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The Visual Opsin Gene Repertoires of Teleost Fishes: Evolution, Ecology, and Function

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Abstract

Visual opsin genes expressed in the rod and cone photoreceptor cells of the retina are core components of the visual sensory system of vertebrates. Here, we provide an overview of the dynamic evolution of visual opsin genes in the most species-rich group of vertebrates, teleost fishes. The examination of the rich genomic resources now available for this group reveals that fish genomes contain more copies of visual opsin genes than are present in the genomes of amphibians, reptiles, birds, and mammals. The expansion of opsin genes in fishes is due primarily to a combination of ancestral and lineage-specific gene duplications. Following their duplication, the visual opsin genes of fishes repeatedly diversified at the same key spectral-tuning sites, generating arrays of visual pigments sensitive to the ultraviolet to red spectrum of light. Species-specific opsin gene repertoires correlate strongly with underwater light habitats, ecology, and color-based sexual selection.

Contents

1. INTRODUCTION

Many animals rely on vision—that is, the ability to perceive a narrow wave band of electromagnetic radiation flanking the peak of the solar emission spectrum in the range of 350–700 nm—for a number of essential tasks. Among other things, their ability to perceive light and see permits animals to adjust their circadian rhythm, to obtain a real-time overview of their immediate surroundings, to navigate through their environment, to track down edible items, to recognize predators and flee and/or hide from them, and to seek potential mating partners (Cronin et al. 2014, Land & Nilsson 2012). The various tasks and demands that vision has to fulfill in different animals, together with the varying light environments that the different species are exposed to, are manifested in a diverse array of adaptations and modifications of the visual sensory system (Cronin et al. 2014). This becomes apparent in the great structural and morphological diversity of animal eyes and the associated parts of the central nervous system, including the retina and the visual cortex (Land & Nilsson 2012).

Visual opsin genes expressed in the photoreceptor cells of the retina constitute a core component of vision at the molecular level (Lamb 2020, Yokoyama 2008). Numerous adaptations in visual opsin genes and their regulation have recently been documented, not least because of advances in next-generation sequencing technologies and broader taxonomic sampling. In this review, we focus on the visual opsin genes of teleost fishes. With currently more than 34,000 species catalogued, the infraclass Teleostei within the class Actinopterygii (the ray-finned fishes) represents by far the most species-rich clade of vertebrates, with over half of all vertebrate species included in it. We provide an overview of the general trends in visual opsin evolution in teleosts and delve deeper into some specific cases of opsin gene proliferation in species found in places such as the deep sea. We then take a closer look at attempts to explain, at least in part, the enormous diversity of visual opsin genes found in fishes.

2. THE VISUAL SENSORY SYSTEM OF TELEOST FISHES

In this section, we give a short introduction to the visual sensory system of vertebrates and some of its main components such as the eye, the retina, and the visual opsin genes. Throughout we highlight features that are specific to teleost fishes.

2.1. The Vertebrate Eye

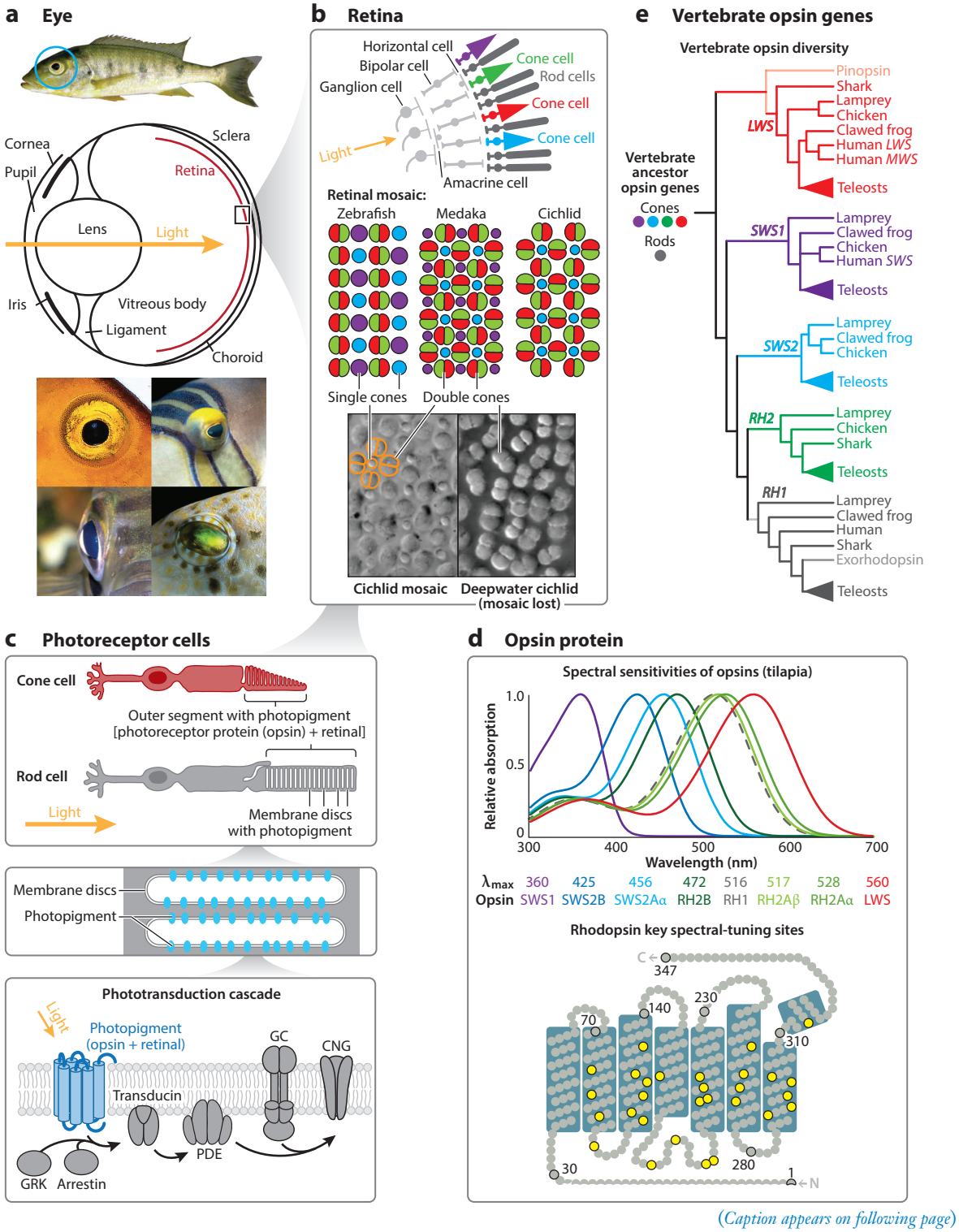
Eyes are organs of the visual sensory system that are present in almost all animal phyla (Land & Nilsson 2012). However, the eyes in most phyla are rather simple and permit only directional photoreception or low-resolution vision, whereas high-resolution image-forming eyes are restricted to arthropods (compound eyes in insects and crustaceans), mollusks (the camera-style eye in cephalopods), chordates (the camera-style eye in vertebrates), and perhaps annelids (alciopid polychaetes) (Land & Nilsson 2012, Nilsson 2013, Randel & Jékely 2016).

The vertebrate eye (**Figure 1*a***) is almost entirely surrounded by a light-impermeable and protective sclera on the outside and a choroid coat on the inside, discontinued only in the areas where light enters and where the optic nerve exits the eye. The point of light entry, consisting of the pupil surrounded by an iris, is shielded from the ambient medium by the cornea, which the incoming light has to penetrate before entering the eye. While the pupil and iris control the amount of light that enters the eye, the cornea and lens are responsible for focus adjustment, which is achieved by moving the lens forward and backward (as in teleost fishes and amphibians) or by dynamically changing the shape of the lens or the cornea using specific muscles and ligaments (as in mammals, reptiles, and birds) (Ott 2006). The inner surface of the vertebrate eye, especially in the part of the sphere opposite the lens, is lined with the retina, a membrane consisting of multiple layers of neurons, including the photoreceptor cells through which the inverted mirror image projected by the lens is perceived (Cronin et al. 2014, Land & Nilsson 2012). This basic blueprint of a camera-style eye is common to the jawless lampreys and all jawed vertebrates (therefore also to teleost fishes), suggesting that this feature was already present in the last common vertebrate ancestor (Fain 2020, Lamb et al. 2007).

The eyes of fishes are similar in structure to those of other vertebrates, except that the diameter of the pupil is fixed in lampreys and almost all teleosts, whereas rays and sharks do possess a muscular iris to regulate aperture (Helfman et al. 2009). In addition, there are a number of adaptations to and constraints on the fishes' eyes in response to their waterborne lifestyles. For example, because the refraction index of water is similar to that of the cornea, light is refracted at the lens, favoring spherical lenses with a relatively short radius (Collin 2009). Such lenses are, in turn, susceptible to spherical aberration, in which light passing through the lens is focused at different points, which is compensated for by a graded refraction index from the center to the outside of the lens (Collin 2009). To minimize chromatic aberration, in which different wavelengths are focused at different focal planes or at different points of the same focal plane, fishes have multifocal lenses (Kröger et al. 1999). Moreover, many fishes have pigmented corneas and lenses that contain mycosporine-like amino acids or yellow pigments to filter out shorter ultraviolet (UV) wavelengths (<400 nm) and to shift the spectral sensitivity toward longer wavelengths (Muntz 1973, Siebeck & Marshall 2001, Thorpe et al. 1993). Some fishes, especially nocturnal and deep-sea species, have reflective tapeta at the back of their retina that reflect unabsorbed photons back to the photoreceptors to increase sensitivity [reviewed in de Busserolles et al. (2020)].

