W. Ford Doolittle: Evolutionary Provocations and a Pluralistic Vision

This is the penultimate draft of a chapter to appear in *Dreamers, Romantics and Visionaries in the Life Sciences*, edited by Michael Dietrich and Oren Harman (forthcoming, University of Chicago Press). Please check first before citing or using this draft.

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Introduction

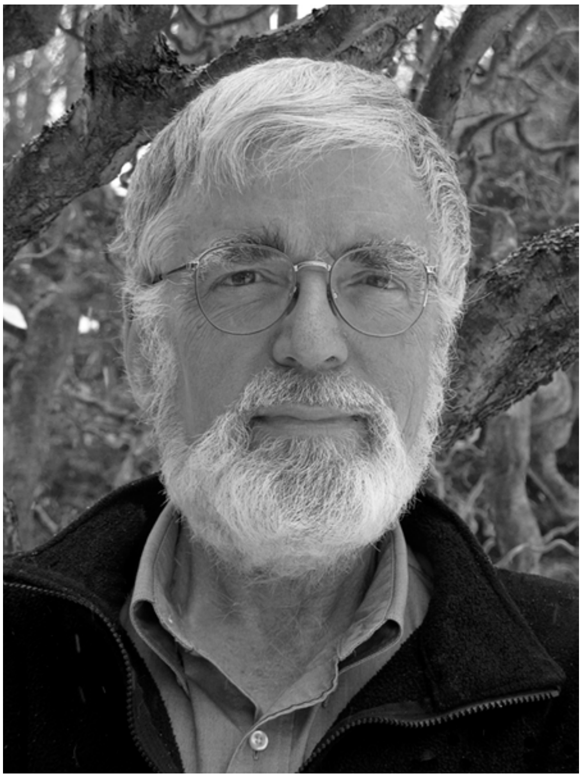
Although many scientists see their work as distinct from academic endeavors that are not classified as natural science, others draw resources from more distant disciplines. Ford Doolittle has maintained throughout his career a deep interest in the humanities and arts, which might be explained to some extent by his father's academic interests. His father was a professor of Art (painting) at the University of Illinois in Champaign-Urbana, the city in which Ford was born in 1942. As an undergraduate at Harvard, Doolittle was torn between science and literature. Science won, at least in part because his applications to literature programs were knocked back.[1] When he was interviewed in 1970 for a position at Dalhousie University (Halifax, Nova Scotia, Canada), the Department Head asked him what he would do if he didn't get the job. 'Write science fiction', said Doolittle, suggesting an alternative career that was not utterly unimaginable to people who knew him at the time.[2] Non-counterfactually, Doolittle pursued part-time for several years a degree in Fine Arts at the Nova Scotia College of Art and Design (completed in 2012). Working in several media, his photography in particular has engaged with his scientific world-view and been exhibited in its own right. Some of the more postmodern theory that informs the study of art these days may also have crept into his philosophical research. As he says, "in both science and art I struggle to be deconstructive, in a polite way."[3]

As part of this 'deconstructive' approach, philosophy has been an implicit and explicit spur to Doolittle's work for at least two decades. The explicit commitments began with the formation of Dalhousie's Evolution Studies Group in the 1990s. Its members include philosophers of science and mathematics, moral philosophers, psychologists, cognitive scientists, economists, anthropologists, sociologists, biophysicists and a huge variety of biologists. The group appointed a postdoctoral fellow with Doolittle's funding in 2001 (the author of this essay), and now, with a Herzberg award (often called Canada's highest science honor), Doolittle has chosen to invest a large portion of it in more philosophy research, including the appointment of two more postdoctoral fellows.

As well as advancing discussion on core topics in philosophy of biology, such as function, phylogeny, adaptation, and evolutionary theory generally, Doolittle has used the philosophy of science to reflect on his own meta-methodology, and the nature of the scientific debates in which he has been involved. Increasingly of late he has been working out his commitments to pluralism, and – ultimately – the relationship of artistic creativity to scientific sensibility.

