Some of the populous nations have a very real case owing to their rapid rate of natural increase, although some of them are taking steps to increase their numbers instead of reducing them. A natural easement of internal pressure might of course be afforded through emigration. At present freedom of migration has become very much restricted and promises to become still more so. It is perhaps an encouraging symptom that the centralized control of migration has been discussed at two of the international congresses on population problems. Migration is no panacea for population difficulties, but it may afford a means of relief to over-populated countries until such time as measures to check undue multiplication have had time to become effective. How to regulate migration and at the same time respect the sovereignty of peoples and their right to work out their destinies in their own way will afford many delicate problems for the statesmen of the future. The art of cooperative instead of competitive statecraft is, I fear, still in its infancy. Were the nations of the earth to unite in a population policy aimed to insure to each nation an optimum number it would go far toward removing occasions for war and would contribute greatly to the continued progress of mankind. At present this may seem to be a utopian ideal, but with a growing realization of the importance of regulating population growth in the interest of human welfare, we may at least hope that it may come to have more influence in shaping the policies of nations in their dealings one with the other.

NEWER BIOLOGICAL ASPECTS OF PROTEIN CHEMISTRY

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FOR a long time it has been unquestioned that proteins are an indispensable requisite of the living organism. Serological investigations have apparently established the fact that each species possesses characteristic and specific proteins. The classical chemical experiments of Emil Fischer have demonstrated that protein molecules are, essentially, many-membered peptide chains. This investigator pointed out that such polypeptide chains allow an overwhelming number of different structures when one varies the number, the nature and the order of the constituent units. These observations appeared to offer an explanation for the vast number of different proteins found in nature but, on the other hand, with this variety of structure there appeared to be no prospect of ever being able to elucidate the exact structure of a single high molecular weight protein.

Fortunately, recent investigations have indicated that the above view can be modified, as it has been found that the natural proteins are not simply polypeptide chains of every conceivable length and configuration, but that their structures are defined by a general stoichiometrical law which greatly limits the number of possible formulae. The nature of this stoichiometrical law can be demonstrated by considering the composition of the four proteins presented in Table 1. These compounds were selected because of their widely different physiological significance.

The first value in each column of Table 1 is the total number of amino acids produced by the hydrolytic degradation of the protein molecule under consideration, and the subsequent values represent the amounts of the various individual amino acids. For

TABLE 1

THE NUMBER OF AMINO ACID RESIDUES IN THE MOLECULES OF CATTLE HEMOGLOBIN, CATTLE FIBRIN, CHICKEN EGG ALBUMIN AND SILK FIBROIN

Amino acid	Number of amino acid residues per molecule			
	Cattle hemoglobin	Cattle fibrin	Chicken egg albumin	Silk fibroin
All amino acids ...	$2^6 \times 3^2$	$2^6 \times 3^2$	$2^5 \times 3^2$	$2^5 \times 3^4$
Arginine	$2^2 \times 3^1$	$2^5 \times 3^0$	$2^2 \times 3^1$	$2^2 \times 3^1$
Lysine	$2^2 \times 3^2$	$2^4 \times 3^1$	$2^2 \times 3^1$	$2^2 \times 3^0$
Histidine	$2^5 \times 3^0$	$2^2 \times 3^1$	$2^2 \times 3^0$	$2^0 \times 3^0$
Aspartic acid	$2^5 \times 3^0$	$2^5 \times 3^0$	$2^4 \times 3^0$	
Glutamic acid	$2^4 \times 3^0$	$2^3 \times 3^2$	$2^2 \times 3^2$	
Glycine				$2^4 \times 3^4$
Alanine				$2^3 \times 3^4$
Tyrosine	$2^2 \times 3^1$		$2^3 \times 3^0$	$2^1 \times 3^4$
Proline	$2^2 \times 3^1$	$2^5 \times 3^0$		
Tryptophane		$2^1 \times 3^2$		
Cysteine	$2^0 \times 3^1$	$2^0 \times 3^2$	$2^2 \times 3^0$	
Methionine		$2^2 \times 3^1$	$2^2 \times 3^1$	

example, in the case of cattle hemoglobin it was found that the molecule is composed of 576 or $2^6 \times 3^2$ amino acid residues, and of this total number there are 12 arginine residues, 32 histidine residues, 36 lysine residues, etc. The total number of amino acid residues (N_t), the number of the individual amino acid residues (N_i), and the frequencies of the individual amino acid residues ($F_i = \frac{N_t}{N_i}$) that are contained in a molecule of protein can be expressed by the following equations:

(1) $N_t = 2^n \times 3^m$ where n and m are positive whole numbers.

(2) $N_i = 2^{n'} \times 3^{m'}$ where n′ and m′ are either zero or positive whole numbers.

