Limits to Evolution

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What do Sleipnir, Goro, Shiva, gryphons, angels, centaurs and pegasuses (pegasi?) have in common? Beside the fact that these creatures are all fictional or mythological, they are all vertebrates with 3 (or more) pairs of limbs. The funny thing is, there are no real vertebrates with more than two pairs of limbs. Despite the usefulness of an extra set of arms (Goro) or legs (Slepnir) this has never arisen during the hundreds of millions of years that vertebrates have been evolving. Vertebrates such as snakes, eels, amphisbaenians and so-called legless lizards have lost limbs, but none have gained any extra. Why is this? A few extra limbs would be useful to at least some species, somewhere. So why haven't we seen it?

Questions such as this one raise an interesting issue, what are the limitations to the process of evolution? Despite what Ian Malcolm says in *Jurassic Park*, nature does not "always find a way." In fact, evolution is very limited. For example, why aren't there any insects with more than six legs? There are arthropods with more legs (centipedes, millipedes, spiders, etc.), but none of the descendants of the common ancestor of all insects has evolved extra legs. In evolution it seems, once you're an insect, you're stuck with only six legs. Not to mention the fact that all these insects have three body regions (head, thorax and abdomen), never in the hundreds of millions of years insects have been around would it have been handy to get a new body segment?

That there are limitations to evolution should not be surprising. Evolution is a shortsighted process that involves a lot of chance events and random factors, it is not some unstoppable juggernaut headed towards biological perfection. In fact, evolution as a process is not "headed" anywhere. Evolution is just the byproduct of differential rates of survival and reproduction among various organisms that possess different qualities that are inherited. This survival and reproduction is often confounded by random factors (trees can still fall on the biggest and best) or the shortsightedness of generation-to-generation survival rather than any long-term survival prospects (resistance to a disease can be lost if the disease isn't around and resistance makes the organism slightly less healthy otherwise). Even the fuel for evolution—new characteristics brought about by mutations—is very rare and random events may easily eliminate individuals with wonderful adaptations. As an example, if a new mutation gives a fitness advantage of 5 percent (that is, individuals with this trait have 5 percent more offspring on average), mathematical models show that it only has a 10 percent chance of becoming the norm for the population; 90 percent of the time it will be lost. The general result is that a new mutation with a fitness benefit of a given percentage has twice that percentage chance of becoming fixed in the population (that is, all individuals in the population at a later date have this new gene). Actual measurements from nature are hard to come by, but most advantageous mutations provide quite small fitness increases so most new beneficial mutations are lost. Of all the great adaptations we see in nature, far more were lost.

Rather than being some pseudomystical force for the good of all life, evolution is the result of a bunch of not very intelligent organisms trying to survive and breed while facing a random and capricious environment. Despite this however, evolution is effective because there are so many organisms surviving and breeding. The high number of organisms means that mutations happen fairly frequently if you look at the populations as a whole. In only 100 million years mammals have gone from being shrewlike also-rans to becoming the dominant large creatures on the land, in the air, and to some extent in the ocean. From the basic rodentlike (not a rodent) ancestor we have gotten whales, apes, camels, sloths, tigers, bats, moles and any number of other weird mammals in a length of time only about 2 percent of the age of the planet. Yet as I mentioned earlier, there seem to be definite limits. For instance, in all that time mammals have essentially kept the same number of neck vertebrae (seven), whether they have long necks or no necks. No mammals have gills or more than two eyes for that matter either. So what gives?

Evolutionary biologists have identified three basic limits to the evolution of life as we know it. These constraints affect how often new mutants will be generated, survive and then reproduce. If the new mutants don't arise or can't reproduce then evolution won't proceed. Evolution can't act on a feature that isn't there and such a feature will never become the norm for a species in nature. The first constraint is one in which the new trait can arise by a mutation in a gene, but this mutation is always associated with some other effect (such a gene that controls two distinct features is called pleiotropic) that dooms the new mutant. We will call this a pleiotropic constraint. The second constraint is such that the process of development in the candidate organism just doesn't allow mutations to arise that have the new beneficial character we are imagining. We will call a constraint of this type a **developmental constraint**. The third type of constraint is one in which mutations that confer the new feature do occur, but these features are somehow bad for the survival of the mutant and it dies before reproducing. We will call these **functional constraints**. For the remainder of this article I will describe these constraints in more detail and give examples of each.

