globin by X-ray methods. The present position is that while projections of the molecule are available which tell us how much material lies in the line of sight in a given direction, more detailed information can only be obtained by making projections of thin slices of the molecule.

Certain specific groups have, however, been located by labelling them with heavy-metal atoms which show up on X-ray diffraction analysis. It has been found, in this way, that the —SH groups of horse hæmoglobin are arranged in close pairs. As Riggs in the United States has recently shown that the —SH and hæm groups have a close functional relationship, it is not impossible that they may be close to one another in the molecule.

Very recently a striking new advance has been made in the study of sickle-cell anæmia. In this condition the hæmoglobin differs from normal in the number of its —SH groups, its solubility and in the remarkable property of forming a gel on reduction. Dr. Ingram has now found, using a combination of paper chromatography and paper electrophoresis, that a peptide appears regularly among the products of tryptic hydrolysis of sickle-cell hæmoglobin which is not present in similar hydrolysates prepared from normal human hæmoglobin. As sickle-cell anæmia is the result of change in a single gene and is inherited in a strict Mendelian way, the possibilities of an increase in our understanding of the relation between genes and proteins synthesis are obvious.

After an interval, Prof. Q. H. Gibson described some applications of flash photolysis to the study of hæmoglobin kinetics. The observations, so far, have been made with a simple apparatus in which the solution to be examined is exposed to the photolysis flash in an integrating sphere and the changes in light absorption are recorded by means of a continuous light source, photocell, and cathode-ray oscillograph. The systems studied are arranged so that at equilibrium the chief compound present is carboxyhæmoglobin, which, as is well known, is sensitive to light. On firing the photolysis flash, this carboxyhæmoglobin is caused to dissociate, setting free reduced hæmoglobin. After the flash ends, the recombination of the reduced hæmoglobin with carbon monoxide or with other ligands forming compounds less stable than carboxyhæmoglobin can be studied.

One application of the method has led to a dramatic confirmation of the difference in kinetic properties between the different intermediate compounds of carbon monoxide with hæmoglobin. By reducing the power of the photolysis flash, partially saturated intermediates can be formed in the solution in calculable quantities. It is found that when large proportions of the intermediate $Hb_4(CO)_3$ are formed, the recombination reaction involving the addition of the fourth and last molecule of carbon monoxide to combine takes place up to sixty times faster than when only fully reduced hæmoglobin is present. It is satisfactory that such good agreement can be reported between the widely different approaches to the kinetic problem described at this meeting, since this rapid reaction was predicted from measurements of the upper end of the dissociation curve and the velocity of dissociation of the first molecule of carbon monoxide from fully saturated hæmoglobin.

Another application reported was to the study of hæmoglobins from invertebrates. Here the advantage of the flash method is its economy in material. This economy must now be approaching its highest possible degree, since the same material can be used repeatedly in duplicate experiments or in runs under altered conditions. It is interesting to reflect that in the thirty-three years since Hartridge and Roughton made the first measurements of the reaction velocity of hæmoglobin with gases, the pigment requirements have been reduced some 100,000 times. It is now readily possible to examine the hæmoglobin from a single specimen of *Arenicola*, say, or of *Chironomus*, but it would seem that several specimens of *Daphnia* would still be needed.

In the final paper of the meeting, Prof. F. J. W. Roughton described the application of some of the kinetic work to the problems of passage of gases from the alveoli into combination with the hæmoglobin. This process, at first sight deceptively simple, must in fact be split up into a number of component steps, each of which plays its part in determining the rate of the overall process. The gas molecules concerned must first diffuse through the alveolar membrane, then through the plasma to the erythrocyte, through the cell membrane of the latter, and finally through the interior of the cell until they meet a hæmoglobin molecule with a vacant gas-binding group.

It has now been possible to evaluate the importance of each of these factors in contributing to the final physiological result. It has been found that the resistance of the alveolar membrane and the resistance in the erythrocyte contribute about equally to the difficulty met with in the uptake of carbon monoxide or oxygen from the alveoli into combination with hæmoglobin. In the erythrocyte, the chemical combination reactions with oxygen and nitric oxide are so rapid that the actual rate of gas uptake is determined primarily by the rate of diffusion through the red-cell membrane and the interior of the cell modified only slightly by the rate of the chemical reaction. With the slower reaction of the displacement of oxygen by carbon monoxide, the rate of the chemical reaction already plays an important part; and when we come to consider the dissociation of carboxyhæmoglobin the picture is reversed, the chief rate-limiting factor now being the chemical reaction, which is slow as compared with the rates of diffusion in the blood and across the membranes.

The new quantitative descriptions of the exchange processes in the blood and lungs have been applied to determine anew the diffusing capacity of the lung membranes and the volume of blood in the lung capillaries. The greater certainty about these processes should lead to advances in fields as diverse as clinical medicine, long-distance running, and in knowledge of how life is carried on at high altitudes.

OBITUARIES

Prof. Carl Neuberg

On May 30 Prof. Carl Neuberg died in New York at the age of seventy-nine. With Neuberg's death ended a succession of brilliant German organic chemists, born and trained in the last century and devoting their life-work mainly to the application of newly developed chemical methods to the study of the components of living matter, their composition, structure and metabolic changes; among them were Friedrich Wöhler, Justus v. Liebig, Felix Hoppe-Seyler, Adolf v. Bayer, Albrecht Kossel, Emil Fischer, Franz Hofmeister and Richard Willstätter.

Equipped with a broad knowledge of, and deep insight into, organic chemistry, possessed by a passionate interest in the material changes of living matter and endowed with a rare skill for devising methods suitable to a direct approach to the problem, Neuberg was one of the founders of modern biochemistry.