Amongst the several major contributions Doolittle has made to the scientific literature, perhaps the best known, for a general audience, is what he has had to say about organisms promiscuously passing around genetic material, and the implications of that for the very possibility of phylogenetic reconstruction (the graphic representation of evolutionary lineages and their divergence points). But just as ground-breaking are numerous other debates that Doolittle has either initiated or transformed during his engagement with them. I will show how his broad research agenda is driven by a commitment to questioning orthodoxy, by examining its assumptions and implicit limitations. I suggest it is philosophical because it proposes a view of how science should proceed (sometimes by going backwards, and often by moving sideways); moreover, it is a practical philosophy that serves as a meta-methodology allowing innovative thinking to flourish. Its aim is explicitly to strengthen scientific inquiry, not weaken it, and several themes in Doolittle's career attest to how such an approach can produce novel insight.

Figure 1: W. F. Doolittle, courtesy of W. F. Doolittle



Early Career

After an undergraduate degree in biochemistry at Harvard, Doolittle did his PhD at Stanford with Charles Yanofsky of co-linearity and tryptophan biosynthesis fame. Doolittle's PhD topic involved an analysis of the transcriptional repression of tryptophan in *Escherichia coli*.[4] Yanofsky was a product of the Beadle-Tatum 'biochemical genetics' lineage,[5] and it is in this illustrious tradition that Doolittle forged his own trajectory in molecular mechanisms and their evolution. Just as Yanofsky saw his career as one that attested to the value and creativity of basic science,[6] so too have these aspirations guided Doolittle throughout his subsequent career.[7]

From Stanford, Doolittle returned to Illinois in 1968 for a postdoctoral fellowship with Sol Spiegelman (1914-1983). Spiegelman, whom Doolittle has described as "a major figure who should have gotten the Nobel Prize"[8] – something it seems Spiegelman himself felt rather bitter about[9] – was renowned for his ground-breaking work on RNA and particularly DNA-RNA hybridization.[10] Doolittle had already gained some undergraduate experience in Spiegelman's lab, primarily as a dishwasher and laboratory drudge, but he had also been exposed to the excitement and sheer dedication of laboratory work.[11] As a postdoctoral fellow he shared more equally in these sentiments, and made strong connections to Spiegelman's colleagues. Notable amongst them were Carl Woese (1928-2012), running his own 'revolutionary' research program down the hallway,[12] and Norman Pace, a postdoc of Spiegelman, who also collaborated with Woese. Doolittle took up a subsequent postdoc with Pace, and they worked together on ribosomal RNA[13] – a molecule that Woese was revealing as central to understanding evolution. In 1971, Doolittle carried these interests with him to Dalhousie University where he developed the research that has made him famous.

Doolittle became interested in Dalhousie after making a connection with Stanley Wainwright (1927-2003), a biochemist who had come to Dalhousie via Yale, Columbia, and the Pasteur Institute. Wainwright's wife, Lillian Schneider Wainwright had worked and published with molecular biology illuminati Francis Ryan (1916-1963) and Joshua Lederberg (1925-2008). Despite Dalhousie being a somewhat out-of-the-way place from an American perspective, the omens were therefore good for settling into a strong scientific community. Not only that, but as Doolittle has observed himself, there was none of the heavy pressure to be a star that existed at more prestigious institutions across the border.[14] Be that as it may, Doolittle rapidly became one of Dalhousie's stars, but by working with and shining alongside local scientific talent. A major collaboration developed with Michael Gray. He and Doolittle did the formative molecular work that established once and for all the endosymbiont hypothesis of chloroplast origins, plus much of the groundwork doing the same for the origin of the mitochondrion.[15] Gray and Doolittle's solid evidential anchoring of the then slightly dodgy endosymbiont hypothesis may have looked like the positive reinforcement of an idea whose time had finally come. Eventually, however, this work connected with another radical agenda about lateral acquisitions, as we shall see below ("Upsetting the tree of life").

Doolittle's proclivity for doubting orthodoxy began much earlier with questions about the power of adaptationism.

Questioning adaptationism

Although as a PhD student Doolittle encountered "panadaptationist" thinking, the very nature of working with molecules meant that he would have to grapple with non-adaptive or neutral evolution at work in nucleotide and amino acid sequences.[16] In fact, Doolittle has claimed that Gould and Lewontin's "Spandrels" paper advocating a reconsideration of panadaptationism was his greatest influence.[17] Doolittle's advocacy for non-adaptationist explanations was honed during his involvement in a major debate about the evolution of introns. In 1977, which was a "big year"[18] because it also saw the discovery of Archaea (the non-bacterial prokaryotes), eukaryote protein-coding genes were found to have introns. These genes are "interrupted by 'silent' DNA", said Walter Gilbert (of subsequent sequencing technique fame), who then tried to explain why these "intergenic regions" – for which he coined the word "intron," in contrast to "exon" for the coding regions – were selected.[19] "What are the benefits of this intronic/exonic structure for genes?" Gilbert mused, taking for granted there would be benefit. His answer was that evolution puts aside some "scattered" genes in the form of introns so that the potential for variation and speedy evolution is preserved. Introns are thus "both frozen remnants of history and … the sites of future evolution."[20]

