EPILOGUE

As a parent of two young children, I find myself spending a lot of time lately in zoos, museums, and aquaria. Being a visitor is a strange experience, because I've been involved with these places for decades, working in museum collections and even helping to prepare exhibits on occasion. During family trips, I've come to realize how much my vocation can make me numb to the beauty and sublime complexity of our world and our bodies. I teach and write about millions of years of history and about bizarre ancient worlds, and usually my interest is detached and analytic. Now I'm experiencing science with my children—in the kinds of places where I discovered my love for it in the first place.

One special moment happened recently with my son at the Museum of Science and Industry in Chicago. We've gone there regularly over the past three years because of his love of trains and the fact that there is a huge model railroad smack in the center of the place. I've spent countless hours at that one exhibit tracing model locomotives on their little trek from Chicago to Seattle. After a number of weekly visits to this shrine for the train-obsessed, Nathaniel and I walked to corners of the museum we had failed to visit during our train-watching ventures or occasional forays to the full-size tractors and planes. In the back of the museum, in the Henry Crown Space Center, model planets hang from the ceiling and space suits lie in cases together with other memorabilia of the space program of the 1960s and 1970s. I was under the presumption that in the back of the museum I would see the trivia that didn't make it to the major exhibits up front. One display consisted of a battered space capsule that you could walk around and look inside. It didn't look significant; it seemed way too small and jerry-rigged to be anything really important. The placard was strangely formal, and I had to read it several times before it dawned on me: here was the original Command Module from *Apollo 8,* the actual vessel that carried James Lovell, Frank Borman, and William Anders on humanity's first trip to the moon and back. This was the spacecraft whose path I followed during Christmas break in third grade, and here I was thirty-eight years later with my own son, looking at the real thing. Of course it was battered. I could see the scars of its journey and subsequent return to earth. Nathaniel was completely disinterested, so I grabbed him and tried to explain what it was. But I couldn't speak; my voice became so choked with emotion that I could barely utter a single word. After a few minutes, I regained my composure and told him the story of man's trip to the moon.

But the story I can't tell him until he is older is why I became speechless and emotional. The real story is that *Apollo 8* is a symbol for the power of science to explain and make our universe knowable. People can quibble over the extent to which the space program was about science or politics, but the central fact remains as clear today as it was in 1968: *Apollo 8* was a product of the essential optimism that fuels the best science. It exemplifies how the unknown should not be a source of suspicion, fear, or retreat to superstition, but motivation to continue asking questions and seeking answers.

Just as the space program changed the way we look at the moon, paleontology and genetics are changing the way we view ourselves. As we learn more, what once seemed distant and unattainable comes within our comprehension and our grasp. We live in an age of discovery, when science is revealing the inner workings of creatures as different as jellyfish, worms, and mice. We are now seeing the glimmer of a solution to one of the greatest mysteries of science—the genetic differences that make humans distinct from other living creatures. Couple these powerful new insights with the fact that some of the most important discoveries in paleontology—new fossils and new tools to analyze them—have come to light in the past twenty years, and we are seeing the truths of our history with ever-increasing precision. Looking back through billions of years of change, everything innovative or apparently unique in the history of life is really just old stuff that has been recycled, recombined, repurposed, or otherwise modified for new uses. This is the story of every part of us, from our sense organs to our heads, indeed our entire body plan.

What do billions of years of history mean for our lives today? Answers to fundamental questions we face—about the inner workings of our organs and our place in nature—will come from understanding how our bodies and minds have emerged from parts common to other living creatures. I can imagine few things more beautiful or intellectually profound than finding the basis for our humanity, and remedies for many of the ills we suffer, nestled inside some of the most humble creatures that have ever lived on our planet.

NOTES, REFERENCES, AND FURTHER READING

CHAPTER ONE FINDING AN INNER FISH

I have included a mix of primary and secondary sources for those interested in pursuing the topics in the book further. For accounts that use exploratory paleontological expeditions as a vehicle to discuss major questions in biology and geology, see Mike Novacek's *Dinosaurs of the Flaming Cliffs* (New York: Anchor, 1997), Andrew Knoll's *Life on a Young Planet* (Princeton: Princeton University Press, 2002), and John Long's *Swimming in Stone* (Melbourne: Freemantle Press, 2006). All balance scientific analysis with descriptions of discovery in the field.

The comparative methods that I discuss, including the methods used in our walk through the zoo, are the methods of cladistics. A superb overview is Henry Gee's *In Search of Deep Time* (New York: Free Press, 1999). Basically, I present a version of the three-taxon statement, the starting point for cladistic comparisons. A good treatment with background sources is found in Richard Forey et al., "The Lungfish, the Coelacanth and the Cow Revisited," in H.-P.

Schultze and L. Trueb, eds., *Origin of the Higher Groups of Tetrapods* (Ithaca, N.Y.: Cornell University Press, 1991).