Pleiotropic constraints

Pleiotropy is a general term for the scenario in which a single gene has multiple effects. Contrary to news reports about "the gene for alcoholism" or "the gene for obesity", life is rarely so simple as to have a one to one relationship between a single gene and a single physical or biochemical trait. As an example, white cats with blue eyes are also generally deaf because the gene that produces the white coat and blue eye color also has a negative effect upon the development of their sense of hearing. Clearly this relationship will prevent an evolutionary future in which all white cats have blue eyes. Basically, mutations that create a new trait are possible, but genetic side effects cause the organisms with the trait to die before passing it on to their offspring, which is what evolution is all about.

The neck vertebrae that I mentioned earlier are a possible example of this sort of constraint on evolution. While other vertebrates vary widely in the number of cervical vertebrae they have, almost all mammals (with only two exceptions, sloths and manatees) have seven cervical vertebrae. No more and no less. Whales with no necks and giraffes with super necks have the same number of vertebrae in their necks. There is no apparent physical reason why mammalian necks shouldn't have more bones—

swans have 23-25 vertebrae in their necks, and they do just fine. Giraffes (with the swan-length necks of the mammal world) can hardly bend their necks at all because of the small number of bones and this is why they have such difficulty drinking at waterholes. Rather than bend their necks down gracefully, they must spread their legs wide apart and lower their entire neck to the water like a heavy loading ramp. This is obviously dangerous due to the risk from predators, so why haven't they evolved extra cervical vertebrae to make drinking less arduous?

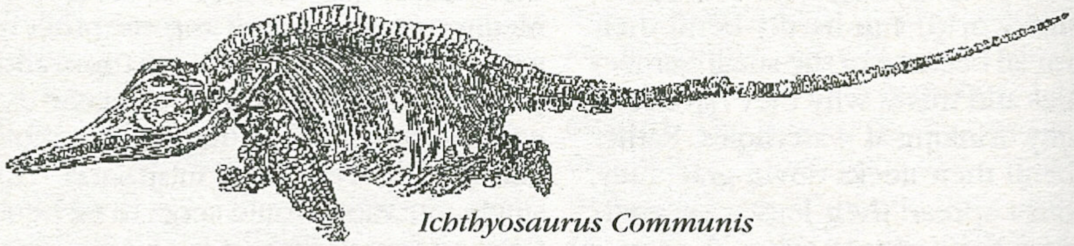
The answer may lie in cancer. Mutations of vertebrae are possible; occasionally in humans mutations occur that lead to the changing of cervical vertebrae into thoracic vertebrae (small ribs appear on the neck vertebrae). However, the childhood cancer rate of people with these mutations is extremely high—one in nine individuals afflicted get a deadly cancer (120 times higher than the normal rate). It seems that the genes responsible for determining vertebral identity are also associated with cancerous cells in the body. Recently, Frietson Galis has proposed that the genes involved are the genes known as *Hox* genes, which determine body segment identity during development as well as influence cell proliferation and growth in general. Galis goes on to make an interesting proposal: if cancer is the threat preventing modification of mammal ribs then maybe it is less effective in mammals naturally more resistant to cancer—those with very low metabolisms. In fact, the only mammals with a number of cervical vertebrae other that seven are manatees and sloths, two groups of mammals with very slow metabolisms. This suggestive observation needs more examination, but it implies that the pleiotropic effect of mutations in the *Hox* genes may be the reason we don't see many mammals with more or less than seven cervical vertebrae.

Another example of a pleiotropic constraint is the evolution of malaria resistance in humans. Malaria is a deadly disease rampant in Northern Africa and the Mediterranean (as well as some other regions in the world), killing thousands yearly. A single mutation in the gene that encodes a part of the hemoglobin molecule confers resistance to malaria. This single mutation would seem to be beneficial to humanity and is seen in many people in these regions. Unfortunately, this mutation also screws up the regular functioning of the hemoglobin molecule, inducing a genetic disease, sickle-cell anemia. This mutation will never become the norm for an entire population because individuals with two copies (humans have two copies of every gene except sex-specific genes, the old XX and XY story from high school biology) die young. Only those fortunate people with one mutant gene and one regular gene enjoy both resistance to malaria and efficient hemoglobin function. This is not a unique case since there is another mutation that provides similar resistance to malaria, but causes a different genetic disorder, thalassemia.

