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Behavior-Specific Computations in the Vertebrate Retina

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Abstract

Since Lettvin and colleagues' seminal discovery of bug detector neurons in the frog retina, understanding how retinal circuits support behavioral demands has been a central goal of visual neuroscience. Recent advances in machine learning, genetic tools, and neural recording have transformed our understanding of these circuits, particularly in the mouse retina. With a focus on mice, we examine how species-specific visual sampling strategies determine the behavioral relevance of retinal computations and review recent insights into circuits underlying reflexive behaviors, threat detection, prey capture, color vision, and night vision. We also highlight how the behavioral state itself influences retinal processing through direct neuromodulation and pupillary changes, challenging the traditional view of purely feedforward retinal processing in mammals. These findings confirm the retina as a sophisticated computational engine whose circuits have evolved to meet species-specific behavioral demands. While Lettvin's discovery of dedicated retinal circuits for innate behaviors launched the field, new tools now promise to expand our understanding of retinal contributions to naturalistic and flexible behaviors across species.

1. INTRODUCTION

Retinal cell types: cell types are categorized by function, anatomy, molecular profile, and brain projections, illustrating the complexity of defining retinal cells

In their seminal work "What the frog's eye tells the frog's brain," Lettvin et al. (1959) suggested that, rather than taking a point-by-point video of the environment, the retina extracts visual features relevant to frog behavior. They tested this theory by presenting the frog's visual system with a variety of naturalistic stimuli, including a small black dot moving on a large color photograph of the frog's habitat. From these experiments, they identified net convexity detectors or bug perceivers: a population of retinal ganglion cells selective for the small moving black dot (Lettvin et al. 1959). Their approach began with a description of the frog's visual behaviors, then they adopted a top-down approach to search for retinal neurons that detect features relevant to those behaviors (**Figure 1*a***). Neurons are considered selective for specific features if they (*a*) respond strongly to the feature and, importantly, (*b*) are invariant to other visual features. This review examines recent work that continues the tradition established by Lettvin et al. (1959), a top-down understanding of retinal circuits for detecting behaviorally relevant features.

1.1. Visual Sampling Strategies Shape the Behavioral Roles of Retinal Computations

How animals sample their visual world has shaped how their retinal circuits process information. Animals with a fovea, such as primates, and those without, such as mice, exhibit markedly different visual sampling strategies that reflect their distinct ecological needs and behaviors. Primates, with their forward-facing eyes and extensive binocular overlap (~130°), have evolved a fovea-centered approach that requires active scanning of the environment through rapid eye movements (saccades) to build detailed visual representations (**Figure 1*b***, **subpanel *i***). In contrast, many vertebrates without a high-resolution fovea, such as mice, rely on compensatory eye movements along with head movements to stabilize their visual field (Meyer et al. 2020, Michaiel et al. 2020) (**Figure 1*b***, **subpanel *ii***). Mice have lateral-facing eyes that provide extensive monocular visual fields (~180°) with limited binocular overlap (~40°). The stabilization allows different regions of the mouse retina to consistently align with specific areas of the visual environment. This alignment enables retinal circuits in each region to evolve specialized processing that directly supports survival behaviors. Recent studies have revealed numerous examples of such computations, making mice particularly valuable for understanding how early visual processing directly serves behavioral needs (Huberman & Niell 2011, Meyer et al. 2018, Gupta et al. 2023, Pinke et al. 2023, Spinelli et al. 2024).

1.2. Architecture, Cell Types, and Neural Circuits of the Vertebrate Retina

Since Lettvin et al.'s (1959) seminal work, advances in anatomical, functional, and genetic approaches have enabled a comprehensive classification of vertebrate retinal cell types (Baden et al. 2016, Shekhar et al. 2016, Bae et al. 2018, Vlasits et al. 2019, Goetz et al. 2022, Hahn et al. 2023). The vertebrate retinal circuit (Masland 2012) (**Figure 1*c***) begins with photoreceptors (PRs)—high-sensitivity rods for low-light conditions and cones for light detection in brighter environments. PRs synapse onto excitatory interneurons called bipolar cells (BCs) and inhibitory interneurons called horizontal cells (HCs). BCs are a major stage of divergence in the retina, with different types having distinct anatomy, structures, stimulus preferences, release kinetics, and connectivity. Like PRs, BCs synapse onto both excitatory and inhibitory neurons [ganglion cells and amacrine cells (ACs), respectively]. Retinal ganglion cells (RGCs) are the output neurons of the retina, sending action potentials through the optic nerve to the central brain. Different RGC types have distinct, but often overlapping, projection patterns in the brain (Martersteck et al. 2017, Reinhard et al. 2019, Kerschensteiner & Feller 2024).

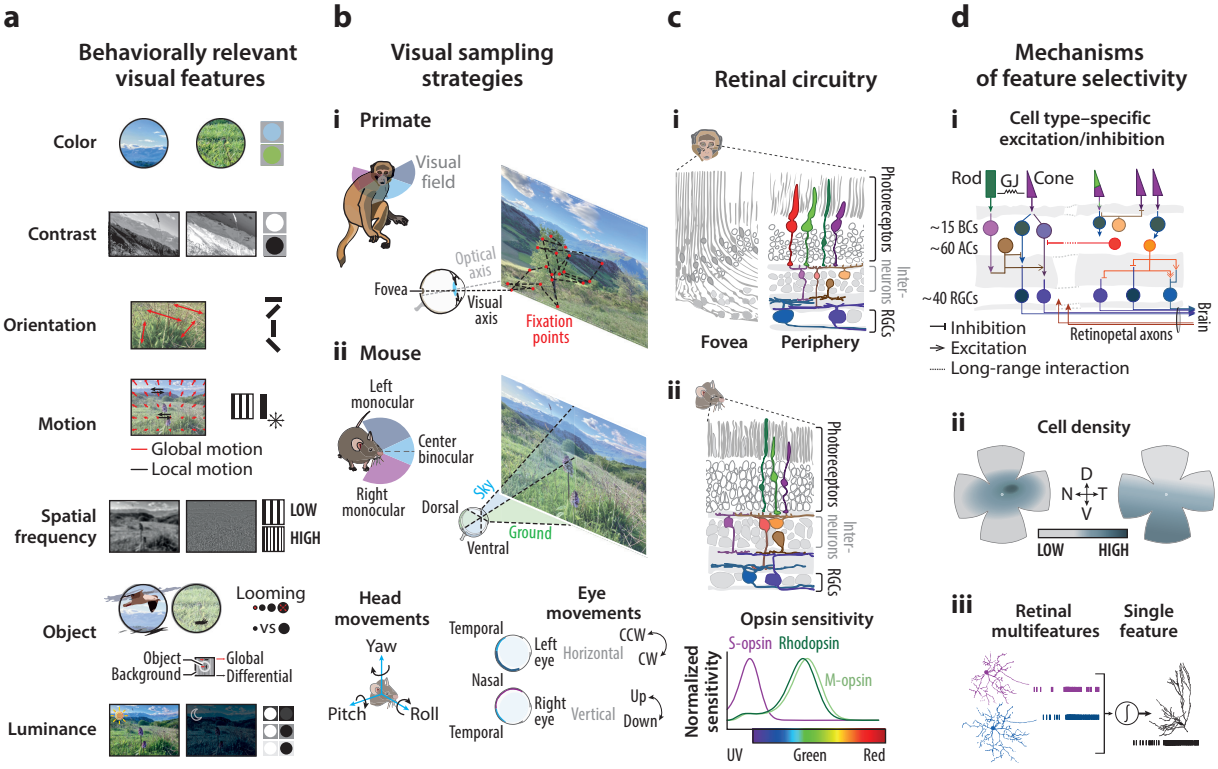

Figure 1

Species-specific visual sampling strategies affect the relationship between retinal computations and behavior. (*a*) Fundamental visual features processed by the retina: color, contrast, orientation, motion (global and local), spatial frequency, object segregation, and luminance. Left pictures show naturalistic images that differ along the respective feature, and adjacent stimuli illustrate well-established parametric stimuli used to probe these features. (*b*) Visual field organization and sampling strategies in (*i*) primates and (*ii*) mice. Primates have forward-facing eyes with a large binocular field (*light blue*) and foveal-centric vision, using saccades to scan scenes (*red*). Mice have laterally positioned eyes with a smaller binocular field, relying on coordinated eye and head movements for image stabilization. Specifically, head motion (i.e., pitch, roll, and yaw) is compensated by eye movements in horizontal (CW and CCW) and vertical (up and down) axes. (*c*) Retinal circuit organization comparing (*i*) primate schematic retinal architecture, emphasizing foveal-peripheral specialization, and (*ii*) mouse retinal structure, with corresponding photoreceptor opsin sensitivity profiles. (*d*) Feature selectivity of retinal neurons arises through different mechanisms. (*i*) Feature-selective retinal circuits are formed by the interplay of retinal cell types, providing cell type–specific excitatory and inhibitory input to RGCs. (*ii*) Nonuniform cell density distributions across the retina. (*iii*) Integration of retinal feature channels in downstream neurons. Abbreviations: AC, amacrine cell; BC, bipolar cell; CCW, counterclockwise; CW, clockwise; D, dorsal; GJ, gap junction; M, medium wavelength; N, nasal; RGC, retinal ganglion cell; S, short wavelength; T, temporal; V, ventral.

