doi:10.1111/j.1558-5646.2011.01304.x

EVOLUTIONARY INSIGHT FROM THE MOLECULAR LANDSCAPE

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Received March 15, 2011
Accepted March 15, 2011

Stillman, B., D. Stewart, and J. Witkowski, eds. Evolution The Molecular Landscape. 2009. Cold Spring Harbor Symposia on Quantitative Biology. Volume LXXIV, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. 484 pp. HC $155, PB $63, ISBN 978–087969871-3.

This volume is organized around the central themes of the "contribution of molecular biology to our understanding of evolution" and the "extent to which evolutionary biology can be viewed in a molecular and often genomic framework" (Foreword). Given the timing of this publication (200th year since Darwin's birth, 150th anniversary of Darwin's publication *On the Origin of Species*), the broad influence of its predecessor (24th symposium on *Genetics and Twentieth Century Darwinism*) and the subject, I expected both retrospective and prospective visions of the contribution of molecular biology to our understanding of evolutionary process. Perhaps a comprehensive approach is impossible, but the limited composition of the authors placed unnecessary circumscription on the scope of questions and approaches addressed. Of the 51 chapters, 11 were authored by contributors linked to Harvard or Edinburgh, and relatively few authors were affiliated with non North American institutes (sans Edinburgh). Although the volume presents a narrow vision of evolution, the composition of the majority of authors provided a perspective not normally presented in the pages of *Evolution*. Contributions were from Howard Hughes Institutes (5), Cold Spring Harbor (2), medical schools (7), chemistry departments (7), and only about 12 of the chapters had any citations (of the ∼3800 in the entire volume) from the journal *Evolution*. Thus be forewarned, many contemporary and core evolutionary topics will not be found here. Although much is missing, reading this volume broadened my horizons and will likely do so as well to those evolutionary biologists who regularly read this journal, you.

The landscape metaphor has rich meaning in evolutionary biology, evoking concept and theory underlying the genetic mechanisms of the evolutionary process as well as the trajectory of evolution in phenotypic space. My initial assumption of the use of the landscape metaphor in the volume's title was different as I assumed that having "landscape" in the title reflected a variety of perspectives that together would provide a wide, if not coherent understanding of evolution. Thus, I optimistically accepted the review assignment hoping that the volume would provide the blueprint for future studies leading to a greater understanding of evolutionary process. My world vision spans evolutionary genetics and the selective forces that result in the biodiversity that drew many of us into the discipline. It is this connection between genes and phenotype, between the ecology of the organism and the genetic changes at the sequence level that I sought insight from this volume, a vision reflecting the first use of the landscape metaphor, yet I found something very different, though informative. The landscape metaphor is expressed in this volume as contributions that seek an understanding of the fitness landscape of genes, as well as attempts to bring many perspectives together. The metaphor also reflects a third and dominant fugue, requiring less-intellectual extrapolation, namely the actual level at which many of the studies are conducted, that is, at the molecular and cell levels. That all three themes are represented in one

volume contributes to the strengths as well as the weakness of this endeavor.

The very first pages, a pithy introduction by E.O. Wilson, set the challenge that I hoped would be addressed in the ensuing chapters: to connect the world of natural history to the genes that comprise an organism, that is, ultimate questions with proximate answers defining a new paradigm of systems biology, linking processes from molecules to ecosystems. This challenge was similarly raised by Stebbins in the 1959 volume who bemoaned the false dichotomy between organismal and cellular biology and was also eloquently articulated by Dobzhansky in his Presidential address to the American Society of Zoologists (Dobzhansky 1964; see Quammen 2011 for further discussion) in which he stated that "life can be studied from two points of view-that of its unity and that of its diversity." Unity represents the commonality among organisms including cellular organization and molecules of inheritance and diversity represents the process by which all organisms arise. The questions we address at these two levels are "how things are" and "how things got to be that way." Fundamental to both levels of inquiry is that "nothing makes sense in biology except in the light of evolution" because, of course, even questions addressed at the former level (how things are) only provide universal answers because of the patterns resulting from common ancestry. Both Stebbins and Dobzhanksy were adamant that the two types of questions and approaches are neither alternatives nor competing but rather, complementary.

