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Animal muscle proteins are stated by Rose (10) to contain 21 amino acids of which 10 must be derived directly from the food while 11 can be modified by transamination provided some other primary amino acid is supplied. Although storage and particularly seed proteins are relatively simple in their structural pattern and amino acid content, herbivorous, and eventually all, animals derive their amino acids entirely from plant products. It seems reasonable to assume, therefore, that leaf proteins are comparable in complexity and amino acid distribution to muscle proteins.

The essential amino acids have molecular weights of less than 200 with an average weight of perhaps 138, or 120 in the peptid linkage. The simplest albuminoid proteins are assigned molecular weights in the neighborhood of 36,000 (12) and would thus contain some 300 amino acids in each molecule. If 300 molecules from 21 different amino acids are drawn at random and arranged in all possible combinations we could get: $21^{300} = 4.63 \times 10^{396}$ different kinds of proteins. With nucleo proteins having molecular weights of one to several million, and containing 8,300 or more amino acid units per molecule, the minimum figure becomes: $21^{8300} = 2.67 \times 10^{10,974}$, a number of such incomprehensible size as to have been defined as an adequate example of infinity.

When plant or animal proteins are hydrolyzed they break down to a series of successively simpler compounds, usually classed as: Proteins —→ proteoses —→ peptones —→ peptids —→ amino acids, where each of the intermediate groups represents a limited series of compounds rather than a specific substance, although they tend to be specific for a given protein. The statistical probabilities of mass action lead to the assumption that the processes of digestion will be reversed in synthesis, with two amino acids combining to form a dipeptid, two dipeptids to form a tetrapeptid and so on.

The Specificity of Proteins

The random condensation of amino acids into proteins would result in the formation of any one of the possible combinations and orders, and in the probability that no two of the protein molecules formed would be identical or even closely similar. Actually, however, the proteins from a given tissue of any species are very similar and probably identical.

Hay fever or other allergy sufers can testify to the specificity of the various proteins, and the sensitive individual is perhaps the best indicator of the presence of traces of a particular protein. We assume that allergies are due to specific chemical properties of the protein molecule, and the best explanation of uniformity of chemical reaction is identity of structure. Certainly we must assume identity of significant bonds within the molecule, and, as we shall

show later, complete identity might be more easily achieved than partial identity.

Serological tests show a similar uniformity of protein structure (8). The proteins of closely related plants or animals show similar precipitin reactions with immune serum. Those of less closely related species show some similarity, and species that we consider widely divergent normally show no relationship. The serological test seems to depend upon certain key linkages within the protein molecule, and so is not completely specific. Its reactions, however, fit the theory that the proteins of related organisims are more and more alike as the relationship becomes closer, and we might assume that the members of a plant family started with one type of protein molecule which has become modified with time and evolution in a manner analagous to changes in the visible characters of the species.

Cytological and cyto-chemical evidence suggests that the genes which determine the inheritance of an organism are groups of specific, complex protein molecules (5, 6). Some genes, for example those controlling the respiratory processes, act so uniformly throughout the biological world as to indicate that they have been transmitted without essential modification through all the steps of organic evolution from the very beginning of life. Irradiation of chromosomes with X-rays (9) or treatment with chemicals which might be expected to change their chemical composition (1) gives a certain percentage of reproducible gene mutations. These mutations suggest that even small changes in the gene molecule modify its genetic effect and support an hypothesis of complete chemical identity among like genes. The frequency of gene mutations also suggests that small changes, and probably any change, in the molecule alters its physiological action. The possibility that specific genes composed of specific, complex protein molecules have been transmitted unchanged through hundreds of millions of years suggests an unchallenged record of precision mass-production. It suggests also, however, that these genes have been sufficiently basic and complex in their action that all modifications have proven lethal. Precision production plus exacting inspection.

