Development Influences Evolution

A range of factors—including genetics and physics, location and timing—can either constrain an animal's features or amplify changes

Katherine E. Willmore

In the animal kingdom, specific traits distinguish one group of animals from another. The beaks and feathers of birds, for example, set them apart from mammals and amphibians. Furthermore, variations in those traits differentiate one kind of bird from another. For instance, ducks have long, wide and flat beaks, and geese have shorter, thinner and taller beaks. Nonetheless, birds also share many features—eyes, feet, legs, a tail and so on—with many mammals and amphibians. What allows some traits to vary so greatly, while other features remain relatively similar across a wide range of animals?

Some might say that a shared evolutionary history creates similarities, and adaptive responses to selective forces trigger differences. This answer provides some insight, but it does not explain all of nature's variation. For example, similar traits can arise independently in different animal lineages by a process called *convergent evolution*. In convergent evolution, different developmental processes form similar structures.

Many biologists point to the development of human and octopus eyes as an example of convergent evolution. Both eyes have an eyelid, iris, lens, pupil and retina, but they are formed by completely different mechanisms. The human eye is an extension of the brain, whereas an in-pocketing of the

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skin creates the octopus eye. Functionally, these eyes differ as well. Our eyes receive light through rod and cone cells that point backward. In the octopus, rod and cone cells point forward. In addition, the focal length of the octopus lens is fixed; the octopus focuses by moving the entire lens relative to the retina. In humans, changing the shape of the lens focuses the eye on objects at varying distances.

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Figure 1. Specific traits distinguish animals. Among birds, for example, beaks come in many sizes and shapes. The roseate spoonbill *(left)* has a long, flat and wide beak, but a curlew's *(upper right)* is long and thin. On the other hand, a Leadbeater's ground-hornbill *(lower right)* relies on a robust bill that is relatively long and quite tall. Through evolutionary developmental biology, scientists can explore the constraints on animal traits, including bird beaks, as well as their history.

This human-octopus example hints at what can be learned from the field of evolutionary developmental biology, or *evo-devo*. Evo-devo is the study of how developmental processes interact with selective forces to produce evolutionary change. In this context, development refers to the formation of physical traits and physiological systems, from conception onward. A major focus of evo-devo is to determine how development is constrained or biased and to assess how that affects evolution. Although many evolutionary modifications could arise, not all outcomes are equally feasible. For instance, some traits are not possible in specific animals because of their developmental toolkit. Developmental toolkits can be compared to Lego building blocks, because both dictate what can be built. A standard set of rectangular LEGO blocks, for example, can serve as building material for many unique structures, but nothing with truly rounded edges. In the same way, an organism relies on limited developmental processes, pathways and interactions.

In this article, I highlight the role that development plays in the evolution of the variety of natural forms. An understanding of this developmental role reveals a set of rules that bias the direction of evolutionary change, and these rules help to demystify the complexities of form that nature creates.

35 Shapes Fit All

Every living animal fits one of 35 distinct shapes, or body plans, all of which originated in the Cambrian period around 500 million years ago. Because these new animal shapes appeared relatively rapidly, the event is referred to as the Cambrian explosion. In this case, "rapid" is based on an evolutionary timescale; the explosion occurred over a period of at least 5 to 10 million years.

A common body plan often explains many of the similarities among different types of animals. For example, humans are part of the phylum Chordata. All members of the Chordata share four common traits at some point during their development: a series of openings that connect the inside and outside of the throat; a bundle of nerve fibers that runs down the back, connecting the brain with other structures; a post-anal tail (literally, a tail behind the anus); and a cartilaginous rod that supports the nerve cord. Humans share these physical traits with amphibians, birds, fish and even sea squirts.

Even after many millions of years—10 times as long as the Cambrian explosion itself—no new body plans have evolved, despite major changes, including the movement from living in water to living on land. Consequently, developmental processes might constrain the possibilities.

