one of the neuronal groups that receives the incoming axons of the auditory nerve, also has a structure very similar to that of the cerebellar cortex complete with granule cells that form parallel fibers, efferent cells that send their dendrites into the layer of parallel fibers and many other characteristics of the cerebellum [1,12].

Evolution of the Cerebellum
Although there are some striking differences between and even within vertebrate classes, the cerebellum generally has remained relatively conservative in its evolution. Some of the major changes in the cerebellum that accompanied the transition to land have been the appearance of new types of inhibitory cells, the development of multiple deep cerebellar nuclei, and the elaboration and expansion of the corpus cerebelli in mammals and birds [1,2].

References

Evolution of Cranial Nerves
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- Evolution of Auditory System: in Mammals
- Evolution of Auditory System: in Reptiles and Birds
- Evolution of Mechanosensory and Electroreceptive Lateral Line Systems
- Evolution of Hindbrain
- Evolution of Oculomotor System
- Evolution of Olfactory and Vomeronasal Systems
- Evolution of Terminal Nerve
- Evolution of the Trigeminal Sensory System and Its Specializations
- Evolution of Vestibular System

Evolution of Corticospinal Motor Systems
- Evolution of Motor Systems: Corticospinal, Reticulospinal, Rubrospinal and Vestibulospinal Systems

Evolution of Eyes

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Synonyms
Eye evolution; Phototransduction; Lens evolution; Opsin evolution

Definition
Eye evolution is the process through which eyes evolved in the animal kingdom. Eyes are organs that compare light from different directions to produce an image. Information carried by light is transduced by specialized photoreceptor cells in the eye into neural information to be used by the brain. Many eyes have lenses that serve to collect and focus light, and these proteins have an independent evolutionary history.

Characteristics
Light has been exploited by organisms for energy via photosynthesis and information through the evolution
of photoreceptors and ultimately eyes in animals. Darwin first wondered how such a remarkable organ as the eye could have evolved. We now know that the many adaptations of different eye types among widely different organisms concealed some interesting constraints on eye evolution. Morphological comparisons of differences in eye structures first suggested eyes are polyphyletic, evolving possibly 40–60 times, but studies of eye development identified some molecules used to build eyes in many species, suggesting eyes are monophyletic. Most studies compared eyes using ciliary photoreceptors found primarily in vertebrates with eyes using microvillar photoreceptors found primarily in invertebrates. Each eye type uses different members of the rhodopsin (type 2) protein for phototransduction and have remarkably different molecular cascades that convert photons into information. Recently, this controversy has been resolved with evidence that both primary eye types existed in ancestral bilaterians, and both are present in extant vertebrates and invertebrates. This means that at least these two eye types and probably many more were present in the urbilateria, prior to the Cambrian explosive speciation. Moreover, the novel functional photodetection system, the cryptochromes that exist widely in both plants and animals is as ancient. Thus, the eyes we know are certainly polyphyletic in origin and more surprises await us.

Constraints on Eye Evolution from Physical Laws

Although there seems to be a large variety of eyes in the animal kingdom, physical laws have constrained solutions for collecting and focusing light to just eight types of eye optics [1].

Animal eyes are not simply photon detectors but organs that produce an image by comparing light from different directions using pinholes, lenses or mirrors to focus an image on photoreceptors. Light travels in straight lines and information is carried by wavelength, intensity and/or polarization, setting limits on eye dimensions and detection systems. Of ca. 33 animal phyla, about one-third have no specialized organ for detecting light, one-third have light sensitive organs, and the rest are animals with what we would consider eyes. Image-forming eyes appeared in six of the 33 extant metazoan phyla (Cnidaria, Mollusca, Annelida, Ophychophora, Arthropoda, and Chordata), and these six contribute about 96% of the known species alive today.

