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Seeing Beyond Violet: UV Cones Guide High-Resolution Prey-Capture Behavior in Fish

Johan Westö¹ and Petri Ala-Laurila^{1,2,*}

¹Neuroscience and Biomedical Engineering, Aalto University, Espoo, Finland

²Molecular and Integrative Biosciences Research Programme, University of Helsinki, Helsinki, Finland

*Correspondence: petri.ala-laurila@helsinki.fi
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How can fish see tiny underwater prey invisible to human eyes? In this issue of *Neuron*, Yoshimatsu et al. (2020) show that ultraviolet light and a rich set of fine-tuned anatomical and neural specializations originating in ultraviolet-sensitive cones underlie high-resolution prey-capture behavior in larval zebrafish.

Vision provides us with a rich sensation of the world around us across a wide range of light wavelengths from 400 nm (blue) to 700 nm (red). The word “ultraviolet” (UV) originates from Latin, meaning “beyond violet,” and refers to the high-energy, short-wavelength radiation that is practically invisible to us although abundantly available in sunlight. Many other animal species have specific UV-sensitive visual pigments, but the precise role of UV light in visually guided behavior has remained mainly unresolved (Cronin and Bok, 2016). In this issue of *Neuron*, Yoshimatsu et al. (2020) show that the prey-capture behavior of larval zebrafish relies on UV cones. The paper highlights an ensemble of anatomical and neural specializations in UV cones that allow larval zebrafish to detect their tiny prey.

David Marr famously postulated that fundamental understanding of a complex information processing system requires the understanding of the computation that the system is aiming to perform as well as the algorithms and the mechanistic implementations by which this is achieved (Marr, 1982). However, in mod-

ern neuroscience, the eagerness to generate large datasets and vast neural connectivity maps oftentimes overrides the need to understand the functional context of the data. The integrative study of Yoshimatsu et al. (2020) beautifully counters this trend, following the key principles of Marr in resolving the UV-light-dependent computations of the prey-capture behavior of larval zebrafish while at the same time applying a *tour de force* set of approaches to resolve their anatomical and physiological implementation. Finally, they link the behavioral performance of the fish to its neural implementation using computational modeling to show how the anatomical and physiological specializations facilitate the detection of prey. This paper sets an example for the neuroscience field by showing the importance of an end-to-end characterization of visual computations in well-defined behavioral tasks.

Why is UV light potentially useful for vision? Short-wavelength radiation penetrates deeper in water compared to longer wavelengths, giving oceans their beautiful deep-blue hue. However, UV light scatters

strongly in water, potentially making objects that are invisible or transparent at other wavelengths detectable. Yoshimatsu et al. (2020) now test this hypothesis on paramecia—a typical prey for larval zebrafish—and show that they become uniquely visible in UV light. To assess the visibility of paramecia in distinct spectral channels defined by the cone types of larval zebrafish, Yoshimatsu et al. (2020) utilized a hyperspectral camera with filters matched to the absorption spectra of the UV-sensitive and red/green-sensitive cone opsins of the fish. The resulting videos, captured in naturalistic daylight conditions, elegantly demonstrate that paramecia shine as tiny UV bright spots even if they are essentially invisible to red/green-sensitive cones (Figure 1). Next, the authors attacked the second part of the hypothesis by showing that the behavior indeed utilizes UV light: behavioral experiments on wild-type larval zebrafish and transgenic fish lacking UV cones showed that both UV cones and UV light were required for normal feeding behavior.