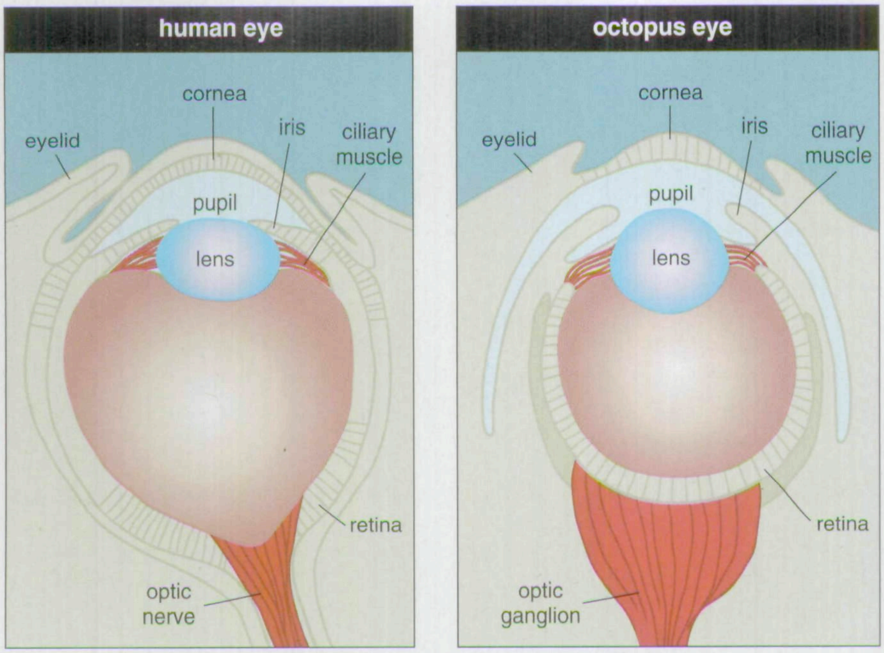

Figure 2. Human and octopus eyes demonstrate convergent evolution, in which different developmental processes form similar structures. As shown here, both of these eyes—from very different organisms—consist of largely similar features: cornea, lens, retina and so on. This is even more compelling given that human and octopus eyes develop along completely different pathways.

For one thing, structural constraints impede some forms. Consider the fictional King Kong, a scaled-up version of a gorilla. All of his proportions are the same as a normal gorilla, but his overall size is much larger. In real animals, the structural properties of bone limit the size and proportions of the creatures, especially ones that live on land. Here's a simplified mathematical explanation of Kong's impossibility based only on the thigh bone, or femur.

Let's say that King Kong is five times taller than a normal-sized gorilla. A bone's strength depends on its cross-sectional area, which is a function of the square of its radius. King Kong's femur is five times bigger in all dimensions, including its radius, so its strength will be increased by 5^2, or 25. King Kong's volume, on the other hand, varies with the product of length and cross-sectional area, which means that it increases by the product of 5 and 25, or 125. With this giant gorilla's weight increasing five times more than his strength, his legs would be crushed. Such a discrepancy between strength and weight would apply to the rest of Kong's body as well. So apes could increase in size, but structural constraints impose limits.

A Collection of Constraints

Elements beyond physics, such as the organization of a genome, also constrain development. Certain genes and gene families can be found in a wide range of animals and serve similar functions in different animals. For example, the Hox genes make up a well-studied set of these *conserved genes* that have been identified in a variety of animals including but not limited to, frogs, fruit flies, humans, mice and worms. Hox genes help to set up an animal's basic body plan, organizing how structures get arranged along the body from the head to the tail. Moreover, the physical order of the Hox genes along the chromosomes corresponds to the order of the structures of the body that they affect—starting with genes that affect the head, then the thorax and then the abdomen. Hox genes are also arranged along the chromosome in the same order as the timing of their effects on body structures. That is, the genes in the complex that affect the head are turned on first, followed by the genes that affect the thorax, and finally the genes that affect the abdomen.