The correlation between the fossil record and our "walk through the zoo" is discussed in several papers. A sampling: Benton, M. J., and Hitchin, R. (1997) Congruence between phylogenetic and stratigraphic data in the history of life, *Proceedings of the Royal Society of London,* B 264:885–890; Norell, M. A., and Novacek, M. J. (1992) Congruence between superpositional and phylogenetic patterns: Comparing cladistic patterns with fossil records, *Cladistics* 8:319–337; Wagner, P. J., and Sidor, C. (2000) Age rank/clade rank metrics—sampling, taxonomy, and the meaning of "stratigraphic consistency," *Systematic Biology* 49:463–479.

The layers of the rock column and the fossils contained therein are beautifully and comprehensively discussed in Richard Fortey's *Life: A Natural History of the First Four Billion Years of Life on Earth* (New York: Knopf, 1998). Resources for vertebrate paleontology include R. Carroll, *Vertebrate Paleontology and Evolution* (San Francisco: W. H. Freeman, 1987), and M. J. Benton, *Vertebrate Paleontology* (London: Blackwell, 2004).

For the origin of tetrapods: Carl Zimmer reviewed the state of the art in the field in his highly readable and well-researched *At the Water's Edge* (New York: Free Press, 1998). Jenny Clack has written the definitive text on the whole transition, *Gaining Ground* (Bloomington: Indiana University Press, 2002). The bible of this transition, Clack's book will bring a novice to expert status quickly.

Our original papers describing *Tiktaalik* appeared in the April 6, 2006, issue of *Nature.* The references are: Daeschler et al. (2006) A Devonian tetrapod-like fish and the origin of the tetrapod body plan, *Nature* 757:757–763; Shubin et al. (2006) The pectoral fin of *Tiktaalik roseae* and the origin of the tetrapod limb, *Nature* 757:764–771. Jenny Clack and Per Ahlberg had a very readable and comprehensive commentary piece in the same issue (*Nature* 757:747–749).

Everything about our past is relative, even the structure of this book. I could have called this book "Our Inner Human" and written it from a fish's point of view. The structure of that book would have been strangely similar: a focus on the history humans and fish share in bodies, brains, and cells. As we've seen, all life shares a deep part of its history with other species, while another part of its history is unique.

CHAPTER TWO GETTING A GRIP

Owen was by no means the first person to see the pattern of one bone–two bones–lotsa blobs–digits. Vicq-d'Azyr in the 1600s and Geoffroy St. Hilaire (1812) also made this pattern part of their worldviews. What distinguished Owen was his concept of the archetype. This was a transcendental organization of the body, reflecting the design of the Creator. St. Hilaire was searching less for an archetypical pattern hidden in all structure than for "laws of form" that govern the formation of bodies. A nice treatment of these issues is in T. Appel, *The Cuvier-Geoffroy Debate: French Biology in the Decades Before Darwin* (New York: Oxford University Press, 1987), and E. S. Russell, *Form and Function: A Contribution to the History of Morphology* (Chicago: University of Chicago Press, 1982).

A recent volume edited by Brian Hall is one-stop shopping for information on limb diversity and development and contains a number of important papers on different kinds of limbs: Brian K. Hall, ed., *Fins into Limbs: Evolution, Development, and Transformation* (Chicago: University of Chicago Press, 2007). Useful references for exploring the shift from fins and limbs in more detail include Shubin et al. (2006) The pectoral fin of *Tiktaalik roseae* and the origin of the tetrapod limb, *Nature* 757:764–771; Coates, M. I., Jeffery, J. E., and Ruta, M. (2002) Fins to limbs: what the fossils say, *Evolution and Development* 4:390–412.

CHAPTER THREE HANDY GENES

The developmental biology of limb diversity has seen a number of reviews and primary papers. For a review of the classic literature see Shubin, N., and Alberch, P. (1986) A morphogenetic approach to the origin and basic organization of the tetrapod limb, *Evolutionary Biology* 20:319–387; and Hinchliffe, J. R., and Griffiths, P., "The Pre-chondrogenic Patterns in Tetrapod Limb Develoment and

Their Phylogenetic Significance," in B. Goodwin, N. Holder, and C. Wylie, eds., *Development and Evolution* (Cambridge, Eng.: Cambridge University Press, 1983), pp. 99–121. Saunders's and Zwilling's experiments are now classic, so some of the best accounts are now seen in the major textbooks in developmental biology. These include S. Gilbert, *Developmental Biology,* 8th ed. (Sunderland, Mass.: Sinauer Associates, 2006); L. Wolpert, J. Smith, T. Jessell, F. Lawrence, E. Robertson, and E. Meyerowitz, *Principles of Development* (Oxford, Eng.: Oxford University Press, 2006).

For the first paper describing *Sonic hedgehog*'s role in limb patterning, go to Riddle, R., Johnson, R. L., Laufer, E., Tabin, C. (1993) *Sonic hedgehog* mediates the polarizing activity of the ZPA, *Cell* 75:1401–1416.

Randy's work on *Sonic* signaling in shark and skate fins is in Dahn, R., Davis, M., Pappano, W., Shubin, N. (2007) *Sonic hedgehog* function in chondrichthyan fins and the evolution of appendage patterning, *Nature* 445:311–314. Subsequent work from the lab on the origin of limbs, at least from a genetic perspective, is contained in Davis, M., Dahn, R., and Shubin, N. (2007) A limb autopodial-like pattern of *Hox* expression in a basal actinopterygian fish, *Nature* 447:473–476.

