NEUTRAL THEORY OF MOLECULAR EVOLUTION

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The neutral theory of molecular evolution holds that most evolutionary changes at the molecular level, and most of the variation within and between species, are due to random genetic drift of mutant alleles that are selectively neutral. The theory applies only for evolution at the molecular level, and is compatible with phenotypic evolution being shaped by natural selection as postulated by Charles Darwin. The neutral theory allows for the possibility that most mutations are deleterious, but holds that because these are rapidly removed by natural selection, they do not make significant contributions to variation within and between species at the molecular level. A neutral mutation is one that does not affect an organism's ability to survive and reproduce. The neutral theory assumes that most mutations that are not deleterious are neutral rather than beneficial. Because only a fraction of gametes are sampled in each generation of a species, the neutral theory suggests that a mutant allele can arise within a population and reach fixation by chance, rather than by selective advantage.

The neutral theory of molecular evolution was first proposed by Motoo Kimura in 1968, and independently by Jack King and Thomas Jukes in 1969. At the time, studies on genetic sequences were showing that the previous idea which postulated that most of the differences between species were caused by selection on advantageous mutations was actually not true.

The neutral theory instead proposed that the majority of molecular changes, such as in DNA sequence, are caused by random processes acting on selectively neutral mutants, meaning they inferred no advantage or disadvantage.

• Mutation rate refers to the rate at which changes are incorporated into a nucleotide sequence during the process of reproduction, i.e., the probability that an allele in an organism differs from the copy of that in its parent from which it was derived.

• An allele substitution occurs when a newly arisen allele completely replaces other alleles in a population in which it arises, i.e., when a newly arisen allele becomes fixed in a population. Substitution rate refers to the rate at which allele substitutions occur.

Neutral mutations

The neutral theory asserts that alternative alleles at variable protein loci are selectively neutral. This does not mean that the locus is unimportant, only that the alternative alleles found at this locus are selectively neutral.

– Glucose-phosphate isomerase is an esssential enzyme. It catalyzes the first step of glycolysis, the conversion of glucose-6-phosphate into fructose-6-phosphate.

– Natural populations of many, perhaps most, populations of plants and animals are polymorphic at this locus, i.e., they have two or more alleles with different amino acid sequences.

– The neutral theory asserts that the alternative alleles are selectively neutral.

• By selectively neutral we do not mean that the alternative alleles have no effect on physiology or fitness. We mean that the selection among different genotypes at this locus is sufficiently weak that the pattern of variation is determined by the interaction of mutation, drift, mating system, and migration. This is equivalent to saying that $N_e s < 1$, where N_e is the effective population size and s is the selection coefficient on alleles at this locus.

– Experiments in Colias butterflies, and other organisms have shown that different electrophoretic variants of GPI have different enzymatic capabilities and different thermal stabilities. In some cases, these differences have been related to differences in individual performance.

– If populations of Colias are large and the differences in fitness associated with differences in genotype are large, i.e., if $N_e s > 1$, then selection plays a predominant role in determining patterns of diversity at this locus, i.e., the neutral theory of molecular evolution would not apply.

– If populations of Colias are small or the differences in fitness associated with differences in genotype are small, or both, then drift plays a predominant role in determining patterns of diversity at this locus, i.e., the neutral theory of molecular evolution applies.

In short, the neutral theory of molecular really asserts only that observed amino acid substitutions and polymorphisms are effectively neutral, not that the loci involved are unimportant or that allelic differences at those loci have no effect on fitness.

The rate of molecular evolution

The rate of allelic substitution, under the hypothesis that mutations are selectively neutral. To get that rate we need two things: the rate at which new mutations occur and the probability with which new mutations are fixed. In a word equation

rate of substitution = rate of mutation × probability of fixation

$$\lambda = \mu_0 p_0$$

In a diploid population of size N, there are 2N gametes. The probability that any one of them mutates is just the mutation rate, μ, so

$$\mu_0 = \mu \,.$$

Diversity in populations

Protein-coding genes consist of hundreds or thousands of nucleotides, each of which could mutate to one of three other nucleotides.2 That's not an infinite number of possibilities, but it's pretty large. It suggests that we could treat every mutation that occurs as if it were completely new, a mutation that has never been seen before and will never be seen again.

Conclusions

The neutral theory does a job of dealing with at least some types of molecular data. According to this “ Neutral Theory” of molecular evolution most mutations are disadvantageous and are quickly removed bynatural selection, a vanishingly small proportion are advantageous and are quickly brought to fixation, while the vast majority of fixed (and therefore observed) mutations are selectively neutral. That most mutations are disadvantageous and rarely observed is in agreement with the previously prevalent views. Selectionists and neutralists also agree that adaptation must be the result of advantageous mutations that are brought to fixation by natural selection. The main point of difference concerns the fraction of mutations that are advantageous: the extreme selectionist view is that almost all observed mutations are advantageous, while the neutralist believes that practically all observed mutations are neutral with respect to fitness. Today, we have many examples of mutations that appear to have been fixed by natural selection, but there is also a great deal of evidence for the importance of neutral mutation and genetic drift. The truth probably lies somewhere between the two extreme viewpoints.