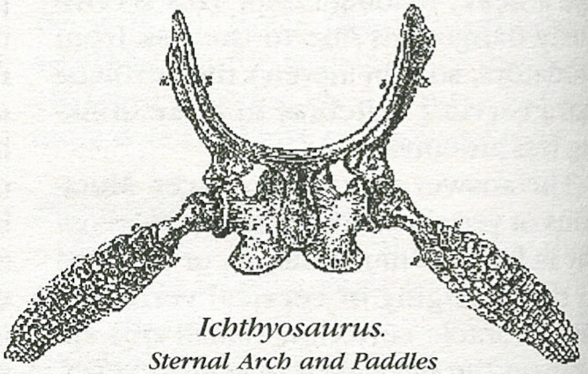
Developmental constraints

The production of an organism is a complicated process with many genes interacting in many more ways, some changes may just be impossible because they would require too many simultaneous changes in a large number of genes.

As an example, all flies (the order Diptera within the class Insecta) have one pair of wings and a tiny set of pseudo-wings called halteres behind them. There is a mutation seen occasionally in laboratory flies occasionally called "bithorax", where the flies have two pairs of full-sized wings and no halteres. This would seem to be a case where mutations to recover four wings (the ancestor of flies had four wings, dragonflies and other non-dipterans retain this state) can occur. But when we look in nature there are no cases where a dipteran species has evolved another pair of



Ichthyosaurus Communis



Ichthyosaurus.
Sternal Arch and Paddles

Fin and phalanges of Ichthyosaurs. Note the large number of undifferentiated phalanges in each fin. The high number of structures is possible due to the relaxation of developmental controls on each individual structure.

Drawings from Buckland, 1841.

wings; all dipterans and their evolutionary ancestors have two wings. The answer lies in closer analysis of the laboratory mutation. While the external wing is duplicated, the underlying muscles and nerves required for functionality are not. The mutation to get an extra wing is there, but it would have to be accompanied by other mutations that provide muscles and nerves as well. Since the immobile extra set screws up flying with the front pair of wings, these mutations would all have to happen simultaneously for a fly with four wings to survive and reproduce. Mutations are very rare, so double mutations would almost never happen. Without these double mutants, no viable four-winged flies will arise and natural selection can't move the evolution of a fly species in that direction.

Developmental constraint may explain why no vertebrates have more than two pairs of limbs. The developmental pathway of vertebrates just doesn't seem to allow the formation of extra limbs. Sure, some animals occasionally sport extra limbs, but they are often placed in weird locations and the heritability (not to mention usefulness) of these extra limbs is low. These extra limbs seem to be due to unusual events and mistakes during development that have little to do with heritable genetic changes. Limbs are not the only feature that vertebrates lack variation in, there are no vertebrates that have more than one nose, one head, two ears, one mouth, etc. These features can be lost, such as limbless snakes, but never have we seen a gain.

Other developmental constraints in vertebrates are more subtle. During forelimb development in almost all vertebrates (newts and salamanders are the only exceptions), digits II and III are formed first, then IV and finally I and V (digits are numbered starting from the thumb and moving out to the "pinky"). Because eliminating an early digit would disrupt the limb's development more severely than a later digit, when individual digits are lost in evolution they are always digits I or V, followed by the other, then IV and finally II and III. Fossils from horses clearly show the loss of digits I and V followed by the drastic reduction of II and IV in the historical path to a single toe (III) on horse limbs. While this constraint may not seem severe, if the function of digits I or V must be preserved yet there exists a pressure to reduce the number of digits, an evolutionary tension would result in which an optimum is impossible to achieve.

