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CHEMICAL NATURE AND MODE OF FORMATION OF PEPSIN, TRYPSIN AND BACTERIOPHAGE¹

By Dr. JOHN H. NORTHROP

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THE field of enzymes has always been a sort of no-men's land between the fields of chemistry and biology. In the early days of science reactions occurring in, or caused by, living organisms were grouped together as fermentations and were supposed to be qualitatively different from the reactions of inorganic material. In the course of the nineteenth century the work of Payen and Persoz, Schwann, Kühne and Buchner and many others showed that most of these reactions were caused by the presence of unknown substances formed by the living cells, but which were not living. These substances were called "enzymes" by Kühne. Berzelius early pointed out that these reactions were very similar

to the catalytic reactions of inorganic chemistry, and the work of Tammann, Arrhenius, Henri, Michaelis, Nelson, Euler, Willstätter, Warburg and other chemists has shown that this view was correct. It is only recently, however, that enzymes have been accepted as a part of chemistry and it is very gratifying that research on enzymes should be selected for a chemical award.

The chemical nature of the enzymes themselves remained quite unknown until a few years ago. In the last eleven years a number of enzymes have been isolated and crystallized and have been found to be proteins. The hydrolytic enzymes, urease (Sumner), pepsin² (Northrop), trypsin,² chymo-trypsin² (Kunitz and Northrop), carboxypeptidase² (Anson), amylase

¹ Lecture delivered on the occasion of the presentation of the Charles Frederick Chandler Medal of Columbia University on October 27, 1937. The lecture was illustrated by lantern slides.

² Photographs of these preparations are reproduced in Harvey Lectures, 1934-35, p. 229.

AN ASBESTOS KCL BRIDGE AND A SIMPLE CALOMEL ELECTRODE

THE potentiometric determination of the O/R potential and pH at different depths in anaerobic oval tubes¹ measuring 360 mm in length and only 6×14 mm in cross section required the use of a small bore KCl bridge to form a junction between the medium and the calomel half cell. The liquid KCl bridge, the agar bridge and the ground glass sleeve commonly used for such measurements are impracticable for this purpose. Therefore an asbestos KCl bridge has been improvised which has proved to be entirely satisfactory, is easy to prepare and sufficiently sturdy to withstand sterilization. Visiting physicists and chemists who have seen this apparatus have suggested a multiplicity of applications for the asbestos KCl bridge so it is described in hopes of helping others, and without any claim for originality in the simplicity of the design.

Small threads of asbestos are freed of mineral impurities by bleaching in dilute HCl and water. Then each thread is heated to incandescence in a gas flame, after which it is sealed through the end of a glass tube of the desired length and diameter. The tubes can be filled with the KCl solution either with a long capillary pipette or by immersing in a vessel containing the hot solution and permitting it to cool.

We have prepared asbestos KCl bridges 400 mm long and only 0.2 mm in diameter, although in most of our work tubes 1.0 to 3.0 mm in diameter have been used. The asbestos thread provides for a slow leak of the KCl solution, thereby insuring a perfect ionic contact. The rate of leakage is controlled by the size of the asbestos fiber used. Satisfactory results have been obtained with tiny threads through which less than 0.01 cc of KCl solution leaks per hour.

The use of the asbestos KCl bridge was further expedited by connecting it directly to a calomel electrode, the design of which is illustrated by Fig. 1. It can be constructed in several ways, depending upon the desired dimensions of the apparatus and one's skill as a glass-blower. If the diameter of the tube AAB exceeds 3 mm, it is a matter of ease to seal on the short side-arm CD which serves as a receptacle for

the mercury and calomel. A platinum wire sealed through the bottom of the side-arm tube CD provides for an electrical connection to the potentiometer. The top of the tube AAB may be flared at E to facilitate the introduction of the KCl solution with which the apparatus is filled after the asbestos fiber has been sealed through the bottom of the tube at B. The mercury and calomel paste are placed in the side-arm CD by means of a capillary pipette.

In case it is desirable to have the tube AAB smaller than 3 mm in diameter, it has been found simpler to construct the apparatus by sealing the tube to a short length of a larger tube EF, to which the side-arm CD is connected as illustrated. However, it is possible for any amateur laboratory technician to construct the entire apparatus from a fifteen-cent Y-tube in fifteen minutes. A platinum wire is sealed in one fork of the Y-tube and will serve as the receptacle for the mercury and calomel. The other fork is pulled out in a flame to give the desired length and diameter, after which an asbestos fiber is sealed through the end. The other end of the Y-tube is flared to facilitate the introduction of the solutions and the apparatus is ready to use.

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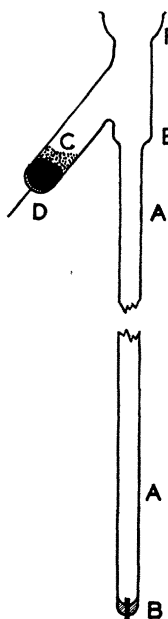


FIG. 1

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HATCH, A. B. *The Physical Basis of Mycotrophy in Pinus*. Pp. x + 168. 16 plates. Black Rock Forest, Cornwall on the Hudson, New York.
MUSKAT, M. *The Flow of Homogeneous Fluids through Porous Media*. Pp. xix + 763. 284 figures. McGraw-Hill. \$8.00.
PAGE, IRVINE H. *Chemistry of the Brain*. Pp. xvii + 444. Thomas. \$7.50.
Studies of the Institutum Divi Thomae. Vol. I, No. 1. Pp. 135. Illustrated. Institutum Divi Thomae, The Athenaeum of Ohio, Cincinnati, Ohio.
Television. Pp. viii + 452. Illustrated. RCA Institutes Technical Press, New York.
WELD, LEROY D., Editor. *Glossary of Physics*. Pp. x + 255. McGraw-Hill. \$5.00.
YATES, RAYMOND F. *These Amazing Electrons*. Pp. vii + 326. Illustrated. Macmillan. \$3.75.

Erratum: In the article by H. L. Hodes, G. I. Lavin and L. T. Webster, entitled "Antirabic immunization with culture virus rendered avirulent by ultra-violet light," printed in the issue of SCIENCE for November 12, 1937, the line "fatal dose of test virus, as contrasted with only one of" immediately before the table on the first column of page 448 was misplaced in the paging. It should be transferred to make it the last line of the text in that column.

¹ S. C. Rittenberg, D. Q. Anderson and C. E. ZoBell; *Proc. Soc. Exp. Biol. and Med.*, 35: 652, 1937.

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