Common Pathways of Illumination

Humans and squid may literally look at things the same way

by Stephen Jay Gould

Ashley Montagu, one of our century's greatest writers of popular science, once gave me a marvelous lesson in the distorting power of half statements. We were having breakfast together at his hotel when two particularly obnoxious men intruded on our conversation, insisting that Ashley identify himself, since they were sure they had seen him on TV. Ashley, cool as could be, replied that he was "just a traveling salesman"—and all their complaints of "aw, c'mon, I know I seen ya on TV" could not budge him. When they had retreated out of earshot, Ashley turned to me and whispered "traveling salesman of ideas."

But the art of semistatement finds more frequent use, alas, in less benevolent attempts to distort an author's meaning for nefarious purposes. No semiquotation from Darwin's *Origin of Species* has been so frequently cited as the following partial passage from his section on "organs of extreme perfection and complication" in the chapter that he so honestly titled "Difficulties on Theory."

> To suppose that the eye, with all its inimitable contrivances for adjusting the focus to different distances, for admitting different amounts of light, and for the correction of spherical and chromatic aberration, could have been formed by natural selection, seems, I freely confess, absurd in the highest possible degree.

Antievolutionists continually cite this passage as supposed evidence that Darwin himself threw in the towel when faced with truly difficult and inherently implausible cases. But if they would only read the very next sentence, they would grasp Darwin's real reason for speaking of absurdity "in the highest possible degree." (Either they have read these following lines and have consciously suppressed them, an indictment of dishonesty; or they have never read them and have merely copied the half quotation from another source, a proof of inexcusable sloppiness.) Darwin set up the overt "absurdity" to display the power of natural selection in resolving even the most difficult cases—the ones that initially strike us as intractable in principle. The very next lines give three reasons—all supported by copious evidence—for resolving the absurdity and accepting evolutionary development as the cause of optimally complex structures:

> Yet reason tells me, that if numerous gradations from a perfect and complex eye to one very imperfect and simple, each grade being useful to its possessor, can be shown to exist; if further, the eye does vary ever so slightly, and the variations be inherited, which is certainly the case; and if any variation or modification in the organ be ever useful to an animal under changing conditions of life, then the difficulty of believing that a perfect and complex eye could be formed by natural selection, though insuperable by our imagination, can hardly be considered real.

In other words, natural selection can evolve the most intricate organs of vision, given (1) the existence of a graded array in complexity of eyes (as clearly found in a sequence from pigment spots able to detect light and darkness but not to form images, to simple pinhole cameras, to the lens eye of several phyla, including vertebrates, insects, and squid); (2) variation in size and form of eyes among individuals within populations (providing the "raw material" for natural selection to work); and (3) the potential utility of some of these variations (another requirement for the operation of natural selection).

While I criticize creationists for their incomplete quotation, I must also state that evolutionists miss a crucial and fascinating aspect of Darwin's full argument by generally failing to cite the very next line after his three arguments to refute absurdity (although, in this case, my colleagues do not distort Darwin, either intentionally or unintentionally, but merely lose out on something interesting and important). Darwin continues:

> How a nerve comes to be sensitive to light, hardly concerns us more than how life itself first originated; but I suspect that any sensitive nerve may be rendered sensitive to light, and likewise to those coarser vibrations of the air which produce sound.

