensitive regions that reflect the underlying topographic organization, suggesting that these two dimensions are related. Further, functional connectivity
patterns between category-selective regions and early visual cortex also reflect topographical organization (Baldassano et al. 2012). Another possible interpretation is that each of these areas is actually a combination of multiple whole cortical areas. Our data suggest that this interpretation is also not likely, as these areas typically did not fully encompass any individual visual field map. As such, this would require the existence of single cortical areas within each visual field map, which by definition has a complete, non-redundant representation of visual space. Instead, our data suggest that these category-selective “areas” are neither a single cortical area, nor multiple whole cortical areas, but instead are multiple parts of several visuotopic areas. This does not take away from the high degree of category-specificity within these regions of cortex, but implies that such response properties only capture part of the complex computations within individual cortical areas.
6 The Organization of Anatomical and Functional Connectivity Across Visual Cortex

Cortical maps are thought to act as discrete processing units, with the pattern of connections between areas forming a complex network at multiple scales. As a general principle, neurons with overlapping representations of visual space are interconnected within and between visual maps. This topography of connectivity facilitates the local processing of a scene in a metabolically efficient manner (Kaas 1997). Theories about optimal organization of individual visual maps have been extended to propose that maps involved in similar computational processing form distinct ‘clusters’ anchored around a common foveal representation (Wandell et al. 2005; Brewer et al. 2005). This grouping minimizes the distance of connections between visual maps within a cluster, though such a pattern of connectivity has yet to be directly tested.

Much about the organization of connectivity across human visual cortex is inferred from the known anatomical connectivity of macaque visual cortex (e.g. Boussaoud et al. 1990; Felleman & Van Essen 1991; Felleman et al. 1997; Lewis & Van Essen 2000). However, a detailed account of connectivity across the human visual system is difficult to infer from the macaque. The visual system has undergone much cortical expansion from macaques to humans and it is unclear how to relate areas between species, as anatomical landmarks do not always provide a good predictor of similar functions (e.g. V3a and MT). The topographic maps we identified in both species offer a framework for relating connectivity measurements in the human with the known anatomical pathways in the macaque. In chapter 4, we showed that separate topographic pathways made up of several visual field maps linked these smaller clusters together. We investigated the functional and anatomical connectivity of this complex
topographic network using DTI and connectivity analyses on resting-state data. Both anatomical and functional data reveal large-scale patterns of connectivity that parallel known connections in the macaque.

6.1 Materials and Methods

**Subjects:** For human participants, eight healthy subjects (25-36 years old, 5 male) gave informed consent to participate in the study, which was approved by the Institutional Review Panel of Princeton University. Each subject participated in one scan session for the acquisition of diffusion-weighted data. Each subject also participated in two or more scan sessions to topographically map visual cortex (See Chapter 4). All subjects had normal or corrected-to-normal vision.

**Data acquisition:** *Diffusion scans:* Diffusion-weighted images (DWI) were acquired using an eddy-current compensated double spin-echo, echo-planar pulse sequence (22). Images with 2.0 mm³ resolution were collected using 60 different isotropic diffusion directions (*Jones et al. 1999*) (66 contiguous transverse slices; anterior to posterior phase-encode direction; FOV = 256 mm; 128 x 128 matrix; slice thickness = 2.0 mm; TR = 10 s; TE = 95 ms; interleaved acquisition; \(b\)-values = 0 and 1,000 s/mm²; 1,776 Hz/pixel bandwidth; 0.61 ms echo spacing). To improve the baseline SNR signal and to decrease the bias in tensor estimation, the ratio of DWI to non-DWI images acquired was increased from the scanner default 60:1 ratio to a 12:1 ratio (*Jones et al. 1999; Zhu et al. 2008*). Cardiac gating was used to minimize artifacts due to pulsatile motion (*Wheeler-Kingshott et al. 2002; Nunes et al. 2005*). A total of six 60-direction
sets of diffusion-weighted data was acquired for subsequent averaging. A gradient echo field map and a magnitude image with slice prescriptions identical to the diffusion-weighted images were also acquired to perform geometric unwarping during preprocessing (TR = 500 ms; TE = 5.23 / 7.69 ms; flip angle = 55°; 1,502 Hz/pixel bandwidth). All diffusion-weighted images were aligned to a high-resolution anatomical scan taken at the end of each session (MPRAGE sequence, same parameters as above anatomical scans). Total scan time for each subject was approximately 2 hours.

Functional scans: Data were acquired with a 3T Skyra magnetic resonance imaging (MRI) scanner (Siemens) using a sixteen-channel head coil. All functional acquisitions used a gradient echo, echo planar sequence with a 64 square matrix (slice thickness of 4mm, interleaved acquisition) leading to an in-plane resolution of 3 x 3 mm² [field of view (FOV), 192 x 192 mm²; 32 slices per volume for resting state and 27 for movie stimuli; repetition time (TR) = 1.8s for resting state and 1.5s for movie stimuli; echo time (TE) = 30 ms; flip angle = 72°]. High-resolution structural scans were acquired in each scan session for registration to surface anatomical images (MPRAGE sequence; 256 matrix; TR, 2.5s; TE 4.38ms; flip angle 8°, 1 x 1 x 1 mm resolution).

Data analysis: Data were analyzed using the AFNI software package (Cox & Hyde 1996), FreeSurfer (Dale et al. 1999; Fischl et al. 1999), SUMA (http://afni.nimh.nih.gov/afni/suma), MATLAB (The MathWorks, Natick, MA), and FSL (Smith et al. 2004).
Defining Regions of Interest (ROIs): Whole visual cortex ROIs were drawn on the surface to include occipital, ventral temporal, and posterior parietal cortex. Visual field map ROIs were identified from topographic mapping studies described in studies 1.1 and 1.2. In order to align the ROIs to the DTI data, the anatomical scan acquired during the topographic mapping sessions was skull-stripped using FMRIB’s Brain Extraction Tool (BET; Smith 2002) and registered using FMRIB’s Linear Registration Tool with a 6 DOF affine registration (FLIRT; Jenkinson & Smith 2001) to the anatomical scan acquired during the DTI scanning session to derive a transformation matrix between the two spaces. This transformation matrix was subsequently applied to the ROI masks from the fMRI scanning sessions to register them to the DTI structural volume. The ROI masks were then transformed into DWI space, and visually inspected for proper alignment, prior to probabilistic tractography analyses.

Probabilistic diffusion tractography: All DWI were corrected for eddy currents and head motion using affine registration (12 DOF) to a non-DWI reference volume, and then averaged to improve the signal-to-noise ratio (Jenkinson & Smith 2001). Next, images were geometrically unwarped with FMRIB’s Utility for Geometrically Unwarping EPIs (FUGUE) using an averaged, skull-stripped non-DWI reference volume. The anatomical volume was skull-stripped using BET, and co-registered to the averaged non-DWI reference volume with 12 DOF affine using FLIRT to derive the transformation matrix between the two spaces.

Tractography analyses were conducted using FMRIB’s Diffusion Toolkit (FDT). For each subject, probability distributions of fiber direction at each voxel (two fiber populations modeled per voxel) were calculated using previously described methods (Behrens et al. 2003a;
Behrens et al. 2003b). Briefly, these probability distributions’ widths correspond to fiber direction uncertainty due to MR noise, artifacts, and incomplete modeling of the diffusion data. With the probability distributions, we ran three separate probabilistic diffusion tractography (PDT) analyses.

