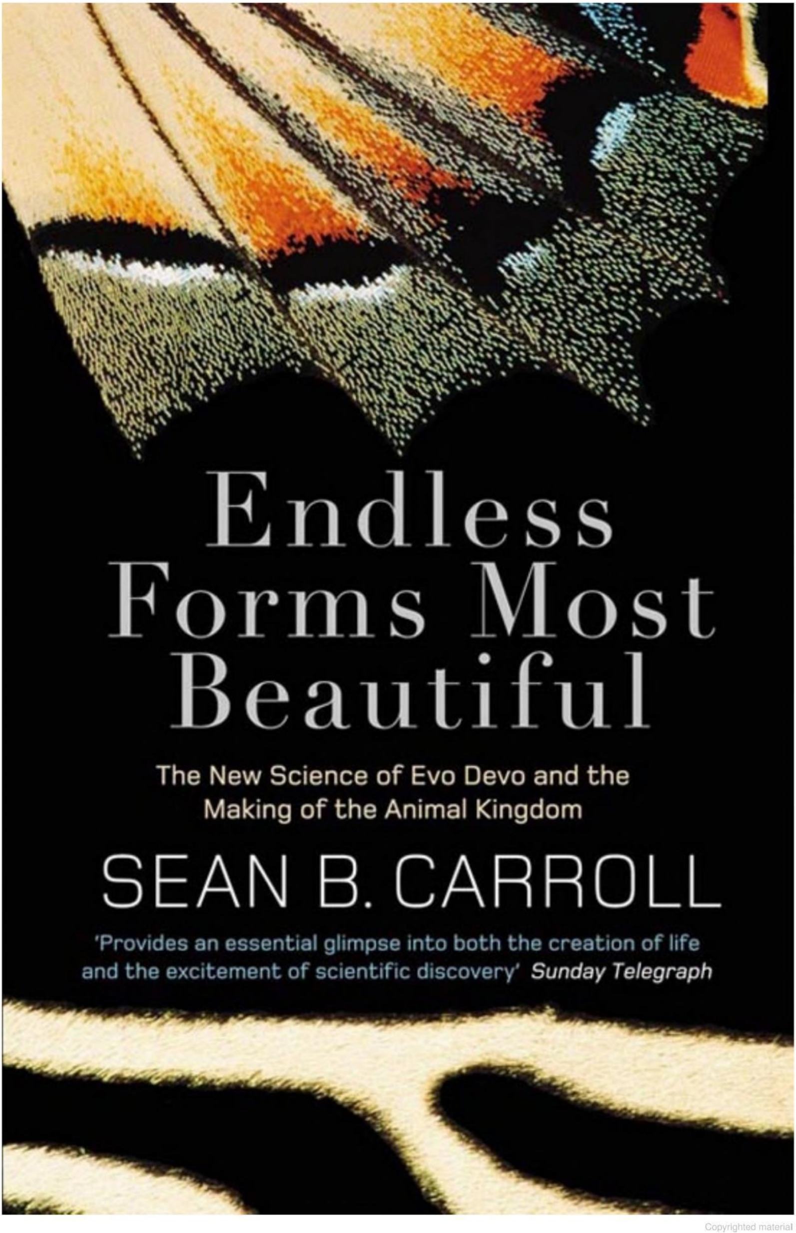
Endless Forms Most Beautiful
The New Science of Evo Devo and the Making of the Animal Kingdom
SEAN B. CARROLL
'Provides an essential glimpse into both the creation of life and the excitement of scientific discovery' Sunday Telegraph

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Preface
Revolution #3

> You say you want a revolution
> Well, you know
> we all want to change the world.
> You tell me that it's evolution,
> Well, you know
> we all want to change the world…
> You say you got a real solution
> Well, you know
> we'd all love to see the plan. …
>
> —John Lennon and Paul McCartney
> "Revolution 1" (1968)

THE PHYSICIST AND NOBEL laureate Jean Perrin once stated that the key to any scientific advance is to be able "to explain the complex visible by some simple invisible." The two greatest revolutions in biology, those in evolution and genetics, were driven by such insights. Darwin explained the parade of species in the fossil record and the diversity of living organisms as products of natural selection over eons of time. Molecular biology explained how the basis of heredity in all species is encoded in molecules of DNA made of just four basic constituents. As powerful as these insights were, in terms of explaining the origin of complex visible *forms,* from the bodies of ancient trilobites to the beaks of Galapagos finches, they were incomplete. Neither natural selection nor DNA directly explains *how* individual forms are made or how they evolved.

The key to understanding form is *development*, the process through which a single-celled egg gives rise to a complex, multi-billion-celled animal. This amazing spectacle stood as one of the great unsolved mysteries of biology for nearly two centuries. And development is intimately connected to evolution because it is through changes in embryos that changes in form arise. Over the past two decades, a new revolution has unfolded in biology. Advances in developmental biology and evolutionary developmental biology (dubbed "Evo Devo") have revealed a great deal about the invisible genes and some simple rules that shape animal form and evolution. Much of what we have learned has been so stunning and unexpected that it has profoundly reshaped our picture of how evolution works. Not a single biologist, for example, ever anticipated that the same genes that control the making of an insect's body and organs also control the making of our bodies.

This book tells the story of this new revolution and its insights into how the animal kingdom has evolved. My goal is to reveal a vivid picture of the process of making animals and how various kinds of changes in that process have molded the different kinds of animals we know today and those from the fossil record.

I wrote the book with several kinds of readers in mind. First, for anyone interested in nature and natural history who takes delight in animals of the rain forest, reef, savannah, or fossil beds, there will be much said about the making and evolution of some of the most fascinating animals of the past and present. Second, for physical scientists, engineers, computer scientists, and others interested in the origins of complexity, this book tells the story of the enormous diversity that has been created from combining a small number of common ingredients. Third, for students and educators, I firmly believe that the new insights from Evo Devo bring the evolutionary process alive and offer a more gripping and illuminating picture of evolution than has typically been taught and discussed. And fourth, for anyone who may ponder the question "Where did I come from?," this book is also about our history, both the journey we have all made from egg to adult, and the long trek from the origin of animals to the very recent origin of our species.

Endless Forms Most Beautiful

Drawing by Christopher Herr, age ten (Eagle School, Madison, Wisconsin)

Introduction
Butterflies, Zebras, and Embryos

> Well she's walking through the clouds
> With a circus mind that's running round
> Butterflies and zebras
> And moonbeams and fairy tales,
> That's all she ever thinks about. …
>
> —Jimi Hendrix,
> "Little Wing" (1967)

ON A RECENT VISIT to my kids' elementary school, I was enjoying the student art that decorated the hallways. Among the landscapes and portraits were many depictions of animals. I couldn't help noting that of the thousands of species to choose from, the most frequently drawn mammal was the zebra. And the most represented animal of any kind was the butterfly. We live in Wisconsin and, this being the middle of winter, the kids were not drawing what they saw out the window. So, why all the butterflies and zebras?

I am certain that these pieces of art reflect the children's deep connection to animal forms—their shapes, patterns, and colors. We all feel that connection. That's why we visit zoos to see exotic animals, flock to the new phenomenon of butterfly aviaries, go to aquaria, and spend billions on our animal companions—dogs, cats, birds, and even fish. We most often choose our favorite breeds and species on aesthetic grounds. Yet, we are also mesmerized, and sometimes terrified, by the more extreme animal forms: giant squids, carnivorous dinosaurs, or bird-eating spiders.

