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BIOLOGY

# EVOLUTION OF THE EYE

Scientists now have a clear vision of how our notoriously complex eye came to be

*By Trevor D. Lamb*

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**T**HE HUMAN EYE IS AN EXQUISITELY COMPLICATED ORGAN. IT ACTS LIKE A CAMERA TO collect and focus light and convert it into an electrical signal that the brain translates into images. But instead of photographic film, it has a highly specialized retina that detects light and processes the signals using dozens of different kinds of neurons. So intricate is the eye that its origin has long been a cause célèbre among creationists and intelligent design proponents, who hold it up as a prime example of what they term irreducible complexity—a system

that cannot function in the absence of any of its components and that therefore cannot have evolved naturally from a more primitive form. Indeed, Charles Darwin himself acknowledged in *On the Origin of Species*—the 1859 book detailing his theory of evolution by natural selection—that it might seem absurd to think the eye formed by natural selection. He nonetheless firmly believed that the eye did evolve in that way, despite a lack of evidence for intermediate forms at the time.

Direct evidence has continued to be hard to come by. Whereas scholars who study the evolution of the skeleton can readily document its metamorphosis in the fossil record, soft-tissue structures

rarely fossilize. And even when they do, the fossils do not preserve nearly enough detail to establish how the structures evolved. Still, biologists have recently made significant advances in tracing the origin of the eye—by studying how it forms in developing embryos and by comparing eye structure and genes across species to reconstruct when key traits arose. The results indicate that our kind of eye—the type common across vertebrates—took shape in less than 100 million years, evolving from a simple light sensor for circadian (daily) and seasonal rhythms around 600 million years ago to an optically and neurologically sophisticated organ by 500 million years ago. More than 150 years after Darwin published his

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groundbreaking theory, these findings put the nail in the coffin of irreducible complexity and beautifully support Darwin's idea. They also explain why the eye, far from being a perfectly engineered piece of machinery, exhibits a number of major flaws—these flaws are the scars of evolution. Natural selection does not, as some might think, result in perfection. It tinkers with the material available to it, sometimes to odd effect.

To understand how our eye originated, one needs to know something about events that occurred in deep time. We humans have an unbroken line of ancestors stretching back nearly four billion years to the beginning of life on earth. Around a billion years ago simple multicellular animals diverged into two groups: one had a radially symmetrical body plan (a top side and bottom side but no front or back), and the other—which gave rise to most of the organisms we think of as animals—was bilaterally symmetrical, with left and right sides that are mirror images of one another and a head end. The bilateria themselves then diverged around 600 million years ago into two important groups: one that gave rise to the vast majority of today's spineless creatures, or invertebrates, and one whose descendants include our own vertebrate lineage. Soon after these two lineages parted ways, an amazing diversity of animal body plans proliferated—the so-called Cambrian explosion that famously left its mark in the fossil record of around 540 million to 490 million years ago. This burst of evolution laid the groundwork for the emergence of our complex eye.

### COMPOUND VS. CAMERA

THE FOSSIL RECORD shows that during the Cambrian explosion two fundamentally different styles of eye arose. The first seems to have been a compound eye of the kind seen today in all adult insects, spiders and crustaceans—part of an invertebrate group collectively known as the arthropods. In this type of eye, an array of identical imaging units, each of which constitutes a lens or reflector, beams light to a handful of light-sensitive elements called photoreceptors. Compound eyes are very effective for small animals in offering a wide-angle view and moderate spatial resolution in a small volume. In the Cambrian, such visual ability may have given trilobites and other ancient arthropods a survival advantage over their visually impaired contemporaries. Compound eyes are impractical for large animals, however, because the eye size required for high-resolution vision would be overly large. Hence, as body size increased, so, too, did the selective pressures favoring the evolution of another type of eye: the camera variety.

In camera-style eyes, the photoreceptors all share a single light-focusing lens, and they are arranged as a sheet (the retina) that lines the inner surface of the wall of the eye. Squid and octopuses have a camera-style eye that superficially resembles our own, but their photoreceptors are the same kind found in insect eyes. Vertebrates possess a different style of photoreceptor, which in jawed vertebrates (including ourselves) comes in two varieties: cones for daylight vision and rods for nighttime vision.

