Brief Historical Perspectives of the Paper

“THE NEW MUTATION THEORY OF PHENOTYPIC EVOLUTION”

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The following is the author’s account of the history of development of the mutation theory of phenotypic evolution and related matters.

Darwinism

(1) Charles Darwin proposed that evolution occurs by natural selection in the presence of fluctuating variation.

(2) At his time, the mechanism of generation of new variation was not known, and he assumed that new variation is generated by climatic changes, inheritance of acquired characters, spontaneous variations, etc. However, he believed that new variation occurs in random direction and evolutionary change is caused by natural selection.

(3) He assumed that enormous phenotypic diversity among different phyla and classes is the result of accumulation of gradual evolution by natural selection.

Saltationism

Several biologists such as Thomas Huxley, William Bateson, and Hugo de Vries argued that the extent of variation between species is much greater than that within
species and therefore saltational or macromutational change is necessary to form new species rather than gradual evolution as proposed by Darwin. In this view a new species can be produced by a single macromutation, and therefore natural selection is unimportant.

This view was strengthened when de Vries discovered several new forms of evening primroses which were very different from the parental species (*Oenothera lamarckiana*) and appeared to be new species. This discovery suggested that new species can arise by a single step of macromutation. However, it was later shown that *O. lamarckiana* is a permanent heterozygote for two chromosomal complexes and that de Vries’ mutants are merely chromosomal segregants from this unusual genetic form. This was a serious blow to de Vries’s mutation theory.

**Morgan’s mutationism**

Using the fruitfly *Drosophila melanogaster*, Morgan and his colleagues obtained a large number of mutations and showed that most mutations are deleterious but there are a small proportion of nondeleterious mutations, whose phenotypic effects are much smaller than those of de Vries’ macromutations. He then proposed that genetic mutation is the cause of innovative characters and natural selection is merely a sieve to save advantageous mutations and eliminate deleterious ones. This simple theory of mutation and selection was quite popular in the 1920’s and 1930’s. This theory is usually called mutationism.
Neo-Darwinism

However, Morgan’s view was later considered too simplistic, and it was almost obliterated when neo-Darwinism proposed by Fisher (1930), Haldane (1932), and Wright (1932) gained general support. This happened partly because most mutations experimentally obtained were deleterious and these mutations did not seem to be useful for evolution.

Neo-Darwinism asserts that natural selection is the major force of evolution and has the power of creating novel characters in the presence of raw genetic material provided by mutation. Therefore, mutation is of secondary importance. Currently, this view is widely accepted (see many college textbooks).

Molecular evolution

Studies of evolutionary changes of genes and proteins have shown that (1) mutation occurs every generation with an appreciable frequency, (2) on average about 85 percent of amino acid changes are deleterious and are eliminated from the populations, (3) the remaining changes are either neutral or selectively advantageous (adaptive) and are fixed in the population by genetic drift or by selection, and (4) only a small proportion of mutations are adaptive.

Nei’s mutation theory of phenotypic evolution

Nei (1983; 1987) revived and extended Morgan’s mutationism taking into account the properties of molecular evolution. He proposed that evolution occurs primarily by mutation and natural selection is of secondary importance. In addition, a considerable
portion of phenotypic evolution is neutral or nearly neutral. However, the data supporting his view were rather scanty in the 1980’s.

During the last 20 years, an extensive study has been done about the molecular basis of phenotypic evolution. In my PNAS paper, I have made the following observations about the results of this new study.

(1) Most phenotypic characters are controlled by multigene families, and the number of gene copies in a gene family may change drastically by genomic drift (caused by random events of gene duplication and deletion and random genetic drift), and this genomic drift is an important factor of evolution.

(2) The basic genetic factor of phenotypic evolution is the mutational change of the protein-coding and regulatory regions of genes. In both regions of genes major-effect and minor-effect mutations may occur, but it seems that the evolutionary change of phenotypic characters is caused primarily by the major-effect mutations (the major gene-effect hypothesis; Nei 1987). Here mutation includes all kinds of genetic changes including recombination.

(3) There is a significant component of neutral change in phenotypic evolution, and a certain degree of phenotypic variation within species does not seem to be related to fitness (Nei 1987). The variation of gene expression levels within and between closely related species is consistent with the pattern of neutral evolution.

(4) The genes controlling phenotypic characters interact with one another spatially and temporally in the process of development. There are also several signaling pathways for producing the same end character. For these reasons, the effects of deleterious and
advantageous mutations may be mitigated, and this may enhance the chance of neutral evolution.

(5) Natural selection occurs as a consequence of mutational production of different genotypes, and therefore it is not a cause of evolution. In other words, mutation is necessary and sufficient for evolution to occur, though the intensity of natural selection affects the speed of spreading of better-fit genotypes in the population. As a metaphor, consider the development and growth of the automobile industry. Each automobile company produces new models of cars almost every year. This production is done by engineers, who modify previous models. This process is similar to the creation of new genotypes by mutation in evolution. In the automobile industry particular models of cars become popular and dominate in the market because consumers like them. This process is similar to natural selection caused by environmental conditions or changes in evolution. In this case consumers play no roles in producing new models of cars, though they may give some ideas to engineers what types of new models should be developed in the future. In the case of evolution environmental conditions and changes are important in selection but play no role in producing new genotypes. New better-fit genotypes are created by mutation, and natural selection is merely to eliminate the previously existing less-fit genotypes.

(6) Evolution occurs without purpose by mutation and adaptation to new environments, and therefore it is intrinsically unpredictable.

Comments on misunderstandings of mutationism
(1) Richard Dawkins attacked mutationism stating that in this theory new species are assumed to occur by single mutations without natural selection. This criticism applies to Bateson’s saltationism or deVries’ macromutationsim. However, it has nothing to do with my mutation theory (or Morgan’s theory), because I maintain that new species are produced by mutations of many genes that interact with one another in the process of development.

(2) Some people argue that mutation is basically destructive, and therefore it is impossible to produce highly developed complex organisms. This criticism is based on misunderstandings of the process of phenotypic evolution. Complex organisms evolve when new characters due to mutation are added to a simpler form of the previous organism. This occurs whenever new mutations enhance the adaptability of the organism. Harmful mutations are eliminated from the population and leave no trace of evolutionary changes. New mutations are incorporated only when they are beneficial in the genetic background of the previous organism in a given environment or when they are neutral despite their visible effects on phenotypic characters. Therefore, evolution does not occur at random but is constrained by the pre-existing genotypes. Evolution by adaptive mutation may be a slow process, but it does not matter because there has been plenty of time to evolve, over 3 billion years.

(3) It has been stated that evolution obviously cannot happen without mutation but the directional change of evolution is controlled by natural selection in the presence of random mutations (Dawkins 1987). However, as mentioned earlier, natural selection is merely a consequence of existence of different genotypes created by mutation. Therefore, the fundamental cause of evolution is mutation. In the presence of a new environment
only mutant genotypes that are adaptive for the environment can survive, and therefore a
directional evolution may occur.

One may argue that this logic is semantic because both mutation and selection are
involved. However, it is obvious that mutation is the driving force of evolution in this
view.

(4) There are many mathematical theories for the neutral evolution of quantitative
characters, but they are dependent on assumptions of gene effects of which the validity is
unclear. For example, the additive, dominance, and epistatic effects of genes in
quantitative characters are statistically defined, and they are not directly related to the
gene effects considered in developmental biology. More experimental studies seem to be
necessary on this issue.