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PIONEERING PARADIGMS AND MAGNIFICENT MANIFESTOS—LEIGH VAN VALEN'S PRICELESS CONTRIBUTIONS TO EVOLUTIONARY BIOLOGY

Evolutionary biology lost a unique, broad, creative, and influential thinker when Leigh Van Valen[1] passed away on October 16, 2010 in Chicago at the age of 75. He was Professor Emeritus of Ecology and Evolution at the University of Chicago and served on the Committees on Evolutionary Biology, Conceptual Foundations of Science and Genetics. Unwritten ideas still coursed through his ceaselessly active mind as he fought and lost his last battle against phylogenetically distant and diverse microbes.

We are a multiflavored group who wants to honor this extraordinary thinker and teacher, and to bring broad attention to Leigh's life's work, much of which was ahead of his times. We reflect briefly on his work on mammal evolution, energy as an organizing principle in ecology and evolution, adaptation, evo–devo, homology and complexity, even though his "interests go beyond what this blurb indicates," quoting directly from his homepage. Leigh's niche in biology has been to open up new areas of research without attempting to provide final answers to the novel questions he identified. He synthesized empirical observations into a cohesive paradigm that often unified traditional disciplines.

[1]The website Leighvanvalen.com archives, with free access, all of Leigh's papers and all issues of his journal, Evolutionary Theory.

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MAMMALS: BRIDGING NEONTOLOGY AND PALEONTOLOGY

Although Leigh contributed to virtually every aspect of the "evolutionary half of biology,"[2] and addressed issues involving the widest range of taxa, his "main group" was the Mammalia. He used mammals extensively as examples of and sources of insight for much of his conceptual research. Leigh was also an active participant in attempts to clarify the origins and systematics of early mammals, topics vigorously debated at the beginning of his career in the 1960s and 1970s (Van Valen 1960b, 1976c). Far from solely solving systematic puzzles, Leigh applied neontological quantitative techniques for measuring natural selection, variation, and life history to fossil mammals—bridging the conceptual gap between neontology and paleontology that characterized the early years of the Modern Synthesis (Van Valen 1963c, 1969). Leigh showed how fossil species can exemplify the same evolutionary processes that are observed in extant species. The fact that today we regard this fact as unsurprising is testament to the application of quantitative theory to paleobiology by Leigh and others at a time when such an approach was a new idea.

The mammalian fossil record offered for Leigh the most informative direct evidence for how evolution occurred over long time spans. Leigh felt that a true understanding of macroevolution required causal explanations and mechanisms, and he sought them at a variety of scales. He regarded mammalian orders (and other such taxa) as having, at any given time, an adaptive and ecological unity that allowed them to participate in macroevolutionary processes (Van Valen 1971, 1978). Indeed, it is difficult to separate Leigh's most persistent and broad-scale theoretical efforts—selective processes at multiple levels, reformulation of evolutionary processes in terms of energy relations, evolution of whole biotas—from the need to formulate a conception of evolution that was sufficiently general to bring the fossil record into the embrace of a causal evolutionary theory. The Red Queen is a prime example of this effort.

RED QUEEN: ENERGY AS A COMMON CURRENCY

Leigh's most widely cited and perhaps most misunderstood work concerns evolution within adaptive zones and communities. He observed that the extinction probabilities of fossil organisms were age independent, that is, lineages do not become more extinction-resilient over time. The Red Queen's Hypothesis (Van Valen 1973b) is a conceptual paradigm for explaining this observation, and is extendable to communities of interacting entities. The Red Queen states that any gain in the control of energy by a species or higher taxon necessarily means a joint equivalent loss for all other co-occurring taxa in the adaptive zone. Energy as the driving force in evolution is a common thread through many of Leigh's ideas. The Red Queen also reflects the somewhat controversial idea, that competition is important in evolution at all time scales. Viewing energy as a common currency for ecological analyses is a currently rapidly growing perspective (Brown et al. 2004) but a cohesive application of Leigh's energy framework to evolutionary analysis is still lacking.

