Scitable BETA by nature EDUCATION
A Collaborative Learning Space for Science Undergraduates
LEARN MORE
GIVE US YOUR FEEDBACK

The Molecular Clock and Estimating Species Divergence

By: Simon Ho, Ph.D. (*Australia National University*) © 2008 Nature Education

Citation: Ho, S. The molecular clock and estimating species divergence. *Nature Education* 1(1), (2008)

Since its proposal in the 1960s, the molecular clock has become an essential tool in many areas of evolutionary biology, including systematics, molecular ecology, and conservation genetics. The molecular clock hypothesis states that DNA and protein sequences evolve at a rate that is relatively constant over time and among different organisms. A direct consequence of this constancy is that the genetic difference between any two species is proportional to the time since these species last shared a common ancestor. Therefore, if the molecular clock hypothesis holds true, this hypothesis serves as an extremely useful method for estimating evolutionary timescales. This is of particular value when studying organisms that have left few traces of their biological history in the fossil record, such as flatworms and viruses.

The Molecular Clock Is Proposed and Refined

The molecular clock hypothesis was originally proposed by researchers Emile Zuckerkandl and Linus Pauling on the basis of empirical observations, but it soon received theoretical backing when biologist Motoo Kimura developed the neutral theory of molecular evolution in 1968. Kimura suggested that a large fraction of new mutations do not have an effect on evolutionary fitness, so natural selection would neither favor nor disfavor them. Eventually, each of these neutral mutations would either spread throughout a population and become fixed in all of its members, or they would be lost entirely in a stochastic process called genetic drift. Kimura then showed that the rate at which neutral mutations become fixed in a population (known as the substitution rate) is equivalent to the rate of appearance of new mutations in each member of the population (the mutation rate). Provided that the mutation rate is consistent across species, the substitution rate would remain constant throughout the tree of life.

Subsequent research has shown that Kimura's assumption of a strict molecular clock is too simplistic, because rates of molecular evolution can vary significantly among organisms. However, there has been a general reluctance to abandon the molecular clock entirely, because it represents such a valuable tool in evolutionary studies. Instead, researchers have undertaken efforts to retain some aspects of the original clock hypothesis while "relaxing" the assumption of a strictly constant rate.

Such efforts have led to the development of so-called "relaxed" molecular clocks, which allow the molecular rate to vary among lineages, albeit in a limited manner. There are currently two major types of relaxed-clock models. The first type assumes that the rate varies over time and among organisms, but that this variation occurs around an average value. The second type allows the evolutionary rate to "evolve" over time, based on the assumption that the rate of molecular evolution is tied to other biological characteristics that also undergo evolution. For instance, there is some evidence that substitution rates are influenced by an organism's metabolic rate.

Calibrating the Molecular Clock

When using either a strict- or relaxed-clock method of genetic analysis, the most important consideration is how to calibrate the molecular clock. Assume, for example, that researchers have two DNA sequences that have a content difference of 5%. From this information alone, it is not possible to tell whether these sequences have diverged from each other at a rate of 1% per 1 million years over a period of 5 million years, or whether they have diverged at a fivefold higher rate over a period of just 1 million years. Indeed, there is a countless range of possible combinations of rate and time, and with access to only percentage data, the researchers will not be able to determine which combination is correct. This is equivalent to trying to determine the average speed of a car merely by looking at its odometer. To deduce the average speed, one would also need to know the length of time for which the car has been travelling.

Thus, to calibrate the molecular clock, one must know the absolute age of some evolutionary divergence event, such as the split between mammals and birds. An estimate of the timing of this event can be gained by examining the fossil record, or by correlating this particular instance of evolutionary divergence with some geological event of known antiquity (such as the formation of a mountain range that split the geographic range of a species in two, thus initiating a process of speciation). Once the evolutionary rate is calculated using a calibration, this calibration can then be applied to other organisms to estimate the timing of evolutionary events.

Using the Molecular Clock

A recent study by Weir and Schluter (2008) demonstrates the use of different calibration techniques. To estimate the evolutionary rate of the mitochondrial gene encoding cytochrome b in birds, Weir and Schluter chose 90 different calibrations derived from dated fossils and from the formation ages of land bridges, oceanic islands, and mountain ranges. They then used a statistical method to check each of these calibrations and discarded 16 that were found to be inconsistent. Using the remaining 74 calibrations, the duo estimated that cytochrome b genes in birds evolve at an average rate of approximately 1% per 1 million years, meaning that any two bird species are diverging from each other at a rate of 2% per 1 million years. This has long been regarded as a standard quantity in genetic studies of birds and is known as the "2% rule." For example, the 2% rule has been used to test the hypothesis that many modern songbird species originated during pronounced glacial cycles over the past 250,000 years.

Weir and Schluter also noted that the rate of molecular evolution varies significantly among different bird species. Many bird lineages have evolved at a speed relatively close to the average rate of 1% per 1 million years, but some birds were found to be evolving more than four times faster than others. Interestingly, Weir and Schluter did not find any evidence to suggest that this variation was correlated with biological characteristics such as body mass.

The findings of Weir and Schluter demonstrate that it can be unwise to calculate an evolutionary rate using one group of organisms and then extrapolate that rate to another group, even when one is comparing relatively similar species. If applied correctly, however, the molecular clock can yield enlightening date estimates for evolutionary events that would otherwise be difficult to study from the fossil record alone. Scientists can use relaxed-clock methods to deal with variation in the rate of the molecular clock. By measuring the patterns of evolutionary rate variation among organisms, they can also gain valuable insight into the biological processes that determine how quickly the molecular clock ticks.

What the Future Holds

In several years' time, the molecular clock will be celebrating its fiftieth birthday. Over its lifetime, the clock has successfully negotiated its way through numerous challenges, undergoing various refinements and improvements, and it thus remains an important tool in evolutionary biology. Moreover, with the rapid accumulation of new genetic data, particularly as a result of the many genomic sequencing projects that are currently underway, it seems that the molecular clock will continue to shed light on the tempo and timescale of evolution for years to come.

References and Recommended Reading

Bromham, L., & Penny, D. The modern molecular clock. *Nature Reviews Genetics* 4, 216–224 (2003) doi:10.1038/nrg1020 (link to article)

Kumar, S. Molecular clocks: Four decades of evolution. *Nature Reviews Genetics* 6, 654–662 (2005) doi:10.1038/nrg1659 (link to article)

Weir, J. T., & Schluter, D. Calibrating the avian molecular clock. *Molecular Ecology* 17, 2321–2328 (2008) (link to article)