The same attraction to and fascination with animal forms has motivated the greatest naturalists for centuries. In cold, gray, damp pre-Victorian England, young Charles Darwin read Alexander von Humboldt's *Personal Narrative*, a 2000-page account of his voyage to and around South America. Darwin was so consumed that he later claimed that all he thought, spoke, or dreamt about were schemes to get to see the sights of the Tropics that Humboldt described. He leaped at the chance when the opportunity to sail on the *Beagle* arose in 1831. Darwin later wrote to Humboldt, "My whole course of life is due to having read and re-read as a youth, this personal narrative." Two other Englishmen, Henry Walter Bates, a twenty-two-year-old office clerk and avid bug collector, and his self-taught naturalist friend, Alfred Russel Wallace, also dreamt of travel abroad to collect new species. Upon reading an American's account of a journey to Brazil, Bates and Wallace immediately decided to head there (in 1848). Darwin's voyage lasted five years, Bates remained in the Tropics for eleven years, and Wallace spent fourteen years over the course of two journeys. These dreamers would, based upon the thousands of species that they saw and collected, launch the first revolution in biology.

There must be something about living in northern climates that inspires dreams of the Tropics. I grew up in Toledo, Ohio, surrounded by city parks and farm fields, near the shores of the less than bountiful Lake Erie. My dreams of paradise were fed by magazines and the TV show *Animal Kingdom* (broadcast in black and white). Decades later, I have been lucky enough to see the animals of the African savannah, the jungles of Central America, and the barrier reefs of Australia and Belize (as a tourist, not as a courageous explorer—trust me). And they are even more awe-inspiring than I had imagined.

On the open grasslands of Kenya, herds of zebras and elephants graze while solitary giraffes, ostriches, and cheetahs stroll by. Striped horses, gigantic gray mammals with six-foot-long noses, and spotted cats that can outrun a Jeep? If these creatures did not exist, they would be almost too incredible to believe.

In the rain forests, the richness is generally in smaller creatures. In the dappled light created by gaps in the canopy, brightly painted butterflies such as the red and yellow *Heliconius* or the sparkling metallic blue *Morpho* dance. In the litter below, red-and-turquoise-splotched poison arrow frogs call and vivid green leaf-cutter ants go about their vast harvesting projects. The big predators come out at night. I shall never forget the thrill of meeting a six-foot-long, deadly fer-de-lance snake in the pitch darkness and absolute quiet of a jungle in Belize, in a place well populated with jaguars (we saw only fresh tracks, but that was close enough!).

The sea holds even more strange and wonderful forms. Plunge into the shallow waters off an Australian coral island and the variety of fish, corals, and shelly creatures will literally hit you in the face. Neon colors, bodies of all shapes and sizes, fantastic geometrical designs are everywhere, and occasionally there’s a glimpse of a giant sea turtle, an octopus, or a darting shark.

The great variety in the size, shape, organization, and color of animal bodies raises deep questions about the origins of animal forms. How are individual forms generated? And how have such diverse forms evolved? These are very old questions in biology, which date back to the time of Darwin, Wallace, and Bates and before, but only very recently have deep answers been discovered, many of them so surprising and profound that they have revolutionized our views on the making of the animal world and our place in it. The initial inspiration for this story is the attraction we all share to animal form, but my aim is to expand that wonder and fascination to *how* form is created—that is, to our new understanding of the biological processes that generate pattern and diversity in animal design. Underlying the many visible elements of animal form are remarkable processes, beautiful in their own right in the way that they transform a tiny, single cell into a large, complex, highly organized, and patterned creature, and over time, have forged a kingdom of millions of individual designs.

Embryos and Evolution

The first approach naturalists took to dealing with the great variety of animals was to sort them into groups, such as vertebrates (including fish, amphibians, reptiles, birds, and mammals) and arthropods (insects, crustaceans, arachnids, and more), but between and within these groups there are many differences. What makes a fish different from a salamander? Or an insect from a spider? On a finer scale, clearly a leopard is a cat, but what makes it different from a domestic tabby? And closer to home, what makes us different from our chimpanzee cousins?

The key to answering such questions is to realize that every animal form is the product of two processes—development from an egg and evolution from its ancestors. To understand the origins of the multitude of animal forms, we must understand these two processes and their intimate relationship to each other. Simply put, development is the process that transforms an egg into a growing embryo and eventually an adult form. The evolution of form occurs through changes in development.

Both processes are breathtaking. Consider that the development of an entire complex creature begins with a single cell—the fertilized egg. In a matter of just a day (a fly maggot), a few weeks (a mouse), or several months (ourselves), an egg grows into millions, billions, or, in the case of humans, perhaps 10 trillion cells formed into organs, tissues, and parts of the body. There are few, if any, phenomena in nature that inspire our wonder and awe as much as the transformation from egg to embryo to the complete animal. One of the great figures in all of biology, Darwin's close ally Thomas H. Huxley, remarked:

> The student of Nature wonders the more and is astonished the less, the more conversant he becomes with her operations; but of all the perennial miracles she offers to his inspection, perhaps the most worthy of admiration is the development of a plant or of an animal from its embryo.
>
> *Aphorisms and Reflections* (1907)

The intimate connection between development and evolution has long been appreciated in biology. Both Darwin, in *The Origin of Species* (1859) and *The Descent of Man* (1871), and Huxley in his short masterpiece, *Evidence as to Man's Place in Nature* (1863), leaned heavily on the facts of embryology (as they were in the mid-nineteenth century) to connect man to the animal kingdom and for indisputable evidence of evolution. Darwin asked his reader to consider how slight changes, introduced at different points in the process and in different parts of the body, over the course of many thousands or a million generations, spanning perhaps tens of thousands to a few million years, can produce different forms that are adapted to different circumstances and that possess unique capabilities. That is evolution in a nutshell.

For Huxley, the nub of the argument was simple: we may marvel at the process of an egg becoming an adult, but we accept it as an everyday fact. It is merely then a lack of imagination to fail to grasp how changes in this process that are assimilated over long periods of time, far longer than the span of human experience, shape life's diversity. Evolution is as natural as development.

> As a natural process, of the same character as the development of a tree from its seed, or of a fowl from its egg, evolution excludes creation and all other kinds of supernatural intervention.
>
> *Aphorisms and Reflections* (1907)

While Darwin and Huxley were right about development as key to evolution, for more than one hundred years after their chief works, virtually no progress was made in understanding the mysteries of development. The puzzle of how a simple egg gives rise to a complete individual stood as one of the most elusive questions in all of biology. Many thought that development was hopelessly complex and would involve entirely different explanations for different types of animals. So frustrating was the enterprise that the study of embryology, heredity, and evolution, once intertwined at the core of biological thought a century ago, fractured into separate fields as each sought to define its own principles.