Several years ago Edward N. Pugh, Jr., then at the University of Pennsylvania, and Shaun P. Collin, then at the University of Queensland in Australia, and I teamed up to try to figure out how these different types of photoreceptors could have evolved. What we found went beyond answering that question to provide a compelling scenario for the origin of the vertebrate eye.

### DEEP ROOTS

LIKE OTHER BIOLOGISTS before us, Pugh, Collin and I observed that many of the hallmark features of the vertebrate eye are the same across all living representatives of a major branch of the vertebrate tree: that of the jawed vertebrates. This pattern suggests that jawed vertebrates inherited the traits from a common ancestor and that our eye had already evolved by around 420 million years ago, when the first jawed vertebrates (which probably resembled modern-day cartilaginous fish such as sharks) patrolled the seas. We reasoned that our camera-style eye and its photoreceptors must therefore have still deeper roots, so we turned our attention to the more primitive jawless vertebrates, with which we share a common ancestor from roughly 500 million years ago.

We wanted to examine the anatomy of such an animal in detail and thus decided to focus on one of the few modern-day animals in this group: the lamprey, an eel-like fish with a funnel-shaped mouth built for sucking rather than biting. It turns out that this fish, too, has a camera-style eye complete with a lens, an iris and eye muscles. The lamprey's retina even has a three-layered structure like ours, and its photoreceptor cells closely resemble our cones, although it has apparently not evolved the more sensitive rods. Furthermore, the genes that govern many aspects of light detection, neural processing and eye development are the same ones that direct these processes in jawed vertebrates.

These striking similarities to the eye of jawed vertebrates are far too numerous to have arisen independently. Instead an eye essentially identical to our own must have been present in the common ancestor of the jawless and jawed vertebrates 500 million years ago. At this point, my colleagues and I could not help but wonder whether we could trace the origin of the eye and its photoreceptors back even further. Unfortunately, there are no living representatives of lineages that split off from our line in the preceding 50 million years, the next logical slice of time to study. But we found clues in the eye of an enigmatic beast called the hagfish.

Like their close relatives the lampreys, hagfish are eel-shaped, jawless fish. They typically live on the ocean floor, where they feed on crustaceans and fallen carcasses of other marine creatures. When threatened, they exude an extremely viscous slime, hence the nickname "slime eels." Although hagfish are vertebrates, their eye departs profoundly from the vertebrate norm. The hagfish eye lacks a cornea, iris, lens and all of the usual supporting muscles. Its retina contains just two layers of cells rather than three. Furthermore, each eye is buried deep underneath a translucent patch of skin. Observations of hagfish behavior sug-

### IN BRIEF

The eyes of vertebrate animals are so complex that creationists have long argued that they could not have formed by natural selection.

