never long in doubt. Napoleon Bonaparte is credited with having said: "There are but two great forces in the world, the sword and the brain and, in the long run, the sword is always beaten by the brain."

Inferiority in population and in endowment of natural resources may be more than counterbalanced by progress in science and in industrial organization and efficiency. As man's scientific knowledge grows, his power becomes less and less dependent upon mere number of population or upon a complete supply of natural resources. In the present troubled condition of the world, that chemist serves his country best who helps it most to self-sufficiency. For "Self-dependent power can time defy, as rocks resist the billows and the sky."

The role of the chemist in the battle to overcome the lack of important raw materials, food, textile fibers, fuels and essential chemicals, has been pointed out repeatedly, with characteristic clarity and power, by Italy's great chemical leader, the distinguished president of this congress and of the International Union, Exc. Prof. Dr. Nicola Parravano.

In the defense of a nation, it is of the utmost importance that every man should be placed where he can render the maximum service. Trained chemists, therefore, should not be permitted to go to the front, if they are more urgently needed behind the lines. It is also imperative that they should be in constant and close contact with other defense forces, whether those forces be military, medical or industrial.

Man's mastery over the physical forces which rule his universe is increasing and expanding so rapidly in all directions that it is entirely appropriate to ask if we are breeding humans who can be safely entrusted with these vast powers.

Daily it becomes more apparent that there are but two paths open to the dwellers upon this planet, depending upon the use they make of this accumulated knowledge. One leads to inevitable ultimate extinction of the race by misuse of these powers. In fact, the opinion has been expressed also by others that science, unless directed into proper channels, may bring about its own obliteration. The other path leads to the development of a race of supermen, superior physically and mentally to any the world has yet seen, and to such a development the biochemist will be an outstanding contributor.

The future of a country and its defense depend not alone upon its birthrate, but also upon the kind of stock it is breeding. It should be a matter of grave concern, therefore, to every nation to make sure that the salaries and living conditions of its intellectuals—its professors and scientific investigators, for example—are not such as to render it difficult or impossible for them to afford the luxury of having children. The real test of a successful life is not how large an estate is amassed, nor how many decorations and other distinctions are won, but how many useful children and grandchildren are left behind you, and how much you did during your lifetime to help protect, teach and train the children of others. It is the human problem which is paramount. The most important crop still remains men and women. We have been so absorbed in making more and better automobiles, airplanes and the host of things which minister to our prosperity or pleasure that we have overlooked completely the far greater need for more and better humans. Things and knowledge are much less important than the nature of the individuals who are to use them, and it is far less difficult to protect ourselves against things than against thoughts.

It is entirely praiseworthy to seek for "the more abundant life," but it does not appear to be understood, except by those well versed in history, that no people can achieve and retain greatness unless they worship sacrifice rather than ease, and crave service rather than support in idleness. As Roger W. Babson so clearly puts it, "progress comes only through truth, security comes only through courage, and freedom comes only through sacrifice."

Scientists are potent factors in maintaining the integrity and progress of a nation, and within that group none have more important roles to play than the chemists. But the chemist must not forget that, in addition to his strictly professional duties, there are other obligations which devolve upon him as a citizen, and to which he can not be recreant. He is a truly great defender of his fatherland who, as expert chemist and loyal citizen, gives to her the best that is in him, in times of peace as well as in war.

RECENT CONTRIBUTIONS TO THE THEORY OF PROTOPLASMIC STRUCTURE[1]

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AN invitation from Sigma Xi is particularly welcome to a worker on protoplasm, for there is no field of research which so perfectly illustrates the need of cooperation as that on which I am to speak this evening.

Theories of protoplasmic structure fall into three categories—solution, emulsion and gel.

Such a grouping is a modern one, but it includes

[1] Lecture delivered on February 28, 1938, at a general meeting of Sigma Xi at Rutgers University.

the older hypotheses: thus, the alveolar structure postulated by Bütschli is but that of an emulsion, the scattered globules of which are under pressure, therefore, hexagonal in cross section, and dodeca- or tetrakaidecahedral in solid form. The micellar hypothesis of Nägeli also has its place in modern theories. X-ray analyses by Sponsler[2] have reestablished the micellar concept for cellulose. The old and familiar fibrillar theory of protoplasmic structure is now generally accepted as the most likely structure of elastic jellies.

