How the Snake Lost its Legs

Curious Tales from the Frontier of Evo-Devo

How did the zebra really get its stripes, and the giraffe its long neck? What is the science behind camel humps, leopard spots, and other animal oddities? Such questions have fascinated us for centuries, but the expanding field of evo-devo (evolutionary developmental biology) is now providing, for the first time, a wealth of insights and answers.

Taking inspiration from Kipling’s Just So Stories, this book weaves emerging insights from evo-devo into a narrative that provides startling explanations for the origin and evolution of traits across the animal kingdom. The author’s unique and engaging style makes this narrative both enlightening and entertaining, guiding students and researchers through even complex concepts and encouraging a fuller understanding of the latest developments in the field. The first five chapters cover the first bilaterally symmetric animals, flies, butterflies, snakes, and cheetahs. A final chapter surveys recent results about a menagerie of other animals.

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Legless or partially legless lizards, some of which resemble snakes to a remarkable extent. Numbers next to legs in each panel (and in parentheses in this legend) are the number of digits per foreleg or hindleg respectively if present. (a) *Lerista dorsalis* (4+4). (b) *Hemiergis decresiensis* (3+3). (c) *Lerista desertorum* (2+3). (d) *Lerista timida* (3+3). (e) *Lerista edwardsae* (0+2). (f) *Anomalopus verreauxii* (3+1). (g) *Ophioscincus truncatus* (0+0). (h) *Pygopus lepidopodus* (0+0). Leg loss is common among lizards and may have occurred for the same reason as leg loss in snakes. All photographs were taken by Mark Hutchinson, South Australia Museum, Adelaide, and are used by permission. For color plate see color section.
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# Contents

**Preface**  
ix  

1  The first two-sided animal  
Why the chordate flipped upside down  
3  
What the urbilaterian looked like  
6  
How the urbilaterian got its symmetry  
11  

2  The fly  
How the fly got its gyroscopes  
15  
How the fly tattooed its arms  
24  
Why the fly twirls his penis  
34  

3  The butterfly  
How the butterfly got its scales  
43  
How the butterfly got its spots  
46  
How the swallowtail got its tail  
60  
How the caterpillar got its hindlegs  
63  
How insects lost their hindlegs  
69  
How insects got their wings  
70  

4  The snake  
How the snake lost its legs  
75  
How the snake elongated its body  
81  
How the snake rebuilt its eyes  
85  
How the snake got its (forked) tongue  
89  
How the snake got its fangs  
91  

5  The cheetah  
Why animals decorate their skin  
95  
How animals decorate their skin  
95  
How the angelfish got its stripes  
100
<table>
<thead>
<tr>
<th>Contents</th>
</tr>
</thead>
<tbody>
<tr>
<td>How the zebrafish got its stripes</td>
</tr>
<tr>
<td>How the zebra got its stripes</td>
</tr>
<tr>
<td>How the cheetah got its spots</td>
</tr>
<tr>
<td>How the mouse makes waves</td>
</tr>
<tr>
<td>How the clouded leopard makes clouds</td>
</tr>
</tbody>
</table>

6 An evo-devo bestiary

<table>
<thead>
<tr>
<th>Contents</th>
</tr>
</thead>
<tbody>
<tr>
<td>How the ant lost its wings</td>
</tr>
<tr>
<td>How the ape lost its tail</td>
</tr>
<tr>
<td>How the bat got its wings</td>
</tr>
<tr>
<td>How the bee got its pollen basket</td>
</tr>
<tr>
<td>How the beetle got its horns</td>
</tr>
<tr>
<td>How the bird got its beak and lost its teeth</td>
</tr>
<tr>
<td>How the camel got its hump</td>
</tr>
<tr>
<td>Why the centipede has odd segments</td>
</tr>
<tr>
<td>How the crocodile got its (facial) scales</td>
</tr>
<tr>
<td>How the deer regrows his antlers</td>
</tr>
<tr>
<td>How the duck got its bill</td>
</tr>
<tr>
<td>How the duck-billed platypus got its bill</td>
</tr>
<tr>
<td>How the echinoderm got its pentamery</td>
</tr>
<tr>
<td>How the elephant got six toes</td>
</tr>
<tr>
<td>How the firefly got its flashlight</td>
</tr>
<tr>
<td>How the flatfish got its (funny) face</td>
</tr>
<tr>
<td>How the frog got its (jumping) legs</td>
</tr>
<tr>
<td>How the giraffe stretched its neck</td>
</tr>
<tr>
<td>How the horse got its hooves</td>
</tr>
<tr>
<td>How the insect got its (stiff) upper lip</td>
</tr>
<tr>
<td>How the jerboa got its (jumping) hindlegs</td>
</tr>
<tr>
<td>How the kiwi almost lost its eyes</td>
</tr>
<tr>
<td>How the ladybird got its elytra</td>
</tr>
<tr>
<td>How the lion got his mane</td>
</tr>
<tr>
<td>How the manatee lost its hindlegs</td>
</tr>
<tr>
<td>How the newt regrows its legs</td>
</tr>
<tr>
<td>How the octopus got its arms</td>
</tr>
<tr>
<td>How the pterosaur got its wings</td>
</tr>
<tr>
<td>How the quagga lost its hind stripes</td>
</tr>
<tr>
<td>How the quetzal got its crest</td>
</tr>
<tr>
<td>Why the quoll kills its babies</td>
</tr>
<tr>
<td>How the remora got its sucker</td>
</tr>
<tr>
<td>How the rhinoceros got its horn</td>
</tr>
<tr>
<td>How the rodent got its incisors</td>
</tr>
<tr>
<td>How the sabertooth cat got its canines</td>
</tr>
<tr>
<td>How the seahorse got its shape</td>
</tr>
</tbody>
</table>
Contents