The specificity of proteins in these reactions can be explained if we assume that gene and cytoplasm proteins are formed on the patterns of pre-existing molecules transmitted in the nuclei and cytoplasm of the gametes from one generation to the next. Strong support for such an hypothesis can be obtained from plant viruses. At least some of these (11) have been shown to be protein molecules of the type found in chromatin materials of the nucleus (6). Protein molecules, no matter how large, would not be expected to show all of the complex phenomena of life. These virus proteins do not respire and will not reproduce in culture. If they are introduced into the cytoplasm of living cells of appropriate species, however, they are *reproduced* rapidly by the host, and in most instances the newly produced molecules are, by every chemical and biological test, exactly like those of the inoculum. If, however, a chemical modification does

arise in one of these non-living protein molecules, it may be reproduced with all the exactness of the original form, and it becomes a virus mutation (4, 7) lending support to a theory of chemical and structural identity of proteins.

Protein Patterns

The synthesis of proteins, like the synthesis of other biological compounds, is presumably dependent upon specific enzymes, and very probably upon a group of enzymes each specific for particular linkages or steps. Such a group of enzymes might account alone for the relatively simple, repetitive amino acid patterns found in some proteins, with no more continuity of inheritance than the genes responsible for the formation of these particular enzymes. Such simple patterns have in fact been built to the level of polypeptids by in vitro synthesis (3) and will undoubtedly be continued to the high molecular weights characteristic of the proteins themselves. We might visualize the cellular mechanism involved here as an enzyme (*A*) which will unite two specific amino acids to form a specific dipeptid, a second enzyme (*B*) which would add a third amino acid, again some particular one, to form a tripeptid, or two dipeptids to form a tetrapeptid, an enzyme (*C*) which would unite these two specific peptids, perhaps with the inclusion of still another amino acid at the linkage. A continuation of such a system could account for a considerable complexity and specificity with repetition and variation on a simple basic pattern. Many natural proteins, including typical seed proteins, have such a structure and their synthesis could be explained on this basis.

The proteins of the genes, the viruses, and the active cytoplasm, however, seem too complex and too specific to be formed by any such enzyme systems acting alone. The genes introduce, also, the problem of thousands of different protein molecules within the same nucleus and subject to the same enzyme system, but with each gene tending to retain its genetic and almost certainly its chemical identity through untold billions of cell divisions. Using the reproduction of an introduced virus protein as our clue, we postulate that these complex proteins are built against the pattern of pre-existing protein molecules. The microscopic picture of chromosome duplication, in which the new chromosome is built in contact with and an exact duplicate of the old at every point, would be repeated at the molecular level. Given any compatible protein as a pattern, the enzymes of the cell would produce and fit amino acids against it, step by step, until they had formed an exact duplicate in every amino acid and linkage.

Such a hpothesis would account for the reproduction of all proteins carried by the macro- or microgametes or of introduced virus molecules. These we might call the primary proteins. The secondary proteins would then owe their origin to specific enzyme patterns, and

it is significant that storage, seed and excretion proteins are simpler in structure and more likely to show similar reactions in two species.

The hypothesis advanced is not new. Fischer (3) suggested it more than a generation ago, and Gulic (5) has speculated on the molecular configuration of gene proteins which would permit a direct contact between the old, pattern molecule and the new one under construction. It is not, however, as generally known and accepted as the facts warrant, and a recent hypothesis of identity of configuration rather than of chemical structure has gained wide acceptance. Emerson (2) assumes that the chemical nature of the genes changes and that only the molds of their forms may remain to transmit the character or to influence the physiology of the cytoplasm. Such a scheme seems too subject to counterfeiting, too lacking in specificity, and too little in accord with the known behavior of molecules in crystal formation, etc.

An Hypothesis

Observations and measurements from a number of fields suggest that genes and viruses are specific protein molecules which are exactly reproduced by the living cell. If we call them autocatalytic we should perhaps use the term in the limited sense that they serve as models or patterns on which the active enzymes of the cell reproduce identical new molecules, arranging amino acids in a manner somewhat analogous to the arrangement of molecules in crystal formation. It is probably that some of the cytoplasmic proteins and possibly some of the enzyme proteins are similarly reproduced from pattern molecules carried in the cytoplasm of the egg cell.

In contrast to these "primary" proteins, many characteristic but relatively simple proteins of storage or excretion products may be formed with equal specificity but less complexity by the action of enzyme systems in which each enzyme is responsible for a definite linkage between molecules of definite size and composition, and in which certain enzymes may vary the basic, repetitive pattern by occasionally inserting, for example, an odd cystine molecule.

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