Beat Lutz, a physiological chemist at Johannes Gutenberg University in Mainz, Germany, and his colleagues demonstrated the functional and spatial conservation of Hox genes between fruit flies and chickens. These researchers experimented with a gene named *labial*, which is necessary for proper head development. With this gene turned off, flies die as embryos, but Lutz and his team showed that these flies can be rescued by placing the *labial* gene in the proper place in the embryo's genome at a specific time during development. Even more amazing, Lutz and his colleagues added a chicken version of *labial* to flies that had *labial* turned off, and that manipulation rescued the flies with the same efficiency as using the fly gene.

Although flies and chickens have markedly different heads, the genetic machinery that drives part of their head development is sufficiently similar to allow swapping genes between the two species. This similarity in genetic framework suggests that some aspects of the basic body plan are constrained.

Beyond genetic constraints, some traits depend heavily on other structures. All structures are burdened somewhat in this way, because no trait exists in isolation. But some traits are more heavily burdened than others. For example, the human vertebral column supports the body, provides a place for muscles to attach and serves as a conduit for nerve and blood supply. If there is a change in the spine, then the structures that interact with it must also change.

A process called *canalization* can also constrain structures. This term came from the idea of depicting, for example, a structure on a landscape of possibilities. If the desired structure lies in a valley, the surrounding ridges depict developmental forces that confine the trait and its development. Canalization is one process that helps developmental systems resist errors. For instance, if a tissue develops from cells that must congregate in a specific location at a specific time, a minimum number of cells must migrate to that spot from different locations or the tissue will not develop properly. On the other hand, if the cells that did migrate properly divided more quickly than normal, the increased division rate could create enough cells to meet the minimum requirements, regardless of any problems with migration.

Breaking Free

Despite the confining power of some developmental systems, variations appear. A mutation with a strong effect or a drastic environmental change can overwhelm the developmental con-