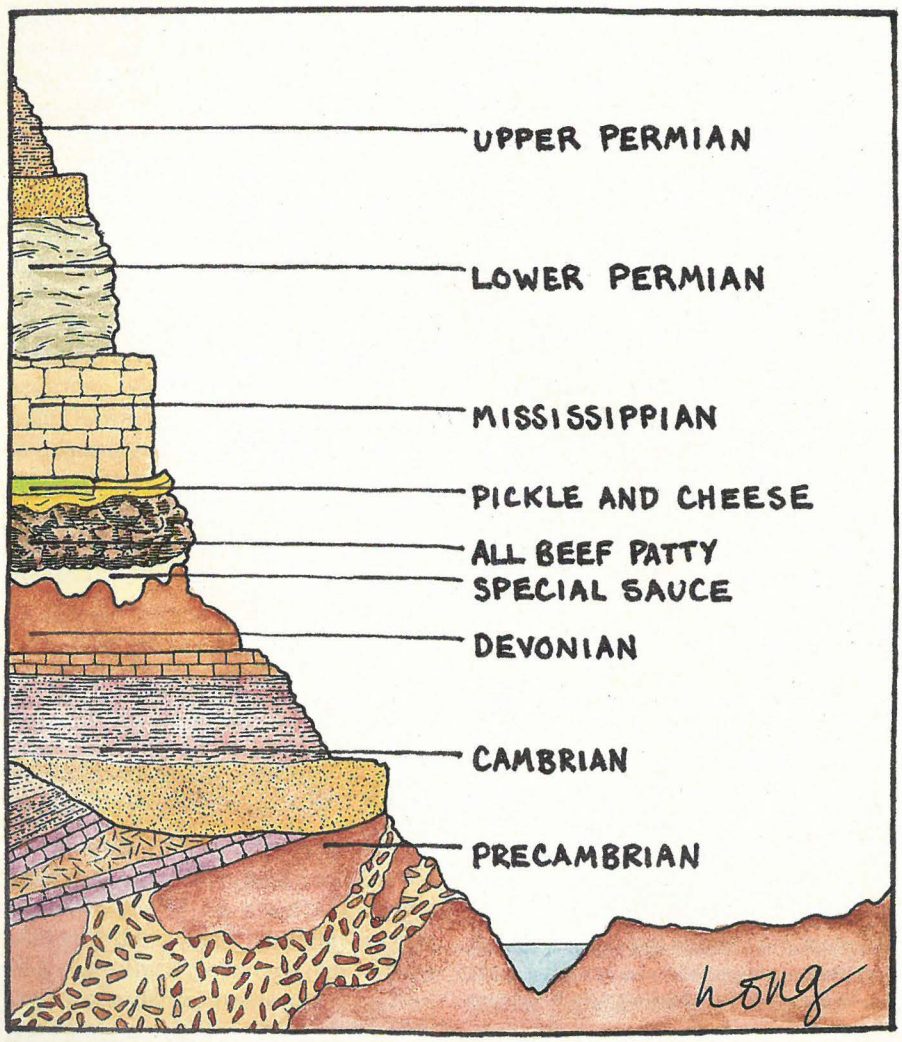
Darwin here discusses the vital historical principle of necessary structural prerequisites. Eyes don't emerge just because they confer such great utility, and therefore such advantages under natural selection. An organism must have the wherewithal for their potential construction beforehand—and since animals don't know their distant futures and cannot prepare the proper materials for later transformation in any conscious or preordained way, fortuity must always play a large role in any major evolutionary innovation. You have to catch a break from your own past.

Many features that would be eminently useful can't evolve because organisms don't maintain the structural prerequisites. A great evolutionist once remarked that even if humans had a capacity for moral perfection (which he greatly doubted), we could never evolve a pair a wings—for our

arms are already committed to other uses and our vertebrate body plan doesn't provide the variation that natural selection would need to fashion a third pair of appendages. In other words, in evolution as in motoring, you can't always get there from here.

This theme of necessary structural prerequisites gains importance because the naïve view of pop-adaptationism—perhaps the most conspicuous of all fallacies in the standard journalistic presentation of evolution—pays the principle no heed and therefore fails to grasp the fascination of evolution's fortuity and frequent failure to do the "sensible" thing. Under pop-adaptationism, useful features manage to emerge because, well, the organism evidently needs them and natural selection is such a powerful force for organic good. In this view, eyes evolve because sight is so advantageous. By extension, needs will be fulfilled and gains rewarded—as evolution follows a sensible pathway toward optimal fit between organism and environment.

But in the rarely quoted passage following his praise for natural selection in the evolution of eyes, Darwin reminds us that vision could never have evolved without a key prerequisite in the structure of neurons—namely, sensitivity to light. He does not know why neurons are so sensitive, and he also recognizes that evolutionists need not resolve this complex question from the cognate field of physiology (just as they don't have to solve the basically chemical problem of how life arose before studying its subsequent history of transformation). But a complete Darwinian argument requires identification and specification of such a structural prerequisite. In other words, we cannot simply say "eyes are so good; therefore natural selection can fashion them." We must also identify a preexisting biological substrate, in structure and variation, that natural selection can use to build this key innovation. Full evolutionary explanations must always combine a statement about structural constraint with an argument about functional advantages.