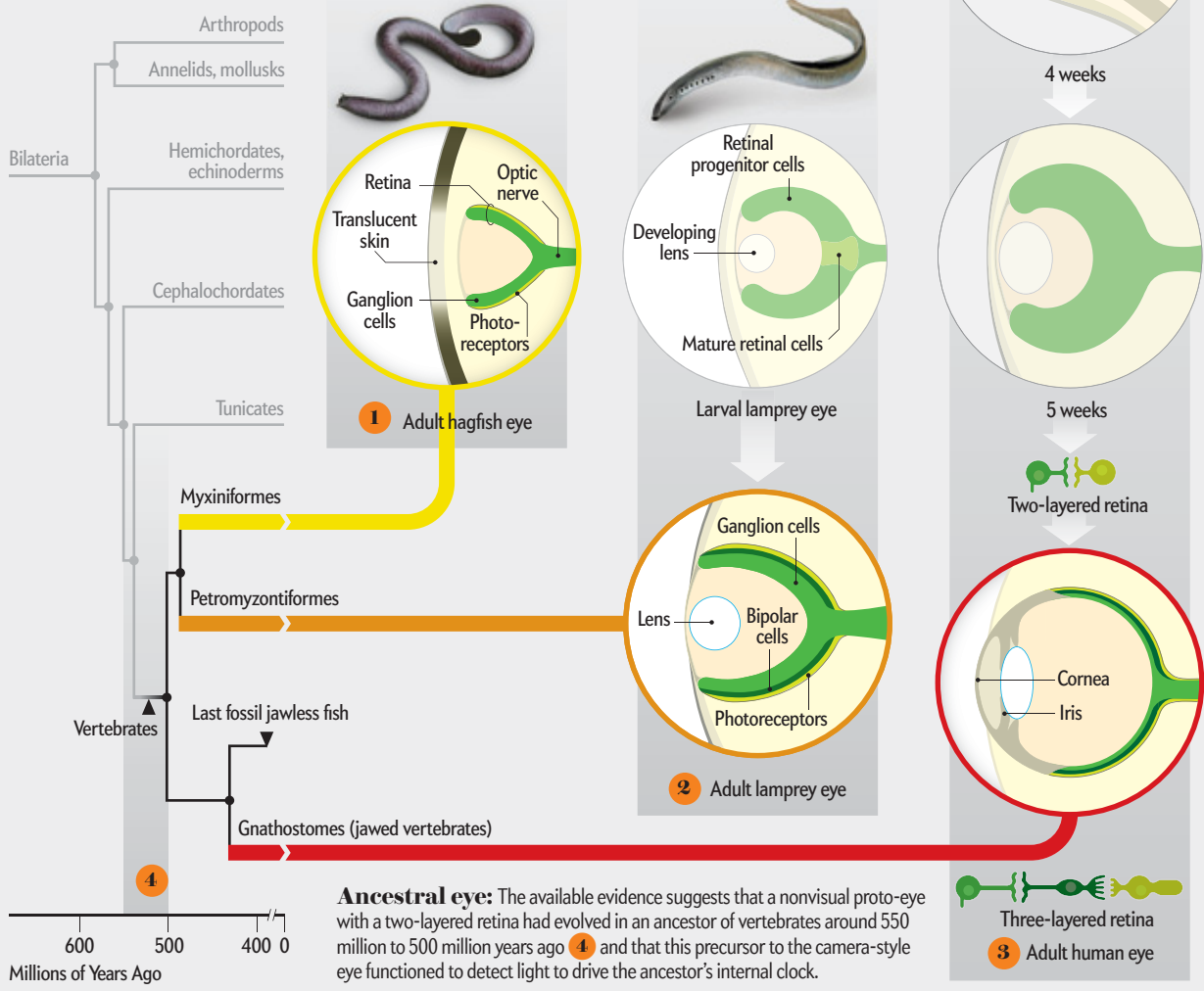
Soft tissues rarely fossilize. But by comparing eye structures and embryological development of the eye in vertebrate species, scientists have gained

crucial insights into the organ's origin. These findings suggest that our camera-style eye has surprisingly ancient roots and that prior to acquiring the

elements necessary to operate as a visual organ it functioned to detect light for modulating our long-ago ancestors' circadian rhythms.

# Echoes of Evolution

Eye structure and embryonic development in the hagfish and lamprey—primitive, eel-like vertebrates—hint at how our camera-style eye evolved and how it functioned in its early stages. The hagfish has a degenerate eye that cannot see but that probably serves to detect light for modulating circadian rhythms **1**. Early in development the lamprey eye resembles the structurally simple hagfish eye, before metamorphosing into a complex camera-style eye **2**. The human eye, too, recalls the hagfish eye during development, passing through a stage in which the retina has just two layers before a third layer of cells emerges **3**. Aspects of the embryonic development of an individual are known to reflect events that occurred during the evolution of its lineage.



gest that the animals are virtually blind, locating carrion with their keen sense of smell.

