ences: It was the introduction of the idea of information and its physical embodiment in DNA sequences of four different bases. Thus, although the components of DNA are simple chemicals, the complexity that can be generated by different sequences is enormous. In 1953, biochemists were preoccupied only with questions of matter and energy, but now they had to add information. In the study of protein synthesis, most biochemists were concerned with the source of energy for the synthesis of the peptide bond; a few wrote about the "patternization" problem. For molecular biologists, the problem was how one sequence of four nucleotides encoded another sequence of 20 amino acids. It should now be evident what is needed to add to physics to account for living systems. The fundamental theory was formulated by Turing in his notion of a universal Turing machine and deployed by von Neumann in his theory of self-reproducing machines. Given a description of any computation, a universal Turing machine can read the description and perform the computation; in the same way, a von Neumann universal constructor can build any machine when provided with its description, but to preserve the self-reproducing property, it is necessary for the parent machine to copy its description and insert a copy into the progeny machine. We can now recognize Schrödinger's mistake: The chromosomes do not contain the means for executing the plan of the organism, but only a description of the means. There are no causal relationships between Turing's and von Neumann's ideas and those of Watson and Crick. They got their ideas of the genetic code from common parlance; Francis Crick once told me that he saw it like the Morse code—as a table transforming the alphabet of letters into the binary code of dots and dashes. The connections exist only in the plane of the history of ideas.

We also can provide the answer for those physicists who looked for new laws of physics in biology: Biology is essentially (very low energy) physics with computation. Fundamental theory in biology is concerned principally with viewing living organisms as the only part of the natural world whose members contain internal descriptions of themselves. That is why I could once tell a Buddhist priest that mountains were not alive: You can't clone a mountain. It is also why the whole of biology must be rooted in DNA, and our task is still to discover how these DNA sequences arose in evolution and how they are interpreted to build the diversity of the living world. Physics was once called natural philosophy; perhaps we should call biology "natural engineering."

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EVOLUTION

Who Speaks with a Forked Tongue?

State-of-the-art molecular and morphological phylogenies for lizards differ fundamentally.

Jonathan B. Losos,[1] David M. Hillis,[2] Harry W. Greene[3]

At the dawn of molecular phylogenetics, much was made of the conflict between results from morphological and molecular data sets. Although molecular data have rarely changed our understanding of the major multicellular groups of the evolutionary tree of life, they have suggested changes in the relationships within many groups, such as the evolutionary position of whales in the clade of even-toed ungulates (*1*). Further investigation has usually resolved conflicts, often by revealing inadequacies in previous morphological studies. This has led to a presumption by many in favor of molecular data, but a recent morphological analysis by Gauthier *et al.* (*2*) argues persuasively that we should reconsider whether DNA is always inherently superior for inferring life's history.

Molecular analysis has clear advantages. Vast quantities of sequence data can be collected rapidly and at ever-lower cost; the sequences can be scored objectively and repeatedly; they often are not as prone to misleading adaptive convergence, and avoid problems of environmentally induced variation. Nonetheless, new molecular phylog-

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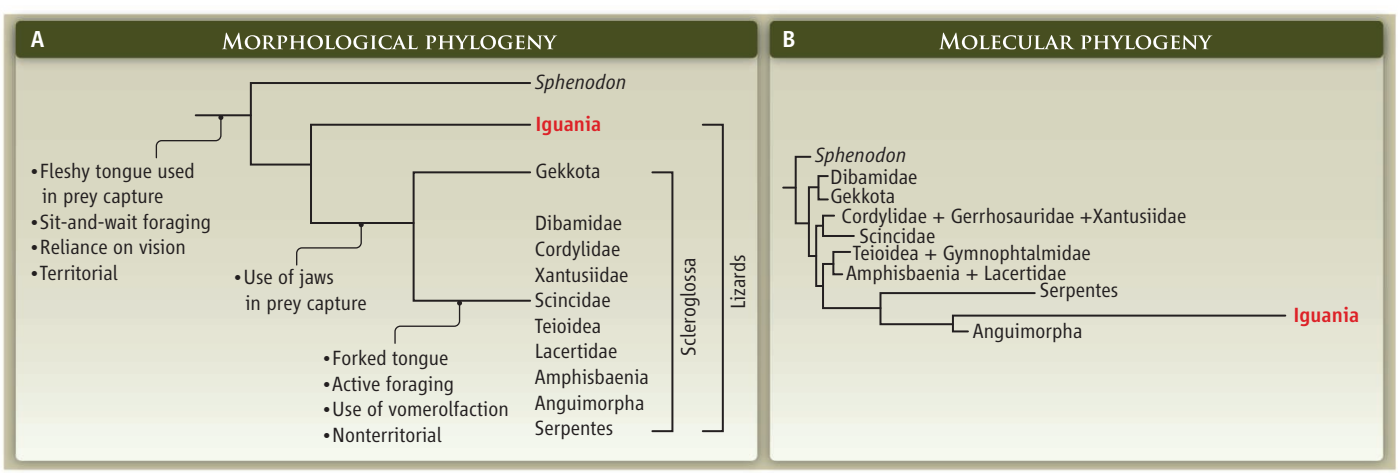

Evolutionary conundrum. (**A**) In the morphology-based phylogeny, many key characters in iguanians are inferred to represent the retained ancestral state. *Sphenodon* is the closest living relative to lizards. [Phylogeny based on (*14*)] (**B**) In the molecular phylogeny, iguanians are placed high in the tree; their supposedly ancestral characters are attributed to evolutionary reversals. Branch lengths are proportional to the number of morphological reversals required by this tree.