How the stalk-eyed fly got its stalks 136
How the stickleback lost its pelvic spines 137
How the swordtail got his sword 137
How tetrapods got their toes 138
How the tiger makes its stripes 138
How the treehopper got its helmet 139
How the turtle got its shell 140
How the uakari went bald 140
How the unicorn got its tusk 141
How the vampire bat reinvented running 143
How the whale got its flippers 144
How the xenarthran stretched its neck 144
How the yeti lobster got its mittens 145
How the zebu got its dewlap 146

Epilogue 147
Glossary 149
References 157
Index 279

Color plate section appears between pages 112 and 113.
Preface

The most famous accounts of animal origins in Western literature are those of Rudyard Kipling (1865–1936). His *Just So Stories* (1902) offered fabulous tales about how the leopard got its spots, how the elephant got its trunk, and so forth. It remains one of the most popular children’s books of all time.

Fables certainly make good bedtime stories, but they are poor substitutes for real understanding. The foundations for modern biology were forged by Charles Darwin (1809–1882) in his *Origin of Species* (1859). Ever since, scientists have been amassing facts about how animal traits arose. Initially, the data came from fossils, embryos, and anatomy. Then, in the first half of the twentieth century, genetics merged with evolution to reveal the causes behind the changes [1420].

Development flirted with evolution for more than a century [46] before their union was consummated around the time of Stephen Jay Gould’s *Ontogeny and Phylogeny* (1977) [828,2311]. Their scion was named “evo-devo” [1599]. Evo-devo initially relied on only a few model organisms [2088], including the fly, the worm, and the mouse. The genetic circuitry of these animals turned out to be surprisingly universal, despite their superficial differences [955].

In 1998 the first animal genome was sequenced – the nematode *Caenorhabditis elegans* [1] – followed in 2000 by flies and humans [81], and more genomes have been added at an increasing pace with each passing year [317]. As pieces of the evo-devo puzzle have come together, various authors have attempted to convey the “big picture” to the general public [1488]. Most notable are Sean Carroll’s *Endless Forms Most Beautiful* [339] and his more advanced *From DNA to Diversity* [344]. Sean’s books would make good primers for anyone who is not already well versed in genetics.

The genome of each species can be thought of as a kind of cookbook for concocting an adult anatomy, starting in most cases with a single fertilized egg. It is also a history book, because it retains remnants of recipes that were previously used by the organism’s ancestors. If we could read all those recipes, then we could decipher development and retrace evolution. Decoding DNA beyond the protein level is hard, however, because genes interact in complex ways [116].

*How the Snake Lost its Legs* was written at the behest of Martin Griffiths, Life Sciences Commissioning Editor at Cambridge University Press. Originally, he had in mind a book along the lines of Wallace Arthur’s majestic *Evolution: A Developmental Approach* (2011) [75]. When I balked at the idea of writing a textbook per se, Martin relented, and we agreed on a more casual format where readers could sample whatever
topics caught their fancy. My aim was to blend Darwin’s rigor with Kipling’s whimsy into a book that could amuse the darling child in all of us. The final product is hence an homage to both *Just So Stories* and *Origin of Species*. It celebrates animal oddities through facts rather than fables.

Truth can be stranger than fiction, and evo-devo is a case in point. Evo-devo defies our intuition in the same way that magicians amaze children by appearing to turn one thing into another.

Once upon a time, for example, snakes really did walk like lizards [2395], whales really did waddle like hippos [1790], and dolphins may have pranced like antelopes [2195], given how they swim as if they were galloping [505]. Relics of these marvels can be seen in their respective embryos, and traces of these transitions can be gleaned from their respective genomes [503]. Researchers around the world have been excavating such insights at an increasing pace, and the impetus to share them with the wider world outside our ivory towers has become almost irresistible. Hence this book.

Chapter 1 introduces concepts that readers will need in order to navigate the rest of the book. It traces key genes and cellular signals back to the common ancestor of all bilaterally symmetric animals. Chapter 2 provides a primer on gene circuitry using the animal whose genetics we know the best – the fruit fly [965]. Chapter 3 examines how some of these circuits arose during evolution and were co-opted for other duties in a related insect – the butterfly. Chapter 4 focuses on one of the strangest animals that has ever lived – the snake, whose quirks reveal its history and thereby allow us to see how natural selection shapes anatomy. Chapter 5 considers animal coat patterns in general, using the cheetah as a handy case study. Finally, Chapter 6 is a potpourri of recent discoveries about a zoo-full of animals that stretches from A to Z. Every chapter is packed with unsolved mysteries that could furnish offbeat topics for term papers, thesis projects, or journal clubs.