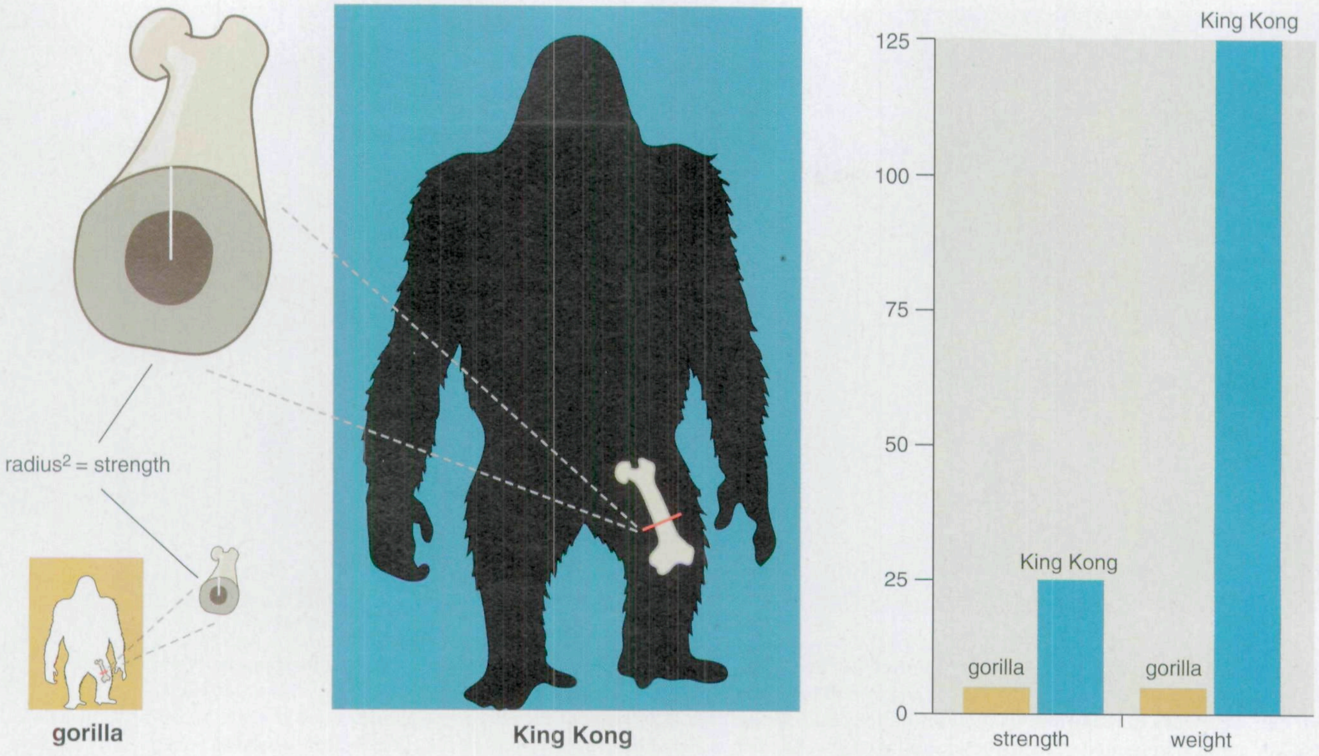

Figure 3. Physical constraints make King Kong impossible. Imagine that King Kong *(blue box)* is five times bigger than an ordinary gorilla *(yellow box)*, but with all proportions maintained. Let's consider only King Kong's thigh bone, or femur. Like the rest of King Kong, his femur *(left)* is five times bigger than an ordinary gorilla's. Bone strength depends on cross-sectional area, which increases in King Kong by 5^2, or 25. Weight, on the other hand, increases as the product of length and cross-sectional area, or 5 × 25 = 125. Consequently, King Kong's weight increases five times faster than his strength, and he would crush himself *(right)*.

straints, driving a modification that is so great that the rest of the system can't hide it. Moreover, one developmental change could even expose previously hidden ones, or ones that had been corrected or compensated for in the past. Taken together, such developmental changes might create vastly different structures. In effect, canalization provides a cache of developmental changes that could be released under some circumstances.

Suzannah Rutherford, a biologist at the Fred Hutchinson Cancer Research Center in Seattle, Washington, and her colleagues elegantly demonstrated this concept in fruit flies by disrupting the normal functioning of heat-shock proteins (HSPs), which exist in the cells of every organism. HSPs help other proteins assume or maintain their proper shape, which is required for proper function. Under stressful conditions—such as exposure to a heat shock or other environmental stressors, including toxins, starvation or infection—some proteins unfold. The same stressful conditions, however, increase the production of HSPs, which fix the damaged proteins.