Because embryology was stalled for so long, it played no part in the so-called Modern Synthesis of evolutionary thought that emerged in the 1930s and 1940s. In the decades after Darwin, biologists struggled to understand the mechanisms of evolution. At the time of *The Origin of Species*, the mechanism for the inheritance of traits was not known. Gregor Mendel's work was rediscovered decades later and genetics did not prosper until well into the 1900s. Different kinds of biologists were approaching evolution at dramatically different scales. Paleontology focused on the largest time scales, the fossil record, and the evolution of higher taxa. Systematists were concerned with the nature of species and the process of speciation. Geneticists generally studied variation in traits in just a few species. These disciplines were disconnected and sometimes hostile over which offered the most worthwhile insights into evolutionary biology. Harmony was gradually approached through an integration of evolutionary viewpoints at different levels. Julian Huxley's book *Evolution: The Modern Synthesis* (1942) signaled this union and the general acceptance of two main ideas. First, that gradual evolution can be explained by small genetic changes that produce variation which is acted upon by natural selection. Second, that evolution at higher taxonomic levels and of greater magnitude can be explained by these same gradual evolutionary processes sustained over longer periods.

The Modern Synthesis established much of the foundation for how evolutionary biology has been discussed and taught for the past sixty years. However, despite the monikers of "Modern" and "Synthesis," it was incomplete. At the time of its formulation and until recently, we could say that forms do change, and that natural selection is a force, but we could say nothing about *how* forms change, about the visible drama of evolution as depicted, for example, in the fossil record. The Synthesis treated embryology as a "black box" that somehow transformed genetic information into three-dimensional, functional animals.

The stalemate continued for several decades. Embryology was preoccupied with phenomena that could be studied by manipulating the eggs and embryos of a few species, and the evolutionary framework faded from embryology's view. Evolutionary biology was studying genetic variation in populations, ignorant of the relationship between genes and form. Perhaps even worse, the perception of evolutionary biology in some circles was that it had become relegated to dusty museums.

Such was the setting in the 1970s when voices for the reunion of embryology and evolutionary biology made themselves heard. Most notable was that of Stephen Jay Gould, whose book *Ontogeny and Phylogeny* revived discussion of the ways in which the modification of development may influence evolution. Gould had also stirred up evolutionary biology when, with Niles Eldredge, he took a fresh look at the patterns of the fossil record and forwarded the idea of *punctuated equilibria*—that evolution was marked by long periods of stasis (equilibria) interrupted by brief intervals of rapid change (punctuation). Gould's book and his many subsequent writings reexamined the "big picture" in evolutionary biology and underscored the major questions that remained unsolved. He planted seeds in more than a few impressionable young scientists, myself included.

To me, and others who had been weaned on the emerging successes of molecular biology in explaining how genes work, the situations in embryology and in evolutionary biology were both unsatisfying, but they presented enormous potential opportunities. Our lack of embryological knowledge seemed to turn much of the discussion in evolutionary biology about the evolution of form into futile exercises in speculation. How could we make progress on questions involving the evolution of form without a scientific understanding of how form is generated in the first place? Population genetics had succeeded in establishing the principle that evolution is due to changes in genes, but this was a principle without an example. No gene that affected the form and evolution of any animal had been characterized. New insights in evolution would require breakthroughs in embryology.

The Evo Devo Revolution

Everyone knew that genes must be at the center of the mysteries of both development and evolution. Zebras look like zebras, butterflies look like butterflies, and we look like we do because of the genes we carry. The problem was that there were very few clues as to which genes mattered for the development of any animal.

The long drought in embryology was eventually broken by a few brilliant geneticists who, while working with the fruit fly, the workhorse of genetics for the past eighty years, devised schemes to find the genes that controlled fly development. The discovery of these genes and their study in the 1980s gave birth to an exciting new vista on development and revealed a logic and order underlying the generation of animal form.

Almost immediately after the first sets of fruit fly genes were characterized came a bombshell that triggered a new revolution in evolutionary biology. For more than a century, biologists had assumed that different types of animals were genetically constructed in completely different ways. The greater the disparity in animal form, the less (if anything) the development of two animals would have in common at the level of their genes. One of the architects of the Modern Synthesis, Ernst Mayr, had written that “the search for homologous genes is quite futile except in very close relatives.” But contrary to the expectations of *any* biologist, most of the genes first identified as governing major aspects of fruit fly body organization were found to have exact counterparts that did the same thing in most animals, including ourselves. This discovery was followed by the revelation that the development of various body parts such as eyes, limbs, and hearts, vastly different in structure among animals and long thought to have evolved in entirely different ways, was also governed by the same genes in different animals. The comparison of developmental genes between species became a new discipline at the interface of embryology and evolutionary biology—evolutionary developmental biology, or “Evo Devo” for short.

The first shots in the Evo Devo revolution revealed that despite their great differences in appearance and physiology, all complex animals—flies and flycatchers, dinosaurs and trilobites, butterflies and zebras and humans—share a common “tool kit” of “master” genes that govern the formation and patterning of their bodies and body parts. I’ll describe the discovery of this tool kit and the remarkable properties of these genes in detail in chapter 3. The important point to appreciate from the outset is that its discovery shattered our previous notions of animal relationships and of what made animals different, and opened up a whole new way of looking at evolution.

We now know from sequencing the entire DNA of species (their *genomes*) that not only do flies and humans share a large cohort of developmental genes, but that mice and humans have virtually identical sets of about 29,000 genes, and that chimps and humans are nearly 99 percent identical at the DNA level. These facts and figures should be humbling to those who wish to hold humans above the animal world and not an evolved part of it. I wish the view I heard expressed by Lewis Black, the stand-up comedian, was more widely shared. He said he won’t even debate evolution’s detractors because “we’ve got the fossils. We win.” Well put, Mr. Black, but there is far more to rely on than just fossils.

Indeed, the new facts and insights from embryology and Evo Devo devastate lingering remnants of stale anti-evolution rhetoric about the utility of intermediate forms or the probability of evolving complex structures. We now understand how complexity is constructed from a single cell into a whole animal. And we can see, with an entirely new set of powerful methods, how modifications of development increase complexity and expand diversity. The discovery of the ancient genetic tool kit is irrefutable evidence of the descent and modification of animals, including humans, from a simple common ancestor. Evo Devo can trace the modifications of structures through vast periods of evolutionary time —to *see* how fish fins were modified into limbs in terrestrial vertebrates, how successive rounds of innovation and modification crafted mouthparts, poison claws, swimming and feeding appendages, gills, and wings from a simple tubelike walking leg, and how many kinds of eyes have been constructed beginning with a collection of photosensitive cells. The wealth of new data from Evo Devo paints a vivid picture of how animal forms are made and evolve.

The Tool Kit Paradox and the Origins of Diversity

The stories of shared body-building genes and of the similarities of our genome to that of other animals have slowly been gaining in public awareness. What is generally neglected, however, is how the discovery of this common tool kit and of great similarities among different species' genomes presents an apparent paradox. If the sets of genes are so widely shared, how do differences arise? The resolution of this paradox and its implications are central to my story. The paradox of great genetic similarity among diverse species is resolved by two key ideas that I will develop in the course of the book and will return to repeatedly. These concepts are crucial for understanding how the species-specific instructions for building an animal are encoded in its DNA and how form is generated and evolves. The substance of these ideas has received scant, if any, attention in the general press, but these ideas have profound implications for understanding great episodes in life's history, such as the explosion of animal forms during the Cambrian period, the evolution of diversity within groups such as butterflies or beetles or finches, and our evolution from a common ancestor with chimps and gorillas.