(3) $F_i = 2^{n''} \times 3^{m''}$ where n″ and m″ are either zero or positive whole numbers.

(4) $n = n' + n''$, and $m = m' + m''$.

(5) $N_t = N_i' + N_i'' + N_i''' + \ldots\ldots\ldots\ldots N_i^x$.

It is of the utmost significance that the experimentally determined values of N_i', N_i'', N_i''', etc., and of F_i', F_i'', F_i''', etc., have led to values of N_t that are whole number multiples of 288 or $2^5 \times 3^2$, and it appears that the molecules of many proteins exhibiting no reversible dissociation contain 288 units or a whole number multiple thereof.

The fact that the stoichiometrical law given above is of general validity for all the simple natural proteins suggests that these substances are constructed on similar structural principles. This general structural principle can be summarized in the statement that every individual amino acid residue in the peptide chain of the protein molecule recurs at constant intervals. For example, each glycine residue in silk fibroin is separated from the adjacent glycine residues by an amino acid residue other than glycine, *e.g.*,

-G-X-G-X-G-X-G-X-G-X-G-X-G-X-G-X-

Each alanine residue is separated from the adjacent alanine residues by 3 other residues, *e.g.*,

-A-X-X-X-A-X-X-X-A-X-X
-X-A-X-X-X-A-X-X-X-A-

Each tyrosine residue is separated from the adjacent tyrosine residues by 15 other residues, *e.g.*,

-X-T-X-X-X-X-X-X-X-X-X-X-X-X-X-X-T
-X-X-X-X-X-X-X-X-X-X-X-X-X-X-X-T-

On combining the above configurations, the structure of a segment of the silk fibroin molecule is obtained, *i.e.*,

G-A-G-X-G-A-G-X-G-A-G-T-G-A-G-X
-G-A-G-X-G-A-G-X-G-A-G-T-G

From the previous discussion it is evident that the structure of the protein molecule is defined by two general principles, *i.e.*, (1) the linking of the individual amino acid residues through the medium of the peptide bond (-CO-NH-CHR-) to form a long polypeptide chain and (2) the recurrence of the individual amino acid residues in a characteristic, periodic manner throughout the entire polypeptide chain. The second principle involving the superposition of many different individual frequencies forces upon the structure of the protein molecule the stoichiometrical law which determines the total number of residues and the number of individual residues in the molecule.

The peptide structure is common to all proteins, but the various natural proteins differ from each other in that their individual amino acid constituents are represented by different frequencies. Thus, the physico-chemical and the biological properties of a particular protein are based, in the last analysis, on the frequencies with which its constituent amino acid residues recur within its peptide chain.

It is recognized that one of the most important functions of the living organism is the maintenance of the individuality of the organism, and it is apparent that the maintenance of the characteristic cellular and tissue proteins provides a chemical basis for this phenomenon. This maintenance of the individual proteins is not to be considered as an act of conservation but rather as a continuous reproduction of characteristic proteins by the organism. Little is known of the actual mechanism by which the organism synthesizes its highly specific and characteristic proteins, but the following line of thought appears suitable as a hypothesis for the experimental investigation of this problem.

As the protein molecule is assembled from hundreds or thousands of amino acids according to a well-defined plan, there appears to be no other choice than to assume that the synthesis of each of these gigantic molecules is controlled by a specific chemical organizer. This chemical organizer must first of all be capable of synthesizing the peptide bond (-CO-NH-CHR-), for the protein molecule is an ensemble of amino acid residues linked in an orderly manner by means of this covalent bond. Second, this chemical organizer must have the ability to select, from all the available amino acids and peptides, a particular amino acid or peptide at the correct moment, so that the unequivocal pattern of the complete protein molecule is adhered to in every stage of the synthesis. It is to be expected that the chemical organizer of a protein molecule will have a type of specificity not as yet encountered in biochemistry. The chemical organizer of each protein molecule must have the ability to promote hundreds of consecutive specific reactions, each of which alters the structure of the substrate and thereby the character of the subsequent specific reactions. For example, the chemical organizer controlling the formation of silk fibroin must provide, at a certain stage, for the successive addition of the residues of the amino acids glycine, alanine, glycine, tyrosine, glycine, alanine, glycine, etc., to the rudimentary molecule.

