his publications. Some of these have been reprinted in the past, such as his remarks on Loudon's "Encyclopedia of Plants" (1832), reprinted in the *Journal of Botany* (38: 225–229, 1900), Fitzpatrick's 1908 reprint of the very rare "Annals of Nature" (1820), the *American Midland Naturalist* series of facsimile reprints (1912–13), including the "Neogenyton" (1825), "Monographie des coquilles bivalves et fluviatales de la rivière Ohio" (1820), "Scadiography of Ombelliferous Plants" (1840) and the "Natural Family of Carexides" (1840). Now the exceedingly rare "Autikon Botanikon" (1840), a two-hundred-page volume, nomenclaturally touching all parts of the world, is available, having been lithoprinted in 1942 under the auspices of the Arnold Arboretum. Because of the cheap, often badly discolored or foxed paper on which many of Rafinesque's works were printed, the modern lithoprint reproductions are much clearer and much easier to consult than are the originals, and are thus even to be preferred to the originals, except from the standpoint of a bibliophile.

Reasons for the great scarcity of many of Rafinesque's publications are the original limited editions (for the "Flora Telluriana" he states that only 160 copies were printed and this probably applies to the "Sylva Telluriana" and the "Autikon Botanikon"), the time and method of publication, the fact that his contemporaries looked on his publications as worthless and thus to be ignored, and his death in 1840 at the height of his publishing career. Rafinesque being in debt at the time of his death, his effects were sold at auction to meet the demands of his creditors and the evidence available seems to indicate that much of his unsold stock of publications was utilized as waste paper. In any case, the "Herbarium Rafinesquianum," published in Philadelphia in 1833, is apparently represented in American libraries by the single complete copy at the New York Botanical Garden and a partial copy containing 44 of its 80 pages at the Arnold Arboretum. Of the "Autikon Botanikon" only about ten or twelve copies are known in all libraries, while the "Flora Telluriana" and the "Sylva Telluriana" are apparently nearly as rare as the "Autikon Botanikon."

Attention is called to the fact that in various scattered papers and volumes published by Rafinesque, there are apparently between 1,200 and 1,500 new, validly published, generic names and binomials that are not as yet listed in "Index Kewensis." Thus, although the numerous generic names in the "Autikon Botanikon" were listed in 1929, several hundred new binomials therein published still remain to be incorporated in that standard work, over a hundred years after the names were published, while none of the numerous new names in the "Herbarium Rafinesquianum" and the "Good Book or Amenities of Nature" (1840) is listed in any of our botanical indices.

In view of the fact that many of Rafinesque's pamphlets and books contain the valid publications of a great many new generic names and binomials—and no matter what the status of these entities may be, their actual publication over a hundred years ago places them in a category that must be considered because of the universally accepted homonym rule in botany—it is highly desirable that all these names be listed. Work on this project is being prosecuted, but it is a complicated matter, as it involves a critical examination of all the very numerous technical botanical papers that Rafinesque published, and it is often difficult to locate copies of essential items. But to make Rafinesque's more important works generally available to working botanists everywhere it is highly desirable that certain other works published by him, particularly the "Herbarium Rafinesquianum" (1833), the "Flora Telluriana" (1837–38), the "Sylva Telluriana" (1838) and the "Good Book" (1840), be reissued in modern facsimile editions. The new data published in these works issued over a hundred years ago touch all parts of the world, a fact that has not been realized by many American and practically all European, Asiatic, African, Australian and South American botanists because these Rafinesque publications are even more rare in foreign libraries than they are in those of the United States. Whether or not it may be possible to reproduce some or all of these works will depend in part on support extended to the recent lithoprint facsimile reproduction of the "Autikon Botanikon." Clearly the prices for these modern reproductions must be kept low if these works are to be made generally available. In my judgment the price should not exceed $0.015 per page, which is in very sharp contrast to over $0.30 per page charged for one modern reproduction of a sixteen-page Rafinesque pamphlet and from $0.03 to $0.10 per page for still others; and all these are scientifically of much less importance than is the "Autikon Botanikon."