Leigh's work on origination and extinction rates was contemporaneous with other such work (Raup 1972), but his view uniquely synthesized the interactions between the biological and the physical world (Van Valen 1973b, 1985a,b). He found that origination rates of families have declined through the Phanerozoic, although extinction rates have been relatively stable (Van Valen 1985a), corroborating his view that "extinction rates measure degree of resistance and external stresses" while "origination rates measure the ease of adaptive change" (Van Valen 1985b). The resilience of a species (or higher taxon) evolves but does not improve temporally because its effective environment declines: this is the Red Queen in action. On the other hand, the ease of adaptive change declines as adaptive zones fill. Since then, prominent studies (Sepkoski 1998; Foote 2000) have brought more attention to large-scale patterns of turnover rates, attracting overdue research on mechanistic explanations. The Red Queen continues to fuel debates on whether evolution on geological time scales is driven by biotic or abiotic forcings (Alroy 2008; Benton 2009). We note, however, that Leigh never intended to exclude physical factors as agents of biotic change, or to attribute evolution to only biotic drivers. Leigh saw that physical forces that can reset equilibrial processes (Van Valen 1984), although he thought "most environmental pressure is biotic rather than physical" (Van Valen 1985b).

Leigh's discussion on "bloom phases, initial crunches, exclusion and saturation" described the macroevolutionary analogue of density dependence (Van Valen 1985b). Recent papers that concern the current version of this model, describing early bursts of speciation and the slowing down of diversification rates as niche space fill ups (Rabosky 2009; Ricklefs 2010), do not mention Leigh's more fully conceptualized model stemming from Lyell and Simpson (Van Valen 1985b). Current research on diversity-dependent

[2]Leigh regularly used this term to underscore the centrality of evolution for biology, and to describe the scope of his research interests. He contrasted the evolutionary "half" with those areas of biology where the focus is on how organisms work, but not on how or why they came to be that way. For Leigh, the evolutionary half includes systematics, comparative biology, ecology, paleontology, behavior, biogeography, population genetics, anatomy, and any other fields where evolution is the underlying theme. See, "Why misunderstand the evolutionary half of biology," (Van Valen 1982b) for a fuller discussion.

diversification will gain handsomely from Leigh's crystal-clear reasoning on the separate contributions of origination and extinction processes to the net result of diversification.

FITNESS AND LEVELS OF SELECTION

Leigh advocated a new and "heretical" notion of fitness, where the fundamental unit of selection is not tallied as the number of offspring, but as the control of free energy (Van Valen 1973b, 1976a, 1989). Like Hamilton who proposed genes as the fundamental unit of selection (Hamilton 1963), Leigh wanted to provide a common currency for fitness that can be used to traverse different levels of biological organization for unified analysis. Leigh often cited Egbert Leigh's remark: "if life evolved elsewhere it would not necessarily need any of the specific chemical materials our life does, but it would need free energy" (Van Valen 1973b, 1976a, 1989). Natural selection follows when organisms have differential control of limited free energy, summarized in Leigh's third Law of Natural Selection (Van Valen 1976a), where "Natural Selection maximizes, at any level or time-scale, expansive energy." Leigh divided fitness into three components, reflecting ways in which energy could be put to use evolutionarily, namely persistence, reproduction, and expansion. Expansion is differential growth: a bryozoan colony crowding out another is natural selection because the relative energy amount of energy each colony controls changes. Although reproduction leads to new adaptations, expansion and persistence confer stability (Van Valen 1989). By characterizing fitness in terms of the control of energy, intra- and interspecific fitness, and evolutionary success in compositionally different systems with diverse histories, heterogeneous parts and incommensurable ecology, even contemporaneous species, and different species sharing an adaptive zone at different times can be compared.

The independent and sometimes antagonistic nature of different levels of selection was a strong focus of Leigh's work (Van Valen 1989), at a time when this view was uncommon. For example, in mammals, large body size is selected for at the organismal level and against at the species level (Van Valen 1975), resulting in an equilibrium body size. Body size is expressed in individual organisms but has consequences for long-term evolution due to its correlation with life-history traits that increase extinction risk. In this way body size illustrates how sometimes the level of selection (in this case the species) can be equivalent to long timescale selection on organismal traits.

HOMOLOGY: THE CONTINUITY OF INFORMATION

Thinking hard about mammals led Leigh not only to his reformulation of fitness and the Red Queen, but also to the conceptualization of homology of morphological characters. The first stage in the elaboration of tooth shape in the stem lineage of mammals is the three-cusped tooth. The commonplace identification of the early mammalian major cusp with the single cusp of the reptilian tooth was embodied in then mainstream "premolar analogy theory" (Hersbkovitz 1971). However, Leigh showed using a detail in the evolution of horse teeth that this whole enterprise was conceptually flawed (Van Valen 1982a).