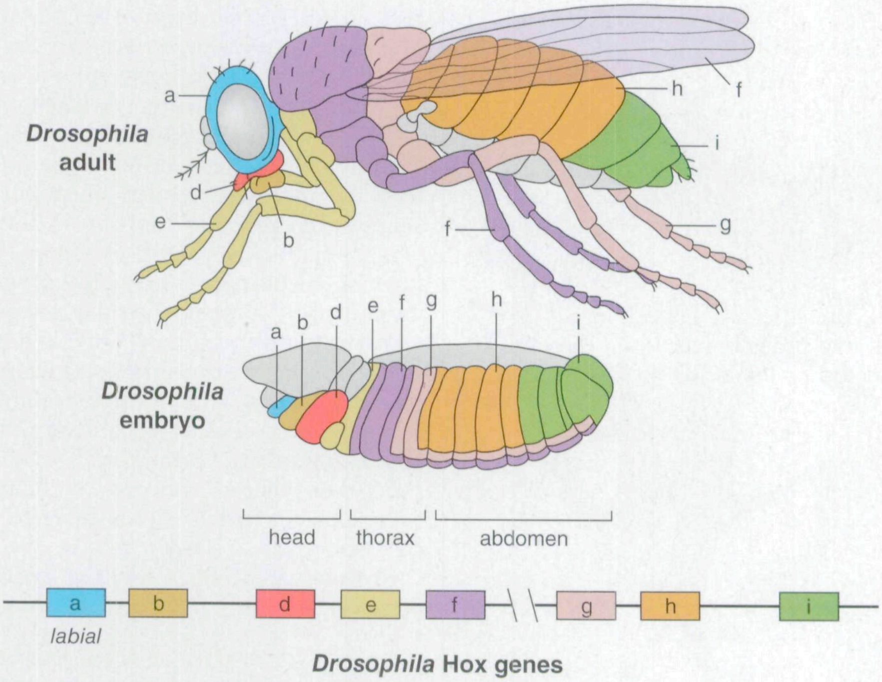

Figure 4. Hox genes play a role in developing the body plan of many animals. As shown here in a fruit fly, the physical order of genes on the chromosome *(bottom)* dictates the order of structures in the embryo *(middle)* and, ultimately, the adult *(top)*. For example, gene *a* (also known as *labial*) appears first in the chromosome and the embryo, and it participates in the formation of the fly's head.

Steve Downer

Edd Westmacott/Alamy

Figure 5. *Heterochrony*, **or changes in the timing of developmental events, explains some of the difference in appearance of a newborn kangaroo** *(left)* **and human** *(right)*. **Although a kangaroo is born at an earlier developmental stage compared with a human, the kangaroo needs the immediate ability to feed from its mother in the pouch. At such an early stage of development, a human could never accomplish that task. In the kangaroo, accelerated production of neural crest cells pushes ahead the development of the facial features needed for this early feeding.**

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Figure 6. *Odontochelys*, **the oldest known fossil turtle, dates to about 220 million years ago. Its lower shell, or plastron, was complete. As shown here, its top shell, or carapace, consisted of plates of bone along the middle, but only ribs along its sides. This partial shell mirrors shell development in some turtles** *(see Figure 7)*.

With high temperatures and mutations, Rutherford and her colleagues disrupted the normal functioning of HSPs in fruit flies. This affected nearly every aspect of the flies—including the antennae, eyes, legs and wings—but not directly. Instead, the disrupted HSPs could not do their usual job of maintaining the shape, and thereby function, of the proteins involved in building these structures. Mistakes in the shaping of proteins can accumulate within cells because HSPs normally fix the proteins before the improper shapes affect protein function in the development of structures. When HSP function is compromised, as it was in these fruit-fly experiments, the build-up of changes in protein shape is revealed, leading to potential changes in form or function. Although the results are often extreme and are unlikely to be advantageous, Rutherford's work shows how the mechanisms that help to canalize a structure can also spawn changes.

Evolutionary change can also arise from adjustments in developmental timing. *Heterochrony* (based on the Greek *hetero*, or change, and *chrono*, or time) describes a change in the timing of a developmental process. When the timing of events relative to sensitive stages of development is shifted, radically different structures can emerge. Marsupials, such as the kangaroo, provide an example of heterochronic change. Compared with placental mammals—such as cats, dogs and humans—marsupials are born very early. At birth, a kangaroo looks more like a fetus than a newborn. The majority of a marsupial's development occurs in its mother's pouch. Therefore, even though marsupials are born relatively undeveloped, they must be able to find the teat within their mother's pouch, attach to it and feed. At a similar stage in development, a placental mammal would not have the facial features or motor skills necessary for this task.

Kathleen Smith, an evolutionary biologist at Duke University, and colleagues discovered that newborn marsupials can feed because the development of their facial muscles and bones is accelerated compared to placental mammals. Specifically, Smith found an earlier production of neural crest cells, which contribute to the development of many facial features.