First, a voxel-wise PDT analysis was performed across the whole visual cortex. Tracking was performed between all voxel pairs to derive a connectivity profile across visual cortex. From each seed voxel, 5000 samples were drawn from the probability distribution (0.2 curvature threshold, 0.5-mm step length, distance corrected), and the proportion of these samples passing through each target voxel were recorded as the probability of connection (PoC) to that target. No thresholding was performed on the PoC for the reported results. Next, voxels were binned by visual field map and averaged to derive PoC profiles for each visual map. To measure the PoC between visual map pairs, voxel pairs between each visual map pair were binned and averaged. Optimal community structure (Brain Connectivity Toolbox: https://sites.google.com/site/bctnet/measures/list) was calculated by subdividing the data into non-overlapping groups in a way that maximizes the number of within-group links, and minimizes the number of between-group links. To visualize the community structure, multidimensional scaling (Matlab: cmdscale) was performed to reduce the data dimensions, and the principle two dimensions were plotted with all links between maps. Visual maps’ PoCs across visual cortex were correlated with each other to assess the similarity of anatomical connectivity between visual maps. Optimal community structure and multidimensional scaling were also performed on these data.
In a second analysis, a probabilistic tracking was performed to inspect the probable paths that pass through medial ventral temporal (PHC-2), lateral ventral temporal (FFA), posterior parietal (IPS-2), and lateral occipital (TO-1) ROIs, individually, for anatomical plausibility. An exclusion mask was used to restrict our analyses to ipsilateral trajectories. The estimated fiber tracts were thresholded by removing the bottom 5% of estimates. To compare the results of each subject, a conjunction analysis was performed on each of the pathways. First, each subject’s anatomical image was skull-stripped with BET, intensity bias field-corrected using FMRIB’s Automated Segmentation Tool (FAST, (Zhang et al. 2001)), and noise-reduced using the FMRIB’s Smallest Univariate Segment Assimilating Nucleus tool (Smith & Brady 1997). Next a linear registration was performed on the processed anatomical image to the MNI 152 template brain using FLIRT to create an affine transform matrix (12 DOF) for use during the nonlinear registration procedure. Using the affine transform matrix, a nonlinear warp transformation for each subject’s original anatomical image was then calculated and applied using the FMRIB’s Nonlinear Image Registration Tool (FNIRT). The resulting nonlinear warp matrices were then applied to each subject’s PHC-2, FFA, IPS-2, and MT pathways using nearest neighbor interpolation to conserve the voxel values of the hard segmentation, and overlaid upon the MNI 152 template brain image. To derive a “group topographic ROIs”, the same conjunction analyses was performed for the ROI masks for early visual, dorsal extrastriate, lateral occipital, and medial, ventral temporal areas.

To directly test the anatomical connectivity within ventral visual cortex, a PDT analysis was performed to estimate the pathways that pass through any voxel in a single seed area (PHC-2), and the probability that such pathways will pass through a voxel in one of the ventral visual
ROIs (hV4, VO-1, VO-2, or PHC-1), a dorsal extrastriate ROI (V3a), a lateral fusiform ROI (FFA), and a lateral occipital ROI (LO-2) (i.e., “single mask seed with classification targets” tractography in the FDT toolkit). From each seed voxel, 5000 samples were drawn from the probability distribution (0.2 curvature threshold, 0.5-mm step length, distance corrected), and the proportion of these samples passing through each target area were recorded as the probability of connection to that target. Identical inter-hemispheric exclusion masks and coronal waypoint masks were used as in the first PDT analysis. We recorded the number of projections to a target area as a proportion of the number going to both targets. We next calculated the mean proportion of projections from PHC-2 to each target area by taking the mean value for all voxels in the seed area, therefore allowing us to compare the projection patterns of the seed areas (Croxson et al. 2005; Ramnani et al. 2006). Mean proportions of projections were averaged across subjects, and repeated-measures analyses of variance (ANOVA) were performed, with factors for target area and hemisphere, followed by paired-samples t-tests for planned comparisons.

Resting-state functional connectivity: Functional data were slice-time and motion corrected. In preparation for functional connectivity analyses, several additional steps were performed on the data: (1) removal of potential “spike” artifacts using AFNI’s 3dDespike; (2) temporal filtering retaining frequencies in the 0.01-0.1 Hz band; (3) linear and quadratic detrending; and (4) removal by regression of several sources of variance: (i) the six motion parameter estimates and their temporal derivatives, (ii) the signal from a ventricular region, and (iii) the signal from a white matter region. The global mean signal (GMS) was not removed in the reported results, though results were consistent, if not marginally stronger, when GMS was
removed. To minimize the effect of any evoked response due to the scanner onset, the initial 20s were removed from each scan. All voxels that fell between the gray and white matter boundaries were mapped to the surface (nodes). No additional spatial filtering was applied on data used for eccentricity-based correlation analyses. The time-series from all nodes spanning occipital, posterior parietal, and ventral temporal cortex, including visuotopic areas V1, V2, V3, hV4, LO-1/2, TO-1/2, OT-1/2, VO-1/2, PHC-1/2, V3a/b, IPS-0-5, SPL as well as posterior fusiform cortex, were extracted into MATLAB for correlation and cluster analyses. Nodes were grouped by visual map for right and left hemispheres separately. The time-series of all nodes were averaged to derive a mean time-series for each visual map. Pearson correlation coefficients were calculated between the mean time-series of maps. Optimal community structure and multidimensional scaling were also performed on these data.

6.2 Results

Detailed visuotopic, anatomical, and functional connectivity organization of the visual system were assessed in twelve participants. Retinotopic organization of the visual system was examined using a conventional travelling wave paradigm in which eccentricity and polar angle maps were collected to define visual areas V1, V2, V3, hV4, V3a/b, IPS-0/2/3/4/5, SPL, LO-1/2, TO-1/2, OT-1/2, VO-1/2, and PHC-1/2 (Materials and Methods). Anatomical connectivity was estimated using probabilistic analyses on diffusion tensor imaging. Functional connectivity organization was probed in two resting conditions in which participants were instructed to: (1) keep eyes open and maintain fixation on a centrally presented dot or (2) keep eyes closed for the duration of the run. In eight subjects, functional connectivity organization was also probed in two
movie viewing conditions in which participants were instructed to: (1) maintain fixation while attending to the movie or (2) freely view the movie.

To investigate the topography of anatomical connectivity across visual cortex, probabilistic estimates of connectivity (PoC) were computed between all voxel pairs within a cortical region of interest spanning occipital, temporal, and parietal cortices and covering all identified visual maps. In individual subjects, voxels were binned based on visual field maps and the mean probability of connection was derived between all visual map pairs. These data were averaged to derive a group anatomical connectivity matrix (Fig 6.1). A clear structure was evident in the group connectivity matrix that largely differentiated early visual, parietal, lateral occipital, and ventral temporal cortices. The group connectivity data was clustered using a local community structure algorithm, which maximizes the number of within-cluster connections and minimizes the number of between-cluster connections. Clustering using unthresholded connectivity data, yielded 3 segmentations: one containing early visual and ventral areas (V1/2/3, hV4, VO-1/2, PHC-1/2), a second containing lateral occipital areas (LO-1/2, TO-1/2, OT-1/2), and a third containing dorsal extrastriate and parietal areas (V3a/b, IPS-1/2/3/4/5, SPL). A similar segmentation was achieved
when thresholding out the bottom 50% of connections, though the first cluster split into two clusters differentiating early visual from ventral temporal cortex. To better visualize this structure, multidimensional scaling was applied to the group connectivity matrix and the top two and three dimensions were plotted (Fig 6.2). Both visualizations illustrate the segmentation of visual areas from the clustering algorithm. The separation between dorsal and ventral visual areas mirrors the known broad two-pathway distinction in the macaque. The distances between areas within many visual field map clusters were smaller (e.g. V3a/b, LO-1/2, TO-1/2, and OT-1/2) than distances between adjacent areas that are parts of separate clusters (e.g. V3a/V3, LO-
To compare the profile of anatomical connectivity across the whole visual cortex between areas, we calculated the mean PoC for all voxels within an area with all voxels in our cortical region of interest. The mean PoC profiles were correlated between areas in individual subjects and then averaged to derive a group mean connectivity similarity matrix. As with the anatomical connectivity matrix, there was a broad distinction between early visual, ventral temporal, lateral occipital, and dorsal / parietal cortices, suggesting that areas that are more directly connected also have similar connectivity profiles across visual cortex.

Next, we investigated the topography of functional connectivity across visual cortex under two task-free “resting” states and during two movie viewing conditions. Pearson correlation coefficients were computed between the mean time series of all areas within the left and right visual cortices in individual subjects and then averaged to derive a group functional connectivity matrix (Fig. 6.3). As with the anatomical connectivity data, there was a qualitative structure in the functional group connectivity matrices that largely differentiated early visual, ventral temporal, parietal, lateral occipital cortices. The connectivity data was then clustered using the same local community structure algorithm utilized in the diffusion data analyses. For task-free, resting-state data, segmentations yielded three large clusters in both datasets: early visual / ventral temporal, lateral occipital, and dorsal / posterior parietal, and one cluster comprised of V1 alone. For movie-viewing data, segmentations yielded four large clusters for fixation datasets: early visual, ventral temporal, lateral occipital, and dorsal / posterior parietal, and three large clusters for free-viewing datasets: early visual / ventral temporal, lateral occipital, and dorsal / posterior parietal cortex. Each area’s connectivity profile was similar between task-free and movie-viewing conditions (avg $r = .93 \pm .02$), suggesting that the general patterns of
connectivity across visual cortex did not differ greatly in the presence and absence of a strong bottom up drive.

To look at the relation between structural and functional connectivity patterns, the resting state connectivity data were correlated with the diffusion connectivity data (Fig 6.4). Each area’s functional and anatomical connectivity profiles were similar regardless of task-free or movie-viewing conditions (across areas, avg $r = .78 \pm .04$ for eyes open, $.81 \pm .04$ for eyes shut, $.81 \pm .04$ for fixation, and $.83 \pm .03$), demonstrating a strong structure-to-function correspondence across visual cortex.