Looking back, unfortunately both Stebbins and Dobzhansky were correct in expressing concern over the growing schism in biology, as traditional taxon oriented departments merged and split along molecular and cellular versus ecological and evolutionary concepts in the ensuing decades. However, currently, contrary evidence of any schism abounds. Technological advances allowed the adoption of molecular approaches across the broad discipline of biology as evinced by the plethora of journals that have either ecology or evolution matched with molecular in their titles. In any given issue of *Evolution*, one half to two-thirds of its empirical (nontheory) articles use molecular approaches or address evolution at the molecular level. Yet in *Evolution The Molecular Landscape* there is a palpable expression that this false dichotomy still exists and is, I believe, reflected in the unevenness of the synthesis presented in this volume. Although every contribution in this volume is extremely well written and individually provides great insight to their respective subjects, they collectively fall short of a synthesis and only in some cases address the challenges set forth by Professor Wilson. Wilson not only posed the general question but raised what he considers as the major challenges for biologists, how to document the role of multilevel selection in the evolution of major transitions, from prokaryote to eukaryote to multicellularity and then to the organization of societies. Wilson's chart of the future is preceded by Browne's delightful description of Darwin as both a theorist and as a skilled experimentalist, resulting in a wonderful synergy between the two chapters highlighting again, the need for observations of nature to supply the major questions with answers supplied by experimental approaches.

If there is cohesiveness in this volume it is in addressing the origins of complexity. The early chapters focus on the origins of life: the synthesis of model protocells (Mansy and Szostak), catalytic properties of ribosomal RNA (Cech), and recombinant RNA molecules are more likely to be present in the population following directed evolution than nonrecombinant molecules, suggesting the utility of sex at the very beginning of life (Joyce). Finally, Ramakrishnanin, provides description of the biochemistry of the ribosome to a sufficient degree to lay the foundation for the previous chapters. All are lucidly written and provide great insight to the early origins of life. Unfortunately, these subjects are rarely the focus of papers in *Evolution*, yet I think they would have much greater influence if published in *Evolution*. Why? Because the questions are as much about the "how to" of biochemistry as they are the "why" of evolutionary biology. Students in EEB departments should just as readily be addressing these questions as students in chemistry departments.

The theme of evolving complexity is continued in the ensuing chapters and to varying success they are able to make the connection between patterns of evolution and the underlying evolutionary processes. Doolittle begins the section with an elegant summary of his life's work to document the evolution of the vertebrate blood coagulation pathway. Not only is it a textbook study of the role of co-option in evolving complexity, but it also illustrates the importance of gene duplication and how incorporating phylogenetic information leads to much greater comprehension of pathway evolution. The work also provides a significant counter point to the creationist argument of irreducible complexity (Miller). The theme of genetic co-option continues with the discussions of the evolution of Metazoan developmental pathways where the genes involved in developmental networks have their antecedents in more primitive organisms (Davidson and Erwin, Richards and Degnan). The former provide a more detailed scenario whereby they conjecture core groups of genes, or highly structured kernels of gene networks operate in cascading fashion during development. The co-option of the earliest kernels from metazoan ancestors define, according to the authors, the extent of explorable morphospace because changes in these early evolved and early acting kernels will have disastrous developmental consequences, mirroring Stebbins (1974), whereby "the essential features of this unit are conserved in all evolutionary descendants." Reducing developmental process underlying the basic morphology of animals to a series of neat and nested boxes suggests possible genetic mechanisms underlying co-option, but also has associative danger of oversimplifying the evolutionary basis of co-option. What is still appealing about Stebbins, in contrast to Davidson and Erwin,

is that he used the terminology common to evolutionary process, for example, pleiotropy and stabilizing selection maintaining core features of organization, whether bilateral symmetry of animals or the presence of single carpels in Leguminosae (the latter example also presented in Cronk) is discussed. Furthermore, rather than invoking different processes associated with higher taxonomic divergence versus lower, it becomes clearer that macroevolutionary patterns can be extrapolated from microevolutionary process. Avoidance of these terms does not lessen the importance of the ideas put forward by Erwin and Davidson, but does, in my opinion, makes them less accessible to the wider audience of evolutionary biologists. In contrast, Moczek's chapter on the developmental mechanisms underlying beetle horn diversification synthesizes both micro and macro evolutionary perspectives. Moczek demonstrates the role of co-option in the evolution of these remarkable structures and that these innovations can be viewed as extrapolations of diversification over time, even providing compelling evidence of the role of contrasting selection pressures acting on inherent trade-offs between horn and copulatory organ investment to explain patterns of diversification (see also Emlem et al. 2005).

