

Symposium

The Richness of Vision in the Mammalian Brain: Neural Codes for Visual Perception and Behavior in Three Dimensions

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Successful navigation and interactions with objects in a complex, three-dimensional (3D) world are essential to survival, yet studies of the neural basis of visual perception and action often treat the world as a flat, two-dimensional (2D) canvas. Here, we review recent discoveries about how the visual systems of different mammals have adapted under the constraint of a 3D world. Many neurons in primate visual cortex are sensitive to 3D depth cues constructed from input differences to the two eyes (binocular disparities). Similar neuronal selectivity has recently been characterized in tree shrews and mice, though constrained anatomically and functionally. Disparity-sensitive receptive field structures can now be assessed noninvasively across human visual cortex and functionally linked to depth perception. At later stages in the nonhuman primate (NHP) ventral (“what”) pathway, supporting object recognition, complex 3D objects are represented as spatial configurations of geometric parts. In studies of the dorsal (“where”/“how”) pathway of NHPs, underlying visuospatial processing, the inclusion of 3D structure in visual tasks has established tighter links between neuronal mechanisms and perception. This has also revealed neuronal representations of 3D object position and orientation that are tolerant to 3D gaze location, providing a basis for robust perception and action. The cross-species analysis presented here provides new perspectives on neural coding mechanisms underpinning the richness of 3D visual experience. Elucidation of these mechanisms will be essential for understanding the neural basis of cognition and behavior, which in turn will enable the development of therapies and neuroprosthetics for those suffering from visual impairments.

Key words: binocular disparity; human; macaque; rodent; tree shrew

Introduction

A unifying constraint shaping brain function is that sensory signals arise within a three-dimensional (3D) world, but visual information is conveyed to the brain as two-dimensional (2D) retinal projections that are ambiguous about the veridical structure of the scene. To interpret the visual world and guide interactions with it, the brain must solve the inverse problem of estimating the scene’s 3D content and organization from these 2D inputs. This makes 3D spatiotemporal processing an essential and general property of neural systems. Primates, cats, and other species compute stereoscopic depth representations from small differences in the two 2D retinal images (Wheatstone, 1838;

Marr and Poggio, 1979). Binocular horizontal disparity selectivity in the visual cortex is a foundation of 3D information processing and underpins perception (Barlow et al., 1967; Nikara et al., 1968; Hubel and Wiesel, 1970; Poggio et al., 1988; Cumming and Parker, 1997; Roe et al., 2007; Fig. 1A). Loss of binocular vision through amblyopia is one of the leading causes of visual impairment in children and young adults, with a prevalence of ~1.5–3.5% (Groenewoud et al., 2010; Fu et al., 2020). Beyond 3D visual impairment, affected persons have an increased lifetime risk of blindness in the healthy eye and deficits in 2D pattern vision (McKee et al., 2003; van Leeuwen et al., 2007; Levi et al.,

Received May 28, 2025; revised Aug. 19, 2025; accepted Aug. 21, 2025.

Author contributions: A.R., H.B., C.E.C., J.M.S., S.T., and K.K. wrote the paper.

We thank Jianhua Cang, Raymond Doudlah, Betina Ip, Lauren Kresser, Hee-kyoung Ko, and Andrew J. Parker for their intellectual and scientific contributions to work described in this review, as well as Betsy Quinlan and Adhira Sunkara for their helpful feedback. A.R. was supported by the National Institutes of Health (NIH; EY029438, EY035005, NS105602, NS128586) with additional Wisconsin National Primate Research Center support from the NIH (OD011106). H.B. was supported by the Medical Research Council (MR/K014382/1, MR/V034723/1), Royal Society, and NIHR Oxford Health Biomedical Research Centre (NIHR203316), with Wellcome Centre for Integrative Neuroimaging support from the Wellcome Trust (203139/Z/16/Z, 203139/A/16/Z). C.E.C. was supported by the

NIH (EY016711, EY011797, EY025223, EY029420, EY037193, EY037065). J.M.S. was supported by the NIH (EY034092). S.T. was supported by NIH (EY026286, EY020950) and Jefferson Scholars Foundation Awards to Jianhua Cang. K.K. was supported by the German Research Foundation (DFG; 520140630, 507082410, 425899996 – SFB 1436), a Wellcome Trust Strategic Award (101092/Z/13/Z), and the Royal Society (UK).

The authors declare no competing financial interests.

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<https://doi.org/10.1523/JNEUROSCI.1316-25.2025>

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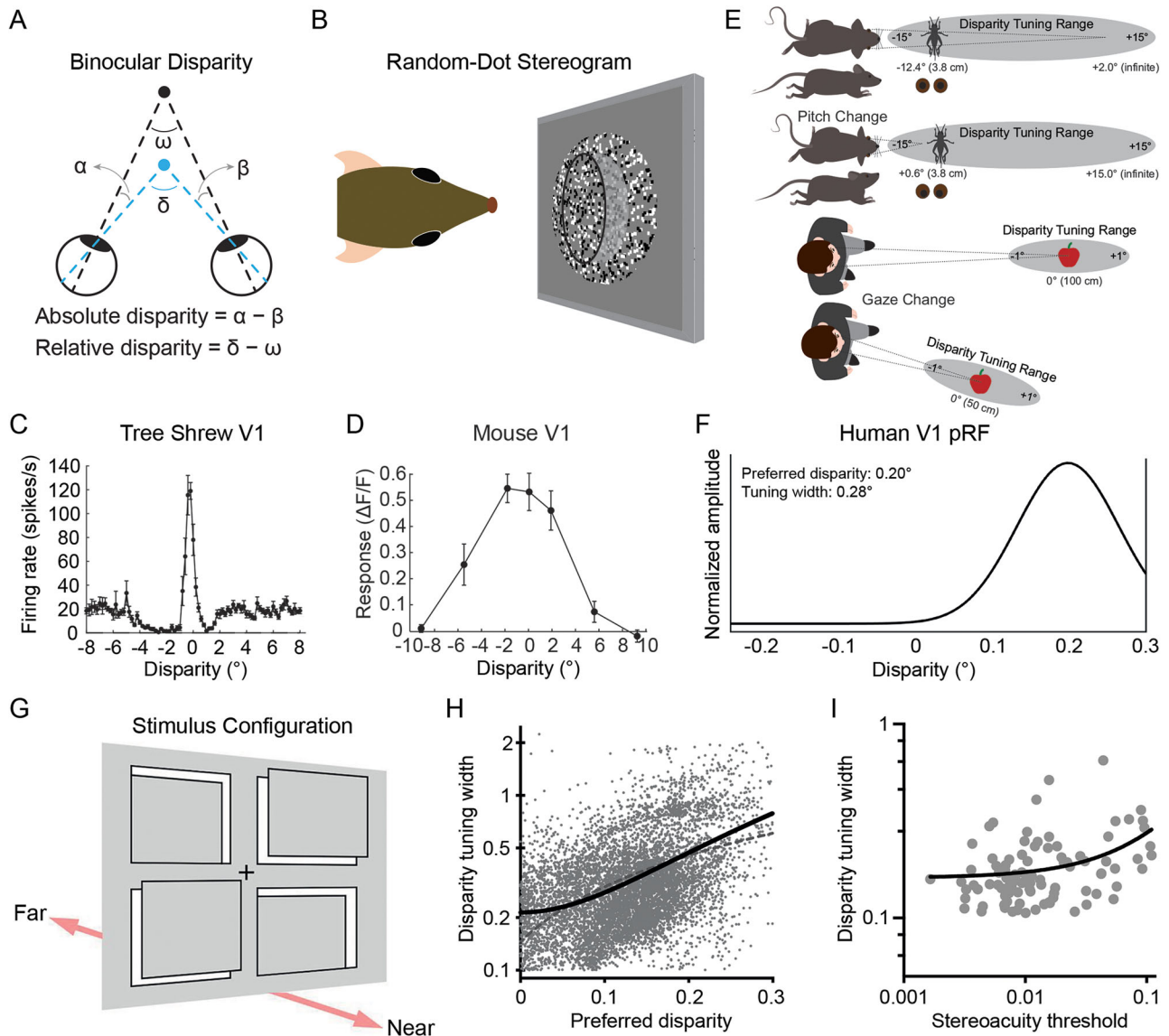