2.2. The Vertebrate Retina

The retina of vertebrates is a multilayered neural tissue that, depending on the species, may contain more than 100 types of neurons, broadly classified into ganglion, amacrine, bipolar, horizontal, and photoreceptor cells (Baden et al. 2020, Masland 2012, Sanes & Masland 2015). Amacrine, bipolar, and horizontal cells are interneurons that process the output of the light-detecting photoreceptors, while the axons of retinal ganglion cells transmit visual information to the brain via the optic nerve (Sanes & Masland 2015). The basic makeup of the retina is such that its boundary layer toward the vitreous humor inside the eye is composed of retinal ganglion cells followed by a stratum containing a mosaic of amacrine, bipolar, and horizontal cells, whereas the light-detecting



(*Caption appears on following page*)

Figure 1 (*Figure appears on preceding page*)

The visual sensory system of teleost fishes. (*a*) The majority of teleost fishes have a camera-style eye typical of vertebrates. Images reproduced with permission of Valerio Tettamanti (*top row* and *bottom right* images of fish eyes) and Zuzana Musilova (fish image and *bottom left* fish eye image). (*b*) The retina of vertebrates is inverted; that is, the photoreceptor cells are located at its outside, facing the choroid. In fishes, photoreceptors are often arranged in regular patterns such as rows (as shown for zebrafish) or square mosaics with (as shown for medaka) or without (as shown for the Nile tilapia, a main model species among cichlids) the corner cones. The photos show (*left*) the single and double cone retinal mosaic of the shallow-water cichlid fish *Konia eisentrauti* and (*right*) the stand-alone double cones of the deepwater species *Konia dikume*, in which the mosaic pattern has been lost; both species are native to the crater lake Barombi Mbo in Cameroon. Photos reproduced with permission from Musilova et al. (2019b). (*c*) The outer segments of rod photoreceptor cells are longer and slimmer compared to those of cone cells, resulting in a longer pathway for the light to travel through and thus increasing sensitivity. Upon the light-induced activation of the chromophore, opsin proteins undergo a conformational change and initiate the phototransduction cascade, which converts the light impulse into a neuronal signal. The main components of the vertebrate phototransduction cascade are shown. (*d*, *top*) The absorption spectra of the visual rod (*dashed line*) and cone (*solid lines*) opsins of the Nile tilapia and their corresponding peak spectral sensitivities (λ_{max}). Spectral sensitivities in panel *d* (*top*) plotted using equations of Govardovskii et al. (2000) and λ_{max} values from Spady et al. (2006). (*Bottom*) Schematic representation of the bovine rhodopsin. The key spectral-tuning sites that are known to shift λ_{max} in RH1 are highlighted in yellow. Panel *d* (*bottom*) key-tuning site data from Musilova et al. (2019a). (*e*) Phylogeny of the vertebrate visual opsin genes. The lamprey used is *Geotria australis*, while the shark is *Callorhinchus milii*. For the teleosts, five to eight representative opsin genes are included. The five basic types of visual opsins were already present in the vertebrate ancestor. Abbreviations: CNG, cyclic nucleotide–gated channel; GC, guanylate cyclase; GRK, G-protein-coupled receptor kinase; *LWS*, long-wavelength-sensitive opsin; *MWS*, middle-wavelength-sensitive opsin; PDE, phosphodiesterase; *RH1*, rhodopsin or rod opsin; *RH2*, rhodopsin-like 2; *SWS1/2*, short-wavelength-sensitive opsins.

photoreceptors are located at its outside, that is, toward the choroid-coated sclera (Land & Nilsson 2012) (**Figure 1*b***). This means that the vertebrate retina is inverted; in other words, photons have to pass through several layers of retinal neurons before reaching the photoreceptors (Cronin et al. 2014, Lythgoe 1979).

There are two basic types of photoreceptor cells in the vertebrate retina, cones and rods (Schultze 1866) (**Figure 1*c***). Cones typically have shorter but relatively wide cone-shaped outer segments and operate in bright-light (photopic) conditions in which they convey color vision, while the longer and thinner outer segments of rods maximize photon capture in dim-light (scotopic) conditions (Land & Nilsson 2012, Yokoyama 2008). Cones can be further subdivided into single and double cones (i.e., two single cones that are joined together and may be optically coupled or that may still work as independent units) (Pignatelli et al. 2010). In teleost fishes, single cones usually express short-wavelength-sensitive opsins, while double cones express medium- and long-wavelength-sensitive opsins (Carleton et al. 2020). In teleosts, single and double cones often form regular mosaics, either in a row (e.g., in zebrafish, cods, and herring) or in a triangular (e.g., in pike) or square (e.g., in medaka, tilapia, and many percomorph fishes) arrangement [see Ali & Anctil (1976)] (**Figure 1*b***). In rare cases, fishes can have triple and quadruple cones, but their functions remain unknown (Bowmaker 1995, de Busserolles et al. 2021).

2.3. The Vertebrate Phototransduction Cascade

The biochemical process by which a stimulus in the form of photons of light is converted into a neuronal—that is, an electrochemical—signal is referred to as phototransduction (Arshavsky et al. 2002, Hunt et al. 2014, Lamb 2020). The phototransduction cascade is initiated by the absorption of photons through visual pigments, which are located in the membranes of the outer segments of photoreceptor cells (**Figure 1*c***). Visual pigments consist of a vitamin A1 (11-*cis*-retinal)– or vitamin A2 (11-*cis*-3,4-dehydroretinal)–based chromophore that is covalently bound to the visual opsin protein via a Schiff base linkage to a conserved lysine residue at amino acid position 296 (Wald 1968) [note that by convention, the alignment positions in visual opsins are referenced to

the bovine rhodopsin (Palczewski 2000)]. Visual pigments have a bell-shaped absorption profile with varying peak spectral sensitivities (λ_{max}), depending on the chromophore type (A2 is longer wavelength–shifted compared to A1) and the opsin protein they are bound to (Hunt et al. 2014, Wald 1968) (**Figure 1*d***).

Visual opsins are G-protein-coupled receptors that, through a conformational change in response to the photon-induced isomerization of the chromophore, activate a heterotrimeric G-protein-signaling cascade involving transducin and a number of other phototransduction proteins (Arshavsky et al. 2002, Lamb 2020) (**Figure 1*c***). Differences in the structure of the rod and cone opsins and the transduction cascade proteins are responsible for the variation in activation, shutoff, and recovery speed of the opsin pigment. Rods are highly sensitive but take longer to recover compared to the cones, which are tolerant to higher light intensities and show faster recovery rates (Cronin et al. 2014, Hunt et al. 2014).

2.4. The Visual Opsin Genes of Vertebrates

Visual opsins are part of a much larger family of opsin proteins that, when bound to a chromophore, are involved in light sensation (Bowmaker 2008). Vertebrates possess five basic types of visual opsins, the rod opsin (RH1) expressed in rod photoreceptors and four cone opsins expressed in the various cone photoreceptors. These visual pigments can be classified according to photoreceptor specificity, phylogeny, and their range of λ_{max}: RH1 typically operates in the blue-green part of the light spectrum (teleost $\lambda_{max} = 447–525$ nm); while for the cone opsins, the short-wavelength-sensitive opsins absorb in the UV (SWS1: teleost $\lambda_{max} = 347–383$ nm) and violet-blue (SWS2: teleost $\lambda_{max} = 397–482$ nm) wave bands; rhodopsin-like 2 (RH2) is most sensitive in the green fraction of the spectrum (teleost $\lambda_{max} = 452–537$ nm); and the long-wavelength-sensitive opsin (LWS) covers the red part (teleost $\lambda_{max} = 501–573$ nm) (Carleton et al. 2020) (**Figure 1*d*,*e***). In some species, only a subset of these photopigment types is present, while in others certain types may occur in more than one copy. Note that a single photoreceptor containing only one visual pigment cannot distinguish differences in intensity or luminance (achromatic vision) from a shift in wavelength (chromatic vision). Therefore, to distinguish color, the relative excitation ratios from at least two differently tuned photoreceptors are required (Krauskopf et al. 1982). Teleost fishes use between two and four differently tuned cone photoreceptors (dichromatic to tetrachromatic vision) to distinguish colors during the day (Marshall et al. 2018, Carleton et al. 2020). Whether higher chromacy exists in fishes and if some species can also see color using their rod photoreceptors (Musilova et al. 2019a) remain to be investigated.

3. THE EVOLUTION OF VISUAL OPSIN GENES IN TELEOST FISHES

While in most vertebrate lineages the ancestral number of visual opsin genes has been maintained (e.g., in birds and diurnal lizards) or become smaller (e.g., in mammals and snakes), the visual opsin genes of teleosts have continued to proliferate (Hunt et al. 2014) (**Figure 2**). This is likely a response to the various light environments that fishes inhabit—ranging from clear mountain streams to the deep sea—as well as to the varied ecologies and lifestyles they exhibit. In this section, we dive into the evolutionary history of visual opsin genes in teleosts in an attempt to synthesize the large body of literature that has emerged on this topic since the beginning of the genomic era. The picture that emerges is one of teleosts varying greatly in their numbers and types of visual opsin genes. Also, it shows that the molecular processes causing this variability differ between lineages and species. Predicting the number and types of visual opsin genes in a given fish species, and what this species can see by virtue of these genes, is thus a precarious endeavor.