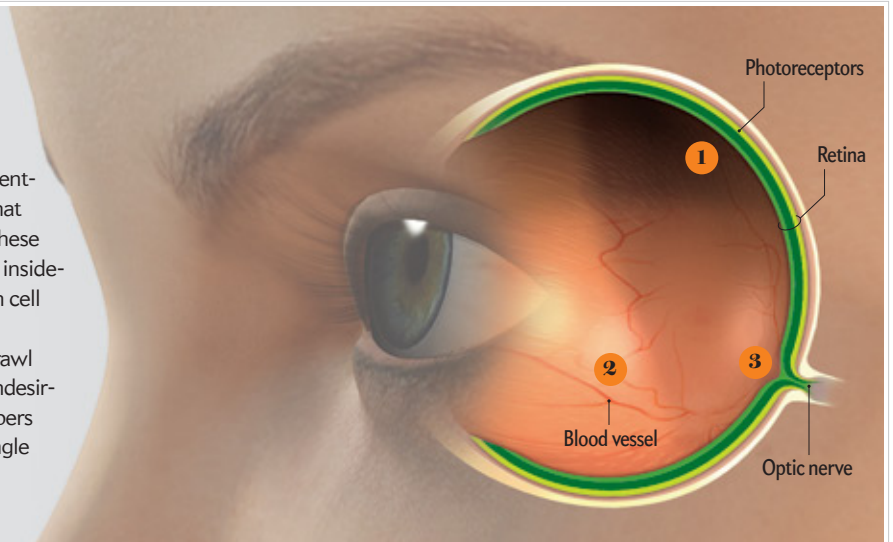
The hagfish shares a common ancestor with the lamprey, and this ancestor presumably had a camera-style eye like the lamprey's. The hagfish eye must therefore have degenerated from that more advanced form. That it still exists in this diminished state is telling. We know from blind cavefish, for instance, that the eye can undergo massive degeneration and can even be lost altogether in as little as 10,000 years. Yet the hagfish eye, such as it is, has hung on for hundreds of millions of years. This persis-

tence suggests that even though the animal cannot use its eye to see in the dim ocean depths, the organ is somehow important for survival. The discovery also has other implications. The hagfish eye may have ended up in its rudimentary state by way of a failure of development, so its current structure may be representative of the architecture of an earlier evolutionary stage. The operation of the hagfish eye could thus throw light on how the proto-eye functioned before evolving into a visual organ.

Hints about the role the hagfish eye might play came from taking a closer look at the animal's retina. In the standard three-

## Scars of Evolution

The vertebrate eye, far from being intelligently designed, contains numerous defects that attest to its evolutionary origin. Some of these flaws degrade image quality, including an inside-out retina that forces light to pass through cell bodies and nerve fibers before hitting the photoreceptors **1**; blood vessels that sprawl across the retina's inner surface, casting undesirable shadows onto the retina **2**; nerve fibers that gather together to push through a single opening in the retina to become the optic nerve, creating a blind spot **3**.



layered vertebrate retina, the cells in the middle layer, known as bipolar cells, process information from the photoreceptors and communicate the results to the output neurons, whose signals travel to the brain for interpretation. The two-layered hagfish retina, however, lacks the intervening bipolar cells, which means that the photoreceptors connect directly to the output neurons. In this regard, the wiring of the hagfish retina closely resembles that of the so-called pineal gland, a small, hormone-secreting body in the vertebrate brain. The pineal gland modulates circadian rhythms, and in nonmammalian vertebrates it contains photoreceptor cells that connect directly to output neurons with no intermediary cells; in mammals those cells have lost their ability to detect light.

Based in part on this parallel to the pineal gland, my collaborators and I proposed in 2007 that the hagfish eye is not involved in vision but instead provides input to the part of the animal's brain that regulates crucial circadian rhythms, as well as seasonal activities such as feeding and breeding. Perhaps, then, the ancestral eye of proto-vertebrates living between 550 million and 500 million years ago first served as a nonvisual organ and only later evolved the neural processing power and optical and motor components needed for spatial vision.

Studies of the embryological development of the vertebrate eye support this notion. When a lamprey is in the larval stage, it lives in a streambed and, like the hagfish, is blind. At that point in its young life, its eye resembles the hagfish eye in being structurally simple and buried below the skin. When the larva undergoes metamorphosis, its rudimentary eye grows substantially and develops a three-layered retina; a lens, cornea and supporting muscles all form. The organ then erupts at the surface as a camera-style vertebrate eye. Because many aspects of the development of an individual mirror events that occurred during the evolution of its ancestors, we can, with caution, use the developing lamprey eye to inform our reconstruction of how the eye evolved.