Figure 1. Disparity tuning in the tree shrew, mouse, and human visual cortex. **A**, Stereoscopic depth is constructed from small differences in where an image falls on the two retinas, namely, binocular disparity. Absolute disparity is defined with respect to fixation. Relative disparity is defined between two objects or points in the world and is unaffected by vergence eye movements. **B**, Random-dot stereograms are used to probe binocular integration and depth selectivity. **C**, Disparity tuning of a highly selective tree shrew V1 neuron. **D**, Disparity tuning of a mouse V1 neuron measured using Ca^{2+} imaging. **E**, Constrained by small, closely spaced eyes, mouse V1 neurons can be tuned for large disparities ($\pm 15^{\circ}$) that represent their entire range of depth. Some neurons tuned to uncrossed disparities ($> 2^{\circ}$) correspond to physically impossible correspondences under head-fixed conditions. Those neurons represent real depths when the head is pitched upward, causing the eyes to converge. Convergence in mice otherwise does not systematically change with gaze shifts or changes in the binocular disparity of objects. Primates instead use convergence to shift a narrow range of binocular disparities ($\pm 1^{\circ}$) onto objects. **F**, Disparity tuning of a pRF in human V1 measured using fMRI. **G**, Using stimuli that temporally modulate in depth allows the preferred disparities and tuning widths of pRFs to be estimated. **H**, Across visual areas (shown for V1), pRF tuning width increased with preferred disparity away from zero ($r = 0.44$; $p < 0.00001$; $N = 8,790$). Curves are linear (dashed gray) and second-degree polynomial (solid black) fits. **I**, In V1, pRF tuning width was significantly correlated with stereoacuity thresholds measured psychophysically ($r = 0.33$; $p = 0.008$; $N = 95$; Bonferroni corrected for nine tested visual areas). The curve shows the linear regression.

2015), suggesting that binocular integration is a fundamental function of the visual system.

In this review, we describe recent advances in the understanding of 3D processing across species as diverse as mice, tree shrews, monkeys, and humans. We begin by comparing how depth signals are represented across these species with an emphasis on recent studies that extend the understanding of mechanisms of stereopsis in nonhuman primates (NHPs) to tree shrews, identify factors constraining stereopsis in mice, and provide insights into human binocular 3D vision. Building on this foundation, we examine how 3D shape representations are constructed in higher cortical areas of NHPs, how conjunctions of visual features in

three dimensions are important for establishing close links between visual processing and perception, and, finally, how extra-retinal signals disambiguate depth representations for stable 3D perception and for guiding interactions with the 3D world. Through cross-species comparisons of the neuronal mechanisms for 3D vision, we can understand how visual functions have adapted through evolution to serve different ecological niches. This work reveals shared yet differentiated mechanisms in the primary visual cortex (V1) of mice, tree shrews, and primates. It shows that higher-level representations in the ventral and dorsal pathways of NHPs underpin the richness of visual perception, cognition, and behavior in three dimensions.

Tree Shrews: An Emerging Model System for Studying 3D Perception and Action

NHPs are an essential model system for studying stereopsis given the homologies to humans, but challenges in establishing techniques for circuit dissection in NHPs compared with other animal models have been an obstacle to progress (Jennings et al., 2016; O'Shea et al., 2017; Tremblay et al., 2020; Raper and Galvan, 2022). Complementary avenues to address these challenges are the continued development of primate-specific genetic tools and the identification of other animal models with stereopsis for which such tools are well established. Tree shrews (*Tupaia belangeri*) skillfully move around arboreal environments in their natural habitat (Emmons, 2000) and jump *ad libitum* from wall to ceiling in enclosures. These behaviors point to the possible usage of stereoscopic vision, making them a candidate for investigating neuronal mechanisms of binocular integration (Tanabe et al., 2022).

V1 is a major site of binocular integration in tree shrews (Conley et al., 1984). As we explore below for humans, based on magnetic resonance imaging (MRI) studies, binocular receptive field (RF) mechanisms of V1 neurons encode the interocular horizontal offset between left- and right-eye images (binocular disparity). A rigorous approach to isolating stereoscopic mechanisms is to measure binocular disparity tuning with random-dot stereograms, because they contain no monocular cues to the 3D image (Prince et al., 2002a; Fig. 1B). Recent experiments using random-dot stereograms found that tree shrew V1 neurons are highly selective for disparity (Tanabe et al., 2022; Fig. 1C).

The disparity selectivity of V1 neurons is one indicator of the extent to which a species relies on stereopsis compared with other cues for processing 3D information, similar to how ecologists characterize the environmental conditions across a species' range when determining its ecological niche. Cross-species comparisons of disparity selectivity measured under similar conditions can therefore inform how the visual cortex of different species has adapted to their anatomy and how they interact with the 3D world. When Tanabe and colleagues compared the disparity selectivity of tree shrew and mouse V1 neurons measured using random-dot stereograms, they found that the mouse neurons were not as highly tuned, even after adjusting the stimuli to account for differences in visual acuity (Tanabe et al., 2022). An example disparity tuning curve of a mouse V1 neuron (Brown et al., 2025; Fig. 1D) with similar disparity preference as the tree shrew neuron (Fig. 1C; an important point of control since, as discussed below, disparity preferences and tuning widths covary) highlights that tuning is substantially broader in the mouse. This species difference in V1 disparity selectivity suggests that mice rely on coarser stereopsis cues to process the 3D structure of their environment than tree shrews. We return to this point in the next section, through an assessment of aspects of mouse anatomy and physiology that limit stereovision.