The first idea is that diversity is not so much a matter of the complement of genes in an animal's tool kit, but, in the words of Eric Clapton, "it's in the way that you use it." The development of form depends upon the turning on and off of genes at different times and places in the course of development. Differences in form arise from evolutionary changes in where and when genes are used, especially those genes that affect the number, shape, or size of a structure. We will see that there are many ways to change how genes are used and that this has created tremendous variety in body designs and the patterning of individual structures.

The second idea concerns where in the genome the “smoking guns” for the evolution in form are found. It turns out that it is not where we have been spending most of our time for the past forty years. It has long been understood that genes are made up of long stretches of DNA that are decoded by a universal process to produce proteins, which do the actual work in animal cells and bodies. The genetic code for proteins, a twenty-word vocabulary, has been known for forty years, and it is easy for us to decode DNA sequences into protein sequences. What is much less appreciated is that only a tiny fraction of our DNA, just about 1.5 percent, codes for the roughly 25,000 proteins in our bodies. So what else is there in the vast amount of our DNA? Around 3 percent of it, made up of about 100 million individual bits, is *regulatory*. This DNA determines when, where, and how much of a gene’s product is made. I will describe how regulatory DNA is organized into fantastic little devices that integrate information about position in the embryo and the time of development. The output of these devices is ultimately transformed into pieces of anatomy that make up animal forms. This regulatory DNA contains the instructions for building anatomy, and evolutionary changes within this regulatory DNA lead to the diversity of form.

In order to understand the role and significance of regulatory DNA in evolution, I have some ground to cover. One must first appreciate how animals are constructed and the roles of genes in embryonic development. This will form the first half of the book and it holds many rewards in its own right. I will illustrate some general features of animal architecture and trends in the evolution of body design that are shared among different groups of animals (chapter 1). I will describe some of the spectacular mutant forms that led biologists to the tool kit of master genes that regulate development (chapters 2 and 3). We will see these genes in action and how they reflect the logic of and order to the building of animal bodies and complex patterns (chapter 4). And we will learn about the devices in the genome that contain the instructions for building anatomy (chapter 5).

In the second half of the book, I will tie together what we know about fossils, genes, and embryos in the making of animal diversity. I will highlight some of the most important, interesting, or compelling episodes in animal evolution that illustrate how nature has forged many individual designs from a small number of building blocks. I will examine in depth the genetic and developmental foundations of the Cambrian Explosion that produced many of the basic types of animals and body parts we know today (chapters 6 and 7). I will probe into the origins of butterfly wing patterns as splendid examples of how nature invents by teaching very old genes new tricks (chapter 8). I will tell some stories about the evolution of the plumage of island birds and the coat colors on mammals (chapter 9). These are all very satisfying, aesthetically pleasing tales that provide deep insights into the evolutionary process. But they have more direct ramifications, for they are the case studies that reveal the very kinds of processes that shaped human origins. In the final chapters of the book, I will describe the making of our species, most notable for its "beautiful mind" more than any other physical trait (chapter 10). I will trace our beginning from an apelike ancestor 6 million years ago to track the physical and developmental changes that led to *Homo sapiens*. I will discuss the scope and types of genetic changes that have occurred in the course of our evolution and those that are most likely to account for the evolution of traits we most associate with being human.

The Grandeur in a More Modern Synthesis: Act III

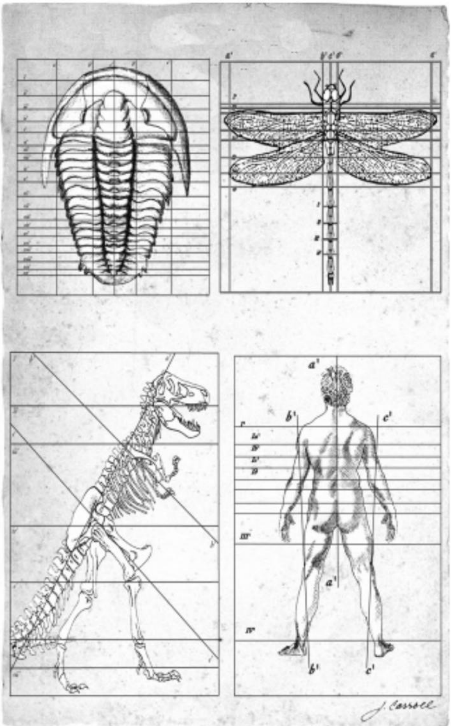
The continuing story of evolution may be thought of as a drama in at least three acts. In Act I, almost 150 years ago, Darwin closed the most important book in the history of biology by urging his readers to see the grandeur in his new vision of nature—in how, "from so simple a beginning, endless forms most beautiful have been, and are being, evolved." In Act II, the architects of the Modern Synthesis unified at least three disciplines to forge a grand synthesis. Here in Act III, there is also a special grandeur in the view embryology and evolutionary developmental biology provide into the making of animal form and diversity. Part of it is visual, in that we can now see how the endless forms of different animals actually take shape.

But beauty, in science, is much more than skin-deep. The best science is an integrated product of our emotional and intellectual sides, a synthesis between what is often referred to as our "left" brain (reasoning) and "right" brain (emotional/artistic) hemispheres. The greatest "eurekas" in science combine both sensual aesthetics and conceptual insight. The physicist Victor Weisskopf (also a pianist) noted, "What is beautiful in science is the same thing that is beautiful in Beethoven. There's a fog of events and suddenly you see a connection. It expresses a complex of human concerns that goes deeply to you, that connects things that were always in you that were never put together before."

In short, the best science offers the same kind of experience as the best books or films do. A mystery or drama engages us, and we follow a story toward some revelation that, in the very best examples, makes us see and understand the world more clearly. The scientist's main constraint is the truth. Can the nonfiction world of science inspire and delight us as much as the imagined world of fiction?

One hundred years ago, Rudyard Kipling published his classic *Just So Stories*, a collection of children's tales inspired by his experiences in India. Kipling's enchanting stories ranged from "How the Leopard Got His Spots" and "How the Camel Got His Hump" to "The Butterfly That Stamped," and wove fanciful tales of how some of our favorite and most unusual creatures acquired prominent features. As delightful as the *Just So* explanations are of how spots, stripes, humps, and horns came to be, biology can now tell stories about butterflies, zebras, and leopards that I contend are every bit as enchanting as Kipling's fairy tales. What's more, they offer some simple, elegant truths that deepen our understanding of all animal forms, including ourselves.

Part I The Making of Animals



Animal architectures, modern and ancient. JAME CARROLL.

1 Animal Architecture: Modern Forms, Ancient Designs

> It is the mystery and beauty of organic form
> that sets the problem for us.
>
> —Ross Harrison, embryologist (1913)

THE AMAZING VARIETY of animal forms does not end with those on land or in the sea. Belowground, buried in as little as a few inches of sand or up to several thousand feet of rock, is the story of 600 million years of animal history—from the enigmatic forms of early animals in Canadian shale, to the enormous bodies of dinosaurs in the buttes and valleys of the American West, and the teeth and skull fragments of our bipedal ancestors in the Rift Valley of east Africa. And some of what lies below the ground can be quite surprising given what breathes just above.

I learned this firsthand only recently in, of all places, Florida, a favorite destination for vacationers and retirees seeking sun, entertainment, and relaxation. It is a land of palm trees, soft sandy beaches, graceful pelicans and ospreys, gentle manatees and dolphins, and *Homo sapiens* in plaid pants … but also of six-foot-long armadillos, tusked mastodons, sixty-foot-long sharks, camels, rhinoceroses, jaguars, and saber-toothed cats?

