	Calculated for $Na_3AsOS_3 + 11H_2O$.	Found. I.	II.
Sodium	15.22	15.58	15.88
Arsenic	16.50	16.71	16.78
Sulphur	21.16	20.26	20.70
Oxygen	3.52	4.26	3.48
Water	43.60	43.19	43.16
Total,	100.00	100.00	100.00

In another case the salt obtained by direct precipitation with alcohol contained 20.80 per cent. sulphur. After the first recrystallization, the sulphur was 21.31 per cent.; and after the second 21.25 per cent., which is very nearly the theoretical value. Sodium trisulphoxyarseniate effloresces rapidly in a hot room; therefore, the crystals should be dried as speedily as possible.

We expect to publish a more complete account of this interesting acid in the near future.

PRINCETON, N. J.,
January, 20, 1904.

REVIEWS.

Recent Work in Biological Chemistry.

By P. A. LEVENE.

THE greater part of cell and tissue constituents is of proteid nature. The conception of protoplasm was always, in a way, associated with that of living proteids. It is, therefore, natural that the efforts of biological chemists for years were directed toward the study of the chemical nature of proteid material. Through these efforts it was established that in the cell the majority of proteids occur in a more or less intimate combination with various substances. The groups binding the proteids in tissues were designated by Kossel as "prosthetic" groups. Until recently, the knowledge of the chemical nature of either of these two groups of the complex molecule of a combined proteid was very limited. However, the work done during the last few years has added much to our knowledge of the subject.

It has been known that both the simple proteids and the prosthetic groups yield, on hydrolysis, certain simple chemical bodies. But no information as to the manner in which the simple substances combined in order to form the complex molecule of proteid, was obtained.

The work of Drechsel, Miescher, Kossel, Schulze and Emil Fischer on hydrolytic cleavage of proteids has resulted in the dis-

covery of many new substances contained in the proteid molecule, and the synthetical experiments of Emil Fischer have elucidated to a great extent the manner in which the amino acids combine in the proteid molecule.

Before the experiments of Drechsel, monoamino acids were known to result on hydrolytic decomposition of proteids. The monobasic acids of that group known to be present in the proteid molecule were glycocoll, alanine, aminovalerianis acid and leucine. Of the dibasic acids of this group, glutamic and aspartic acids were isolated, and only one oxyamino acid, serine, was shown to be present in the proteid molecule. The methods for isolating the individual amino acids from the decomposition products were so unsatisfactory that only a few of the enumerated acids could be obtained on decomposition of every proteid. The chief difficulty in separating the acids lay in the similarity of their salts in regard to their solubility. Their separation, however, at present is greatly facilitated, chiefly owing to the efforts of Fischer. In the course of a study of the different compounds of the acids, Fischer observed that the ethyl esters of the individual amino acids, if distilled, boiled at diminished pressure, at distinct temperatures, the esters of the lower acids having a low boiling-point. Thus it was made possible to separate amino acids by means of fractional distillation at low pressure. The work was facilitated further by an improvement in the method of transforming the hydrochloric salts into the free esters; and further, Fischer made it possible to individualize the different acids by means of their phenyl isocyanide compounds, and by means of their β-sulphonaphthaline compounds. With these new methods a systematic study of the products of hydrolysis of casein, egg albumen, fibrin, gelatine, keratine, oxyhemoglobin, serumalbumin and edestin was undertaken by Fischer and his students. By them it was etablished that most proteids contain in their molecule amino acids with 2, 3, 4, 5 and 6 carbon atoms. It was also shown that some proteids contain little of the lower acids, while others, on hydrolysis, yield chiefly glycocoll and alanine. It was also demonstrated that the hydroxyamino acids, like serine, occur more frequently than had been known. An amino acid of the pyrrol group was demonstrated in all the analyzed proteids and also a hydroxy acid of the same group. Aspartic and glutamic acids were isolated from the products of hydrolysis of all proteids. Also phenylalanine was proved to be a constant component of the proteid molecule.