Thus, may all theories of protoplasmic structure, old and new, be classed into three groups. Of the three, the one which states that living matter is a true solution, pure and simple, and obedient to solution laws, may be immediately discarded, for it is untenable. Protoplasm exhibits the same anomalous behavior as do elastic sols. It possesses not only one viscosity value but many values depending upon the sheering stress. This is easily demonstrated with non-living systems such as gelatine and certain soap solutions, but not so readily in the case of protoplasm; yet Pfeiffer,[3] in his studies on protoplasmic flow through capillaries, has found that curves of deformation-speed plotted against suction-force bear a strong resemblance to the curves of anomalous flow of colloids with structural viscosity. Protoplasm is, therefore, non-Newtonian in behavior. Furthermore, it is exceedingly difficult to conceive of a living system which is devoid of sufficient structural continuity to give a modicum of symmetry and coordination.

The second of the theories of protoplasmic structure is one which formerly found application to hydrated and elastic proteins. It holds that jellies are "emulsoidal," that is to say, "emulsion-like." This belief has long since been given up by the colloid chemists. Superficially, protoplasm is an emulsion, just as is milk, but the physical properties of protoplasm are characteristic of gels, not of emulsions. For example, when protoplasm coagulates, the superficial emulsion plays no part whatever, any more than does the emulsion in milk when milk curdles.

The third of the major theories of protoplasmic structure states that living matter is fibrous. Biological thought was dominated to such an extent by the emulsion hypothesis that the fibrillar concept was forgotten or ignored, and thrown into that heap of discarded cellular artifacts from which so much of value has since been culled. Yet through the years there persisted the thought that living matter possesses a continuity in structure which only fibrous units can adequately impart to it. This concept was expressed by earlier workers in such terms as "spongioplasm" and "reticulum," and by later ones with "cytoskeleton." Conklin[4] has repeatedly emphasized the necessity of regarding protoplasm as an elastic system which recovers its normal form after distortion. Only in such a way are nucleus and other cell inclusions slowly brought back into their usual positions after centrifuging. Needham[5] interprets polarity in the egg in terms of structural continuity, and puts forward the aphorism, "biology is largely the study of fibers." Moore[6] finds that the protoplasm of a slime-mold will of itself pass through parchment paper with pores 5×10^{-5} mm in diameter, but if pressed through silk with pores 5×10^{-2} mm in diameter it will not survive, thus indicating the presence of a structure which, if destroyed, means death.

Particularly significant is the crystalline character of living matter. The polarity of cells and the symmetry of organisms exist in virtue of molecular patterns indicative of the crystalline state. As protoplasm is often fluid, its crystalline nature must be that of liquid crystals. When molecular axes are parallel in all three planes, solid crystals are formed. Para- or liquid crystalline substances have elongated molecules which, distributed at random, yield isotropic liquids, but when the distribution is symmetrical in one or two planes, the liquid crystalline state results. As Needham says, "The paracrystalline state seems the most suited to biological function, as it combines the fluidity and diffusibility of liquid while preserving the possibilities of internal structure characteristic of crystalline solids."

Thus more and more is there unanimity of opinion on the fibrous structure and crystalline nature of organic jellies, in particular, the living jelly, protoplasm.

My own conviction of the presence of fibrous units and structural continuity in protoplasm came through measurements of elasticity twenty years ago. But we can go farther back than this: it is just over a century since Dujardin suggested elastic qualities in protoplasm when he referred to it as a glutinous jelly. The significance of elasticity is now generally recognized; thus, Scarth[7] says it is the best indication we have of the structure of protoplasm.

That a liquid may be elastic, in the sense that it is capable of being stretched, is at first difficult to comprehend, but it is an easy matter to demonstrate the elasticity of certain soap solutions, the viscosity of which is only twice that of water.[8]

The elastic qualities of protoplasm are more readily demonstrated when it is of high viscosity. By stretching protoplasm between mechanically controlled microneedles, its elasticity and tensile strength are made very evident. These qualities rest upon structural

[2] O. L. Sponsler, *Am. Jour. Bot.*, 9: 471, 1922.
[3] *Physics*, 7: 302, 1936; *Nature*, 138: 1054, 1936.
[4] *Jour. Exp. Zool.*, 22: 311, 1917.
[5] "Order and Life," Cambridge, 1936.
[6] *Proc. Soc. Exp. Biol. and Med.*, 32: 174, 1934.
[7] *Protoplasma*, 2: 189, 1927.
[8] W. Seifriz, *Coll. Sym. Mono.*, 3: 285, 1925.

continuity. Fluidity is possible through the shifting of linkages between one unit and another.