There is another line of evidence that indicates that developmental constraints may be responsible for the fixed number of digits in the limbs of mammals. This evidence comes from snake ribs, ichthyosaur fins and whale teeth. In these animals there are far more of each structure than the normal maximum, snakes have many vertebrae with ribs, ichthyosaur fins have more than five digits (each with many phalanges all concealed inside a fleshy paddle—see the picture) and whales can have up to 252 teeth, a number far larger than other mammals. So how have these animals exceeded the normal maximum? This seems to have been accomplished by altering the development of these structures by eliminating individual differences between the repeated structures. Snake vertebrae with ribs are all identical, ichthyosaur digits are all identical and very simple, as are whale teeth. Developmental constraints limit the production of new and distinctly-shaped units, but if having all the units identical serves well then evolution can take this route by switching off the developmental pathways individualized for each structure. The fact that extra ribs, digits and teeth are only seen in cases where they are all identical shows that these extra structures aren't functionally bad, just developmentally constrained.

Functional constraints

Finally some new features don't arise in evolution because they are either physically impossible or their presence would doom the new mutant to a quick death. I am reminded of a Far Side™ cartoon in which a deer has a target-shaped birthmark and another deer remarks something to the effect of, "bummer of a birthmark." A mutant with a novel feature that is bad for the mutant will not survive very well and the feature won't become fixed in the population.

The classical example of a functional constraint involves the maximum size of terrestrial organisms. As an organism gets bigger its body mass will increase roughly as the cube of its increase in length (mass is contained in the entire length times width times depth), assuming the same shape and makeup. By the way, this isn't a new concept—in 1726 Swift alluded to this in "Gulliver's Travels" when the Lilliputian emperor's last proclamation orders Gulliver to be given the rations of 1,728 Lilliputians (they are said to be about six inches tall, one twelfth of a Gulliver, so Gulliver is 12*12*12=1,728 times larger in mass). The problem arises when we consider the strength of the limbs that are needed to support the creature (or thickness of trunk for a tree). The strength of a limb is proportional to its thickness, which is proportional to the width times the breadth, the square of an increase in length. So as the organism's size expands assuming a fixed shape, its mass increases as the cube and the limbs strengthen as the square. At some point the limbs will be too weak relative to the mass of the body to work against the gravity of Earth.

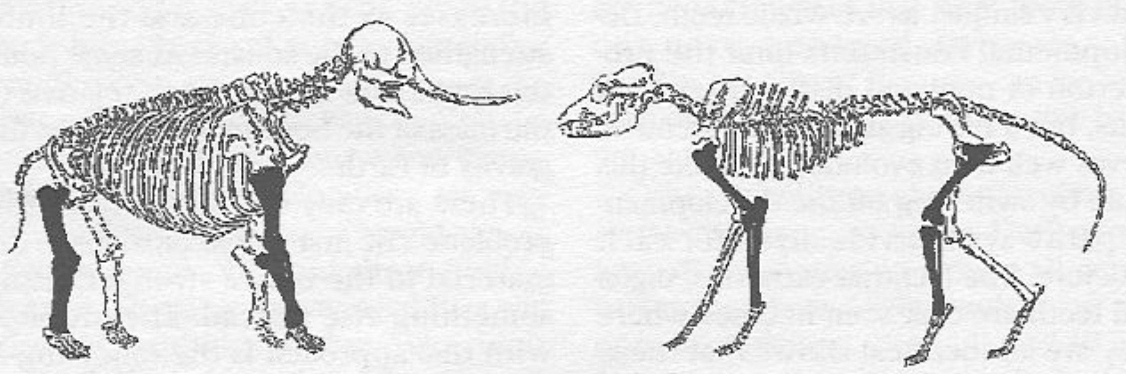
There are only two solutions to this problem. The first would be to make the material in the bones stronger, using something else instead. The problem with this approach is the following—how does an organism suddenly get a whole new set of biochemical reactions to make a brand-new substance and incorporate it into all the bones simultaneously? The generation of a brand-new, harder-than-bone substance is very unlikely. The second solution is to increase the relative size of the limbs so that they can do the work of moving the animal as they could do before. This is what has generally happened in nature.