The high diversity of cell types identified in the retina across vertebrates extends to the primate (**Figure 1*c*, subpanel *i***). There are more RGC types than previously thought (Peng et al. 2019, Kim et al. 2022, Li et al. 2023b, Kling et al. 2024). In addition, the primate retina can detect complex features like motion direction (Kim et al. 2022, Patterson et al. 2022, Wang et al. 2023a). This suggests that, at least in the periphery, primate retinas may resemble those of our mammalian relatives, such as the mouse.

Neural circuits and even the anatomy of single cells can be arranged such that a cell type prefers specific features over others. Inhibition from ACs is thought to play an especially important role in tuning the preferences of RGCs to distinct features (Kerschensteiner 2022) (**Figure 1*d***,

subpanel *i*). Specializations in the layout and location of cell types across the retina can allow for distinct feature selectivity across different parts of the visual field (**Figure 1*d***, **subpanel *ii***). Finally, RGCs may project to brain regions where they interact with downstream partners in distinct ways, providing a further selective filter on the information they convey (**Figure 1*d***, **subpanel *iii***).

1.3. Revisiting the Role of Retinal Processing in Behavior

Two recent developments make revisiting the role of retinal computations in behavior especially relevant. First, advances in machine learning now enable the investigation of retinal processing under naturalistic conditions that better reflect real-world vision. While traditional studies relied on simplified stimuli like flashing spots or moving bars for easier interpretation (reviewed in Turner et al. 2019), deep learning approaches—particularly convolutional neural networks—can effectively analyze neural responses across complex, high-dimensional stimulus spaces without requiring predefined parameters. These models can identify the most exciting inputs for individual neurons and reveal feature selectivity in more naturalistic contexts (Bashivan et al. 2019, Walker et al. 2019, Franke et al. 2022, Höfling et al. 2024). Second, recent evidence has revealed that retinal function is substantially modulated by behavioral state and feedback signals from the brain, even in mammals, where such influences were previously thought to be minimal. This modulation occurs through multiple pathways: direct centrifugal inputs via the optic nerve, neuromodulatory signals associated with arousal and attention, and indirect effects through pupillary adjustments. The discovery of species-specific differences in feedback mechanisms, from extensive systems in birds to more subtle but significant feedback in mammals, suggests that these pathways have evolved to meet specific ecological demands (Nilsson 2021, Baier et al. 2023, Warwick et al. 2024). Together, these advances are transforming our understanding of how the retina supports natural vision through dynamic, context-dependent processing (Baden et al. 2020, Nilsson 2021, Baier et al. 2023, Baden 2024b).

In summary, recent advances in retinal cell type classification, circuit manipulation tools, machine learning approaches, and behavioral tools make this a compelling time to reexamine retinal computations in behavioral contexts. This ecological, evolutionary, and systemic context can provide insights into how the visual system has adapted to solve specific behavioral demands (Baden et al. 2020, Nilsson 2021, Baier et al. 2023, Baden 2024b). In the following sections, we explore how various mechanisms of retinal feature selectivity support visual behaviors (**Figure 1**).

2. FROM RETINA TO BEHAVIOR: EXPLORING RETINAL CIRCUIT CONTRIBUTIONS

Visual processing in the retina supports a diverse array of survival-critical behaviors, from navigation and predator avoidance to prey capture. Following Lettvin's top-down approach, we structure each of the following sections to systematically link ethology to retinal mechanisms. For each behavior, we describe its ecological role, analyze the visual features that trigger it, and detail the underlying retinal circuits that extract these features.

2.1. Visually Driven Reflexive Behaviors

For animals to survive, they must accurately detect food, predators, and obstacles while moving through their environment. Self-generated motion creates constant shifts in visual input that can blur vital signals. The solution lies in reflexive eye movements that automatically compensate for self-motion (Walls 1962). Different species have evolved distinct stabilization strategies (reviewed in Land 2015, Giovannetti & Rancz 2024).

Visual stabilization occurs through coordinated movements of the eyes, head, or body (**Figure 1*b***). Two primary reflexes prevent retinal image blur: the vestibulo-ocular reflex and the optokinetic reflex (OKR). The vestibulo-ocular reflex, driven by inner ear signals, operates during rapid head movements (Wallace et al. 2013, Holmgren et al. 2021), while the OKR responds to visual cues during slower movements (Yonehara et al. 2016, Harris & Dunn 2023). These reflexes work together to maintain visual stability across different movement conditions. Consider an animal moving forward: This creates an optic flow pattern with lateral drift. The OKR generates compensatory eye movements to track the environment, ensuring that approaching objects appear to grow larger while maintaining their position, while peripheral objects move laterally.

Vestibulo-ocular reflex: uses inner ear signals to produce compensatory eye movements opposite to rapid head turns

Optokinetic reflex (OKR): uses visual motion signals to produce compensatory eye movements that stabilize retinal images during sustained head or global motion

Although natural scenes are complex, researchers typically study motion-stabilizing reflexes using simplified stimuli, such as moving stripe patterns. In a classic setup, a head-fixed mouse is presented with rotating stripes that evoke the OKR (**Figure 2*a***). The OKR consists of two phases: a smooth tracking phase, where the eyes follow the moving stripes, followed by rapid resets in the opposite direction to prepare for the next tracking cycle. This reflex shows directional preferences, with a stronger response to upward and anterior motion (Yonehara et al. 2009, Harris & Dunn 2023), and adapts to various stimulus properties (Tabata et al. 2010, Dehmelt et al. 2021, Knorr et al. 2021). The OKR also responds to motion in depth, generating different eye movement patterns when objects move toward or away from the animal (Choi & Priebe 2020). Beyond eye movements, many species also show a whole-body response to visual motion, known as the optomotor response (Wang et al. 2020). Zebrafish exhibit specializations in this response, primarily using their lower temporal visual field during forward swimming, likely because the underwater floor provides reliable motion cues (Alexander et al. 2022).