E. D. MERRILL

QUOTATIONS

ARTIFICIAL ANTIBODIES

IN vitro synthesis of type specific anti-pneumococcus precipitins and agglutinins has been reported recently by Pauling and Campbell[1] of the Department of Chemistry, California Institute of Technology. Sub-

[1] Linus Pauling and Dan H. Campbell, SCIENCE, 95: 440, April 24, 1942.

stances simulating specific antibodies formed outside the animal body were demonstrated thirty years ago by Russian immunologists. Ostromyschlenski and Petroff,[2] for example, incubated a mixture of diphtheria toxin and normal horse serum and obtained an end product with all the therapeutic properties of diphtheria antitoxin. By incubating diphtheria toxin with different protein fractions of normal horse serum, Kryshanowski[3] prepared two artificial diphtheria antitoxins of different therapeutic value. By somewhat different technics, Sdrawosmisslow[4] and Kimmelstiel[5] incubated diphtheria toxin with commercial trypsin and reported the successful test-tube synthesis of a "toxin trypsinate" with the therapeutic properties of an anti-diphtheritic serum. In anticipation of future commercial value, artificial antitoxin made by incubating diphtheria toxin with normal serum plus pancreatin was promptly patented in Germany.[6]

By substituting bacteria for diphtheria toxin, other Soviet investigators[7] successfully synthesized specific agglutinins, bacteriolysins and complement deviating antibodies. This technic was promptly appropriated by German botanists,[8] mainly to avoid the trouble and expense of experimental animals. They incubated plant juices with normal serums and reported the production of artificial precipitins, interchangeable with natural immune precipitins, in their study of biochemical plant relationships. While most of these artificial precipitins were of low titer, Sasse[9] obtained an occasional product with which plant juices could be identified in dilutions as high as 1:6,400. Many unexpected overlapping specificities, however, were reported by other investigators,[10] suggesting plant relationships differing from those suggested by natural immune serums.

The first artificial precipitin for an animal protein was prepared by Kabelik[11] of Czecho-Slovakia. He, however, believed that his synthetic product was not a true antibody but only a biochemical precursor of such an antibody. This conclusion was confirmed by Manwaring,[12] who found that artificial precipitins formed by incubating one part of horse protein with twenty parts of normal rabbit serum usually show zone reactions and other qualitative differences from natural immune precipitins. He concluded that "hybridization" of horse proteins in artificial serum mixtures represents but the initial stage in the natural production of specific antibodies, necessitating the assumption of secondary and tertiary stages in the natural synthesis. It also seemed necessary to assume a continuous, quasi-proliferative process in order to account for the relatively high titer in experimental animals. This proliferative process was conceivably similar to the quasi-proliferation of bacteriophage in symbiosis with bacterial cells.

Subsequent advances in immunochemistry, particularly determination of the chemical nature of haptens and protein molecules, have made possible to-day the formulation of a more definite theory. Pauling,[13] for example, called attention to the fact that globulin molecules are "unfolded" or "uncoiled" under the influence of certain physical or chemical agents much in the way a fern leaf uncoils on approaching maturity. On removal of these conditions the unfolded molecule is again "coiled" to its original surface specificity. Pauling assumes that in the presence of a foreign antigen the refolding is atypical, the globulin molecule coiling around and assuming a surface configuration "complementing the surface regions of the antigen." Dissociated from the adherent antigen, the refolded globulin now functions as a specific antibody or specific receptor for the antigen. Artificial antibodies therefore differ from normal serum globulins only in the way in which the polypeptide chain is refolded or recoiled. This concept is in accord with data currently reported by Wright,[14] who concluded that "horse antibody protein is essentially the same as horse gamma globulin."

In order to test this theory, Pauling and Campbell attempted to prepare antibodies against antigens of known chemical composition. They selected certain antigenic dyes, for example, and type III pneumococcus carbohydrate, bovine gamma globulin being the normal serum protein used in most of their tests. Successful unfolding and refolding of gamma globulin is readily effected by several methods, such as the addition of alkali and slow return to neutrality, the addition and slow removal of urea, or by heating to 65° C. and slowly cooling. Their most satisfactory yield, however, was obtained by incubating the gamma globulin-antigen mixture for several days at 57° C., a process similar to that originally adopted by the Soviet immunochemists.

In a typical experiment, 1 per cent. type III pneumococcus polysaccharide was added to a 1 per cent. solution of bovine gamma globulin and the resulting mixture held at 57° C. for fourteen days. The mixture

[2] Ostromyschlenski and Petroff, *Russ. Gesellsch. f. physical. Chem.*, 47: 263, 1915.

[3] W. N. Kryshanowski, *Centralbl. f. Bakt.*, 110: 1, 1929.

[4] W. H. Sdrawosmisslow and N. E. Kastromin, *Ztschr. f. Immunitätsforsch.*, 54: 1, 1927.

[5] D. Kimmelstiel, *Ztschr. f. Immunitätsforsch.*, 62: 245, 1929.

[6] Patent No. 293055, class 30 h. group 6.

[7] W. M. Sdravomysloff and N. Kistromine, *Bull. Inst. Pasteur*, 21: 941, 1923. N. I. Bashkirzev, *Ztschr. f. Urol.*, 23: 92, 1929.