Yet another quality of living matter is satisfied by its fibrous structure. The high water-holding power of protoplasm requires structural continuity. The jelly-fish consists of two to four per cent. solid matter, or about 97 per cent. water, yet it is rigid enough when stranded to support the weight of a man without collapsing; if left to dry in the sun, it is soon reduced to a thin film. A similar situation exists in the germanium oxide gel which may contain as much as 99.5 per cent. water.

It has long been the conviction of those supporting the fibrillar theory of protoplasmic structure, that protoplasm should prove to be doubly-refractive and give an x-ray pattern comparable to that of gelatine, egg-white, and pepsin. In the case of double refraction, that which was anticipated in protoplasm is the phenomenon described by Freundlich and Disselhorst,[9] and so strikingly illustrated in a vanadium pentoxide sol. On mere stirring, or flowing, this sol shows pronounced double-refraction due to the orientation of linear crystalline particles. Rod-shaped particles in other colloidal suspensions, such as benzopurpurine and viruses, also orient themselves spontaneously, and form structures which exhibit double-refraction. Such substances have been termed "tactoids" by Freundlich, who calls attention to the resemblance of tactoids to that of certain cellular structures, such as the mitotic spindle, which also show double-refraction.

There has never been any question of the presence of optical activity in muscle and all types of connective tissue, but W. J. Schmidt[10] has now shown Amoeba to be doubly refractive; though usually weak, it is nearly always capable of verification and becomes pronounced when the Amoeba prepares for encystment. Double-refraction in the Foraminifera is likewise demonstrable, and at times very prominently so.

In all its properties—elasticity, tensile strength, coagulation, thixotropism, anomalous flow (non-Newtonian behavior), imbibition, high water content, etc.—protoplasm is similar to elastic jellies, and these properties are capable of interpretation in terms of a fibrous structure.

The linear unit postulated for protoplasm is of the same character as that which has long been attributed to proteins; it is the familiar polypeptide chain. To this information, which dates back to the time of Emil Fischer, Astbury[11] has added observations of considerable significance. X-ray diffraction patterns are regarded as the final proof of crystallinity and symmetry in organization. With their aid, Astbury has been able to distinguish between the chain structure of elastic substances, such as wool and hair, and non-elastic substances, such as silk. By means of x-ray analysis, he has shown that the protein chain of silk and stretched hair is fully extended, while that of unstretched hair and wool is folded or waved; to this latter property are due the elastic qualities of proteins. The x-ray photograph of muscle is similar to that of the muscle protein, myosin (a globulin) when freed from the muscle.

I have stated that the linear unit postulated for protoplasm and elastic jellies is the polypeptide chain, but the matter is not so readily disposed of, for the protein molecule is given so extraordinarily high a weight in modern theories that its identity is questioned. Furthermore, the old concept that the colloidal unit of gels is a micelle, or molecular aggregate, still persists. It becomes, therefore, our task to consider the nature of the structural units of protoplasm and protein jellies.

The micellar hypothesis is fairly well established for cellulose, but even here high tensile strength suggests an overlapping of fibrous molecules, so that the micelle begins to lose its identity.

Coagula, in particular gels of the silica type, are unquestionably finely granular and therefore micellar in structure. The silicic acid gel is porous when dry; but with gelatine the situation is not so clear. Here the micellar theory meets with limitations set upon it by the known properties of elastic protein systems. It is quite possible that a hydrated yet firm block of gelatin is homogeneous, *i.e.*, the dispersion is a molecular one. To offset this possibility is the fact that gelatine gels make good ultra-filters, and this suggests porosity, therefore heterogeneity and a micellar structure. Perhaps the whole situation is cleared up by the modern concept of macro-molecules, and the micelle made, so to speak, superfluous; or are the macromolecules themselves micellae?

Our problem is to decide whether hydrated protein units are molecules or molecular aggregates, and in either case whether fibrous or not.

Many high molecular weight compounds tend to unite and form larger aggregates. This is particularly characteristic of proteins with their amino acids and polypeptide chains, and of cellulose, the molecule of which is a fiber of variable length consisting of from 100 to 500 anhydrous glucose units. Indeed, Kraemer[12] has attributed a length of 1.7 μ to the molecule of native cellulose, which brings it well within microscopic dimensions, but not visibility. A similar shape has been postulated for the gelatine molecule which is said to be a slender fiber of great length with a

[9] *Phys. Zeitschr.*, 16: 422, 1915.

[10] Die Doppelbrechung von Zytoplasma, Protoplasma Mono. XI, 1937.

[11] "Fundamentals of Fibre Structure," Oxford, 1933.