We can see an example of this limitation at work if we just look at dogs and elephants. Think of how skinny dog legs are in proportion to their bodies, now think of how legs that skinny would look on an elephant. Ridiculous, right? The elephant's legs are clearly much thicker proportionally and it hasn't even retained the same efficiency in moving the body—elephants can't pounce. The figure shown illustrates the relative thickness of dog and elephant leg bones if the bodies are scaled to about the same size. Another example could be geckos and alligators. Alligator legs are much thicker in proportion to their body than geckos, and they can't even walk upside down or leap very well.

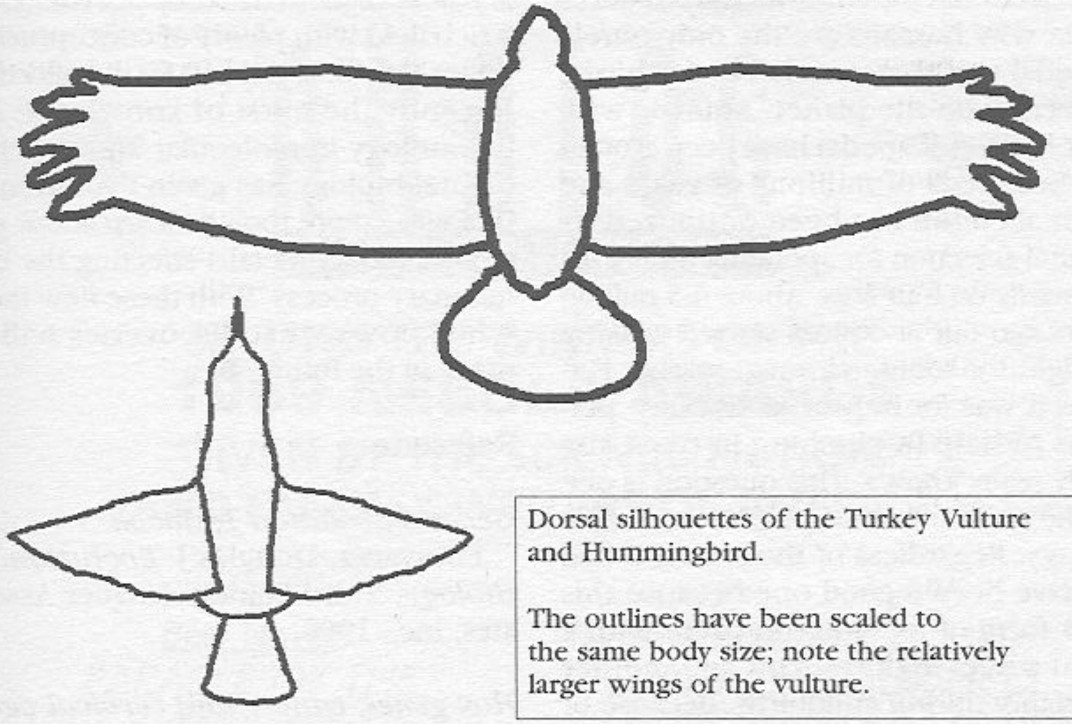
There are plenty of other examples of this general constraint on limb proportions. The same thing goes for the size of wings on birds. Hummingbird wings are smaller than the body, while vulture wings are huge relative to the body (as seen in the figure), and vultures can't fly nearly as well as hummingbirds. Imagine a vulture trying to hover in place. Even trees, which don't move, suffer from this problem. The trunk must get proportionally thicker to support the weight above. Compare the relative thickness of an elm tree to a sequoia, the sequoia is only 3-4 times taller, but the trunk is 8-10 times thicker.

In fact, at a certain point the amount of mass needed to make the bones required to support an animal's weight exceeds the weight of the animal they are trying to support, leaving no room for flesh or blood. Similarly the required mass of a bird's wings would exceed the mass of the bird as a whole, leaving no mass for the body or head. This is why we don't see terrestrial animals anywhere near as big as oceanic animals that don't have to fight gravity to survive.

A related constraint involves the use of an external skeleton versus an internal one. As a creature with an external skeleton increases in size the skeleton must get thicker and thicker proportionally, leaving less and less room for organs on the inside. Think of how little meat there is inside a big crab; it's hardly worth the work at a fancy seafood restaurant to eat a king crab or lobster. This is why we don't see terrestrial arthropods or crustaceans bigger than about one foot long—their skeletons can't take it. An analogy can be seen



Relative Thickness of leg bones in elephant and dog. The bodies have been scaled to the same height; note the larger relative thickness and shortened lengths of the elephant leg bones. Drawings from McGowan, 1999.