Besides the monoamino acids, the proteid molecule also contains diamino acids. They were discovered among the products of hydrolysis by Drechsel. The work on these substances was continued by Kossel and Schulze and their students. The results of their work was reviewed by the author in this Journal,

22, 604, and only the investigations that have appeared since will be discussed in this article.

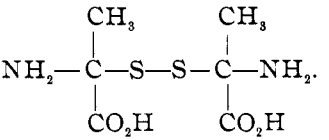
Two diamino acids are known to be present in the proteid molecule, diaminovalerianic and diaminopropionic acids. The former generally appears in the form of a base, arginine. Schulze and Winterstein obtained arginine synthetically from ornithine and cyanimide, and thus have established its nature as a guanidine derivative, namely: guanidine aminovalerianic acid. And Fischer synthetically obtained ornithine and lysine, and thus explained their chemical nature as α,δ-diaminovalerianic acid and α,ε-diaminocaproic acid, respectively. During recent years, nitrogenous substances, belonging to other groups, have been discovered among the cleavage products of proteids. Thus Hopkins and Cole succeeded in preparing a pure "Tryptophan," which they regard as skatolaminoacetic acid. Also Baum and Swain have described a substance of the indigo group and named it skatosine.

By the work of S. Fränkel it has been made probable that there is present in the proteid molecule a base of the pyrimidine group. The base histidine has been generally classified with the diamino acids, the "Hexonbases" of Kossel; according to Fränkel, it is a pyrimidine derivative.

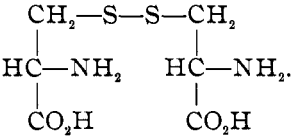
Besides carbon, hydrogen, nitrogen and oxygen, the proteid molecule contains also sulphur, but our knowledge of the form in which the element is present was very limited. It was known that one part of the sulphur of the proteid molecule could be split off by aid of alkalies in the form of hydrogen sulphide and that the other part of the sulphur could not be split off by treatment with the same reagents. Thus it was assumed that the proteid molecule contains its sulphur in two different forms. Attempts to gain better knowledge of the sulphur of the proteid molecule for a long time remained futile. They all, however, corroborated the older observation, and also have established that the two forms of sulphur compounds were present in various proteids in different proportions. During very recent years, however, important work showing the nature of the sulphur-containing substance of proteids, which, on treatment with alkalies, breaks off its sulphur in form of hydrogen sulphide, has been done.

A substance of a similar nature was first observed as a product of abnormal metabolism, and was named cystine. A substance with the elementary composition of cystine was discovered among the cleavage products of proteids.

The chemical nature of the original cystine was explained by Baumann and his co-workers. They showed that it was a derivative of pyrotartaric acid, having the following composition:



Baumann, however, assumed that cystine was not a primary cleavage product of proteids. He based his view on the work of Suter, who failed to detect the substance on hydrolytic cleavage by means of mineral acids. On one occasion Suter, on decomposition of a proteid, found thiolactic acid, and in this Baumann saw a corroboration of his views on the chemical nature of cystine, and also of his view on the presence of cystine in the proteid molecule. K. A. H. Mörner, and later Embden, however, succeeded in obtaining cystine on cleavage of many proteids, and Friedmann demonstrated that cystine thus obtained differs from the one occurring in urine in pathological condition. The proteid cystine has the following composition:



Thus it is related to serine, and might be, as suggested by Friedmann, the mother substance of taurine, which is a normal constituent of bile. This view was very recently corroborated by v. Bergmann, who showed that the production of taurine in the organism increased on feeding with cystine.

It is seen from this summary of the work on the cleavage of proteids that the components of thin molecules are very numerous, and still it is generally admitted that the knowledge of them is not complete. However, even at this stage of our knowledge, attempts have been made to ascertain the way in which the various components are grouped in the proteid molecule.