The stunning genetic similarities in the development of flies, chickens, and humans is discussed in Shubin, N., Tabin, C., Carroll, S. (1997) Fossils, genes, and the evolution of animal limbs, *Nature* 388:639–648; and Erwin, D. and Davidson, E. H. (2003) The last common bilaterian ancestor, *Development* 129:3021–3032.

CHAPTER FOUR TEETH EVERYWHERE

The importance of teeth to an understanding of mammals is evident in the many treatments in the field. Dental structure plays a particularly important role in understanding the early record of mammals. Extensive reviews are found in Z. Kielan-Jaworowska, R. L. Cifelli, and Z. Luo, *Mammals from the Age of Dinosaurs* (New York: Columbia University Press, 2004); and J. A. Lillegraven, Z. Kielan-Jaworowska, and W. Clemens, eds., *Mesozoic Mammals: The First Two-Thirds of Mammalian History* (Berkeley: University of California Press, 1979), p. 311.

Farish's mammal from Arizona is analyzed in Jenkins, F. A., Jr., Crompton, A. W., Downs, W. R. (1983) Mesozoic mammals from Arizona: New evidence on mammalian evolution, *Science* 222:1233–1235.

The tritheledonts we found in Nova Scotia are described in Shubin, N., Crompton, A. W., Sues, H.-D., and Olsen, P. (1991) New fossil evidence on the sister-group of mammals and early Mesozoic faunal distributions, *Science* 251:1063–1065.

A recent review on the origin of teeth, bone, and skulls, in particular the new evolution gleaned from conodont animals, is found in Donoghue, P., and Sansom I. (2002) Origin and early evolution of vertebrate skeletonization, *Microscopy Research and Technique* 59:352–372. A thorough review of the evolutionary relationships among conodonts and their significance is in Donoghue, P., Forey, P., and Aldridge, R. (2000) Conodont affinity and chordate phylogeny, *Biological Reviews* 75:191–251.

CHAPTER FIVE GETTING AHEAD

A wonderfully comprehensive and detailed treatment of the details of skull structure, development, and evolution is found in a three-volume set: *The Skull,* James Hanken and Brian Hall, eds. (Chicago: University of Chicago Press, 1993). This is a multi-author update of one of the classic volumes on head development and structure: G. R. de Beer, *The Development of the Vertebrate Skull* (Oxford, Eng.: Oxford University Press, 1937).

Details of head development and structure in humans can be found in texts on human anatomy and embryology. For embryology, see K. Moore and T.V.N. Persaud, *The Developing Human,* 7th ed. (Philadelphia: Elsevier, 2006). The companion anatomy text is K. Moore and A. F. Dalley, *Clinically Oriented Anatomy* (Philadelphia: Lippincott Williams & Wilkins, 2006).

Francis Maitland Balfour's seminal work is encapsulated in Balfour, F. M. (1874) A preliminary account of the development of the elasmobranch fishes, *Q. J. Microsc. Sci.* 14:323–364; F. M. Balfour, *A Monograph on the Development of Elasmobranch Fishes,* 4 vols. (London: Macmillan & Co., 1878); F. M. Balfour, *A Treatise on Comparative Embryology,* 2 vols. (London: Macmillan & Co., 1880–81); M. Foster and A. Sedgwick, *The Works of Francis Maitland Balfour,* with an introductory biographical notice by Michael Foster, 4 vols. (London: Macmillan & Co., 1885). A successor at Oxford, Edwin Goodrich, produced one of the classics of comparative anatomy, *Studies on the Structure and Development of Vertebrates* (London: Macmillan, 1930).

Balfour, Oken, Goethe, Huxley, and others were addressing the problem known as head segmentation. Just as the vertebrae differ in a regular progression from front to back, so the head has a segmental pattern. A selection of classic and recent resources (all with good bibliographies) to pursue this field further: Olsson, L., Ericsson, R., Cerny, R. (2005) Vertebrate head development: Segmentation, novelties, and homology, *Theory in Biosciences* 124:145–163; Jollie, M. (1977) Segmentation of the vertebrate head, *American Zoologist* 17:323–333; Graham, A. (2001) The development and evolution of the pharyngeal arches, *Journal of Anatomy* 199:133–141.

A recent overview of the genetic basis of gill arch formation is found in Kuratani, S. (2004) Evolution of the vertebrate jaw: comparative embryology and molecular developmental biology reveal the factors behind evolutionary novelty, *Journal of Anatomy* 205:335–347. Examples of the experimental manipulation of one gill arch into another, using genetic technologies, include Baltzinger, M., Ori, M., Pasqualetti, M., Nardi, I., Riji, F. (2005) *Hoxa 2* knockdown in *Xenopus* results in hyoid to mandibular homeosis, *Developmental Dynamics* 234:858–867; Depew, M., Lufkin, T., Rubenstein, J. (2002) Specification of jaw subdivisions by *Dlx* genes, *Science* 298:381–385.