Figure 6.3: Functional connectivity between 23 cortical visual maps during eyes shut and eyes open “resting” conditions. Average connectivity matrix across subjects shows the average correlations between the average time series for all visual map pairs. Each area was generally most strongly correlated (yellow-red) with itself and neighboring areas, and weakly correlated (blue) with distant areas. Five broad patterns are apparent that match rough anatomical regions (color coded). The pattern of correlations was near identical between the two resting state conditions ($r = .93$). The pattern of correlations is qualitatively similar to the DTI connectivity matrix.
Across visual cortex, the patterns of functional and anatomical connections differentiated greatly between parietal, lateral occipital, and ventral temporal cortices. Such a distinction is consistent with our proposition in chapter 4 that the visual field maps in these regions of cortex form separate topographic pathways. Within these pathways, visual field maps cluster around a common, distinct foveal representations. It has been proposed that the functional cluster share computational resources. As such, the local connectivity within clusters should be greater than the connectivity between clusters. We tested this by comparing the strength of connectivity between areas within a cluster (e.g. LO-1 & LO-2) to the strength of connectivity between adjacent areas in different clusters (e.g. LO-2 & TO-1) (Fig. 6.5). Functional connectivity was significantly stronger between areas within a cluster than between clusters ($p < .05$) for all clusters except V3a. Connectivity between V3a and V3b was surprisingly weak, and actually significantly weaker than connectivity between V3a and IPS-0 ($p < .05$). Visual cluster OT was left out of this analysis because it does not directly abut other visual field maps, though the connectivity within was higher than nearby areas hV4 and LO-1/2. Anatomical connectivity was only significantly stronger for connectivity within TO ($p < .05$), but not for any other area. In fact, the connectivity strengths were near identical for LO, VO, and PHC. These data support...
the hypothesis that visual maps within a cluster are involved in similar computational processing, and provide a nice control that the local connectivity patterns that dominate the connectivity profiles are not simply an artifact of signal spread along the cortical surface.

The anatomical data did not show greater connectivity between areas within a cluster. One possibility is that the diffusion data is more sensitive are revealing such local connectivity, and is more sensitive for identifying major pathways linking areas across visual cortex. To test this, we looked at the connectivity of individual maps with the rest of visual cortex, unrestrained by visual area. Three maps were tested and anatomical region where visual maps have not (yet) been identified. Each seed area was located within a different part of cortex: medial ventral temporal (PHC-2), lateral occipital (TO-1), posterior parietal (IPS-2), and a medial region of the lateral fusiform. For the IPS-2 and PHC-2 maps, connectivity was strongest to neighboring visual maps and was largely confined to within the extent of visual field maps (Fig 6.6). Average group connectivity show that the connectivity patterns were largely distinct across these four areas. Connectivity from the three maps was largely confined to the local stream of visual maps. The fusiform anatomical connectivity was largely separate from any of the topographic maps, though partially overlapped with hV4 and

![Figure 6.5: Functional and anatomical connectivity within and between clusters. The strength of connectivity between visual maps within a cluster (light grey) and between clusters (dark grey) was measured for five clusters: V3a/b, LO, TO, VO, and PHC. Functional connectivity was strongest between maps within a cluster than between for all clusters except V3a/b. Only TO showed significantly stronger connectivity between maps within a cluster than between for anatomical data.](image)
likely OT-1/2 posteriorly. We quantified the degree of PoC for one area, PHC-2, with the neighboring and distinct visual maps as well as adjacent anatomical region with no clear visuotopic organization (Fig. 6.7). Connectivity was strongest with neighboring maps and weakest for distant maps (LO-1 and V3a). Connectivity was also significantly weaker with the adjacent lateral fusiform region than PHC-1 and VO-1/2 (p < .05) despite being the closest area to PHC-2. These data suggest that the prominent local connectivity connect visual maps within specific topographic streams, allowing for the communication of information between adjacent map clusters (e.g. VO and PHC).

6.3 Discussion

We investigated the organization of anatomical connectivity across human visual cortex. We compared the large-scale connectivity patterns between visual maps with the functional connectivity patterns observed during conditions in which there was little or no bottom-up input.
(resting-state) and during conditions in which there was a dynamic bottom-up input (movie viewing). We found strong similarities between the patterns of anatomical and functional connectivity across visual cortex. Connectivity was strongest regionally, and formed distinct paths within ventral temporal, lateral occipital and posterior parietal. These paths almost entirely overlapped with separate groups of areas that we proposed in chapter 4 form distinct topographic streams. Within each topographic stream, functional connectivity was greatest between areas within a cluster than between areas in adjacent clusters. The anatomical connectivity did not differentiate between clusters within a topographic stream, but differentiated topographic streams between each other and the surrounding cortex. These data suggest that the prominent connectivity patterns within the visual system are local, connecting individual areas to form a network of topographic streams.

These data are broadly consistent with the known connectivity patterns in the macaque. Methodological differences make comparisons between the degree (or probability) of connectivity in imaging data and macaque tracer data difficult. Tracer studies often only report whether a connection was present or absent, and lack information on the strength of connectivity. Nevertheless, there were several similarities in the large-scale patterns of connectivity between our results and macaque tracer studies. There was a broad distinction in connectivity between...
dorsal and ventral cortex. Such a distinction is also apparent when applying the same analyses to the anatomical connectivity of macaque visual cortex (Supplementary Fig. 6.1). Connectivity patterns across macaque visual cortex also largely differentiate the superior temporal sulcus (STS) from ventral temporal cortex (Morel et al. 1990; Baizer et al. 1991; Knierim & Van Essen 1992; Kravitz et al. 2013). Based on our cross-species comparisons on the organization of visual field maps, the visual maps within human lateral occipital cortex parallel the maps within macaque STS. We found a distinction in the connectivity patterns between human ventral temporal and lateral occipital cortex, paralleling the ventral temporal – STS distinction in macaques. Our data support the distinction of parietal, temporal, and lateral occipital visual maps into three separate regions based on anatomical connectivity.

Within these regional parcellations, functional connectivity was strongest between areas within a visual field cluster. As discussed in chapter 4, visual field map clusters minimize the distances between maps that are involved in similar perceptual processing. In chapter 5, we showed that stimulus-evoked activity was similar for maps within individual clusters. Here, we show, for the first time, that intrinsic functional connectivity is greater between areas within clusters than between clusters. These data support the interpretation that the visual field map cluster is an important organizational principle for the efficient processing of information between areas.

Local, regional connectivity was much more prominent in our imaging data than long-range connectivity. Long-range connections are known to exist in the macaque visual system between dorsal and ventral cortex (Felleman & Van Essen 1991). It is possible that the imaging
methods we used are too locally biased to reveal these long-range connections. We do not think this is the case as we saw strong long-range connections in other parts of cortex known to have prominent long-range connectivity (e.g. IPS to FEF). Connections between areas such as V4 and IPS are apparent in our data, though these connections are much weaker than the local connectivity. Anatomical tracer studies that report strength of connectivity actually show similar gradients of connectivity strength that are locally biased as well (Lewis & Van Essen 2000). This regional connectivity is likely an extension of organizational principles within individual maps and visual clusters that minimizes the distances between clusters that are functionally related. These data suggest that the organization of connectivity throughout the primate visual system minimizes distances between areas that share computational resources at multiple spatial scales and are involved in similar perceptual processing.

The pattern of functional connectivity across visual cortex was strikingly similar during conditions in which there was little or no bottom-up input (resting-state) and during conditions in which there was a dynamic bottom-up input (movie viewing). Our results suggest that the large-scale patterns of communication between visual areas are largely constant regardless of processing with stimulus- and task-based processing occurring within this organization. This is surprising given that decades of research on the primate visual system have demonstrated that stimulus input and task conditions significantly modulate activity within individual areas as well as communication between areas. The observed connectivity and stimulus- / task-evoked activity may reflect different components of neuronal processing via distinct mechanisms (Donner et al. 2013). Studies have shown a close relationship between frequency-specific oscillations and BOLD activity (Logothetis et al. 2001; Fox & Raichle 2007; Goense and Logothetis 2008) as
well as BOLD connectivity (Nir et al. 2008; Wang et al. 2012), and that this relationship reflects local neural computations (Canolty & Knight 2010; Siegel et al. 2012). As such, these connectivity patterns may reflect intrinsic dynamics across visual cortex. These intrinsic fluctuations between areas may simply reflect the topographic organization of visual field maps (Heinzle et al. 2011), but may also reflect a more “global” organization (Nir et al. 2006; Yeo et al. 2011). The structure of the observed connectivity between areas remains to be explored.
7 Large-scale Eccentricity-based Organization of Functional Connectivity Across Visual Cortex

The retinotopic organization of individual areas is thought to provide an infrastructure for the integration of information across areas along the visual hierarchy (Kaas 1997; Wandell et al. 2007). Indeed, anatomical connectivity studies in the macaque visual cortex have demonstrated that neurons with overlapping receptive fields are connected to each other across visual areas (Cragg 1969; Maunsell and Van Essen 1983; Van Essen and Zeki 1978; Zeki 1969). Similarly, using fMRI functional connectivity analyses in humans (Biswal et al. 1995; Fox & Raichle 2007), Heinzle and colleagues (2011) reported retinotopically-organized connectivity between two early visual areas, V1 and V3. In addition to such topographically-local connections between neurons with overlapping receptive fields, large-scale connectivity patterns have been observed between foveal and peripheral visual cortex in macaques (Zeki 1969; Colby et al. 1988; Nakamura et al. 1993; Ungerleider et al. 2008; Gattass et al. 2005; Vincent et al. 2007) and in humans (Dougherty et al. 2005; Yeo et al. 2011). While these patterns may be important for the integration of information across the entire visual field, the governing organization principles of such large-scale connectivity patterns are still unknown.

