HEREDITARY MOLECULES

N. K. Koltsov

from the book "Cell organization", 1936

VII

So we have come to the conclusion that the makings of all hereditary characteristics as the species and the racial and individual enclosed in genonems as a separate, properly placed in a series of units—genes. Genonems usually have a few microns or tens of microns in length with a submicroscopic, and sometimes ultra-microscopic width, oscillating around 0.1 micron. Based on their research on some genes, the prisoners in one of the disks at the end of the X-chromosome in Drosophila, G. Muller and A. Prokofiev conclude that the diameter of a single gene does not exceed 200–300 angstroms (A = 0.0001 microns).

What are the same education in inorganic nature, we can compare these amazing structures?

Back in 1927, in my speech at the Congress of Zoologists in Leningrad, I developed a hypothesis that genonem is nothing like an enormous protein molecule, or the same bundle of long molecules—the micelles. While this hypothesis may seem paradoxical, because the chemists were not known molecules such gigantic proportions, or even any approaching this size. But even then, some chemists have started talking about the fact that cellulose and its derivatives are built of very long molecules or bundles of molecules, micelles, in which the composition of $C_6H_{10}O_5$ linked with primary valences. But the reporter, G. Mark, had asserted that view at the congress of German naturalists and physicians in Duesseldorf in 1926, has met strong opposition. Only gradually this view of the structure of long molecules of cellulose and other complex organic compounds solidified in chemistry. Played a big role here analysis of macromolecular compounds with X-rays. In his book, "The structure of high-polymer organic natural compounds," published in 1930, Kurt Menner and G. Mark the first of the chemists mentioned, and referring to my work, the opportunity to make a protein molecule, the length of the chromosome. They find that the length of the small chromosomes only ten times the length of the famous long chain molecules. Goes even farther G. Staudinger, who argues that the length of the chain molecules of rubber reaches 0.8 microns, therefore, closely approaching the length of the small chromosomes. But he is far from mind to consider this magnitude limit the length of the molecule and suggests that protein molecules with a molecular weight of 500,000 or more must be much longer than the rubber molecules. Staudinger pointed out that such an explanation can be applied to the chromosomes. He says plainly here about single molecules, refusing to impose an idea of the molecular beam—micelles.

The same point of view on the possible existence of large protein chain molecules develops in his recent book English organic chemist Astbury (1933).

So I find myself in a right to think that I expressed eight years ago, the idea of a chromosome as the molecule is now is not so paradoxical as it may seem early.

Even more paradoxically, seemed to put me at the same time suggested that the complex molecules of protein compounds can not be created in the body again and that we are not able to rely on the artificial synthesis of even some peptides, as the latter has a trillion isomers. I formulated this idea in the thesis: "*Omnis molecula e molecula*", i.e., every (of course, a complex organic) molecule occurs from the surrounding solution only if the molecule is already finished, and the corresponding radicals are placed by apposition (van der Waals forces of attraction or forces of crystallization) on the items available there, and serves as a seed molecule, which are the same radicals.

The process of assimilation of protein compounds in the cytoplasm, nucleus and chromosomes are, in my opinion, is nothing like the growth of crystals in the presence of ready-made crystal lattices. It was nice to see six years after this hypothesis was published by me in German biological journal, found that a chemist Staudinger expressed same idea, repeated in almost the same words.

My hypothesis on the molecular structure of chromosomes I can illustrate with the scheme, which was published by me in 1928 (Fig. 20). The figure shows a chromosome, within which are two genonems as it is usually happens long before cell division. Each genonem is a bunch of long molecules, of which the figure shows only two. All four molecules shown have exactly the same structure and consist of a series of protein radicals linked with primary bonds. Each beam of similar molecules are constrained by the lateral connections. Most of the chromosomes between the shell and genonem chromosome shell (chromolemm) filled with chromoplasm and chromatin, composed as part of metabolism consists of the same radicals—the genes that comprise genonem, or particles, fragments of these radicals, as well as nucleic acid. With the growth of genonem molecular beam these radicals are positioned the same as during the crystallization, in precisely those areas of the crystal lattice, where are the same radicals. The diagram shows on the inside of genonem a few already existing segments. When the thickness of genonem molecular beam by fouling reaches a certain limit, genonem splits along. At different moments in life of cell the exchange of radicals can go in different directions: either from the nucleoplasm into the chromosome, or from chromosome to nucleoplasm.