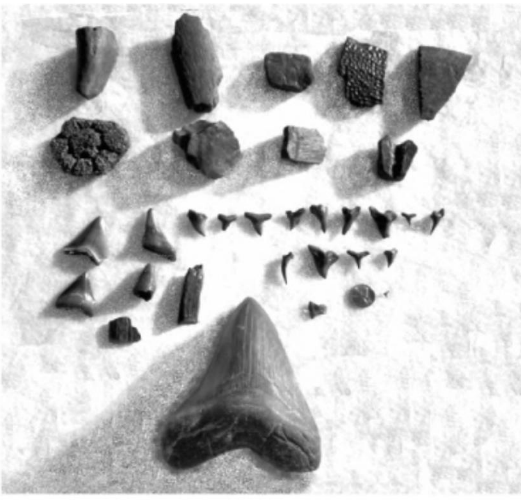


FIG. 1.1 **Fossils from a Florida riverbed**. Mammal bone, turtle shell fragments, and shark teeth abound. Note the variety of shapes and sizes. The largest tooth is from the enormous shark *Charcharadon megalodon*. FOSSILS COLLECTED AND PHOTOGRAPHED BY PATRICK CARROLL

Yes, indeed. Well, it depends on where you look.

Journey inland to a river cutting through the sandy soil and a shovel of gravel from the riverbed might contain teeth from any of ten species of shark, from the intricately serrated and curved snaggletooth, to the absolutely terrifying six-inch flesh rippers of the long extinct behemoth *Charcharadon megalodon* (figure 1.1). In the same gravel there will also be bones of Florida's geologically recent past—of tapirs, sloths, camels, horses, glyptodonts, mastodons, dugongs, and other species now vanished.

The diversity of living and fossil animal forms in just this one locale frames the two central mysteries at hand: How are individual forms made? And, how have so many different forms evolved?

At first, the variety of animal forms may seem overwhelming. But there are some general, long established trends in animal design that we can make sense of. In this chapter, we'll search for some generalities in animal architecture and evolution that will help us reduce this mind-boggling diversity to some basic themes.

The Construction of Animals from Building Blocks

A basic theme of animal design becomes obvious when one tries to figure out just what bone or tooth one has found in that shovelful of Florida river gravel. The challenge of the game is both to match the fossil to a species, and also to determine where in the animal it belonged. Why is this so hard? This is one demonstration of a basic fact of animal design. Related animals, such as vertebrates, are made up of very similar parts.

Now say, with a bit of expert help, one is able to figure out that a piece of bone is from a dugong (an extinct sea cow). But if it is a rib, which rib? Or, if a toe bone is from an extinct horse, which toe is it? From individual bones, it is really difficult to tell. Why this is the case punctuates a second basic fact of animal design—that individual animals are made up of numbers of the same kinds of parts, like building blocks.

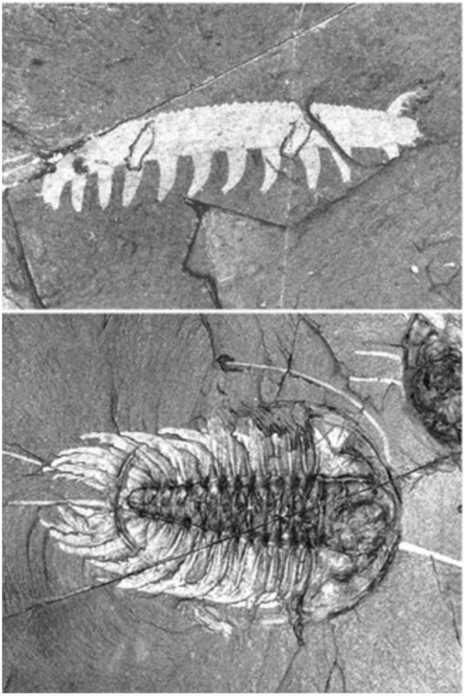


FIG. 1.3 **The modular architecture of Cambrian animals**. The lobopodian *Ayshaeia pedunculata* (above) and trilobite *Olenoides serratus* (below) display repetitively organized, modular body forms. PHOTOS COURTESY OF CHIP CLARK, SMITHSONIAN INSTITUTION

FIG. 1.4 **The modular design of a human hand**. The finger bones revealed by an × ray display a serially reiterated architecture. COURTESY OF JAMIE CARROLL

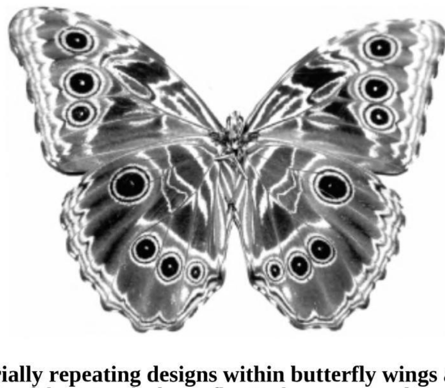


FIG. 1.5 **Serially repeating designs within butterfly wings** are shown in the underside of this *Morpho* butterfly. Each wing is made up of serially reiterated subunits demarcated by two veins and the wing edge. Each subunit contains variations of the same elements—eyespots, bands, and

chevrons. BUTTERFLY GIFT OF NIPAM PATEL, PHOTO BY JAMIE CARROLL

From just these few descriptions, we can begin to appreciate the immense task of development—to build large, complex animals beginning with only a tiny single cell. There are millions of details, and the details count. A small shift in an early process would have a cascade of later effects. What processes can assemble both a massive dinosaur and paint the delicate details of a spot on a butterfly?

Given such enormous differences in scale, and such great variety in animal forms, it would seem that the details of development would present what molecular biologist Gunther Stent described only twenty years ago as "a near infinitude of particulars which have to be sorted out case by case." But biologists have been surprised and delighted to find there are generalities we can make about form and, fortunately, these generalities also extend far more deeply than outward appearances, into the genetic machinery of development. I'll start with the outward similarities here and work my way down to the genes that do the job in the next two chapters.

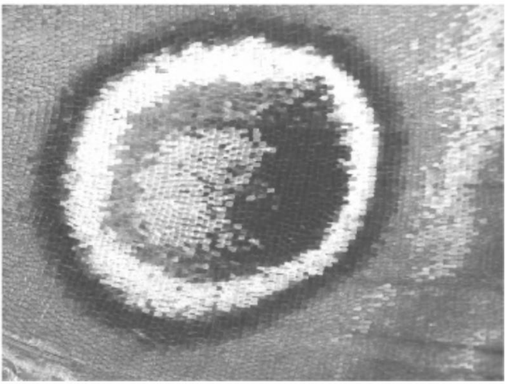


FIG. 1.6 **Repetition on a fine scale**. The scales of a butterfly wing are like the strokes of a pointillist painting, each stroke being a single scale of a particular color; collectively they form geometric pattern elements. PHOTO BY STEVE PADDOCK

Evolution as Variations in Number and Kind

The modular and repetitive aspects of animal design reflect an order to animal forms. Anatomists have long appreciated that no matter how diverse their outward appearance, animal bodies and their parts are constructed along some perceivable themes. More than a century ago, some of these themes were formally defined by the English biologist William Bateson. His perspective turns out to be a very helpful framework for thinking about the logic of animal design and understanding how variations on basic themes evolve.