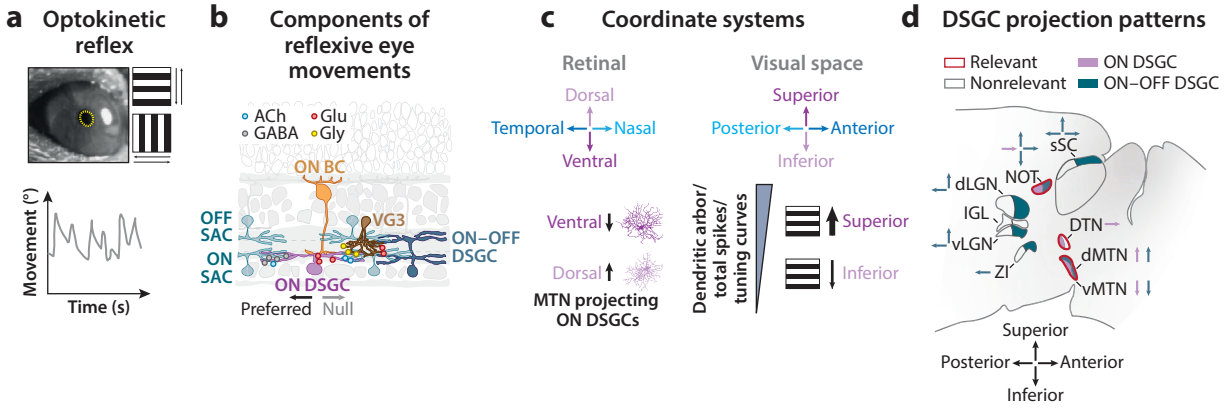

Figure 2

Eye movement-based image stabilization. (*a*) The optokinetic reflex generates involuntary eye movements that stabilize retinal images during head motion, as well as simulated motion using drifting gratings. (*b*) Schematic neural circuit showing key cellular components of reflexive eye movements: ON BCs, OFF and ON SACs, VG3 ACs, and DSGCs. Neurotransmitters used to create respective feature selectivity (i.e., direction, motion, and speed selectivity) include GABA, Glu, Gly, and ACh. (*c*, *top*) Coordinate systems in retinal and visual space. The arrows indicate preferred motion directions and are color-coded within the two systems. (*bottom*) Asymmetric tuning in ON DSGCs projecting to the MTN of the accessory optic system drives directional bias in the vertical optokinetic reflex. (*d*) DSGC projection patterns in the brain, including the sSC, dLGN, vLGN, IGL, ZI, and accessory optic system nuclei (NOT, DTN, MTN). Arrows indicate preferred DSGC motion directions in visual space. Brain areas involved in eye movement–based image stabilization are highlighted in red. Abbreviations: ACh, acetylcholine; BC, bipolar cell; dLGN, dorsal lateral geniculate nucleus; dMTN, dorsal medial terminal nucleus; DSGC, direction-selective ganglion cell; DTN, dorsal terminal nucleus; GABA, gamma-aminobutyric acid; Glu, glutamate; Gly, glycine; IGL, intergeniculate nucleus; MTN, medial terminal nucleus; NOT, nucleus of the optic tract; SAC, starburst amacrine cell; sSC, superficial superior colliculus; VG3, VGluT3; vLGN, ventral lateral geniculate nucleus; vMTN, ventral medial terminal nucleus; ZI, zona incerta.

Visual reflexes, including eye movements and whole-body adjustments, enable critical behaviors such as estimating running speed and calculating object distances (Saleem et al. 2013). Direction-selective ganglion cells (DSGCs), shown in **Figure 2*b***, mediate these reflexive eye movements in mice. These neurons respond robustly to motion in their preferred direction while remaining silent to opposite motion. Originally discovered in rabbits (Barlow & Hill 1963), DSGCs have been characterized across species and recently confirmed in primates (Patterson et al. 2022, Wang et al. 2023a).

Direction selectivity arises through inhibition from starburst amacrine cells (SACs) (Yoshida et al. 2001, Euler et al. 2002). DSGCs include three main types: ON, OFF, and ON–OFF. ON–OFF DSGCs respond to both light onset and offset along four cardinal directions (nasal/posterior, dorsal/inferior, temporal/anterior, and ventral/superior in retinal and visual space coordinate systems) (Wei 2018) (**Figure 2*c***). ON DSGCs align with vestibular semicircular canals (Sabbah et al. 2017) and exhibit distinct speed preferences. While ON–OFF DSGCs respond to broad speeds, ON DSGCs prefer slower motion (around 5°/s), matching OKR tuning. VGluT3 (VG3) ACs regulate this speed sensitivity (Summers & Feller 2022, Mani et al. 2023) (**Figure 2*b***).

The role of ON DSGCs in the OKR is well-established. ON DSGCs have been identified in several species such as primates, where they are asymmetrically distributed with peak density along the horizontal midline (Giolli et al. 2006, Wang et al. 2023a). This suggests similar gaze stabilization roles across species. ON DSGCs project exclusively to the accessory optic system (AOS), a group of brainstem nuclei that control reflexive eye movements (Yonehara et al. 2008, 2009; Dhande et al. 2013) (**Figure 2*d***). Disrupting SACs, SAC–DSGC connectivity, or DSGC–AOS connections eliminates the OKR response (Yoshida et al. 2001, Yonehara et al. 2016, Al-Khindi et al. 2022). The AOS processes vertical and horizontal motion components through specialized nuclei: the medial terminal nucleus handles vertical motion, while the nucleus of the optic tract and dorsal terminal nucleus process horizontal motion. In natural scenes, the ground plane limits depth variation in the lower visual field, which may require specialized retinal processing. In general, ON DSGCs exhibit stronger responses in the dorsal retina, with ventral motion–preferring ON DSGCs spiking more than their dorsal motion–preferring counterparts across all retinal quadrants (Harris & Dunn 2023) (**Figure 2*c***). This asymmetry in the morphology and tuning properties of the medial terminal nucleus projecting superior versus inferior motion–preferring DSGCs leads to asymmetries along the vertical axis, which may accommodate for the limited depth variation in the lower visual field.

While ON DSGCs have a clear role in the OKR, the behavioral significance of ON–OFF DSGCs remains less understood. Unlike ON DSGCs, ON–OFF DSGCs project to multiple targets, including the AOS, dorsal lateral geniculate nucleus (dLGN), ventral lateral geniculate nucleus (vLGN), and superficial superior colliculus (sSC). Although ON–OFF DSGCs contribute to direction-selective responses in the superior colliculus (SC) (Shi et al. 2017), their function in the dLGN and broader motion perception requires further investigation.

2.2. Innate Behaviors: Predator Avoidance and Prey Capture

Sensory systems have evolved to process survival-critical signals through hard-wired feature selectivity. This enables rapid, robust, and stereotyped responses without prior learning. Despite being innate, these behaviors can exhibit flexibility, and animals can refine their responses over time. Here, we focus on two such behaviors: threat detection and prey capture.

2.2.1. Responses to visual threat. One of the most fundamental threatening visual stimuli is an object that appears to be approaching rapidly, which manifests as an expanding shape on the retina (**Figure 3*a***). This looming stimulus has proven valuable for studying threat responses