Ongoing work continues to establish the tree shrew as a model for linking neuronal mechanisms of stereopsis to cortical organization and behavior. Similar to some mammalian species including primates, but not others like rodents, tree shrew V1 is organized such that neuronal orientation preferences vary across the cortical sheet in a systematic orientation map (Bosking et al., 1997). Tree shrews therefore offer an opportunity to investigate if the functional response properties of individual neurons depend on their cortical milieu (Nauhaus et al., 2008). For instance, Tanabe and colleagues are currently using two-photon imaging to test if the strength of a V1 neuron's disparity

tuning is correlated with its location in the orientation map. They are also evaluating how disparity tuning in V1 might underpin naturalistic behaviors by recording tree shrews jumping across gaps and quantifying how the binocular visual field relates to the jump trajectory. Through such efforts, tree shrews have the potential to become a valuable model system in biomedical research for studying with cell-type specificity the neurodevelopment and circuitry of stereovision, including the pathophysiology of disorders such as amblyopia.

Anatomical and Physiological Constraints on Mouse Stereopsis

Whether mice are a suitable model system for stereoscopic 3D vision has been debated in part because, as a predominantly prey species, their eyes are directed laterally. However, they do possess 40° of binocular overlap within the central visual field (Drager, 1978; Drager and Olsen, 1980; Scholl et al., 2013; Samonds et al., 2019; van Beest et al., 2021). Mice also make gaze changes to move the binocular region onto objects of interest (Meyer et al., 2020; Michael et al., 2020; Johnson et al., 2021). These observations suggest that mice rely, at least to some extent, on stereovision to process 3D scenes.

Notably, stereopsis is constrained in several ways by the close spacing (separated by ~1 cm) and small size (~3 mm diameter) of mouse eyes (Chalupa et al., 2008). First, the closeness of their eyes means that the convergence angle is very small even at modest distances (Samonds et al., 2019), limiting the utility of stereoscopic signals since smaller convergence angles produce smaller, less discriminable disparity differences (McKee et al., 1990). Thus, mice likely employ stereopsis mostly at very close distances. Consistent with this, they struggle to capture a cricket immediately in front of them if binocular vision is chemogenetically ablated (Johnson et al., 2021). Humans likewise depend most on stereoscopic vision for tasks requiring hand–eye coordination such as threading a needle (McKee et al., 1990). Mice also use binocular vision within 7.5 cm of a surface when choosing to exit onto the near surface in the pole descent cliff task (Boone et al., 2021). For tasks requiring distance judgments beyond 10 cm, such as jumping across a gap, perspective cues appear to mediate their performance (Parker et al., 2022). Second, small eyes mean that even small eye movements produce large visual field changes. Binocular alignment varies on average by >3° even in head-fixed mice (Samonds et al., 2022; Brown et al., 2025). When moving *ad libitum*, they make rapid head and eye movements to change their gaze or to stabilize an image on the retina (Michael et al., 2020). Due to the orientation of their eyes, pitch rotations of the head necessitate large convergence changes to maintain gaze (Fig. 1E, first vs second row). Under naturalistic conditions, this means that binocular alignment deviates on average by 8° (Meyer et al., 2020). These variations in binocular alignment may limit mouse stereoscopic discrimination to differences of no less than ~3° of disparity (Samonds et al., 2019; Boone et al., 2021). Third, small eyes mean their optics differ substantially from larger mammals. For example, their small pupil causes the depth of field to be large, making accommodation unnecessary (Chalupa et al., 2008). Correspondingly, mice do not appear to converge based on stimulus disparity. Instead, they have neurons tuned for large disparities ($\pm 15^\circ$), representing their entire range of depth (La Chioma et al., 2019; Samonds et al., 2019; Fig. 1E, top). In contrast, accommodation and convergence are tightly coupled in primates (Tait, 1933; Cumming and Judge, 1986; Sprague et al., 2016), which use

changes in convergence to focus a narrow range of disparities ($\pm 1^\circ$) onto objects (Prince et al., 2002b; Fig. 1E, bottom).

Despite differences in the spatial scale and strategies for stereoscopic vision between mice and other mammals, fundamental similarities exist across the representations of binocular disparity (Samonds et al., 2019; La Chioma et al., 2020). Indeed, studies with mice have made important contributions to our understanding of 3D vision. For example, developmental studies have provided detailed insight into how the ocular dominance and tuning properties of binocular neurons change from eye opening to the end of the critical period, when the visual cortex is highly plastic (Wang et al., 2010; Tan et al., 2022; Brown and McGee, 2023; Brown et al., 2025). This plasticity involves specific inhibitory cell types and molecules (McGee et al., 2005; Kuhlman et al., 2013; Gu et al., 2016; Yaeger et al., 2019), pointing to cellular processes supporting binocular integration that can be pursued in mammals which rely more on stereopsis to interpret and interact with the 3D world. Work with mice has further underscored how geometric analyses have informed our understanding of stereopsis in multiple species, even theropod dinosaurs (Stevens, 2006), and are likely to have an important role in the ongoing development of the tree shrew model of stereopsis.

Bridging Mechanisms of Disparity Processing and Depth Perception in Humans

Despite the fundamental nature of depth perception, the use of noninvasive imaging techniques to untangle the mechanisms of disparity processing has remained challenging. In this section, we discuss recent advances in MRI approaches that provide a more detailed understanding of disparity processing in the human brain.

Knowing the preferences and sensitivities of disparity selective neuronal populations allows the investigation of their functional links to depth perception (Parker and Newsome, 1998). Population RF (pRF) mapping provides a method for determining such properties in small regions of the cortex. In standard usage, a salient stimulus is moved through the visual field, while the BOLD signal is measured in humans (Dumoulin and Wandell, 2008; Wandell and Winawer, 2015; Benson et al., 2018) or NHPs (Ip and Bridge, 2021; Klink et al., 2021). For any given voxel in the visual system, the response increases when the stimulus is within the pRF.

This method was recently adapted to investigate disparity tuning and depth perception in humans (Alvarez et al., 2021, 2025). First, the investigators compared pRFs measured using checkerboard stimuli (which elicit retinotopically confined visual responses) and disparity-defined stimuli. Consistent with earlier findings in macaque neurophysiology (Nienborg et al., 2004) and human MRI (Barendregt et al., 2015), the disparity-defined stimulus resulted in larger pRFs than the checkerboard stimulus in V1, whereas there was no difference in the pRF size in extrastriate visual areas. This stimulus dependence of the pRF size in V1, which was attributed to the spatial offset between left- and right-eye components of binocular RFs in a disparity energy model, implies that V1 is also a key site of binocular integration in humans.