In this study we used fMRI to investigate the relationship between functional connectivity patterns and the retinotopic organization of individual areas to evaluate local- and large-scale functional organizational principles. Functional connectivity analyses were performed on data collected during task-free conditions (eyes closed and fixation), and during real-life movie viewing conditions (fixation and free-viewing). To evaluate the local
connectivity, we examined the pattern of correlations between areas with overlapping visual field representations. To evaluate large-scale connectivity, we examined the pattern of correlations across areas with non-overlapping visual field representations. First, our data provide additional support for the well-documented connectivity between areas based on overlapping receptive fields. In addition, our analysis reveals a novel large-scale organization pattern based on eccentricity representation, in which areas with non-overlapping visual field representations, but with matching eccentricity representations, are correlated. The eccentricity-based functional connectivity was consistent between upper and lower visual fields as well as between hemispheres. Moreover, the eccentricity-based correlation pattern was apparent across all conditions (rest, movie viewing, fixation and free viewing), demonstrating that this pattern cannot be accounted for by confounding factors such as cortical distance, eye movements, stimulus induced correlation, or intrinsic artifacts. This novel eccentricity-based large-scale organization principle provides a new functional parcellation scheme of the visual cortex, which is orthogonal to the standard retinotopic parcellation.

7.1 Materials and Methods

Participants. 12 subjects (aged 24-34 years, 6 females) participated in the study, which was approved by the Institutional Review Panel of Princeton University. All participants were in good health without history of psychiatric or neurological disorders and gave their informed written consent. Subjects had normal or corrected-to-normal visual acuity.

General Procedure. All subjects participated in 3 scanning sessions, during which resting state scans were collected, high-resolution structural images were acquired for cortical surface
reconstructions, and polar angle and eccentricity measurements were obtained to delineate retinotopic areas. 10 subjects participated in 2 additional scanning sessions, during which subjects viewed movie clips.

**Resting State.** Each subject participated in two versions of resting state: (1) fixation; (2) eyes closed. During the fixation scans, subjects were instructed to maintain fixation on a centrally presented dot (0.3° diameter) overlaid on a mean grey luminance screen background for 10 minutes. During the eyes closed scans, the projector was turned off and subjects were instructed to keep their eyes closed for 10 minutes. Two runs were collected per resting condition.

**Movie Conditions.** Ten subjects participated in two versions of movie viewing where a movie clip with audio from the film, *Dog Day Afternoon*, was presented: (1) free-viewing; (2) fixation. During the free-viewing scans, subjects were instructed to watch the movie and were allowed to freely move their eyes. During the fixation scans, subjects were instructed to attend to the movie, but maintain fixation on a centrally presented dot (0.3° diameter). Movie stimuli subtended 20° horizontally and 16° vertically. Two runs were collected per condition with each run lasting 5 minutes 45 seconds.

**Retinotopic Mapping.** Polar angle and eccentricity representations were measured using a standard traveling wave paradigm consisting of a colored checkerboard wedge or rings, respectively (Swisher et al. 2007, Arcaro et al. 2009, 2011). For eccentricity mapping, the annulus increased on a logarithmic scale over time in size and rate of expansion to approximately
match the human cortical magnification factor of early visual cortex (Horton and Hoyt, 1991; Swisher et al. 2007). Each run consisted of eight 40s cycles. For each subject, 4-5 polar angle runs and 2-3 eccentricity runs were collected. Visual areas V1, V2, V3, hV4, V3a/b, LO-1/2, IPS-0 (V7) were defined using criteria previously reported (Sereno et al. 1995, DeYoe et al.1996, Engel et al. 1997, Brewer et al. 2005, Wandell et al. 2007; Arcaro et al. 2009). Areas VO-1/2 and PHC-1/2 were defined using a similar experiment, targeting ventral-temporal cortex. For more details, see Arcaro et al. 2009, 2011.

Data Acquisition and Preprocessing. Data were acquired with a 3T Skyra magnetic resonance imaging (MRI) scanner (Siemens) using a sixteen-channel head coil. All functional acquisitions used a gradient echo, echo planar sequence with a 64 square matrix (slice thickness of 4mm, interleaved acquisition) leading to an in-plane resolution of 3 x 3 mm² [field of view (FOV), 192 x 192 mm²; 32 slices per volume for resting state and 27 for movie stimuli; repetition time (TR) = 1.8s for resting state and 1.5s for movie stimuli; echo time (TE) = 30 ms; flip angle = 72°]. High-resolution structural scans were acquired in each scan session for registration to surface anatomical images (MPRAGE sequence; 256 matrix; TR, 2.5s; TE 4.38ms; flip angle 8°, 1 x 1 x 1 mm resolution).

Data Analysis. Data were analyzed using AFNI (Cox, 1996) (http://afni.nimh.nih.gov/afni/), SUMA (http://afni.nimh.nih.gov/afni/suma/), MATLAB, and FreeSurfer (Dale et al. 1999; Fischl et al. 1999) (http://surfer.nmr.mgh.harvard.edu/). Functional data were slice-time and motion corrected. In preparation for functional connectivity analyses, several additional steps were performed on the data: (1) removal of potential “spike” artifacts using AFNI’s 3dDespike; (2)
temporal filtering retaining frequencies in the 0.01-0.1 Hz band; (3) linear and quadratic
detrending; and (4) removal by regression of several sources of variance: (i) the six motion
parameter estimates and their temporal derivatives, (ii) the signal from a ventricular region, and
(iii) the signal from a white matter region. The global mean signal (GMS) was not removed in
the reported results, though results were consistent, if not marginally stronger, when GMS was
removed. To minimize the effect of any evoked response due to the scanner onset, the initial 20s
were removed from each scan. All voxels that fell between the gray and white matter boundaries
were mapped to the surface (nodes). For node-based correlations and cluster analyses, data were
spatially filtered using a Gaussian filter to a maximum smoothness of 4 mm full-width at half-
max (FWHM) (by estimating the FWHM before spatial filtering), ensuring uniformity across the
surface and maintaining spatial specificity while increasing the signal-to-noise ratio (SNR) (Chung et al. 2005). No additional spatial filtering was applied on data used for eccentricity-based
correlation analyses. The time-series from all nodes spanning occipital, posterior parietal, and
ventral temporal cortex, including visuotopic areas V1, V2, V3, hV4, LO-1/2, VO-1/2, PHC-1/2,
V3a/b, IPS-0 (V7) as well as posterior fusiform cortex, were extracted into MATLAB for
correlation and cluster analyses.

Eccentricity-based Correlation Analysis. For each experimental scan, nodes were grouped by
visual area (V1, V2, V3, hV4, V3a/b) for right and left hemispheres separately. Visual areas V1,
V2, and V3 were separated into dorsal and ventral parts. For each visual area, nodes were further
subdivided into 12 equidistant bins spanning 0 log⁰ to 12 log⁰ eccentricity. Though the
eccentricity values measured using an annulus with a logarithmic scaling do not directly
correspond to visual degrees, eccentricity values from a log-scaled stimulus were used for the
current analyses because: (1) the cortical magnification factor in early visual cortex is accounted for, yielding an even distribution of nodes across eccentricity bins; (2) subsequent cluster analyses on the data yielded eccentricity-based segmentations that did not reflect cortical magnification. To ensure that the log-scaled eccentricity stimulus was not confounding the results, analyses were re-run using eccentricity values that were converted into visual degrees. Comparable eccentricity-based connectivity effects were observed in this control analysis. For each visual area, the time-series of all nodes within each eccentricity bin were averaged to derive a mean time-series for each eccentricity bin. Pearson correlation coefficients were calculated between the mean time-series of all eccentricity bins within as well as between visual areas. For each pair of visual areas, connectivity matrices were created containing all possible eccentricity bin correlations. Correlation coefficients varied considerably between connectivity matrices. To illustrate the consistency in the pattern of correlations across connectivity matrices in the display figures, and not the overall magnitude differences between them, correlation coefficients were z-scored within each connectivity matrix. Connectivity matrices were averaged for repeat runs to yield an average connectivity matrix for each task (resting-fixation, resting-eyes shut, movie-free viewing, movie-fixation).