Since earliest evolution occurred in water which transmits only a limited range of wavelengths, the mechanisms for photon response converged on biochemical solutions that set the course for subsequent evolution [1]. The evolution of eyes very likely proceeded in stages. First were eye-spots, found in nearly all major animal groups, with a small number of receptors in an open cup of screening pigment. Eye-spots are able to distinguish light from dark but cannot represent complex light patterns. Second, invagination of this eyespot into a pit adds the capacity to detect the direction of incident light. Third, increasing the number of receptors, either by adding them in an existing pit or duplicating the pit in its entirety, probably led in two directions: adding receptors may have led to a chambered eye, while duplication of receptors may have led to a compound eye [1]. Fourth, adding an optical system that increases light collection and produces an image significantly increases the usefulness of an eye. Early in the Cambrian period (570–500 million years ago), very simple eyespots, useful for detecting light but not for processing directional information, were present. Explosive speciation, or the “Big Bang” of animal evolution, happened during the Cambrian period, and existing eye types improved radically, coincident with the appearance of carnivory and predation. Whereas primitive eyes can inform about light intensity and direction, more advanced eyes deliver more sophisticated information about wavelength, contrast and polarity.

Other Photodetection Systems

In addition, a second family of photodetection is found in archaea and eukaryotic microbes based on an independently evolved family of rhodopsin molecules (rhodopsin 1). Evolution produced this solution for harvesting light for energy, guiding phototaxis and serving other yet undiscovered functions. Genetic sequencing of organisms in large water samples has increased the number of known type 1 opsins (>800). Despite remarkable convergence in molecular details of their function, there is no phylogenetic relationship between the gene sequences of opsin types 1 and 2. Nonetheless, both are seven transmembrane domain proteins, both use an associated retinal moiety to capture light and, in both, retinal is attached in a Schiff base linkage via a lysine residue in the seventh helix. However, type 1 opsins function within the membrane to pump ions or signal other integral membrane proteins as opposed to signaling via intracellular G proteins. Finally, the two retinal molecules are photoisomerized quite differently. Progenitors of the type 1 opsins probably existed in earliest evolution before the divergence of archaea, eubacteria and eukaryotes, meaning that a light driven ion transport mechanism for deriving energy used in association with opsin 1 preceded the evolution of photosynthesis as a means for using the sun’s energy. These photodetection systems can trigger movement in response to light direction and intensity and thus might be considered “proto-eyes.” Comparing these two opsin systems reveals the power of natural selection to generate independent inventions which, when coupled with strong functional constraints, yield complex, convergent biological systems.
Capturing Photons

The transduction of photons into neural signals uses seven-transmembrane opsin proteins (30–50 kDa) combined with a photon sensitive vitamin A-derived non-protein retinal chromophore attached via a specialized binding pocket. These opsin proteins, or visual pigments, which control sensitivity to light of different wavelengths, appeared before eyes and evolved into seven or eight distinct families, diverging from an ancestral type before fish split from other vertebrates (Fig. 1). It is now clear that all animals have multiple opsin types, and opsin was present before deuterostomes split from protostomes suggesting that a common ancestor had multiple opsin genes, a surmise recently verified. Multiple new opsin genes, as well as new genes for other photo transduction specific families (e.g., G proteins, nucleotide-gated channels etc.) arose early in vertebrate evolution during extensive chromosome duplications and very likely facilitated retinal specializations, providing the raw material for natural selection. For example, opsin gene duplication was responsible for the independent evolution of three color (trichromatic) vision in both Old and New World primates, and opsin gene duplications in lepidoptera (butterflies) followed by increased rate of evolution produced a diversity of pigments sensitive to visual spectra important for specific species. Photoceptor wavelength absorption spectra are exquisitely modulated by a small collection of amino acid side groups adjacent to the chromophore binding site in the seventh transmembrane domain of opsins where the effects of natural selection are now most evident.

An example of how color vision shapes cone opsin evolution is in the visual systems of cichlid fishes in the East African lakes. In one riverine species, ancestral to the lake species, seven cone opsin genes are present due to gene duplications. Though only four cone opsin are found in the adult retina and hence can contribute to wavelength discrimination by the animal, the rest are expressed variously during ontogeny. This preservation of opsin genes may offer a substrate for Rapid selection of different visual chromatic sensitivities in response to selective pressures.

The two best known photoreceptor types use distinct families of opsins packed in quite different membrane specializations and, importantly, use different mechanisms of transduction (Fig. 2).