It is surprising that all the properties that are demanded of the chemical organizer of proteins are to be found only among the intracellular proteinases (papainases), and it appears likely that the intracellular proteinases are in reality the protein organizers. The intracellular enzymes are able to degrade proteins through hydrolysis of the peptide bond, and recently it has been demonstrated that this splitting proceeds so far that lower molecular weight peptides and even amino acids are formed. On the other hand, these same intracellular enzymes are capable of promoting

the synthesis of the peptide bond, thereby forming higher order peptides from the lower molecular weight protein hydrolysis products. It appears that the reason that the intracellular enzymes are able to promote hydrolysis and synthesis under the same experimental conditions, with the result that these two reactions are in competition with each other, is that small differences in the structure of the substrate coupled with the very exactly tuned specificity of the individual intracellular enzymes determines whether or not and to what degree synthesis or hydrolysis shall occur. The organizing ability of the individual intracellular proteinases is concomitant with the possession of the above properties.

To-day there are no fundamental obstacles in the way of an experimental study of the organizing ability of the intracellular enzymes. The old axiom of physiology, which held that the proteinases are engaged solely in the splitting of high molecular weight proteins and are not capable of hydrolyzing low molecular weight peptides, has been shown to be erroneous. This fact permits a new approach to the problem of protein organization, for it sanctions the use of simple "protein models."

The enzyme papain, as has been shown in recent work done in cooperation with Dr. H. Fraenkel-Conrat, acts upon the two very similar peptide-like compounds, benzoylglycine amide and benzoylglycine anilide, in an entirely opposite manner. Benzoylglycine amide is quantitatively hydrolyzed by the enzyme yielding benzoylglycine and ammonia. In contrast, benzoylglycine anilide not only is not split by the enzyme but is actually synthesized in the presence of the enzyme from benzoylglycine and aniline.

$$C_6H_5CONHCH_2CONH_2 \xrightarrow[\text{hydrolysis}]{\text{enzymatic}} C_6H_5CONHCH_2COOH + NH_3$$

$$C_6H_5CONHCH_2CONHC_6H_5 \xleftarrow[\text{synthesis}]{\text{enzymatic}} C_6H_5CONHCH_2COOH + C_6H_5NH_2$$

In this "model" experiment the amide plays the rôle of the extracellular proteins, and the anilide that of the intracellular proteins. It is decisive for the economy of the living cell that the hydrolysis of the extracellular proteins (amide) and the synthesis of the intracellular proteins (anilide) are capable of being accomplished under the same general conditions.

In the living cell the hydrolysis of extracellular proteins and the synthesis of intracellular proteins may proceed simultaneously, thus providing for the immediate utilization of the degradation products of the extracellular proteins in the synthetical reactions. In order to achieve a still greater economy than is possible through the above hydrolytic and synthetic reactions, the living organism is able to transform the extracellular proteins directly, and without the necessity of a complete degradation, into intracellular proteins by means of a special type of enzymatic transformation. This new type of enzymatic reaction was disclosed by the formation of benzoylglycine anilide in the presence of papain from benzoylglycine amide and aniline by a direct replacement reaction.

$$C_6H_5CONHCH_2CONH_2 + C_6H_5NH_2 \longrightarrow C_6H_5CONHCH_2CONHC_6H_5 + NH_3$$

The present concept of protein synthesis *in vivo,* then, may be described as follows. When the intracellular enzyme has at its disposal a number of protein fragments of different size and structure, it subjects these fragments to a series of transformations by synthesis, hydrolysis and replacement and thereby reconstructs one peptide bond after the other, until there is produced a protein pattern which is stable in the presence of the enzyme. Thus the protein fragments available under the individual environments and the specificity of the enzyme together determine the individual pattern of the synthesized protein.

The knowledge that the structural pattern of a protein, in all its details, is a consequence of the specificity of the intracellular proteinases greatly increases the biological significance of these enzymes. Formerly these proteinases were considered essentially as agents responsible for the degradation of proteins in the tissues, and were therefore accessories to the proteinases of the gastro-intestinal tract. In addition to their traditional rôle as "wreckers," these intracellular proteinases must now be considered as the "architects" and "builders" of the characteristic and indispensable individual proteins. If the proteins are to be considered as an essential requisite for the phenomena of life, then the organizing proteinases are indeed of primary importance in life processes. As the maintenance of the individual is controlled in a constant and fixed manner by the reproduction of individual proteins, it is evident that both growth and cell division are associated with the production of individual proteins under the positive influence of the intracellular proteinases. The reproduction of the organism is a complicated sequence of interrelated chemical syntheses wherein the function and the definite production of the highly specific individual proteins is predetermined throughout all the intermediate stages and in the final result. The many manifestations of the phenomena of life are dependent upon the existence of numerous individual proteins which, in turn, are dependent upon the existence of the enzymes that synthesize these proteins and upon the unparalleled specific mechanism of these en-