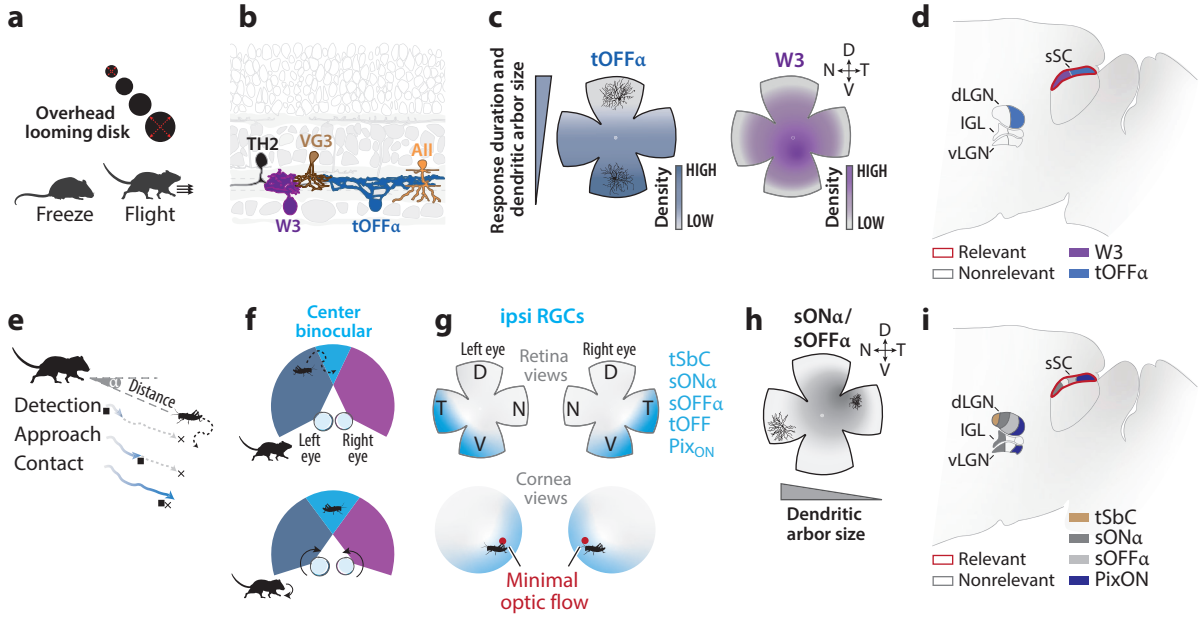

Figure 3

Retinal circuits for threat detection and prey capture behaviors. (*a*) A looming overhead stimulus elicits defensive freeze or flight responses in mice and many other animals. (*b*) Three retinal cell types (W3, VG3, tOFFα) form neural circuits with selectivity for dark looming stimuli. (*c*) tOFFα and W3 RGCs show ventral retina specialization with smaller dendritic arbors and, for tOFFα RGCs, more transient responses when sampling the sky. (*d*) W3 and tOFFα projections to downstream brain areas, with areas involved in threat detection behaviors indicated in red. (*e*) Prey hunting in mice can be broken down into distinct phases: detection, approach, and contact. Small dark moving objects located in the lower visual field elicit prey capture. (*f*) Prey targeting utilizes binocular vision. Mice perform converging eye movements to increase the binocular field during the approach phase. (*g*) Efficient prey approach relies on binocular vision and, therefore, ipsilateral-projecting RGCs. The binocular visual field also overlaps with an area of least optic flow, which may also stabilize prey images on the retina. (*h*) sONα/sOFFα RGCs are present at higher density and have smaller dendritic arbors in the temporal retina's binocular zone. (*i*) Brain projections of prey capture–relevant cells (tSbC, sONα, sOFFα, Pix$_{ON}$) to the sSC, dLGN, vLGN, and IGL. The areas involved in prey hunting are indicated in red. Abbreviations: D, dorsal; dLGN, dorsal lateral geniculate nucleus; IGL, intergeniculate leaflet; ipsi, ipsilateral-projecting; N, nasal; Pix$_{ON}$, pixel encoder cell ON; RGC, retinal ganglion cell; sOFFα, sustained OFF α; sONα, sustained ON α; sSC, superficial superior colliculus; T, temporal; TH2, tyrosine hydroxylase type 2; tOFFα, transient OFF α; tSbC, transient suppressed-by-contrast; V, ventral; VG3, VGluT3; vLGN, ventral lateral geniculate nucleus.

in laboratory settings. When faced with looming stimuli, animals exhibit various defensive behaviors, including avoidance, blinking, ducking, escape, or freezing. From insects (Card & Dickinson 2008) to vertebrates, threat responses are often executed as stereotyped, reflexive motor patterns. The processing of looming threats involves two key neural stages. First, the visual system must detect the approaching threat. Second, this information must be processed by specialized brain regions that determine whether escape is warranted and coordinate evasive action.

Mice, as prey animals of aerial predators, display stereotyped defensive responses when confronted with looming stimuli: actively escaping to seek cover if a shelter is present or freezing in place (Yilmaz & Meister 2013, De Franceschi et al. 2016). Each strategy offers distinct advantages. Escaping provides direct protection, while freezing reduces detectability and enhances visual processing by minimizing retinal motion blur (Lojowska et al. 2015). Mice can initiate escape while freezing (De Franceschi et al. 2016), suggesting that responses extend beyond simple reflexes. The selection process depends on visual stimulus characteristics, environmental context,

and behavioral state (Yilmaz & Meister 2013, Vale et al. 2017, Tafreshiha et al. 2021, Lenzi et al. 2022, Li et al. 2023a, Solomon et al. 2023).

Center–surround receptive field (RF): Consists of a circular excitatory center antagonized by a concentric inhibitory surround

In rodents, key insights into neural threat detection mechanisms have emerged from systematic stimulus manipulations. The ability to trigger escape responses from the upper visual field suggests that threat detection originates in the inferior retina (Yilmaz & Meister 2013). A dark expanding disk at specific velocities triggers flight responses, highlighting the retinal OFF channel's role, while a sweeping disk triggers freezing. This velocity-dependent transition from freezing to flight (De Franceschi et al. 2016) is similar in fish, where larger dark objects and faster stimuli elicit stronger escape reactions (Preuss et al. 2006, Temizer et al. 2015).

In rodents, several key retinal cell types have been shown to be involved in processing visually threatening looming stimuli. Recent evidence suggests that distinct types of RGCs independently contribute to the choice between freezing and escaping depending on shelter availability (Lee et al. 2024). This underscores the role of specific retinal cell types in regulating these complex behaviors. *Kcnip2*-positive transient OFF α (tOFFα) RGCs play a crucial role, with their activation triggering escape and their ablation abolishing defensive responses (Wang et al. 2021). Ablation of all α RGCs reveals deficits in escaping to a shelter but no effect on freezing behavior in the absence of a shelter (Lee et al. 2024). Meanwhile, ablation of ON–OFF DSCGs using a Cart-Cre mouse line, which targets vertically tuned ON–OFF DSGCs, shows no critical involvement in freezing or escape responses (Lee et al. 2024). VG3 ACs are essential, as shown by reduced looming responses in VG3-knockout mice (Kim et al. 2020). W3 RGCs contribute to local motion signal detection (Zhang et al. 2012) (**Figure 3*b***). Together, these results suggest that specific RGC types contribute to distinct pathways underlying responses to visual threats.

Looming detection involves sophisticated circuit interactions. tOFFα RGCs integrate excitatory signals from OFF cone BCs and VG3 ACs (Kim et al. 2020) with ON AII ACs providing inhibitory signals that are relieved during looming stimuli (Münch et al. 2009). VG3 ACs and W3 RGCs detect looming motion onset through push–pull between transient excitation and sustained inhibition (Lee et al. 2014, Kim et al. 2015, Krishnaswamy et al. 2015).

These threat-detection signals are primarily processed in the SC. tOFFα RGCs innervate the superficial SC layers, where their terminal activation triggers defensive responses. Other RGC types, including SC-projecting W3 RGCs (Kim et al. 2010, Wang et al. 2021), likely contribute to full behavioral responses (**Figure 3*d***). tOFFα RGCs also project to the dLGN, relaying information to the primary visual cortex (Huberman et al. 2008). In zebrafish, similar principles apply, with RGCs projecting to the tectum, which integrates motion, looming, and brightness information (Temizer et al. 2015, Heap et al. 2018). Open questions remain regarding tOFFα and W3 RGCs' contributions to selectivity for objects approaching from above (**Figure 3*c***), as these cells exhibit a nonhomogeneous sampling of the visual field (Zhang et al. 2012, Warwick et al. 2018).

2.2.2. Prey capture. Prey capture is a dynamic, challenging task involving detecting, approaching, capturing, and killing or eating prey (**Figure 3*e***). Specialized visual circuits have evolved to improve prey capture success, extracting and transmitting prey-related features while the hunter is in motion. This process begins in the retina, with specializations observed across species, particularly in mouse hunting of crickets and zebrafish hunting of paramecia. Several visual features aid prey detection, including object size, color, texture, and movement patterns relative to the background. Both mice and zebrafish approach virtual objects meeting specific criteria, allowing one to test prey stimulus parameters. Many retinal cells detect local motion through center–surround receptive fields (RFs) (Gaynes et al. 2022, Strauss et al. 2022), suggesting that initial prey detection may not require specialized circuits. For mice, ~2 cm objects, either stationary or moving at

2–15 cm/s, evoke approach behaviors rather than freezing (Procacci et al. 2020). Prey detection involves two parts: initial movement detection followed by judgments based on object characteristics, processed in the sSC through wide- and narrow-field cells (Hoy et al. 2019), with wide-field cells handling initial detection and narrow-field cells managing approach transition (Hoy et al. 2019).

A different specialization is key for the zebrafish detection of *Paramecium*: color. Paramecia are more salient in the UV spectrum (Zimmermann et al. 2018). Zebrafish target prey in an acute zone of their visual field, the frontal horizon, corresponding to the temporal midline of the retina. Here, zebrafish have specialized UV cone PRs that highlight prey (Yoshimatsu et al. 2020). These cones are located in the binocular zone of the zebrafish eye, and activating single cones evokes stereotyped prey capture behavior.