Doolittle, who was then on sabbatical in Gilbert's lab, elaborated on this historical scenario of the ancient emergence of introns.[21] According to Doolittle, genes may have been interrupted from their very origin, and prokaryotes (which don't have the sorts of introns being discussed) were then streamlined from this primordial architecture. Rather than thinking of the tidy prokaryote genome as "primitive" and the messy eukaryote genome as an evolutionary refinement, this view of "introns early" (i.e., the basic state of genome organization) undercut a very traditional simple-to-complex view of the evolution of life. Moreover, argued Doolittle, Gilbert's adaptationist explanation was teleological, because it suggested that introns were retained by selection for the future benefit of the lineages carrying them.[22]

The "introns early" perspective was eventually overwhelmed by the "introns late" view (the position that spliceosomal introns originated in eukaryotes, and prokaryotes never had them). Doolittle himself produced some of the evidence undermining his original position, which he then announced as "untenable."[23] He was ultimately able to explain the evolution of these introns as an example of "constructive neutral evolution" (see below).[24] It may be the case that introns-early is not completely dead, though it would have to be considerably different from the original simple view. In Eugene Koonin's recent revisionary efforts, the introns-early hypothesis, which tried to explain important differences between prokaryotes and eukaryotes while acknowledging their shared features, "incorporated too many good ideas to just go out with a whimper."[25] So although Doolittle's early perspective was wrong (likewise Gilbert's, though that is still not admitted), it was nevertheless productive and helped steer the future development of research in this area.

Several other lines of Doolittle's research have questioned adaptationist thinking, including his groundbreaking work on selfish DNA, and some early collaboration with Arlin Stoltzfus, who put these discussions into print as the theory of constructive neutral evolution.[26] The "selfish gene" paper Doolittle wrote with graduate student Carmen Sapienza is his second-most cited article with more than 1,600 citations.[27] It argues that there is no theoretical or empirical reason to expect most of the DNA in a genome to be phenotypically functional – the very opposite, in fact, is more likely to be the case. Transposable elements were the focus of the paper's discussion of this "non-phenotypic selection." Published at the same time in *Nature* was Leslie Orgel and Francis Crick's 1980 outline of the same phenomenon and explanation.[28] They too had converged on the importance of this idea, in an era of molecular biology that was not very strongly based in population genetics, and when assumptions of adaptive function tended to be the default. Both papers argued that this was a dangerous default.

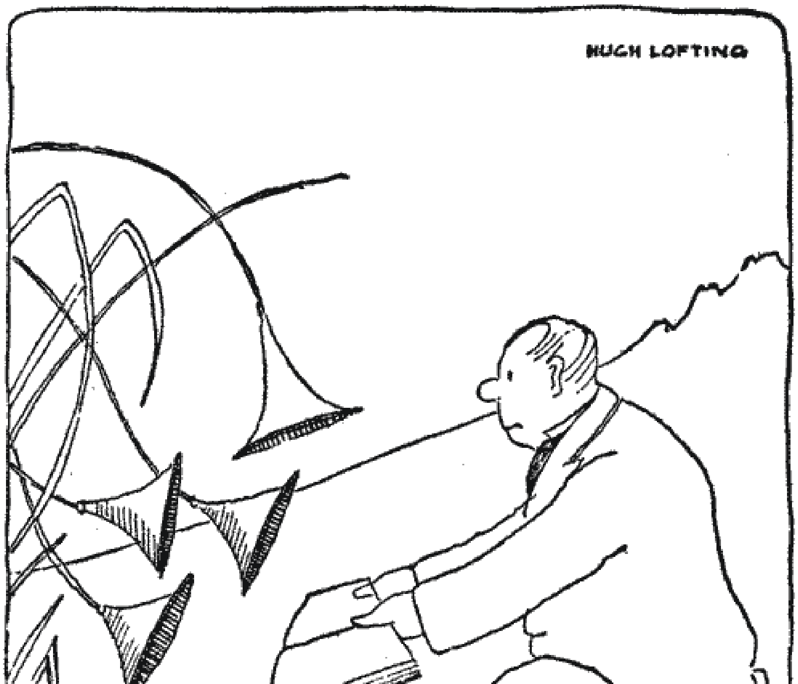
Doolittle's proclivity to question adaptationist claims especially but not only at the molecular level found its strongest voice in response to the ENCODE debate. ENCODE (the Encyclopedia of DNA Elements) was and still is a huge sequencing project that aims to discern the function of the DNA in the human genome. By conflating an evolutionary (selected) definition of function with a minimalist biochemical definition (i.e., "some sort of reaction will occur"), ENCODE's publications triggered scientific outrage, especially when associated media releases suggested almost the entirety of the human genome was functional.[29] Although many of these objecting papers attacked the underlying definition, Doolittle[30] and Graur et al.[31] were the only ones to dwell on classic philosophical discussions of function. They distinguished "selected effects" from "causal roles" to tear apart ENCODE's overweening claims.[32] But even though it could appear to many readers as if there were clearly a wrong and a right side to the debate, Doolittle was doing something more nuanced. His subsequent musings on the role of provocation and debate in science make this clear.

