CHAPTER 1

Background

If aliens had surveyed Earth 10 million years ago (MYA), they might have concluded that our planet not only lacked intelligent life but also had no obvious prospects for acquiring any. After all, how could they have known that East Africa would dry out, forcing some of its hairy tree dwellers to venture onto the plains, walk upright, utter sentences, make tools, and build skyscrapers?

What role did chance play in our origin?

It is sobering to think that our species might never have arisen without the timely uplift and desiccation of the Rift Valley [341], but that incident was only the latest in a long string of haphazard events that made humanity possible [515]. Indeed, the African continent itself only emerged by chance when Gondwana cracked randomly into half a dozen pieces ~140 MYA [1450,2662]. Our luckiest break was undoubtedly 65 MYA when a wayward meteor collided with Earth, killing off the ruling reptiles and making room for our mammalian ancestors to spread, colonize, multiply, and diversify.

If we ever do encounter aliens on our future voyages into outer space, they might be able to deduce our home planet just by studying our bodies and behavior. They could guess Earth's mass from the thickness of our bones, the depth of its atmosphere from the size of our diaphragm, the rate of its rotation from our sleep–wake cycle, and the spectrum of its sun by the optics of our eyes.

Humans are not alone in bearing the stamp of our planet in our anatomy. All Earthlings do [592]. However, mythology and science fiction are full of creatures that could not have evolved here because they would violate physical laws [81,2595]. Steven Spielberg's character "E.T." (the Extra-Terrestrial) is a case in point. His cantilevered head was simply too heavy to be supported by his thin neck—assuming that his spine contained the same sort of bony vertebrae as ours does [242].

Other species could have evolved but never did because of the vagaries of how history happened to unfold [1050]. For example, babies that look like mermaids are occasionally born to normal parents [1841,2665], as are one-eyed cyclopes [488], but neither of these "monsters" typically survives to adulthood due to side effects of their respective syndromes [1047,1524,1599]. However, if having a propulsive tail fin or a median eye had proven adaptive for hominins, then such traits might have been refined incrementally by natural selection [142], with their associated afflictions subsiding as felicitous mutations accrued over time [2589].

Physics thus restrains the conceivable to the possible [2137,2700], whereas history confines the possible to the actual (Fig. 1.1) [967,1266,1493,1792]. The beings that have populated Earth constitute a single, rather limited experiment in biological evolution, albeit a long one, spanning ~3.5 billion years. Only in the last 0.01% of that history did our species arise, spread, and come to rule the planet. If the movie of life were rerun, the likelihood of humans ever evolving again is nearly nil considering how many chance events chiseled our anatomy as our ancestors were nudged from niche to niche [341,729,970,2007,2400]. We are, in short, "a glorious accident" [978].

One historical constraint that profoundly affected the shape of our body was the molecular machinery that moves our muscles [830,2699]. A minimum of two opposing muscles is necessary to maneuver any given bone because muscles can only exert force by pulling [48,2213]. Muscles cannot push because myosin ratchets along actin fibers in only one direction [1563,2448]. If the gadgetry had instead relied on microtubule (*vs.* actin) fibers [328], then muscles could both pull and push because the motor proteins kinesin and dynein walk in opposite directions [2786].

Had we evolved push–pull muscles instead of pull-only ones, we would obviously look quite different [50,655]. Some of our organs have nevertheless managed to achieve some impressive feats of gymnastic flexibility despite the pull-only limitation [1490]. Our tongue, for example, extends or retracts without any bony support [2502] by alternately contracting transverse versus longitudinal muscles [50,2419,2806], our irises dilate or constrict our pupils by alternately contracting radial versus circular muscles [1478], and the penis of adult males rises hydraulically without any muscles at all by valving the flow of blood through spongy tissue [1362,2698].

How much did internal factors influence our evolution?

