

Evolution: Neutralist View

Introductory article

Andreas Wagner, *University of New Mexico, New Mexico, USA*

The neutralist view of molecular evolution maintains that the vast amount of molecular variation seen in natural populations is largely due to neutral mutations.

Copies of the same gene in different individuals of a population usually differ at multiple positions in their deoxyribonucleic acid (DNA) sequence. Similarly, the proteins they encode differ at multiple positions in their amino acid sequence. Mutations, either point mutations or small insertions or deletions, cause these differences. Such mutations fall into three classes. The first class consists of neutral mutations, causing a change in DNA or amino acid sequence that does not affect gene function and thus leaves an organism's fitness unchanged. A second class comprises beneficial mutations, mutations that improve the function of a gene and that increase an organism's fitness. Natural selection will increase the frequency of genes carrying such mutations in a population. A third class consists of deleterious mutations, which adversely affect the function of a gene, decrease the fitness of an organism and are thus eliminated from populations. For this reason, deleterious mutations do not contribute to observed molecular variation, even though they are usually the most frequent mutations. It is unclear whether most observed variation stems from neutral mutations or beneficial mutations. According to the neutralist view, the vast majority of occurring mutations are neutral, and the variation we see in natural populations is thus mostly neutral variation. Motoo Kimura's neutral theory of molecular evolution makes specific predictions about the fate of such neutral mutations. The rate at which neutral mutations arise that will eventually go to fixation, that is, attain a frequency of 1, equals the rate of neutral mutations itself and is thus constant and independent of population size. The time they take to go to fixation is proportional to the size of the population. Because more mutations arise in large populations than in small populations, and because mutations take longer to go to fixation in large populations, much observed variation may be due to neutral mutations on their way to fixation. These simple predictions do not hold for beneficial mutations, whose fate also depends on the amount of fitness benefits they confer.

The neutralist view has since been modified to include weakly deleterious mutations as a major source of observed genetic variation. In populations of N individuals, mutations that reduce an organism's fitness by less than $1/2N$ have effects that are too weak to be detected by natural selection. Such weakly deleterious mutations are thus effectively neutral and could be a source of observed variation.

A variety of tests exist that aim at detecting whether neutral or beneficial mutations are primarily responsible for observed variation. They test predictions of the neutral theory of molecular evolution. One such prediction is that the mean and variance of the number of mutations going to fixation in different lineages should be approximately equal.

Molecular systematics, the area of contemporary biology concerned with the reconstruction of evolutionary history using DNA or protein sequences, assumes that DNA changes accumulate at constant rates, a key prediction of the neutral theory, and thus that the neutralist view is approximately valid at least for some genes.

See also

Evolution: Selectionist View
Evolution: Views of
Kimura, Motoo

Further Reading

- Kimura M (1983) *The Neutral Theory of Molecular Evolution*. Cambridge, UK: Cambridge University Press.
- Kreitman M and Akashi H (1995) Molecular evidence for natural selection. *Annual Review of Ecology and Systematics* **26**: 403–422.
- Ohta T (1992) The nearly neutral theory of molecular evolution. *Annual Review of Ecology and Systematics* **23**: 263–286.
- Sayer SA, Dykhuizen DE and Hartl DL (1987) A confidence interval for the number of selectively neutral amino acid polymorphisms. *Proceedings of the National Academy of Sciences of the United States of America* **84**: 6225–6228.

Encyclopedia of the Human Genome

Volume 2

Editor in Chief

David N Cooper
University of Wales College of Medicine

- Volume 1 Absolute Pitch: Genetics – DiGeorge Syndrome and Velocardiofacial Syndrome (VCFS)
- Volume 2 Digital Image Analysis – Gene Trees and Species Trees
- Volume 3 Genome Databases – Mitochondrial Genome: Evolution
- Volume 4 Mitochondrial Heteroplasmy and Disease – Relatives-based Tests of Association
- Volume 5 Renal Carcinoma and von Hippel–Lindau Disease – Zuckerkandl, Emile



A. 3769482

Lesesale 193,93 : 2