Next, the disparity between eccentricity values for each bin pair were calculated such that the disparity between 2-3 log-degrees bin and the 4-5 log-degrees bin was 2 and the disparity between 1-2 log-degrees bin and the 7-8 log-degrees bin was 6. An eccentricity disparity matrix was created containing the disparity in eccentricity representations between all correlation bin pairs (Fig. 2B, left). Correlation coefficients within each connectivity matrix were grouped as a function of this eccentricity disparity matrix (Fig. 2B, center). This yielded several correlation
estimates for each eccentricity disparity. Grouped correlation coefficients were averaged to yield mean correlation coefficients for each eccentricity disparity from 0 – 11. Though the total number of correlation estimates varied between eccentricity disparities, this only affected the variance estimate in individual subjects, not the mean correlation. The magnitude of correlation coefficients varied across subjects and visual area pairs. To minimize this magnitude variability but preserve the relation of correlations across eccentricity disparities, correlation coefficients were normalized to the mean correlation coefficient at an eccentricity disparity of 0 (iso-eccentricity) as follows: 

\[ 1 - (r_{0\text{disparity}} - r_{X\text{disparity}}), \]

yielding a scale where 1 equals the correlation value of 0 disparity. Values smaller (larger) than 1 indicate that the correlations decrease (increase) with increased eccentricity disparity. Normalized correlation coefficients were averaged across subjects to derive group mean normalized coefficients. The correlation between the magnitude of the normalized coefficients and eccentricity disparities was calculated for each visual area pair in individual subjects. These correlations were Fisher Z-transformed for statistical tests.

For each visual area pair, two-tailed t-tests were performed on these values to assess whether the correlation reliably differed from 0. Statistical significance was further tested using a non-parametric permutation test where the disparity labels for each correlation were shuffled prior to grouping. This permutation was run 10,000 times, and the 97.5% and 2.5% bootstrap intervals were compared to the non-permuted data. A linear regression was performed on the disparity correlations (non-normalized) for each visual area pair in each subject. The slopes were used to evaluate the strength of eccentricity-based connectivity between area pairs and across conditions. Group mean slopes were calculated for each visual area pair.
The same correlation analyses were performed using polar angle data in which each area was divided into 12 polar angle bins, and correlations based on polar angle disparities between bins were derived. Correlations were calculated in two ways: 1) by calculating the smallest difference between polar angle values; 2) by reflecting polar angle values across the vertical and horizontal meridians and then calculating the smallest difference between these values. The former case tested for pure polar angle-based connectivity and the later tested for mirror symmetrical polar angle connectivity along the horizontal and vertical meridians.

**Cluster Analysis.** For each experimental scan, functional connectivity matrices were calculated by computing Pearson correlation coefficients for all possible node pairs within (intra-) as well as between (inter-) hemispheres. Connectivity matrices were averaged for repeat runs to yield an average connectivity matrix for each task (resting-fixation, resting-eyes shut, movie-free viewing, movie-fixation). K-means (least-squares) segmentation was used to partition each average connectivity matrix into k clusters in which each node belongs to the cluster with the nearest mean. The number of clusters (k) in the k-means segmentations was set by the experimenter. K-means segmentation was conducted with 2, 4, 8, and 16 clusters. The segmentation was run 5 times on each dataset, each with a new set of initial cluster centroid positions, and the iteration with the lowest variance was kept. Since the initial set of cluster centroid positions was random, cluster numbering varied across iterations of the algorithm even for the same data. Cluster numbers were anchored to a common source by computing the mean time series in each cluster and correlating each cluster’s mean time series with that of a foveal cluster within early visual cortex. The cluster numbers were reordered relative to the strength of
their correlation with the fovea cluster. C-means and Louvain clustering (not reported) yielded, qualitatively, a very similar clustering organization.

7.2 Results

Detailed retinotopic and functional connectivity organization of the visual system were assessed in twelve participants. Retinotopic organization of the visual system was examined using a conventional travelling wave paradigm in which eccentricity and polar angle maps were collected to define visual areas V1, V2, V3, hV4, V3a/b, IPS-0 (V7), LO-1/2, VO-1/2, PHC-1/2 (Materials and Methods). Functional connectivity organization was probed in two resting conditions in which participants were instructed to: (1) keep eyes open and maintain fixation on a centrally presented dot or (2) keep eyes closed for the duration of the run. In addition, in ten of these participants we also assessed the functional connectivity organization during two viewings of a real life dynamic movie in which participants were instructed to (1) attend to the movie, but maintain fixation on a centrally presented dot or (2) freely view the movie.

To investigate the topography of functional connectivity across visual cortex, Pearson correlation coefficients were computed between the time series of all surface node pairs within the left and right visual cortices. For illustration of the raw functional connectivity results, we present fixation resting-state correlation maps for four example seed locations in subject S1 (Fig. 7.1, top) and fixation movie-viewing correlation maps for four example seed locations in subject S2 (Fig. 7.1, bottom). The response time course in each of the four seeds was sampled from a single node within dorsal (or ventral) V2, and the seed location was gradually shifted from foveal...
(leftside panels) to peripheral (rightside panels) representations as defined from a separate eccentricity localizer experiment (rightmost panel). Evidently, the strongest correlations (red) for each seed spanned several visual areas along an elongated band of eccentricity roughly corresponding to that of the seed area. Interestingly, this correlation pattern was seen within both dorsal and ventral visual cortex, which are comprised of several areas that represent the lower and upper visual field, respectively. The correlations between dorsal and ventral visual cortex at corresponding eccentricities were even stronger than correlations at large eccentricity disparities.
(> 4° difference) within V1, V2, and V3 (Fig. 7.1), suggesting an eccentricity-based connectivity that deviates from topographically-local connectivity based on overlapping receptive fields.

To further characterize the large-scale eccentricity-based functional connectivity structure that was observed in the raw correlation maps, data were grouped by visual area and then sub-divided into 12 bins with each bin containing a 1 log° range of eccentricity values between 0 log° and 12 log° (Fig. 7.2A left panel). Pairwise correlations were limited to visual areas V1, V2, V3, hV4, and V3a/b, which have extensive surface area allowing for fine-scale binning of eccentricity data. We first present the raw correlations for three distinct bins at the fovea, mid-periphery and far periphery of dorsal V3 with all bins of ventral V3 for subject S3 (Fig. 7.2, top). Dorsal portions of visual areas V1, V2, and V3 represent the same visual quadrant, making true eccentricity-based connectivity difficult to evaluate relative to local connectivity based on overlapping receptive fields. Further, the shortest cortical distances between adjacent dorsal areas are typically at corresponding eccentricity representations, making local correlations difficult to distinguish from cortical distance-based correlations. In contrast, dorsal and ventral portions of visual area V3 (as well as V2) only border each other at the fovea, and represent different parts of the visual field (lower and upper, respectively). Thus, correlation analyses between these areas allowed us to test for large-scale eccentricity-based connectivity patterns that were orthogonal to effects driven by cortical distance or overlapping receptive fields. Figure 7.2B provides the expected correlation matrix in area V3 as predicted based on eccentricity disparity (left gray panel) and based on cortical distance (right gray panel). While cortical distance predicts that correlations will be weaker between distanced bins with iso-eccentricity (e.g., V3 ventral and dorsal periphery), eccentricity disparity predicts a strong correlation between iso-eccentricities despite large cortical distances.
For each of the selected dorsal V3 bins, correlations with ventral V3 bins were strongest at corresponding iso-eccentricities, irrespective of a cortical distance effect (Fig. 7.2A, lower
The entire correlation matrix for all eccentricity locations between dorsal and ventral V3 (Fig. 7.2B, center panel), revealed a similar pattern, where correlations were strongest among ventral and dorsal bins with iso-eccentricity (the diagonal line), and weaker for bins with large eccentricity disparities (e.g., fovea vs. periphery). Thus, the measured group connectivity was strongly correlated with the predicted eccentricity disparity connectivity ($r = 0.87$) and was uncorrelated to the predicted cortical distance connectivity matrix (Fig. 7.2B). The predicted eccentricity disparity connectivity was consistently observed in individual subjects (mean $r = .47$; $T(11) = 6.27, p < 0.0001$).