Bateson recognized that many large animals were constructed of repeated parts, and many body parts themselves were constructed of repeated units. In considering particular groups of animals, it appeared that some of the most obvious difference between members of a group were in the *number* and *kind* of repeated structures. For example, while all vertebrates have a modularly constructed backbone made up of individual vertebrae, different vertebrates possess different numbers and kinds of vertebrae. The number of vertebrae from head to tail differs greatly, from fewer than a dozen in frogs, to thirty-three in humans, and up to a few hundred in a snake (figure 1.7). There are also different kinds of vertebrae such as cervical (neck), thoracic, lumbar, sacral, and caudal (tail) vertebrae. The main differences between these types in any one animal are their size and shape and the presence or absence of structures attached to them, such as ribs. There is great diversity in the number of each type in different vertebrates.

A similar pattern applies to arthropod form and diversity. Arthropod bodies are made up of repeating segments, which in the trunk (behind the head) may vary from about eleven segments in insects to dozens in centipedes and millipedes. Groups of segments are distinguished from one another (e.g., the thoracic and abdominal segments) by their size and shape and especially by the appendages that project from them (e.g., the thoracic segments in insects each bear a pair of legs while the abdominal segments do not).

These two groups of animals have successfully exploited every environment on earth (water, land, and air) and are the most complex animals in terms of anatomy and behavior. Both groups are constructed of repeated assemblages of similar parts. Is there a connection between modularity of design and the success in evolutionary diversification? I certainly think so. The challenge for biologists has been to figure out how these animals are built, beginning from just a single cell, and how all sorts of variations on a body design evolve. The modular construction of vertebrates and arthropods, and their variation in the number and kinds of modules, are important clues to the processes involved.

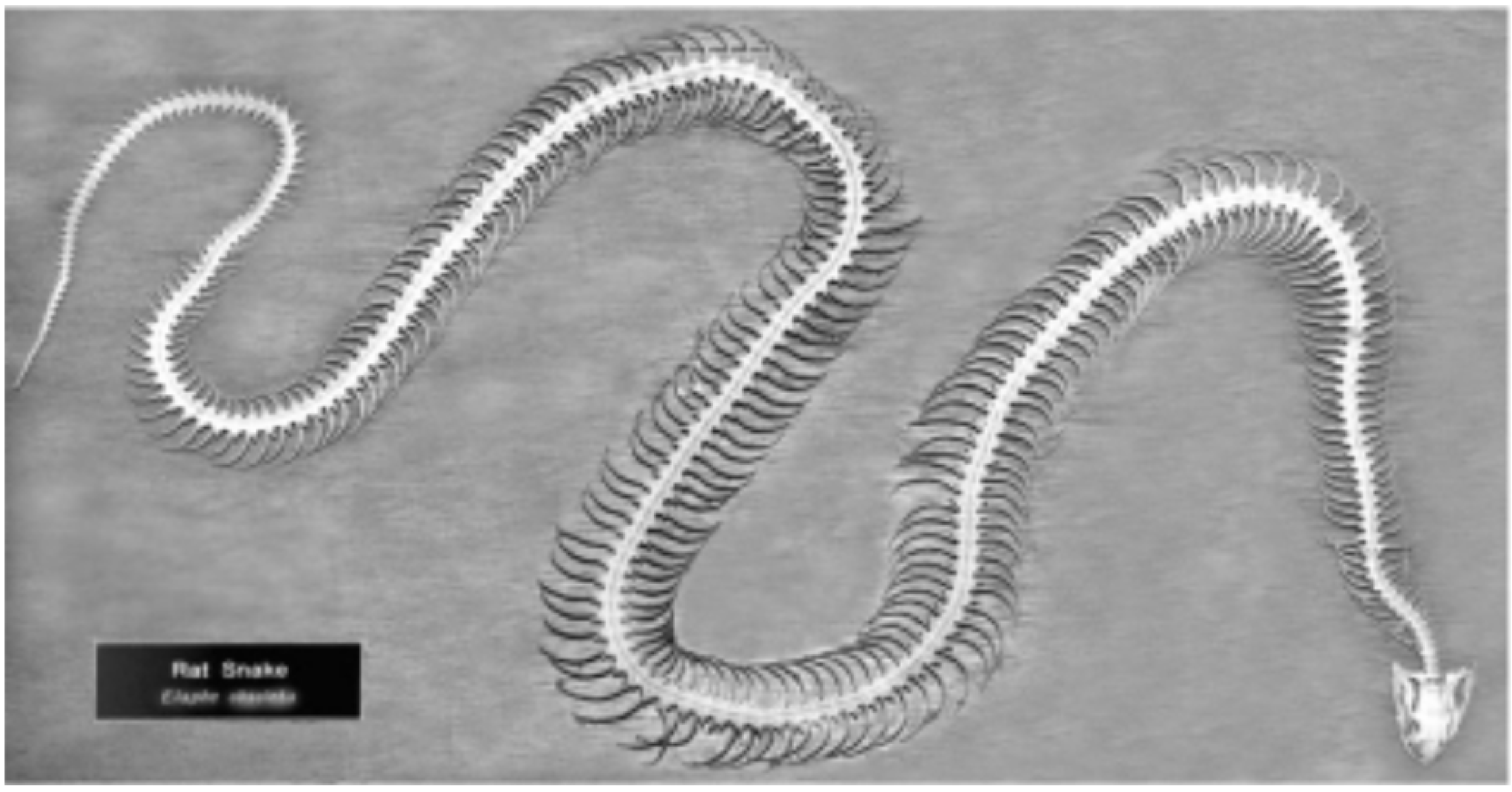


FIG. 1.7 **Snake skeleton**. Hundreds of repeating vertebrae and ribs make up the snake body form. COURTESY OF DR. KURT SLADKY, UNIVERSITY OF WISCONSIN

Body parts that are often modular and constructed of similar units often differ between species largely in number and kind. The limbs of four-legged vertebrates (tetrapods) usually bear one to five digits. We recognize five distinct types of digits on our own hands (thumb, forefinger, etc.) and feet. The similarities among digits are obvious, the differences largely a matter of size and shape. The tetrapod limb has been adapted to many functions in a great variety of designs, and the basic five-digit design has persisted for more than 350 million years, although digit number has evolved extensively such that anywhere from one to five digits may be present (for example, camels have two toes, rhinos have three, etc.). The variations on the tetrapod theme are spectacular, as a sample of × rays among vertebrates highlights (figure 1.8). Interestingly, closely related animals can differ widely; some groups have evolved many species that differ from one another in digit number.