In *heterotopy*—a combination of the Greek for change, and *topo*, or

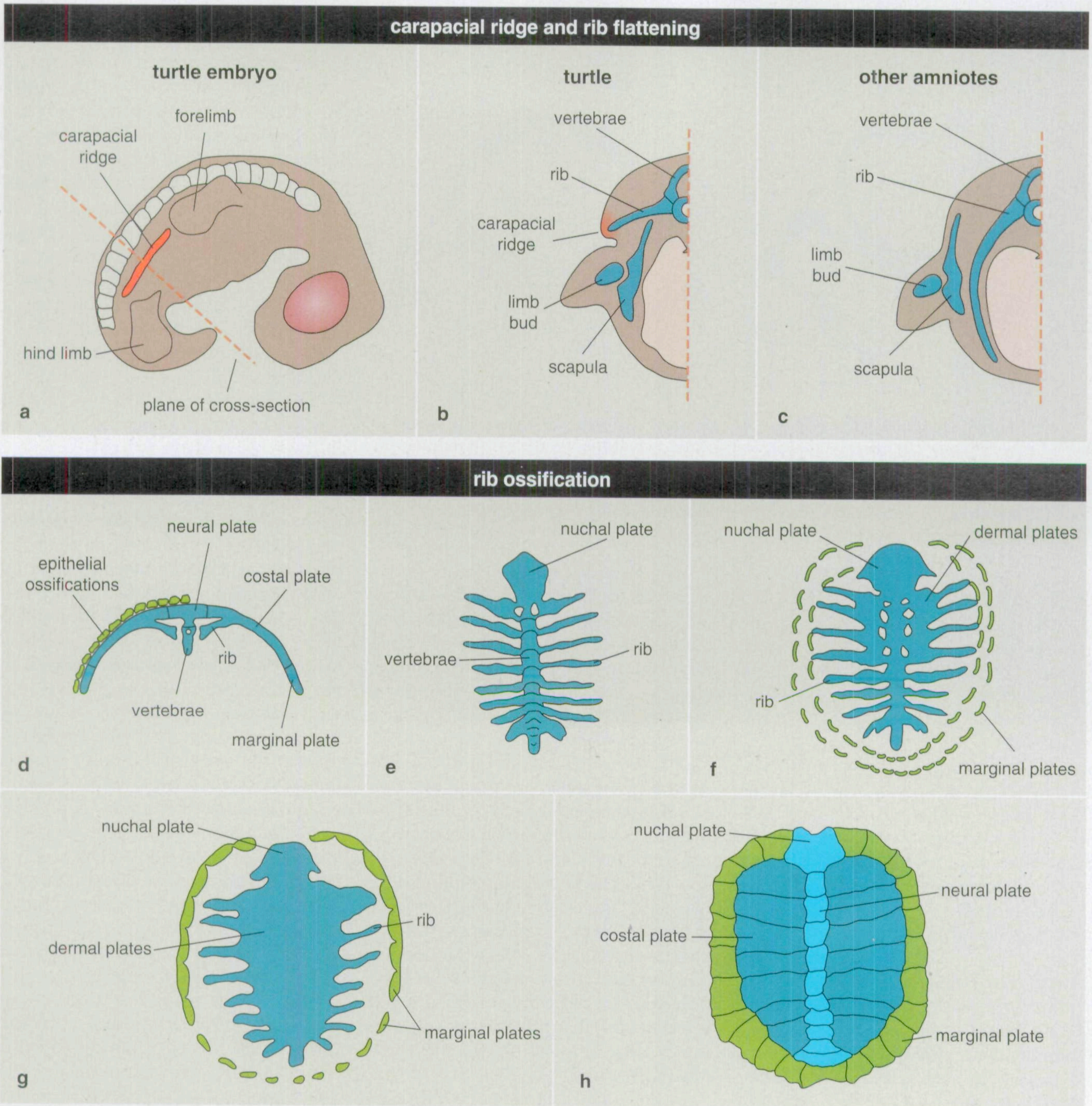

Figure 7. Turtle shell development starts with a carapacial ridge (CR) *(a, red)*. As shown in cross section *(relative to the dashed red line in a)*, the CR entraps the ribs, which get pulled to the side *(b)*, unlike other amniotes in which the ribs grow forward, toward the breastbone *(c)*. As development continues, a turtle's ribs grow toward the sides even more *(d* and *e)*. Then, dermal bones start to form around the ribs *(f* and *g)*. Eventually, the dermal bones fuse to form the complete shell *(h)*.

place—change arises from a suite of developmental processes taking place in a new location. Relocation places the developmental structures in contact with others from which they are normally separated. The result can be the production of extra parts in a new location, such as an extra set of legs or wings, or entirely unique structures.