It has been known from the work of Kühne and his pupils, Chittenden and Neumeister, that on digestion with proteolytic enzymes proteids undergo gradual transformation into proteoses and these into peptones. The relation of the mother substance to the proteid molecule had not been definitely established. Theoretically there were two possibilities: The proteid molecule is a condensation product either of the various albumoses, or of the simple crystalline substances. In the latter case its transformation into albumose could be explained by a gradual losing of some of the crystalline substances. The question, thus, was whether the various albumoses were totally different in their composition, or whether they could be transformed one into another. The older writers characterized individual albumoses chiefly by their solu-

bility and by their behavior toward different mineral salts. They distinguished, however, two groups of digestion products, the anti- and the hemi-groups, and the proteid molecule was supposed to consist of the two moieties. The point of distinction between the two groups lay in the fact that the anti-group could not be hydrolyzed by proteolytic enzymes into simple crystalline components. These problems were the subject of numerous investigations during recent years.

The old methods of Kühne were improved by Hofmeister, and a systematic separation of the proteoses and peptones was carried out in his laboratory, chiefly by Pick and by Zunz. These workers succeeded in isolating a greater number of proteoses than had been known. They demonstrated further that the various fractions differed not only in their solubility and elementary composition, but also in their behavior towards certain reagents. Thus, one fraction was characterized by the intensity with which it responded to the furfural test; another was individualized by its power to decompose lead acetate into the sulphide upon heating with an alkali; again, a third fraction failed to form indol on fusion with potassium hydroxide. It was inferred from this that the albumoses of the first fraction contain much carbohydrate, that those of the second contain much cystine or an analogous substance, and that the albumoses of the third group lack in their molecule the substances of the indigo group.

Another method of establishing the relationship of the primary digestion products of proteids was to compare the crystalline cleavage products in the various fractions of proteoses. Thus Pick, Hart and Haslam demonstrated that the hetero- and proto-albumose differ by the quantities of basic substances in their molecules, and Levene showed that primary and secondary gelatoses differ in the content of glycocoll in their molecules.

Much attention has been devoted to the question of "anti-peptone." As already mentioned, Kühne designated by that name the part of the proteid molecule that could not be decomposed further by tryptic digestion. New investigations undertaken in Drechsel's laboratory on the nature of peptone, have demonstrated that it contains, besides the biuret-giving substance, also simple crystalline bases, commonly occurring on hydrolysis of proteids. A more thorough analysis of the so-called "gland peptone" was undertaken by Kutscher, who came to the conclusion that the product consists of simple crystalline substances only. He, therefore, cast considerable doubt on the existence of an anti-group in the proteid molecule. This view, however, was disputed by Siegfried. This author succeeded in obtaining a substance with the properties of peptone and having a constant composition, a definite rotation, and other characteristic physical properties. He, therefore, modified Kühne's theory thus: On

hydrolysis of proteids with trypsin the following substances are formed: Amino acids, bases and peptones which cannot be decomposed further by the action of the enzyme. The existence of peptones in the sense of Siegfried was recently demonstrated by E. Fischer and Abderhalden.

On the ground of recent investigations it does not seem improbable that a definite relation similar to the one demonstrated by Fischer for carbohydrates and glycolytic enzymes exists between proteids and proteolytic enzymes. Thus trypsin may exercise a stronger action on the proteids of the pancreatic gland than on any other. The observation of Kossel and Mathews that protamines are not affected by pepsin and do undergo cleavage when acted upon by trypsin, supports this assumption.

The *manner in which the amino acids combine in the proteid molecule* remained absolutely unknown until very recently. It is made probable, especially by the work of E. Fischer, that the acids are combined in the molecule after the type of acid amides. Fischer has succeeded in condensing in this manner various amino acids and designates them as peptides. The polypeptides may be formed on condensation of one or more acids. They all resemble, in a degree, true peptones, and Fischer states that he has succeeded in obtaining a similar substance on a partial hydrolysis of proteids.

Some progress has also been made toward a rational *classification* of proteids. The older classification was based chiefly on their solubility and their relation to mineral salts. No information as to the distinction of their chemical composition existed. The methods of obtaining the basic decomposition products were recently improved by Kossel and Kutscher to such an extent that they can be applied for their quantitative estimation. The method of Fischer made it possible to estimate some amino acids with exactness and others with approximation. By the aid of the new methods, considerable work on the estimation of decomposition products of various proteids has been done in the laboratories of Kossel, Hoffmeister, Fischer, and Osborne, from which the existence of two distinct groups of proteids may be regarded as established. To one belongs those composed chiefly of the lower amino acids, glycocoll and alanine. The other components enter the molecule of these proteids in rather small quantities. To the second group belong proteids with a markedly high content of basic substances. Most proteids approach one or the other of the two groups. Proteids differ also by the preponderance of one or another of their basic components.