Yoshimatsu et al. (2020) next sought to understand how the fish retina



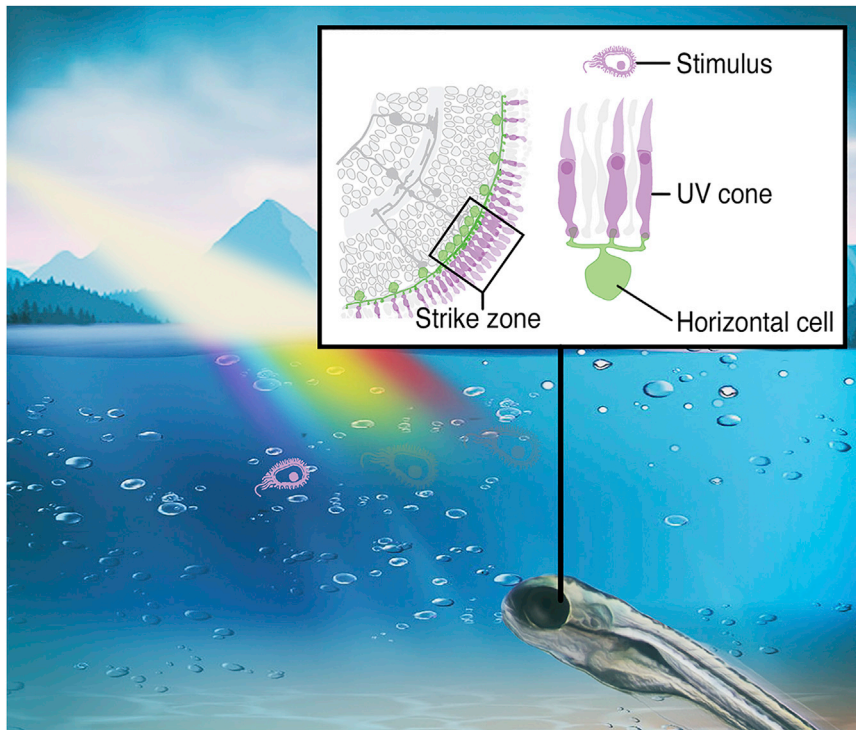


Figure 1. Larval Zebrafish Rely on UV Light for Prey Detection

The results of Yoshimatsu et al. (2020) show that paramecia (larval zebrafish prey) scatter UV light and appear uniquely as bright spots in the UV range of the spectrum. UV cones in the retinal region utilized in prey capture (the strike zone) are highly tuned anatomically and physiologically for detecting tiny UV bright spots (inset). These specializations let larval zebrafish detect their prey up to distances where the projection of the prey is comparable in size to a single UV cone (inset). Credits: Juha Haapala, Aarni Seppänen, and Baden lab.

implements UV-light-dependent visual computations. To boost the detection of UV light, it would be natural to maximize the capture of these high-energy photons. Therefore, Yoshimatsu et al. (2020) first focused on seeking specializations for UV capture in the anatomical structures of the strike zone (SZ) of the larval zebrafish retina—the region utilized in prey capture. Interestingly, they found substantial anatomical specializations enhancing the detection of small UV bright spots within the SZ: the density of UV cones was 3-fold higher, and they had up to 10-fold longer outer segments in the SZ when compared to other regions of the retina. These findings demonstrate pronounced spatial asymmetries in the larval zebrafish retina serving high-resolution UV-light capture. In comparison with the primate fovea, these findings show that spatial asymmetries in cone anatomy and function can take distinct forms across species to support high-resolution visually guided behavior.

In addition to the anatomical facilitation of UV sensitivity, Yoshimatsu et al. (2020) found a set of fine-tuned neural mechanisms providing an additional neural boost to the signaling of UV bright spots within the SZ. First, synaptic calcium imaging *in vivo* in SZ UV-cone pedicles revealed an elevated gain for encoding bright objects as compared to UV cones in other regions of the retina. Photoreceptor transcriptomics and computational modeling jointly attributed this regional bias for bright objects to a differential expression of phototransduction genes, especially for the second-messenger protein transducin. Second, the authors found that UV-cone responses were slowed down within the SZ via horizontal cell feedback, thus allowing downstream readout mechanisms to pool signals more effectively. Interestingly, slowed-down kinetics have also been identified in primate foveal cones (Sinha et al., 2017), suggesting that such kinetic adjustments can subserve

similar computational needs for regionally enhancing spatial acuity across species. As a real technical accomplishment, the authors finally validated their findings of synaptic mechanisms via UV-cone-driven glutamate release in the live fish eye at single pedicle resolution.