Vertebrate photoreceptors use members of the ciliary opsin (r-opsin) family named because they are incorporated into specialized cilia, while invertebrate photoreceptors use members of the rhodopinic opsin (r-opsin) that are typically formed into structures called rhodopsin. Each receptor type uses different heterotrimetric guanine nucleotide-binding proteins (Gp protein), named transducin in vertebrates, and the Gq family in invertebrates. Vertebrate photoreceptors produce hyperpolarizing potentials via a phosphodiesterase cascade while invertebrate photoreceptors are depolarizing and use a phospholipase C cascade. The site of biochemical signal amplification is quite different between these receptor types, as are the mechanisms for terminating the response. Moreover, opsins in vertebrates are fixed to their membranes, allowing polarization detection while those in invertebrates are not. It is clear that these photoreceptor types arose independently and co-existed in urbilateria before bilateria arose.

Eyes have evolved to extract information about the environment exploiting the same properties of light: intensity differences produce contrast, and wavelength differences produce hue. However, no unique neural solutions exist for extracting this information, and specializations that evolved to process intensity and wavelength differ among species, reflecting how natural selection can solve similar problems via diverse mechanisms. For example, mammals and bees use long wavelength photoreceptors for intensity and color vision, while flies and birds have evolved separate sets of photoreceptors for these two purposes. Similarly, blowfly and monkey photoreceptors are equally effective in compressing a wide range of light intensities and in converting detected intensity variations into useful visual contrast using vastly different mechanisms. Thus, blowfly and monkey photoreceptors evolved independently, use different molecular mechanisms, signal processing and other physiological steps, yet essential information about the world delivered to the nervous system is nearly identical. These few examples reveal the different routes natural selection has taken during the evolution of eyes in response to the information available in light.

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**Evolution of Eyes, Figure 1** A schematic molecular phylogenetic tree inferred by the neighbor-joining method showing the seven known opsin subfamilies [Simplified from Terakita A. (2005) The opsins. Genome Biology 6:213.1–213.9].

G<sub>q</sub>-coupled invertebrate opsins (r-opsins)

G<sub>q</sub>-coupled melanopsin

Encephalopsin/ tmt opsin

G<sub>q</sub>-coupled vertebrate opsins (c-opsins) & non-visual opsins

G<sub>q</sub>-coupled opsin subfamily

Neuropin subfamily

Peropsin subfamily

Photoisomerase (RGR) subfamily
Evolution of Eyes. Figure 2  Schematic illustration showing the key differences between a simplified representation of: (TOP) canonical vertebrate ciliary phototransduction and: (BOTTOM) invertebrate rhabdomeric phototransduction where hv represents incident photon energy. The two different opsins types (c-opsin and r-opsin) are contained in distinctly different membrane types, ciliary and rhabdomeric. The opsins are coupled to different families of G proteins that act via different types of transduction cascades. Amplification occurs during phototransduction in ciliary receptors and during channel opening in rhabdomeric receptors. These cascades produce signals of different sign. Gt, transducin; PDE, phosphodiesterase; cGMP, cyclic guanosylmophosphate; Gq, guanine nucleotide binding protein α15; PIP2, phosphatidylinositol-4,5-biphosphate; DAG, diacylglycerol.

Lenses
Eye lenses collect and focus light, leading to increased sensitivity and allowing information to be spatially resolved. More advanced eyes collect light through an aperture and focus it with a lens onto a layer of photoreceptor cells. Lenses are made from proteins, so could their phylogenetic relationships provide insight into eye evolution?

Vertebrate lenses contain high concentrations of soluble proteins called crystallins because they maintain transparency while lens proteins of most invertebrate eyes are secreted by specialized cells. Three major gene families of crystallins are widely expressed in vertebrate lenses and account for most of the protein in aquatic and terrestrial vertebrates: α-crystallins [2–3], β-crystallins [6+] and γ-crystallins [2–16]. Though it was once thought that these proteins had uniquely evolved to function as lenses, some are found expressed in heart, brain and other tissues of the eye. The remaining vertebrate lens proteins are a diverse, non-conserved group, each of which serves as enzymes elsewhere in the body having been co-opted from other functions, such as enzymes, and typically the same gene encodes both the enzyme and lens protein. This molecular opportunism has also occurred both in cephalopods (octopus, cuttlefishes, etc.) and in Drosophila [1]. The common strategy of assembling lenses from diverse proteins seems to be a convergent evolutionary solution that has occurred independently many times in vertebrates with the source of protein quite variable.