zymatic processes. From this point of view, increased importance must be attached to the old question of whether the proteinases themselves are proteins or contain proteins as an essential constituent. In the event that the proteinases are not proteins or do not contain proteins, it would be necessary to postulate the existence of another group of substances capable of equal multiplicity of form in order to explain the organization of the numerous individual proteins. If, on the other hand, the individual organizing proteinases are wholly or partially proteins, no special postulates are necessary and the known examples of proteins with catalytic properties would be increased by an additional and extensive group of substances. The intracellular proteinases would then have to be regarded as proteins endowed with the property of catalyzing the formation of specific proteins from the materials at their disposal. This view-point is worthy of discussion, since it leads to interesting consequences and new experiments. If the proteinases themselves are proteins and at the same time have the ability to synthesize other individual proteins, then there must exist proteinases which have the ability to synthesize replicas of their own structural pattern and therefore are able to "multiply" in suitable surroundings. Such a type of proteinase when placed in the presence of a suitable host organism would cause the continuous production of foreign protein. It is evident that this property is similar to that described by Stanley for the tobacco mosaic virus, and it would appear desirable to investigate this and other viruses for possible proteinase activity.

SCIENTIFIC EVENTS

CONGRESSIONAL APPROPRIATIONS FOR SCIENTIFIC WORK

A SUMMARY of legislation enacted by the seventy-fifth Congress is printed in *The New York Times*. A list of appropriations for agriculture and for the work of the Department of the Interior are as follows:

Appropriations of $630,381,208 are made for the Department of Agriculture and Farm Credit Administration for the fiscal year 1938.

Among the major items are $6,232,500 for agricultural experiment station payments to states, Hawaii, Alaska and Puerto Rico; $1,200,000 for the department's special research fund; $13,690,672 for the Agricultural Extension Service; $4,703,049 for the Weather Bureau; $10,373,098 for the Bureau of Animal Industry; $703,694 for the Bureau of Dairy Industry; $4,833,048 for the Bureau of Plant Industry; $18,892,182 for the Forest Service; $1,425,431 for the Bureau of Chemistry and Soils; $5,711,398 for the Bureau of Entomology and Plant Quarantine; $2,127,840 for the Biological Survey; $167,500,000 for the Bureau of Public Roads; $6,212,698 for the Bureau of Agricultural Economics; $500,000 for the enforcement of the Commodity Exchange Act; $2,227,758 for the Food and Drug Administration; $24,390,780 for the Soil Conservation Service; $340,000,000 for carrying into effect the provisions of the Soil Conservation Act plus not to exceed $100,000,000 for that purpose of the funds made available for the fiscal years 1937 and 1938 by Section 32 of the Act of August 24, 1935; $12,500,000 for forest roads and trails; $4,000,000 for the Farm Credit Administration plus $2,950,000 from funds made available under Section 5 of the Emergency Crop Loan Act of 1934; $15,000,000 for the Federal Farm Mortgage Corporation.

Appropriations of $132,732,499.85 for the various activities of the Department of the Interior during the fiscal year 1938 include $14,483,000 for vocational education; $13,000,000 for the Grand Coulee Dam project; $12,500,000 for the Central Valley reclamation project in California; $3,050,000 for the Boulder Dam, plus $1,500,000 for the All-American Canal phase of that project; $1,500,000 for the Yakima, Wash., reclamation project; $1,000,000 for the Boise, Idaho, reclamation project; $900,000 for the Colorado-Big Thompson tunnel project in Colorado; $700,000 for the Gila reclamation project in Arizona; $750,000 for the Provo River reclamation project in Utah; $500,000 for the Owyhee project in Oregon; $650,000 for the Casper-Alxova reclamation project in Wyoming; $700,000 for the Shoshone reclamation project in Wyoming, and $500,000 for the Colorado River irrigation project.

THE LEVERHULME FELLOWSHIPS IN GREAT BRITAIN

AWARDS of thirteen Leverhulme research fellowships in 1937 and fourteen grants to research workers have been announced.

The awards in the sciences are as follows:

D. H. BANGHAM, professor of inorganic chemistry, Egyptian University, Cairo. The wetting of solid surfaces and the phenomena of spreading liquids thereon.

MISS D. E. CHARLES, research fellow, department of social biology, London. The mechanism of population decline with special reference to Scottish population problems.

C. W. DAVIES, senior lecturer in chemistry, Battersea Polytechnic. Adsorption at liquid surfaces.

J. R. FIRTH, senior lecturer in phonetics, University College, London. Research in the phonetics of four principal languages of India.

O. V. S. HEATH, research worker, Institute of Plant Physiology, London. Study of carbon assimilation by the green plant.

J. DE GRAAFF HUNTER, lately director, survey of India, Leverhulme research fellow. Planning and execution of geodetic triangulation of great extent. (Renewal of present fellowship.)

G. W. B. HUNTINGFORD, farmer, Kenya Colony, mem-