Dorsal silhouettes of the Turkey Vulture and Hummingbird.

The outlines have been scaled to the same body size; note the relatively larger wings of the vulture.

when we compare the largest exoskeleton building, castles, and the largest internal skeleton buildings, skyscrapers; the latter are capable of reaching far larger sizes and having greater relative internal space than the former. If you've ever bumped your head in a very narrow castle staircase you know what I mean.

Hollywood, of course, has missed this point. A prime example of a creature violating this functional constraint can be seen in the otherwise scientifically feasible (sarcasm here) movie *Starship Troopers*. In the film, insectlike creatures more than ten feet tall (some far larger) roam around killing soldiers. Of course, an argument may be made that these are alien creatures with some magical super-tough chitin. Yet the movie shows that the carapaces are not that strong: an early dissection scene shows how easy it is to pull apart a carapace apart using only bare hands and later Johnny Rico has no problem shooting through the very thin carapace of a fire-breathing bug. In reality these creatures would not be able to support their own weight and would collapse anywhere other than in an aqueous environment or on a very low gravity planet.

But what about features that we would think may be very helpful, might they have some hidden detrimental effects? Consider the life of a whale; it spends all of its time in the ocean, but must constantly surface to breathe. It would be advantageous for whales to evolve some system of gills so that they could spend all their time in the depths feeding and hiding from predators (and whaling ships). The problem with gills in whales is one of temperature. For gills to be effective they must have a large surface area with blood vessels exposed to the water (think about how fish gills consist of so many little filamentous layers full of blood vessels underneath the hard exterior operculum). Unfortunately this would spell the doom of any warm-blooded seagoing creature. The cold ocean water would cool the blood dramatically and the whale would lose all its insulation from the environment; its blubber would be useless. Only by minimizing exposure of the blood to the cold do mammals stay warm in cold water, the exact opposite of what a functional gill requires. This is a good explanation for why whales, seals, otters and manatees have never evolved gills.

Functional constraints may also explain why humans are the only purely bipedal vertebrates (except for birds) currently on the planet. Animals with four limbs (tetrapods) have been around for hundreds of millions of years and their skeleton has been optimized by natural selection for spending their lives primarily on four legs. About 4.5 million years ago our ancestors started walking upright for some unknown reason. Perhaps it was for improved visibility, perhaps to help in climbing in trees, nobody really knows. This question is one of the great unsolved puzzles in anthropology. Regardless of the reason it had to have been a good one because this new form of locomotion came with a great price: higher infant and mother mortality during childbirth. Because of the way our hips had to be redesigned to support the entire weight of the body instead of just the rear half, there is now very little room for the relatively gigantic head of a human baby to squeeze through the birth canal of a human mother. This is what causes labor and the usually extreme pain of childbirth. Before modern medical practice women used to die all the time in childbirth and the babies didn't do so well either. No other animal has anywhere near this much trouble giving birth, because in their four-legged stance there is plenty of room for a large birth canal to let the baby out. The traumatic nature of giving birth from a bipedal body has limited the number of times we see this feature in evolution, despite how useful having better visibility or free hands might be.

Too often people treat evolution as some almost mystical force or limitless internal energy of life. It is neither. Evolution is a complex and intricate system of processes that has led life down many twisted paths to generate the various organisms we see today. As this essay has shown evolutionary biologists encounter significant complexity when they seek to understand the evolutionary story of life. The study of evolution is a rich field with plenty of conceptual avenues for study, not just fossil collecting. Recently the burst of knowledge and technology in molecular and developmental biology has given evolutionary biologists more tools to learn about previously hidden details affecting the evolutionary process. With these new tools, who knows what discoveries will be made in the future? ■

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Ashley J. R. Carter is a graduate student in the department of Ecology and Evolutionary Biology at Yale University. He is currently using theoretical and computer simulation models to study the role of genetic duplications in molecular evolution. Ashley would like to dedicate this article to the memory of an exceptional professor, Donna M. Carr.