Functionally, the exquisite gradient of refractive index necessary to allow spherical lenses to focus light [2] is a convergent solution that has evolved in water-dwelling vertebrates and invertebrates alike. What remains unknown is how genetic programs assemble differing amounts of diverse proteins to preserve the essential functional properties of lenses and whether there is any rhyme or reason to which specific proteins are used in different taxa.

Origins of Eyes
In the past 100 years, ideas about whether eyes evolved from many origins (polyphyletic) to one origin (monophyletic) have switched back and forth. Originally, it was thought that there could have been many origins of eyes, but when it was discovered that opsin proteins were central to phototransduction in all eyes, a monophyletic origin was posited. Subsequent morphological comparisons suggested that eyes evolved 40 or more times independently based on, among other things, the distinct ontogenetic origins of eyes in different species. For example, the vertebrate retina arises from neural ectoderm and induces head ectoderm to form the lens, while cephalopod retinas result from invaginations of lateral head ectoderm, ultimately producing an eye without a cornea. These observations and many others suggested eyes had multiple origins.
that converged onto a limited number of forms dictated by the physics of light.

Multiple origins were also supported by the apparent ease of eye evolution, shown by an elegant simulation model [3]. Starting from a patch of photoreceptive epithelium, the simulation, under selection for improved visual acuity, produced a focused camera-type eye in less than $4 \times 10^3$ generations. For animals with generation times less than a year, this would be less than a half million years.

The idea that eyes arose multiple times independently was challenged by the discovery that a single developmental gene, *pax6*, could initiate eye construction in diverse species. However, subsequent work has shown that *pax6* does not act alone, but that building an eye requires many interacting genes. Nonetheless, discussion about eye origins was invigorated by the discovery that homologous genes can trigger construction of paralogous systems for photodetection, just as homologous *hox* genes do for paralogous body parts across phyla.

Eye development proceeds via morphological transformations of newly generated tissue that are regulated by multiple genes with expression patterns that overlap in time and space. Identifying clear control pathways is difficult because gene products are tightly regulated, and many are used repeatedly. Functions for at least 15 transcription factors and several signaling molecules have been described for human and mouse eye development, many of which are also widely expressed in other tissues. For *Drosophila* photoreceptor arrays, it is now known that seven genes, encoding transcription factors and two signaling molecules, collaborate. These genes ([*Eyeless* (ey), *twin of eyeless* (toy)](both of which are *pax6* homologs), *sine oculus* (so), *eyes absent* (eya), *dachshund* (dac), *eye gone* (eyg) and *optix*) and signaling systems, including the Notch and receptor tyrosine kinase pathways, act via a complex regulatory network. Deletion of any one of these genes causes a loss of *Drosophila* eye. Yet in collaboration with certain signaling molecules, any one of these genes, except *sine oculus*, can also cause an eyeless phenotype. Like other developmental cascades, a network of genes is required for organogenesis. Notably, *Six1*, *Dach* and *Eya* are important in the formation of the kidney, muscle, and inner ear, as well as eyes, suggesting that this suite of genetically interacting gene products may have been recruited repeatedly during evolution for organogenesis of other structures.

It seems highly probable that photodetection systems came first in evolution. Appearance of photodetection probably happened many, possibly hundreds of times until selection produced at the very least the two independent, main types of photoreceptor types known today – ciliary and rhabdomeric (e.g., Fig. 2). Clearly, though, the other opsin families also have photodetection capacities mediated by unknown structures for functions also unknown. Although these two main photoreceptor types were thought to be strictly segregated in vertebrate animals (ciliary) and invertebrate animals (rhabdomeric), recent studies show that elements of both photoreceptor types probably co-exist in most organisms.