A comprehensive, well-illustrated, and informative resource for early fossil records of skulls, heads, and primitive fish is reviewed in P. Janvier, *Early Vertebrates* (Oxford, Eng.: Oxford University Press, 1996). The paper describing *Haikouella,* the 530-million-year-old worm with gills, is Chen, J.-Y., Huang, D. Y., and Li, C. W. (1999) An early Cambrian craniate-like chordate, *Nature* 402:518–522.

CHAPTER SIX THE BEST-LAID (BODY) PLANS

The origin of body plans has been the subject of a number of book-length treatments. For one with an exceptional scope and bibliography, go to J. Valentine, *On the Origin of Phyla* (Chicago: University of Chicago Press, 2004).

There have been several biographies of von Baer. A short one is Jane Oppenheimer, "Baer, Karl Ernst von," in C. Gillespie, ed., *Dictionary of Scientific Biography,* vol. 1 (New York: Scribners, 1970). For more detailed treatments, see *Autobiography of Dr. Karl Ernst von Baer,* ed. Jane Oppenheimer (1986; originally published in German, 2nd ed., 1886). See also B. E. Raikov, *Karl Ernst von Baer, 1792–1876,* trans. from Russian (1968), and Ludwig Stieda, *Karl Ernst von Baer,* 2nd ed. (1886). All these resources have large bibliographies. See also S. Gould, *Ontogeny and Phylogeny* (Cambridge, Mass.: Harvard University Press, 1977), for a discussion of von Baer's laws.

Spemann and Mangold's experiments are discussed in embryology textbooks: S. Gilbert, *Developmental Biology,* 8th ed. (Sunderland, Mass.: Sinauer Associates, 2006). A modern genetic perspective on the Organizer is contained in De Robertis, E. M. (2006) Spemann's organizer and self regulation in amphibian embryos, *Nature Reviews* 7:296–302, and De Robertis, E. M., and Arecheaga, J. The Spemann Organizer: 75 years on, *International Journal of Developmental Biology* 45 (special issue).

For access to the huge literature on *Hox* genes and evolution, the best starting reference is Sean Carroll's recent book *Endless Forms Most Beautiful* (New York: Norton, 2004). A recent review and interpretation of the ways that genes allow us to understand the common ancestor of bilaterally symmetrical animals is in Erwin, D., and Davidson, E. H. (2002) The last common bilaterian ancestor, *Development* 129:3021–3032.

A number of investigators argue that a genetic "flip" between the body plan of an anthropod and the body plan of a human happened sometime in the distant past. This idea is discussed in De Robertis, E., and Sasai, Y. (1996) A common plan for dorsoventral patterning in Bilateria, *Nature* 380:37–40. Historical perspective on St. Hilaire's views, as well as other controversies in the early years of comparative anatomy, are found in T. Appel, *The Cuvier-Geoffroy Debate: French Biology in the Decades Before Darwin* (New York: Oxford University Press, 1987). Data from acorn worms does not easily fit this model, and suggests that in some taxa the map between gene activity and axis specification may have evolved. For this work, see Lowe, C. J., et al. (2006) Dorsoventral patterning in hemichordates: insights into early chordate evolution, *PLoS Biology online access:* http://dx.doi.org/journal.0040291.

The evolution of the genes that determine the body axes is reviewed in Martindale, M. Q. (2005) The evolution of metazoan axial properties, *Nature Reviews Genetics* 6:917–927. Body plan genes in cnidarians (jellyfish, sea anemones, and their relatives) are discussed in a series of primary papers: Martindale, M. Q., Finnerty, J. R., Henry, J. (2002) The Radiata and the evolutionary origins of the bilaterian body plan, *Molecular Phylogenetics and Evolution* 24:358–365; Matus, D. Q., Pang, K., Marlow, H., Dunn, C., Thomsen, G., Martindale, M. (2006) Molecular evidence for deep evolutionary roots of bilaterality in animal development, *Proceedings of the National Academy of Sciences* 103:11195–11200; Chourrout, D., et al. (2006) Minimal protohox cluster inferred from bilaterian and cnidarian *Hox* complements, *Nature* 442:684–687; Martindale, M., Pang, K., Finnerty, J. (2004) Investigating the origins of triploblasty: "mesodermal" gene expression in a diploblastic animal, the sea anemone *Nemostella vectensis* (phylum, Cnidaria; class, Anthozoa), *Development* 131:2463–2474; Finnerty, J., Pang, K., Burton, P., Paulson, D., Martindale, M. Q. (2004) Deep origins for bilateral symmetry: *Hox* and *Dpp* expression in a sea anemone, *Science* 304:1335–1337.

Three key articles review the origins and evolution of bodies and offer an integrative perspective on genetics, geology, and ecology: King, N. (2004) The unicellular ancestry of animal development, *Developmental Cell* 7:313–325; Knoll, A. H., and Carroll, S. B. (1999) Early animal evolution: Emerging views from comparative biology and geology, *Science* 284:2129–2137; Brooke, N. M., and Holland, P. (2003) The evolution of multicellularity and early animal genomes, *Current Opinion in Genetics and Development* 13:599–603. All three papers are well referenced and offer a good introduction to the topics of the chapter.