Molars appear to have been derived from premolars by the addition of cusps. However, apparently corresponding cusps among adjacent premolar teeth in *Orohippus*, an early horse genus, in fact arose from different positions. There was selection for increased grinding surface over the course of horse evolution where each premolar tooth added cusps in similar locations but had different derivations either de novo or from nearby ancestral cusps. Leigh interpreted this as a breakdown of homology assessment among tooth cusps, meaning that tooth cusps lack historical continuity beyond that among highly related species (Van Valen 1982a). Leigh's interpretation is confirmed by recent work where "It is unlikely that there is a simple "gene to phenotype" map for dental characters. Rather, the whole cusp pattern is a product of a dynamic developmental program manifested in the activation of the developmental modules" (Jernvall and Jung 2000).

What Leigh recognized, earlier than most, was that homology only applies to body parts that are developmentally and genetically individualized. This is the first step in a long struggle toward understanding the mechanistic basis of homology. Leigh also proposed a new definition of homology, namely, correspondence based on continuity of information. He anticipated that this definition did not require homologous parts to be based on identical genetic information, a point now clear from comparative developmental genetics. He was a pioneer in realizing that the true challenge in understanding homology is identifying the molecular mechanisms that provide continuity to the phenotype in the midst of a sea of genetic change, but nobody had the means to follow his lead until 20 years after the publication of "Homology and Causes."

INFORMATION AND DEVELOPMENTAL COMPLEXITY

Deep in a paper on multivariate statistics in natural history lies a portal to the heart of developmental complexity (Van Valen 1974), a measure called "information" or "nonredundancy." Here, information is the number of degrees of independence in a multivariate dataset. In development, it is the number of independent factors needed to account for the observed phenotypic-developmental variation.

For two measured variables, $I = 2 - \rho^2$, where I is information and ρ^2 is the squared correlation coefficient. I is maximal and equal to 2 when the correlation is zero and there are two underlying developmental factors. I is minimal and equal to 1 when the correlation is 1 and there is really only a single factor at work. Leigh also gave a multivariate version: $I = 1 + (n - 1)(1 - \rho_n^2)$, where n is the number of measured variables and $(1 - \rho_n^2)$ is the mean proportion of each variance that is independent of all the other variables.

So I is a count—albeit on a continuous scale—of independent factors. It is also, therefore, complexity (in one sense). The more independent factors, the greater the dimensionality of the space in which change occurs, and the greater the number of possible phenotypes. Evolutionary biology has long suspected that complexity may be hugely important in evolution, but we have lacked apt measures of it. Leigh's I provides a measure, allowing us to ask questions, for example, about trends. Is a human more developmentally complex than a reptile? Is there a trend in developmental complexity within this or that group, or over the history of life?

Importantly, I is—unlike certain other measures of complexity—function-free, or adaptation-free. An organism with greater I may or may not be a better adapted one. Also, I is not a measure of "morphological integration" (Olson and Miller 1958). For one thing, what I measures is not integration but disintegration. For another, the goal is different: morphological integration is concerned with a range of issues, from the relationship between integration and speciation to the identification of specific developmental mechanisms. But the mission implicit in Leigh's I is even more general, seeking not actual mechanisms, but a measure of the "diversity" of those mechanisms, the "generative diversity" of the organism.

Interestingly, there is a close connection between I and modern treatments of modularity and evolvability, some containing measures of independence that correspond closely with I (Hansen 2003; Hansen and Houle 2008). However, the concern in the modern treatment is with the effect of a character's independence on its ability to respond to selection, not with complexity understood as a variable in its own right.

VARIATION: GENETICS, PHENOTYPES, AND PIONEERING EVO–DEVO

Leigh was uniquely co-mentored by arguably the greatest microevolutionist (Dobzhansky) and macroevolutionist (Simpson) alive at that time. This provided him with a seamless perspective of the evolutionary process that kept him from falling into traps not always avoided by some of his prominent contemporaries. However, despite having written five papers on *Drosophila* genetics in top ranking journals, Leigh's research on the genetics of extant organisms, unlike his other contributions, has not been particularly enduring.

Leigh's lasting contributions in this area focused on phenotypic rather than genetic variation. In a series of early papers, Leigh measured selection on phenotypic traits in natural populations, including extinct ones (Van Valen 1963c,b, 1965b; Van Valen and Weiss 1966). Related works explored if wider niches correlated with more variable traits (Van Valen 1965a) and reviewed the genetics of variation in paleontology (Van Valen 1969). Although the case studies in this latter paper have been almost entirely superseded by modern works, few of its main conclusions need to be altered. An early statistical paper on measuring multivariate variation and covariation (Van Valen 1974) anticipated later problems arising in the study of morphological disparity (Foote 1992), morphological integration, modularity and complexity, as noted above (see also (Van Valen 1965c)). Leigh's seminal work on fluctuating asymmetry (FA) also exemplifies the depth of his thinking on how phenotypic variation is related to underlying developmental processes (Van Valen 1962). A bibliographic search reveals about 7990 articles published with this phrase in their titles or abstracts since, much of which Leigh did not approve, because they pursue what he viewed as highly questionable correlations between asymmetry signals and fitness. The fundamental issue Leigh addressed originally is the precision of developmental processes and why natural selection has shaped developmental systems so as to minimize the noise that FA indirectly measures.