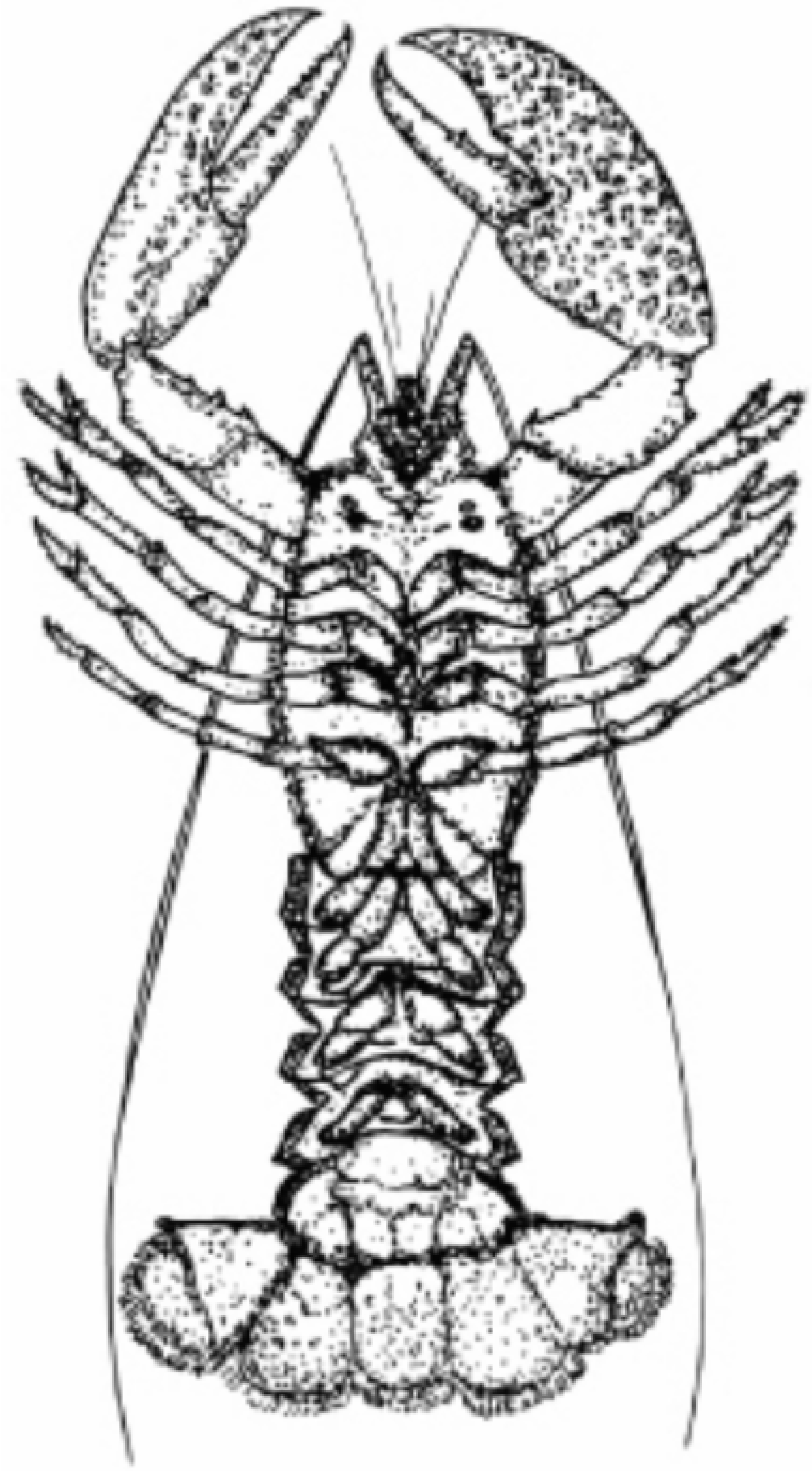


FIG. 1.9 **The diversity of the serially repeated appendages of a lobster**. The antennae, claws, walking legs, swimmerets, and tail structures are all modifications of a common limb design. DRAWING BY JAMIE CARROLL

A second example of serially homologous parts would be the teeth you used to mince and crush that lobster. Our jaws host a variety of teeth (canines, premolars, incisors, molars, etc.). Again, one of the obvious differences among all sorts of vertebrates are the number and kind of teeth. Primitive reptiles, like great marine forms, had a mouth full of mostly similar teeth, but later species evolved different kinds of teeth, adapted for biting, tearing, and compacting food. The differences in dental hardware reflect differences in diet, with carnivores bearing incisors and canines and grazers bearing mostly molars (figure 1.10). We differ from our primate relatives in our dentition (figure 1.11). You may be aware that teeth make hardy fossils and such finds have played a major role in deciphering the identity and lifestyle of our ancestors.

The evolutionary trends in the number and kinds of repeated structures are so pronounced that the paleontologist Samuel Williston declared in 1914, "it is [also] a law in evolution that the parts in an organism tend toward reduction in number, with the fewer parts greatly specialized in function." Williston was studying ancient marine reptiles. He noted that in the course of evolution, earlier groups tended to have large numbers of similar serially reiterated parts, but that later groups exhibited reduced numbers and specialized forms of these structures. Furthermore, the specialized pattern rarely reverted to the more general form. One interesting case is that when digits first evolved in tetrapods, there were as many as eight digits per foot. But among these eight, there were no more than five types, which eventually reduced to five digits that were specialized, or further reduced, in later species. Laws in biology are few, and those dared to be articulated are almost certain to be broken by some organisms. Yet Williston's Law is a useful observation that seems to pertain to trends in more than just the ancient marine reptiles he was writing about. The trend appears to be that once expanded in number, serial homologs became specialized in function and reduced in number. The specialization of vertebral, tooth, and digit morphology in vertebrates, and of legs and wings in arthropods, was in fact generally accompanied by a reduction in the number of these repeated structures. Williston and Bateson appear to have captured some simple truths about animal design and evolution, allowing us to boil down the vast history and variety of some of the largest and most diverse groups into some generalities.

FIG. 1.10 **Teeth in a primitive vertebrate**. In mosasaurs (bottom), all teeth appear mostly similar, whereas later vertebrates (top; here a horse) had teeth of distinct types. RECONSTRUCTION OF *PLATECARPUS PLAIFRONS* COURTESY OF MIKE EVERHART, OCEANS OF KANSAS