Although that work relied on a disparity-defined stimulus, the pRF mapping was still in 2D. To investigate the relationship between disparity preference and tuning width (Fig. 1F), the third dimension must be mapped by varying disparity. Alvarez et al. (2025) used a ministereoscope (Ip et al., 2022) in the MR scanner to present stimuli that were temporally modulated in

depth (Fig. 1G). By fitting a Gaussian function over depth, it was possible to extract the preferred disparity and tuning width (as in Fig. 1F). Across the visual cortex, a consistent pattern of greater tuning width with a preferred disparity further away from zero was found (shown for V1 in Fig. 1H). However, the disparity tuning width for the most sensitive pRFs correlated with perceptual stereoacuity thresholds in V1 only (Fig. 1I), suggesting that V1 disparity tuning may provide the limit for depth perception.

These studies collectively revealed distinctions between V1 and extrastriate cortex. To understand the mechanistic differences, functional magnetic resonance spectroscopy was used to investigate the roles of GABA and glutamate in disparity selectivity (Matuszewski et al., 2025). Specifically, their concentrations were measured during the presentation of binocularly correlated stimuli (where the luminance polarity of corresponding stimulus elements in the two eyes was matched, e.g., both “white” or both “black”), which lead to depth perception, and binocularly anticorrelated stimuli (where the luminance polarity of the corresponding stimulus elements was reversed, e.g., “white” vs “black,” leading to “false matches” or “unmatched” dots), which do not (both compared with rest). Although the original hypothesis was that GABA would increase during the presentation of correlated stimuli leading to a perception of depth, this condition instead led to an increase in glutamate concentration and the excitation:inhibition balance in V1. This may indicate a facilitated response to correlated but not anticorrelated stimuli. In contrast, in the lateral occipital cortex within the ventral visual pathway, the anticorrelated condition showed an increase in the excitation:inhibition balance. Why facilitation may occur in this region for anticorrelated stimuli remains unclear, but one possibility is that in the absence of a coherent depth percept, more (unmatched) dots may be perceived. In the next sections, we explore the contributions of neurons in higher visual areas of NHPs to 3D processing as investigated with neurophysiological methods.

3D Object Representations in the Primate Ventral Visual Pathway

Higher levels of the visual cortex achieve the goal of representing the 3D world we inhabit. The ventral pathway of primates transforms massive, implicit, unstable 2D retinal images into compressed, explicit (easy to process and decode), stable representations of 3D objects, animals, people, and scenes. This transformation builds on compression (Attneave, 1954; Barlow, 1961) and explicit coding that begins in the retina and continues in V1, with compressive, explicit coding of orientation (Hubel and Wiesel, 1968) and position in depth based on absolute disparity (Poggio et al., 1988; Cumming and Parker, 1999). Area V2, a target of V1, also uses implicit image cues and relative disparity to begin to resolve relative position in depth (Zhou et al., 2000; Thomas et al., 2002).

Area V4, a target of V2 and V3A, is the beginning of the ventral pathway proper (Felleman and Van Essen, 1991; Ungerleider et al., 2008). While V1 and V2 process position in depth, V4 contains explicit signals for 3D shape-in-depth. The finding of 3D orientation selective neurons in V4 (Hinkle and Connor, 2002; Hegdé and Van Essen, 2005) was recently extended to V3A (Doudlah et al., 2022). This selectivity is essential for a world where edges of visual stimuli are often not frontoparallel (Rosenberg et al., 2013, 2023; Burge et al., 2016). Disparity-based 3D orientation tuning that remains consistent

across changes in 2D position (within the RF) and depth, as shown in V4, provides an explicit, compressed, stable representation of orientation with the full dimensionality of the natural world.

On the scale of V4 RFs, the 3D world remains largely smooth but with variations in orientation. These variations can be gradual and smooth (as with surface curvature) or abrupt (as with curvature singularities, i.e., sharp edges). V4 generates 3D surface and curvature signals, concentrated in patches that alternate with 2D shape tuning (Srinath et al., 2021). Curvature tuning compresses a larger number of smaller orientation signals, just as orientation tuning compresses a number of position signals. V4 neurons show tuning for the position and orientation of curvature fragments in an object-centered reference frame. For example, a V4 neuron might respond to a specific surface fragment only when it is near the top of the object, even if the object moves within the RF (Pasupathy and Connor, 2001). This reference frame transformation, from retinotopic to object-centered, enables stable coding of objects regardless of their 3D position relative to the eyes.

Signals from V4 feed into the inferotemporal cortex (IT; Kravitz et al., 2013). IT neurons are tuned for 3D spatial configurations of multiple simpler 3D fragments encoded in V4 (Janssen et al., 1999, 2000; Yamane et al., 2008; Hung et al., 2012). An example neuron, shown in Figure 2, was studied with abstract, evolving 3D shapes rendered with stereoscopic and shading cues for depth. Stimulus evolution was controlled by a genetic algorithm in which the neuron's response defined fitness to produce descendant stimuli in subsequent generations. The highest response stimuli across eight generations are shown in Figure 2A (lowest in Fig. 2B). Responses to a given 3D shape were consistent across a variety of 3D depth cue changes

(Fig. 2C). The neuron's tuning for two surface fragment configurations is quantified in Figure 2D, with the fragments projected onto the surface of a high-response stimulus in Figure 2E.

Tuning for 3D fragment geometry and object-relative position is indicative of compositional coding, in which ensembles of neurons represent complete shapes as a handful of constituent geometric fragments. Fragment position is represented in a reference frame centered on and sized to the shape, producing a stable representation (Marr and Nishihara, 1978; Biederman, 1987; Pasupathy and Connor, 2002). In addition to being compressive, explicit, and stable, compositional coding is theoretically appealing because of its productivity. Like letters of an alphabet, a finite set of geometric fragment signals, in different combinations, can represent the virtual infinity of imaginable shapes. An abstract statue by Henry Moore (Fig. 2F) provides an illustrative example of how an initially unfamiliar object can be represented by an ensemble of IT neuron tuning functions (here, projected onto the surface of a model; Yamane et al., 2008).