One of the most striking discoveries of recent years is the application of a new *biological test for the differentiation of proteids.* It was observed by Tschistowitch, Bordet, v. Dungern, and especially by Meyers, that the serum of an animal that had

received subcutaneous injections of a proteid acquires the property of precipitating that proteid from its solution. It was assumed that the serum contained a specific precipitin. Thus, a serum of an animal that had been injected with egg albumen acquired the property of precipitating only egg albumen. This serum thus could serve to differentiate egg albumen from all other proteids, while, on the other hand, the formation of specific precipitins was regarded as a proof of the chemical individuality of different proteids. It has, however, been demonstrated by Levene, Lemoine and Lavasseur that precipitins do not possess that strict specificity that has been claimed for them. By the aid of the precipitin test, proteids are shown to possess a certain biological relationship. Thus albumins and globulins obtained from one animal, or from animals of the same species, can be precipitated by one precipitin, while all albumins of animals of different species do not form precipitates with a serum active for one of them.

COMBINED PROTEIDS.

In the cell and tissues most proteids occur in combinations with other substances, designated by Kossel as their prosthetic group. Such groups of the haemoglobin, of the nucleoproteids and of the glucoproteids have attracted, in recent years, much attention.

Haemoglobin.—To haemoglobin belongs the most important function of supplying tissues with oxygen. The carrier of oxygen is an iron-containing substance, haematin. Also the color of haemoglobin is due to the same substance. However, our knowledge of its chemical constitution, as well as of its relation to other animal pigments, was rather meager. Through the efforts of Nencki, Kuster, Zaleski, Schwink and Marchlewski, considerable knowledge as to the constitution of the substance, and its relation to other animal chromatins, and to chlorophyl, has been gained. It has been shown that haematin is a pyrrol derivative. Upon treating haematin with strong acids a substance, free from iron, is obtained. According to the work of Küster, Nencki and Zaleski, the substance had the composition of $C_{16}H_{18}N_2O_3$, but in a very recent publication Zaleski claimed that the true composition is $C_{32}H_{38}N_4O_6$. This substance can be reduced by hydriodic acid in the presence of phosphonium iodide into a substance of the composition $C_8H_{13}N$. This oxygen-free derivative shows all the properties of pyrrol and is assumed to be isobutyl pyrrol.

Relationship between haematin and bile pigments was again demonstrated by the fact that haemopyrrol, on exposure to air, is transformed into urobilin. It is also transformed into this substance if injected subcutaneously into the organism of a rabbit. On the other hand, it is known that by means of reduction urobilin is transformed into bilirubin.

The relationship between haematin and chlorophyl was established on the ground of the following observations. A substance analogous to haematoporphyrin was obtained from chlorophyl. It has the composition of $C_{16}H_{18}N_2O$, and accepting the formula of $C_{16}H_{16}N_2O(OH)_2$ for the first, it differs from the blood pigments only by two oxygen atoms. Further, on reduction the phyloporphyrin forms the same haemopyrrol as the blood derivative. The pyrrol nature of haematin may also serve to explain its origin from proteids, since the presence of a pyrrol ring in the molecule of all proteid material is quite certain.

Nucleoproteids.—After haemoglobin the next in importance among the combined proteids are the derivatives of nucleic acid. It was established through the researches of Miescher, Kossel, Lilienfeld and Malfatti, that the chromatin of a cell is a phosphorus-containing proteid, possessing certain acid properties. Substances with the staining properties of chromatin could be extracted from cells and tissues. They are all phosphorus-containing, and possessed, in some degree, acid properties. It has been accepted by biologists that the most important functions of the cell are controlled by its chromatin, and it is natural that the study of the chemical nature of these substances attracted considerable attention. Nucleoproteids of two distinct groups are described. To one group belong the derivatives of a proteid-free nucleic acid of a very complex nature, designated as the true nucleic acid. The substances of the second group are apparently direct derivatives of phosphoric acid, and are known as paranucleoproteids.