Conjectures, refutations, and fruitful lines of inquiry

A more abstract change of direction in Doolittle's views occurred in relation to discussions of Gaia. In 1974 Lynn Margulis (1938-2011), of endosymbiont hypothesis fame,[33] joined forces with James Lovelock to advance a cybernetic view of the Earth as a single organism-like biosphere.[34] Using both theory and evidence (particularly biogeochemical), Margulis and Lovelock pushed the notion of a feedback-controlled system that was regulated from a planetary level to maintain the Earth in the state it currently and optimally is. Not everyone was convinced. Although much of the criticism was directed at the idea of the Earth as a homeostatic system, Doolittle went on the attack via an evolutionary argument, as did Richard Dawkins.[35] If Gaia were like an organism and had evolved by natural selection to be that way, as Margulis and Lovelock had argued,[36] then how would selection have worked, asked Doolittle.[37] There is only one putative Gaia, and no competition to be had, and therefore selection – the operation of which is often used to identify living systems – could not be at work. In addition, just as for introns, the subsystems (organisms) could not structure their efforts to benefit a future entity.

Doolittle used an analogy with another famous Dolittle, notably the fictional one who talked to animals and, in one volume of a popular series,[38] went to the moon. On the species-diverse moon, Dr. John Dolittle found that instead of competition, the animals and plants (all of them sentient and enormous) had formed a council to regulate their interactions. The council's aim and accomplishment was to eliminate warfare at every level, and bring about a "balance." No such top-down mechanisms exist on Earth, nor indeed balance, observed Doolittle,[39] and there was no choice but to understand all evolutionary hypotheses in light of individual Darwinian fitness.

Figure 2: Dr. Dolittle experimenting with sentient plants on the moon, to determine their cognitive capacities and distance-communication abilities.[40]