One of the subtle charms of the volume is the juxtaposition of chapters that have very different perspectives on similar subjects. For example, Bell's chapter espouses the oligogenic view of adaptation, whereby evolution at a few, identifiable and perhaps predictable loci is stated as fact, "supported by theory, laboratory experiments and detailed analyses of selection in natural populations (p. 143)." However it is sandwiched between chapters by Greenspan mostly focused on *Drosophila* and Ehrenreich et al. studies of crosses between genotypes of baker's yeast that provide much contrary evidence for a polygenic and complex basis of adaptation. One of the defining features of *Drosophila* selection studies, according to Greenspan, is the discrepancy between the loci involved in selection response and the loci identified through standard mutagenesis as affecting the very same phenotype. Greenspan attempts to reconcile these differences using reasoning harkening back to Mayr's, Carson's and Templeton's theories of genetic revolutions (best summarized in Coyne and Orr 2004). Greenspan suggests that major genes, of the type identified in mutagenic studies, eventually contribute to adaptive response only following the evolution of genetic background effects. I appreciate Greenspan's attempt to bridge the schism between cellular and organismal approaches, but my guess is that there is a far simpler explanation. Rather the discrepancy reflects the differing contribution of standing genetic variation versus new mutation in selection response, a topic that I will return to shortly. Charlesworth (summary chapter) cites work by Carroll and colleagues that does not appear in the volume but was instead published elsewhere (Rebeiz et al. 2009), where a *cis* regulatory region is involved in adaptive melanism in a Ugandan population of *D. melanogaster* and this evolution reflects five sequence changes or "steps" demonstrating that even "single" loci may evolve in ways consistent with a polygenic perspective.

Examining Bell's rationale for the universal role of major effect alleles contributing adaptive response is important because I think false dichotomies are having undo influence on our understanding of the genetic architecture of adaptive evolution. Let us focus on three specific examples Bell uses to support his contention of the oliogenic basis of adaptation. The presence or absence of armor in the three-spined stickleback is now known to be controlled by the locus *Eda*. The reduction of plates appears to be an adaptation to invasion of fresh water, and is mirrored in experimental evolution studies in microcosms (Barrett et al. 2008). However my interpretation is that loss of armor mirrors loss of function, which is much more likely to occur through a single mutation than the gain of function, in this case gain of armor in the lineage giving rise to sticklebacks. Similarly, one may find mutations in species with zygomorphic (bilaterally symmetric) flowers that give rise to phenotypes with actinomorphic (radially symmetric) flowers, but never the reverse (Cronk). Thus I agree that a simple and perhaps predictable genetic mechanism may underlay adaptation, especially if it involves loss of function, however, my guess is that gain of function is what underlies most evolutionary innovations. The second example used by Bell is the finding that beak shape in *Geospiza* species is strongly correlated to the expression of *Bmp-4*, which codes for a bone morphogen (Abzhanov et al. 2004). Bell and others conclude that "selection on this quantitative character may act primarily through alleles of a single gene to produce adaptation" (p. 142). It makes sense that expression patterns of *Bmp-4* contribute to species differences, after all candidate loci do sometimes contribute to the genetic mechanisms underlying natural phenomenon. However, we do not know at this point to what extent *Bmp-4* regulation contributes to the pattern of phenotypic variation of beak shape in the medium ground finch or how many loci underlay variation in its expression (Grant and Grant 1989). We have plentiful evidence that co-option of the same genes are involved in diversification of morphology in both plants and animals, respectively (the predictable component of Bell's argument), e.g., *CYCLOIDEA/TEOSINTE BRANCHED1 (CYC/TB1)* like genes have been implicated in the development and evolution of floral symmetry in numerous Angiosperm lineages (Bartlett and Spect 2011). But how likely is it that the very same genetic changes responsible for their deployment in the correct tissues at the right time occur in some 70 or more independent transitions from radial to bilateral asymmetry (Citerne et al. 2010)? I will bet very unlikely. The third example, also the focus of the chapter by Linnen and Hoekstra, is the evolution of cryptic coat color patterns in mice. To say this elegant example of natural selection acting on phenotype understood at the sequence level is typical is virtually stating that studies of natural selection

