More than 100 years ago, Charles Darwin systematically charted relationships of organisms in space and time. What emerged was the concept of the Tree of Life, a cornerstone in evolutionary theory that, as well as classifying organisms, has the potential to make sense of all biology. What kind of tree is it and where are we on it? Many are comfortable with the idea that humanity occupies the apex of a symmetrical Christmas fir, but disturbed by the growing realization that we are really just clinging to a minor twig of a ragged old eucalypt. The discovery of the structure of DNA 50 years ago, combined with our increasing understanding of the history of life, helps us to relate branches to one another and deduce how the Tree grew at a genomic level. We can now use evolution not only to answer the “how does it work?” questions but to move on to the ones of ultimate significance to humans: “why?”

Until a decade ago, it seemed an impossible dream to unravel the genetic message of a bacterium, let alone a human, and to pick out genes, sequence them, and figure out what they do individually. At first glance, most of the human genome appears to encode nothing meaningful, although this “junk” increasingly appears to harbor cryptic controls and switches. The precious informative bits seem to be copied into confusingly permuted messages and translated into a bewildering variety of proteins networked in complex ways. Like the infinity of space, the hugeness of the human genome, and the varieties of ways in which it is expressed, can evoke helpless awe. But the proliferation of sequencing projects threatens to bury us all in mountains of leaves from the Tree of Life. How can we establish the rules of life, and can they be simplified?

Our most powerful tool for making sense of the genome data is variation. Within species, mutations (spontaneous or engineered) and population variation provide insight into gene function, gene change, and gene flow. Even more powerful for understanding the big picture of life are comparisons among species: species that are closely related, such as human and chimpanzee, and distantly related, such as fish and flies, worms and yeast; and species from the fossil record, which also mark evolutionary events. Details of genome organization, recombination, duplication and translocation, mutation and epigenetic modification, and repeated sequences and retrotransposition in different branches of the Tree will help to answer the “how” questions and may even allow us to tinker with life forms (including our own) in, hopefully, beneficial ways.

We edge ever closer to answering the big “why” questions: Why is a human different from a chimp or a mouse? Why do selective forces drive gene birth and death and reshape groups of genes to modify physiology and behavior? And what are those forces? Ultimately, we wish to understand what drives genome change and to formulate the unifying principles that built the Tree of Life, even if the most general rule is just “whatever works.”

The promise of proteomics for unscrambling how genes network to establish phenotypes is exciting, but I hope we will not rush through the genomics era to the postgenomics haven longed for by die-hard protein biochemists. Microarray analyses deliver enormous amounts of data on gene expression patterns, so we need more than ever to understand evolutionary variation to deduce how proteins took on their shapes and found new functions. By grouping proteins into domains and families that are understandable in terms of gene duplication and rearrangement, genetic complexity can become accessible. All biologists will need a working knowledge of the rules governing this complexity—both those of genetics and of evolution.

A change in our approach to genetics, genomics, and evolution as a whole must feed quickly into the education system, so that future generations can see through the complexity of biology to the underlying principles being revealed and find answers to their own “whys.” Just as the details of cracking the DNA code (which, as I recall, dominated graduate courses in the 1960s) are encapsulated in a single table in today’s biology primers, details that seem impossibly complicated now must resolve into an introductory chapter in the school textbooks of 2008. The concept of the unity of life—the most simple and general rules of molecular structure, chemistry, and genetics that apply to all organisms—should be introduced in grade school. These rules can be linked firmly to an understanding of the way in which the genome has gradually changed over the more than 3 billion years that life has been unfolding. The fascinating descriptive biology of diverse organisms that my generation grew up on can come later, once there is a framework to hang it on. That way, future generations will be able to appreciate the beauty of the Tree of Life without its form being obscured by the tangle of twigs and leaves.

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The Tree of Life: View from a Twig
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