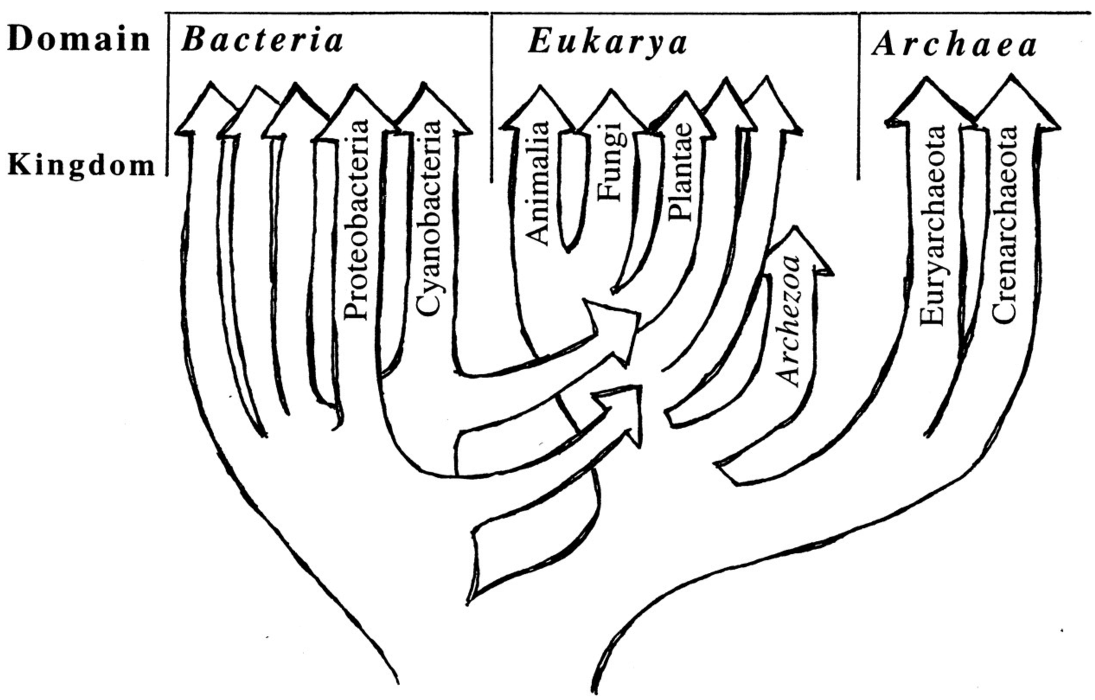


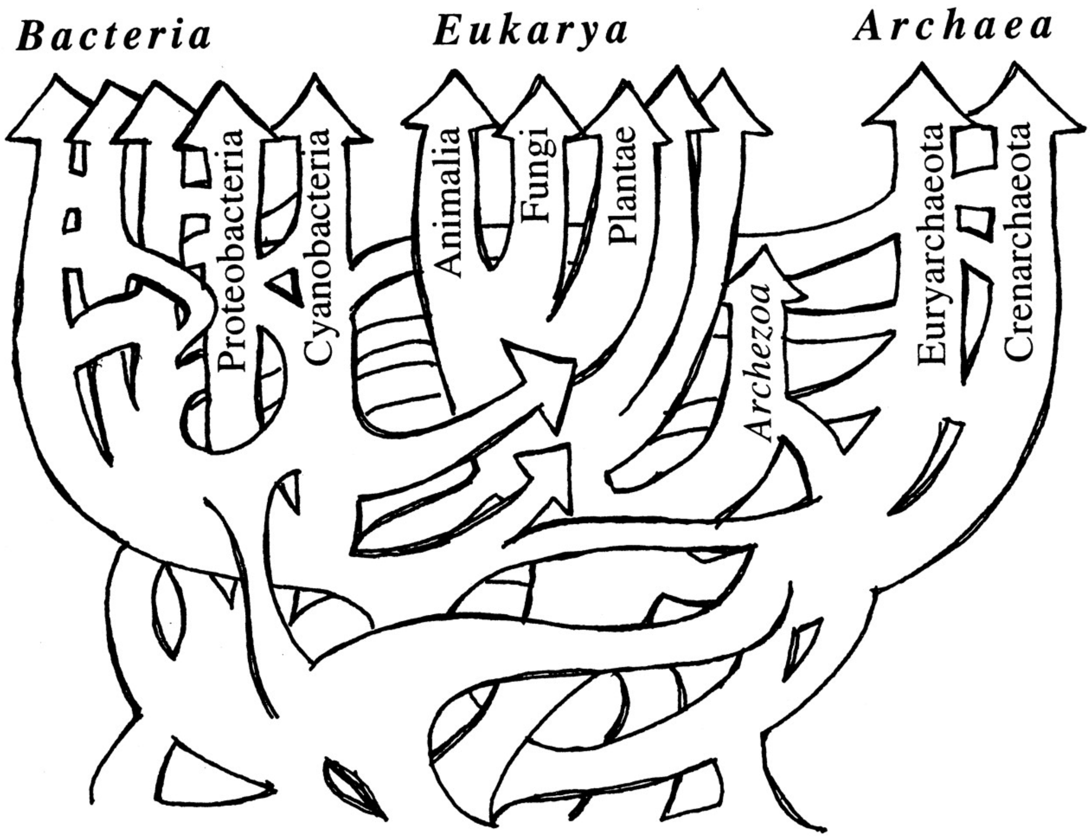
However, even though these criticisms were widely acclaimed (despite being published in a rather obscure journal), Doolittle has gone on to rethink some of his argument.[41] In particular, he has reflected on the notion that not all evolving systems need to reproduce to have fitness, and that outcompeting other entities might not be as crucial to evolutionary fitness as he had supposed. Gaia might be a persisting entity ("immortal"), and thus a living system evolving in a way that is not captured by classical Darwinian tenets. What might be the point of making this quite abstract argument, which in the end does not vindicate the Gaia concept? A major reason for Doolittle is that it fills in some Darwinian gaps by adding “selection by survival” to everyday natural selection.[42] He believes that this kind of persistence can be understood as minimally Darwinian (rather than paradigmatically Darwinian), and is thus in accord with Peter Godfrey-Smith’s philosophical efforts to describe the continuum of Darwinian individuality created by varying combinations of different processes.[43] More generally, I suggest, this sort of philosophical turn is part of Doolittle’s effort to understand science itself as a dynamic evolving process that rewards serious consideration of non-orthodox ideas – even when they are found ultimately to be wrong.

