

the South Carolina Section of the American Chemical Society and the South Carolina Section of the Southern Society for Psychology and Philosophy, on Saturday, May 1, 1937. More than two hundred members attended.

The morning session was devoted to papers of more general interest and the address, "The Ubiquitous Insect," of the retiring president, Professor Franklin Sherman, of Clemson College. The afternoon session was divided into sections of biology and chemistry.

At the business session the following officers for 1937-38 were elected:

*President:* Dr. J. E. Mills, Sonoco Products Company, Hartsville, S. C.

*Vice-president:* Dr. G. G. Naudain, Winthrop College, Rock Hill, S. C.

*Secretary-Treasurer:* Dr. F. W. Kinard, Medical College, Charleston, S. C.

*Curator:* Dr. J. E. Copenhaver, University of South Carolina, Columbia, S. C.

*Editor:* To be appointed.

*Executive Committee:* Professor A. C. Carson, University of South Carolina; Professor Franklin Sherman, Clemson College; Dr. C. B. Waller, Wofford College; Dr. Velma Matthews, Coker College; Dr. J. C. Kinard, Newberry College.

The Jefferson Medal for the outstanding paper was awarded to Dr. Roe E. Remington, of the Medical College, for a paper entitled "A Quantitative Technique in the Study of Goitre." The 1937 Research Fund was granted to Drs. J. Hampton Hoch and Hillyer Rudisill, Jr., of the Medical College.

The next meeting will be held in the spring of 1938 at Charleston, South Carolina.

F. W. KINARD,  
*Secretary*

## SPECIAL ARTICLES

### ON THE STRUCTURE OF INSULIN

It has recently been shown<sup>1</sup> that the cyclol theory of protein structure,<sup>2</sup> originally developed with special reference to the structure both of unimolecular protein films<sup>3</sup> and of the multi-laminar proteins, logically implies the existence of "space-enclosing" protein molecules; these contain certain specific numbers of amino acid residues. In particular a certain series of space-enclosing cyclols  $C_1, \dots, C_2, \dots, C_n, \dots$  which comprise  $72, 288, \dots, 72n^2, \dots$  amino acid residues have been constructed. The theory thus passes the test, to which any theory of protein structure must submit, of predicting in general terms the body of facts relating to the "globular" proteins established by Svedberg and his collaborators.<sup>4</sup>

In view of the fact that considerable data relating to insulin are now available, including the x-ray analysis of the structure of insulin crystals,<sup>5</sup> it was deemed worth while to investigate in detail how far any of these space-enclosing cyclol molecules which have now been constructed can be used as a basis for a discussion of the structure of insulin. The molecular weight of insulin is known accurately enough for it to be plain that  $C_1$  is much too light and  $C_3$  much too heavy. The only cyclol of the series which comes into question is therefore  $C_2$ . Here the number of residues is of the right order of magnitude.

<sup>1</sup> D. M. Wrinch, *Nature*, 139: 1937 (in the press).

<sup>2</sup> D. M. Wrinch, *Nature*, 137, 411; 138, 241 and 651; 1936. *Proc. Roy. Soc. Lond. A.*, 160: 59, 1937.

<sup>3</sup> I. Langmuir, V. Schaefer and D. M. Wrinch, *SCIENCE*, 85: 76, 1937.

<sup>4</sup> T. Svedberg *et al.*, *Koll. Z.*, 51: 10, 1930. *Trans. Far. Soc.*, 26: 72 and 737, 1930. *SCIENCE*, 79: 327, 1934. *Biol. Bull.*, 66: 191, 1934. *Chem. Rev.*, 14: 1, 1935, and a series of papers in *Jour. Am. Chem. Soc.*, from 1929.

<sup>5</sup> D. Crowfoot, *Nature*, 135: 591, 1935.

Each space-enclosing molecule consists of a piece of the cyclol fabric shown in Fig. 1, which by bending

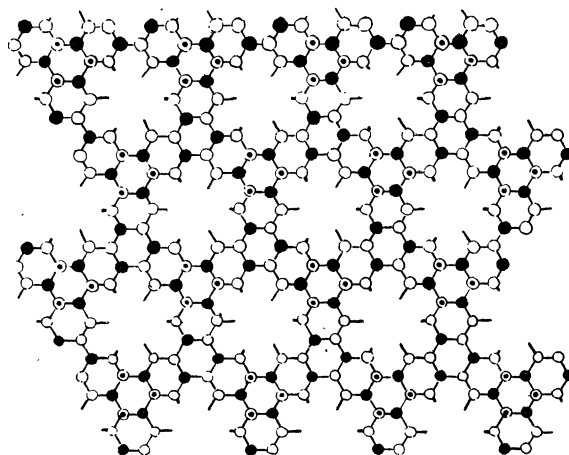


FIG. 1. The cyclol pattern. The median plane of the lamina is the plane of the paper. The lamina has its "front" surface above and its "back" surface below the paper.