We have realized how natural selection drives anatomical evolution ever since Darwin put forward the argument in his magnum opus *On the Origin of Species*

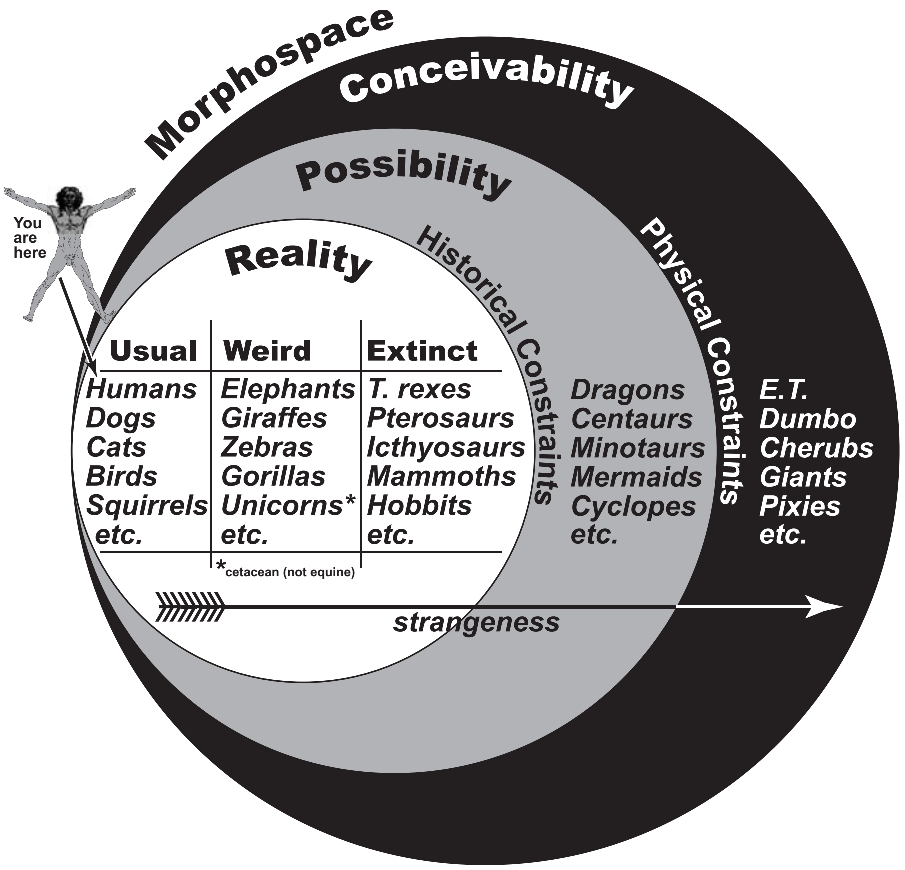


Figure 1.1. Real, possible, and conceivable subsets of vertebrate "Morphospace" [959,2600] in Venn diagram format. The arrow points from the familiar to the fantastic. City dwellers routinely see only a tiny part of the animal world: pets, birds, and the occasional squirrel. As children, we first met exotic animals (elephants, giraffes, etc.) at the zoo or circus and extinct dinosaurs at the museum. The thrill we felt at the novelty of those beasts has faded, but we can still get a similar frisson when we see science-fiction monsters in movie theaters. Some of those fabulous creatures could have evolved if Earth's history had unfolded differently [970], whereas others could not because they violate the laws of physics. For instance, centaurs could have evolved if the first fish to come on land had possessed three pairs of fins instead of two [823,959,2544], as some other groups of fish did at that time [2417]. Examples of conceivable, but impossible, animals include (1) Steven Spielberg's E.T. (the Extra-Terrestrial), whose neck was too thin to support his cantilevered head [2305], and (2) Walt Disney's Dumbo (the flying elephant), whose ears were too small (despite frantic flapping) to lift him into the air [49,1335]. The same is true for cherubs with their impotent wings. Mythical giants like Paul Bunyan could never stand because their proportionally scaled legs would not support their overly massive torso [955], nor could Disney's pixies like Tinkerbell exist because their brains would be too tiny to afford intellect. On the other hand, hobbits (~1 m tall à la Tolkien) not only *could* have evolved but *did* [92,2611], at least on one small island [407,2212]. Unicorns also evolved, albeit in aquatic form as narwhals [298,795], and, as noted by Aristotle {PoA:3:2:663a23} [137], the Indian rhino is technically a unicorn as well, given its median nasal horn [2085]. Heavier- or lighter-gravity planets may have fostered a rich assortment of alien faunas [556,1049], which we may someday encounter. Sadly, our Moon is lifeless, and although we like to think of it as colonizable, we are ill suited to walking there [1764,2685]. Indeed, the *Apollo* astronauts resorted to hopping and skipping to get around [50,1812].