These compounds were first described by Kossel, Hammarsten and Milroy. They occur in the unfertilized egg as vitellin and in milk as casein. Comparatively little has been known of their chemical nature. Recently P. A. Levene and C. Alsberg published the results of their investigation regarding the nature of the substance. They were led to the conclusion that paranucleoproteids are derivatives of a paranucleic acid. This is a substance with a fairly constant composition, and probably a protein-ester of phosphoric acid. An identical substance could be obtained from the egg of fowls and from that of fish. E. Salkowski obtained an analogous compound from casein.

The number of researches on the nature of true nucleic acid was considerably greater. They were conducted in the laboratories of Kossel, Miescher, Schmiedeberg, Hammarsten, Osborne and Levene. There are two objects in all these researches, one, simply to find the chemical composition of the acid, the other, to ascertain whether the acids vary in their composition in cells with distinct functions. On hydrolysis of nucleic acid there were obtained phosphoric acid, bases of the purine and pyrimidine groups and carbohydrates, a pentose and possibly a hexose. Of

the purine bases two, namely, adenine and guanine, and three bases of the pyrimidine group, namely, thymine, cytosine, and uracyl, were found. *A priori* it seemed possible that there would exist nucleic acids of different complexity. Bang actually succeeded in obtaining a substance much simpler in its composition than the usual acid. It yielded, on hydrolysis, only phosphoric acid, glycerol and guanine pentose. Adenine and the bases of the pyrimidine group were absent from the molecule of that substance. All the other acids contain pyrimidine bases. There is, however, a marked distinction between the acids derived from the animal and that derived from the plant cell. Most of the acids of the first group form, on hydrolysis, the three named pyrimidine bases, while those of the second group contain only cystosine and uracyl. Thymine was first discovered by Kosel, and its constitution as 5-methyl-2,6-hydroxypyrimidine was established by Fischer and by Steudel. Uracyl, 2,6-hydroxypyrimidine, was discovered in yeast, nucleic acid by Ascoli in Kossel's laboratory; it was then found in the wheat embryo by Osborne and Harris. In the acids of animal origin uracyl was first observed by Levene and then by Kossel and Steudel. Cytosine was discovered simultaneously and independently by Kossel and Steudel and by Levene. Its composition as 2-hydroxy-C-amino-pyrimidine was established by Wheeler. Thus at present a distinction can be made between the acids of animal and of plant origin, but there is no evidence in favor of making a distinction between individual acids of animal or plant origin.

To the third group of combined proteids belong the *glucoproteids*. It is as yet uncertain whether or not all the substances of this class are derivatives of one prosthetic group. The chief obstacle in the way of solving the problem lies in the fact that it is very difficult to remove the proteid from the prosthetic group without breaking it up. Until recent years only one substance of the class was successfully isolated and analyzed. It was obtained by Schmiedeberg from cartilage and designated by him as chondroitinsulphuric acid, and was supposed to consist of sulphuric acid, of a hexosamin, of glucoronic and acetic acids. The other proteids of this class were supposed to be derivatives of a polysaccharide, designed by Landwehr as animal gum.

Both these substances have been the subject of renewed investigation recently.

Attempts to ascertain the nature of the carbohydrate entering the molecule of the prosthetic group of glucoproteids have been rather successful. Through the efforts of Fr. Müller and Neuberg, v. Fürth, Langstein and Steudel, it has been established that in the majority of substances of this group, the carbohydrate is a hexosamin. Müller, v. Fürth and Langstein have obtained it in the form of its benzoyl derivative, which they could then