This theme has particular relevance to the evolution of eyes because, ironically (despite Darwin's own explicit reminder), the subject of structural constraint has been so generally ignored, and that of adaptation so emphasized and even celebrated. The three largest animal phyla have all evolved complex eyes with evident utility in the formation of images—the compound eye of insects and other arthropods and the single-lens eye of vertebrates and mollusks (squid and octopuses in particular). These eyes seem to follow markedly different evolutionary pathways in their origin. The compound eye is so distinct in design that no structural homology (descent from a common ancestor with eyes of similar form) can be claimed with vertebrates and mollusks. The single-lens eyes of squid and vertebrates, on the other hand, are strikingly similar in basic structure. Nonetheless, clear and fundamental differences in the architecture of embryological development also identify these eyes as separate evolutionary innovations.

Therefore, the independent evolution of complex, image-forming eyes in all these groups has become our classic textbook illustration of the enormous power of natural selection to produce similar (and eminently useful) results from disparate starting points, a phenomenon called "convergence" (and particularly emphasized for the structurally similar, but developmentally different, eyes of squid and vertebrates). Darwin himself discussed convergence at the end of his section on the evolution of eyes:

> I am inclined to believe that in nearly the same way as two men have sometimes independently hit on the very same invention, so natural selection, working for the good of each being and taking advantage of analogous variations, has sometimes modified in very nearly the same manner two parts in two organic beings, which owe but little of their structure in common to inheritance from the same ancestor.

Thus, eyes have become our standard illustration of natural selection's power and the organism's almost infinite malleability—like clay before a sculptor, to cite a metaphor often advanced at this point in the discussion. But are organisms so puttylike, and is natural selection so potent a builder? Of course no professional biologist would go so far in extolling selection and relegating preexisting structure to infinitely flexible raw material. Nonetheless, celebration of natural selection and de-emphasis of structural con-

straint has been the characteristic bias of evolutionary theory since the 1930s, when modern Darwinism began its deserved triumph. And eyes provide the premier illustration of such an attitude, for flexibility must dominate over constraint if such complex and similar structures—paired organs up front, complete with lenses and retinas and, in the case of squid and vertebrates, of such comparable design—can evolve so often in total independence.

But is the independence so complete? Might a structural constraint of common inheritance be operating after all, despite the admitted differences in form (compound versus single-lens eyes) and developmental pathways (vertebrates and squid)? Might some inherited predisposition of anatomy or development, preserved in all eyed groups (despite half a billion years of evolutionary separation among vertebrates, mollusks, and arthropods), be providing a boost to the development of eyes from the past? Maybe natural selection doesn't have to start from formless raw material and then do all the work itself.

Such a contribution from common ancestry would have seemed almost risible as few as five or ten years ago—for strict Darwinians then argued that such a long evolutionary separation among phyla had permitted natural selection to tailor all initially common genetic sequences to the specific uses of each lineage—thus wiping out all important signs of shared genetic and developmental ancestry. In my view, the most exciting event in evolutionary theory during the past decade resides in the disproof of this assertion (one of the linchpins of education in my graduate student days during the 1960s, and thus requiring some major clearing of cobwebs from my own mental architecture).

Our modern ability to map detailed sequences of DNA, and to trace the operation of genes in early embryology, has finally permitted us to assess the role of genetic structure in the building of organisms. As the biggest surprise of this work, astonishing conservation of intricate genetic detail has been discovered across genealogically distant phyla, and for genes that are most crucial in building the basic body plan of organisms. Most strikingly, a set of genes in fruit flies and other arthropods, called the *HOM,* or homeotic, complex and crucial for proper differentiation of segments along the front–back axis (building antennae, mouthparts, and legs in the right places, for example), can also be found in vertebrates, where these genes maintain virtually the same DNA sequence and must therefore be products of shared ancestry. (In vertebrates, these genes, called the *Hox,* or homeobox, complex, have been duplicated and now exist as four copies on four different chromosomes.)

For nearly 150 years, since the death of the visionary French scientist Etienne Geoffroy Saint-Hilaire in 1844, no one had taken seriously the possibility of homology (similarity due to shared inheritance) between insects and vertebrates in the basic architecture of segmentation and differentiation of organs front to back. (Geoffroy had argued, wrongly in detail but correctly in spirit, as we must now recognize, that all complex animals are built on the same shared body plan, with the vertebra as an archetypal structure. He compared the jointed, external skeleton of insects with the backbone of vertebrates and actually argued that insects lived within their own vertebrae.) Ironically, Geoffroy was quite wrong in homologizing insect segments with the vertebrae of our spine—but he was right in arguing for homology of basic design. The comparable structure in vertebrates, however, turns out to be the transient segmentation of midbrain and hind brain during embryology—for the *Hox* genes of vertebrates influence the architecture of these structures in the same way as the nearly identical *HOM* genes of *Drosophila* regulate segments of developing fruit flies.