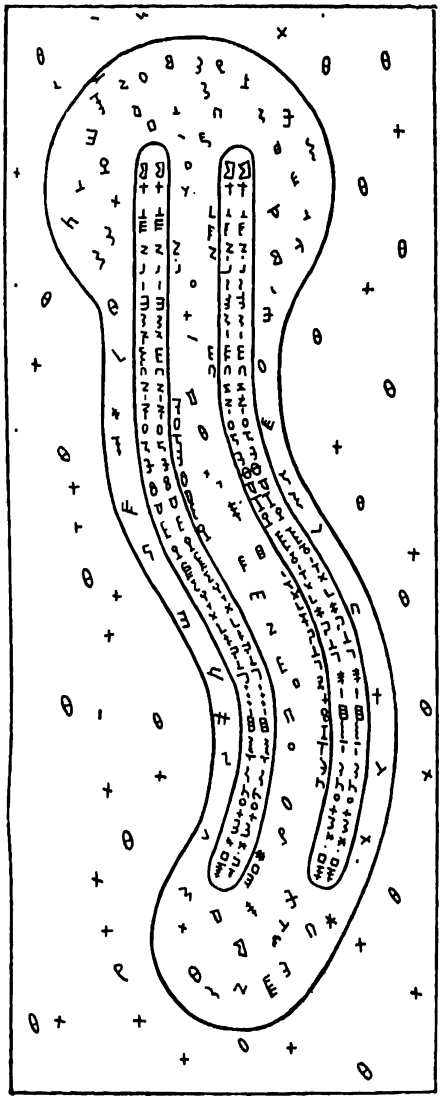

Fig. 20. The scheme of chromosome by Koltsov (1928).

Presented on the scheme radicals of genonem molecules are consistent with genes. American geneticist Demerets criticizing my hypothesis in a private letter, asked me a question: how can cross over happen, in which two chromosomes exchange their segments? But this is—the common chemical reaction of exchange, in which two molecules exchange their ions, such as simple $NaCl + AgNO_3 \rightarrow NaNO_3 + AgCl$.

I also wondered why the inversion, i.e., the rotation of a piece of chromosome to 180°, which dramatically changed the order of the radicals in the genonem molecule and isomer appears, does not entail the usual dramatic change or even death of the organism. But, first, in such huge molecules, changing the order of the radicals should affect, likely to be much weaker than in small molecules. And, secondly, with inversions and translocations, according to the latest works (in America—Stertevant and in USSR—Dubinin and Sidorov, and later Mueller and Prokofiev), every time you move a gene from one place to another there is usually some change in its manifestations (so-called "position effect").

What is the chemical nature, we can assign to individual genes, which are radicals of genonem molecule? Here we are, of course, in the field of pure speculation and can not justify them. Just as an example I put in my 1927 paper peptide structure representing seventeen amino acids of the main valence in one longitudinal chain (Fig. 21). This circuit has a length of about 100 angstroms, i.e., 0.01 micron, and the thickness is less than 10 angstroms in the molecular weight of 2446. For a protein molecule, the molecular weight of which may exceed half a million, it is certainly a very simple particle. Demerets in his article "What is a gene?" shows, but also as an example, the plan of another molecule, which is close to the timonucleic acid that comprises the mass of chromatin. But this is also a very simple molecule consisting of only 170 atoms. Perhaps, some genes are indeed similar to that: genonem, consists of thousands of such radicals, will be a very complex entity.

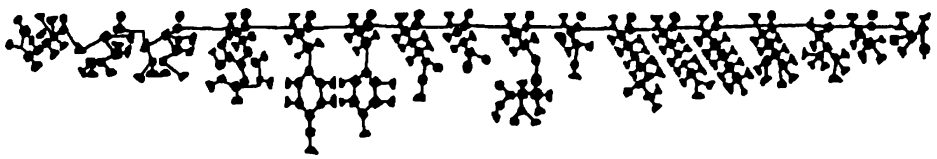

Fig. 21. Diagram of the simplest protein molecule compound—a polypeptide. The circles denote oxygen atoms, semicircles—hydrogen, squares and triangles are carbon and nitrogen.