The morphology of cheek pouches—structures that carry food—provide an example of heterotopy. The cheek pouches of squirrels and many mice represent the original condition. Their pouches are found on the inside of their cheeks and are lined with mucus. These pouches develop from an in-pocketing of the skin on the inside of each cheek. Some other animals, including pocket gophers and kangaroo rats, develop fur-lined pouches on the outside of their cheeks. In these animals, the in-pocketing takes place closer to the front of the face and allows for the skin of the lip to be included. In this more forward position, the developing pouch comes in contact with hair-forming cells, initiating the development of hair follicles inside the pouch. Additionally, the forward placement of the pocket places it in a new group of cells that follow a different growth pathway. These cells

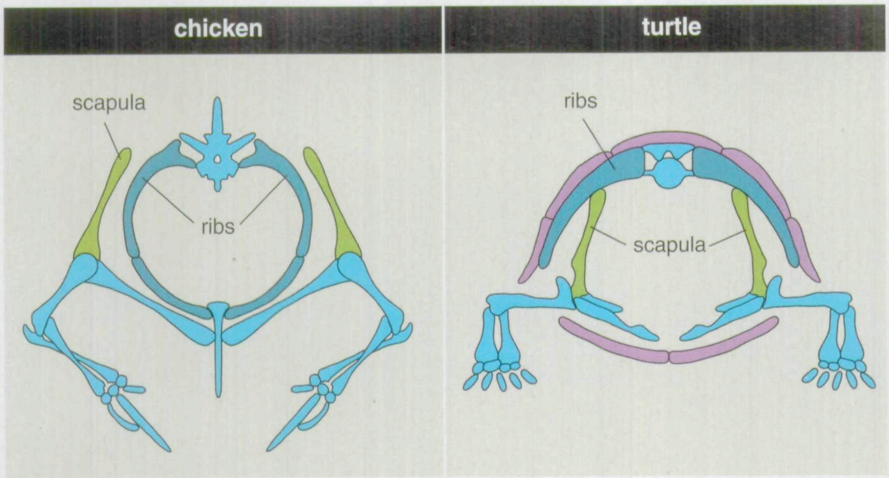

Figure 8. Scapula location *(green)* distinguishes a turtle *(right)* from a chicken *(left)*, as well as all other vertebrates. The developmental events related to building a turtle's shell pull the ribs *(blue)* over the scapula, leaving them inside. In the chicken, the development of the ribs pulls them into a semicircle from the spinal column to the breastbone, thereby leaving the scapula outside the rib cage. As this shows, one developmental change can trigger others, leading to significant differences in animals.

pull the fur-lined pocket so that it lies on the outside of the cheek. The same processes are used to develop both types of cheek pouches, but a slight displacement of the initial developmental steps lead to vastly different structures.

Every animal is a mixture of constrained and unique features. Therefore, the development of an animal involves a combination of many of the developmental phenomena described above. Turtles provide a great example of how these phenomena combine to produce interesting structures.

Building a Turtle

Although turtles have roamed the Earth for at least 220 million years, making them one of the most primitive animals, they possess several distinctive features, including a shell and uniquely placed shoulder blades. Both of these traits arise from simple tweaks of existing developmental programs.