During embryological development the mammalian eye, too, exhibits telltale clues to its evolutionary origin. Benjamin E. Reese and his collaborators at the University of California, Santa Barbara, have found that the circuitry of the mammalian retina starts out rather like that of the hagfish, with the photoreceptors connecting directly to the output neurons. Then, over a period of

several weeks, the bipolar cells mature and insert themselves between the photoreceptors and the output neurons. This sequence is exactly the developmental pattern one would expect to see if the vertebrate retina evolved from a two-layered circadian organ by adding processing power and imaging components. It therefore seems entirely plausible that this early, simple stage of development represents a holdover from a period in evolution before the invention of bipolar cell circuitry in the retina and before the invention of the lens, cornea and supporting muscles.

### RISE OF THE RECEPTORS

WHILE WE WERE STUDYING the development of the three layers of the retina, another question related to the eye's evolution occurred to us. Photoreceptor cells across the animal kingdom fall into two distinct classes: rhabdomeric and ciliary. Until recently, many scientists thought that invertebrates used the rhabdomeric class, whereas vertebrates used the ciliary class, but in fact, the situation is more complicated. In the vast majority of organisms, ciliary photoreceptors are responsible for sensing light for nonvisual purposes—to regulate circadian rhythms, for example. Rhabdomeric receptors, in contrast, sense light for the express purpose of enabling vision. Both the compound eyes of arthropods and the camera-style eyes of mollusks such as the octopus, which evolved independently of the camera-style eyes of vertebrates, employ rhabdomeric photoreceptors. The vertebrate eye, however, uses the ciliary class of photoreceptors to sense light for vision.

In 2003 Detlev Arendt of the European Molecular Biology Laboratory in Heidelberg, Germany, reported evidence that our eye still retains the descendants of rhabdomeric photoreceptors, which have been greatly modified to form the output neurons that send information from the retina to the brain. This discovery means that our retina contains the descendants of both classes of photoreceptors: the ciliary class, which has always comprised photoreceptors, and the rhabdomeric class, transformed into output neurons. Pressing an existing structure into use for a new purpose is exactly how evolution works, and so the discovery that the ciliary and rhabdomeric photoreceptors play different roles in our eye than in the eye of invertebrates adds still more weight to the evidence that the vertebrate eye was constructed by natural pro-

cesses. We wondered, though, what kinds of environmental pressures might have pushed those cells to take on those new roles.

To try to understand why the ciliary photoreceptors triumphed as the light sensors of the vertebrate retina, whereas the rhabdomeric class evolved into projection neurons, I analyzed the properties of their respective light-sensing pigments, or rhodopsins, so named for the opsin protein molecule they contain. In 2004 Yoshinori Shichida of Kyoto University in Japan and his colleagues had shown that early in the evolution of vertebrate visual pigments, a change had occurred that made the light-activated form of the pigment more stable and hence more active. I proposed that this change also blocked the route for reconversion of the activated rhodopsin back to its inactive form, which for rhabdomeric rhodopsins uses the absorption of a second photon of light; thus, of necessity, a biochemical pathway was needed to reset the molecule in readiness to signal light again. Once these two elements were in place, I hypothesized, the ciliary photoreceptors would have had a distinct advantage over rhabdomeric photoreceptors in environments such as the deep ocean, where light levels are very low. As a result, some early chordates (ancestors of the vertebrates) may have been able to colonize ecological niches inaccessible to animals that relied on rhabdomeric photoreceptors—not because the improved ciliary opsin conferred better vision (the other essential components of the camera-style eye had yet to evolve) but because it provided an improved way of sensing the light that enables circadian and seasonal clocks to keep time.