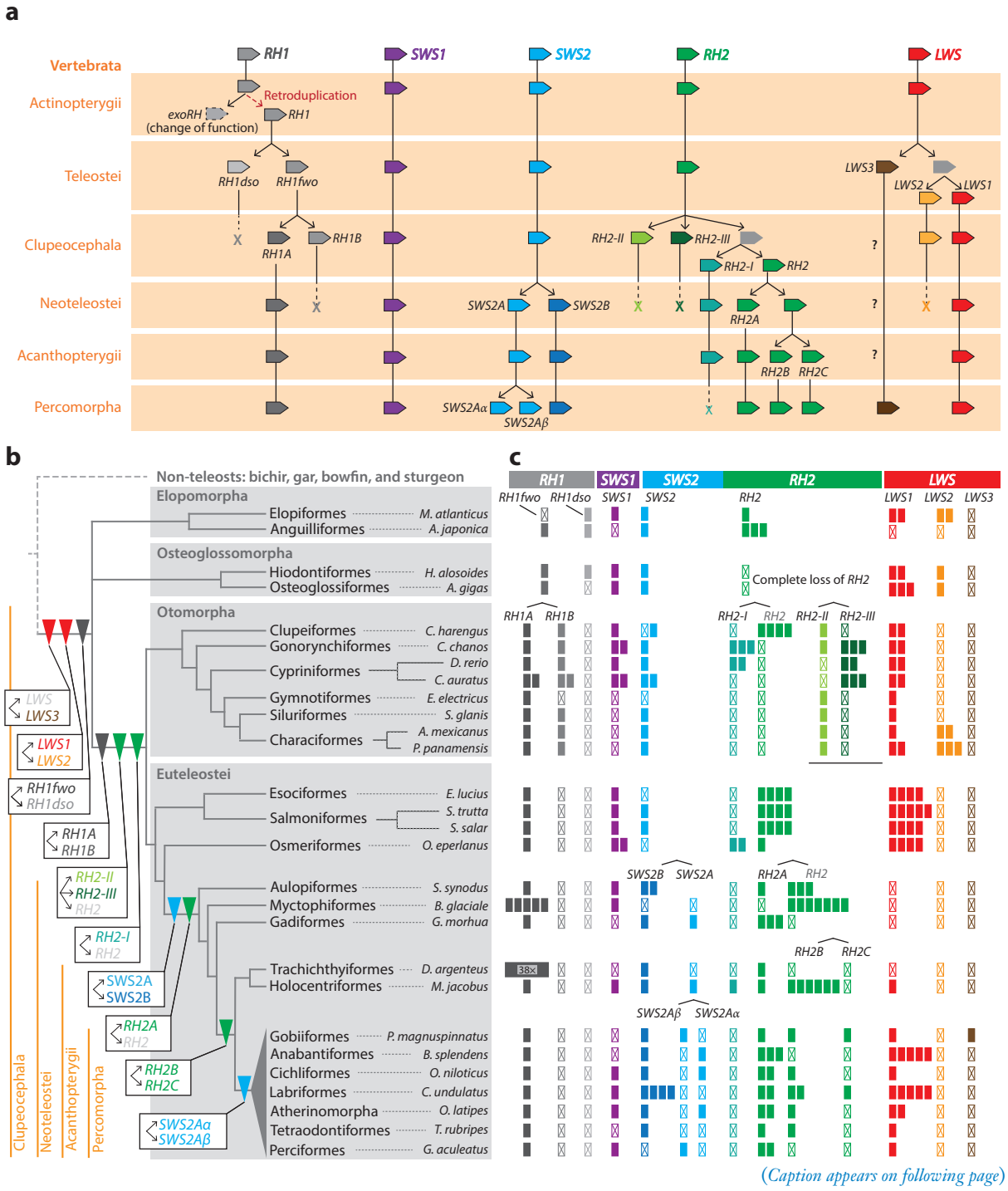


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Figure 2 (*Figure appears on preceding page*)

The visual opsin gene repertoire of teleost fishes. (*a*) The gene duplication history of visual opsin genes from the vertebrate ancestor to the percomorph fishes, the most species-rich crown group of teleosts. (*b*) A simplified phylogenetic tree of teleost fishes at the level of orders, illustrating ancestral duplications in visual opsin genes. The numerous lineage-specific duplications are not shown. Tree in panel *b* adapted from Betancur-R et al. (2017) and Musilova et al. (2019a). (*c*) Diversity of the rod and cone opsin genes across teleost fishes. Filled rectangles indicate the presence of a particular visual opsin gene in a given genome (and the number of copies), while crossed out rectangles indicate its absence. Panel *c* based on data from Chen et al. (2018), Cortesi et al. (2015, 2021), Liu et al. (2019), Musilova & Cortesi (2021), and Musilova et al. (2019a) and complemented by additional data from GenBank. Abbreviations: *LWS1–3*, long-wavelength-sensitive opsins; *RH1*, rhodopsin or rod opsin; *RH2*, rhodopsin-like 2; *SWS1/2*, short-wavelength-sensitive opsins.

3.1. Molecular Mechanisms Involved in Opsin Gene Evolution in Fishes

Gene (and genome) duplications and the subsequent diversification of the newly emerged gene copies are known to provide the substrate for functional novelty (Ohno 1970). This is also the case for visual opsins, in which arguably the most crucial functional modifications relate to shifts in λ_{max}. Teleosts feature an extended set of functionally distinct visual opsins compared to other vertebrates (Carleton et al. 2020, Cortesi et al. 2020, Musilova et al. 2019a). That opsin gene evolution is more dynamic in teleosts than in other vertebrates is further illustrated by the fact that they possess the largest numbers of visual opsin gene copies for all vertebrate opsin types: 38 copies of *RH1* in the silver spinyfin, *Diretmus argenteus* (Diretmidae) (Musilova et al. 2019a); three *SWS1* copies in anemonefish (Amphiprioninae; Pomacentridae) [two functional copies and one pseudogene (Mitchell et al. 2020)]; four copies of *SWS2* in the humphead wrasse, *Cheilinus undulatus* (Labridae) (Dong et al. 2020); eight copies of *RH2* in soldierfish (Myripristinae) (Musilova et al. 2019a); and five copies of *LWS* in wrasses (Labridae), fighting fish (Osphronemidae), and brown trout (Salmonidae) (Cortesi et al. 2021, Dong et al. 2020) (**Figure 2*c***). In the following, we outline the main molecular mechanisms that are responsible for this diversity.

3.1.1. Whole-genome and tandem gene duplications. The five basic types of visual opsin genes in vertebrates—that is, the four cone opsins and the rod opsin—are the product of two rounds of whole genome duplications (2R), likely starting from an initial set of two opsin genes (*LWS* and *SWS*) in their common ancestor (Lamb 2020, Larhammar et al. 2009). The evolutionary lineage leading to modern teleosts underwent an additional (third, or 3R) round of genome duplication (Meyer & Van de Peer 2005). This teleost-specific genome duplication is also traceable in the visual opsin genes of some fishes. For example, Elopomorpha (eels) and Osteoglossomorpha have retained their two ancestral rod opsins (*RH1*s) (Chen et al. 2018), and characins, bony tongues, tarpons, and gobies have two ancestral types of the red-sensitive *LWS* opsin (Adrian-Kalchhauser et al. 2020, Cortesi et al. 2021, Escobar-Camacho et al. 2020, Liu et al. 2019) (**Figure 2**).

Apart from the expansion through three rounds of whole-genome duplications, several additional ancestral and numerous lineage-specific opsin gene duplications have occurred in fishes (Cortesi et al. 2015, Lin et al. 2017, Liu et al. 2019, Musilova & Cortesi 2021, Musilova et al. 2019a) (**Figure 2*a*,*b***). The most common way of opsin gene expansion in fishes is via tandem duplication, whereby the resultant sister copies (paralogs) end up being located next to each other on the same chromosome, as exemplified by the *RH2* gene arrays found in many species (Lin et al. 2017, Musilova & Cortesi 2021). Interestingly, while tandem duplications prevail in the cone opsins [all *SWS2* duplicates, most *SWS1* and *LWS* duplicates, and many of the *RH2* duplicates derive from tandem duplications (Lin et al. 2017)], this is usually not the case for *RH1* (Musilova et al. 2019a), probably because of the somewhat unique evolutionary history of the teleost *RH1* (see Section 3.1.2).

3.1.2. Duplication by retrotransposition. Gene duplication may also occur via retrotransposition, whereby mature messenger RNA post-splicing is retrotranscribed and reinserted into the genome. Two such cases have been documented in fish: The first involves *RH1*, which is a single-exon gene in all ray-finned fishes but bichirs (Fujiyabu et al. 2019) and has originated from the retrotransposition of its common ancestor with the extraocular rhodopsin (exorhodopsin) (Bellingham et al. 2003) (**Figure 2*a***). While the new intron-less copy retained the ancestral function in vision, exorhodopsin expression mainly became restricted to the pineal gland in extant fishes, where it is involved in circadian regulation (Mano et al. 1999, Pierce et al. 2008). The second case occurred in Cyprinodontiformes (guppies, killifish, and related species), in which three *LWS* copies emerged through tandem duplication and a fourth through retrotransposition (Sandkam et al. 2017, Ward et al. 2008).