In summary, Yoshimatsu et al. (2020) showed that prey capture relies on UV-cone-driven vision in a highly specialized region of the retina (the SZ, see Figure 1). They established an ensemble of regional mechanisms that boost the necessary neural computations anatomically and functionally at the level of photoreceptors, synapses, and horizontal-cell-driven feedback. Together, these specializations let larval zebrafish detect and localize tiny UV bright paramecia relying on their UV cones.

How good is the spatial resolution of UV-light-driven prey capture in zebrafish? Yoshimatsu et al. (2020) estimate that the image of the UV bright prey falling onto the back of the retina is comparable in size to a single UV cone. Interestingly, this suggests that behavioral decision making is based on a sparse code originating in individual UV cones. Evolution tends to push specializations of high survival value to the extreme. For example, at the absolute sensitivity limit of vision, single-photon absorptions in a few rods among millions of rods in the retina can guide behavior (Kiani et al., 2020). When judging the performance of UV-light-driven prey capture in zebrafish, one may note that human foveal vision can read out signals from individual cones and that humans can exceed the acuity limit set by the spacing of individual cones by up to 10-fold in the detection of misalignments between line stimuli (Westheimer, 1975). This raises the question of whether UV vision provides a special opportunity for high-resolution vision. On the one hand, chromatic aberration of short-wavelength light poses big challenges for the optics (Cronin and Bok, 2016). On the other hand, cone noise has been shown to be the dominant noise source in ganglion cells at photopic light levels (Ala-Laurila et al., 2011), and UV pigments are particularly stable, providing an exceptionally low-noise visual channel for high-resolution computations. Further work will be needed to resolve the neural mechanisms setting fundamental limits on spatial resolution in UV light.

It is likely that the neural specializations for UV-light detection extend to downstream signal processing, thus making UV-light-dependent computation in retinal circuits and in the brain an exciting target for future studies. Zimmermann et al. (2018) have observed that bipolar cells within the SZ are primarily short-wavelength ON cells, and Zhou et al. (2020) found that ganglion cells within the SZ also exhibit an ON-type bias with slowed-down kinetics to more effectively integrate the sparse UV signal. These results line up nicely with the recent findings of Smeds et al. (2019) suggesting that the brain preferentially utilizes the neural code originating from ON-type ganglion cells for reading light increments. The transparent larval zebrafish will offer a remarkable possibility to further study signal processing in UV-light-dependent prey-capture behavior across the whole brain through *in vivo* imaging. This direction is now ready to be pursued in a well-defined

functional context according to the principles of Marr and in a model animal with a rich set of genetic and other tools available. This is thanks to the beautiful study of Yoshimatsu et al. (2020).

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Two Is Greater Than One: Binocular Visual Experience Drives Cortical Orientation Map Alignment

Rolf Skyberg,¹ Seiji Tanabe,² and Jianhua Cang^{1,2,*}

¹Department of Biology, University of Virginia, Charlottesville, VA 22904, USA

²Department of Psychology, University of Virginia, Charlottesville, VA 22904, USA

*Correspondence: cang@virginia.edu

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One hallmark of the mature visual cortex is binocularly matched orientation maps. In this issue of *Neuron*, Chang et al. (2020) show that three different maps exist at vision onset and that binocular visual experience aligns them into a single unified representation.

To create an accurate perception of the world, the brain must integrate information from multiple sources, both within and across modalities. For example, although we see the world with two eyes, we have a single visual percept, indicating that the brain must combine the two monocular inputs coherently. Research in mice has revealed that this integrative process is not a hardwired feature of the visual system, but instead

requires a normal binocular visual experience (Wang et al., 2010). At vision onset, before the critical period of visual development, binocular cells in the mouse primary visual cortex (V1) often display different orientation preferences through the two eyes. During the following two weeks, the mismatch in monocular orientation preference is reduced to create a binocularly matched representation of stimulus orientation (Wang et al., 2010,

2013) (Figure 1A). This matching process requires the animal to experience normal vision with both eyes. Such an experience-dependent integration of multiple streams of input has been shown to underlie the development of many sensory and motor processes, such as the alignment of visual, auditory, and motor maps in the barn owl optic tectum (Cang and Feldheim, 2013) and learned vocalizations in songbirds (Mackevicius and Fee, 2018).