- = N.
- = C(OH), peptide hydroxyl upwards.
- ⊙ = C(OH), peptide hydroxyl downwards.
- = CHR, direction of side chain initially outwards.
- = CHR, direction of side chain initially upwards.

across one line after another joins up and so surrounds a portion of space. For simplicity of exposition, the cyclol fabric may be replaced by its median network in which the C-C-N atoms in the constituent residues are replaced by points midway between linked atoms. Various views of a model of the median network of the molecule  $C_2$  are shown in Fig. 2. This network lies on the surface of a truncated tetrahedron and

possesses four triangular faces and four hexagonal faces. This polyhedral configuration is in agreement with Svedberg's deduction that insulin is a "globular"

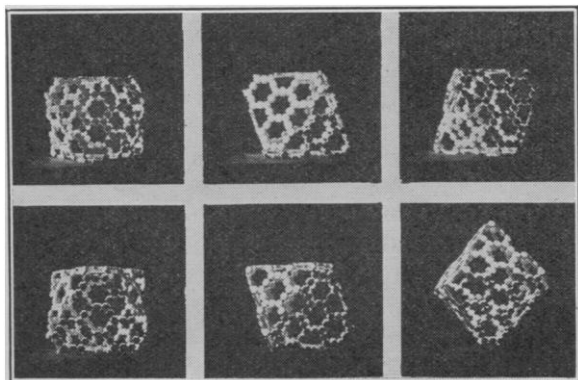


FIG. 2

molecule with low asymmetry number<sup>6</sup> and in fact offers an interpretation of the nature of this "globularity," which may be useful in the future in a quantitative interpretation of the asymmetry numbers of megamolecules in general. Further, since the  $C_2$  structure (like all  $C_n$  structures) is a condensation of amino (or imino) acid molecules, no prosthetic group is required, in accordance with the chemical evidence.

The most stringent test of any proposed structure is afforded by the x-ray findings.<sup>5</sup> In the first place the insulin lattice has space group  $R3$ , and the unit cell is rhombohedral and contains one molecule only. Strictly interpreted, this means that the molecule itself has trigonal symmetry. Now for all the space-enclosing cyclols, the median network (which is to be regarded as a shorthand notation for the molecular structure, from which its essential features can be deduced) has four trigonal axes, if the distribution of different amino acids be left out of account. This symmetry requirement can then be met by any  $C_n$  and at the same time interpreted to mean that in the insulin molecule one hexagonal and one triangular face have the various residues trigonally arranged, while the three other hexagonal faces and also the three other triangular faces have identical arrangements of residues.

Next, the unit rhombohedral cell has  $a = 44.3\text{\AA}$  and  $\alpha = 115^\circ$ . On working out the detailed geography of the structure proposed, it is found that the cyclol molecule  $C_2$  (whose median network is shown in Fig. 2) fits easily and elegantly into this cell; furthermore, its structure suggests actual mechanisms of coordination in this megamolecular lattice. Thus the coordination between a molecule and its neighbors above and below at a distance  $30.2\text{\AA}$  along the trigonal axis appears to be due to the simultaneous linking of a number of peptide hydroxyls. On the other hand

each molecule appears to be linked severally to its six neighbors at distances  $44.3\text{\AA}$  along the edges of the primitive rhombohedron by means of groups belonging to side chains, probably by the phenolic groups of tyrosine residues, which are held together by zinc (or other) cations. This mechanism accounts for the data of Scott which establish the fact that in insulin crystals there is a stoichiometric relation between the insulin content and the content of zinc, of cadmium or of cobalt.<sup>7</sup> The proportion is three cations to one molecule of insulin, which is in accordance with the mechanism of coordination suggested above, assuming that each insulin molecule has a half share of the six cations, located on the rhombohedral edges. The present suggestions thus fit in with and explain the view that crystalline insulin contains the metals as chemically combined constituents and not as mere impurities, and throws light also upon the fact<sup>7</sup> that the best acidity for the crystallization of insulin in the presence of certain metals is pH 6.0 to 6.2 on the alkaline side of the isoelectric point<sup>8</sup> pH 5.0–5.5.

Full details of the work will appear shortly.

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#### THE DIFFUSION COEFFICIENT AND MOLECULAR SIZE OF VISUAL PURPLE

IN order to secure some notion of the molecular dimensions of visual purple, we have determined its diffusion coefficient by the method of Northrop and Anson.<sup>1</sup> This involves measuring the rate with which a dissolved substance passes from an enclosed solution into an outer solvent through a porous glass or alundum disk calibrated with substances of known diffusion coefficient.

The two basic properties of visual purple are its color and its light sensitivity. We have therefore relied on these criteria for measuring its diffusion. Using three different glass disks and four preparations of visual purple, we have obtained apparent diffusion coefficients of 0.0153, 0.0125, 0.0161 and 0.0152, with an average of 0.0148 sq. cm. per day at  $6^\circ\text{C}$ .

These values are probably not the real diffusion coefficients, because the glass disks become clogged during the manipulations. The clogging happens rapidly and then stops; after diffusion equilibrium with visual purple has become established over night the rate usually remains constant for as long as we have measured it, in one case for a week.

To estimate this clogging factor we calibrated the disks as usual with 2 M NaCl before the visual purple

<sup>7</sup> D. A. Scott and A. M. Fisher, *Biochem. Jour.*, 29: 1048, 1935.

<sup>8</sup> F. O. Howitt and E. B. R. Prideaux, *Proc. Roy. Soc. Lond. B.*, 112: 13, 1932.

<sup>1</sup> J. H. Northrop and M. L. Anson, *Jour. Gen. Physiol.*, 12: 543, 1929.

<sup>6</sup> T. Svedberg and I. B.-Eriksson-Quensel, *Tabulae Biologicae Periodicae*, 5: 351, 1935–36.