3.1.3. Pseudogenization, gene loss, and gene conversion. The evolution of opsin genes in fishes is also characterized by the frequent occurrence of gene losses and pseudogenization, often in connection with a peculiar light environment (see Section 4). Gene conversion, that is, the unidirectional exchange of information between sequences, is yet another mechanism that reduces opsin diversity due to its homogenizing effect on paralogs (Cortesi et al. 2015, Sandkam et al. 2017). This can even lead to the resurrection of a no-longer-functional gene copy, as found in the *SWS2* genes of the Asian swamp eel (*Monopterus albus*) and the roughhead grenadier (*Macrourus berglax*). In both species, a segment of a functional gene was replaced by a homologous sequence derived from a pseudogene (Cortesi et al. 2015). Ultimately, it is the interplay between gene duplications, gene loss, pseudogenization, and gene conversion that determines the number of visual opsin genes in a given teleost genome.

3.1.4. Point mutations and adaptations of teleost visual opsins. Bovine RH1 was the first G-coupled protein to have its crystal structure fully resolved (Palczewski 2000). Even before this feat, a plethora of studies have been looking into how changes in gene sequence affect amino acid composition and, thus, the function of visual opsin genes. Some point mutations affecting so-called key spectral-tuning sites have directly been implicated with shifts in λ_{max} (Yokoyama 2008) (**Figure 1*d***, **Figure 3**). These sites are usually inside of or close to the retinal binding pocket and have traditionally been identified on the basis of phylogenetic comparisons, that is, by correlating amino acid sequences with the spectral sensitivity a visual pigment conveys (Yokoyama 2008, Chang & Donoghue 2000). *In vitro* opsin protein regenerations (Yokoyama 2008) and—as of late—atomistic molecular simulations (e.g., Patel et al. 2018) have also been used to infer the contribution to shifts in λ_{max} of specific amino acid substitutions if *in situ* spectral absorbance measurements using microspectrophotometry or similar techniques are not feasible [e.g., for deep-sea fishes (de Busserolles et al. 2017)]. Although a number of key-tuning sites have been identified so far [e.g., for RH2 (Yokoyama & Jia 2020) and RH1 (Musilova et al. 2019a)], ongoing research on reconstituted opsin proteins and increasing phylogenetic coverage are likely to keep adding to this list. Notably, in some cases, sites found to be involved in the spectral tuning of one type of visual opsin are also relevant in others (Yokoyama & Jia 2020) (**Figure 3**). For example, mutations in amino acid site 292 lead to shifts in λ_{max} in RH1, RH2, LWS, and SWS2 (Musilova et al. 2019a, Yokoyama 2008, Yokoyama & Jia 2020). The question remains as to what extent at least some key-tuning sites may be able to universally tune any type of visual opsin gene.

The contribution of amino acids other than the classical key spectral-tuning sites to functional shifts in λ_{max} is not very well understood. One reason is that multiple amino acid sites —whether or not they are key-tuning sites—may interact in determining λ_{max} (Yokoyama 2008). For example, atomistic molecular simulations have recently uncovered a disulfide bridge between two amino

acid sites of RH1 (111 and 188) that cause a substantial blue shift in the rod opsins of deep-sea spinyfins (Musilova et al. 2019a). Also, the general background of the coding sequence may impact the function of visual opsins, as suggested by the signatures of positive selection in nucleotide substitutions that do not affect key-tuning sites (Nozawa et al. 2009).

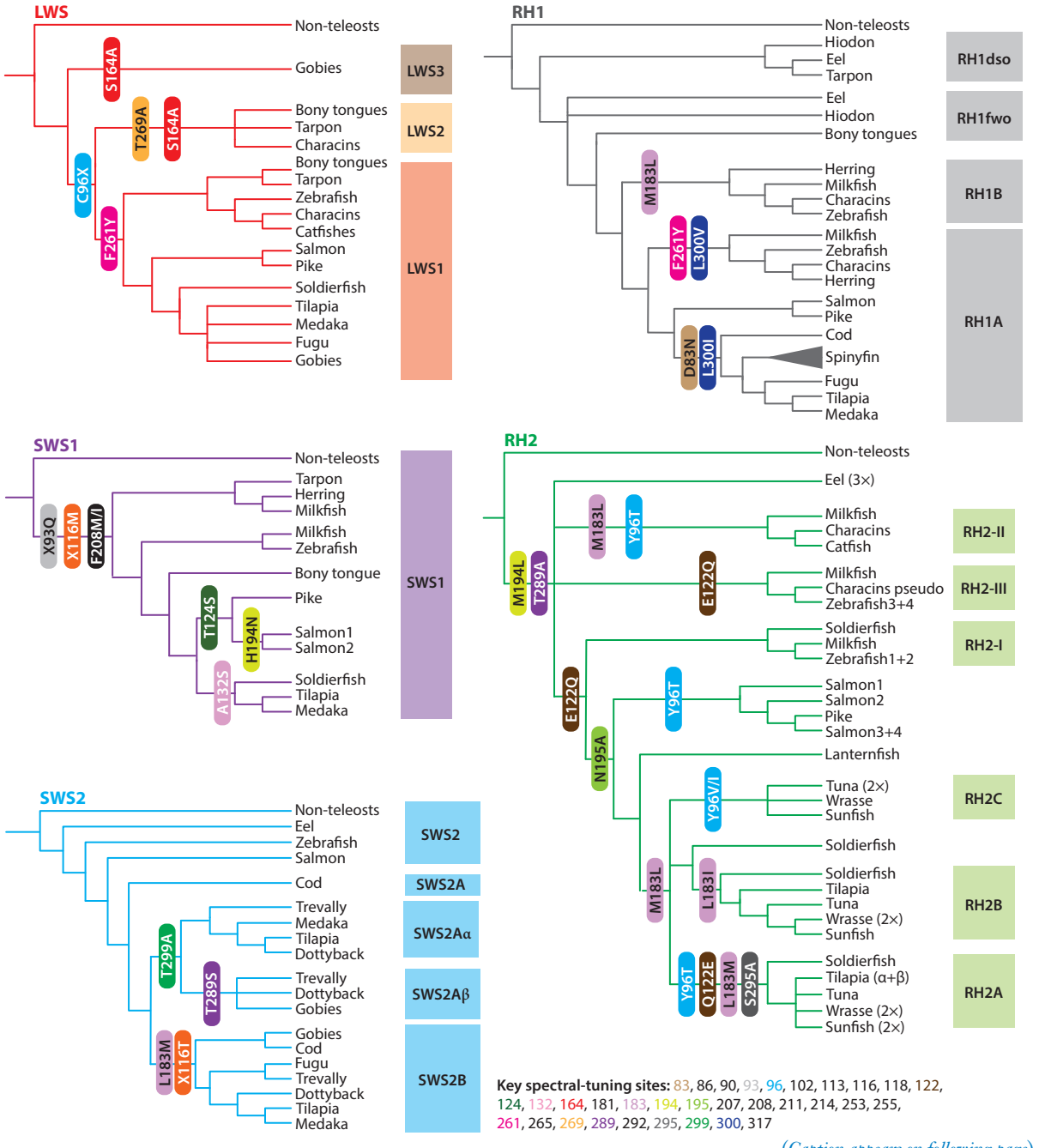

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Figure 3 (*Figure appears on preceding page*)

The functional diversification of visual opsin genes in teleost fishes. Shown are individual gene trees (simplified) of the teleost visual opsin genes (rod *RH1* and cones *SWS1*, *SWS2*, *RH2*, and *LWS*). The bottom right depicts a list of 32 key spectral-tuning amino acid sites based on Musilova et al. (2019a), Yokoyama (2008), and Yokoyama & Jia (2020). Amino acid alignment positions are referenced in relation to the bovine rhodopsin (Palczewski 2000). Changes in key spectral-tuning sites (following the color coding in the list) characteristic for a particular visual opsin gene or larger subclades of teleosts are mapped on the respective branches of the gene trees. Gene tree data are based on an analysis of more than one hundred fish genomes reported in Cortesi et al. (2015, 2021), Musilova & Cortesi (2021), and Musilova et al. (2019a) and complemented by additional data from GenBank. Abbreviations: LWS1–3, long-wavelength-sensitive opsins; pseudo, pseudogene; RH1, rhodopsin or rod opsin; RH2, rhodopsin-like 2; SWS1/2, short-wavelength-sensitive opsins.

Mutations at sites that do not alter λ_{max} may also concern functions unrelated to spectral sensitivity. For example, in Andean and Amazonian catfishes, variants of RH1 (L59Q and M288L) have been identified that are specific to populations living at high altitudes and show accelerated protein kinetics (Castiglione et al. 2017). In addition, in several deep-sea fishes, four amino acid sites (159, 196, 213, and 275) have been implicated to have lower opsin dimer compressibility and, hence, greater stability under high hydrostatic pressure (Porter et al. 2016).