Binocular zone: the region of visual space where the fields of view from both eyes overlap, enabling depth perception through stereopsis and enhanced visual acuity

The next step is the approach, where the visual system estimates prey distance. Binocular vision and depth from defocus are key strategies. Both mice and jumping spiders use defocus for estimating jump distances (Nagata et al. 2012, Parker et al. 2022). However, for mice, defocus alone is insufficient, given their poor monocular hunting performance (Johnson et al. 2021). Binocular vision occurs where input from both eyes overlaps (**Figure 3*f***). Both mice and zebrafish exhibit ocular convergence, which enlarges the binocular zone (Bianco et al. 2011, Michaiel et al. 2020). This temporal retinal region has higher acuity through increased RGC density, improving detail and depth perception (Bleckert et al. 2014, Yoshimatsu et al. 2020) (**Figure 3*f***). Binocular vision, achieved through contralateral and ipsilateral RGC axon projections, is essential for approach behavior in mice. When ipsilateral-projecting RGCs, comprising less than 2% of RGCs (**Figure 3*g***), are eliminated in adult mice, prey approaches fail (Johnson et al. 2021).

Approach requires tracking prey during movement through visual–motor integration and maintaining stable gaze in the high-acuity zone (Hoy et al. 2016, Michaiel et al. 2020, Holmgren et al. 2021) (**Figure 3*f***). Zebrafish use visually guided orienting movements, striking when prey enters the binocular zone at specific distances (Patterson et al. 2013). Mice approach with pitched-forward heads to keep prey centered in their binocular field (Holmgren et al. 2021, Johnson et al. 2021). The mouse binocular zone experiences minimal optic flow (Holmgren et al. 2021), potentially facilitating prey movement detection through separate peripheral and acute zones (**Figure 3*g***).

Cell types in the retina could be specialized for prey capture or repurposed in the acute zone. Johnson et al. (2021) found that several ipsilateral-projecting RGC types detect cricket-sized moving bars. However, these cells are mostly contralateral projecting throughout the retina (**Figure 3*g***), suggesting functional repurposing. In the acute zone, sustained ON α (sONα) RGCs have distinct features supporting prey detection (Oesterle et al. 2025) (**Figure 3*b***). RGCs may multiplex the information they send to the brain, with specific information used by downstream circuits for prey capture. For example, DSGCs provide input to narrow-field cells in the SC (Krizan et al. 2024). While these direction-tuned narrow-field cells are critical for prey approach orientation (Hoy et al. 2019), the RGC inputs' direction selectivity is not required for prey capture (Krizan et al. 2024). Which RGC-encoded information guides successful prey capture remains an active research area.

A new frontier in prey capture research is understanding its developmental emergence. Zebrafish larvae begin hunting within a day of hatching, with innate behavior improving over days (Oldfield et al. 2020). Mice present an interesting case, as juveniles with underdeveloped binocular vision exhibit prey capture deficits (Allen et al. 2022). Hu et al. (2024) found that SC binocular cells display a critical period affecting hunting success. Beyond this period, mice show experience-dependent improvements in prey capture (Procacci et al. 2020, Galvin et al. 2021).

Understanding how the brain refines prey signal interpretation and integrates visual–motor responses remains an exciting frontier in visual learning research.

2.3. Nonimage-Forming Vision

The most dramatic change in an animal's visual environment is the difference in luminance between day and night. In recent years, the behaviors and physiological processes that are influenced by changes in luminance both on short timescales and circadian and circannual timescales have begun to grow. Many of these behaviors do not appear to require spatial vision. Instead, these nonimage-forming behaviors take advantage of retinal neurons that monitor changes in luminance over longer timescales. Information about changes in luminance is primarily thought to be relayed by RGCs that express the opsin protein melanopsin. Melanopsin-expressing RGCs are capable of directly detecting photons (reviewed in Aranda & Schmidt 2021). They are thus known as intrinsically photosensitive RGCs (ipRGCs).

Beyond well-described roles in circadian entrainment, pupil control, and image-forming vision, ipRGCs are now thought to supply luminance information to a wide variety of brain centers. Light information via ipRGCs modulates activity in the perihabenula to influence mood (Fernandez et al. 2018, Weil et al. 2022), the central amygdala to cause anxiety (Wang et al. 2023b), and the prefrontal cortex to influence cognition (Lazzerini Ospri et al. 2024, Zangen et al. 2024). In addition, projections from ipRGCs to the supraoptic nucleus of the hypothalamus can mediate light's influence on maternal behaviors and social memory (Berry et al. 2023, Huang et al. 2023) and modulate glucose metabolism (Meng et al. 2023). Many behaviors are indirectly modulated by light via the suprachiasmatic nucleus, which controls the central circadian clock. However, both body temperature (Rupp et al. 2019) and breathing (Jones et al. 2024) are regulated by light separately from the central clock.

The retina is capable of sending luminance information on a variety of timescales to the brain. This is accomplished through mechanisms at the level of molecules, circuits, and populations. Different ipRGC subtypes harness distinct G protein–coupled signaling cascades to tune their sensitivity to light and the duration of their firing (Contreras et al. 2021). In addition, melanopsin has multiple stable conformations, with short wavelengths of light activating the protein and long wavelengths deactivating it (Emanuel & Do 2015). At the circuit level, ipRGCs receive input from the canonical retinal circuits in addition to their cell-intrinsic sources of light information.

At the level of the brain, the neurotransmitter released by ipRGCs shapes how these cells influence downstream brain circuits. Some RGC types, including ipRGCs, release gamma-aminobutyric acid (GABA) rather than glutamate (Sonoda et al. 2020, Yuan et al. 2024). This inhibitory input from ipRGCs is important for tuning the luminance sensitivity of circadian entrainment and the pupil response (Sonoda et al. 2020). Finally, ipRGCs carry important information about absolute light intensity at the population level through differences in their luminance tuning. This population code has been observed in both mice and primates (Milner & Do 2017, Liu et al. 2023). Population codes may be further refined by nonuniform tiling of the retina (Dyer et al. 2024), which restricts luminance sampling to specific regions of the visual field.

2.4. Color Vision

For most animals, vision relies heavily on color sensation and perception (reviewed in Gerl & Morris 2008). Although color vision—the ability to sense and distinguish different wavelengths of light—is not a behavior in itself, it underpins numerous behaviors across species, from object detection to mating rituals. Color vision stands as a classic example of our comprehensive

understanding of retinal contributions to perception and, consequently, behavior. In this section, we examine the retinal mechanisms underlying color vision, with a specific focus on recent discoveries in mice.

Color vision operates by comparing signals from PR types responsive to specific ranges of light wavelengths. This comparison occurs through various retinal circuits (reviewed in Baden & Osorio 2019, Thoreson & Dacey 2019), broadly categorized into two types: those with PR type selective wiring, which is found in many vertebrates, and those with random, unselective wiring, such as red–green opponency in primates. While color vision was long thought to rely exclusively on cone PRs, recent research has revealed an additional mechanism: rod–cone opponency, in which differences in wavelength sensitivity between rods and cones support color comparisons (Joesch & Meister 2016, Szatko et al. 2020, Rhim & Nauhaus 2023).

The strategies for color processing vary across animal species. In primates, color information is transmitted by a small number of distinct retinal cell types to downstream visual areas (reviewed in Thoreson & Dacey 2019), where the representation of color remains partially segregated from other visual features (Zeki 1978, Livingstone & Hubel 1988; but see Garg et al. 2019). In contrast, other vertebrates (e.g., zebrafish, birds) and invertebrates (e.g., *Drosophila*) show color processing that is distributed across many neuron types (Johnson et al. 2010, Zhou et al. 2020, Longden et al. 2023, Seifert et al. 2023) and is not easily separated from the processing of other visual features. Mice appear to follow the latter strategy (Szatko et al. 2020, Khani & Gollisch 2021, Mouland et al. 2021, Rhim & Nauhaus 2023), with a large number of retinal output types encoding color information alongside other visual features.