Primate Dorsal Visual Pathway Areas Are Adapted for Motion Perception in 3D Space

Representations of visual motion and contributions to vision for action are defining characteristics of the primate dorsal pathway (Goodale and Milner, 1992). This characterization is exemplified by extrastriate visual area V5/MT (Allman and Kaas, 1971; Dubner and Zeki, 1971), where seminal studies established robust links between single neuron activity and motion perception (Newsome et al., 1989; Salzman et al., 1990; Britten et al., 1996). The selectivity and perceptual relevance of V5/MT signals is increased further when motion discrimination is probed in different 3D depth configurations that match the stimulus and

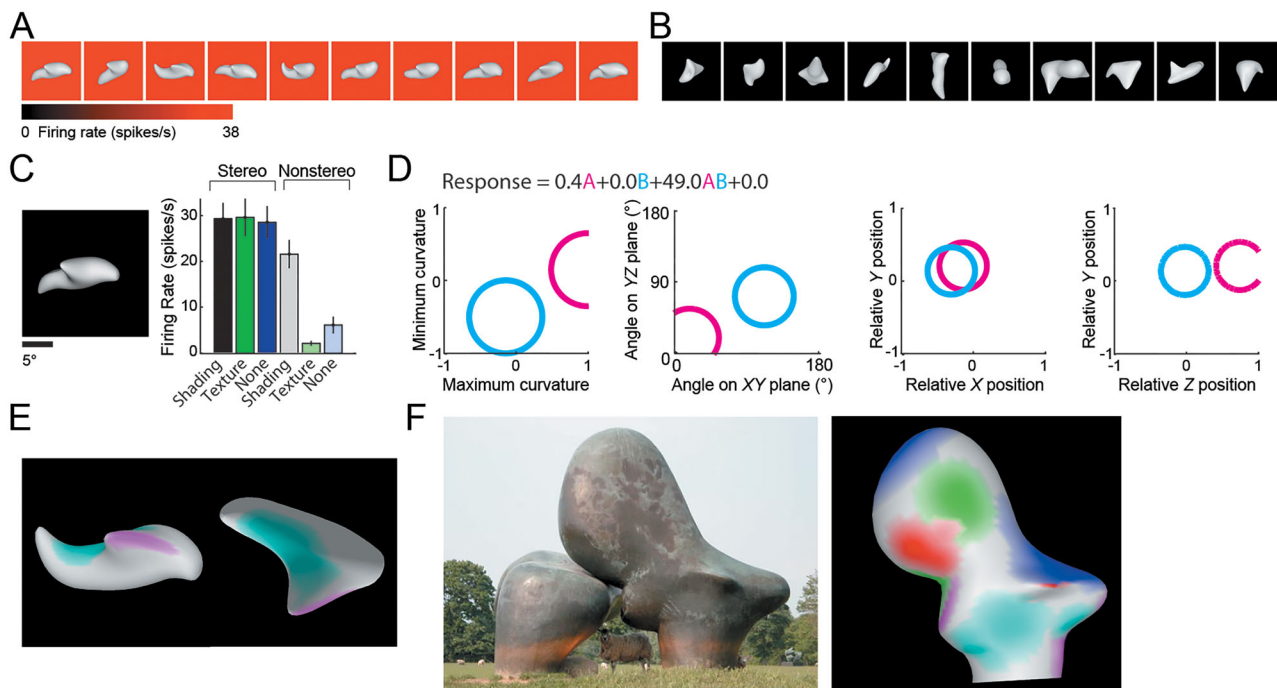


Figure 2. Compositional coding of 3D shape by a macaque IT neuron. **A**, High-response shapes for an IT neuron evolved through a genetic algorithm. **B**, Low-response shapes for the same neuron. **C**, High responses to the shape at the left were consistent across different combinations of cues, including stereoscopic only and shading only (right). **D**, Quantification of tuning for surface fragment configurations. Circles represent 1 standard deviation ranges of tuning for curvature, orientation, and position. One surface fragment (blue) comprises slightly concave surfaces facing upward and positioned above object center. Another fragment (magenta) comprises sharp, extended ridges, facing toward the viewer and positioned at the front of the object. **E**, Projections of the two fragments (in blue and magenta) onto the surface of a high-response stimulus, seen from two viewpoints. **F**, An abstract statue by Henry Moore (left) with an ensemble of neuronal tuning functions measured in IT projected onto its surface (right).

task to the neurons' conjoint encoding of direction and binocular disparity (Dodd et al., 2001; Krug and Parker, 2011; Krug et al., 2013).

Beyond V1, selectivity for binocular disparity is found in many dorsal pathway areas, which were initially thought to primarily encode depth with reference to the fixation distance (absolute disparity; Maunsell and Van Essen, 1983; Roy et al., 1992; Uka and DeAngelis, 2006; Parker, 2007; Fig. 1A). However, many V5/MT neurons also show tuning to the relative disparity between two transparent 2D planes of moving dots placed at different depths (Krug and Parker, 2011). For a direction selective, relative disparity-tuned V5/MT neuron, the steepness of the tuning function for the depth of a 2D plane of dots moving in the preferred direction increases when another 2D

plane of dots moving in the antipreferred direction is superimposed. This nonlinear interaction enhances visual processing in 3D space.

Beyond RF structures, the specialization for conjoint depth-motion encoding is also evident in the perceptual contribution of neurons. Trial-by-trial correlations between single neuron activity and behavioral reports, measured as choice probabilities, are found in V5/MT for direction and depth discrimination. For direction discrimination, an average choice probability of 0.56, significantly above the chance level of 0.50, was reported (Britten et al., 1996). For depth discrimination, a similar choice probability of 0.59 was reported (Uka and DeAngelis, 2004). However, when V5/MT neurons were probed with structure-from-motion stimuli matching their direction and disparity