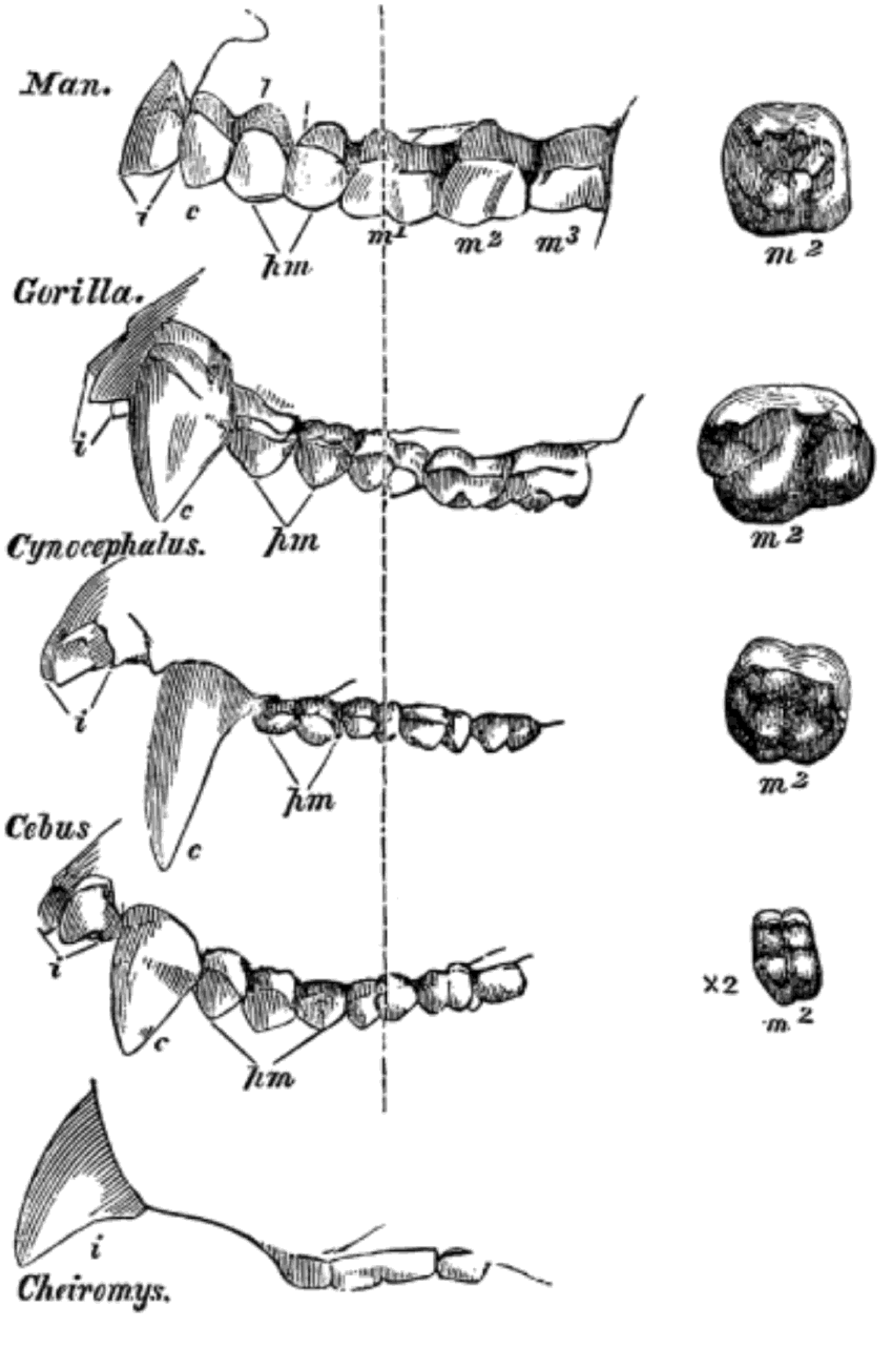


FIG. 1.11 **The diversity of primate dental hardware**. Primates differ in the number and shape of canine, premolar, and molar teeth. FROM T. H. HUXLEY, *MAN'S PLACE IN NATURE* (1863)

Symmetry and Polarity

In addition to the repetition of modular parts, animal bodies and body parts usually display two additional features—*symmetry* and *polarity*. Most familiar animals are bilaterally symmetrical in that they have matching right and left sides with a central axis of symmetry running down the middle of the long axis of the body. This design also imposes a front/rear orientation to animals and has enabled the evolution of many efficient modes of locomotion. Some animals exhibit other symmetries, such as the pentaradial (five-fold) echinoderms, a group including sea urchins, sand dollars, and a spectacular variety of other species (figure 1.12). The axes of symmetry in an animal are clues to how the animal is built.

So, too, is the polarity of an animal and its parts. In most animals there are three axes of polarity: head to tail, top to bottom (back and front in ourselves, since we stand up), and near to far from the body (in reference to structures that project from the main body—such as a limb whose parts are organized perpendicular to the main body). Individual structures also have polarity. Think of the hand, which has three axes oriented by the thumb to pinkie, back to palm, and wrist to fingertip directions.

How Is Form Encoded in the Genome?

Modularity, symmetry, and polarity are nearly universal features of animal design, certainly of larger, more complex animals such as butterflies and zebras. These features and the evolutionary trends noted by Williston and Bateson suggest that there is order and logic to animal architectures. They suggest that underneath the great variety of animal forms, there are some general "rules" to be discovered about how animals are built and evolve.

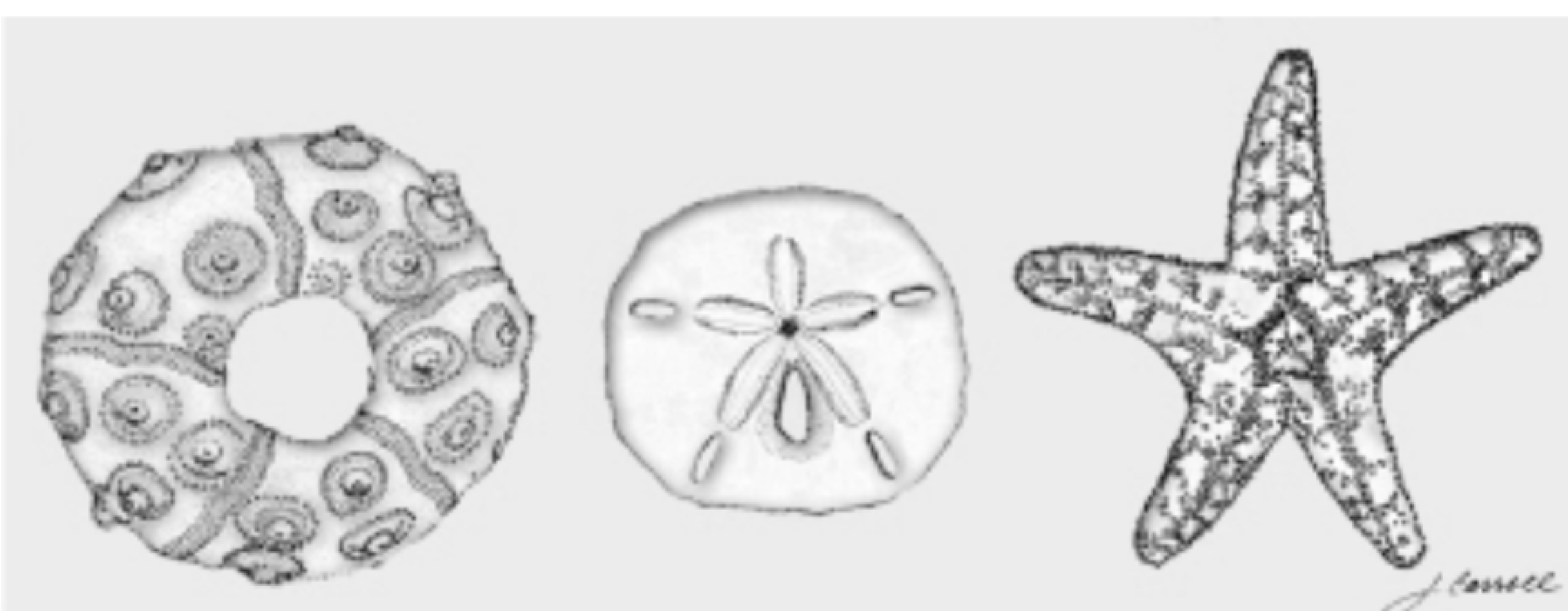


FIG. 1.12 **Other symmetrical animal forms**. Echinoderms such as sea urchins (left), sand dollars (center), and starfish (right) are radially symmetrical. DRAWING BY JAMIE CARROLL

In the course of this book, I will focus on four main questions:

1. What are some of the major "rules" for generating animal form?
2. How is the species-specific information for building a particular animal encoded?