For stimulating treatments of the consequences of the origin of bodies and of other new forms of biological organization, see L. W. Buss, *The Evolution of Individuality* (Princeton: Princeton University Press, 2006), and J. Maynard Smith, and E. Szathmary, *The Major Transitions in Evolution* (New York: Oxford University Press, 1998).

The story behind the Ediacarian animals is covered, with references, in Richard Fortey's *Life: A Natural History of the First Four Billion Years of Life on Earth* (New York: Knopf, 1998), and Andrew Knoll's *Life on a Young Planet* (Princeton: Princeton University Press, 2002).

The experiment that yielded "proto-bodies" from "no-bodies" is described in Boraas, M. E., Seale, D. B., Boxhorn, J. (1998) Phagotrophy by a flagellate selects for colonial prey: A possible origin of multicellularity, *Evolutionary Ecology*

12:153–164.

CHAPTER EIGHT MAKING SCENTS

The University of Utah has an effective website, Learn. Genetics, that provides a wonderfully simple kitchen protocol for extracting DNA. The URL is http://learn.genetics.utah.edu/units/activities/extraction/

The evolution of the so-called odor genes or, more precisely, olfactory receptor genes has a large literature. Buck and Axel's seminal paper is Buck, L., and Axel, R. (1991) A novel multigene family may encode odorant receptors: a molecular basis for odor recognition, *Cell* 65:175–181.

Comparative aspects of olfactory gene evolution are treated in Young, B., and Trask, B. J. (2002) The sense of smell: genomics of vertebrate odorant receptors, *Human Molecular Genetics* 11:1153–1160; Mombaerts, P. (1999) Molecular biology of odorant receptors in vertebrates, *Annual Reviews of Neuroscience* 22:487–509.

Olfactory receptor genes in jawless fish are discussed in Freitag, J., Beck, A., Ludwig, G., von Buchholtz, L., Breer, H. (1999) On the origin of the olfactory receptor family: receptor genes of the jawless fish (*Lampetra fluviatilis*), *Gene* 226:165–174. The distinction between aquatic and terrestrial olfactory receptor genes is described in Freitag, J., Ludwig, G., Andreini, I., Rossler, P., Breer, H. (1998) Olfactory receptors in aquatic and terrestrial vertebrates, *Journal of Comparative Physiology A* 183:635–650.

Human olfactory receptor evolution is discussed in a number of papers. This selection reflects the issues discussed in the text: Gilad, Y., Man, O., Lancet, D. (2003) Human specific loss of olfactory receptor genes, *Proceedings of the National Academy of Sciences* 100:3324–3327; Gilad, Y., Man, O., and Glusman, G. (2005) A comparison of the human and chimpanzee olfactory receptor gene repertoires, *Genome Research* 15:224–230; Menashe, I., Man, O., Lancet, D., Gilad, Y. (2003) Different noses for different people, *Nature Genetics* 34:143–144; Gilad, Y., Wiebe, V., Przeworski, M., Lancet, D., Paabo, S. (2003) Loss of olfactory receptor genes coincides with the acquisition of full trichromatic vision in primates, *PLoS Biology online access:* http://dx.doi.org/journal.pbio.0020005.

The notion of gene duplication as an important source of new genetic variation traces to the seminal work of Ohno almost forty years ago: S. Ohno, *Evolution by Gene Duplication* (New York: Springer-Verlag, 1970). A recent review of the issue that contains a discussion of both opsins and olfactory receptor genes is found in Taylor, J., and Raes, J. (2004) Duplication and divergence: the evolution of new genes and old ideas, *Annual Reviews of Genetics* 38:615–643.

CHAPTER NINE VISION

Opsin genes in the evolution of eyes have been described in a number of papers in recent years. Reviews of the basic biology and the consequences of opsin gene evolution include Nathans, J. (1999) The evolution and physiology of human color vision: insights from molecular genetic studies of visual pigments, *Neuron* 24:299–312; Dominy, N., Svenning, J. C., Li, W. H. (2003) Historical contingency in the evolution of primate color vision, *Journal of Human Evolution* 44:25–45; Tan, Y., Yoder, A., Yamashita, N., Li, W. H. (2005) Evidence from opsin genes rejects nocturnality in ancestral primates, *Proceedings of the National Academy of Sciences* 102:14712–14716; Yokoyama, S. (1996) Molecular evolution of retinal and nonretinal opsins, *Genes to Cells* 1:787–794; Dulai, K., von Dornum, M., Mollon, J., Hunt, D. M. (1999) The evolution of trichromatic color vision by opsin gene duplication in New World and Old World primates, *Genome* 9:629–638.

