Rethinking the Tree of Life

Even though lateral gene transfers tend to undermine this beloved metaphor, the underlying theory of evolution is very much intact

W. Ford Doolittle

Two decades ago, rumors began to spread that something was seriously wrong with the universal Tree of Life (TOL). Since the middle 1960s, evolutionists had been comparing molecular sequences—first proteins, then ribosomal RNAs, then protein-coding genes, and later genomes—to reconstruct evolutionary relationships. Tacit assumptions in this pursuit, called molecular phylogenetics, were that all genes would tell pretty much the same story, enabling us to trace back through a series of branchings to some single last universal common ancestor (LUCA).

However, in the 1990s, some evolutionists realized that for prokaryotes, at least, such assumptions might not be safe. Because of lateral gene transfers (LGT), analyses of different genes can yield different trees. Moreover, nothing can guarantee that any gene will have escaped being transferred sometime during four billion years of life. Several of us thus began to ask if it would still be possible to construct a universal TOL and whether such a tree would be meaningful.

Tree Huggers versus Bashers

That two-decade debate between those who answer yes to both those questions (the “tree-huggers”) and those who answer no (the “tree-bashers”) leaves us with a conceptual conundrum. We can construct what looks like a TOL, but whether it is valid depends on what we want that concept to be, more a matter of philosophy than biology. Here I ask whether the TOL is (i) what Darwin meant it to be, (ii) proof of the theory of evolution, (iii) a tracing of the history of cells and species, (iv) singly rooted, (v) a sensible framework for systematics, or (vi) essential in the battle against creationism.

My response, perhaps predictably, is none of the above six, despite there being some value in each possibility. My reservations deal mainly with the prokaryote part of the TOL. For one thing, LGT is surely less frequent in complex multicellular plants and animals, especially those with differentiated germ lines. Although there are reliable reports of LGT among unicellular eukaryotes, especially phagotrophic protists, prokaryotes comprise the majority of living things on this planet, excluding viruses. So for the TOL, accommodating prokaryotes and LGT looms as the most critical challenge.

Considering the Six Possibilities: Darwin’s Version

Biologists were drawing trees centuries before Darwin, and similar efforts to organize physical observations or concepts into categories and subcategories go back at least as far as the Greek philosophers. Assigning organisms into hierarchical schemes based on phenotypic similarities and differences—branching trees—seems natural. Thus, for example, all birds are more like each other than any is to any fish, and vice versa, while birds and fishes are more closely related to each other than to flowering plants. In biological systematics we argue about what the truth is, but not...
about whether there is one. Before 1859, why any biological classification should be true was a philosophical or theological matter. For Christians it was easy: an orderly classification reflected the orderly mind of a Creator.

**Possibility One: a Naturalistic Hypothesis**

Darwin did not set out to challenge Christianity, but he did seek a non-supernatural explanation for the orderliness and seeming naturalness of biological classifications. He found it in evolution. “All true classification is genealogical,” he wrote in *On the Origin of Species*. Moreover, he thought the pattern would be tree-like all the way down: “The affinities of all beings of the same class have sometimes been represented by a great tree. I believe this simile largely speaks the truth . . . [a ‘great tree,’ whose] ramifying branches may well represent the classification of all extinct and living species in groups subordinate to groups.”

Those comments are part of what Eric Bapteste and I call Darwin’s “Tree of Life Hypothesis (TOLH).” He and other systematists saw a tree-like pattern of natural classification based on phenotype, and he inferred an underlying tree-like process producing that pattern. Darwin called this process “descent with modification,” but we just call it “evolution.” The TOLH is a hypothesis rather than a fact because a branching evolutionary process is not the only way to explain tree-like classifications (Fig. 1).

Although the Tree of Life Hypothesis should be testable, for many prokaryotes, it is not. For them, we have no widely accepted “natural classification” other than that based on ribosomal RNA (rRNA) sequences, widely taken to represent the underlying evolutionary process. Of course this pattern and process agree, because they are part of a circular claim. But an independent hierarchical prokaryotic classification—like earlier ones for animals and plants based on phenotypic similarities and differences—would often differ from one based on the rRNA tree, sometimes drastically.

When trying to infer phenotype from genes in any genome, this problem shows up at all taxonomic levels. With species, there can be disagreement between phenotype and strain position in an rRNA-based phylogeny. At the phylum level, there are instances like the Thermotogales, which are sister taxa to Aquificales based on ribosomes, but fall within Firmicutes with the majority of their other genes. And, at the domain level, the

---

**FIGURE 1**

Both branching processes with congruent gene trees and a pattern of biased LGT will lead to these trees, with many phylogenetic reconstruction methods. For biased gene transfer, taxa A, B, and C need have no recent common ancestors, and the nodes 1 and 2 in that tree do not correspond to ancestral taxa.
widely accepted closer relationship of Archaea and eukaryotes is based only on a minority of genes: the majority show a bacterial/eukaryotic affinity.