3.2. The Specifics of Rod and Cone Opsin Evolution in Fishes

As detailed in Section 3.1, visual opsin genes in teleost fishes have diversified along multiple axes, and these processes have involved a variety of mechanisms. The median number of visual opsins in teleost fish genomes has been estimated at seven [six cones and one rod opsin (Musilova et al. 2019a)]. Despite this higher number compared to other vertebrates, there is no substantial overlap in the λ_{max} range of the cone opsin types in fishes (Carleton et al. 2020). Therefore, processes such as gene conversion and the convergent evolution of key spectral-tuning sites appear to be keeping different cone opsins constrained to specific spectral ranges. However, these constraints might be released once an opsin type is lost. For example, analogous to what has happened in primates, including humans, osteoglossomorph fishes have lost the green-sensitive *RH2* gene and instead use a second *LWS* copy that has shifted its spectral sensitivity from red to green (Liu et al. 2019). Notably, the cone opsins that are sensitive to the edges of the light spectrum (the UV-sensitive *SWS1* and red-sensitive *LWS*) are more variable compared to the ones sensitive to the middle, blue-green part of the spectrum [*SWS2* and *RH2* (Carleton et al. 2020)]. This is likely a consequence of the optical properties of water, in which the short and long wavelengths are first absorbed and scattered as a function of water depth (or of distance from the light source).

3.2.1. Rod opsin evolution. Rods are active during dim light and, in the majority of vertebrates, contain only a single RH1-based visual pigment used to discriminate between differences in brightness (Hunt et al. 2014). However, some teleost lineages possess two or more copies of *RH1* that have functionally diversified and are expressed, for example, during different developmental stages (Zhang et al. 2000) or in different areas of the retina (Morrow et al. 2017). Most Otomorpha contain two *RH1* genes that are likely derived from a duplication event in the clupeocephalan ancestor (Chen et al. 2018, Musilova et al. 2019a) (**Figure 2**). Cyprinids have up to four *RH1* copies, which are associated with an additional round of genome duplication in this group. A special case of convergent *RH1* gene proliferation has occurred in three deep-sea fish lineages that possess between 5 and 38 *RH1* copies due to lineage- or species-specific gene duplications (Musilova et al. 2019a). Because these *RH1* copies do not all occur in tandem, they may be the product of repeated (retro)transposition events.

3.2.2. Cone opsin evolution. Teleosts, on average, have two to three *RH2* copies within their genomes (Musilova & Cortesi 2021, Musilova et al. 2019a). The spectral sensitivity of *RH2* to

blue-green light overlaps largely with that of *RH1*. Note that *RH1* (and the teleost exorhodopsin) and *RH2* share a common ancestry (**Figure 1*e***) but are active during different light intensities and have evolved functional independence. Expansions of *RH2* have primarily occurred in fish living in blue-green-dominated marine habitats, with species with five and more *RH2* copies either inhabiting the deep sea or the pelagic open ocean or showing nocturnal activities on coral reefs (de Busserolles et al. 2020, Musilova et al. 2019a).

The largest number of red-sensitive *LWS* copies has been found in species inhabiting shallow aquatic environments rich in long-wavelength light, such as rivers and lakes or shallow coral reefs [tropical fighting fish (*Betta splendens*) and temperate brown trout (*Salmo trutta*) as well as wrasses (Cortesi et al. 2021, Dong et al. 2020)]. Some freshwater lineages (salmonids, pike, percids, and livebearers) have also expanded their *LWS* gene repertoire (Cortesi et al. 2021). In contrast, *LWS* tends to be lost in deeper-living species (Musilova et al. 2019a).

Fishes generally have fewer copies of the shorter wavelength–sensitive opsins (*SWS1* and *SWS2*) compared to the longer wavelength–sensitive opsin genes. Only a handful of species, such as damselfishes (Pomacentridae), smelts, and salmonids, have been found to have two UV-sensitive *SWS1* copies (Mitchell et al. 2020, Musilova et al. 2019a). These copies are derived from tandem duplications or from lineage-specific whole-genome duplications, and there is no evidence for ancestral duplications of *SWS1* within teleosts. Moreover, many species in the deep sea and the shallows have lost this gene altogether (see Section 4). Most teleosts possess between one and three copies of the violet-blue-sensitive *SWS2*, which is largely due to two ancestral duplications, one specific to neoteleosts and the other to percomorphs, the most species-rich crown group of teleosts (Cortesi et al. 2015). Up to three copies (*SWS2Aα*, *SWS2Aβ*, and *SWS2B*) can be found in the genomes of several coral reef or pelagic species (Cortesi et al. 2015), and the humphead wrasse has four copies of *SWS2B* (Dong et al. 2020) (**Figure 2**).

3.3. Visual Opsin Gene Expression and Its Regulation

Besides mutating the amino acid–sequence shifting λ_{max}, visual adaptations may also be achieved by changing the type or amount of visual opsin expressed or coexpressed within a given photoreceptor. Alterations in gene expression are very common and rather straightforward to assess, but their genetic underpinnings remain difficult to uncover. Changes in gene expression may also be plastic and under the control of epigenetic rather than genetic mechanisms. Either way, changing the type of opsin that is expressed and coexpressing multiple opsins within a single photoreceptor type appear to be quick ways by which fish vision can be adapted to changes in the light environment (Carleton et al. 2020).

3.3.1. Variation in opsin gene expression. A common observation in teleosts is that only a particular subset of their visual opsin genes is expressed at any one time. Opsin gene expression often differs between closely related species. For example, alternative gene expression profiles (referred to as opsin palettes) are common between closely related cichlid species that differ in their ecology and/or the light environment they inhabit (Hofmann et al. 2009, Musilova et al. 2019b, O'Quin et al. 2010). Visual opsin palettes may also differ within an individual, for example, along a developmental axis. Cone opsins are typically the first visual opsins to be expressed during ontogeny, with rod opsin only being switched on later (e.g., Lupše et al. 2021). Within the cone opsins, there are species that first express the shorter wavelength–sensitive (*SWS1* and *SWS2*) opsins [e.g., groupers (Kim et al. 2019) and salmonids (Cheng et al. 2007)], while others start their lives expressing the longer wavelength–sensitive (*RH2* or *LWS*) opsins [e.g., zebrafish and goldfish (Cheng et al. 2007)].

3.3.2. Opsin gene regulation. We are just beginning to understand how opsin gene expression is regulated, and what we have learned so far is limited to a few species such as zebrafish and some cichlids. Generally, both *cis*- and *trans*-regulatory processes are thought to drive the expression of cone opsins, while rod opsin regulation seems to rely more on *cis*-regulation (Tsujimura 2020). A number of candidate gene regulatory elements as well as the locus control regions for some of the visual opsins in fishes have been described. For instance, thyroid hormone receptor beta, which is also known to play a role in the expression of mammalian cone opsins (Roberts et al. 2006), has been shown to be essential for the expression of *LWS* (Suzuki et al. 2013) and *SWS1* (Alvarez-Delfin et al. 2009) in zebrafish. The transcription factor Tbx2a has been shown to simultaneously regulate the expression of *LWS* and *RH2* in cichlids (Sandkam et al. 2020), and its paralog Tbx2b has been shown to regulate *SWS1* in trout (Raine & Hawryshyn 2009). Also, the transcription factors Six6b and Six7 have been shown to regulate the expression of *SWS2* and *RH2* in zebrafish (Ogawa et al. 2019). However, while their binding sites have been identified in the promoter regions of *RH2* and *LWS*, the complete regulatory machinery remains elusive. Clearly, more work is needed to establish the link between changes in opsin gene expression and habitat, ecology, and behavior in the tens of thousands of teleost species.

4. VISUAL OPSIN DIVERSITY IN FISHES: ENVIRONMENT, ECOLOGY, AND FUNCTION

As shown in Section 3, recent advances in sequencing technology have made it possible to reconstruct the evolution of teleost visual opsins across a large number of species. At first glance, it appears that fishes possess many more opsin genes than necessary to perform a given visual task. In the following section, we review some general trends in visual opsin evolution in fishes and highlight, in more detail, some specific cases of environmental factors driving the opsin gene diversity in this group. Caution must be exercised, however, in interpreting such trends, as adaptive advantages often remain correlative rather than causative. Hence, understanding whether the diversity of opsin genes in fishes and the resulting spectral sensitivities are tightly linked to specific functions or whether fish vision evolved to be good enough to serve multiple purposes remains a challenge (Marshall et al. 2015).

4.1. Visual Opsin Genes and the Light Environment

The spectral sensitivities of the photoreceptors of aquatic animals tend to correlate with—albeit not always exactly match (Munz & McFarland 1977)—the light environment of their respective habitats {e.g., crustaceans [Cronin et al. 2001, Marshall et al. 1999], cetaceans and pinnipeds [Dungan et al. 2016, Fasick & Robinson 2000, Meredith et al. 2013], squamates [Seiko et al. 2020, Simões et al. 2020], and teleosts [reviewed in Bowmaker (1995), Munz & McFarland (1977), Schweikert et al. (2018, 2019)]}. In the most extreme cases of fishes that live in constant darkness, such as in caves, in the deepest depths of the ocean (see the sidebar titled The Deep Sea: Extreme Visual Adaptations to Extreme Conditions), or in deep rivers and lakes, the trend is toward the loss or reduction of eye structures, often accompanied by changes in the regulation of and/or the loss of genes relevant for vision (Aardema et al. 2020, Gore et al. 2018, Jeffery 2009, McGaugh et al. 2014, Musilova et al. 2019a).