Scott Gilbert [783] and others [994,1473,1602,2377] have advocated using evo-devo to teach about evolution in general. With this goal in mind, I have cited all sources (numbers in brackets) as links to the literature. Only by consulting original articles can students appreciate the richness of data, the nuances of arguments, or the thrill of discoveries. The References section offers instructors a reservoir that they can tap for tidbits to spice up their lectures. Two outstanding “must reads” concern snakes, elephants, and manatees in one case [886] and tigers, cream horses, and silver chickens in the other [2470].

To enhance its didactic utility, I have punctuated the narrative with take-home lessons. To ensure accessibility, I have culled as much jargon as possible, compiled a glossary (albeit a spartan one), used a case-study approach, and perforated the book with “rabbit-holes.” Readers can enter this Wonderland by studying the schematics, browsing the bestiary (Chapter 6), sampling the glossary, or just looking at the pictures. Like Alice, readers can then explore whatever piques their curiosity.

Because so many key genes were discovered and characterized in flies [761], the conventions of fly nomenclature will be followed here. Thus, gene names are italicized and can begin with either a capital (due to the first mutant allele being dominant; e.g., *Serrate*) or a lower-case letter (recessive; e.g., *engrailed*). Protein names are in roman type and always capitalized (e.g., Serrate or Engrailed). Key concepts are set
in **boldface** and are defined in the Glossary. Quotes are set apart from narrative text as indented, blocked paragraphs in smaller, non-serif typeface. The abbreviation “MY” denotes millions of years, and the slang term “app” means an application, as in computer software.

Reconstructing past events can be as tricky as solving a Sherlock Holmes mystery because there is some margin of error in every inference. Authors must assemble the evidence for their arguments as methodically as a lawyer, and readers must weigh the soundness of all theories as carefully as a juror. Some lessons can be learned from cases where lovely ideas were subsequently overturned in various investigations of fish, stick insects, insect wings, turtles, treehoppers, leopards, and acel flatworms. The benchmarks listed below may also offer some helpful guidance in this regard.

Plausibility is the first criterion that any evo-devo scenario must meet, but it cannot be the last, lest we run the risk of believing stories that seem valid only because alternatives have not been adequately assessed. Too often we assume that a structure must have served the same function in the past as it serves today. In fact, structures need not have served any function at all when they first arose.

Testability is the second hurdle that any proposal must meet, and every attempt will be made to frame hypotheses so that they can be easily tested. Indeed, this venue is where the evo-devo approach has proven to be so valuable. The field has matured to the point where we can now manipulate the genes that we think caused specific changes in evolution to see whether we can re-create those events in the laboratory.

Ultimately, fidelity to phylogeny is the best way to be sure that the trends we deduce are real. Evolutionary trees furnish a framework within which developmental deviations can be plotted, and the more robust the trees the better. Only by knowing the historical sequence of species (A begat B begat C), for instance, can we show that a certain structure was lost (by B) and regained (by C).

Kipling’s iconic rubric of “how the [blank] got its [blank]” is retained here despite there being no such thing as the leopard or the zebra. Indeed, there are many kinds of leopards and several species of zebras. The old notion of Platonic types was disproven in 1859 and supplanted by the Darwinian concept of variations as the raw material for evolution. There is no need to re-fight that war.

Another shorthand that needs to be clarified concerns genes. When I refer to “cuticle-stiffening genes” for beetle elytra in Chapter 6, for example, I do not mean that the genes themselves have stiffening properties, but rather that the expression of such genes leads to hardening via agents such as enzymes. Genes alone do not cause form! Likewise, when I say in Chapter 4 that “snakes were inventive” in solving an anatomical problem, I am not implying some sort of serpentine Sanhedrin that met to plot an adaptive strategy, though I am a big fan of Gary Larson’s *Far Side* cartoons.

The final delusion that must be dispelled is that evo-devo is only about animals. Plants offer enchanting stories as well, but including them would have diluted the Kipling conceit.

Drafts of the entire book were kindly critiqued by Richard Blanton, John (Trey) Fondon, Joseph and Anne Frankel, Ellen Larsen, Jack Levy, and Jeffrey Thomas. Individual
Preface

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Other colleagues tutored me in the finer points of bats (Robert Bradley, Tigga Kingston, and Caleb Phillips), birds (Arhat Abzhanov, Nancy McIntyre, and Ken Schmidt), centipedes (Michael Akam), jerboas (Cliff Tabin), leopards (Kristofer Helgen), lizards (Gad Perry), seahorses (Sam Van Wassenbergh), skunks (Adam Ferguson), squirrels (Cody Thompson), and, of course, snakes (David Cundall and Lou Densmore).

I accept responsibility for any flaws that remain.

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