REFLECTIONS ON FIGURE 1.1

Given how blasé we are today about the natural world, it is hard to imagine how amazed Europeans must have been when they first saw African wildlife in the 1700s [501] and dinosaur fossils in the 1800s [1472]. We take too much for granted in our anatomy (and behavior). One aim of this book is to rekindle our sense of wonder about life in general [594] and ourselves in particular. "The way we walk, for example, teetering on long, paired stilts of articulated bone, is unique among mammals, and as preposterous in its way as elephant trunks and platypus feet. We also communicate by tossing oddly intricate noises at one another, which somehow carry complex packages of feeling, thought, and information. We share and understand these sounds as if they were scents drifting on the wind, and our minds . . . sniff the fragrance of their meaning" [2737].

During the Middle Ages, narwhal tusks were marketed as "unicorn horns" and sold for 10 times their weight in gold [1876]! Now, of course, we know better: they're just teeth after all, so they sell nowadays for only $125/foot. But wait! If you think that narwhal tusks are any less mysterious, majestic, or magical just because we "know" what they really are, then you haven't thought about (1) what it takes for them to develop or (2) what it took for them to evolve (*cf.* Fig. 2.4). You should read Richard Dawkins's *Unweaving the Rainbow* [594] . . . or just read on.

This book was written as a kind of amusement park. Its thematic "pretend game" is to inspect each body part through the eyes of an alien visitor who asks, "Why is it *this* way and not *that*?" (*cf.* [2037]; his p. 523). Why, for instance, is there no Earthling that makes its skeleton out of metal, considering the ubiquity of metal ions and their use in other roles [2699]? In the face of such questions, the neophyte is on an equal footing with the expert. *No one* knows! Therein lies the *fun* of interrogating Nature. Asking the right questions is an art form unto itself, and some people are naturally gifted. Darwin was one of them.

For an even wilder ride through Fantasyland, see Dougal Dixon's *Man After Man: An Anthropology of the Future* (1990, St. Martin's Press, New York).

by Means of Natural Selection [832]. The essential idea is exquisitely simple [109,596,1336]. Individuals vary. When the environment changes, those best suited to the new conditions leave more offspring than those less suited, so that the population's average anatomy shifts in the next generation [664]. Over time, the population's gene pool may deviate enough to establish a new species [531]. Species thus manage to adapt to new ecological niches [2007,2460]. However, if the demands of the environment exceed the supply of useful variations, then a population or species can go extinct [330]. Surprisingly, extinction has been the fate of the vast majority (≥97%) of all the species that have ever lived [1684,2461].

In short, the genome proposes, and nature disposes. Evolution is a groping, ratcheting, trial-and-error process fueled by hereditary variations [588,1234,1607]. The supply of those variations can thus limit its rate [118,375, 587,1065]. The possibility that variations might also constrain its direction was proposed by William Bateson (1861–1926) [1058], who actually coined the term "genetics" [1556]. His classic treatise on this subject was called *Materials for*

Cambridge University Press
978-0-521-51848-2 - Quirks of Human Anatomy: An Evo-Devo Look at the Human Body
Lewis I. Held
Excerpt
More information

the Study of Variation, Treated with Especial Regard to the Discontinuity in the Origin of Species (1894) [151]. As the title suggests, he concluded that traits can vary stepwise *before* nature winnows them, rather than smoothly in all directions [44,2262]. He stated his thesis clearly in his Introduction (boldface is his):

> If then all the individual ancestors of any given form were before us and were arranged in their order, we believe they would constitute a series. . . . In proportion as the transition from term to term is minimal and imperceptible we may speak of the series as being **continuous**, while in proportion as there appear in it lacunae, filled by no transitional form, we may describe it as **discontinuous**. . . . Variation has been supposed to be always continuous. . . . That this inference is a wrong one, the facts will show. [151] (p. 14*ff*.)