To quantify the effects across all eccentricity disparities, the mean correlation coefficients of each connectivity matrix were normalized for each subject to the mean correlation coefficient at the 0 disparity (Materials and Methods). A normalized coefficient of 1 would be equal in connectivity strength to the correlation at the 0 eccentricity disparity with values < 1 indicating weaker connectivity relative to 0 disparity and values > 1 indicating stronger connectivity relative to 0.

Figure 7.3: Intra-run eccentricity-based connectivity analyses for resting-state and movie viewing conditions. Group mean correlations are plotted as a function of eccentricity disparity between the upper and lower visual fields (top), right and left visual fields (middle), as well as across both left and right and upper and lower visual fields (bottom) for all four conditions. All correlations were strongest at the 0 eccentricity disparities and monotonically decreased at larger disparities for all conditions.
disparity. We calculated the strength of correlation as function of visual disparity between the upper and lower visual fields, right and left visual fields, as well as across both left and right and upper and lower visual fields (see graphic illustrations in Fig. 7.3).

The correlations between dorsal and ventral portions of V2 and V3 were strongest at the 0 eccentricity disparities, and monotonically decreased at larger disparities for all conditions (Fig. 7.3). We observed similar patterns of correlations as a function of eccentricity disparity across hemispheres, both along the horizontal plane (e.g., RH V2v and LH V2v) and across the upper and lower visual fields (e.g., RH V2v and LH V2d). This suggests that correlations in signal fluctuations between two areas are strongest at matched eccentricities spanning the whole visual field. The monotonic decrease in connectivity strength at larger eccentricity disparities yielded significant negative correlations for the V2 pairs (mean r (across conditions): -0.91, max: -0.77 min: -0.95; for rest Ts(11) < 7.54, ps < 0.0001; for movies Ts(9) < 4.69, ps < 0.001) and for the V3 pairs (mean r (across conditions): -0.86, max: -0.79 min: -0.92; Ts(11) > 5.91, ps < 0.001; for movies Ts(9) > 4.73, ps < 0.001). These negative correlations survived permutation testing where the labels of eccentricity bins were scrambled before deriving mean correlations for each eccentricity disparity (Materials and Methods). Finally, we observed the same correlation patterns at rest and during the processing of the movie, and during fixation, eye closed, and free viewing, attesting to the robustness of the effect, and excluding many potential confounds (see discussion).

Next, we explored the relation of this eccentricity-based connectivity to stimulus-dependent and stimulus-independent processing. Intrinsic neural dynamics during the resting and
movie conditions that are not related to the processing of visual stimuli, as well as non-neuronal artifacts (e.g., respiratory rate, motion), can only influence the pattern of connectivity within each run, but cannot induce correlations between runs. Cross-run correlations showed similar eccentricity-based connectivity patterns for the movie conditions, both for the free-viewing and fixation conditions (Fig. 7.4). The slope of anti-correlation as a function of eccentricity disparity for movie data was, however, weaker for the inter-run relative to intra-run analyses (Figs. 7.3 & 7.4). This was statistically significant for all intra-hemisphere comparisons and for most (112/128) inter-hemisphere comparisons ($p < .05$). Cross-run correlations on resting state data showed no effects of eccentricity-based connectivity (all $p > .05$), validating the assumption that noise correlations should not be reliable across runs. These data indicate that the observed global eccentricity-based correlations can be coupled to the processing of the incoming information during viewing of real life stimuli. Moreover, it seems there are run specific components that also contribute to the effect.

Figure 7.4: Inter-run eccentricity-based connectivity analyses for resting-state and movie viewing conditions. Group mean cross-run correlations on movie data between hemispheres as well as between dorsal and ventral portions of V2 and V3 were strongest at the 0 eccentricity disparities and monotonically decreased at larger disparities for all conditions. Cross-run correlations on resting state data showed no effects of eccentricity-based connectivity. See Figure 3 for conventions.
Similar group connectivity matrices were obtained between all areas tested for both intra- and inter-hemispheres for all four conditions (Fig. 7.5). For resting state and movie viewing experiments, the strongest correlations (red / yellow) were consistently between bins at comparable eccentricity locations (diagonal in each sub-matrix), even for correlations between dorsal and ventral visual areas and between hemispheres, which represent non-overlapping parts of visual space (Fig. 7.5, black bounding boxes). For all visual area pairs, correlations were strongest at the 0 disparity and monotonically decreased at larger disparities for all conditions (see Supplementary Fig. 7.1). The monotonic decrease in connectivity strength at larger eccentricity disparities yielded significant negative correlations for all intra-hemisphere and inter-hemisphere area pairs (fixation: mean $r$ (across areas) = -0.82, min = -0.96, max = -0.60; eyes shut: mean $r$ (across areas) = -0.75, min = -0.95, max = -0.44) and movie viewing (fixation: mean $r$ (across areas) = -0.85, min = -0.95, max = -0.61; freeview: mean $r$ (across areas) = -0.85, min = -0.97, max = -0.61) experiments.
For each visual area pair, the Fisher-transformed individual subject correlations were reliably different from zero for resting state (fixation: \( Ts(11) > 2.54, ps < 0.05 \); eyes shut: \( Ts(11) > 2.56, ps < 0.05 \)) and movie viewing (fixation: \( Ts(9) > 3.67, p < 0.005 \); freeview: \( Ts(9) > 2.59, ps < 0.05 \)) experiments.), demonstrating that this effect was reliable across subjects. This effect was strongest among early visual areas (fixation: \( Ts(11) > 4.88, ps < 0.0005 \); eyes shut: \( Ts(11) > 3.38, ps < 0.01 \)) and movie viewing (fixation: \( Ts(9) > 4.77, ps < 0.001 \); freeview: \( Ts(9) > 4.70, ps < 0.001 \)).

In addition to eccentricity, angular distance from the horizontal plane is a principle organization of visual space within individual retinotopic maps. Although we did not see evidence for angular-based connectivity in the initial seed-based analysis, we nonetheless tested for angular-based connectivity by grouping data into polar angle bins (Figs. 7.6 & Supplementary Fig. 7.2). We
tested angular mirror symmetry connectivity along the horizontal and vertical meridians as well as pure distance angular connectivity (See Methods). For V2 and V3, the pattern of correlations between dorsal and ventral visual cortex was inconsistent with the predicted pattern for mirror symmetric angular disparity (Fig. 7.6A). As with the eccentricity data, we calculated the strength of correlation as a function of visual disparity for the upper and lower visual fields, right and left visual fields, as well as across both left and right and upper and lower visual fields (see graphic illustrations in Fig. 7.6B). There was no effect of either angular-based connectivity between dorsal and ventral visual cortex for intra- and inter-hemisphere V2 and V3 correlations. The magnitude of mirror symmetric correlations between dorsal and ventral areas was not highest at 0 disparity, but in the mid-disparity range for most conditions (Fig. 7.6B, top & bottom). There was a weak effect of angular-disparity for inter-hemispheric connectivity (mirror symmetric along the vertical meridian) with the strongest correlations at or around the 0 disparity and weaker correlations at larger disparities (Fig. 6B, middle). Across all area pairs, the angular connectivity was qualitatively weaker and more variable than the eccentricity connectivity. The only consistent effect of connectivity between dorsal and ventral cortex was for pure angular-based correlations within V1, though these correlations could be influenced by signal spread along the cortical surface (i.e., cortical distance). In summary, large-scale polar angle-based connectivity effects were only observed for inter-hemispheric connectivity (mirror symmetric along the vertical meridian).

In addition to evaluating large-scale connectivity across the visual field, correlations between areas with overlapping representations of the visual field were used to evaluate topographically-local connectivity. As expected, correlations were strongest at iso-eccentricity
bins between areas with overlapping representations of the visual field (Supplementary Fig. 7.1). It should be noted that areas with overlapping receptive fields share, by construction, similar eccentricity biases, and as such are a sub group of areas that show large-scale eccentricity-based connectivity. Moreover, in contrast to the large-scale eccentricity-based connectivity organization, it is harder to distinguish the local connectivity from effects of cortical distance, especially for adjacent areas as discussed above (e.g., V1 and V2). However, the correlations between non-adjacent areas (e.g., V1 and hV4) and between areas with separate foveal representations (e.g., V1 and V3a/b) are less susceptible to the cortical distance confounding factor. Correlations were also strongest at iso-polar angle bins between areas with overlapping visual field representations (Supplementary Fig. 7.2). For most areas containing overlapping polar angle representations, there was some effect of pure angular-based disparity with correlations generally strongest at 0 disparity and weaker at larger disparities. Although eccentricity-based correlation patterns between these areas are difficult to distinguish from cortical distance-based connectivity (as noted above), this is less of an issue given that neighboring polar angle maps are mirror reversals or each other. Taken together, these correlations suggest some effect of connectivity based on overlapping visual field representations.