Born on July 29, 1877, at Hannover (Germany), he received his scientific training in the Universities of Berlin and Würzburg. In 1898 he joined E. Salkowski in the Chemical Division of the Pathological Department of the University of Berlin; in 1909 he was appointed head of the Chemical Unit of the Department of Animal Physiology at the Agricultural College, Berlin, and in 1913 he became assistant director of the Kaiser Wilhelm Institute for Experimental Therapy under August v. Wassermann, whom he succeeded in 1925. The Institute became one of the foremost centres of biochemical research. Although Neuberg had given signal service to his native country both in peace and in the First World War, he was forced by the Hitler regime to leave it in 1939. He found refuge in the United States, where he was at first research professor at the College of Arts and Sciences of New York University and then professor at the Brooklyn Polytechnic Institute and at the New York Medical College.

Neuberg's main contribution to science was the elucidation of the principal mechanism underlying alcoholic fermentation of sugar by yeast. This process, though the subject of violent controversy between the most illustrious chemists of the last century, remained an unsolved mystery until Harden and Young in London and the Neuberg school at Berlin entered the field. The first step in unravelling the integrated series of reactions by which the carbon chain of the sugar molecule is disrupted was the demonstration that pyruvic acid is readily and quantitatively transformed to carbon dioxide and acetaldehyde by a yeast enzyme named carboxylase. The next step was the trapping by sodium sulphite of the intermediary acetaldehyde in the course of glucose fermentation. The hydrogen becoming available through the formation of the carboxyl group of pyruvic acid, but deprived of its physiological acceptor acetaldehyde, was traced in glycerol, produced in stoichiometric quantity to the trapped acetaldehyde. The interpretation of these findings was given by Neuberg in a fermentation scheme the main features of which were: (1) dehydration and de-aldolization of one mole D-glucose to two moles of a 3-C-aldehyde assumed to be methylglyoxal, (2) oxidation of the ketoaldehyde to pyruvic acid, and (3) reduction of the decarboxylated pyruvic acid to alcohol.

The concept of alcoholic fermentation as the balanced sequence of an energy-yielding dehydrogenase reaction and a reaction in which a hydrogen acceptor derived from the first reaction combines with the hydrogen atoms released proved to be one of the most fruitful theories in the realm of fermentation and respiration. Neuberg demonstrated clearly that the end-products of sugar fermentation by yeast vary with the nature of the hydrogen-accepting system available. The ideal fermentation equation of Gay-Lussac is never verified because yeast on metabolizing sugar forms a variety of competing hydrogen-acceptors, their quality and quantity depending on the conditions imposed. Neuberg realized the key position of pyruvic acid in the metabolism of fungi and bacteria and ascribed the great diversity of products formed in the various types of fermentation mainly to the formation of a wide range of hydrogen-acceptors from pyruvic acid. It may be said with confidence that the production of pyruvic acid, isolated in high yield from fermenting sugar solutions by Neuberg in 1929, is the central stage of a carbohydrate degradation pathway very common in living cells; this central stage is preceded by phosphorylating and desmolatic steps and followed in respiration by the Krebs cycle, in fermentation (glycolysis) by reduction of pyruvic acid or a derivative thereof.

In addition to carboxylase, Neuberg discovered the enzymes β-glucuronidase, methylglyoxalase, phenolsulphatase, chondrosulphatase, polyphosphatase and metaphosphatase. His wide interest and experimental skill are documented by many other notable achievements. Among them are studies on the structures of raffinose, inositol and phytin, first non-enzymatic preparation of phosphorylated sugars and amino-acids, discovery of fructose-6-phosphate (Neuberg ester), first observation of the carboligatic reaction and synthesis of the various phosphoglyceric acids.

Neuberg's work has done much to shape present trends in biochemistry and his contributions to knowledge will long be remembered. In 1906 he founded the *Biochemische Zeitschrift* and edited no less than 278 volumes in the next thirty years. Among the many honours bestowed upon him were the Emil Fischer, Delbrück, Pasteur, Berzelius, Scheele and Leblanc Medals, and the Carl Neuberg Medal established by the American Society of European Chemists and Pharmacists in 1950. He received several honorary degrees, and was a member of many scientific academies. Of Neuberg may be said what he himself said at the funeral of his predecessor A. v. Wassermann in 1925: "He belonged to the small band of scientists who visibly moved the hand of the clock recording the advancement of science".

ALFRED GOTTSCHALK

Dr. Gunnar Dahlberg

DR. GUNNAR DAHLBERG, who died on July 25, was born in Lofta, Sweden, in 1893 and was educated in the University of Upsala, graduating M.D. in 1926. It was in Upsala where his career was spent, for he was director of the Statens Rasbiologiska Institut there from 1936 until his death. He was also dean of the Faculty of Medicine at Upsala during the critical year 1939–40 when Swedish mobilization faced the University with administrative problems, into which he threw his energies with enthusiasm as one of the leading Swedish intellectuals with uncompromising hostility to the Nazi challenge. From the start a vigorous critic of the Nazi creed, he was at all times a friend of the British cause when the Second World War became inevitable. In 1948 he received from Britain the King's Medal for Service in the Cause of Freedom in recognition of the part he played.

As a man of science, Dahlberg is remembered for his early work on twin resemblance, his pioneer publications on the genetical theory of inbreeding and more especially for his concept of the population isolate. Above all, he strove to develop human genetics as a branch of medical science dissociated from its discreditable associations with racialist propaganda. He edited a monumental semi-popular