Possibility Two: Proof of the Theory of Evolution

Simply expanding hierarchical classification by adding more taxa and improving tree-construction algorithms does not prove the theory of evolution. Hierarchical classification is a fact of nature to be explained, and it cannot logically be then re-employed to prove that explanation. The circularity of such reasoning is embedded in *The Origin*, as the late Alec Panchen of the University of Newcastle and Niles Eldredge of the American Museum of Natural History pointed out decades ago. Thus it is the convergence (consilience) of many independent lines of evidence from systematics, phylogenetics, molecular biology, biogeography, and developmental biology that so robustly supports the modern theory of evolution, not any one alone.

What most distinguishes Darwin’s TOLH from the “orderly mind of the Creator” theory? The “ancestral” nodes deep within the great tree that Darwin embraced as a “simile” correspond to ancestors within a historical sequence. God’s creating all taxa in a few biblical days, however, leaves no room for such an extended history and no ancestors.

Some nontheologically motivated tree bashers also question the extent to which ancestral nodes in the TOL correspond to real ancestral taxa. Two bacterial species A and B that exchange genes with each other frequently will inevitably come to resemble each other closely in gene composition or gene sequence even if they share no common ancestor. Treeing methods will show A and B as “sister” taxa (Fig. 1). For this second and fully logical reason, constructing trees does not by itself prove Darwin’s theory.

Possibility Three: Tracing the History of Cells and Species

Tree huggers generally admit that LGT is far more pervasive than was thought when molecular phylogenetics was conceived. Because of LGT, gene trees will disagree and there can be no unambiguous single “tree of genomes.” However, because genomes replicate only within organisms, there is in principle a tree of organisms and cells, comprising all speciation events and (for asexual lineages) all cell divisions back to the beginning of time. Tree bashers might protest that this concept privileges some cellular processes over others, but it is not incoherent.

We might construct a presumptive tree of species and cell divisions, in several complementary ways. First, we could build the tree with “core” genes that are present in all or most genomes. Ribosomal RNA, ribosomal protein, and other translation-related genes are favored for this building process not only because they are universal but also because they appear to be difficult to transfer over substantial phylogenetic distances. Moreover, it was rRNA on which the late Carl Woese based his groundbreaking microbial phylogeny. However, even if we could be sure that ribosomal and other core genes never transfer, such genes are very few. One attempt to construct a universal TOL from 31 core genes was famously derided as “the Tree of One Percent.”

Second, we might construct trees on the basis of shared gene content, without attention to sequence divergences within gene families. In following this approach, for example, Thermochoiales would be nested within the Firmicutes. Third, we might try super-tree, super-matrix, or consensus approaches to reconcile incongruent individual gene trees, forcing them into a minimally conflicting structure, which might be thought of as the “central tendency” of the data. Fourth, newer hybrid methods aim to reinforce core or supertree approaches by recognizing that LGTs at the base of clades make excellent shared characters for defining them.

All these approaches might work despite rampant LGT, if LGT were random, occurring at similar frequencies regardless of the evolutionary distance between or ecological preferences of donors and recipients. However, LGT is not random. Within species, homologous recombination can be very frequent, leading trees for strains to differ gene by gene. Two routes for between-species LGT, conjugation and transduction, typically show some degree of host specificity, while transformation should be more difficult the greater the phylogenetic distance between donor and recipient, because of divergence in informational machinery. The consequences of such a “phylogenetic bias” on LGT might be seen as harmless or beneficial to tree-building, with LGT
reinforcing the true evolutionary signal. Still, such trees are at best “fuzzy.”

Ecological bias is a more serious problem. LGT is more frequent between donors and recipients that live in the same sorts of places and do similar things. None of the four methods is immune to this bias, and there will be instances where gene-based reconstructions do not accurately reflect the history of speciation.

Possibility Four: Singly Rooted
The last sentence of the first edition of *The Origin* begins, “There is grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one . . .” This last small equivocation notwithstanding, most scholars see that the Tree of Life had but a single root.

Woese imagined something more inchoate, with Bacteria, Archaea, and Eukarya arising as cellular lineages independently from a “progenote” state. If we define life as replicating information and see it emerging first at the level of RNA, it is possible that many forms rather than one cooperated before cellular life took off. However, most tree-huggers talk in terms of a single last universal common ancestor, and some but not all imagine it to be a single cell.