To characterize the pattern of connectivity across visual cortex, k-means clustering was performed on the correlations between all node pairs. Data were segmented into 2, 4, 8, and 16 clusters (Materials and Methods). Data clustering resulted in one of two patterns. For half of the rest (6 eyes shut and 6 fixation) and 19 of 20 movie-viewing data, separating the data into 2 parcellations yielded a cluster within the fovea of early visual cortex, extending into lateral-
temporal and lateral-parietal cortices, and a second cluster of the surrounding cortex (Fig. 7.7A). At greater segmentation sizes, clusters spanned several visual areas across portions of both dorsal and ventral visual cortex and encircled a cluster within the fovea of early visual cortex. Thus, these clustered data appeared to resemble the eccentricity topography as defined by using an independent expanding and contracting ring localizer (Fig. 7.7B).

To compare the topographic structure of the cluster data across runs with the large-scale eccentricity and polar angle organization of visual cortex in individual subjects, the cluster numbers were reordered relative to their correlation strength with the fovea cluster. This correlation of large-scale clustering relative to the fovea yielded an organization parallel to that of eccentricity maps and orthogonal to that of polar angle maps (Fig. 7.7B). As seen in two exemplar subjects, nodes within the fovea of early visual cortex were typically clustered together (red), and elongated clusters were observed in the parafovea (yellow), mid-periphery (green) and the periphery (blue). Clusters strongly correlated with the fovea were also evident in lateral ventral temporal and parietal cortex, consistent with prior studies on the topographic organization of those regions (Hasson et al. 2002; Brewer et al. 2005; Swisher et al. 2007; Arcaro et al. 2009). The same functional connectivity organization was observed when the clustering was based on intra-hemispheric (Fig. 7.7B, left column) and inter-hemispheric (Fig. 7.7B, right column) correlations.

In about half of the resting state data (but not in the movie data), the clustering method revealed a different and complex second pattern, suggesting that clustering of resting state data may be influenced by other factors beside the large-scale eccentricity-based organization.
Figure 7.7: *Cluster analyses on resting state and movie viewing data.* (a) K-means clustering for resting state, fixation and movie, fixation viewing in subject S4 at cluster sizes of 2, 4, 8, and 16. Clusters spanned several visual areas across portions of both dorsal and ventral cortex and encircled a foveal cluster. For the cluster size 16, the color of a cluster reflects the strength of correlation with the foveal cluster. (b) K-means clustering of nodewise intra- and inter-hemispheric correlations for resting state in subject S5 and for movie viewing in subject S6. Clusters were color-coded based on their correlation strength with a foveal cluster (red = strongest, blue = weakest). Clusters spanned several visuotopic areas and are parallel to each subject's eccentricity organization.
(Supplementary Fig. 7.3). For 11 of 24 resting-state segmentations, separating the data into 2 parcellations yielded two clusters largely separating V1/V2 from the rest of visual cortex (Fig. S3, top). Such a distinction in the strength of correlations between early and extrastriate visual cortex was recently reported during similar resting-state conditions (McAvoy et al. 2012). In 6 of these 11 segmentations, the division between V1/V2 and extrastriate cortex remained at greater segmentation sizes with the additional clusters forming no discernable pattern (Fig. S3, top). However, even in these 6 datasets, the bin analyses revealed an effect of eccentricity-based connectivity. In 10 of 24 resting-state segmentations, clusters at greater segmentation sizes formed a mixture of the two patterns with clusters spanning both dorsal and ventral visual cortex and encircling a fovea cluster, but also maintaining a distinction between V1/V2 and extrastriate cortex (Fig. S3, middle). In one resting-state and one movie dataset, there were no discernable patterns at any of the tested cluster sizes. Finally, the cluster analyses did not reveal an organization that reflected polar angle organization, nor, individual visual areas (aside from the coarse segmentation of early visual areas from extrastriate cortex for a subset of the resting-state data).

The majority of the cluster analyses revealed large-scale eccentricity-based functional parcellations similar to the bin analyses. Although cluster analyses also revealed a broad separation of early and higher order visual cortex in about a quarter of the parcellations, an effect of eccentricity-based connectivity was evident in this sub-group using the bin analyses. Our results suggest that segmentation patterns from cluster analysis of individual subject fMRI data will be quite variable, especially with complex data containing multiple underlying patterns. As such, interpretation of functional connectivity patterns in fMRI data from cluster analyses alone
is difficult. However, our data-driven cluster analyses do complement our region-of-interest bin analysis by demonstrating converging results in the majority of datasets. Further, cluster analysis assigns each voxel into a discrete group even in cases of gradual smooth transitions. Our detailed analysis of the functional correlation bin matrices revealed a gradual transition of connectivity strength as a function of eccentricity disparity (Fig. 7.5). As such, the borders between clusters in our data (Figs. 7.7 & Supplementary Fig. 7.3) are likely less informative about the organization of functional connectivity than the large-scale pattern of clusters and their topological relation to each other (Figs. 7.1-7.4).

7.3 Discussion

We investigated the organization of functional connectivity across human visual cortex using fMRI during conditions in which there was little or no bottom-up input (resting-state) and during conditions in which there was a dynamic bottom-up input (movie viewing). We found strong evidence for a large-scale organization of connectivity based on eccentricity, which spanned the entire visual field. We found moderate evidence for a functional organization based on polar angle symmetry between hemispheres, but no evidence for polar angle-based connectivity between dorsal and ventral visual cortex. In agreement with prior reports, we also found evidence for topographically-local connectivity based on overlapping representations of visual space.

We observed eccentricity-based connectivity at rest and during the processing of the movie regardless of eye position, supporting our interpretation that this organization is not the
result of stimulus-evoked activation, and cannot be attributed to ocular movement. Our analyses did not reveal individual, functionally specialized areas, which would be expected if the correlations were driven by stimulus response properties. However, cross-run correlations on movie data, but not the rest data, showed that the observed organization of eccentricity-based correlations can be coupled to the processing of the incoming information during viewing of real life stimuli, and rule out the possible influence of non-neuronal artifacts (e.g., respiratory rate, motion) on the results.

Our results underscore the importance of relating functional connectivity data to known functional (or anatomical) organization of the brain. The detailed retinotopic organization of visual areas allowed for a unique opportunity to systematically compare functional connectivity with the known underlying functional organization of the visual system. Across subjects, experiments, and seed-based analyses, we found stronger connectivity between areas at matched eccentricities than within areas at large eccentricity disparities, suggesting that functional correlation analyses are more sensitive at revealing intra-areal connectivity than the localization of individual functional areas within the visual system. Similarly, most of the cluster analyses revealed functional parcellations spanning several visual areas along iso-eccentricities, not individual retinotopic areas. Thus, we propose that functional connectivity analyses are useful for revealing such large-scale organization principles, and will prove important for identifying the functional pathways for the integration of information across individual, functionally specialized areas.
Functional connectivity between visual areas likely reflects both direct and indirect anatomical connections (Honey et al. 2009). Consistent with prior studies demonstrating topographically-local anatomical (Cragg 1969; Maunsell and Van Essen 1983; Van Essen and Zeki 1978) and functional (Heinzle et al. 2011) connectivity, we found both polar angle- and eccentricity-based correlations between areas with overlapping visual field representations. Topographically-local wiring is necessary for the integration of information within focal points of our visual environment. Our data also demonstrate a novel, large-scale organizational principle of functional connectivity across visual cortex based on eccentricity with connections not limited to overlapping representations of visual space. The large-scale correlation structure may be facilitated by direct anatomical connections between neurons with non-overlapping receptive fields or between neurons with multi-focal receptive fields (Pigarev et al. 2001), but also could be the result of indirect, polysynaptic anatomical connections between neurons with partially overlapping receptive fields. Such indirect anatomical connectivity has been shown to link dorsal and ventral visual cortex at the horizontal meridians (Jeffs et al. 2009) and both hemispheres at the vertical meridians (Hubel and Wiesel 1967; Van Essen and Zeki 1978; Newsome & Allman 1980; Kennedy et al. 1986; Cusick et al. 1984). Some preliminary evidence for eccentricity-based wiring was provided by a diffusion tensor imaging study showing that the organization of callosal fibers from visual cortex reflects eccentricity in the human splenium (Dougherty et al. 2005; Saenz & Fine 2010). It is important to note that phase-locked fluctuations of regions with co-eccentricity do not necessarily imply that these regions are directly interconnected, and the relationship between the eccentricity-based functional connectivity and anatomical pathways should be further investigated.
Our data provide a link between the functional organization of early and higher order visual cortex. Previous studies have proposed eccentricity as a large-scale functional organizing principle for higher order visual cortex (Levy et al. 2001; Hasson et al. 2002; Malach et al. 2002). Higher order areas with foveal biases tend to be specialized in face and object recognition, and areas with peripheral biases tend to be involved in scene analysis (Levy et al. 2001; Hasson et al. 2002; Malach et al. 2002; Arcaro et al. 2009). Perceptually, these recognition processes require different visual acuities. For example, while fine acuity is needed for the featural discrimination among similar face and object exemplars (Fiorentini et al. 1983; Goffaux et al. 2005; Keil 2008), a coarser acuity is needed for mapping the surrounding layout necessary for navigation in space (Oliva & Schyns 1997; Oliva & Torralba 2006). Further, eye movement patterns during scene perception are related to the types of information within a scene (Buswell 1935; Henderson et al. 1999). People tend to foveate on faces while orienting their peripheral vision at landscape features and room contours (Yarbus 1967). Our data show that through eccentricity-based connectivity, the divergence in the computational processes necessary for these recognition processes seems to be already evident in early visual cortex.