One drastic kind of discontinuity that Bateson analyzed was "homeosis" (another term he coined) [1535,1703]—the transformation of one body part into another [2689]. Most of the human homeoses he listed involved odd vertebrae—for example, a neck vertebra sprouting ribs as if it were a thoracic vertebra. Whether this phenomenon has any relevance to evolution is debatable, and it has been vigorously debated [661,957,1040,2475,2858]. The most extreme hypothesis—that homeosis is the main driving force behind macroevolution—was proposed by Richard Goldschmidt (1878–1958) [930,931]. He thought of homeotic mutants as "hopeful monsters" [662,2733] that could launch whole new species under the right circumstances [1163,2589]. Evolution may have followed this route in rare instances [1163,2179,2589], but its usual mode is decidedly more gradual [38,101,916,2790].

Bateson is famous not only for cataloguing homeoses but also for discovering an odd geometry of abnormally branched legs in animals as different as cockroaches and salamanders [819,1135]. Such legs, he found, always manifest new planes of mirror symmetry that obey what is now called "Bateson's Rule" [150,304]. Evidently, limb development is limited to a predictable subset of morphologies whenever disturbances occur. In a similar way, perhaps, homeoses tend to be confined to certain organs when they are induced by teratogens [1479,1958]. For example, fly embryos exposed to ether vapor show a nonheritable conversion of haltere to wing but few other abnormalities [1166].

Internal constraints apply not only to mutant individuals but to normal ones as well [943,960,1492]. One oft-cited example is the mollusk shell. The spectrum of naturally occurring shell shapes (from conch to nautilus to clam) is produced as a function of only three developmental parameters: (1) the rate of growth of the shell's mouth, (2) its rate of revolution around a vertical line, and (3) its rate of translation along that line [2132]. These internal variables define the axes of an imaginary cube in which most mollusk species can be plotted

Cambridge University Press
978-0-521-51848-2 - Quirks of Human Anatomy: An Evo-Devo Look at the Human Body
Lewis I. Held
Excerpt
More information

as single points (*x*, *y*, *z*) [465,2133]. Not all regions of this "Morphospace" are occupied [959,2600], mainly because of the contingent conditions (*i.e.*, *historical* constraints) that governed how the various lineages of mollusks happened to evolve [2325,2499,2729].

If shell growth, revolution, and translation are independent of one another in how they are controlled genetically, then mutations will tend to steer a species along a trajectory that is parallel to one axis of the Morphospace at a time [45,2498,2728]. The same applies to any species (mollusk or otherwise) with generative determinants that are likewise uncoupled. Under such conditions, which do indeed apply to many anatomical features [265,2109], certain paths through the pertinent Morphospace will tend to be well traveled, whereas others remain untrodden [793]. The evolutionary routes available to any given anatomy at any particular time will thus depend on its cellular program of development [44,1344,1687], which in turn will depend on the circuitry within its genome [1782,2816].

Here we have hit on the raison d'être for the hybrid field of "evo–devo" (evolutionary–developmental biology) [1143,2238]. Only by deciphering how genes control development can we hope to discern how evolution tinkers with anatomy [98,2110,2721].