Detlev Arendt and Joachim Wittbrodt's work on photoreceptor tissues was originally described in a paper from the primary literature: Arendt, D., Tessmar-Raible, K., Synman, H., Dorresteijn, A., Wittbrodt, J. (2004) Ciliary photoreceptors with a vertebrate-type opsin in an invertebrate brain, *Science* 306:869–871. An associated commentary appeared with the piece: Pennisi, E. (2004) Worm's light-sensing proteins suggest eye's single origin, *Science* 306:796–797. An earlier review by Arendt provides the larger framework that he uses to interpret the discovery: Arendt, D. (2003) The evolution of eyes and photoreceptor cell types, *International Journal of Developmental Biology* 47:563–571. Further commentary can be found in Plachetzki, D. C., Serb, J. M., Oakley, T. H. (2005) New insights into photoreceptor evolution, *Trends in Ecology and Evolution* 20:465–467. Still more commentary on Arendt and Wittbrodt's work by Bernd Fritzsch and Joram Piatigorsky appeared in a later issue of *Science,* with a comment-reply that discussed the notion that the origin of eyes may be extremely ancient, and traced to a very deep branch of our evolutionary tree. This text can be found in *Science* (2005) 308:1113–1114.

A review of Walter Gehring's work on *Pax 6* and its consequences for eye evolution is contained in a personal account: Gehring, W. (2005) New perspectives on eye development and the evolution of eyes and photoreceptors, *Journal of Heredity* 96:171–184.

Papers that look at the different possible relationships between conserved eye formation genes and the evolution of eye organs include Oakley, T. (2003) The eye as a replicating and diverging modular developmental unit, *Trends in Ecology and Evolution* 18:623–627, and Nilsson D.-E. (2004) Eye evolution: a question of genetic promiscuity, *Current Opinion in Neurobiology* 14:407–414.

The relationship between the lens proteins in our eyes and those of larval sea squirts is discussed in Shimeld, S., Purkiss, A. G., Dirks, R.P.H., Bateman, O., Slingsby, C., Lubsen, N. (2005) Urochordate by-crystallin and the evolutionary origin of the vertebrate eye lens, *Current Biology* 15:1684–

1689.

CHAPTER TEN EARS

The genetics of inner ear evolution is discussed in Beisel, K. W., and Fritzsch, B. (2004) Keeping sensory cells and evolving neurons to connect them to the brain: molecular conservation and novelties in vertebrate ear development, *Brain Behavior and Evolution* 64:182–197. Ear development and the genes behind it are discussed in Represa, J., Frenz, D. A., Van de Water, T. (2000) Genetic patterning of embryonic ear development, *Acta Otolaryngolica* 120:5–10.

The transformation of the hyomandibula into the stapes is reviewed in comprehensive book-length treatments of the evolution of primitive fish or the origin of land-living animals: J. Clack, *Gaining Ground* (Bloomington: Indiana University Press, 2002); P. Janvier, *Early Vertebrates* (Oxford, Eng.: Oxford University Press, 1996). It is also discussed in recent research papers, including Clack, J. A. (1989) Discovery of the earliest known tetrapod stapes, *Nature* 342:425–427; Brazeau, M., and Ahlberg, P. (2005) Tetrapod-like middle ear architecture in a Devonian fish, *Nature* 439:318–321.

The origin of the mammalian middle ear is discussed from the perspective of a scientific historian in P. Bowler, *Life's Spendid Journey* (Chicago: University of Chicago Press, 1996). Key primary sources include: Reichert, C. (1837) Uber die Visceralbogen der Wirbeltiere im allgemeinen und deren Metamorphosen bei den Vogeln und Saugetieren, *Arch. Anat. Physiol. Wiss. Med.* 1837:120–222; Gaupp, E. (1911) Beiträge zur Kenntnis des Unterkiefers der Wirbeltiere I. Der Processus anterior (Folii) des Hammers der Sauger und das Goniale der Nichtsäuger, *Anatomischer Anzeiger* 39:97–135; Gaupp, E. (1911) Beiträge zur Kenntnis des Unterkiefers der Wirbeltiere II. Die Zusammensetzung des Unterkiefers der Quadrupeden, *Anatomischer Anzeiger,* 39:433–473; Gaupp, E. (1911) Beiträge zur Kenntnis des Unterkiefers der Wirbeltiere III. Das Probleme der Entstehung eines "sekundären" Kiefergelenkes bei den Säugern, *Anatomischer Anzeiger,* 39:609–666; Gregory, W. K. (1913) Critique of recent work on the morphology of the vertebrate skull, especially in relation to the origin of mammals, *Journal of Morphology* 24:1–42.

Major literature on the origin of the mammalian jaw, chewing, and the three-boned middle ear includes Crompton, A. W. (1963) The evolution of the mammalian jaw, *Evolution* 17:431–439; Crompton, A. W., and Parker, P. (1978) Evolution of the mammalian masticatory apparatus, *American Scientist* 66:192–201; Hopson, J. (1966) The origin of the mammalian middle ear, *American Zoologist* 6:437–450; Allin, E. (1975) Evolution of the mammalian ear, *Journal of Morphology* 147:403–438.