The large-scale eccentricity-based organization of connectivity could also support the integration of information across the visual field necessary for holistic perception. Intrinsic intra- and inter-areal connectivity at corresponding eccentricities could provide a means for the automatic detection and grouping of similar image features across the visual environment in the absence of directed attention. Behavioral research on feature grouping and symmetry perception generally supports the view that such visual regularities are processed pre-attentively (Barlow & Reeves 1979; Wolfe & Friedman-Hill 1992; Wagemans 1995). Several fMRI studies have shown
that many extrastriate visual areas are engaged during symmetry perception (Sasaki et al. 2005; Tyler et al. 2005; Kietzmann et al. 2012). Our data make the prediction that perceptual principles such as feature grouping and symmetry perception should exhibit large-scale eccentricity biases. As such, eccentricity-based connectivity could support perceptual behaviors such as the bilateral visual field advantage (Dimond & Beaumont 1972; Banich & Belger 1990; Sereno & Kosslyn 1991), in particular for homotopic (vs. heterotopic) stimulus presentations (Desjardins & Braun 2006). Future studies will be aimed at characterizing the influence of this eccentricity organization on the processing of information across the visual system.
8 Concluding Remarks

In this dissertation, I discussed a series of experiments investigating the organization of visual field maps across the visual system, their relation to other functional topographies, and their connectivity. We identified 26 visual field maps in humans (23 cortical and 3 subcortical) and 15 cortical visual field maps in macaques. Several of these maps were identified in regions of cortex thought to lack any organized representation of space. Indeed, in both species, these maps spanned most of visually-responsive cortex. Visual field maps formed a network of topographic pathways covering posterior parietal, lateral occipital, and ventral temporal cortex. The functional and anatomical connectivity between human visual areas closely paralleled the large-scale topographic organization found in macaque visual cortex. The pattern of connectivity across visual cortex was tightly coupled to the organization of visual maps. Functional connectivity between areas was largely organized by eccentricity representations.

We identified visual maps throughout most of visual cortex. Even in regions of cortex where visual maps have not been identified, spatially specific modulations were observed across subjects. It may be that these areas contain additional topographic organization that has yet to be classified. These data demonstrate that the topographic organization of space is not just a major organizing principle for early visual cortex, but for most, if not all, of the visual system. Since visual field maps facilitate the local processing of a scene in a metabolically efficient manor by minimizing the distance of connections (Young 1992; Kaas 1997), the prevalence of maps throughout the visual system may simply be good design for the efficient integration of information across areas. The organization of visual field maps into clusters extends this efficiency principle to a coarser scale by minimizing connection distance between groups of
areas (Wandell et al. 2007). Our results support this extension by demonstrating greater connectivity between maps within clusters than between clusters. We also found that clusters that border each other are more connected than to non-bordering clusters or adjacent cortex lacking visual maps. Our data suggest that the organization of visual field maps throughout the primate visual system minimizes distances at multiple spatial scales between areas that are involved in similar perceptual processing.

At the beginning of the dissertation, I proposed that visual field maps could provide objective criteria for comparing the functions of the visual system between species. Our results demonstrate several similarities in the topographic organization of the visual system at multiple spatial scales between species. For every map we identified in the macaque, we identified a potential parallel in the human. Maps that formed clusters in the macaque tended to have parallel maps in the human that also formed clusters. The topographic relations of clusters to each other were also similar between species. There were notable differences, however. We identified many more visual maps in human than in macaque posterior parietal cortex and we did not identify any maps in macaque ventral temporal cortex. These extrastriate areas may fundamentally differ in their organization between species. However, lack of identifying organized topography is difficult to interpret. Further, when visual field maps were first identified in human posterior parietal cortex, only two maps, IPS-1 and IPS-2, were identified (Schluppeck et al. 2005; Silver et al. 2005). Improvements in imaging methods enabled subsequent identification of additional maps within parietal cortex. It is perhaps not a coincidence that the most anterior map we were able to identify in the macaque is proposed to parallel IPS-2 in humans. Improved coils and
better experimental paradigms that employ an attentive task may be needed to identify additional maps in the macaque.

Despite many similarities in topographic organization, it seems highly unlikely that the functional organization of human and macaque visual systems would be identical, given that our genomes diverged over 25 million years ago. It may be that the organization of topographic maps within visual cortex is generally similar between species, but the functional specializations of individual areas have diverged. For example, V3a in humans is motion sensitive, 2D shape sensitive, and involved in 3D structure-from-motion, whereas V3a in macaques is not (Orban et al. 2004). Given this differentiation, one might be tempted to conclude that these areas are not truly homologous across the species. However, V3a has a similar topographic organization between species and is sensitive to stereopsis in both species. These similarities provide good cause to relate and compare these areas between species, and suggest that the functional differentiation in V3a between species is an evolutionary change. Our results provide a framework for such detailed comparisons of visual cortex between humans and monkeys.

Together, these studies provide new insights into the topographic organization of the primate visual system. Our data demonstrate that the visual field map is a major organizational principle for most – if not all – of the primate visual system. This organization extends previous theories on the organization of connections between visual field maps and suggests that the primate visual system is organized to efficiently communicate information at multiple spatial scales by broadly minimizing distances between areas involved in similar computational processes.
References


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Supplementary Figure 6.1: Multidimensional scaling and cluster analysis of macaque tracer data from Felleman & Van Essen (1991). 2- and 3-dimensional scaling was performed on a binary matrix of macaque visual cortex connectivity from Felleman & Van Essen 1991. Data were clustered into 2 segmentations that largely separated dorsal and ventral visual areas. Early visual cortex was included as part of the dorsal segmentation.
Supplementary Figure 7.1: Intra-areal and V1 connectivity for all conditions. (a) Group mean intra-areal, intra- (top) and inter- (bottom) hemisphere correlations. (b) Group mean V1 inter-areal, intra-hemisphere (top) and inter-hemisphere (bottom) correlations with areas containing overlapping (top-left) and non-overlapping (top-right) visual field representations. In each condition, the strongest correlations were strongest at the 0 eccentricity disparities and monotonically decreased at larger disparities for all conditions. See Figure 3 for conventions.
Supplementary Figure 7.2: Intra- and inter-areal polar angle-based connectivity. (a) Group mean intra-areal, intra- (top) and inter- (bottom) hemispheric correlations. (b) Group mean inter-areal, intra-hemisphere (top) and inter-hemisphere (bottom) correlations for ventral (left) and dorsal (right) areas containing overlapping visual field representations. In each condition, the strongest correlations were strongest at the 0 eccentricity disparities and monotonically decreased at larger disparities for all conditions. See Figure 3 for conventions.
Supplementary Figure 7.3: Alternate pattern from cluster analyses on resting state data. K-means clustering for resting state in subject S7 (top), subject S1 (middle). In a subset of clustered resting state data, segmenting the data into 2 parcellations yielded clusters largely separating V1/V2 from the rest of visual cortex. In half of these data, clusters at greater segmentation sizes formed a mixture of patterns #1 and #2 with clusters spanning both dorsal and ventral cortex and encircling a fovea cluster, but also maintaining a distinction between V1/V2 and extrastriate visual cortex. As can be clearly seen in the correlation maps from resting-state dataset in subject S4 that showed this second cluster pattern, the correlation coefficients within V1/V2 were much larger than with the rest of visual cortex. The 6 resting-state datasets that only showed a division between early visual and extrastriate cortex in the clustering still showed an effect of eccentricity-based connectivity in the pairwise correlation analyses. The effect was weaker than compared with the 6 best resting-state datasets, suggesting that the cluster analyses only reveals the dominant pattern in each dataset.