[12] E. O. Kraemer, *Jour. Ind. Chem. Eng.*, 30: in press, 1938.

diameter of but a few Ångstrom units. Such macromolecules are of enormous weight, values up to 15,000,000 being given them, which is alone reason enough to suspect them of being aggregates. Possibly the controversy is unreal from the kinetic point of view, that is to say, the molecular concept falls out altogether.

Svedberg[13] states that "particles" of native, undenatured, proteins in solution are true molecules, for the "particle weight" is completely defined by environment, and all the "particles" have the *same* mass. One is, therefore, entitled to speak of "molecular weight" just as one does in the case of N_2O_4 and other "polymerized molecules." Kruyt[14] answers with the statement that osmotic laws are generally applied to true solutions and therefore we are accustomed to identify the thus measured number of particles with that of the molecules present, but this is an arbitrary identification. What we really do is count kinetically active particles, and thus obtain only micellar numbers and micellar weights.

We may disagree with Kruyt to this extent and say, while kinetic measurements give only particle numbers and weights, *it can not be definitely said whether the particles are molecules or micelles.*

Another fact in Svedberg's favor is that the kinetically active units of proteins are of *uniform* size. This indicates the absence of association, for aggregates formed by coagulation always result in non-uniform sizes. Furthermore, under certain conditions, some of the proteins of homogeneous particle weight dissociate into products of lower, but still homogeneous particle weight, the weights of the original and final particles being related as simple whole numbers. When the original conditions are restored, the dissociated particles reunite to give again uniform particles of the same size as the original ones. Thus, the evidence that the kinetically active unit of a protein solution is a single molecule is better than that ordinarily obtained for some simple substances of low molecular weight.

A significant feature of the work of Svedberg is that the protein particle in solution is not an accidental one resulting from the conditions of preparation, but—and here we may include the basic structural unit of protoplasm—it is a particle built to a definite size by the living cell.

The biologist must await a decision from the chemists, but whatever the outcome may be, it will not materially affect interpretations of protoplasmic behavior, for *mammoth-sized molecules satisfy the conditions of colloidality as well as molecular aggregates.* The molecule-micelle uncertainty also does not affect the concept of fibrous units. There is, however, another question which bears directly upon the fibrous, or non-fibrous, character of the structural units in elastic organic systems.

There has of late crept into the literature information purporting to support spherical protein molecules.[15] It is difficult to do anything structurally with a spherical particle. If the globular molecule is hollow, *i.e.,* a porous cage, high water content is as easily interpreted as in the case of fibrous units, but other properties can not at all be satisfied by a globular unit. A spherical protein molecule in solution will mean Newtonian behavior, yet if there is one firmly established property of many protein solutions it is their anomalous flow. Mechanical properties, such as elasticity and tensile strength, are equally difficult of interpretation. To attempt to satisfy these physical properties with a spherical molecule is rather like asking a weaver of cloth to make his fabric of sand instead of threads.

While spherical or "globular" molecules are said to occur in globulins, such as edestin, and in normal albumin (egg-white), this is true only in dilute solutions, and not when the molecules are on surfaces. Furthermore, all yield x-ray photographs when denatured.

For a time, each will have to interpret the behavior of proteins as he thinks best. The globular molecule has some advantages; the unwieldy polypeptide chain, with its thousands of atoms and hundreds of residues along a single thread, becomes a two or three dimensional pattern. To offset this advantage is the far greater difficulty of adding to a sphere than to an open chain. The globular molecule of 35,000 molecular weight is complete and closed; what, then, of those of higher weight?

It is, further, not necessary to resort to a hollow sphere, for the *folded* polypeptide chain will do as well. According to Astbury,[16] the supposed "globular" protein molecule is a folded polypeptide chain in which the linear fiber (A, Fig. 1) has been thrown into a series of rings, possibly the form shown in B, Fig. 1.

In some proteins, the natural configuration is an extended chain, which may be quite fully extended as in silk, β-keratin, and β-myosin, or regularly folded in one dimension, as in the α- and supercontracted forms of keratin and myosin. When the chains are fully folded, so-called "globular" proteins result, such as egg albumin, haemoglobin, pepsin, and insulin. The "globular" proteins unfold on denaturation, and the liberated polypeptide chains may then sometimes be spun into artificial protein fibers. In the living cell there is probably an unlimited number of reversible interchanges between various states of folding.