The evolutionary origin of *Pax 2* and *Pax 6* and the evolutionary link of ears and eyes to box jellyfish is discussed in Piatigorsky, J., and Kozmik, Z. (2004) Cubozoan jellyfish: an evo/devo model for eyes and other sensory systems, *International Journal for Developmental Biology* 48:719–729.

Links of sensory receptor molecules to different molecules in bacteria are discussed in Kung, C. (2005) A possible unifying principle for mechanosensation, *Nature* 436:647–654.

CHAPTER ELEVEN THE MEANING OF IT ALL

The methods of phylogenetic systematics are discussed in a number of sources. Key primary literature includes the classic work of Willi Hennig, published originally in German (*Grundzüge einer Theorie der phylogenetischen Systematik* [Berlin: Deutscher Zentralverlag, 1950]) and translated into English more than a decade later (*Phylogenetic Systematics,* trans. D. D. Davis and R. Zangerl [Urbana: University of Illinois Press, 1966]).

Methods of phylogenetic reconstruction, which form the basis for the chapter, are discussed in detail in P. Forey, ed., *Cladistics: A Practical Course in Systematics* (Oxford, Eng.: Clarendon Press, 1992); D. Hillis, C. Moritz, and B. Mable, eds., *Molecular Systematics* (Sunderland, Mass.: Sinauer Associates, 1996); R. DeSalle, G. Girbet, and W. Wheeler, *Molecular Systematics and Evolution: Theory and Practice* (Basel: BirkhauserVerlag, 2002).

A comprehensive treatment of the phenomenon of independent evolution of similar features is in M. Sanderson and L. Hufford, *Homoplasy: The Recurrence of*

Similarity in Evolution (San Diego: Academic Press, 1996).

To see the tree of life and the different hypotheses for the relationships between living creatures, visit http://tolweb.org/tree/.

The notion that our evolutionary history has medical implications has been the subject of several good recent books. For comprehensive and well-referenced treatments, see N. Boaz, *Evolving Health: The Origins of Illness and How the Modern World Is Making Us Sick* (New York: Wiley, 2002); D. Mindell, *The Evolving World: Evolution in Everyday Life* (Cambridge, Mass.: Harvard University Press, 2006); R. M. Nesse and G. C. Williams, *Why We Get Sick: The New Science of Darwinian Medicine* (New York: Vintage, 1996); W. R. Trevathan, E. O. Smith, and J. J. McKenna, *Evolutionary Medicine* (New York: Oxford University Press, 1999).

The apnea example I derived from discussions with Nino Ramirez, chairman of the Department of Anatomy at the University of Chicago. The hiccup example is derived from Straus, C., et al. (2003) A phylogenetic hypothesis for the origin of hiccoughs, *Bioessays* 25:182–188. The human-bacterial gene switch used in the study of mitochondrial cardioencephalomyopathy was originally discussed in Lucioli, S., et al. (2006) Introducing a novel human mtDNA mutation into the *Paracoccus denitriticans* COX 1 gene explains functional deficits in a patient, *Neurogenetics* 7:51–57.

ONLINE RESOURCES

A number of websites and blogs carry accurate information and are updated frequently.

http://www.ucmp.berkeley.edu/ Produced by the Museum of Paleontology at the University of California–Berkeley, this is one of the best online resources on paleontology and evolution. It is continuously updated and revised.

http://www.scienceblogs.com/loom/ This is Carl Zimmer's blog, a well-written, timely, and thoughtful source of information and discussion on evolution.

http://www.scienceblogs.com/pharyngula/ P. Z. Myers, a professor of developmental biology, writes this accessible, informative, and cutting-edge blog. This is a rich source of information, well worth following.

Both Zimmer's and Myers's blogs are at http://www.scienceblogs.com, a site that contains a number of excellent blogs also worth following for information and commentary on recent discoveries. Blogs relevant to the theme of this book at that site include Afarensis, Tetrapod Zoology, Evolving Thoughts, and Gene Expression.

http://www.tolweb.org/tree/ The Tree of Life Project provides a regularly updated and authoritative treatment of the relationships among all groups of life. Like the UCMP page at Berkeley, it also includes resources for learning about how evolutionary trees are made and interpreted.

ACKNOWLEDGMENTS

All the illustrations, except where noted, are by Ms. Kalliopi Monoyios (www.kalliopimonoyios.com). Kapi read drafts of the manuscript and not only improved the text but designed art that matched it. I have been truly fortunate to work with someone with so many talents. Scott Rawlins (Arcadia University) generously gave permission to use his elegant rendering of *Sauripterus* in Chapter 2. Ted Daeschler (Academy of Natural Sciences of Philadelphia) graciously provided his superb photos of the great *Tiktaalik* "C" specimen. Thanks are due to Phillip Donoghue (University of Bristol) and Mark Purnell (University of Leicester) for permission to use their rendering of the conodont tooth array, McGraw-Hill for permission to use the textbook figure that started the hunt for *Tiktaalik,* and Steven Campana of the Canadian Shark Research Laboratory for the photos of shark organs.

One of the greatest debts students of anatomy have is to the people who donate their bodies so that we can learn. It is a rare privilege to learn from a real body. Sitting through long hours in the lab, one feels a very profound connection to the donors who make the experience possible. I felt that connection again while writing this book.