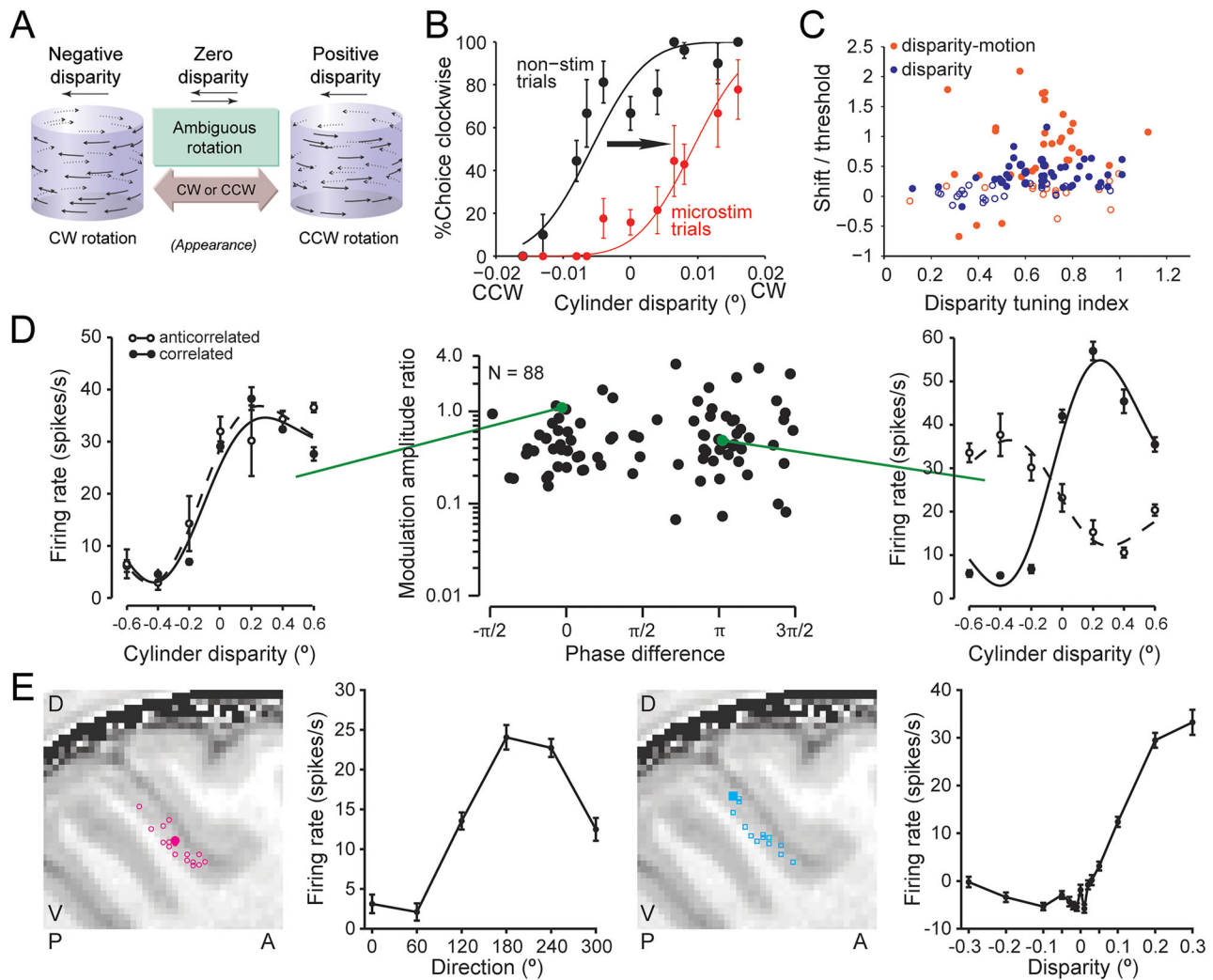


Figure 3. Conjoint motion and depth perception signals in the dorsal pathway of macaques. **A**, Bistable, structure-from-motion cylinder stimuli are disambiguated by separating the rightward and leftward moving dots in depth, so that the cylinder rotates unambiguously clockwise (CW) or counterclockwise (CCW; adapted from Parker and Krug (2003)). **B**, Shift in perceptual reports with focal electrical microstimulation of a V5/MT site. **C**, For the same disparity tuning strength (quantified using a disparity tuning index), microstimulation biases perception more strongly in a structure-from-motion rotation discrimination task ("disparity-motion," orange) than in planar random-dot stereogram depth judgments ("disparity," blue) [adapted from Krug et al. (2013)]. Filled (open) circles indicate (non)significant shifts of the behavioral responses. **D**, For anticorrelated structure-from-motion cylinders, which do not yield a coherent depth percept, a similar proportion of V5/MT neurons respond with an inverted tuning preference as with the same tuning preference compared with their responses for binocularly correlated structure-from-motion cylinders, which generate depth percepts. A phase difference of 0 between fitted tuning functions for binocularly correlated and anticorrelated structure-from-motion cylinders indicates the same disparity tuning preference (left example neuron). A phase difference of π indicates inverted tuning preferences (right example neuron). If these neuronal populations were pooled, tuning for the false (anticorrelated) binocular matches would disappear—commensurate with no coherent depth percept for anticorrelation [adapted from Krug et al. (2004)]. **E**, In neurophysiological recordings from area LIP (locations shown on a parasagittal slice of a structural MRI; D, dorsal; V, ventral; P, posterior; A, anterior), many neurons were tuned to motion direction (pink circles) or binocular disparity (cyan squares), including some to both. Example tuning curves are shown to the right of the MRIs (their recording locations marked with filled symbols).

preferences (Fig. 3A), responses showed a considerably stronger functional link with perception, with a choice probability of 0.67 (Dodd et al., 2001; Krug et al., 2004). This increase is not simply a function of higher firing rates but attributable to conjoint stereo-motion sensitivity (Krug et al., 2016) and stronger correlated activity within the local pool of neurons with similar tuning properties (Wasmuht et al., 2019). The conjoint activation of motion and depth features also translates to a stronger causal link between focal electrical microstimulation of V5/MT neurons and perception (Fig. 3B). Microstimulation lead to a consistently larger effect on the perceived rotation direction of a 3D structure-from-motion cylinder than on the depth judgment for a planar random-dot stereogram (Krug et al., 2013; Fig. 3C). These results collectively showed that V5/MT neurons make a stronger contribution to perception when the direction and depth of a stimulus match their tuning preferences and conjointly generate new properties like object shape.

A key distinction in the encoding of binocular depth is that ventral pathway neurons are less susceptible to false matches than neurons in early visual areas or the dorsal pathway. For example, they do not show tuned responses for anticorrelated random-dot stereograms that do not yield a depth percept (Janssen et al., 2003). In contrast, dorsal pathway neurons display consistently inverted tuning responses to false matches in planar anticorrelated random-dot stereograms, as predicted by a standard disparity energy model. These responses are frequently reduced in amplitude, but not eliminated, unlike what has been observed in the ventral pathway (Takemura et al., 2001; Janssen et al., 2003; Parker, 2007; Yoshioka et al., 2021). However, for anticorrelated structure-from-motion cylinders, V5/MT neurons can show an inverted tuning response (Fig. 3D, right panel) or a tuning response with the same preference (Fig. 3D, left panel) as for correlated disparities, in roughly equal proportion (Fig. 3D, middle; Krug et al., 2004). If the responses of these neurons were pooled, the tuned population response for anticorrelated disparity would disappear. This suggests that the correspondence problem (i.e., identification of retinal image elements across the two eyes that correspond to the same visual input in the 3D world) may also be solved in the dorsal pathway, at least for stimuli conjointly defined by motion and depth, as occurs in nature.