only matters for those traits that segregate into Mendelian ratios, which is déjà-vu all over again (see e.g., Provine 1971 for discussion of the false controversy between Mendelian geneticists and biometricians). Likely Hoekstra and colleagues study these color coat systems because they behave as Mendelian traits, as elucidated 80 years ago by Sumner (reviewed in Wright 1978, pp. 330–351), and are amenable to ecological genetics (see e.g., Ford 1964). Finally, Bell's reference to the Kearsey and Farquhar (1998) review of QTL studies in the plant literature demonstrating that typically 4 QTLs are reported per trait and only one per chromosome as evidence of oligogenic based adaptation is, in my opinion, a misinterpretation. I do not think Kearsey and Farquhar would ever endorse their review as providing evidence for the oligogenic basis of adaptation, rather that only a few loci of many may have phenotypically detectable allelic variants in the particular segregating populations used in the mapping populations; thus less a statement about genetic architecture and more a statement on the limits of QTL analyses to date.

I believe that discussion of whether adaptations reflect evolution at many or few loci is a distraction, and deflects from the main point, which is, whether evolution is selection or mutation limited. Biology is not physics. Biology is rampant with contingency, and so it should not be surprising that the evolution of some traits reflect evolution at one locus, several loci, or perhaps at many loci. The primary question is what role does standing genetic variation play in the evolution of adaptations, and what processes are responsible for the maintenance of this genetic variation (e.g., Kelly and Willis 2001)? This topic was underrepresented in the volume.

On a more intimate evolutionary scale, Arnold's chapter demonstrates the power of the evolutionary design algorithm, a.k.a., directed evolution, a method utilizing artificial selection concepts to engineer a protein or RNA with desirable properties not found in nature, and provides insight on the fitness landscape for protein evolution. Arnold describes how directed evolution on the bacterial enzyme cytochrome P450 to have completely new function was acquired via small steps, reflecting the accumulation of 23 mutations. Key mutations in this process had little effect on enzyme function per se, but stabilized the structure of the protein while it acquired the necessary amino acid replacements, that is, these functionally neutral mutations stabilized the proteins three-dimensional structure allowing "functionally important but destabilizing mutations to be accepted." In my view, this is a form of epistasis, although at the within locus level.

Both Arnold's work on the fitness landscape of one protein's evolution and Carroll's work with the enhancer region of ebony (Rebiez et al. 2009) evoke Fox and Hastings (1992) definition of a gene in terms of functional fitness determined by the ratio of s:r (selection:recombination), with the ratio >1 defining coadapted groups of nucleotides and thus a functional gene in terms of fitness. Given the important role of linkage disequilibrium in evolutionary models, I was disappointed by the coverage of this topic, especially the degree of linkage disequilibrium and how many functional domains of selection there may be in the genome. However the two chapters that did examine linkage disequilibrium, Barton's on sex and recombination and Charlesworth's et al. on genetic recombination and molecular evolution are insightful commentaries that reflect long thought on these topics. Both chapters are unified in their view of the importance Hill–Robertson (HR) effects, (where selection at one site effects selection at other linked sites, Hill and Robertson 1966) in understanding the adaptive advantage of sex. Barton emphasizes the role of strong or episodic selection for the maintenance of high rates of recombination and sex while Charlesworth et al. note the complexity of discriminating between background selection and hitchhiking, given HR effects. The relationship between genetic variation and selection response likely will require much more in the way of conjoining theory with empirical data. Lenski's (Barrick and Lenski) and colleagues heroic selection experiment on *E. coli* ($>$53,000 generations to date) and future experiments with sexual organisms may provide the detailed information necessary for a complete understanding of the genetics underlying selection response. With their ability to sequence the "fossil" record of his experiments and detect the introduction and subsequent fate of a mutation, Lenski and colleagues will provide the details necessary to comprehend selection response in a way that traditional quantitative genetics cannot do because of its reliance on focusing on the emergent properties of the genome rather than on its details (Hill 2010).

Rather than examining the outcome of selection, Obunugafor et al. attempt to predict future selection response based on selection for genetic robustness, defined in their experiments as the ability of the organism (RNA phage virus) to maintain high fitness following mutation accumulation. These differing abilities then translate into differing capabilities to evolve to novel thermal environments with more robust lineages better able to evolve/adapt, or in the current parlance, manifesting greater evolvability. The notion that genomes have differing evolvabilities based on their ability to absorb and use new mutations mirrors the work of Arnold discussed above. This work differs from previous concepts of evolvability (e.g., Houle 1992), such as h^2, or its multivariate equivalent, the **G** matrix, in that it is focused on the role of mutation in adaptive evolution versus standing genetic variation. It would have been useful if Obunugafor had compared the different concepts of evolvability, mutation versus standing variation based, and what lessons can be drawn from the different approaches.