Mice are dichromats with UV- and green-sensitive cones and green-sensitive rods (**Figure 1*c***, **subpanel *ii***), exhibiting an asymmetric distribution of cone opsin types across their retina (Szél et al. 1992, Baden et al. 2013). The ventral retina, which primarily encodes light from the sky, is most sensitive to short wavelengths (UV), while the dorsal retina, which is responsible for encoding light near the ground, is most sensitive to medium wavelengths (green) (**Figures 1*b*** and **4*a***). This distribution likely evolved as an adaptation to the inhomogeneous distribution of achromatic contrast across natural scenes (Baden et al. 2013) (**Figure 4*a***).

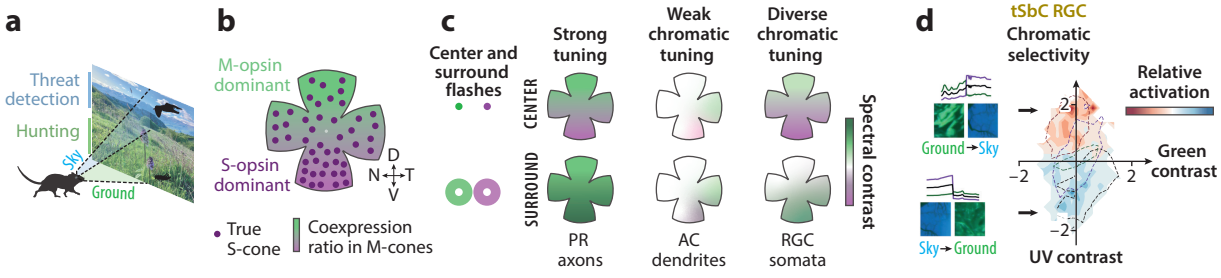

Figure 4

Color processing in the mouse retina. (*a*) The ground and sky of natural images, which have distinct chromatic statistics, project onto the dorsal and ventral parts of the retina, respectively. (*b*) Cone opsin distribution across the mouse retina. The color gradient illustrates the coexpression of UV-sensitive S-opsin in M-cones, which increases toward the ventral retina (Nadal-Nicolás et al. 2020). True S-cones exclusively expressing S-opsin are homogeneously distributed across the retina, with a slightly higher density in the ventral retina. (*c*) Maps illustrating the spectral contrast preferences of different neuron classes in the center–surround RFs, obtained from the presentation of the colored center and surround stimuli shown on the left. From left to right, the maps show the spectral contrast selectivity of PR axon terminals, AC dendrites, and RGC somata. (*d*) Chromatic contrast tuning showing that tSbC RGCs respond strongly to changes occurring in ground-to-sky transitions. Abbreviations: AC, amacrine cell; D, dorsal; M, medium wavelength; N, nasal; PR, photoreceptor; RGC, retinal ganglion cell; RF, receptive field; S, short wavelength; T, temporal; tSbC, transient suppressed-by-contrast; V, ventral. Panel *d* adapted from Höfling et al. 2024.

Despite the complications posed by an asymmetric opsin arrangement, behavioral studies using parametric stimuli have shown that mice can discriminate different colors (Jacobs et al. 2004, Denman et al. 2018), particularly in their central and upper visual fields (**Figure 4*b***). Recent research has revealed widespread rod–cone opponency in the mouse retina, particularly prominent in the ventral region, which may underlie the superior color discrimination in the upper visual field. This mechanism compares UV-sensitive cone signals with green-sensitive rod signals (Joesch & Meister 2016, Szatko et al. 2020, Khani & Gollisch 2021, Rhim & Nauhaus 2023) by integrating cone signals from the RF center with rod signals from the RF surround. The enhanced chromatic processing in the ventral retina appears to be an adaptive specialization driven by the greater chromatic contrast in the sky (Qiu et al. 2021), which may facilitate aerial predator detection (**Figure 4*a***). Evidence for rod–cone opponency has also been observed in monochromatic humans (Reitner et al. 1991), suggesting a broader presence of these circuits across mammals. At the level of ACs and RGCs, diverse patterns of chromatic RFs emerge, with many cell types across both ON and OFF pathways showing specialized color preferences (Szatko et al. 2020, Khani & Gollisch 2021). Cells within AC types, identified based on nonchromatic features, often display different chromatic preferences (Korympidou et al. 2024), creating a distributed and multiplexed color representation in the retinal output (**Figure 4*c***).

Machine learning approaches applied to neural responses from natural stimuli promise to reveal how retinal color processing guides behavior in natural environments. Using natural mouse movies (Qiu et al. 2021), researchers identified novel chromatic selectivity in transient suppressed-by-contrast RGCs (Höfling et al. 2024) (**Figure 4*d***). These cells show selective responses to green–OFF/UV–ON contrasts, corresponding to transitions between ground and sky views in natural scenes. This selectivity may help detect the horizon and ground/sky transitions, where identical visual features can signal different behavioral imperatives. For instance, a small dark moving object could represent a predatory bird when spotted against the sky but potential prey when seen on the ground.

Color processing extends from the retina to higher visual areas, with color-opponent signals particularly prominent in the posterior cortex, which receives ventral retinal input (Rhim & Nauhaus 2023, Franke et al. 2024). This region shows specialized responses for detecting dark objects against UV-rich skies and exhibits maximal color processing under bright conditions (Franke et al. 2024). While rod–cone opponency provides one mechanism, cone-to-cone comparisons remain essential for cortical color representation, with the dLGN serving as a key relay point that refines these signals (Mouland et al. 2021).

From an evolutionary perspective, the distributed code of color processing observed in mice and other species might offer adaptive advantages. Different PR types sensitive to distinct wavelength bands may have evolved primarily to reduce lighting noise in early vertebrates' natural environments (discussed in Maximov 2000, Kelber et al. 2003), with chromatic signals potentially serving to boost specific environmental contrast aspects rather than color discrimination alone (discussed in Baden 2024a). For example, UV sensitivity aids in detecting prey, predators, and food by increasing their contrast against the background (reviewed in Peichl 2005, Cronin & Bok 2016). Future studies combining unrestrained behavioral paradigms with ecologically relevant stimuli will be crucial in understanding the role of color vision in natural mouse behaviors, while comparative studies across species will help uncover general principles governing vertebrate color processing.

2.5. Vision at Its Sensitivity Limits

While the visual system operates across diverse light levels, most behavioral studies focus on bright conditions. Yet mice, being primarily nocturnal, depend critically on detecting subtle luminance

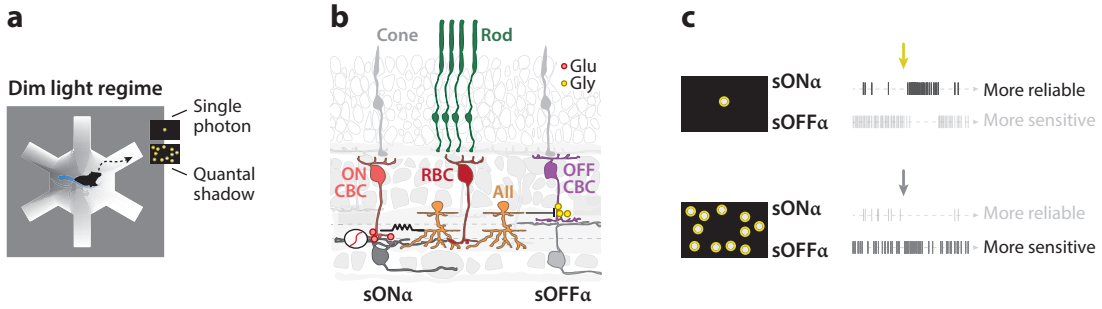

Figure 5

Neural circuits for single-photon detection and quantal shadow processing in the retina. (*a*) Behavioral paradigm for testing visual sensitivity under dim-light conditions: a radial water maze where mice must discriminate between arms based on the presence of either single photons or quantal shadows. (*b*) Retinal circuit schematic showing parallel processing streams: Rod and cone PRs connect to RBCs and CBCs, respectively. These signals converge via AII amacrine cells and glycinergic transmission onto two types of RGCs—sONα and sOFFα RGCs. (*c*) Functional characterization of sONα and sOFFα responses: sONα RGCs exhibit greater reliability in single-photon detection (*top*), while sOFFα RGCs show enhanced sensitivity to quantal shadows (*bottom*). Abbreviations: CBC, cone bipolar cell; Glu, glutamate; Gly, glycine; RBC, rod bipolar cell; RGC, retinal ganglion cell; sOFFα, sustained OFF α; sONα, sustained ON α.

changes in near darkness (**Figure 5*a***). At vision's absolute threshold, rod PRs achieve remarkable sensitivity, capable of detecting and signaling single-photon absorptions (Baylor et al. 1979, 1984; reviewed in Field et al. 2005). These signals follow a specialized pathway (**Figure 5*b***): Rods connect to dedicated rod BCs—ON-type BCs that exclusively receive rod input (Kolb & Nelson 1983). Rod BCs then transmit to AII ACs (Sterling et al. 1988), which serve as critical integration hubs. AII ACs route rod signals into cone pathways through two distinct mechanisms: electrical coupling to ON cone BCs and glycinergic inhibition of OFF cone BCs. This dual-channel organization ultimately enables both ON and OFF RGCs to relay rod-driven visual information to the brain (Sterling et al. 1988, Bloomfield & Dacheux 2001).

