

# Techniques used to infer pathways of protein evolution found unreliable

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A key assumption that biologists have relied on widely over the past quarter-century in studying the evolution of protein molecules is "highly questionable," according to an article published in the November issue of *BioScience*.

The article, by Shozo Yokoyama, a vision researcher at Emory University, summarizes experimental work that involved creating and measuring the properties of dozens of reconstructed ancestral versions of visual pigments found in the eyes of [vertebrates](#), including humans, as well as deliberately altered variants. Yokoyama concludes that the studies he assessed "cast serious doubt" on the "fundamental principle of molecular adaptation," the bedrock of thousands of published papers based on reconstructions of [evolutionary changes](#) in a wide range of proteins. The statistical tools used by such studies are "not reliable," he writes.

In attempting to understand how proteins and their properties might have changed over time, [biologists](#) have typically made simplifying assumptions. One is that a known change at a particular spot in a protein would affect the properties of ancestral and modern forms of proteins in similar ways. That simplification makes it relatively easy for computers to infer the likely evolutionary paths that led to the forms of the proteins found in modern organisms—for example, the visual pigments found in deep-sea fishes (which live with no [ultraviolet light](#)) and the different pigments found in shallow-water fishes.

Yokoyama tested the assumptions by making the hypothesized ancestral pigments and variants of them that might have been produced by mutation, then accurately measuring their properties. The results were disturbing: the properties of related versions of proteins would often change in very different ways when the same mutation was introduced into each. Consequently, standard computational and [statistical methods](#) would rarely have identified the experimentally supported evolutionary pathway. Yokoyama expresses the hope that other researchers will start to make and test the properties of reconstructed ancestral proteins to evaluate hypotheses about their evolution, rather than relying on computational approaches.

Provided by American Institute of Biological Sciences

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