Although experimental evolution or artificial selection studies have demonstrated many important principles (Falconer 1992; Falconer and Mackay 1996), and should do so in the future, it should be emphasized that there are inherent biases in these

studies. For example, response to artificial selection is reduced in small populations of *Drosophila melanogaster* relative to larger populations (Frankham and Weber 2000), because small populations reduce the efficiency of selection relative to drift ($N_eS < 1$, Wright 1931). Thus in the experiments that incorporate small population size, it is more likely that alleles of larger effect will contribute to selection response based on standing genetic variation. On the other hand if response is due to new mutations, then small populations will be biased to responding with mutations of small effect (Burch and Chao 1999) or whatever mutations are available. As long as these assumptions are understood then sound conclusions can be drawn, but if they are not understood then false conflicts may emerge, that is, inferring the role of mutations of major and minor effect in the adaptive process from artificial selection experiments.

Nine of the 51 contributions specifically address human evolution. I stress to my classes that the study of human evolution is a way of learning to know thyself (and so is reading Hesse's Narcissus and Goldmund) and Dobzhansky (1964) was also clear in his presidential address that the question "what is man" is one of the key questions in biology and requires both organismic and molecular approaches. However, human evolution does not, per se, necessarily provide great insight into understanding the origin of biodiversity. Given the role of humans as agents of biotic change, perhaps it is important that we know as much about ourselves as humanly possible. But, in terms of what we can learn about the evolution of other organisms these chapters, as with any sample of a particular taxon, do not necessarily provide great insight. Based on ISI searches, roughly five of the top 100 cited papers for the topic "evolution" for any journal that typically publishes on evolution (including *Evolution*, *Nature*, etc.) will be on human or primate evolution. Thus the nearly 20% allocation of space to human evolution in this volume, seems exaggerated, especially considering that there are only three contributions on plant evolution from a molecular perspective. Although White's contribution on the history of interpreting hominid fossils is tremendously helpful if one teaches evolution, and a model of clarity, many of the remaining chapters will not greatly influence the broader field of evolution nor do they attempt to place their findings within a broader evolutionary context. For example Lambert and Tishkoff report on genetic structure in African populations and the consequence for interpreting human evolutionary history in the context of the coalescence. It is a well-written introduction to the broader topic of population structure as well as coalescence, but adds nothing new to our understanding of the contribution of population structure to evolutionary process. A chapter on the contribution of mtDNA evolution to human adaptive evolution by Wallace, mostly conjecture, is interesting in itself, yet fails to cite studies that clearly demonstrate the role of mtDNA and other cytoplasmically inherited genomes to adaptive evolution in other organisms (Galloway and Fenster 2001; Rand et al. 2004; Leinonen et al. 2011), and thus fails in putting their ideas in any meaningful context. Some of the papers in this section, and also many others in the volume, are not motivated by the deep conceptual questions that often motivate our work, and are more concerned with the highly successful molecular paradigm of identifying gene with function. In defense, it may be that these contributions reflect a fresh view of the landscape and may generate new paradigms. For example two chapters use a feature of genome organization, segmental duplications as a strategy to identify genes contributing to both adaptation and disease. Taking the premise that rapid and recent evolutionary change will be found in recently duplicated regions of the DNA, Marques-Bonet and Eichler demonstrate that the human great ape lineage experienced an accelerated rate of duplications. They make somewhat of a leap by stating it will be in these regions that we will find the genetic changes that make us uniquely human, including increased cognitive abilities. They provide some support in that many neurocognitive and behavioral diseases reflect mutations (due to unequal crossing over) in these regions. Dumas and Sikela use this same concept but focus on those newly evolved duplications that reflect the greatest copy number evolution. Using this approach they show that the novel protein domain, DUF1220, demonstrates dramatically increased copy number in the human lineage and this increased copy number is associated with numerous diseases associated with cognitive dysfunction. However more evidence, for example, evidence of selective sweeps, is needed before we can say whether these newly arisen duplications are associated with both adaptation and disease and not just the latter. Furthermore (and it may not need to be stated here), many adaptations may not be derived from recent duplications (e.g., the origin of the genus *Arabidopsis* and even more recently, the recolonization of Europe postglaciation by *A. thaliana* has occurred tens of millions of years since the most recent wide-spread gene duplication event in this lineage), thus focus on duplications alone will likely lead to only partial answers.