Bateson was one of the first theorists to sense this connection. Another was his mentor Francis Galton (1822–1911), who is famous for advocating the use of fingerprints in forensics [2484] and *in*famous for advocating the use of eugenics in social engineering [704]. Galton devised a clever way to illustrate how development constrains evolution [854]. He imagined the organism as a polyhedron that rests on one facet at a time [959,960]. If pushed hard enough by natural selection, the polyhedron will topple onto one adjacent facet, and then another—thus following a trajectory governed by its geometry. The analogy stands in obvious contrast to the behavior of a billiard ball, which responds compliantly in both direction and degree to every nudge of natural selection [965,968]. Figure 1.2 sketches this metaphor and two others that have proven useful in this field. Galton actually fancied the polyhedron more for its tendency to stay put than for its ability to constrain evolution (boldface added) [916]:

> The mechanical conception would be that of a rough stone, having, in consequence of its roughness, a vast number of natural facets, on any one of which it might rest in "stable" equilibrium. That is to say, when pushed it would somewhat yield. . . . **On the pressure being withdrawn, it would fall back into its first position.** But, if by a powerful effort the stone is compelled to overpass the limits of the facet on which it has hitherto found rest, it will tumble over into a new

Cambridge University Press
978-0-521-51848-2 - Quirks of Human Anatomy: An Evo-Devo Look at the Human Body
Lewis I. Held
Excerpt
More information

> position of stability, whence just the same proceedings must be gone through as before, before it can be dislodged and rolled another step onwards. [854] (p. 369)

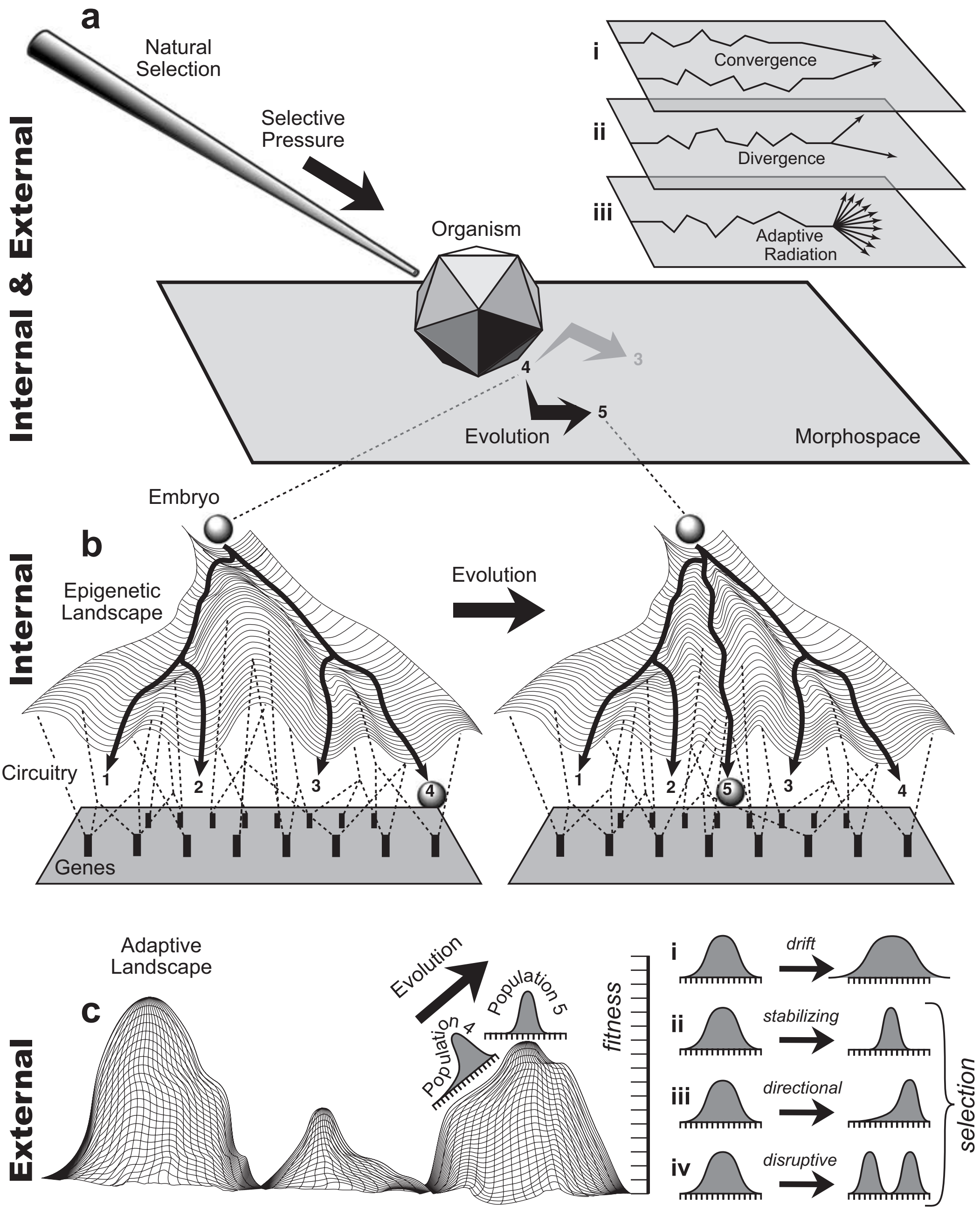
Stability in the face of perturbing forces was also an issue for Conrad Waddington (1905–1975) [1054], but instead of facets on a solid, he imagined grooves in a landscape (Fig. 1.2b) [905,2283,2712]. The deeper the grooves, the greater the resilience of the pathways. If the embryo were a ball rolling down a groove, then mutations might alter its path by reshaping the landscape [99]. Waddington coined the term "canalization" to denote the stability of pathways in the face of mutations [2714,2813]. At the genetic level, it involves "buffering" [693,784,899,1999]. The fact that humans normally have five fingers is a manifestation of this phenomenon [844].