Upsetting the tree of life

Doolittle’s anti-orthodoxy is most recognized in his revision of how the tree of life is understood. Molecular phylogeny had become by the late 1980s the new gold standard of evolutionary tree reconstruction.[44] However, at the same time molecules made phylogeny possible for organisms without much morphology (i.e., prokaryotes), they also revealed wayward genetic movements behind minor and major organismal differences. Lateral gene transfer (LGT) occurs between organisms (often unicells but not exclusively) and involves the “gift” of genetic material that may have a very different evolutionary history from that of the recipient. Rather than orthodox bifurcating lineages with strict genetic continuity, LGT requires messier web-like representations. The impact of LGT on phylogeny is the theme that brought Doolittle’s work to a broader audience. His paper in *Science* in 1999, which has also been cited over 1600 times, spelled out the conceptual implications for phylogeny if LGT were as common as recent data indicated it was.[45] The hand-drawn cartoon with which Doolittle illustrated the alternatives played a central role in bringing home the conclusions of his argument.

Figure 3: Doolittle’s 1999 cartoons of the standard Tree of Life (top) and the alternative “net” of life (bottom).[46] Reproduced with permission of AAAS.





What is crucial to understand here is that Doolittle was not a lone voice crying out in the wilderness of orthodoxy. The message was indeed revolutionary, but several other members of the evolutionary community were simultaneously reflecting broadly on the theoretical and phylogenetic implications of LGT.[47] The distinctiveness of Doolittle's contribution was how he framed it. This framing has implications for how he is interpreted as a “visionary” scientist. My point is not that he and his colleagues were right, and radically so (such that their position now is the new orthodoxy), but that Doolittle’s special contribution was and is meta-methodological in a philosophical way.

Any understanding of Doolittle as a visionary “dreamer” needs to bear in mind that he couched his argument about LGT conditionally. As he noted subsequently, “I only wanted to point out how interesting the consequences for phylogeny would be *if* lateral gene transfer were a major force.”[48] The way in which the conditionality of this statement was lost, as reams of data accumulated in its favor, has been covered by numerous review articles – scientific, philosophical and historical.[49] How Doolittle sees this transformation, however, is not exclusively as an episode of careful data gathering and evaluation of competing hypotheses, but as an instance of giving entrenched frameworks a good kick to see what gets dislodged. In other words, “the debate … shows how strongly unstated philosophical commitments can influence how we collect and interpret hard facts.”[50] Much of his career, including many of its challenges to well-accepted ways of thinking, can be understood as a disciplined inquiry into the philosophies guiding and even driving the science.

Pluralism

One of Doolittle’s high-profile recent papers (at 350+ citations, it is ‘only’ near the bottom of his top-20 most-cited publications) is one he wrote with Eric Bapteste (then a postdoctoral fellow at Dalhousie) for Doolittle’s inauguration as a member of the National Academy of Sciences (USA) in 2009. This paper explores what it means to be a pluralist in phylogenetic practice.[51] Doolittle and Bapteste outline “pattern pluralism” as “the recognition that different evolutionary models and representations of relationships will be appropriate, and true, for different taxa or at different scales, or for different purposes.”[52] In other words, just as the modern synthesis of evolution embraces mutation, drift and recombination in addition to natural selection, so must phylogeny be pluralist.[53] Phylogeny needs “a versatile and well-stocked *explanatory toolkit*,” argues Doolittle, not only for the sake of science but also for its public reception.[54]