The ON and OFF pathways show distinct characteristics in darkness, reflecting their specialized roles. In both primates and mice, the ON pathway includes a thresholding nonlinearity that is absent in the OFF pathway (Ala-Laurila & Rieke 2014, Smeds et al. 2019) (**Figure 5*b***). This nonlinearity means that ON cells prioritize reliability over sensitivity; when active, they reliably signal the presence of light. OFF cells show the opposite trade-off: greater sensitivity at the cost of reliability. Smeds et al. (2019) found that at vision's sensitivity limit, mouse behavioral detection of light increments primarily depends on the more reliable thresholded input from sONα RGCs. Additional studies revealed that mice optimize behavioral strategies to maximize visual sensitivity during nighttime (Koskela et al. 2020). This reliance on sONα RGCs rather than the potentially more informative gaps in sustained OFF α (sOFFα) RGC firing at vision's sensitivity limit aligns with findings in humans (Kilpeläinen et al. 2024).

While extensive research has focused on rod detection of single photons, less attention has been paid to how nocturnal animals detect light decrements or quantal shadows—a crucial ability for avoiding predators (Sampath et al. 2005). Recent work by Westö et al. (2022) revealed that at very dim backgrounds, sOFFα RGCs excel at detecting light decrements compared to sONα RGCs. Behavioral experiments with mice performing a visual discrimination task using a radial water maze confirmed that sOFFα RGCs operate near the limits set by light's Poisson distribution and retinal noise. Further investigation is needed to understand the roles of specific OFFα RGC types in predator avoidance near the absolute visual threshold, particularly considering potential dorsal–ventral variations in retinal activity during natural behaviors such as navigation.

3. FROM BEHAVIOR TO RETINA: MODULATION OF RETINAL SIGNALING

Brain arousal states: in this context, arousal refers to diverse physiological, emotional, and cognitive states rather than a singular process influencing neural activity and behavior through factors like locomotion, circadian rhythms, and motivation

How does the brain influence the eye? While traditionally we focus on how the eye communicates with the brain, recent research has revealed a more complex bidirectional relationship between the eye and the brain. Consider a mouse actively exploring its environment—running, pausing, and scanning for threats or food. During these behaviors, the brain not only processes visual input but also modulates how the retina interprets the world through two primary pathways: direct neuromodulation and pupillary changes.

3.1. Direct Brain-to-Retina Neuromodulation

The anatomical foundation for direct brain-to-eye communication was first discovered over a century ago when Ramón y Cajal (1889) identified retinopetal axons in birds. Subsequent studies revealed similar projections across vertebrates, including mammals (Repérant et al. 1989). Although these axons are few in number in mammals, they branch extensively throughout the retina. Their cell bodies, situated in the posterior hypothalamus and dorsal raphe nucleus, release histamine and serotonin, respectively (Gastinger et al. 2006, Reggiani et al. 2023, Tripodi & Asari 2024, Warwick et al. 2024).

At the neuronal level, brain regions including V1, the dLGN, and the SC modify their spontaneous and visually evoked activity in response to varying arousal levels (Niell & Stryker 2010, Erisken et al. 2014, Vinck et al. 2015, Aydın et al. 2018, Socha et al. 2024). These modulations arise from local neuromodulators, top-down feedback, or changes in local circuitry. Significantly, recent studies demonstrate that these arousal-driven changes also affect retinal output. By imaging hundreds of individual retinal axonal terminals in the dLGN (Liang et al. 2020) and the SC (Schröder et al. 2020) in awake, head-fixed mice, researchers observed shifts in retinal output corresponding to the animal's arousal state. Additional changes in retinal output correlating with locomotion or pupil size suggest even more intricate brain-state influences on retinal processing (Liang et al. 2020, Schröder et al. 2020).

Recent work by Warwick et al. (2024) has demonstrated that the mouse retina receives direct modulation from the brain's arousal system through histamine-releasing neurons projecting from the hypothalamus (**Figure 6*a***), putting to bed the traditional view of the mammalian retina as an autonomous circuit. They showed that histamine application affects the baseline activity of RGCs and enhances DSGCs' ability to respond to fast-moving stimuli (**Figure 4*b***). During periods of arousal, the brain releases histamine into the retina, enhancing certain retinal neurons' ability to track rapid motion. This mechanism appears to be evolutionarily conserved, as an antihistamine drug has been shown to modulate visual sensitivity nonuniformly in humans. This pathway's presence is advantageous: During high arousal states when animals move quickly through their environment, enhanced processing of fast motion—also demonstrated in flying flies (Jung et al. 2011)—may aid in navigation, hunting, and threat avoidance.

3.2. Behavioral State and Pupillary Regulation of Retinal Processing

Pupil size is influenced by two well-established factors: ambient luminance and brain state, such as arousal. Regarding the latter, pupil size has emerged as a crucial metric for tracking brain arousal states, providing a noninvasive window into neural dynamics and behavioral contexts (Grujic et al. 2024). Behaviorally driven changes in pupil size are a common feature shared across most vertebrates (reviewed in Larsen & Waters 2018). However, why the pupil is modulated by arousal is still debated (reviewed in Larsen & Waters 2018, Joshi & Gold 2020).