It is perhaps surprising that Leigh, the staunch adaptationist (Van Valen 2009), was an early and influential advocate of incorporating development into evolutionary theory, because much of the early work in evo–devo revolved around developmental constraints as alternatives to adaptation as explanations for evolutionary change. Leigh's perspective was however different, taking the view that development should be woven into the fabric of evolutionary explanation. Leigh's oft misquoted aphorism "... evolution is the control of development by ecology ... " (Van Valen 1973a) was meant to point out that development (and ecology) had been short-changed in evolutionary biology. Much of his earlier work shows an intense interest in the origination of variation through development. For example, Leigh discussed the implications of dysmorphic incisor growth in rats for the characterization of Rodentia (Van Valen 1966). In his analysis of developmental or morphogenetic fields in mammalian teeth (Van Valen 1970), Leigh drew a prescient connection between the developmental field concept and homeotic mutations in *Drosophila* —decades before the homeobox gene story was revealed.

His combined interest in development and variation also led him to seize the significance of correlations among traits. Rediscovering Olson and Miller (1958), Leigh saw the implications of morphological integration for how developmental processes structure the expression of phenotypic variation (Van Valen 1965c). He succinctly hypothesized that "The tendencies of functionally related structures to be similar in form or adjacent to each other explains developmentally only part of this relationship. It seems necessary to postulate selection specifically for developmental patterns that affect functional complexes as a whole." This concept is very close to current ideas on modularity and its importance in evolution, a theme that also runs through his work on serial homology (Van Valen 1994).

MALADAPTATIONS: EXCESSES AND WASTE

The self-proclaimed adaptationist not only pioneered evo–devo and estimated that adaptation is overwhelmingly prevalent in features of organisms (Van Valen 2009), but also had long been interested in nonadaptations and apparently maladaptive traits (Van Valen 1960a). Expanding his early treatment on the mechanisms of nonadaptive evolution in a study of female reproduction (Van Valen 2003), Leigh proposed that selection among oocytes explained two seemingly unrelated and maladaptive phenomena. What looks at birth to be (1) an inexhaustible number of oocytes dwindles to zero in mid-life, followed by (2) decades of sterility (menopause). The energy used to produce the ill-fated eggs could presumably be used adaptively, and models that propose a fitness advantage to reproductive cessation are unconvincing. Using germ-cell counts across the life span, Leigh calculated an exponential decline in oocytes, culminating in menopause. With a constant probability of atresia per day, selection for additional germ cells is relatively ineffective in extending the reproductive life. Menopause, then, is not an adaptation but a result of a trade-off between cost and reproductive life span.

NOT JUST A BIOLOGIST

Leigh wrote about the nature of interdisciplinary research, the role of laws in explanations, the types of laws that can be found in biology, the role of deduction in scientific reasoning, topics worthy of a professional philosopher (Van Valen 1963a, 1976b, 1988, 2009), and is often quoted by philosophers of biology. Although other biologists (e.g., Dobzhansky, Mayr, Lewontin) had genuine philosophical interests, Leigh to a unique degree emphasized best the symbiosis between philosophical commitments and scientific hypotheses. Leigh's philosophical discussions on ultimate processes in nature beyond consensual scientific approaches, include "Three paradigms of evolution" and "Biotal evolutional: manifesto" (Van Valen 1989, 1991). Beyond the search for definitional and logical adequateness, his questioning of what is a biological individual and what to make of the fuzzy boundaries of entities expressed the types of ontological concerns that philosophers have been dealing with for centuries. Leigh cared about laws (universal statements that allow for deductions), but also deeply recognized that the role of induction and its relationship to causal inferences must not be minimized (Van Valen 1982b). In going beyond common scientific intuitions to identify the most logically coherent theoretical approach, Leigh was a philosopher and a biologist.

FINAL UTTERANCES

Leigh left us with promising signposts in disparate fields but also many unanswered questions. Numerous portals he opened are still unexplored. The search for causal theory in macroevolution still remains; the full significance of energy in evolution still eludes us; conceptual gaps between neontology and paleontology still run deep. Leigh may no longer be among us, but his paradigms and manifestos remain to inspire many of us in our quest to understand the evolutionary biology.

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