Methodologically, Doolittle calls himself an “instinctive” reductionist.[55] By this he simply means a tendency to ask molecules for biological answers. It does not imply this is the only level at which to work, but it is where some very good data can be obtained and successful explanations generated. For philosophers, pluralism can be divided into a metaphysics of plurality (i.e., the nature of things is not fixed) and an epistemic stance (sometimes but not always associated with the metaphysical position): that multiple explanatory frameworks can capture the phenomenon of interest. Certainly, with regard to species and the tree of life, Doolittle could be read as an ontological pluralist.[56] But it is unlikely that he regards all or even many phenomena in this way (e.g., “junk” DNA is simply not on a par with “functional” DNA given the explanatory frameworks in which such discussions are rightfully held). Explanation is what it’s about then. And explanatorily, in a number of discussions throughout his career, Doolittle has come down hard on “wrong” accounts of biological phenomena: the ENCODE account of function, the Gaia view of evolution ("unquestionably false"),[57] and the autogenous (non-endosymbiotic) account of the chloroplast and mitochondrion.[58] How do we interpret Doolittle's pluralism in light of such assessments?

What pluralism seems to be associated with for Doolittle, when trying to understand his career-wide research trajectory, is his reluctance to restrict inquiry to a single "metanarrative" or "monistic view,"[59] and his openness to novel hypotheses and innovative explanations. Yes indeed, emerging and existing explanations all need to be evaluated rigorously, but shutting down the creative side of hypothesis generation seems to be anathema to his view of how science works. "I try to find alternatives to the standard evolutionary explanations for biological patterns and processes," he says,[60] "in part because I believe that scientists are as liable as other humans to cling to dominant theories or attitudes, even when obvious alternatives become equally tenable." In articulating this view, Doolittle draws some important parallels between Art and Science.

Both the arts and the natural sciences, from Doolittle's point of view, are very similar in that they possess "potential purity of motive" and "internal enemies, which are laziness and self-deceit."[61] There is, however, a big difference: "scientists are not supposed to be too deliberately playful with their audience, not supposed to speculate wildly in order to evaluate the response [to their work]. That's what artists must do to survive, and I think we [scientists] could learn from them," argues Doolittle.[62] He believes that self-regulated constraint in interpretation often occurs out of fear of appearing unconventional and "un-objective." But such a belief is built on a limited view of what science is: it is not an aggregation of rational self-policing individuals (though that comes into it, albeit via the back door), but is instead a social institution that assesses and adjudicates at the institutional level. It has room for more wayward but occasionally productive interpretations, and may even need them. That is the reason behind his opposition to increasingly commercial requirements of scientists, and an advocacy for basic science driven by curiosity.

On the other hand, he observes that "Science is way too uncritical of itself" and needs more people like Rosie Redfield, who is well known for debunking the notorious arsenic life claims.[63] Redfield, herself an iconoclastic evolutionary microbiologist fond of deflating a variety of allegedly puffed-up hypotheses,[64] sometimes hints that Doolittle's "philosophical" musings are mere indulgences and not the stuff of which science is made. As Doolittle explains it, many scientists fear that too much philosophy is not only at too great a remove from the science it purports to analyse, but it can also lead to "analysis paralysis" and an inability to make any further headway.[65] My sketch of how he has interrogated evolutionary and other biological explanations shows how in many respects, the opposite has occurred. For Doolittle and sometimes the entire area in which he is working, philosophical inquiry has brought about liberation from constraining frameworks and a capacity to move into new phases of inquiry. In his ongoing practical engagement with philosophy, Doolittle may be at his most visionary, transgressing some very traditional boundaries and attempting a synthesis of a fairly risky sort.

Concluding thoughts

Ford Doolittle has lead a double life: as a scientist and as an “embedded” philosopher who has challenged assumptions (“deconstructively”) and offered novel and sometimes left-field explanations (“playful speculation”). Although many substantive elements of Doolittle’s research program are visionary in their own right, my suggestion is that underlying it is a normative view of how science works that offers advice about the responsibilities any individual scientist has to his or her community and the broader institution of science. Part of this responsibility, he suggests, is to examine every argument and interpretation, and be willing to doubt even the most established scientific framework. This is not done for destructive purposes, however, but to be constructively open to the expansion of explanatory options. Each of the topics in Doolittle’s oeuvre above shows how valuable a methodology this is, not just for him personally but for the scientific community more generally.

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