The perceptual segmentation and depth order of moving visual features, signaled by V5/MT, is essential for the successful processing of 3D scene information viewed by a moving observer, which we discuss in the next section. These results also have implications for understanding the contribution of other areas to perception and decision-making, especially downstream of V5/MT. For instance, when probed with 2D motion stimuli, lateral intraparietal (LIP) area neurons integrate perceptual evidence for decision-making (Gold and Shadlen, 2007). However, primates naturally make decisions about 3D objects and visually explore 3D space. These behaviors may be mediated by LIP neurons with a distinct visual RF and tuning for 3D depth and motion (Ferraina et al., 2002; Ahmed et al., 2025; Fig. 3E). A full account of perceptual and decision processing must include 3D space.

Mechanisms for 3D Gaze-Tolerant Object Vision in the Primate Dorsal Pathway

Up to this point, we focused on visual coding mechanisms that model the 3D world without explicitly considering the impact of self-motion on 3D representations. Self-motion, especially

eye and head movements for visual exploration, is a key element of strategies used to acquire information about the environment. Because self-motion shifts and rotates visual elements on the retinae and changes their absolute disparities, it inherently complicates 3D spatial encoding. In this section, we discuss mechanisms within the macaque dorsal visual pathway that create representations of the 3D spatial pose (position and orientation) of objects which remain stable across changes in the animal's 3D gaze location (i.e., are gaze-tolerant).

Stable visual perception involves the synthesis of retinal and extraretinal signals including oculomotor command and proprioceptive eye-in-orbit signals (Sun and Goldberg, 2016). Studies in which stimuli and eye movements were confined to a 2D display revealed mechanisms for 2D gaze tolerance in multiple dorsal pathway areas, including V3A (Galletti and Battaglini, 1989; Galletti et al., 1990; Nakamura and Colby, 2002), LIP (Duhamel et al., 1992), and 7a (a target of LIP; Andersen and Mountcastle, 1983; Andersen et al., 1990; Felleman and Van Essen, 1991). Visual exploration, however, also involves fixating at different distances, such that vergence eye movements profoundly alter a scene's absolute disparity structure. For instance, if an observer moves their fixation from in front of an object to behind it, the absolute disparities change from "far" to "near."

Relative disparity (Fig. 1A) mechanisms that potentially provide resilience to changes in fixation distance begin to emerge in V2 and become more prevalent in some higher visual areas (briefly discussed above; Thomas et al., 2002; Parker, 2007; Umeda et al., 2007; Krug and Parker, 2011; Verhoef et al., 2016). However, it is unclear whether those mechanisms contribute to 3D gaze-tolerant visual perception because fixation distance was not varied in that work. Other studies have tested the 3D gaze tolerance of neuronal responses to object distance in the medial superior temporal area (Roy et al., 1992), LIP (Genovesio and Ferraina, 2004), parietal reach region (Bhattacharyya et al., 2009), and ventral intraparietal area (Caziot et al., 2025) by varying both the absolute disparity of stimuli and the fixation distance. Those studies found that the disparity tuning curves of individual neurons could change with fixation distance in several ways, including gain changes with no shift in disparity preference, preference shifts that partially offset the vergence changes, and gain changes with partial shifts in preference. Thus, the neurons did not directly represent object distance. Instead, their responses were consistent with those of units in intermediate layers of in silico network models that synthesize retinal and extraretinal inputs to create gaze-tolerant representations of object position (Deneve et al., 2001; Seilheimer et al., 2014).

Other work implicates V3A and its little-studied target, the caudal intraparietal (CIP) area, in performing hierarchical, 3D visual computations. Visual selectivity in these areas is intriguingly heterogeneous. Similar to V1, some V3A neurons implement low-level spatiotemporal filtering or absolute disparity detection (Gaska et al., 1988; Anzai et al., 2011). Correspondingly, experiments that tested for 3D object pose selectivity by varying the orientation and distance of planar surfaces with fixation held at a single distance (Fig. 4A) found that the responses of some neurons can be straightforwardly attributed to absolute disparity signals (Rosenberg et al., 2023; Fig. 4B). In stark contrast, other neurons, which are more prevalent in CIP than V3A (Chang et al., 2020a; Doudlah et al., 2022), show high-level selectivity for 3D object pose (Fig. 4C). The defining property of 3D pose-selective neurons is that joint tuning for orientation and distance is multiplicatively separable,