Waddington depicted his landscape (in later versions) as a corrugated canopy, much like a sagging circus tent. The shape of the canopy is set by a cobweb of guy wires beneath it (= gene circuitry). Those wires, in turn, are anchored by pegs (= genes) [2713]. Given this hierarchy, the effect of uprooting any single peg at the ground level (= null mutation) on the final anatomy (= fate of the rolling ball) is hard to predict because cross-links in the wire matrix (= *epi*genetic network) preclude a 1:1 relationship between specific pegs and parts of the landscape [1374,2195].

One upshot of this genetic cooperativity is that tweaks at the gene level can have complex, wide-ranging, and counterintuitive effects at the phenotypic level [1545,2379], and herein lies much of the fun in studying embryos. They often surprise you, and their mutant syndromes are typically as challenging as a Sherlock Holmes mystery or a Sunday *New York Times* crossword puzzle [414,1137].

Over the past century, the field of developmental genetics, which Waddington helped found [2711,2712], has deciphered thousands of etiologies and, in so doing, has uncovered a few "emergent properties" [576,2147] that characterize genomic control systems in general [190,331,571,1413,1741]. Those properties include robustness (resistance of pathways to perturbations) [133,846], pleiotropy (involvement of single genes in multiple circuits) [753,1175,1400,2720], nonlinearity (dosage-independent effects due to redundancy, etc.) [335,2773], thresholds (tipping points) [1536,1782,1798,1821], and feedback (dampers or auto-activators) [165,269,814,2018,2594]. However, the system property that has exerted the greatest constraint on *gross* anatomy has probably been allometry [479,882,1531,2421]—an inherent (canalized) divergence of growth rates in certain body parts relative to the body as a whole [323,871]. Wherever allometric

Cambridge University Press
978-0-521-51848-2 - Quirks of Human Anatomy: An Evo-Devo Look at the Human Body
Lewis I. Held
Excerpt
More information



links exist, they cause a change in body *shape* whenever there is a change in body *size* [716,2305,2477]—for example, antlers getting disproportionately larger as deer grow bigger [952]. D'Arcy Thompson (1860–1948) was one of the first to show how startling such reshaping can be [953], and his grid transformations are iconic in the evo-devo literature [100,1702,2231]. Allometry is relevant to our own history because it may have boosted hominid brain size beyond the level

