M. V. Vol'kenshteĭn. *Evolution of biopolymers and biological evolution.* The modern theory of evolution incorporates molecular biology and biophysics, synergetics, and information theory. The relationship with molecular biology was recognized a long time ago. Homologous proteins and nucleic acids of different types are closer to each other in composition and primary structure, the closer the types. Evolution trees can be constructed on this basis. The simple thought arises that each unit of a biopolymer has been selected by evolution. A Darwinian selection, however, is necessary at the level of phenotypes but apparently not at the molecular level.

In globular proteins, the polypeptide chains are coiled into a compact globule—an aperiodic solid. A globule consists of ordered regions of a secondary structure—α-helices and/or β-ribbons—alternating with disordered regions. The protein performs its biological function (primarily an enzymatic function) at an active center in a globule. The rest of the globule serves as a framework. In the active region, the substrate molecules undergo sorption and catalytic conversion; the framework participates in this conversion as a medium having a conformational mobility. The functioning of the protein is determined by the electronic-conformational interactions—chemical, i.e., electronic, degrees of freedom at the active center interact with conformational degrees of freedom both at the center and in the framework. This interaction may be thought of as the propagation of a "conformon": a formation somewhat similar to a polaron.

The correlation between the spatial and secondary structures of a protein and the sequence of amino acid groups in the chain is of course degenerate. In several cases, significant changes in the primary structure have essentially no effect on the structure of a globule and thus essentially no effect on its function. Mutational replacements of groups may not affect the properties of the protein if these replacements do not affect key groups in the active center.

As far back as 1966 it was shown that the genetic code has a high noise immunity: Most unit replacements in DNA do not change the framework of the amino acid which is coded or its hydrophoby. The way in which the groups are encountered in the proteins correlates with the numbers of codons which are responsible for these groups. The average primary structures of proteins are similar to a random distribution of groups. O. B. Ptitsyn has shown that the distribution of the lengths of the α- and β-regions and also of $\alpha\beta$ clusters agrees with the statistical distribution found for protein models based on groups of two types: polar (hydrophilic) and nonpolar (hydrophobic). A protein may be thought of as an "edited statistical copolymer." The editing occurs through natural selection and affects primarily the active center. It may be that the metal ions Zn^{2+}, Fe^{3+}, Cu^{2+}, and Mo^{2+} play an important role in this process. About a third of all enzymes have such ions in their active centers. These ions seem to be important to the origin of life in sea water.

The statistical nature of the structure of proteins has been demonstrated in the well-known experiments by Fox, who obtained protein-like substances—proteinoids—by heating mixtures of amino acids in the presence of a dehydrating substance: a phosphate.

The structure of a protein is the result of the storage of a random choice; it is a relic of events which occurred when life first appeared. A study of the statistical and evolution-selected properties of proteins is important to protein engineering—to the artificial production of proteins with given properties.

The Japanese geneticist Kimura has developed a neutral theory of evolution, according to which most mutational replacements in nucleic acids occur at random, without being subject to the pressure of natural selection. There is a "molecular clock" of evolution. The number of point mutations in biopolymers turns out to depend in a linear way on the evolutionary time which has elapsed, which is estimated from the times of the divergence of species established in paleontology. The molecular clock runs in different ways for different groups and different proteins. For example, a substitution of 10^{-9} per unit of the chain per year would amount to 9.0 for fibrinopeptides, 1.4 for hemoglobin, and 0.006 for histon HIV. The substitution rate in the active center of hemoglobin is an order of magnitude lower than in the remainder of the protein, to which this number refers. The reason for the low evolution rate of histon is that the entire molecule is active here. These figures show that if the molecular clock were determined by natural selection the universe would not have existed long enough for the formation of proteins. The construction of the hemoglobin chain through the selection of each unit would have required 10^{11} yr, and the corresponding time for histon would have been 10^{13} yr.

If a mutation brings a small amount of damage, the mutation behaves as if it were neutral. An essential neutralization of harmful mutations occurs as the result of a series of compensatory processes. In contrast with machines made by human hands, biological systems necessarily have "tolerances" and "free play," which determine the homeostasis.

Mutations in biopolymers do not have any direct relation to speciation. A comparison of the 44 proteins of man and chimpanzee shows that they differ in composition by less than 1%. The crux of the matter is that several factors are important for evolution: not only the structure of the

proteins but also the amount of protein, the time it was synthesized, and the place it was synthesized in the organism—the exact answers to the questions, how much, when, and where.

Evolution is inseparably related to individual development, the possibilities for which sharply restrict the paths of natural selection. The directionality of evolution is set by the structure and possibilities for changes in the preceding organisms. Darwin recognized this circumstance. Proteins which have already formed are used in many ways in the course of ontogeny and phylogeny. Ansers to these questions are given by the regulation of the action of genes in space and time. It has been established that new proteins arise in evolution in several cases not through point mutations but in the course of large-scale changes: reorganizations of regions of the primary structure.

For gene regulation there are many possibilities involving the duplication of genes, their activation, and their repression. So-called homeotypical mutations, which include or exclude entire groups of genes, have been discovered. Genes are not immobile; they are observed to undergo transposition in chromosomes and "horizontal transfer": the incorporation of foreign genetic material in a gene. One observes "transpositional explosions," i.e., transpositions which involve a set of genes. These events play an important role in evolution.

In the modern theory of evolution there is a sharp debate between the proponents and opponents of gradualism and puctualism—between concepts of gradual and sharp, abrupt changes in characteristics in speciation and macroevolution. Belintsev and the present author have shown that these processes are of the nature of phase transitions. The contradiction between gradualism and puctualism is therefore erased: The phase transition may be more or less sharp and more or less time-consuming, as is observed in paleontology.

It follows from these arguments that by no means all characteristics have accommodative, adaptive value. This nonadaptationalism is closely related to punctualism. Neutralism at the molecular level also follows from puctualism and nonadaptationalism, since substitutions in biopolymers are gradual and not adaptive: They do not have any direct effect on speciation. This triad of interrelated features explains several questions in the modern theory of evolution, whose unshakable foundation is Darwin's theory. Its importance in biology might be compared with the importance of classical mechanics or electrodynamics in modern physics.

It is usually asked how could there have been enough material and enough time for the development of the biosphere by evolution. There is sufficient material, since the variability within a given population is determined not by rare point mutations but by the ample reserve (up to some tenths) of genetic recombinants and heterozygotes. The question regarding time is answered by the aforementioned triad. Punctualism, i.e., phase transitions in speciation and macroevolution, nonadaptationalism of many characteristics, and neutralism at the molecular level determine the high rate of evolution. Far less time is required to "edit protein texts" than to "write" them.

These are qualitative considerations. The task of the theory is to develop rigorous quantitative models. At this point, several factors have been identified which determine the high rate of evolution.

Future development of an evolutionary theory will require that we overcome, on the one hand, unjustified criticism of Darwin's theory and the synthetic theory of evolution and, on the other, an overly orthodox Darwinism which rejects new ideas, in particular, the neutral theory of evolution.

Several of the questions mentioned in this paper are set forth in more detail in Refs. 1–4.

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