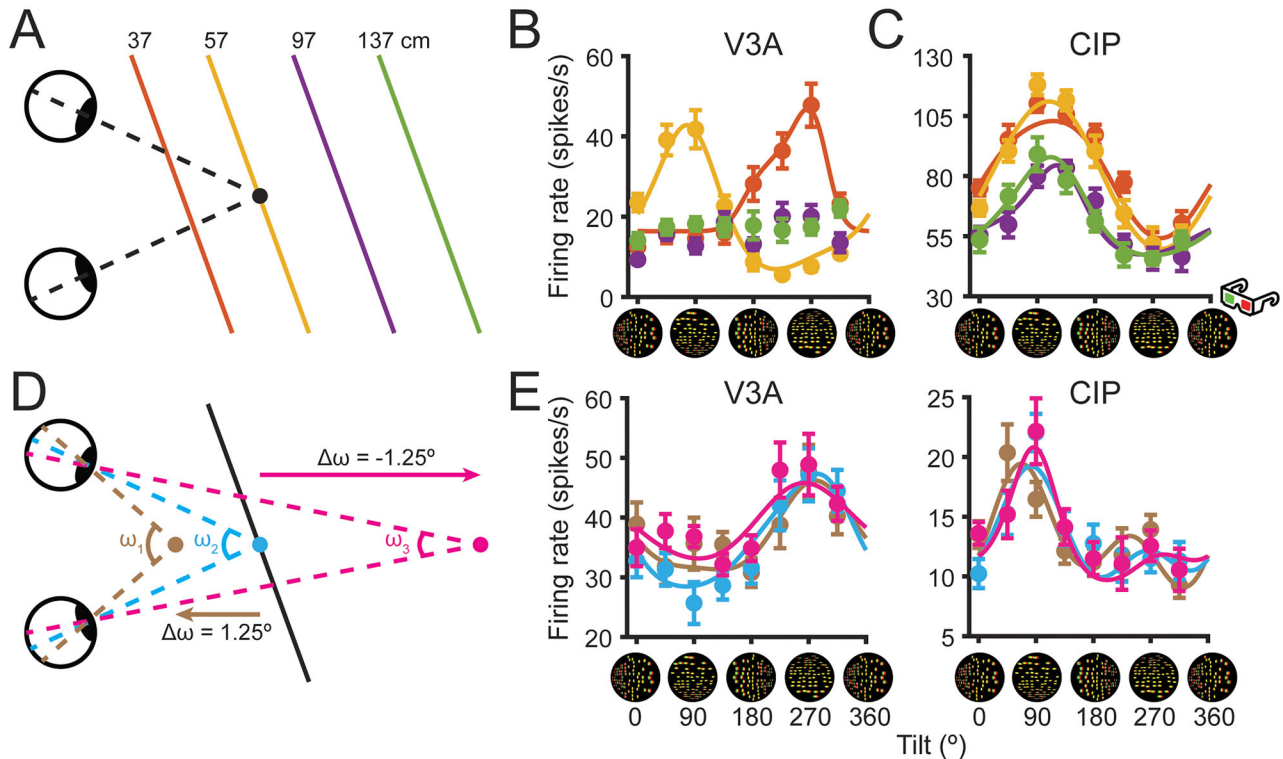


Figure 4. 3D object pose tuning and gaze-tolerant representations in the macaque dorsal pathway. **A**, Stimulus conditions for evaluating 3D pose (position and orientation) selectivity. Tuning for 3D surface orientation was measured at four stimulus distances, while a constant fixation distance (57 cm) was maintained. Tilt angle indicates which side of the plane was nearest to the subject. **B**, Tilt tuning at each distance for a V3A neuron. The strong dependence of tilt preference on distance implies selectivity for lower-level disparity signals. **C**, Tilt tuning at each distance for a CIP neuron. The high degree of similarity in tilt preferences across stimulus distances (despite profound differences in the absolute disparities) together with parametric modulation of response amplitude (gain) indicates selectivity for the object's 3D spatial pose. **D**, Stimulus conditions for evaluating 3D gaze tolerance. Tuning for 3D surface orientation was measured at one stimulus distance but three fixation distances (vergence changes and corresponding disparity pedestals of $\pm 1.25^\circ$ from the middle condition). **E**, Tilt tuning at each fixation distance for V3A (left) and CIP (right) neurons. The high degree of similarity in tilt preferences across fixation distances with minimal gain change (again despite profound differences in the absolute disparities) indicates 3D gaze tolerance. That is, the representation of the object's 3D pose was stable with respect to the subject, even as their gaze moved through the 3D space. Solid curves are Bingham function fits (Rosenberg et al., 2013). Planar surfaces along the abscissae of the tuning curve plots illustrate a subset of presented tilts as red–green anaglyphs.

such that orientation preferences are distance tolerant and distance is signaled by the response gain. Several findings point to generalized roles for V3A and CIP in stable, cohesive visual perception. Neurons in both areas multiplex visual and saccade signals (Doudlah et al., 2022), which may be the mechanistic basis for the 2D gaze tolerance of V3A neurons noted above. Similarly, the visual orientation preferences of some V3A and CIP neurons rotate with changes in head orientation as a result of vestibular/proprioceptive signals, which may help anchor visual perception to a gravitational reference frame (Sauvan and Peterhans, 1999; Rosenberg and Angelaki, 2014a). Lastly, the 3D orientation selectivity of many CIP neurons is driven by both stereoscopic and perspective cues (Tsutsui et al., 2001; Rosenberg and Angelaki, 2014b).

Ongoing experiments are now testing for 3D gaze-tolerant neuronal responses in V3A and CIP by comparing 3D orientation tuning curves measured at a fixed stimulus distance with gaze held in front of, at, or behind a planar surface (Fig. 4D). For many neurons in both areas, initial results suggest that fixation distance minimally effects the gain and shape of the 3D orientation tuning curve (Fig. 4E). Given that 3D pose selectivity is stronger in CIP, confirmation that 3D gaze tolerance is strong and similarly prevalent in V3A and CIP has fundamental implications for the order in which functions are performed along the dorsal pathway. Specifically, it would imply that gaze-tolerant visual perception is achieved first through the synthesis

of lower-level visual representations and extraretinal signals, after which object pose is computed for stable 3D visual perception and successful manipulation of objects in 3D space.

Glancing toward the Future with Two Eyes

Depth perception is integral to the proper functioning of the visual system. This is evident from the wide-ranging visual and oculomotor deficits associated with the loss of binocular integration, disparity processing, and depth perception in amblyopia (Levi et al., 2015). To perceive and interact with the 3D world, the brain must model it from ambiguous and dynamic 2D retinal images. Here, we described studies investigating the neural basis of stereopsis which revealed parallels and distinctions between how the visual systems of different mammals adapted to process 3D information. A common feature is that binocular disparity selectivity in V1 reflects an animal's ecological niche and appears to shape their reliance on stereoscopic cues to interpret the world. Higher visual areas in primates are characterized by specialization for 3D processing linked to stable perception and interacting with objects. In addition to stereopsis, perspective and other cues play prominent roles in 3D vision (Mamassian et al., 1998; Knill and Saunders, 2003; Chang et al., 2020b; Thompson et al., 2021; Parker et al., 2022). The cross-species approach taken here provides a roadmap for future research investigating how multiple 3D cues are integrated within neural circuits for cohesive perception of objects and scenes. An additional

important direction for future research is to understand how statistical regularities across 3D scenes are learned and exploited to improve information-gathering and guide interactions with objects (Hibbard, 2007; Sprague et al., 2015).

Following the principles of the 3Rs—replacement, reduction, and refinement—it is important for research elucidating the neural basis of 3D vision to rely both on humans and animal models best suited to specific experimental questions and approaches. Further development of noninvasive human and animal neuroimaging techniques as well as intervention approaches at the neuronal circuit level in animal models will be essential for a deeper understanding of the mechanistic links between neural processing and depth perception across computational scales. Experiments with species which have different reliance on stereopsis, cognitive and motor abilities, and developmental timelines will elucidate the diversity of cellular and circuit mechanisms enabling rich visual perception and behavior. Genetic tools currently available for mice allow the activity of large neuronal populations to be monitored with cell-type specificity as well as highly targeted optical and chemical manipulations of neural circuits (Huberman and Niell, 2011; Priebe and McGee, 2014). The refinement of these techniques in NHPs, an essential model system because of their homologies to humans (Eldridge et al., 2016; Poo, 2023), and other species with robust stereopsis, like tree shrews, will create new, important avenues for discovering brain mechanisms underlying cognitive function directly relevant to human behavior. Recent fMRI studies of human 3D vision build directly upon findings from NHPs (Rosenberg et al., 2008; Thompson et al., 2023), underscoring that animal research will continue to guide the discovery of human biological processes (Wen et al., 2025a,b). For instance, as discussed above, open questions remain regarding the roles of GABA and glutamate signaling in the responses of the human visual cortex to binocular stimulation. At the same time, nonanimal approaches, such as in silico modeling, will play a valuable role in understanding the detailed workings of distributed, network-level brain computations. Together, these complementary research strategies promise to reveal therapeutic targets and yield scientifically validated treatments for visual impairments that afflict humans, including amblyopia and blindness, by providing a deeper comprehension of fundamental biological processes underpinning perception, cognition, and behavior.

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