If the long hand of the past so constrains the fundamental building plan of two such distinct phyla, must we not rethink our previous assumption that convergence and independent evolution, not shared ancestry, lie behind such similar organs as the eyes of squid and vertebrates? In August 1994, in the most exciting advance in evolutionary studies of development since the finding of *HOM* and *Hox* homologies, Rebecca Quiring, Uwe Walldorf, Urs Kloter, and Walter J. Gehring announced the discovery of homology in an important gene crucial to the embryology of eyes in both fruit flies and vertebrates ("Homology of the *Eyeless* Gene of *Drosophila* to the *Small Eye* Gene in Mice and *Aniridia* in Humans," *Science,* vol. 265, pp. 785–89).

We have known for a few years about genetic homology of some common building blocks in visual systems. For example, all opsins, an important protein component of visual pigments in all phyla, show such similarity in their DNA sequences that they must be products of common ancestry, rather than separately evolved (for no convergence can be precise enough to produce near identity in thousands of DNA bases along a linear chain; only a common starting point can explain this de-

gree of similarity). In discussing this example in his 1990 article on "Optimization, Constraint, and History in the Evolution of Eyes" (*Quarterly Review of Biology,* vol. 65), Yale biologist Timothy H. Goldsmith wrote: "The eyes of cephalopods [squid and octopuses], arthropods, and vertebrates are not homologous, yet at the molecular level some of their constituent elements are."

These data are interesting, and they do contradict the previously favored notion that visual pigments must be convergent rather than homologous across phyla, but homology of something so far from the form of a building as bricks and mortar does not pack a powerful wallop for constraint. After all, we have known for some time that the basic molecules of life are widely shared—the nucleic acids themselves, ATP as the energy-storing compound of all organisms. Opsins are a bit more specific and impressive, but still ever so far from an eye.

The excitement of the latest discovery lies in its well-documented claim for homology in the actual, detailed pathway for building eyes as paired organs at the front end of an animal. I am not greatly moved to learn that my outhouse and the Great Wall of China both use bricks of similar composition and construction based on an inherited tradition of learning (not everyone agrees, but one common argument traces knowledge of both Western and Eastern brick making to a Babylonian source). But common blueprints for designs of integrated and complex structures indicate historical constraint of a far more comprehensive kind. (We do not doubt that the automobiles of China and the United States derive from a common tradition of invention and construction.) Homology in some singular molecular components of eyes seems interesting but unsurprising; homology in complex genetic and developmental pathways for building eyes (as has now been discovered) was both unexpected under usual views of evolution and downright revisionary in forcing a rethinking of many previous certainties.

To appreciate the impact of this latest discovery, we must review the history and comparative anatomy of eyes—especially in the light of Darwin's first argument about a series of transformations from rudimentary to most elaborate. The first stage is structurally and easily accomplished—a simple eyespot, on a surface or in a shallow pit, made by the aggregation of a small number of receptor cells (usually one to one hundred). These "eyes" cannot form images but can detect light and darkness, and therefore provide important information about environments. Ease of construction and evident utility led to the multiple evolution of such eyespots. In a famous article written in 1977, my colleagues L. von Salvini-Plawen and Ernst Mayr estimated that eyespots evolved independently among animals some forty to sixty-five times. Michael F. Land and Russell D. Fernald add, in their excellent article "The Evolution of Eyes" (*Annual Reviews of Neuroscience,* vol. 15, pp. 1–29, 1992), that only about five of some thirty-five recognized animal phyla failed to develop rudimentary eyes of this type.

From this nearly universal substrate, six animal phyla evolved eyes capable of forming images: the Cnidaria (where a few jellyfish have lens eyes); the Annelida, or segmented worms; the Onychophora (a fairly obscure group today, best represented by the velvet worm *Peripatus,* but much more common in the early fossil record of multicellular animals); and the three great phyla previously mentioned, Mollusca (where eyes grace members of all major subgroups, snails, clams, and cephalopods), Arthropoda, and our own Chordata. Both a structural series and a riotous display of diversity may be identified among image-forming eyes.