transform into the hydrochlorate. Neuberg demonstrated the appearance of nitroso saccharic acid on oxidation of some of the glucoproteids with nitric acid, and Steudel identified glucosamine by its phenyl isocyanate derivative. Only in one proteid was the reducing substance shown to be galactosamine by F. N. Schultz and Ditthorn. Recent investigations, however, failed to corroborate the old views of the chemical composition of animal gum and of the chondroitinsulphuric acid. Folin repeated, under the direction of Hammarsten, the old experiments of Landwehr, with the result that he obtained a nitrogenous substance, which he designated mucalbumose, instead of animal gum. Orgler and Neuberg undertook a new study on Schmiedeberg's chondroitinsulphuric acid, and came to the conclusion that it did not contain in its molecule either glucosamine or glucoronic acid. They discovered in it a new hydroxyamino acid. Thus the true nature of the substance remains to be explained. At the same time, the substance has been shown to have a much wider occurrence than had been known. Thus Müller has adduced evidence for the belief that in the mucin the carbohydrate is present in form of an acetyl derivative. P. A. Levene has shown the presence of a substance closely resembling Schmiedeberg's chondroitinsulphuric acid in the molecule of tendomucin, and of another substance of the same group in the spleen. Panzer has assumed that ovarial colloid is also a derivative of chondroitinsulphuric acid.

noAther complex substance yielding, on hydrolysis, glucosamin has been isolated by S. Fränkel from egg albumin and designated albamine. It is probable that the substance had the composition of $2(C_6H_9O_4NH_2)+H_2O$.

Thus it may be regarded as established by the investigations of recent years that the carbohydrate of combined proteids is nitrogenous, that the old conception of animal gum was erroneous, and that in many glucoproteids the carbohydrate is present in form of a complex ester of sulphuric acid.

Of the other cell-constituents, some attention has been given to the study of *lecithin* and *cholesterin*. From the researches of Overton and Hans Meyer, it seems probable that the action of different narcotics is dependent upon the coëfficient of their solubility in water and fatty or lecithin-like substances; and Koch has demonstrated that the antagonistic action of different ions on the life of a cell is to some extent dependent on their power to precipitate the lecithans from a colloidal solution.

As lecithans, Koch designates waxy, hygroscopic substances composed of orthophosphoric acids, nitrogenous groups and of glycerin. He has demonstrated that the ratio of nitrogen to the methyl group varies in individual substances of this class.

During life, cell-constituents undergo constant changes. The mechanism through which the transformation of cell-components

takes place has been the subject of many researches during recent years. It is practically established that most of the chemical reactions occurring in the life of a cell or of an organism are due to the presence in them of enzymes. It was generally known that enzymes are capable of bringing about a decomposition of complex into simple substances, and it was accepted that enzyme action was exothermic under all conditions. The natural conclusion was that they could act only in one direction. Observations, however, have shown that a decomposition of 100 per cent. of the original substance through enzyme action is a very rare occurrence under the most favorable conditions. Most generally the products of enzyme action consist of a mixture of the original substance and of its decomposition products. Recent investigations have demonstrated that this is due, not to a deficient cleavage power of the enzyme, but to the fact that the action of an enzyme is reversible. Thus Hill has stated that the yeast enzyme is capable not only of transforming starch into sugar, but also of transforming glucose into maltose. Emmerling has proved that the product of the reversible action of this enzyme is isomaltose. Cremer has shown that yeast plasma is also capable of forming glycogen from glucose. Hanriot and Kastle and Loevenhart here has demonstrated that lipase also possesses a reversible action, and, according to Emmerling, amygdalin can be formed synthetically through the action of yeast maltase. These discoveries are of very great biological importance as tending to explain the mechanism of the synthetical work of the living cell and organs.

Considerable work has also been done toward the explanation of the nature of individual enzymes.

Of very great biological importance is the enzyme causing coagulation of blood, plasma-fibrin ferment. It is chiefly through the work of Buchanan and Alexander Schmidt that the existence of this substance has been made probable. There are, however, authors who have denied its existence. In recent years Huiskamp has attempted to show that the coagulation of blood is caused not by enzyme action but by the action of nucleoproteids. On the other hand, Bordet and Gengou have succeeded in obtaining, by means of immunization, an antifibrin ferment, and thus have adduced new evidence in support of the theory of Schmidt. Arthus has shown that the coagulation of fluor plasma can be caused only by the ferment. Thus, notwithstanding the work done during recent years in this direction, the subject still remains a matter of controversy.