Rampant LGT means that most if not all the genes in such a cell will have been lost or replaced by homologs or nonhomologous genes with the same or different functions, unless some genes can never be lost, gained, or replaced. Thus, LUCA’s genes are not directly necessarily ancestral to contemporary members of the gene family to which they belong. Even were it sensible to imagine a single root to the TOL we cannot be sure what genes the organism corresponding to that root had or of anything about its phenotype.

Possibility Four: a Sensible Framework for Systematics
Systematics is as much a legalistic practice as a science. In principle it can be divorced from evolutionary theory, and in the 1950s and 1960s pheneticists and numerical taxonomists insisted that it should be. Phenetic classifications, based on assessing overall similarities objectively, are unquestionably useful in inferring evolutionary (cladistic) relationships, and branching processes. But if classifications already incorporate inferences about evolution, we are trapped in circular reasoning. Indeed, Darwin’s TOLH is that branching evolution explains tree-like phenetic classification, not that these are identical, conceptually or in practice. However, since Darwin we tend to assume, simplistically, that proper classifications are genealogical. For many, “classification” and “phylogeny” are synonyms.

LGT makes genealogy less tree-like and requires that we again separate phenetics from cladistics. Indeed, some argue that networks rather than trees should be the basis of systematics. It is hard to beat dichotomously branching hierarchies, however, and most of us would probably be uncomfortable saying that *Thermotoga maritima* is not only a member of the phylum Thermotogae but also of the phylum Firmicutes. *Bergey’s Manual* adopted rRNA phylogenetics as the “backbone” for its taxonomy at higher ranks, and this system seems the best bet when facing discoveries of new life forms and methodological innovations. Such enshrinement should nevertheless not be taken as a guarantor of the truth, or evidence that there is only one simple truth about relationships.

Possibility Six: Essential in the Battle against Creationism
Several biologists who defend the theory of evolution argue as if the TOL were essential for that defense. For Creationists, “organisms would not have common ancestry, but would simply result from an instantaneous creation of forms designed de novo to fit their environments,” notes Jerry Coyne at the University of Chicago. “Under this scenario, we wouldn’t expect to see species falling into a nested hierarchy of forms that is recognized by all biologists.” Richard Dawkins, in an amusing exchange with Craig Venter, seems to hold a similar view (https://www.youtube.com/watch?v=MXrYhINutuI).

They and other experts conflate “common ancestry” with “common ancestor.” The analogous mistake in human evolution would be to assume that because all men might trace their ancestry by their Y chromosomes back to one single “Y-chromosome Adam” and all women might trace their mitochondria back to a single “mitochondrial Eve,” that these two were a couple. Current thinking is that they lived in different populations thousands of years apart. Moreover, our non-Y,
nonmitochondrial autosomal alleles trace back to still different individuals.

Because of sex and recombination, common ancestry does not mean that there is a single common ancestor or ancestral couple. Similarly, because of LGT, there was not a single cell or species in which the last common ancestors of all genes in prokaryotes were present. Moreover, there will always be nodes, but these need not always be ancestors. The “nested hierarchy of forms that is recognized by all biologists” is not proof of process.

Such a proof is not needed to counter the claims of Creationists. All we need to assert is that genetic and ecological processes and forces of which we have by now a very good understanding are adequate when extrapolated over three or four billion years to explain the adaptedness and diversity of life on this planet. Our explanatory toolkit is very robust and, though the theory of evolution is more complex and nuanced than Darwin imagined, he would surely be pleased our progress in elaborating it.

Conclusion

Tree huggers and many tree bashers accept that the TOL is a robust or “good-enough” metaphor and a logical basis for universal classification. However, it may be inappropriate in many specific contexts. Sometimes the pattern will be reticulate and sometimes tree-like, and the hierarchical level of analysis matters. There logically is a single tree of animal phyla, but within (sexual) animal species there is no single tree of individuals, nor is there one of genomes or genes (because of recombination). Only at the level of nucleotides is there again in principle only one tree. Much of the heat in the debate over the TOL comes from conflating the “Tree of Genomes,” which does not exist, with the historical tree of cells and species, which might. Molecular phylogenetics encouraged this conflation.

It is not necessary to make the truth of a TOL a bulwark in our defense of the theory of evolution. Newer “network” methods may more accurately represent evolutionary relationships, though it is hard to see how they will ever achieve the convenience of hierarchical schemes for organizing knowledge and identifying species. We might be wise to relax the requirement that “all true classification is genealogical.” The truth is more complex than Darwin knew or could have known.

Suggested Reading