4.1.1. Vision and depth. Due to the absorbing properties of water and the scattering effect of particles in the water column, the light intensity decreases, and the light spectrum becomes narrower (blue-light shifted) with increasing depth (Jerlov 1976) (**Figure 4*a***). Consequently, fishes that inhabit shallow and clear waters tend to rely during the day on cone-based visual systems that

THE DEEP SEA: EXTREME VISUAL ADAPTATIONS TO EXTREME CONDITIONS

Visual adaptations in the deep sea have mostly one aim: to catch more photons. Having larger eyes is only one way to do so. Some deep-sea fishes have peculiar eye morphologies, including upward-looking tubular-shaped eyes that may contain accessory, sideward-looking mirror eyes (diverticula) without lenses. Other deep-sea fishes possess thick multibank retinas with rod cells stacked in layers, or they may have a single layer containing modified, exceptionally long rod photoreceptors. The longer the rod outer segments are, the more efficient they are at capturing photons. No wonder, then, that the longest rods among fishes are found in those of the deep sea. Other adaptations include the photopigments themselves. The silver spinyfin's 38 rod opsin genes, which produce a plethora of differentially tuned proteins, represent one more record among vertebrates. Yet another unique visual adaptation is present in some deep-sea dragonfishes that use red photophores under their eyes. By using a bacteriochlorophyll-derived photosensitizer inside their rod photoreceptors, the spectral sensitivity of these photoreceptors is heavily shifted to the far red. Because red wavelengths and red vision are extremely rare in the deep sea, red bioluminescence might serve as a private communication channel or to illuminate red-blind prey. For an in-depth review on the topic see de Busserolles et al. (2020).

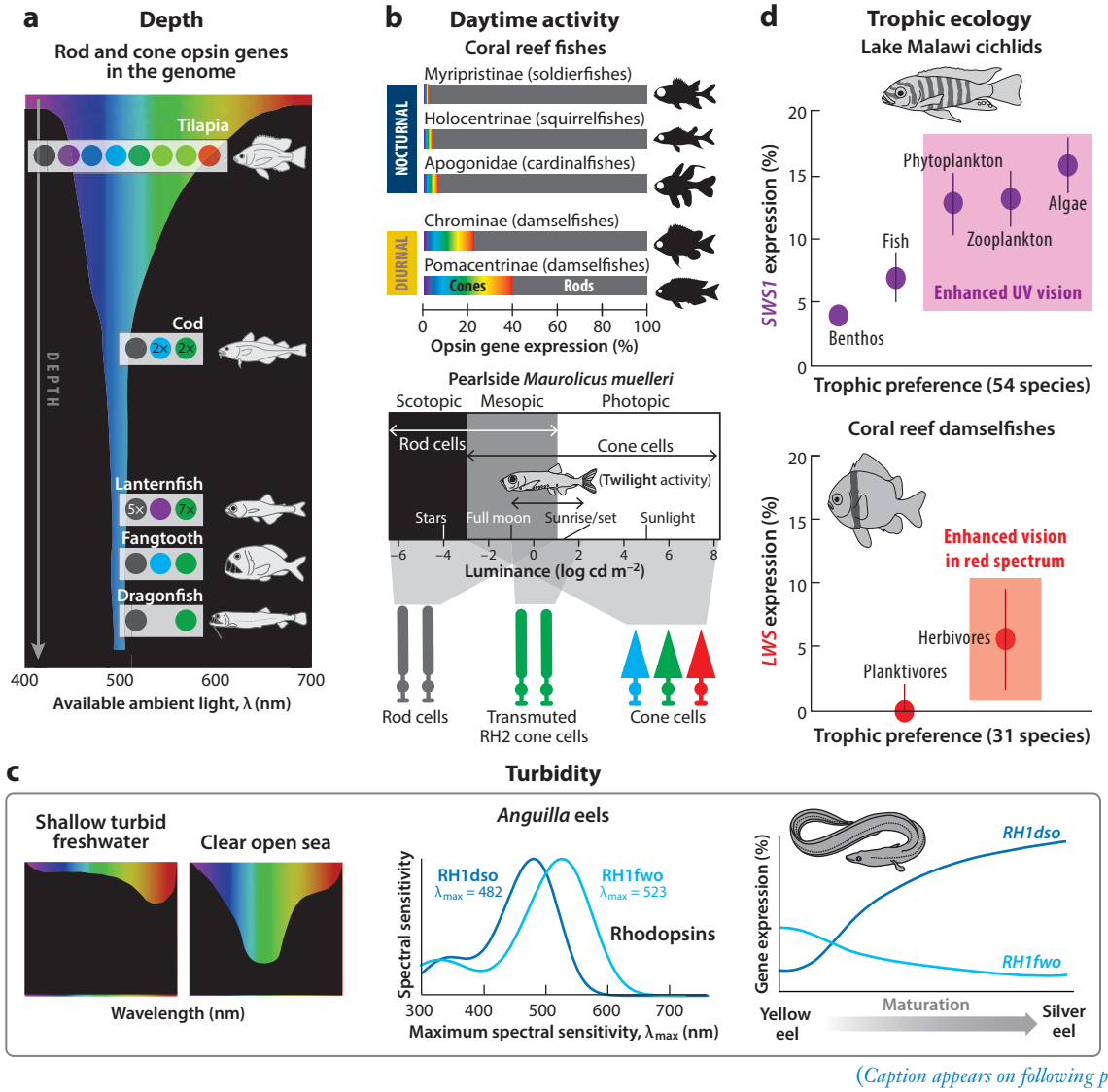
are sensitive to a broad spectrum of light. Deeper-living species, however, feature visual systems that rely on cones and/or rods tuned toward the blue-green spectrum of light. At water depths below 200 m, the remaining downwelling light is dim and spectrally narrow, as is bioluminescence emitted by deep-sea organisms. Accordingly, most deep-sea fishes use purely rod-based visual systems sensitive to blue wavelengths (~480 nm) [reviewed in Carleton et al. (2020), de Busserolles et al. (2020), and Munz & McFarland (1977)]. This correlation between water depth, light environment, and visual phenotype has been reported for a great number of fish species inhabiting both freshwater [e.g., sculpins (Hunt et al. 1996, Luk et al. 2016), salmonids (Eaton et al. 2020), cichlids (Hofmann et al. 2009; Musilova et al. 2019b; Sugawara et al. 2005; Terai et al. 2006, 2017)] and marine habitats [e.g., damselfishes (Stieb et al. 2016), holocentrids (Munz & McFarland 1973, Yokoyama & Takenaka 2004), and deep-sea fishes (de Busserolles et al. 2020, Douglas et al. 1998)].

Recent studies (Lin et al. 2017, Musilova et al. 2019a) based on whole-genome sequencing data have revealed that the water depth at which a species lives is not only reflected in repeated changes in the same key spectral-tuning sites but also is a robust predictor of the opsin gene repertoire (**Figure 4*a***). Shallow-living species have opsin complements rich in *SWS2*, *RH2*, and particularly *LWS*, conferring sensitivity across the visible light spectrum. Notably, although the UV-sensitive *SWS1* is more prevalent in fishes experiencing UV-illuminated environments, not all shallow-living species possess this gene (Musilova et al. 2019a). UV light may damage the eye (Ivanov et al. 2018) and is also scattered quickly in clear water (Rayleigh scattering), causing unwanted visual noise that limits contrast detection over distance (Muntz 1973). Hence, both of these properties are likely to have driven the evolution of UV-absorbing lenses and similar structures, which in turn might have facilitated the loss of *SWS1* (Escobar-Camacho et al. 2017, Hofmann et al. 2009, Losey et al. 2003, Siebeck & Marshall 2001).

In contrast, the genomes of deeper-living fishes tend to be rich in *SWS2* and *RH2* genes, conferring sensitivities to the more central blue-green part of the light spectrum, while having reduced numbers of *SWS1* and *LWS* genes (Lin et al. 2017, Musilova et al. 2019a) (**Figure 4*a***). In the deep sea, where dim light and bioluminescence prevail, another phenomenon has been observed: Together with colleagues, we have recently shown (Musilova et al. 2019a) that at least three deep-sea fish lineages have independently expanded and functionally diversified their rod opsin repertoires. Why some deep-sea fishes have more copies of *RH1* is not yet entirely clear.

One possible explanation is that these fishes use them for broader spectral absorbance to maximize photon capture; alternatively, the spectrally different rod opsins might be used to distinguish differently colored bioluminescent signals. In the silver spinyfin, there is also a difference in the expression of the various *RH1* copies in different developmental stages (Musilova et al. 2019a), which might likewise be the case for other species with multiple *RH1*s. Interestingly, in common with other deep-sea fishes, spinyfins start their lives as larvae in the shallow, nutrient-rich layers of the pelagic zone, at which point their vision mostly relies on the green-sensitive *RH2* (Lupše et al. 2021, Musilova et al. 2019a). Being exposed to a well-lit environment early in life might explain why species that rely on pure rod retinas as adults still retain cone opsin genes in their genomes.