In 2008, Chun Li of the Chinese Academy of Sciences in Beijing and colleagues described the oldest known fossil turtle, called *Odontochelys*, which dates to about 220 million years ago. In *Odontochelys*, the plastron—the part of the shell next to the belly—is complete but the carapace—the portion on the turtle's back—is incomplete. On this turtle's back, plates of bone developed along the middle, but only ribs are evident along its sides. This partial shell fits well with what is known about shell development in today's turtles.

Early in development, turtle embryos develop a bulge on both sides between the limb buds, the structures that form the front and hind legs. These bulges lengthen along the sides of the turtle embryo, creating a *carapacial ridge* (CR). Two embryonic tissues—*mesenchyme* and *ectoderm*—form the CR. Mesenchyme is the embryonic precursor of blood vessels, blood cells, bones, ligaments and cartilage. Ectoderm gives rise to the brain and nerves, and to skin and other external features, including hair, nails and scales. The CR consists of a mesenchyme core with a thick ectodermal covering. This arrangement of mesenchyme and ectoderm is found repeatedly in animal development and is responsible for initiating and organizing the development of limbs and many other structures.

In shell development, the CR traps the growing ribs. In all other tetrapods, or four-limbed vertebrates, the ribs grow from the spine to the breastbone, thereby forming the rib cage. In turtles, the ribs become ensnared in the CR and are pulled to the side and into the dermis, or the middle layer of the skin. Consequently, turtle ribs are somewhat flattened out to the sides. This heterotopic placement of the ribs within the dermis exaggerates the sideways growth of the CR and ribs. Moreover, a heterochronic growth rate of the dermis—side growth accelerated over front-to-back growth—amplifies the movement of the ribs to the side. As a result, the embedded ribs are pulled to the side faster than they can grow toward the front.

The unique proximity of the ribs to the dermis in turtles allows for another ectodermal (dermis)–mesenchyme (ribs) interaction. Initially cartilage forms the ribs, but through interactions with the CR, the cartilage is replaced with bone. The new bone in the ribs sends signals to the surrounding skin that initiate further bone formation. These bones are called dermal bones. Dermal bones continue to grow until they become fused with each other and the underlying ribs. The heterotopic placement of the ribs within the dermis allows for a new developmental interaction, creating the bony carapace.

Although a turtle shell seems unique among animals, dermal bones also develop in crocodiles and some amphibians and fish. The location of a turtle's scapulae, or shoulder blades, makes up its truly unique aspect. In all other vertebrates, the scapulae lie on the outside of the ribs, but they are on the inside in turtles. When the ribs get trapped in the CR and are pulled to the side and the back, they surround the scapulae. In all other vertebrates, the ribs grow toward the front of the body, leaving the shoulder blades outside. The inward placement of the shoulder blades in turtles represents a break from the common tetrapod body plan and is a major evolutionary modification.

As turtles demonstrate, small changes early in development can trigger far-reaching effects. Nonetheless, it would be nearly impossible to predict how a slight tweaking of a cell population—like the development of the CR—would create a completely different skeletal arrangement and the development of a bony shell. To recreate the initial appearance of unique structures, we need specific details of each species' developmental program and information about intermediate species. This is yet another example of what makes evolution so complex—and so utterly fascinating.

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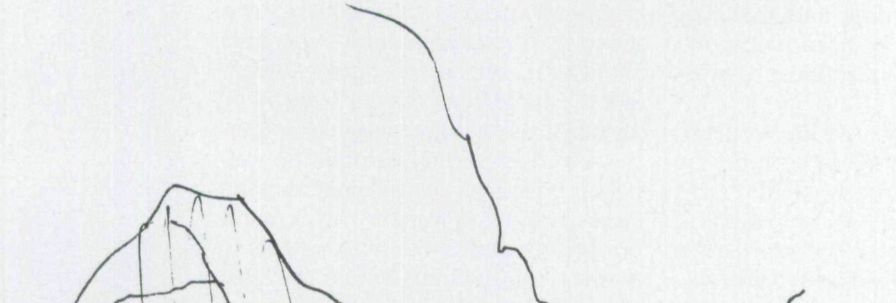

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