For these ancient chordates dwelling in darker realms, the less sensitive rhabdomeric photoreceptors they had in addition to the ciliary ones would have been virtually useless and so would have been free to take on a new role: as neurons that transmit signals to the brain. (At that point, they no longer needed opsin, and natural selection would have eliminated it from these cells.)

### AN EYE IS BORN

NOW THAT MY COLLEAGUES and I had an idea of how the components of the vertebrate retina originated, we wanted to figure out how the eye evolved from a light-sensing but nonvisual organ into an image-forming one by around 500 million years ago. Here again we found clues in developing embryos. Early in development, the neural structure that gives rise to the eye bulges out on either side to form two sacs, or vesicles. Each of these vesicles then folds in on itself to form a C-shaped retina that lines the interior of the eye. Evolution probably proceeded in much the same way. We postulate that a proto-eye of this kind—with a C-shaped, two-layered retina composed of ciliary photoreceptors on the exterior and output neurons derived from rhabdomeric photoreceptors on the interior—had evolved in an ancestor of vertebrates between 550 million and 500 million years ago, serving to drive its internal clock and perhaps help it to detect shadows and orient its body properly.

In the next stage of embryological development, as the retina is folding inward against itself, the lens forms, originating as a thickening of the embryo's outer surface, or ectoderm, that bulges into the curved empty space formed by the C-shaped retina. This protrusion eventually separates from the rest of the ectoderm to become a free-floating element. It seems likely that a broadly similar sequence of changes occurred during evolution. We do not know exactly when this modification happened, but in 1994 researchers at Lund University in Sweden showed that the optical components of the eye could have easily evolved with-

in a million years. If so, the image-forming eye may have arisen from the nonvisual proto-eye in a geologic instant.

With the advent of the lens to capture light and focus images, the eye's information-gathering capability increased dramatically. This augmentation would have created selective pressures favoring the emergence of improved signal processing in the retina beyond what the simple connection of photoreceptors to output neurons afforded. Evolution met this need by modifying the cell maturation process so that some developing cells, instead of forming ciliary photoreceptors, instead become retinal bipolar cells that insert themselves between the photoreceptor layer and the output neuron layer. This is why the retina's bipolar cells so closely resemble rod and cone cells, although they lack rhodopsin and receive input not from light but instead from the chemical (called a neurotransmitter) released by the photoreceptors.

Although camera-style eyes provide a wide field of view (typically of around 180 degrees), in practice our brain can sample only a fraction of the available information at any given time because of the limited number of nerve fibers linking our eye to our brain. The earliest camera-style eyes no doubt faced an even more severe limitation, because they presumably had even fewer nerve fibers. Thus, there would have been considerable selective pressure for the evolution of muscles to move the eye. Such muscles must have been present by 500 million years ago because the arrangement of these muscles in the lamprey, whose lineage dates back that far, is almost identical to that of jawed vertebrates, including humans.

For all the ingenious features evolution built into the vertebrate eye, there are a number of decidedly inelegant traits. For instance, the retina is inside out, so light has to pass through the whole thickness of the retina—through the intervening nerve fibers and cell bodies that scatter the light and degrade image quality—before reaching the light-sensitive photoreceptors. Blood vessels also line the inner surface of the retina, casting unwanted shadows onto the photoreceptor layer. The retina has a blind spot where the nerve fibers that run across its surface congregate before tunneling out through the retina to emerge behind it as the optic nerve. The list goes on and on.

These defects are by no means inevitable features of a camera-style eye because octopuses and squid independently evolved camera-style eyes that do not suffer these deficiencies. Indeed, if engineers were to build an eye with the flaws of our own, they would probably be fired. Considering the vertebrate eye in an evolutionary framework reveals these seemingly absurd shortcomings as consequences of an ancient sequence of steps, each of which provided benefit to our long-ago vertebrate ancestors even before they could see. The design of our eye is not intelligent—but it makes perfect sense when viewed in the bright light of evolution. ■

#### MORE TO EXPLORE

Evolution of the Vertebrate Eye: Opsins, Photoreceptors, Retina and Eye Cup. Trevor D. Lamb et al. in *Nature Reviews Neuroscience*, Vol. 8, pages 960–975; December 2007.

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