4.1.2. Vision during twilight and at night. In shallow and clear waters, the light spectrum changes considerably with the time of the day: Daylight is characterized by a broad spectrum



(Caption appears on following page)

Figure 4 (*Figure appears on preceding page*)

Environmental drivers of visual opsin evolution in teleost fishes. (*a*) Water depth and the associated light environment are main predictors of the visual opsin gene repertoire of teleosts. Shallow-living species exposed to the entire light spectrum typically exhibit the full range of visual opsins, including the UV-sensitive *SWS1* (*purple dot*) (shown here for the Nile tilapia), while species living in the depths, where blue light prevails, often lack the shortest- (*SWS1*) and longest-tuned (*LWS*) (*red dot*) visual opsins but show expansions of *RH2* (*green dots*) and *RH1* (*gray dot*) (as illustrated for cod, lanternfish, fangtooth, and dragonfish). Blue dots indicate *SWS2* opsins. Panel *a* is based on data from Musilova et al. (2019a). (*b*) The time of day when a species is active is reflected in the expression patterns of its visual opsin genes. (*Top*) The visual system of nocturnal fishes is based mostly on rods, and these fishes express comparatively lower quantities of cone opsins than do diurnal species (as shown here for coral reef fishes). Panel *b* (*top*) is based on data from de Busserolles et al. (2021), Luehrmann et al. (2019), and Stieb et al. (2017). (*Bottom*) Deep-sea pearlsides feature transmuted cones with a rod-like appearance but a molecular machinery of cones (as shown here for *Maurolicus muelleri*). Panel *b* (*bottom*) adapted with permission from de Busserolles et al. (2017). (*c*) Turbidity and the associated shifts in the light spectrum impact the visual system of fishes. Migratory eels (*Anguilla* spp.) exhibit an ontogenetic shift in the expression of their two *RH1* copies (*RH1dso* and *RH1fwo*) whereby juveniles living in turbid freshwater habitats primarily express the longer-wavelength-shifted *RH1fwo* and adults migrating into clear marine waters express the shorter-wavelength-shifted *RH1dso*. Panel *c* (*right*) adapted with permission from Zhang et al. (2000). (*d*) Trophic ecology determines visual opsin expression in fishes. (*Top*) Planktivorous and algivorous cichlids from Lake Malawi exhibit higher expression levels of the UV-sensitive opsin *SWS1* compared to benthic feeders or fish eaters. Panel *d* (*top*) adapted with permission from Hofmann et al. (2009). (*Bottom*) Herbivorous coral reef damselfishes (Pomacentridae) express higher levels of *LWS* than do their planktivorous relatives. Panel *d* (*bottom*) adapted with permission from Stieb et al. (2017). Abbreviations: *dso*, deep sea opsin; *fwo*, freshwater opsin; *LWS*, long-wavelength-sensitive opsin; *RH1*, rhodopsin or rod opsin; *RH2*, rhodopsin-like 2; *SWS1*, short-wavelength-sensitive opsin; UV, ultraviolet.

of high-intensity light; during crepuscular hours, the intensity decreases and the light environment is mostly blue-wavelength dominated; and at night, the moon and the stars are the main sources of light, whereby the light intensity is from 8 to 9 orders of magnitude lower than during the day, and longer wavelengths predominate despite a fairly broad light spectrum (McFarland 1986). Consequently, nocturnal fishes show visual adaptations that are similar to those of deep-sea fishes, including large eyes and rod-dominated retinas to maximize sensitivity [reviewed in Cortesi et al. (2020) and Munz & McFarland (1977)]. However, because green light prevails at night, the rod spectral sensitivities of nocturnal shallow-water fishes are shifted toward longer wavelengths (~490–520 nm λ_{max}) compared to those of deep-sea fishes [reviewed in Munz & McFarland (1977) and Schweikert et al. (2019)].

The twilight period (also referred to as the quiet period) is of special interest because the intensity of light during the crepuscular hours leads to the simultaneous activity of both cones and rods, albeit with neither of them working at their optimum (Munz & McFarland 1973, Stockman & Sharpe 2006) (**Figure 4*b***). While many animals avoid being active during this time of day, one group of fishes stands out by taking advantage of this so-called antipredation window (Clark & Levy 1988). The pearlsides (*Maurolicus* spp.) are deep-sea fishes found in water depths of ~200 m during the day. However, in contrast to other mesopelagic fishes that venture to the surface at night to find food, pearlsides migrate to the surface during crepuscular hours (Giske et al. 1990). Accordingly, their visual system shows unique adaptations to twilight conditions (de Busserolles et al. 2017) (**Figure 4*b***). For example, they rely mainly on rodlike cone cells that express *RH2* and genes belonging to the cone-photoreceptor cascade. Also, the spectral sensitivities of their transmuted photoreceptors are shifted toward blue wavelengths (~430–440 nm λ_{max}). Thus, pearlsides appear to have combined the properties of rod photoreceptors (high sensitivity) and cone photopigments (tolerance to higher light intensities and rapid pigment recovery) to optimize vision during twilight hours (de Busserolles et al. 2017).

Nocturnal fishes often show reduced activity during the day (Helfman 1986). Their visual systems may therefore be adapted to both dim- and bright-light conditions, as is the case for two reef-dwelling nocturnal families, the cardinalfishes (Luehrmann et al. 2019) and the holocentrids (de Busserolles et al. 2021). Holocentrids have large eyes, and their single *RH1* is expressed in rods

that are arranged in multiple banks stacked on top of one another—an adaptation usually found in deep-sea fishes (de Busserolles et al. 2020, 2021). Depending on the water depth at which they occur, the different holocentrid species have rod pigments with different spectral sensitivities: Shallow-dwelling species have rods tuned to green wavelengths (~500–507 nm λ_{max}), while the photoreceptors of deeper-living holocentrids are tuned to blue wavelengths (~480–485 nm λ_{max}); species living at intermediate depths have rods with intermediate sensitivities (~490–495 nm λ_{max}) (Munz & McFarland 1973, Yokoyama & Takenaka 2004). In addition, holocentrids retain few but large cones that express a single blue-sensitive *SWS2A* and up to two copies of the green-sensitive *RH2* (de Busserolles et al. 2021, Musilova et al. 2019a). Having large cones and a multibank retina seems especially favorable for vision during twilight hours and at night, presumably to increase sensitivity and/or to allow color discrimination in dim light (de Busserolles et al. 2021).

4.1.3. Vision in turbid waters. The color of fresh and brackish waters, but also that of marine water in inshore and outer reef habitats, may differ substantially between locations and seasons due to changes in solar angle and irradiance as well as varying levels of phytoplankton (chlorophyll), dissolved organic matter, and silt in the water column (Jerlov 1976, Munz & McFarland 1977). An increasing number of fishes have been found to have visual systems adapted to such differences in photic environments [e.g., snappers (Lythgoe et al. 1994), cichlids (Carleton & Yourick 2020), sticklebacks (Marques et al. 2017, Novales Flamarique 2013), killifish (Fuller et al. 2003), herring (Hill et al. 2019), Atlantic tarpons (Schweikert & Grace 2018, Taylor et al. 2011), tuna (Loew et al. 2002), and cardinalfishes (Luehrmann et al. 2020)]. Cone opsin losses and red-shifted spectral sensitivities (Escobar-Camacho et al. 2017, Liu et al. 2016, Weadick et al. 2012) are common in species that live in turbid waters, presumably due to the reduced levels of UV light and shifts toward longer wavelengths, respectively. For example, amino acid site 261 of RH1 has converged to a red-shifted phenotype (Phe261Tyr) at least 20 times independently as teleosts transitioned from blue-shifted marine environments to red-shifted brackish or freshwater habitats (Hill et al. 2019, Musilova et al. 2019a), and the same switch has also been found between closely related freshwater species (Eaton et al. 2020). Similar scenarios involving repeated changes in key spectral-tuning sites when transitioning between differently colored waters are also common in cone opsins (Lin et al. 2017, Musilova et al. 2019a, Yokoyama 2008). This illustrates the somewhat limited scope under which opsins can operate, as the light environment exerts strong selective pressures, leading to convergent visual phenotypes.

Adaptations to turbid waters can also occur at the chromophore level: Cichlids that live in the relatively clear Lake Malawi and in some crater lakes of Nicaragua use more of the shorter-shifted A1-derived chromophore, while those that live in the murky large lakes of Nicaragua use increased amounts of the longer-shifted A2-derived chromophore (Härer et al. 2018, Muntz 1976, Torres-Dowdall et al. 2017). This shift is likely catalyzed by *Cyp27c1* (Enright et al. 2015, Torres-Dowdall et al. 2017). As shown recently in fishes that inhabit the Panama Canal, changes in chromophores can be dynamic and occur over short periods of time (Escobar-Camacho et al. 2019). Chromophore switches might sometimes also be tied to ontogeny such as in eels that migrate between fresh and marine waters (eels also switch the rod opsin they use; **Figure 4*c***) (Archer et al. 1995, Wood & Partridge 1993). Arguably the fastest way to adapt to differences in light environments, though, is by changing opsin gene expression itself (Carleton et al. 2020).

4.1.4. Vision in variable light environments. Plasticity in the expression of visual opsin genes is remarkably widespread in teleosts and can occur over different timescales (Carleton et al. 2020). In many species, opsin gene expression is plastic during development [e.g., flounder (Savelli et al. 2018), cichlids (Carleton et al. 2008, Dalton et al. 2015, Härer et al. 2017), killifish (Fuller

et al. 2005, 2010), and black bream (Shand et al. 2008)]. These changes are often associated with ontogenetic habitat transitions, for example, in the dusky dottyback, *Pseudochromis fuscus*, which changes opsin gene expression between pelagic larvae and juvenile and adult stages on the reef (Cortesi et al. 2016). However, in some species, opsin gene expression might be more hardwired, showing barely any changes with development [e.g., cod (Valen et al. 2018), salmon (Novales Flamarique 2018), and surgeonfishes (Tettamanti et al. 2019)]. Shifts in the photic environment, for example, from clearer waters in winter to greener algae- and phytoplankton-dominated waters during summer [e.g., damselfishes (Stieb et al. 2016)] or due to seasonal changes in temperature and day length [e.g., medaka (Shimmura et al. 2017)], may also cause adult fishes to change gene expression. In some species, adults are even able to change opsin gene expression within weeks or days when exposed to different light conditions in laboratory experiments [e.g., damselfishes and cardinalfishes (Luehrmann et al. 2018), cichlids (Nandamuri et al. 2017), and killifish (Fuller & Claricoates 2011)]. Other ways to adapt to variable photic environments are by expressing different opsin complements in different parts of the retina or by coexpressing multiple opsins within the same photoreceptor cell [e.g., archerfish (Temple et al. 2010), cichlids (Dalton et al. 2014, Torres-Dowdall et al. 2017), flatfish (Iwanicki et al. 2017), and salmon (Cheng & Novales Flamarique 2004)]. For example, the eyes of the four-eyed fish (*Anableps anableps*) are adapted for simultaneous vision above and below the water, whereby the lower part of the eye that looks down into the turbid water expresses a longer wavelength–shifted opsin complement compared to that of the upper part that looks into air (Owens et al. 2012).