Cambridge University Press
978-0-521-51848-2 - Quirks of Human Anatomy: An Evo-Devo Look at the Human Body
Lewis I. Held
Excerpt
More information

Figure 1.2. Metaphors for evo-devo that illustrate internal factors, external factors, or both. Modified from ref. [1135].

a. Galton's polyhedron analogy [960]. Francis Galton thought that species go from one stable anatomy to another when exposed to selective pressure [855]. He likened the stability to a polyhedron that stays poised on one facet unless pushed hard enough to topple it onto an adjacent facet. The organism would thus zigzag through its available "Morphospace" [2129]—the set of all possible shapes (*cf.* Fig. 1.1) [493,1702]. Insets (*upper right*) depict some trends in this context, where the y axis represents a one-dimensional Morphospace and the x axis is time. **a.i.** Convergence. Similar anatomies often evolve in separate lineages [1989,2821] because of physical constraints that allow few solutions for any given problem [1105,1176]. Similar *behavioral* traits can also evolve independently—for example, intelligence in humans and dolphins [1651]. **a.ii.** Divergence. Splitting of lineages is thought to occur mainly through geographic separation (*i.e.*, allopatric speciation), where different niches demand different adaptations [1154,2007,2580]. Initially, the splitting may only entail subspecific morphological specializations (*e.g.*, dog breeds), but the greater the differences become, the more likely they will lead to reproductive isolation (*i.e.*, separate species) [531]. **a.iii.** Adaptive radiation [870,2209]. Species can ramify rapidly into multiple offshoots [1523,2265] when they colonize ecosystems full of vacant niches [2108,2304,2446]. Mounting evidence suggests that the stress of habitat colonization itself may reveal hitherto-untapped potential for wild variability, on which natural selection can then act [1180,2525,2790].

b. Waddington's epigenetic landscape [2712,2713]. In his original metaphor, the ball was an embryonic cell that rolls to a differentiated state [905]. Here the analogy is broadened to the entire cohort of cells (*i.e.*, the embryo) and their collective destiny (*i.e.*, the adult). The canopy (~circus tent) is shaped by a network (circuit) of guy wires tied down by genes (pegs). Its grooves correspond to facets of the polyhedron in **a.** Initially, the species has anatomy #4 because this is the ball's path of least resistance (*i.e.*, lowest energy). If the environment changes, then any mutations (deviant tensions on the network) that happen to change anatomy to a more favorable state will be selected for [738]. As the landscape's shape changes (diagram to right of the thick arrow), the ball may fall into a prior groove (#1–3), or, as shown here, one that arises *de novo* (#5) [1064]. If the transition between grooves is sudden, then anatomy could change abruptly [151,930] (but see critiques [38,2858]).

c. Wright's adaptive landscape [869,2857]. In this imaginary example, height (scale at right) denotes fitness of genotypes (points in the mesh) [613]. If the environment changes (not shown), then contours would change accordingly. The three hills represent different ways to elevate fitness [593] (*cf.* [1304]). One interbreeding population is plotted as a bell curve, where the height of each point denotes the number of individuals having the genotype beneath it on the hill. The population is plotted before (Pop. 4) and after (Pop. 5) selection has exerted an effect, where 4 and 5 correspond to anatomies from the pathways shown in **b.** Panels at the right show how selection varies with topography [815]. **c.i.** On terrain that is relatively flat, there is negligible selection, so the span of genotypes can broaden via random mutation and recombination [118,738,1840]. In small populations, this "genetic drift" [1480,1606] can lead to fixation of neutral (or even deleterious) mutations [891,1224,2581,2632]. A case in point was the bottleneck ~5 MYA that led to fixation of our chromosome #2 from a harmless (but useless?) fusion of two ape chromosomes [1317]. **c.ii.** At an adaptive peak (hilltop) any deviations from the mean will be disfavored, thus narrowing ("stabilizing") the bell curve. **c.iii.** While a population is in the process of climbing a hill, individuals at the leading edge will leave more offspring, thus skewing the distribution ("directional" selection) [714]. Climbing can only occur by (1) mutational creation of new alleles or (2) recombination of old ones, both of which are random events. **c.iv.** If a population straddles a valley, then cohorts will be pulled apart ("disruptive" selection) [1702], and this divergence can lead to speciation [1407].