I expected more contributions reflecting the explosive growth of studies quantifying differentiation of gene expression, as well as the genetic changes underlying gene expression evolution. Several chapters demonstrate the utility of high-throughput gene expression profiling that can provide great insight into the evolution of nonmodel organisms. Allen and Little provide a scheme for quantifying the genetic changes underlying coevolution, and Soltis et al. describe how gene expression data inform us of the nature of constraints and flexibility by quantifying patterns in the independent evolution of polyploid *Tragopogon* taxa. However, perhaps the most novel use of gene expression data is presented by Cibrián-Jaramillo and Matienssen who use gene expression data to resolve the relationships among major lineages of plants and then use the phylogenetic framework for "identifying genes

of functional importance in plant diversification." Several of the major nodes, were represented by genes associated with posttranscriptional silencing by small RNAs (split between *Amborella* and the rest of the angiosperms and monocots vs. eudicots), whereas other nodes reflected genes associated with plant adaptation to major environmental stresses. Mapping genes of functional or developmental significance onto major lineage divergence must surely lead to a greater understanding of the selective forces and genetic architecture underlying angiosperm divergence. What is completely missing in the volume as a whole is a discussion of the role of regulatory loci, and *cis* vs. *trans* regulation in particular, in evolution. Although at least seven chapters highlight the role of evolution at *cis*-regulatory loci, none mention the review by Hoekstra and Coyne (2007) that concluded that neither data nor theoretical arguments support an important role of *cis*-regulatory mutations in evolution. I would have appreciated the expression of counterpoints to Hoekstra and Coyne (e.g., Carroll 2008) and it is this general lack of appreciation of the evolutionary conceptual literature that devalues the contribution as a whole.

There are other studies that I do wish to draw positive attention too. Linnen and Hoekstra deftly link evolution at the molecular level with natural selection acting on the phenotype. Foster's weaving of kin selection, group selection, and altruism to shed light on the major questions of sociobiology is remarkable in both scope and clarity. Ridley's discussion of the role of the exchange of ideas in cultural evolution, sex at the level of culture, is delightful, and fits my world view of the importance of universities as idea sources, where thoughts are freely exchanged and this exchange leads to the amazing outpouring of creativity that brings us to our desks each morning (if only university administrators were universal in their understanding of this). Forrest's summary of what intelligent design is and Miller's short account on how to defend evolution in the face of these challenges are must reads for evolutionary biologists and at the very least should have broad influence on our pedagogy in the USA and perhaps other countries.

To reiterate, contributions in the volume are mainly not firmly anchored with the conceptual framework that is found in papers published in *Evolution*. The problem may be that some of the organizers subscribe to the view that molecular biology is a discipline in and of itself as opposed to the view by many contributors to and readers of *Evolution* that it is a tool to address specific questions. This issue may be at the heart of what I think is the failing of the volume to address the challenges raised by Professor Wilson. Ultimately the phenotype is the focus of evolutionary studies and it is the synthesis of the cycle of observation (fieldwork) and experiments (including unraveling the molecular underpinnings of the observations) that leads to a fuller understanding of the evolutionary processes responsible for the origins and maintenance of biodiversity. Another prime example of this in addition to my criticisms above is that little mention is made of the environmental context of evolution and how this interfaces with sequence change. Note that in a keyword search *in Evolution*, "environment" comes up nearly as frequently as "sex" and more than "inbreeding" or "mutation." That is, to paraphrase Hutchinson (1965), we are offered insight into the evolutionary play at the molecular level but only in the briefest sense of the theatre in which it is performed. You will find no stories here of dead woodsmen found with nary a sign of struggle but a newt in their coffee pot all of which has led to deep insight on the coevolution between garter snakes and their toxic newt prey and the molecular basis thereof (Brodie 2011).

The strength of the volume relative to the weaknesses described above is that it allows one to glimpse the future of a horizon of endless questions on the origin of biological diversity to be addressed with molecular approaches. However, I strongly believe these questions are more likely to be addressed and addressed in an efficient manner if they were better represented in the pages of our journal, and in the symposia that anchor our meetings.

ACKNOWLEDGMENTS

J. Kelly, J. Kostyun, F. Stearns and especially M. Dudash provided helpful comments. They are absolved of all opinions or misstatements expressed in this review.

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Associate Editor: J. Thompson