All of the abovementioned examples testify that the light environment determines what fish can see. Therefore, it may come as a surprise that, within a given envelope of light, spectral sensitivities can vary substantially in fish, even between closely related species (Carleton et al. 2020; Marshall et al. 2015, 2018; Schweikert et al. 2018). In the next section, we discuss different aspects of the biology of fishes that might, at least in part, explain this variation.

4.2. Visual Opsin Genes and Life History

4.2.1. Vision and feeding ecology. Intra- and interspecific differences in visual opsin gene expression and, by extension, spectral sensitivity may arise in response to different feeding habits, which is especially evident for the shortest- and the longest-tuned photoreceptors expressing *SWS1* and *LWS*, respectively. For example, the contrast of zooplankton against the background light is increased via the absorption or reflection of short wavelengths of light, which is thought to confer a benefit to species with UV sensitivity [e.g., cichlids (Hofmann et al. 2009, Jordan et al. 2004, O'Quin et al. 2010) (**Figure 4*d***), zebrafish (Novales Flamarique 2016, Yoshimatsu et al. 2020), perch (Loew et al. 1993), and sticklebacks (Rick et al. 2012)]. Changes in UV sensitivity may also occur during development: Fishes are often sensitive to UV light during the planktonic larval stage but shift their sensitivities to longer wavelengths later in life when settling and changing diet (Job & Bellwood 2007, Siebeck & Marshall 2007, Thorpe & Douglas 1993). The rainbow trout (*Oncorhynchus mykiss*), for example, undergoes such an ontogenetic switch from UV sensitivity (when being zooplanktivorous) to blue sensitivity (when starting to feed on invertebrates and small fishes) (Browman et al. 1994, Hawryshyn et al. 1989). The expression of *LWS*, however, may benefit herbivorous fishes such as some damselfishes (Stieb et al. 2017) and blennies (Cortesi et al. 2018), as the (far-)red reflectance of chlorophyll sharply contrasts with the gray to brown color of a rubble-filled or sandy background (Marshall et al. 2003).

4.2.2. Vision, color, and sex. Interestingly, both UV and red sensitivity have also been associated with color signaling, communication, and sexual selection in both freshwater and marine

fishes [reviewed in Carleton et al. (2020) and Marshall et al. (2018)]. UV vision is common in smaller teleosts that live in clear waters, while bigger fishes tend to be insensitive to shorter wavelengths of light (Marshall et al. 2018, Siebeck et al. 2006). UV-reflecting body patterns are common in these smaller species and are thought to be used to secretly communicate with one another, hidden away from the UV-blind predatory fish [e.g., damselfish (Siebeck et al. 2010, Stieb et al. 2017), swordtails (Cummings et al. 2003), and guppies (Smith et al. 2002)]. For example, the Ambon damselfish (*Pomacentrus amboinensis*) has been shown to use its UV-reflecting facial markings to distinguish conspecifics from heterospecific intruders (Siebeck et al. 2010). The white stripes in the iconic anemonefishes strongly reflect in the UV (Marshall et al. 2006), and in the Barrier Reef anemonefish (*Amphiprion akindynos*), single-cone photoreceptors located in a small, highly acute area of the forward-looking part of the retina coexpress *SWS1* and *SWS2B*, which might help in discerning a conspecific intruder from a member of their own group (Stieb et al. 2019).

Vision at longer wavelengths of light—and with it the functional diversification of *LWS*—has been associated with color-selective mating in freshwater fishes such as cichlids (Seehausen et al. 2008), guppies (Sandkam et al. 2018), and sticklebacks (Boughman 2001). Similarly, a strong association between *LWS* expression and red coloration has also been reported in marine fishes such as the wrasses (Marshall et al. 2003, Michiels et al. 2008, Phillips et al. 2016). The idea behind this sensory drive is that the visual system is initially shaped by a species ecology and the light environment, which in turn drive the coevolution of colorful signals, ultimately leading to the formation of new species (Cummings & Endler 2018, Endler 1992). Support for this scenario comes from cichlids from Lake Victoria (Miyagi et al. 2012, Terai et al. 2006). In the genus *Pundamilia*, for example, a shallow-living species (*P. pundamilia*) expresses a blue-shifted *LWS* opsin and the males are blue-colored, while a deeper-living species (*P. nyererei*) has red-colored males and females express a red-shifted *LWS* copy, facilitating color-assortative mating (Seehausen et al. 2008). However, even in these cichlids, unambiguous evidence for sensory drive remains difficult to establish (Wright et al. 2020).

Notably, in long-wavelength-sensitive species that prominently feature orange or red colors, such as the wrasses and guppies, the *LWS* genes have expanded substantially (Sandkam et al. 2018; Cortesi et al. 2020, 2021). Similarly, in damselfishes and salmonids, which rely on UV vision for feeding and communication, *SWS1* has been duplicated (Mitchell et al. 2020, Musilova et al. 2019a).

5. CONCLUSION

Visual pigments, which are composed of an opsin protein and a retinal chromophore, are at the core of animal vision. Phylogenetic comparative approaches and *in vitro* protein reconstructions have revealed that changes in the key spectral-tuning sites of the opsin protein lead to shifts in their spectral sensitivity, permitting a direct link between opsin genotypes and visual phenotypes. The vertebrate ancestor possessed five types of visual opsin genes, a rod opsin and four cone opsins sensitive from the UV to the red light ranges. In the most species-rich clade of vertebrates, teleost fishes, the visual opsin genes continued to proliferate and to functionally diversify. This has happened primarily through ancestral as well as many lineage-specific gene duplications. Why fishes have so many visual opsin genes is not entirely clear, but correlations can be drawn with the respective light environment, ecology, and coloration of a species. Based on the work of previous generations of scientists and aided by the technological advances of the last decade, contemporary vision researchers are now able to move beyond correlations in their attempts to unravel the mechanistic links causing the astonishing diversity of visual opsin genes in fishes.

SUMMARY POINTS

1. The vertebrate ancestor possessed five types of visual opsin genes, one rod opsin (*RH1*) and four cone opsins (*SWS1*, *SWS2*, *RH2*, and *LWS*). In teleost fishes, visual opsin gene copy numbers continued to expand, as they did in no other vertebrate lineage.
2. The evolution of visual opsin genes in teleosts is primarily driven by differences in the light environment that the various species inhabit. Differences in (feeding) ecology and coloration may also play a role in the fine-tuning of the visual sensory system.
3. Shallow-living species have opsin gene repertoires that may contain all four cone opsin types, with photoreceptor peak spectral sensitivities that range from the ultraviolet (UV) to the red spectrum (350–600 nm λ_{max}).
4. Many deeper-living species have lost the UV- and red-sensitive cone opsins (*SWS1* and *LWS*) and their photoreceptors are sensitive to the center, blue-green part of the light spectrum (~440–520 nm λ_{max}).
5. The green-sensitive *RH2* cone opsins have by far the most dynamic evolutionary history in teleost fishes with many ancestral, lineage-, and species-specific gene duplications and losses.
6. *LWS* paralogs in characins, mormyrids, and tarpons are most likely remnants of the teleost-specific whole-genome duplication. A more distinct *LWS* paralog in gobies suggests that an even earlier gene duplication event also took place.
7. An unusual example of opsin gene proliferation exists in deep-sea fishes, in which *RH1* was independently duplicated in at least three different lineages. The most extreme case is that of the silver spinyfin, *Diretmus argenteus*, which has 38 functionally diversified *RH1* copies.
8. Many fishes appear to have more visual opsins than are necessary to complete a given visual task. These seemingly extra visual opsins may be used at different developmental stages, in different seasons (or shorter time frames), or in different parts of the retina. They may also be the result of phylogenetic inertia or drift.

FUTURE ISSUES

1. While some vision-related genes (especially the visual opsins) are well studied, others are not. Future research should focus on the entire network of genes underlying vision (Mehta et al. 2021).
2. Except for the zebrafish model system, little is known about the neuronal circuits that mediate visually guided behavior and light responses in teleosts beyond the photoreceptors (Baden et al. 2020). Recent technological advances such as *in vivo* calcium imaging and reverse-genetic approaches in non-model teleosts as well as sophisticated behavioral experiments will greatly facilitate future comparative studies.
3. How opsin gene expression is controlled remains for the most part unknown. Single-cell RNA sequencing coupled with functional (epi)genomics and reverse genetics will provide the opportunity to elucidate these pathways going forward.

4. Visual opsins may also function as light receptors outside the eyes; this is an area that we expect to receive increased attention in the future.

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.

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