bequest was accompanied by an endowment of $5,000 for the extension and maintenance of the library.

THE first issue of *Wrightia,* the botanical journal of the Southern Methodist University at Dallas, has appeared. Each volume, which will contain approximately five hundred pages, will consist of a series of numbers to be issued at irregular intervals.

AS an aid in the study of legislation on science now before the Congress, the Subcommittee on War Mobilization of the Senate Military Affairs Committee has issued a select bibliography on "The Social Impact of Science." The bibliography has been prepared by the Library of Congress. It lists more than five hundred titles of books, pamphlets, articles and Congressional bills and reports dealing with the social and economic problems arising from scientific progress. A special section covers the available literature on atomic power, including several volumes yet in press.

SPECIAL ARTICLES

FORCES INVOLVED IN THE REACTION BETWEEN ANTIGEN AND ANTIBODY MOLECULES

THE nature of the reaction between antigen and antibody molecules is far from being completely understood at the present time.[1] Though of major importance from the standpoint of biology, the reaction also offers a very interesting example of the physical forces involved between large molecules. Thus for the past few years the author has been engaged in a study of the serological reactions occurring between a film of antigen deposited on a metal slide and a solution of antibodies brought in contact with that slide. From this work, which will be published shortly in detail, some surprising facts have recently come to light which appear to be of sufficient interest to justify their publication in this note.

Previously published work has shown that the specific fixation of homologous antibodies occurs even when the antigen molecule is completely unfolded and 6 to 8A thick.[2] The specific fixation of antibodies has been demonstrated by an increase in the adsorbed layer on the plate after treatment with homologous antibodies. The accuracy with which small increments in film thickness can be measured is now greatly improved by an apparatus named the "ellipsometer," recently described, which permits the measurement of film thickness increments with an accuracy of $\simeq \pm 0.3$A.[3] The method is based on the change that takes place in ellipticity of the light reflected after a metal slide has been coated with films whose thickness is of molecular dimensions. The technique employed is briefly this: Highly polished stainless steel slides are first covered with an optical gauge of 1 and 3 (or 2 and 4) layers of a reference film (stearic acid). Films of antigen (bovine albumin, egg albumin) spread on an Adam Langmuir trough are transferred on the slides according to the procedure of Blodgett and Langmuir.[4] Two unfolded films 6 to 8A thick can easily be transferred on such slides.

It is very difficult to transfer more than two layers. However, if the slide is first treated with a dilute solution of uranyl acetate, a very large number of protein films can be transferred. This demonstrates that the uranium ions strongly polarize the first layer, which in turn polarizes the second, and so on along the successive layers. This polarization prevents the films from slipping back on the surface of the trough when the slides are taken out. A drop of the antisera to be tested, diluted 1/10 in buffered saline solution, is deposited on slides covered with the antigen films. After a few minutes, the slides are washed with saline and water and the increment of thickness is determined. Some of the results have been condensed in Table 1.

TABLE 1

SPECIFIC REACTION OF FILMS OF BOVINE ALBUMIN WITH RABBIT ANTIBODIES

Number of bovine albumin layers	Increase in thickness in A units after adsorption of antibovine albumin serum	Increase in thickness in A units after adsorption of antiegg albumin serum
1	39	4
2	57	4
4	104	−3
6	136	−8
8	149	

It is evident from the data that films of bovine albumin react in an unexpected way. The amount of adsorbed antibody molecules increases with the number of underlying layers of bovine albumin up to four double layers. Thickness increments of antibodies obtained with five underlying double layers are about the same as those obtained with four double layers.

Quite a different result is obtained with egg albumin. With films of this protein, the amount of adsorbed homologous antibodies is independent of the number of underlying layers of antigen. Constant increment of antibodies of about 20A is obtained and

[1] K. Landsteiner, "The Specificity of Serological Reactions," Cambridge, Harvard University Press, p. 262. 1945.

[2] A. Rothen and K. Landsteiner, *Jour. Exp. Med.,* 76: 437, 1942.

[3] A. Rothen, *Rev. Sci. Inst.,* 16: 26, 1945.

[4] K. B. Blodgett and I. Langmuir, *Phys. Rev.,* 51: 964, 1937.

no increase is observed upon treatment with a heterologous serum at the dilution used.