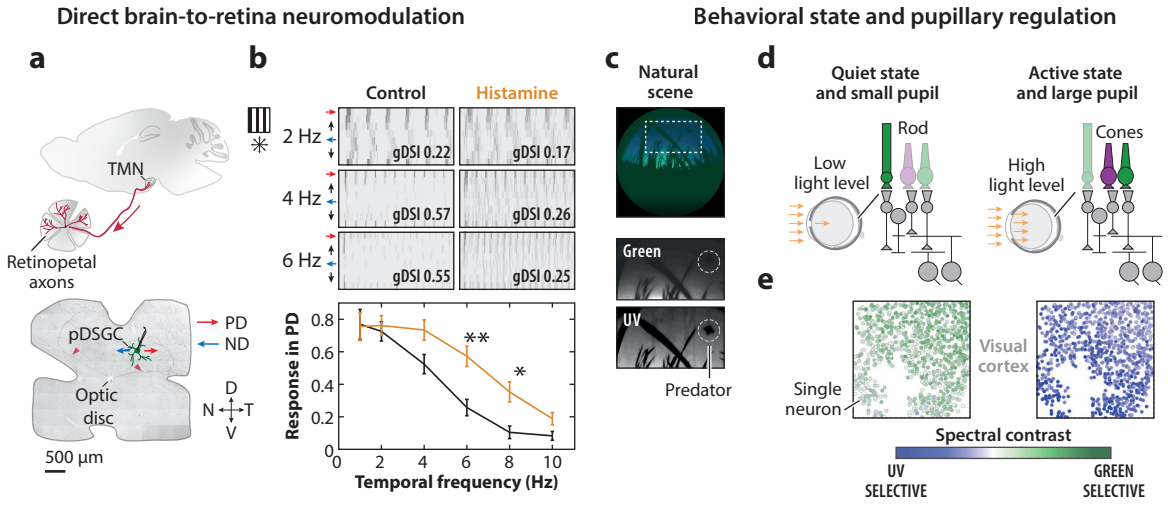

Figure 6

How behavioral state shapes retinal information processing—neuromodulation and pupil control. (*a*, *top*) Schematic of the mouse brain illustrating retinopetal axons from the brain to the eye, originating from histaminergic neurons in the TMN. (*bottom*) Image of the retina displaying two prominent histaminergic fibers extending from the optic disc. Histamine in the retina affects the tuning of pDSGCs. (*b*) Responses of DSGCs in the retina to histamine application reveal shifts in the frequency tuning toward higher frequencies. (*c*) Natural scene recorded with a camera sensitive to UV and green light, similar to the mouse. The scene was recorded during twilight while a drone was flying in the sky. The drone is better detectable using the UV channel. (*d*) Pupil dilation during an active behavioral state such as locomotion results in higher levels of retinal illumination and, thereby, a switch from rod- to cone-dominated visual responses. (*e*) Spectral contrast selectivity of neurons in the visual cortex of mice for different states. The quiet state results in rod-mediated responses, which are green sensitive, and the active state results in cone-mediated responses, which are UV sensitive. Abbreviations: D, dorsal; DSGC, direction-selective ganglion cell; gDSI, global direction selectivity index; N, nasal; ND, null direction; PD, preferred direction; pDSGC, posterior motion–preferring direction-selective ganglion cell; T, temporal; TMN, tuberomammillary nucleus; V, ventral. Panels *a* and *b* adapted from Warwick et al. (2024). Panels *c–e* adapted from Franke et al. (2022).

Franke et al. (2022) revealed that arousal-mediated pupil dilation directly alters visual information encoding in the visual cortex by shifting the balance between rod and cone PR activation (**Figure 6*e***). This finding aligns with work in anesthetized mice showing that artificial pupil dilation switches visual processing from rod to cone dominated (Rhim et al. 2021), even under constant ambient light levels. This rapid switching between rod and cone PRs may affect numerous aspects of vision beyond color perception, such as spatial and temporal resolution.

Another recent study by Fitzpatrick et al. (2024) has uncovered a novel retina-driven mechanism controlling pupil size—the pupillary contrast response (PCoR). The study demonstrates that the pupil actively constricts in response to temporal contrast in visual scenes, independent of overall luminance changes, in both mice and humans. The authors identify a specific retinal circuit mediating this response, from rod PRs through type 6 BCs to M1 ipRGCs. They demonstrated that pupil constriction primarily functions to enhance spatial contrast and visual acuity. The PCoR works in concert with eye movements to optimize visual processing, and its disruption in mice impairs both basic visual behaviors and complex tasks like prey capture.

Complementary to these findings, by imaging dLGN axon activity in the primary visual cortex in awake mice, researchers have shown that nasal visual motion can trigger pupil dilation, occasionally leading to locomotor activity, and enhances responsiveness in the visual pathway (Socha et al. 2024). These pupil size changes modulate neuronal activity in dLGN axons, influencing direction and orientation selectivity. Notably, such stimulus-driven behavioral modulations are weakened

during high-arousal states, such as locomotion, and absent under anesthesia, underscoring their dependence on quiet wakefulness.

These studies reveal distinct mechanisms by which pupil size actively shapes visual processing. Arousal-mediated dilation and the PCoR might operate together in a dynamic visual processing system. The apparent contradiction of rods both driving constriction and being suppressed by dilation might represent a sophisticated feedback system that helps maintain visual stability across different behavioral states.

3.3. Future Directions

While extensive feedback circuits have been well-documented in other species (Repérant et al. 1989), the relatively sparse feedback projections observed in mammals have historically led to an underestimation of their functional significance. A key emerging question is to what extent brain-to-retina feedback can dynamically modify retinal output signals. Current evidence primarily derives from studies in head-fixed animals using simplified visual stimuli. Recent technological advances, particularly in adaptive optics and miniature microscopes, offer promising approaches for in vivo recordings from retinal circuits in behaving mice. This dual influence of behavior on retinal processing—through pupillary changes and direct neuromodulation—challenges the traditional view of purely feedforward sensory processing from eye to brain.

4. DISCUSSION

While the elegant concept proposed by Lettvin et al. (1959) that individual retinal cell types serve discrete behavioral functions remains appealing to retinal physiologists, the picture is more complex than that. This one-to-one mapping between cell types and behaviors likely holds true primarily for innate, stereotyped responses, where retinal outputs can directly trigger specific behavioral programs. However, more sophisticated visual behaviors probably emerge from the intricate interplay of multiple cell types and extensive downstream processing.

This complexity is evident even in well-studied cells like DSGCs. Despite our detailed understanding of their response properties in simplified contexts, we still struggle to explain how these neurons contribute to motion processing during complex natural behaviors. The gap between our knowledge of cellular function and behavioral output suggests that retinal signals undergo substantial transformation and integration before driving behavior.

The primate visual system offers a particularly striking example of this principle. The fovea, despite its extraordinary acuity and behavioral importance, operates with a surprisingly limited repertoire of retinal cell types. As the retina scans the environment through eye movements, downstream circuits must construct complex visual representations from this relatively simple set of inputs. This organization stands in marked contrast to species with more specialized retinal circuits, which supports the notion that increased behavioral complexity may require relatively unfiltered input from the retina. Both may be happening within the retinas of single species, including primates. For primates, the fovea may provide a more unfiltered specialization while the periphery takes on stereotyped functions such as eye reflexes.

This species-specific organization of visual processing underscores the importance of studying each animal model in its appropriate ecological context. The mouse exemplifies how technological advances and ecological perspectives can reshape our understanding of sensory processing. Initially valued primarily for its genetic and anatomical tools, the mouse was often studied using paradigms borrowed from primate research, leading to an underestimation of its visual capabilities when evaluated with tasks such as grating orientation discrimination. Recent years have witnessed a paradigm shift in mouse vision research. Studies of freely moving animals

have revealed sophisticated visual behaviors—from tracking and pursuing prey to avoiding aerial predators to navigating complex environments using depth information. This turn toward naturalistic behaviors highlights that mouse visual circuits, while different from primates, are precisely tuned to their behavioral needs.

Looking forward, this emphasis on natural contexts in mouse vision research offers valuable lessons for studying retinal computation across species. Success lies in matching experimental approaches to ethologically relevant contexts, rather than assuming universal solutions across the animal kingdom. As we develop increasingly sophisticated tools for analyzing behavior and retinal activity in awake behaving animals, we have unprecedented opportunities to uncover how retinal circuits implement computations that support species-specific visual behaviors.

SUMMARY POINTS

1. Animals use different visual sampling strategies to extract behaviorally relevant features from their environment, which influences the role of retinal computations in behavior.
2. Advances in anatomical, functional, and genetic studies have revealed a greater diversity of retinal cell types, each contributing to specific feature extraction circuits.
3. Feature selectivity arises from the organization of excitatory and inhibitory cells into specialized retinal circuits, asymmetric distribution of cell types across the visual field, and convergence or filtering in downstream visual areas.
4. While some retinal circuits serve specific behaviors (such as direction-selective cells for image stabilization), others may serve an array of behaviors.
5. Retinal processing is shaped by behavioral state through direct neuromodulation and pupillary responses.
6. Understanding retinal computations requires examining naturalistic contexts and considering how retinal circuits are shaped by species-specific environments and behaviors.

FUTURE ISSUES

1. How do retinal circuits process visual information during complex natural behaviors that require the integration of multiple features, and how can we study these computations in freely moving animals?
2. What is the full extent of brain-to-retina feedback, and how does this modulation adapt retinal processing to meet changing behavioral demands?
3. How do different retinal cell types work together to support flexible behaviors, moving beyond the one-to-one mapping of cell types to specific functions?
4. How do developmental programs establish regional specializations in the retina, and how plastic are these specializations in response to experience?
5. How do parallel retinal channels interact with downstream circuits to enable context-dependent processing of visual information?

6. How conserved are retinal computational principles across species, and how can comparative studies inform our understanding of vision evolution?

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

AUTHOR CONTRIBUTIONS

The authors contributed equally to all aspects of this work and share authorship.

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