[8] C. Mez and H. Ziegenspeck, *Botanisches Arch.*, 12: 163, 1925.

[9] F. Sasse, *Beitr. z. biol. Pflanzen*, 16: 351, 1928.

[10] E. Nahmacher, *Beitr. z. biol. Pflanzen*, 17: 1, 1929.

[11] J. Kabelik, *Biologicke liste* (Prague), 1927, p. 31.

[12] W. H. Manwaring, *Jour. Immunol.*, 19: 155, August, 1930.

[13] L. Pauling, *Jour. Am. Chem. Soc.*, 62: 2643, 1940.

[14] G. G. Wright, *Jour. Infect. Dis.*, 70: 103, March–April, 1942.

was then freed from pneumopolysaccharide by a precipitation or salting out method. The resulting free modified gamma globulin ("purified antibody") was found to precipitate type III pneumopolysaccharide *in vitro* but gave negative reactions with type I or type VIII polysaccharide. The modified gamma globulin would also agglutinate type III pneumococci *in vitro* but not types I or II. Mouse protection tests and swelling tests have not yet been carried out.

The earlier Russian attempts to synthesize specific antibodies were mainly undertaken for their theoretical interest, since substitution of relatively low titer artificial antibodies for high titer natural immune serums was of little clinical promise. With the wide use of human plasma banks at the present time, however, practical interest is aroused. If a conversion of normal human plasma globulins into immune globulins is feasible, artificial immune human plasma banks may become a subject of future clinical research. In this eventuality the California biochemists will have rendered a distinct service to clinical medicine by suggesting a definite chemical theory to replace the tentative metaphors of the earlier immunologic theorists.—*Journal of the American Medical Association.*

SCIENTIFIC BOOKS

THE FOURIER SERIES

Fourier Series and Orthogonal Polynomials. Number Six of the Carus Mathematical Monographs. By DUNHAM JACKSON. viii + 234 pages. Chicago: Open Court Publishing Company. 1941.

THE topics dealt with in the above monograph bulk large both in the literature of pure and of applied mathematics. The study of Fourier series and related developments in orthogonal functions, together with their application to problems of mathematical physics, dates back to the middle of the eighteenth century. Such study has had a continuous development since that time at the hands of many mathematicians of first rank, as well as lesser lights, and continues to be a live and important part of current mathematical research.

In preparing a book of moderate size on subject-matter of such scope which will be within the comprehension of readers having an adequate grasp of the calculus, the problem of selection of material is a difficult one. No two writers would be likely to make precisely the same selection, but the reviewer agrees in the main with the judgment of the author. The theory of Fourier series itself is dealt with in sufficient detail to enable the reader to appreciate the analytic difficulties that arise in justifying mathematically the formal solutions of the important boundary problems in mathematical physics. Other developments of greater complexity, such as the Legendre and Laplace series and the developments in Bessel functions are naturally treated with less detail but are dealt with in such a manner as to exhibit their analogy with trigonometric series.

In most cases the rigorous treatment of the properties of the development in question, needed to justify the formal solutions of the physical problems, are available in other literature cited by the author when not given in the book. An exception is found in the case of the developments in Bessel functions. One would naturally expect that reference to a work of such an encyclopedic character as Watson's "Theory of Bessel Functions" would cover this point, but this is not the case. For most of the standard boundary value problems, the uniform convergence (or the uniform summability by some regular method) of the development in the neighborhood of the origin is needed to justify the formal solutions. Such uniform convergence and uniform summability have been established in two papers by the reviewer.[1] They can not be inferred from the discussion of convergence and summability in Watson's treatise or from other standard discussions of these questions.

From the standpoint of readers of SCIENCE who are more interested in the application of the theory of orthogonal functions to the solution of boundary value problems of mathematical physics than in the mathematical refinements of the subject, a valuable feature of the book is found in the rapid but elegant approach to such application that is found in Chapters IV and V. It is quite feasible to begin with these chapters and take up later the more delicate questions of analysis that are involved. The references to preceding chapters that are contained in the chapters in question facilitate such a process.

It is natural to expect that in a book on orthogonal functions by one of the leading authorities on orthogonal polynomials a considerable percentage of space would be devoted to the theory of such polynomials, and this is the case. In addition to the discussion of Legendre polynomials, to which reference has been made, there is a chapter on the general theory of orthogonal polynomials, followed by separate chapters on Jacobi polynomials, Hermite polynomials and Laguerre polynomials, and a chapter on the convergence of developments in such functions. In the discussion of Hermite and Laguerre polynomials applications are given which connect up with Schrödinger's wave equation.

To sum up the book as a whole, it can be regarded

[1] Transactions of the American Mathematical Society, Vol. XII (1911) and Vol. XXI (1920).