In the "Nature" of December 22, 1934, there is an interesting message from Ms. Ranch: "The behavior of chromosomes in terms of molecular structures." She completely shares the my view that genonem is a long chain molecule and enters one simplifying assumption, which I think deserves attention. Ranch accepts that the basis of genonem molecule is a chain of monotonously repeating simple units, as determined for the molecule of cellulose or paraffin. The author even offers a specific structure for the backbone of the chromosome of the molecule, namely the structure of clupein—polypeptide, which derive a significant amount of fish sperm. Clupein molecule consists of a connected chain links, each of which is a polypeptide consisting of several successive amino acid residues: arginine (A) and [proline] (M): MAAAMAAAMAA.

Hydrogen arginine residues can be easily replaced by various radicals—different in different links of the chain, which enables differentiation of an infinite chain, and satisfies the requirements of geneticists. In a brief communication, the author does not develop her views with complete clarity, but by associating his thoughts with the views that I have long been developing, I can portray such a scheme of the chromosome structure of the molecule and its evolution (Fig. 22).

Initially, when the protozoa were constructed genonem molecules for the first time, they have been represented by homogenous and more or less long chains of identical units, such as keratin or sericin. Each part consisted of a few simple radicals. With the further evolution of the body, these molecules gradually become more complex by attaching to some of the side links of the radicals, receiving the value of genes. Gradually the number of these side chains located at certain points of genonem proliferate, and radicals become more complicated. Microscope picture of chromosomes in the saliva glands of *Drosophila* is now already a very highly differentiated genonem. If we assume that the transverse discs correspond to genes, here we have to put it side-chain radicals, or radicals, which adsorb strongly stained chromatin. In this case colorless segments in which we see longitudinal threads, should be major chains, not complicated by complex lateral appendages. But when further differentiation happened, here can join the side radicals—new genes; on the other hand, existing side radicals can be complicated or simplified in the mutation process.

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Let us recall the session of the Congress of Naturalists and Physicians, which took place forty years ago: extremely complicated structure of chromosomes by Menzbir and minimization of the complexity to a few molecules by Kolli. Both thesis and antithesis were placed correctly in their apparent contradiction. But for forty years, our knowledge about the structure of chromosomes and the structure of protein molecules underwent a profound change. As a result, views which seemed to be incompatible, are now closer due to increase of our knowledge. For us, chromosome still is an extremely complex structure, but this does not preclude us take for its basis one giant protein molecules.

Of course, we should not get involved in that progress, especially since its chemical parts, they are far from complete, in fact—is still very controversial. After our present synthesis will come a new antithesis, but it will be a new stage of scientific development. And it is unlikely, at least in our Union, there is at least one scholar who dared to declare after the Lev Tolstoy, all these scientific researches futile and useless.

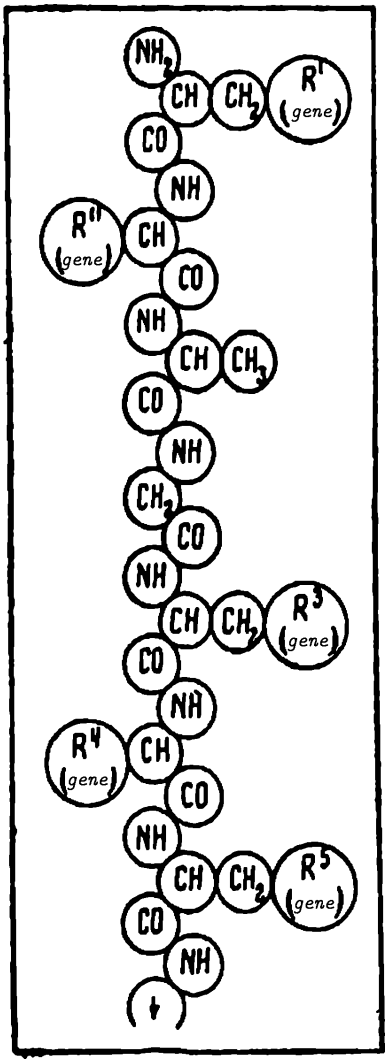

Fig. 22. Scheme of genonem molecular structure. Side radicals—the genes—are associated with individual links dipeptide chains alanine glycine (silk fibroin).