An overlooked hint about the existence of multiple photodetection systems came from the discovery of both depolarizing and hyperpolarizing responses to light stimuli from cells located in different layers of a scallop retina (*Pecten irradians*). Depolarizing potentials, characteristic of invertebrate photoreception, arise from the proximal layer, and hyperpolarizing potentials, characteristic of vertebrate photoreception, arise from the distal layer. In 2004, Arendt and colleagues found that the polychete ragworm (*Platyneris dumerilii*) had ciliary photoreceptors in the brain in addition to rhabdomeric photoreceptors in its eyes [4]. The canonical opsins associated with each photoreceptor type were localized only with its type (e.g., vertebrate c-opsin with ciliary receptors in the brain and invertebrate r-opsin with rhabdomeric receptors in the eye). Thus both main types of “eyes” exist in a worm. Correspondingly, in vertebrates, Berson and colleagues [5] had found a small population of intrinsically photosensitive retinal ganglion cells (the neural output of the retina), use melanopsin, a member of the r-opsin family. Melanopsin in these neurons, functions via transduction pathways like those in invertebrates and signals presence or absence of light in parallel to and collaboration with the well known image-forming visual system.

Arendt and colleagues also proposed that rhabdomeric photoreceptors might be the evolutionary ancestors of vertebrate ganglion cells based on use of r-opsin and the expression of a constellation of transcription factors including *pax6*, *Math5*, *Bm3* and *BarH*. Further, they suggested that other retinal processing neurons, horizontal and amacrine cells, might also share in this rhabdomeric photoreceptor ancestry but have lost photosensitivity. Taken together, these data show that at least two kinds of photoreception existed in the *Urbilateria*, before the split into three *Bilateria* branches at the Cambrian. Moreover, each branch of the family tree still carries versions of both of these photoreceptor types, along with other opsin dependent photo detection systems yet to be fully described. In the course of evolution, vertebrate vision favored ciliary photodetection for the pathway that delivers images, while invertebrates favored rhabdomeric photodetection for their main eyes, although why this might be remains unknown. Along both evolutionary paths, secondary photodetection systems remained to give additional information about light, possibly to instruct circadian
rhythms, phototaxis or other light dependent behaviors. But, if vertebrates are an example, these two photodetection systems functioned together rather than remaining separate. Although the remaining five families of opsins have not been fully characterized, it seems probable that they also respond to light, and organisms use the information they provide. Understanding whether and how they extract information from light and how animals use that information is now a major challenge.

References

Evolution of Forebrain

Evolution and Embryological Development of Forebrain

Evolution of Midbrain

Evolution of Optic Tectum in Anamniotes
Evolution of Optic Tectum: In Amniotes

Evolution of Motor Systems: Basal Ganglia

Evolution and Embryological Development of Forebrain

Evolution of Motor Systems:
Corticospinal, Reticulospinal,
Rubrospinal and Vestibulospinal Systems

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Synonyms
Evolution of corticospinal motor systems; Evolution of reticulospinal motor systems; Evolution of rubrospinal motor systems; Evolution of vestibulospinal motor systems

Definition
The descending pathways from the forebrain and brainstem to the spinal cord represent the instruments by which the central nervous system (CNS) steers movements of the trunk, the tail and the extremities. All vertebrates have a common repertoire of descending brainstem pathways in common [1-3]. Reticulospinal projections form the most ancestral descending motor system by which the vertebrate brain exerts control over movements in all classes from cyclostomes to mammals. Vestibulospinal projections were also present early in evolution for control of equilibrium and postural activities. With the appearance of extremities, the development of an adequate neural control system for the steering of limb movements became apparent. It is likely that the rubrospinal tract plays an important role in this mechanism [4]. Goal-directed limb movements are controlled mainly by the rubrospinal tract, and in mammals also by the corticospinal tract.

Characteristics
Reticulospinal Projections
The ancestral vertebrate motor system included myomeric axial musculature, spinal motoneurons, a spinal network composed of at least two types of interneurons (excitatory interneurons and inhibitory commissural interneurons) and reticulospinal neurons to activate the spinal networks [5]. Throughout vertebrates, reticulospinal neurons are large. Their coarse axons conduct rapidly and make direct contact with spinal motoneurons and interneurons [6]. For rapid escape movements, a pair of specialized very large cells in the brainstem, the Mauthner cells, has been formed. These features of the early motor system were retained in living amniotes. Major changes occur among amniotes such as the break-up of the myomeres into a large number of discrete axial