ADVANCES IN ENZYMOLOGY

AND RELATED SUBJECTS OF BIOCHEMISTRY

Volume IV

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THE CHEMICAL FORMULATION OF GENE STRUCTURE AND GENE ACTION

By

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I. Introduction

For the past four decades, since the rediscovery of Mendel's laws, the science of genetics has been progressing consistently from the status of a group of formal abstract propositions toward a more concrete science dealing with specialized strings of material particles possessed of certain outstanding attributes. These particles—genes—belong to the order of magnitude of megamolecules, and to the extent that the chemist has undertaken the study of megamolecules he can claim them as within his field. Thus, chemical genetics is a subject capable of very broad definitions; a chemical geneticist is not a scientist in charge of a particular subdivision of genetics, but is, much of the time, one who differs from other geneticists merely in the mental tools he brings to almost any genetic problem.

Is there any chemical pattern that all genes possess in common? Wherein is found the individuality of each particular gene, without which it could

not serve as a distinctive determinant of some particular characteristic or characteristics? When a gene acts, what is happening, chemically speaking? All such questions come into the field of chemical genetics.

II. Protein Molecules

Our concepts of the constitution of genes are closely dependent upon the structural picture we make of the protein molecule. Here, the latest advances have resulted from several modes of attack: x-ray diffraction studies, centrifugal and other methods for determining molecular size, studies of enzyme hydrolysis and the linkages involved, increasingly precise analysis of amino acid content and, most recently of all, electron microscope shadow pictures of the particles of dissolved homogeneous proteins.

Several lines of evidence tend to confirm the orthodox opinion, coming from Emil Fischer and Franz Hofmeister, that proteins consist fundamentally of polypeptide chains. In the fibrous proteins (keratin, myosin, white connective fiber, silk, etc.) the entire molecule may be a single, exaggeratedly long peptide chain. Protamines are similar strings but shorter, some 15 to 33 amino acid groups in a linear series constituting one molecule.

The peptide linkage by which the amino acids are joined seems even more certain today than it has seemed in the past, since protein-splitting enzymes are being identified more and more universally as splitters of the peptide linkage. It seems probable today that there is no other kind of proteolytic action, hence that the fundamental structural bonds are all of this type.

But not all protein molecules consist of a single, straight, linear fiber; and these less fibrous molecules have been the object of considerable speculation. Are they bundles of parallel fibers, or are they folded fibers, or a flat fabric, or a cage (5, 6, 45, 82, 203–214)? It seems clear that structurally and genetically they stand very close to the fiber proteins, so that only refined physical tests can be trusted to show that they are different. Very gentle physical forces are often sufficient to change the compact type of molecule (sometimes less accurately called "globular") into a film or even a peptide filament. Also, both filamentous and massive proteins are prone to follow the "Svedberg number series" and the "Bergmann ratios," upon which some comment is needed.

The Svedberg series expresses the observation that numerous proteins fall in the series having molecular weights of 16,000 to 17,000, or of 32,000 to 34,000, and multiples, roughly $(2^m \times 3^n) \times$ *ca.* 33,000. The lowest