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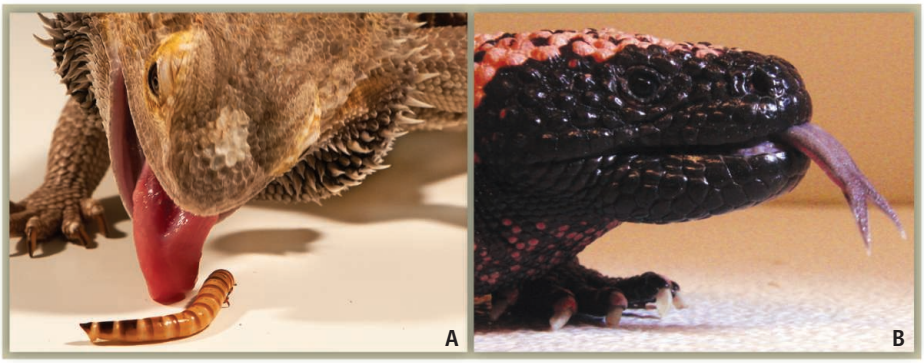

Evolutionary reversal or ancestral state? One of the traits inferred to have reversed evolutionarily in the lizard molecular tree is the ancestral tongue morphology, shown here for the iguanian *Pogona barbatus* (**A**); the scleroglossan *Heloderma suspectum* (**B**) exhibits the derived, bifid state.

enies are not always correct. A 1991 study concluded that guinea pigs are not rodents (*3*), but higher sampling of taxa revealed a methodological bias and showed that they are indeed rodents (*4*). In a similar vein, errors in rooting molecular trees have led to mistaken conclusions, such as that toothed whales evolved multiple times (*5*). Other problems with molecular analyses stem from overly simplistic substitution models that fail to account for details of genome evolution (*6*), confusion arising from gene duplication (*7*), and missing genes (*8*). None of these exemplify inherent problems with molecular data but rather false assumptions about how genomes evolve. A study is not necessarily better just because it uses DNA analysis (*9*).

And that brings us to lizards. The standard view has been that the ~9000 lizard species split at the base of the phylogeny into Iguania (iguanas, chameleons, and relatives) and Scleroglossa (all remaining lizards, including geckos, skinks, monitors, and snakes) (see the first figure, panel A). The straightforward evolutionary scenario from this phylogeny was that iguanians exhibit many ancestral characteristics and that the evolution of scleroglossans reflected a suite of derived and often concerted changes.

In the past decade, molecular phylogenetic analyses, culminating in Wiens *et al*.'s study (*10*), have strongly contradicted this view. Most surprisingly, they find that iguanians evolved more recently, nesting high in the lizard tree close to monitors and Gila monsters (Anguimorpha) and snakes (Serpentes) (see the first figure, panel B). In this view, supposedly ancestral characteristics of iguanians arose because they re-evolved character states shared with more distant relatives but not seen in snakes, monitors, and others among their newfound phylogenetic neighbors (see the second figure).

These findings did not sit well with Gauthier's team of morphologists, who have built an enormous data set, examining 192 species of extant and extinct lizards and 610 variable characters, 247 of them previously unrecognized and most only now accessible through high-resolution x-ray computed tomography. Many systematists likely expected that a greatly enhanced morphological data set, analyzed with state-of-the-art phylogenetic methods, would echo DNA-based studies, but the results could hardly have been more contradictory. The analysis overwhelming supports the traditional phylogeny; not a single anatomical synapomorphy (a shared, derived character that suggests close relationship) supports placement of Iguania high in the lizard tree. Moreover, an enormous number of evolutionary reversals—traits evolving back to the ancestral lizard condition—is required on the branch leading to the Iguania.

When two phylogenies are fundamentally discordant, at least one data set must be misleading. There are two plausible explanations for this conflict. One is that morphological homoplasy [multiple evolution of character states by convergent evolution or reversal (*11*)] is rampant, falsely signaling that iguanians possess a remarkable number of ancestral character states and incorrectly placing them at the base of the lizard tree. Gauthier *et al*. regard this as unlikely, because the synapomorphies of scleroglossans inferred as lost by iguanians in the molecular tree come from many functionally different parts of anatomy. These traits have disparate embryological origins and growth patterns, discounting general explanations based on development. Furthermore, iguanians have diverse lifestyles, ranging from large herbivorous iguanas to ant-eating horned lizards and gliding dragons. It is hard to see how this multifaceted suite of characteristics could reflect adaptation to an overall iguanian lifestyle.

Could the explanation be that the molecular data are providing the false signal? Natural selection operates at molecular as well as morphological levels, and examples of molecular convergence confounding phylogeny bear out this concern (*12*). Moreover, differential selection for base composition or particular codon usage could produce biased patterns of genetic evolution, skewing a phylogenetic analysis (*13*). But what processes are sufficient for the 44 protein-coding genes analyzed by Wiens *et al*. (*10*) to produce a consistent bias and so radically restructure the lizard tree? Higher rates of molecular evolution in iguanians and snakes (*1*) suggest that the genes in these taxa are not evolving like those in other lizard lineages, but it is unclear how this rate heterogeneity might violate assumptions of the underlying models used to infer the molecular phylogeny.

We are left with a conundrum. The molecular data imply an astonishing pattern of morphological homoplasy and suggest very limited knowledge of the functional link between structures and lifestyle; if convergence is so pervasive, what faith can we have in the placement of fossil taxa for which no molecular data are available? Conversely, morphology implies a pattern of molecular evolution that has yet to be explained.

Beyond this intriguing discrepancy, Gauthier *et al*.'s analysis shows the continuing power and importance of morphological and fossil investigation. Lizards are surely not special in harboring so much undescribed and little understood variation, and state-of-the-art technological tools promise revelations never previously imagined.

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