In a first step, a deepening of the pit for receptor cells into an optic cup and a narrowing of the aperture into this cup can produce a pinhole camera without any lens at all. A few mollusks have evolved pinhole camera eyes of this type—most notably the chambered *Nautilus* among cephalopods and the abalone *Haliotis* among clams. The next step, leading to such diversity in complex eyes, adds other layers and structures either to refract or reflect an image upon the retina. The simple lens eye works by refraction. Most aquatic animals use the lens as a primary device for forming an image, whereas many terrestrial groups, including mammals and spiders, develop more optical power in an outer cornea and use the underlying lens primarily for adjusting focus.

Most compound eyes also employ lenses, and each separate unit, called a facet or ommatidium (the fruit fly *Drosophila* has some 800 in each eye), forms a part, one pixel if you will, of a

"It's amazing how well they adapt to an urban environment."

total image, which the organism must then integrate as a single picture. Although compound eyes are best known in the great phylum of arthropods, they have also arisen independently in two other phyla, and in interestingly different anatomical places—on the tentacles of some tube-dwelling annelid worms and on the mantle edge (the "skin" visible at the gape between two valves) of some clams in the family Arcidae.

A far less common, but quite striking, anatomical variant relies upon reflection rather than refraction and places a concave layer of cells (called a tapetum) behind the retina (rather than using refraction through a lens in front of the retina). In some eyes, the tapetum only acts to increase light available to the receptors and does not focus an image, but if the concavity of the tapetum is great enough, and if the retinal surface moves far enough forward, then the tapetum can reflect an image upon the retina.

Some organisms use both refraction and reflection. The mantle-edge eyes of swimming scallops (up to one hundred per animal), for example, have both a lens in front of the retina and a reflecting tapetum behind. In the most interesting use of a posterior tapetum as an imaging device, the deep-water ostracode *Gigantocypris* shapes a large tapetum into the form of a parabolic reflector, focusing light onto the bloblike retina in front (ostracodes are small and little known, but enormously abundant, bivalved marine arthropods). These reflectors may produce a poor image, but they are remarkable light-gathering machines in the low illumination of deeper marine waters.

Lens eyes are enormously variable among organisms, both in position and in form. A pair up front may be canonical in the groups we know best, but animals with different modes of life often evolve eyes in positions more suitable for their activities. Clams often develop a row of eyes along the mantle edge between the two valves or on the ends of their siphons, the tubes that project upward from the closed shell (and function for intake of nutrients and outflow of waste). Most intriguingly, or even amusingly, a group of polychaetes (segmented marine worms) typically move rear end first, rather than the usual vice versa. They have evolved a pair of eyes on their posteriors!

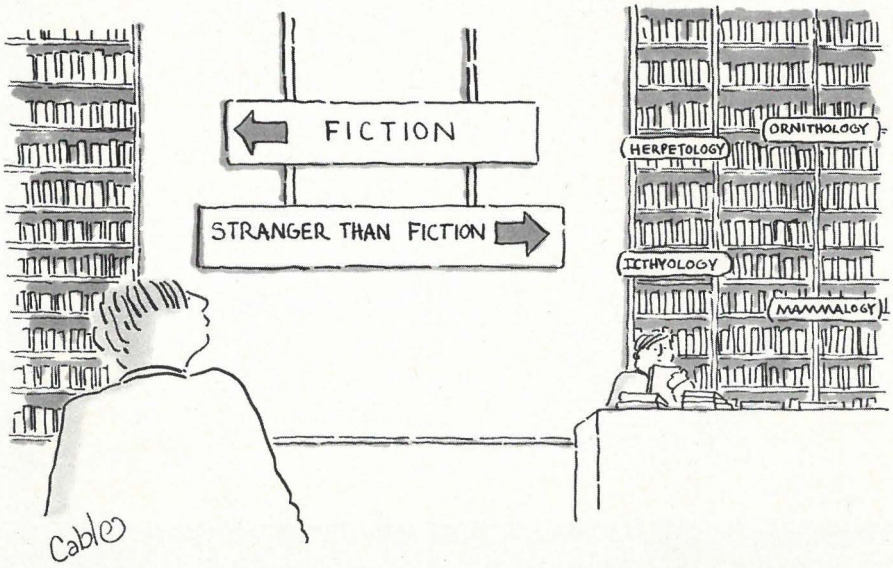
To cite just two anecdotes about variation in form: The copepod *Pontella* develops three lenses in males (two above and outside the eye proper) and two in females. (Copepods are another group of small and little known, but extraordinarily abundant, marine arthropods.) *Copelia,* another copepod, builds a narrow tubular eye with two distant lenses—and the entire structure both resembles and works like a telescope. But the retinal receptors are so few that only a dotlike image can be formed at any moment. Consequently, *Copelia* must constantly move its head and scan its surroundings in order to integrate a more complete image.