13 T. Svedberg, *Nature* (Supplement), 139: 1051, 1937.
14 *Proc. Ninth Internat. Congr. Chem.*, Madrid, 1934.

15 I. Langmuir, V. J. Schaefer and D. M. Wrinch, SCIENCE, 85: 76, 1937.
16 *Nature,* 137: 803, 1936.

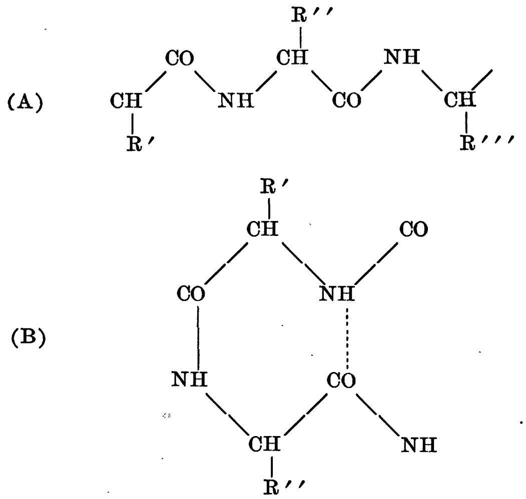

Fig. 1

Knowledge of protein structure has not yet reached the point where it can be indisputably stated that there is but one stereochemistry of the proteins based on the convolutions of the polypeptide chain, even though this conclusion is a likely one. It may be that proteins fall into two groups, morphologically considered, the soluble proteins—egg-albumin, insulin, edestin, etc.—of globular molecular form, and the insoluble proteins—silk, hair, wool, etc.—with chain molecules. Protoplasm will then contain both forms, and to the chain molecules are its elastic, structural, and anomalous properties due.

These are questions which will have to be settled by the organic and x-ray chemists. But the biologist is in the happy position that whatever the answer, he still has sufficient to meet his major demands; namely, a continuity and symmetry in structure which will satisfy the elasticity and non-Newtonian behavior of protoplasm, to which must be added fundamental biological qualities. Among these are certain genetical requirements.

In order that the linear arrangement of genes shall be kept, it is necessary to assume that chromosomes maintain their identity throughout the life of the cell, and not just during mitosis as heretofore believed.

Structural continuity and symmetry in organization are necessary prerequisites of an ordered behavior, and the latter is a fundamental quality of all living matter.

In conclusion, I wish to refer to a recent hypothesis on the mechanism of protoplasmic streaming, in order to indulge in a speculation which makes further use of the theory of protein and protoplasmic structure as here set forth. I made the suggestion[17] that the streaming of protoplasm in slime-molds is due to rhythmic pulsations of the plasmodium, thus attributing to a very primitive form of living matter the same capacity for rhythmic contractiliity possessed by certain tissues of higher organisms. I discarded all older hypotheses of protoplasmic streaming, of which there are several based on surface tension, hydration, and electroendosmosis. In ascribing the outward and inward flow of protoplasm in slime-molds to rhythmic pulsations of the plasmodium, I gave no hint of the possible mechanism of the systolic and diastolic movements. It has occurred to me that these movements may be due to the contraction of folded molecules such as those postulated by Astbury for wool and hair.

As contractility is a property of all living matter, we may make the general postulate that vital contractility, wherever it occurs, whether in the most elementary forms of protoplasm or in highly specialized tissues, is due to the shortening of protein fibers by molecular folding or helical contraction. The energy for this work is supplied by the oxidative processes in the cell.

OBITUARY

WILLIAM WALLACE CAMPBELL

"All of his life William Wallace Campbell did difficult things with high courage. There can be no doubt that the most difficult thing he ever did, and the one which required the highest courage, was to end his own life. Most who take their own lives do it from lack of courage. One can not read the pitiful notes left by Dr. Campbell and bring that charge against him. We can do Dr. Campbell this justice and yield no whit in our disapproval of self-destruction."

All Dr. Campbell's friends, who knew of his condition in recent months, will agree with the statement I have just quoted from an editorial printed in the *San Francisco Chronicle* on June 15, twenty-four hours after his tragic death.

It was an act of highest courage dictated by love for his devoted wife and children and desire to spare them the burden of caring, perhaps for long months, for an invalid rapidly approaching the state in which, by reason of blindness and aphasia, he could not even communicate his thoughts or wants to them. "It is better," he wrote, "that I go away now with my powers nearly all gone."

I shall not here attempt to pass in full review Dr. Campbell's brilliant career as an astronomer and as a great leader and executive, were it only for the reason that space limitations would forbid. At the "Symposium in Appreciation of the Scientific Contributions of William Wallace Campbell," held at Harvard Observatory on March 31, 1938, Dr. Shapley, in his intro-

[17] W. Seifriz, Science, 86: 397, 1937.