The ideas I present here are rooted in research I've done and in classes I've taught. Colleagues and students too numerous to name—undergraduates, medical students, and graduate students—have played a role in the thinking that went into these pages.

I owe a great debt to the colleagues I have worked with over the years. Ted Daeschler, Farish A. Jenkins, Jr., Fred Mullison, Paul Olsen, William Amaral, Jason Downs, and Chuck Schaff have all been part of the stories I tell here. Without these people I would have had no reservoir of experience on which to draw, nor would I have had as much fun along the way. Members of my laboratory at the University of Chicago—Randall Dahn, Marcus Davis, Adam Franssen, Andrew Gillis, Christian Kammerer, Kalliopi Monoyios, and Becky Shearman—all influenced my thinking and tolerated my time away from the bench as I wrote.

Colleagues who gave their time to provide needed background or comments on the manuscript include Kamla Ahluwalia, Sean Carroll, Michael Coates, Randall Dahn, Marcus Davis, Anna DiRienzo, Andrew Gillis, Lance Grande, Elizabeth Grove, Nicholas Hatsopoulos, Robert Ho, Betty Katsaros, Michael LaBarbera, Chris Lowe, Daniel Margoliash, Kalliopi Monoyios, Jonathan Pritchard, Vicky Prince, Cliff Ragsdale, Nino Ramirez, Callum Ross, Avi Stopper, Cliff Tabin, and John Zeller. Haytham Abu-Zayd helped with many administrative matters. My own teachers of anatomy in the Harvard–MIT Health Sciences and Technology program, Farish A. Jenkins, Jr., and Lee Gehrke, stimulated an interest that has lasted over twenty years.

Key advice at the inception of the project, and inspiration throughout, came from Sean Carroll and Carl Zimmer.

The Wellfleet Public Library (Wellfleet, Massachusetts) provided a comfortable home, and much-needed retreat, where I wrote significant parts of the book. A brief stint at the American Academy in Berlin put me in an environment that proved critical when I was completing the manuscript.

My two bosses, Dr. James Madara, M.D. (CEO, University of Chicago Medical Center, Vice President for Medical Affairs, Dean and Sara and Harold Thompson Distinguished Service Professor in the Biological Sciences Division and the Pritzker School of Medicine), and John McCarter, Jr. (CEO, The Field Museum), supported this project and the research behind it. It has been a true pleasure to work with such insightful and compassionate leaders.

I have been fortunate to teach at the University of Chicago and to have had the opportunity to interact with the leadership of the Pritzker School of Medicine there. The deans, Holly Humphrey and Halina Bruckner, graciously welcomed a paleontologist to their team. Through interacting with them I came to appreciate the challenges and importance of basic medical education.

It has been a great pleasure to be associated with The Field Museum in Chicago, where I have had the opportunity to work with a unique group of people dedicated to scientific discovery, application, and outreach. These colleagues include Elizabeth Babcock, Joseph Brennan, Sheila Cawley, Jim Croft, Lance Grande, Melissa Hilton, Ed Horner, Debra Moskovits, Laura Sadler, Sean VanDerziel, and Diane White. I am also grateful for the support, guidance, and encouragement I have received from the leaders of the Committee on Science of the Board of Trustees at The Field Museum, James L. Alexander and Adele S. Simmons.

I am indebted to my agent, Katinka Matson, for helping me turn an idea into a proposal and for advice throughout the process. I feel privileged to have worked with Marty Asher, my editor. Like a patient teacher, he gave me a nurturing combination of advice, time, and encouragement to help me find my way. Zachary Wagman contributed to this project in countless ways by being free with his time, keen editorial eye, and good counsel. Dan Frank made insightful suggestions that stimulated me to think about the story in new ways. Jolanta Benal copyedited the text and improved the presentation immeasurably. I am very grateful to Ellen Feldman, Kristen Bearse, and the production team for their hard work under a tight schedule.

My parents, Gloria and Seymour Shubin, always knew that I would write a book, even before I did. Without their faith in me, I doubt that I ever would have put a word on paper.

My wife, Michele Seidl, and our children, Nathaniel and Hannah, have been living with fish—both *Tiktaalik* and this book—for the better part of two years. Michele read and commented on every draft of this text and supported long weekend absences while I wrote. Her patience and love made it all possible.

 Published in the United States by Pantheon Books, a division of Random House, Inc., New York, and in Canada by Random House of Canada Limited, Toronto.

Pantheon Books and colophon are registered trademarks of Random House, Inc.

All illustrations by Kalliopi Monoyios unless otherwise noted.

Library of Congress Cataloging-in-Publication Data

Shubin, Neil.
Your inner fish : a journey into the 3.5-billion-year history of the human body / By Neil Shubin.—1st ed.
p. cm.
Includes bibliographical references.
eISBN: 978-0-307-37716-6
1. Human anatomy—Popular works. 2. Human evolution—Popular works. I. Title.
QM26.s58 2008 611—dc22 2007024699

www.pantheonbooks.com

v1.0