This riotous diversity seems to make historical constraint and preserved homology from common ancestry even more unlikely. After all, if eyes seem to form in almost any place and with such disparity of form in so many groups, then surely organic material is fully competent to answer any call from natural selection. Therefore, one would suppose the most common design of a single pair at the front end must represent an adaptive optimality for bilaterally symmetrical animals moving in the usual direction (and not ass forward like those rear-eyed polychaetes just described). This usual placement in all three of the most widely discussed lineages—squid, insects, and vertebrates—should represent pure convergence and absolutely independent evolution without any important constraint from retained homologies of common ancestry. And yet, however surprisingly, outstanding genetic homology has just been discovered.

Quiring, Walldorf, and their colleagues worked with a small family of homologous sequences known as *Pax* genes. These genes were first identified in the fruit fly *Drosophila* and owe their name (*Pax* stands for "paired box") to initial discovery of the key sequence within a *Drosophila* gene called *paired. Pax* genes were then identified in all vertebrates studied, from zebrafish to mice to humans. Nine *Pax* genes have been found so far in mammals. *Pax-6,* the best studied, must be a key factor in the development of eyes, for mutations at this locus cause severe ocular disruption. *Sey,* the *small eye* mutation of *Pax-6* in mice, for example, yields eyes of greatly diminished size in heterozygotes (normal copy of the gene from one parent and mutant copy from the other) and no eyes at all in homozygotes (mutant copies from both parents). A mutation of the same gene in humans produces *Aniridia,* a severe condition leading to limited development of the iris, absence of foveae, and malformation of the lens.

The so-called paired domain produced by these *Pax* genes, the major component of their homology, is a sequence of 130 amino acids coded by 390 nucleotides of DNA (remember that the genetic code is triplet, with three nucleotides designating one amino acid). The *Pax* genes of vertebrates retain remarkable similarity in their paired domains, despite a few hundred million years of evolutionary separation between fishes and mammals—a sure sign of homology, or inheritance of these genes from a common ancestor. For example, the paired domains in *Pax-6* of mice and zebrafish differ in only one amino acid out of 130.

Quiring, Walldorf, and colleagues have now identified and sequenced a *Dro-*



sophila gene clearly homologous to *Pax-6* of vertebrates. The paired domain of this *Drosophila* version shares 94 percent identity with the amino acid sequences of mice and humans—a remarkable evolutionary conservatism across more than 500 million years of genealogical separation and between two phyla so apparently different that anyone, even ten years ago, would have scoffed at the idea of such stable homology.

But homology of structure does not establish any argument for genetic or developmental constraint in the evolution of eyes. We need to know what the *Pax-6* homolog in *Drosophila* does for developing fruit flies. Perhaps this gene plays no role in building the eye in insects. Quiring, Walldorf, and colleagues therefore went on to determine the chromosomal location of this *Pax-6* homolog and its function in the developing fruit fly. In their most exciting result, they mapped the *Pax-6* gene to the *ey* (or *eyeless*) locus on the fourth chromosome, a well-known position identified as the site of several mutations affecting the development of eyes. In other words, *Pax-6* is the *ey* gene (previously unsequenced for its DNA structure but known by its developmental effects). *Pax-6* is not only homologous in genetic structure between insects and vertebrates; it also acts as a major repository for the developmental blueprint of eyes in both distantly related phyla.