The proteolytic enzymes also have been the subject of renewed investigation during late years. Attempts have been made to ascertain the chemical nature of the enzymes. Friedlander came to the conclusion that they belonged to the class of nucleoproteids.

That this conclusion was based on insufficient evidence has been shown by Levene. On the other hand, different authors claim to have obtaind extracts from digestive glands, possessing proteolytic power, and at the same time giving no evidence of the presence in them of any proteid material.

The old basis for the classification of the enzymes has been to a great extent modified. They were generally distinguished by the reaction and the medium in which they showed greatest activity. Thus enzymes most active in acid solutions were regarded as belonging to the group of pepsin, and in that of trypsin were classified all those active in alkaline media. The endeavors of recent years have been to classify proteolytic enzymes by the end-products of their digestion. Thus it was found that trypsin may, under certain conditions, accomplish the cleavage of proteids to the crystalline constituents of the proteid molecule, leaving no trace of proteid-like substance. On the other hand, pepsin was supposed to be capable of transforming proteids into peptone. Recently, however, Lawrow and Langstein have demonstrated that the mucous membrane of the gastric wall on prolonged self-digestion also forms the crystalline end-products usual to tryptic digestion. Emmerling has shown, also, that papain is capable of decomposing fibrin to the crystalline products generally obtained on hydrolysis with mineral acids. It thus seems at present that by the end-products of their action proteolytic enzymes do not differ one from another. However, in view of the latest work on intracellular enzymes, this conclusion again needs revision.

A proteolytic enzyme with very peculiar properties has been described by Conheim. It was obtained from the intestinal wall and named erepsin. This enzyme does not affect unaltered proteids, but digests very rapidly proteoses and peptones to their final decomposition products. A very peculiar action of proteolytic enzymes has been noted by Okuneff in the laboratory of Danilewski. Okuneff has observed that soluble peptone subjected to the action of pepsin forms, among other products, a coagulated proteid. Kuraieff has demonstrated also that other proteolytic enzymes possess the same property. A certain analogy between this phenomenon and the reversible action of other enzymes is very suggestive.

A practically new chapter, and yet one of great importance for biology, is that of intracellular enzymes. Theodold Smith and Salkowski have discovered the presence of proteolytic enzymes in surviving tissues. The subject then attracted the attention of many investigators, chiefly Hedin and his co-workers, Hofmeister and his co-workers, especially Jacobi and Conradi and Kutscher The questions investigated have been the most favorable condition for their action, the end-products of their digestion and

their specificity. It has been established that most of them exercise the most effective decomposition in a solution of 2 per cent. of acetic acid. As regards the end-products the following have been obtained: Amino-acids, hexone-bases, purine bases, and pyrimidine derivativs. The results of the author's on the autolysis of different organs vary considerably. This may find an explanation either in the distinct nature of the individual enzymes, or in the fact that the methods employed by different authors were not the same. Regarding the specificity of the intracellular enzymes, Jacobi has made a statement that in distinction from the other enzymes their action is limited only to certain proteids. Of great importance is the observation of Müller, Petri and others, that many pathological formations disappear owing to enzyme action, and Jacobi has demonstrated that atrophic condition of organs may be caused by an increase of the enzymotic action of the organ. The relation between enzyme action and other pathological conditions, known as degeneration, has also been the subject of considerable investigation. Among the intracellular enzymes may be classified also the diastase of the liver and the glycolytic enzyme of the spleen. The existence of the former is again the topic of considerable discussion, and Pick in a recent paper insists on its existence. The presence of a glycolytic enzyme in tissues other than the blood has been demonstrated by Conheim, who also states that the enzymotic action appears only in the presence of pancreatic extract.

The influence of mineral salts on many physiological phenomena has been extensively studied during late years, but the discussion of it belongs rather to the domain of physiology, and will, therefore, be omitted in this place.

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NOTES.

Cereal Foods.—The examination of a large number of cereal foods, representing the products of forty-three manufacturers, has shown that the foods differed only from the grains from which