---

expected from adaptation alone—at least during the initial phases (*cf.* Ch. 7) [770,2181,2212,2309].

Historically, Waddington's metaphor of the "epigenetic landscape" was a derivative of Sewall Wright's notion of an "adaptive landscape" [2410], although

Cambridge University Press
978-0-521-51848-2 - Quirks of Human Anatomy: An Evo-Devo Look at the Human Body
Lewis I. Held
Excerpt
More information

REFLECTIONS ON FIGURE 1.2

Such metaphors give us a feeling for how genes control anatomy. For more on how "Genospace" maps onto "Phenospace," see articles by Lieberman and Hall [1545] and Weiss [2778]. Ultimately, it was our ricocheting through "Ecospace" that caused us to land at the point we now occupy in Morphospace [482,493].

a. In Morphospace, a species would actually occupy an area, not a point, and the size of that area would reflect its span of variation [653]. Indeed, as mentioned in the text, a better metaphor for a species (≈ bell curves in **c**) might be an amoeba that moves over the terrain by extending and retracting pseudopodia. Species can retain their anatomy for eons [833,2750] (*i.e.*, stay put in Morphospace), although structural stasis need not imply genetic stasis [1124]. Darwin called such species "living fossils" and inferred that they must have "inhabited a confined area and . . . thus [were] exposed to less severe competition" [559] (p. 107). **a.i.** One clear example of convergence involves hooves. Any animal that runs *en pointe* (like a ballerina) risks injuring its toes, and the same protective devices evolved separately in even- and odd-toed mammals (*e.g.*, pigs *vs.* horses)—namely, fused toes and thicker toenails ("hooves") [2085]. Convergence also arises when lineages fill similar niches [482,2007,2692]. Thus, marsupials evolved species that look eerily like the placental wolf, cat, mole, squirrel, and anteater [631,2153,2446,2861]. **a.ii.** A classic example of divergence is Darwin's finches [1691,2770]. The molecular basis for finch beak divergence has finally been revealed by some recent evo-devo analyses [8]. **a.iii.** Explosive speciation can be sparked not only by access to uninhabited areas [811,2304] but also by the appearance of novel structures [237,1548,1890,2873]. For example, the debut of the neural crest created jaws that allowed a predatory (*vs.* filter-feeding) lifestyle [1624,1900] and hence spawned clades of carnivorous fish [472,796]. Radiation is aided by founder effects in small populations [1755] (*e.g.*, colonizing of the Galapagos by Darwin's finches [997,998]). Surprisingly, recent data refute the old cliché that mammals only radiated after dinosaurs disappeared [200,1597].

b. The uniformity of the depicted pegs may leave the impression that all genes are equal [2778]. Far from it! A tiny subset (the "toolkit") is most critical for building anatomy [392], and evolution results mainly from mutations therein [390].

the latter was devised for an entirely different purpose [1702,2035]. In Wright's original (1932) formulation [2857], unique combinations of alleles (= individuals) were represented by (x, y) coordinates in a plane, and their fitness for particular environments was denoted by altitude (z value) above the plane [613,1465]. To use a trite example, consider a population of giraffes with neck lengths that vary as a function of each animal's genetic constitution (= x–y plane) [53]. Those with longer necks will be more apt to survive (*i.e.*, have higher z values) when the only leaves that remain are high in the treetops (= natural selection). Such favored genotypes would thus constitute optima (= peaks) in the landscape.

In Figure 1.2c, a population is schematized as a bell-curve distribution that initially does not overlap any optimum in the landscape. If it resides on the side of an adaptive peak, then selective pressure will impel it to climb higher [815,1702]. For giraffes, this might mean evolving longer necks. If a population's