Moreover, modern genetic techniques permit the tracing of a gene's influence through development by probing for changing locations of transcripts (the working products of the gene's action) during embryology. Again, the pattern is strikingly similar in the two groups. In *Drosophila, Pax-6* is first expressed in the imaginal disk of the eye, but not in disks for legs or wings (imaginal disks grow within larval flies as precursor structures for adult organs)—and also in parts of the brain and ventral nerve cord. In mice, transcripts of the homologous gene appear first in the forebrain and hind brain and then along the whole length of the nerve cord. Quiring, Walldorf, and colleagues write: "This pattern of expression resembles the one found in *Drosophila*; the *ey* transcripts are detected first in the central nervous system, in the brain, and the ventral nerve cord." The authors then state their remarkable general conclusion:

> Because *Pax-6* is involved in the genetic control of eye morphogenesis in both mammals and insects, the traditional view that the vertebrate eye and the compound eye of insects evolved independently has to be reconsidered.

Some findings in science are particularly potent because they suggest such obvious, and eminently doable, extensions of great importance. Anyone discovering *Pax-6* homology of structure and developmental function between *Drosophila* and vertebrates would have to ask: How general is this phenomenon? Is *Pax-6* a master builder of eyes in all animals? The first signs of a positive answer are already in hand, based on some intriguing footnotes and side comments (for work in progress but not yet published) in the report of Quiring, Walldorf, and colleagues. They have already found homologs of *Pax-6* in two anatomically simple phyla that have evolved eyespots but not lens eyes—in the flatworm *Dugesia tigrina* and in the nemertean worm *Lineus sanguineus*. But we do not yet know whether these genes build visual structures in these two phyla.

With a good sense of style, Quiring, Walldorf, and colleagues saved the best hint for last. They have indeed looked for the *Pax-6* homolog in the most revisionary of all places—in squid, where convergence, rather than homology, with the vertebrate eyes has, for so long, been a textbook case. Again, tests for similar developmental function have not yet been made, but *Pax-6* homologs have been found in the squid *Loligo vulgaris*. Quiring, Walldorf, and colleagues end their paper by stating:

> Also, the hypothesis that the eye of cephalopods has evolved by convergence with the vertebrate eye is challenged by our recent findings...of *Pax-6* related sequences in the squid *Loligo vulgaris*. These findings may throw some new light on the fascinating problems of eye evolution.

In trying to summarize the importance of this work for evolutionary theory, let me provide an anecdote and a statement. So much of our conventional thinking must be tweaked, if not reversed. We must reassess our views on the weight of past influence and current adaptation. Naturalists tend to work by example as much as by principle, so I will share my first candidate for rethinking. I have always been amazed by the dorsal fin of ichthyosaurs. These seagoing reptiles, living at the same time as dinosaurs, evolved from fully terrestrial ancestors but look remarkably like marlin or swordfish. They grew a dorsal fin of the same form, and in the same position, as the dorsal fin of fishes. The function of this structure is well understood—a device, primarily, for the prevention of rolling side to side during swimming. Hydrodynamic engineers have found that the dorsal fin is optimal in form and position for this role.

Yet the dorsal fin of ichthyosaurs evolved from absolutely no precursor structure in 100 million years worth of ancestors (for these forebears were fully terrestrial, finless creatures, even though more distant fish ancestors had dorsal fins). Therefore, the ichthyosaur dorsal fin has always been regarded as another stunning example of convergence, or fully independent evolution of an organ by natural selection based on evident utility. But this view may not be right. If all or most animals hold *Pax-6* in their genetic repertoires, using the developmental consequences to build eyes of enormous variety, then perhaps the ancestors of ichthyosaurs retained unexpressed developmental information for building dorsal fins—a legacy from more distant fish ancestors—throughout the 100 million years of terrestrial evolution. Perhaps this reptilian dorsal fin (although not homologous in structure with that of fishes, for the ichthyosaur version contains no fin rays) could be built at all because distant ancestry provided a prerequisite—making the fin as much a consequence of constrained history as of immediate adaptation.

We have an unfortunate habit of regarding constraint as entirely negative, as limitation, in this case imposed by a restricted array of inheritances. But constraint, in both concept and language, also bears a positive meaning of providing a directed possibility, of channeling for potential benefit. Organisms need structural constraints of ancestry to build anything of interest. Constraints do restrict the range of outcomes, but their absence may preclude any outcome at all. Construct organisms with no neural sensitivity, as Darwin argued, and eyes might never evolve. Lose the genetic architecture encoded by *Pax-6* (and, no doubt, many other factors), and all reasonable possibility of generating an eye might evaporate. But lineages that retain these developmental pathways may then evolve and permute organs of vision into a wondrous variety of form and function. The past may only be prologue, as Shakespeare said, but the past is also promise. Let there be light, but also the wherewithal for perception.

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