Further, the investigation of the screening action of films transferred on the slide on top of the antigen films brought out most surprising results, which are, in fact, the main object of this note. It can be seen from the data in Tables 2 and 3 that screens consisting of stearic acid or protein layers do not prevent considerable specific adsorption of antibodies. When the antigen films consist of three double layers of bovine albumin, a specific reaction still occurs in spite of a screen of four double layers of stearic acid. Analogous results were obtained with screens of octadecylamine and mixed screens of octadecylamine and stearic acid.

TABLE 2

SCREENING EFFECT OF STEARIC ACID LAYERS ON THE ANTIGEN-ANTIBODY REACTION

	Antigen films: 3 double layers of bovine albumin (50A)		Antigen films: 1 double layer of egg albumin (16A)	
Screen: Number of stearic acid layers	Increase in A units after adsorption of anti-bovine albumin serum	Increase in A units after adsorption of anti-egg albumin serum	Increase in A units after adsorption of anti-egg albumin serum	Increase in A units after adsorption of anti-bovine albumin serum
2	87	0	18	0
4	61	2	13	5
6	36	6	12	10
8	29	13		

TABLE 3

SCREENING EFFECT OF EGG ALBUMIN LAYERS ON BOVINE ALBUMIN-ANTIBOVINE ALBUMIN REACTION

Antigen: Number of bovine albumin layers	2	2	2	2	2	6	6
Screen: Number of egg albumin layers	2	4	6	8	10	6	10
Increase in A units after adsorption with antibovine albumin serum	41	28	17	9	0	86	58

The interpretation of these results now becomes important. Perhaps the most obvious explanation is that stearic acid or protein films have holes through which the antibody molecules can reach the antigenic film. Such an explanation, however, is scarcely satisfactory if one considers the closely packed structure of stearic films in relation to the size of the antibody molecule (molecular weight $\simeq$ 160,000). Furthermore, an extensive series of experiments carried out in this laboratory have shown that stearic acid films may act as a perfect screen for certain types of reaction. For instance, at the proper pH a layer of insulin molecules 150A thick[5] (molecular weight $\simeq$ 40,000) can be adsorbed on a slide covered by a layer of protamine. Nevertheless, a monolayer of stearic acid deposited on the protamine prevents subsequent adsorption of insulin molecules.

The following explanation of our results is offered tentatively. It is assumed that the effective range of action between a film of antigen and an antibody molecule might extend to an order of hundreds of A instead of a few A as in the case of forces between individual atoms. In order to achieve such a long range, it is considered possible that a field of force of greater magnitude might result from an integrated action of the many elementary units which build up the single large molecules of antigen and antibody in an orderly way. It is a matter of speculation how this field is realized, but it is not impossible that it could result along the lines indicated by London.[6] Under favorable conditions, the field of force of the antigen film could be enhanced as the number of layers is increased, which seems to occur in the case of bovine albumin films. The data reported above may thus be interpreted in the sense that no direct contact is necessary between a film of antigen and the corresponding antibodies to demonstrate a specific interaction.

If this interpretation is correct, it means that in the animal body the sphere of action of antibodies is much greater than commonly supposed. An interaction might even occur through a thin biological membrane.

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METABOLISM IN DIABETIC COMA PRODUCED BY ALLOXAN[1]

IT has been observed that the injection of alloxan in rats will produce varying degrees of diabetes mellitus—even severe coma—which is similar to that seen in human beings.[2,3] Alloxan has, therefore, provided us with a valuable experimental tool, with which to study the metabolism in diabetic coma and the results of therapy.

In human diabetic coma there is a marked elevation in plasma inorganic phosphate which decreases rapidly, following administration of insulin.[4,5] The mechanism of this fall is still obscure. Studies on normal animals show that insulin causes a rise in acid-

[5] G. H. A. Clowes, "Recent Advances in Surface Chemistry and Chemical Physics," The American Association for the Advancement of Science, No. 7, p. 61. 1939.

[6] F. London, "Surface Chemistry," The American Association for the Advancement of Science, No. 21, p. 141. 1943.

[1] These studies were aided by a grant from the Committee on Scientific Research of the American Medical Association.

[2] J. S. Dunn and N. G. B. McLetchie, *Lancet*, 245: 384, 1943.

[3] R. E. Janes and C. E. Friedgood, *Endocrinology*, 36: 62, 1945.

[4] G. M. Guest and S. Rapoport, *Am. Jour. Dis. of Children*, 58: 1072, 1939.

[5] M. Franks, R. F. Berris, N. O. Kaplan and G. B. Myers. In preparation.