tography was resumed. Since the total length of the chromosome was 25 to 30 μ, the 7-μ microspot covered between one-third and one-fourth of its length.

Immediately after irradiation, the bombarded chromosome segment appeared "pale"; that is, its index of refraction was changed so that it no longer appeared blackish by medium-dark phase-contrast microscopy. This "paling" intensified for 20 or 30 min after irradiation and usually came to extend beyond the irradiated segment, so that frequently a considerable fraction of the irradiated chromosome appeared only as a colorless "ghost." Aside from its intrinsic interest, this phenomenon served as a valuable check on the accuracy of the aiming.

In each of 20 chromosomes (group A), the irradiated segment included the kinetochore; the exposure was 3 min. In 15 other chromosomes (group B), the kinetochore was excluded from the irradiated segment; 10 were exposed for 3 min, and the rest for 6 min. Without exception, those of group A failed to join the metaphase plate and drifted until anaphase (Fig. 1). After anaphase, each of these drifters was squeezed into one of the daughter cells by the constriction of the cytoplasm and formed either an accessory nucleus or a lobe on one of the main daughter nuclei. By contrast, all chromosomes of group B joined the metaphase plate before anaphase, even though some of them were exposed twice as long as group A. Moreover, this migration to the plate, in contrast with the drifting after kinetochore irradiation, was normally directed; that is the kinetochore proceeded foremost, with the two "legs" of the chromosome trailing behind.

This experiment shows that when parts of chromosomes are exposed to ultraviolet light, the normal directed movement of the chromosome from centrosome region to metaphase plate is inhibited only if the kinetochore is included in the irradiated part.

Work is in progress to improve visual observation during bombardment by equipping the apparatus with phase-contrast and dark-field illumination. This will permit the use of smaller microspots to determine how well the ultraviolet-sensitive entity corresponds to the morphological kinetochore. Work is also in progress to utilize monochromatic radiation and to measure the energy in the microbeam.

References and Notes

* National Science Foundation Fellow.
1. R. E. Zirkle and W. Bloom, *Science* **117**, 487 (1953).
2. This work was supported by grants from the U.S. Atomic Energy Commission, the Office of Naval Research, and the Abbott Research Fund of the University of Chicago. We are grateful for assistance from Theresa Panny and Robert P. Perry.
3. S. Tschachotin, *Biol. Zentr.* **32**, 623 (1912).
4. ———, in Abderhalden, *Handbuch der biologischen Arbeitsmethoden* 3 (Urban and Schwarzenberg, Berlin, 1938), p. 877.
5. Also see the discussions by H. J. Muller (U.S. Pat. No. 1458143) and by S. Zamenhof (*Rev. Sci. Inst.* **14**, 17, 1943). Tschachotin's technique was extensively used by F. Seidel [*Arch. Entwicklungsmech. Organ.* **132**, 671 (1935)] in experimental embryology.
6. In case the amount of refracting material is not negligible, it can be compensated by suitably adjusting the position of the primary aperture.
7. Details of the apparatus will be described and discussed elsewhere.

Rudolf Höber: His Life and Scientific Work

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PHYSIOLOGY lost another of its great leaders when, on 5 September 1953, in Philadelphia, Rudolf Höber passed away. It was my privilege to work with him years ago in the Kiel laboratory and to see him frequently after he came to America. More than any other man, he has been to me my master in science. He was a fine and true spirit of intelligence and human sympathy, who stimulated the scientific work of a great group of students and colleagues. Through his books and publications, he has had a truly international influence.

Höber was born in Stettin, Germany, on 27 December 1873. From early childhood he was devoted to natural science, spending much time in collecting plants and minerals and in microscopic studies. He early read Darwin and other biological classics. He decided to study medicine, not to practice, but to prepare himself for a life of teaching and research. He attended the Universities of Freiburg, Berlin, and Erlangen. In 1898 he graduated in medicine at Erlangen.

Soon after taking his medical degree, Höber joined the staff of the Physiological Institute of the University of Zürich, directed by J. Gaule. His first scientific paper, an experimental study of wound shock, appeared in 1898. During the next 10 years there followed more than 30 papers from his own pen. At the same time, 22 graduate students wrote their doctoral theses under his direction. Höber's interest ranged broadly over his field. His work included studies of intestinal resorption, the mechanism of catalysis, the permeability of cells, the hydroxyl ion concentration of the blood, the mechanism of narcosis and its influence upon permeability, vital staining, the secretion of the urine, the physiological significance of the colloids, and the effects of ions upon the resting potential of nerve and muscle.

During this period, Höber's basic scientific interest

became fully defined. He wished to understand the nature of the cell membrane, its physicochemical structure and composition, its electric properties, its ability to permit or prevent the movement of material into the cell, its change in permeability during excitation. To this end, he devoted much study to Overton's theory of lipoid solubility (1895) as an explanation for the differing penetrations of various organic substances into cells. He pointed out exceptions to the rule, while supporting the idea with many new experimental demonstrations. He was also intensely interested in Bernstein's "membrane hypothesis" (1902), which explained the electromotive forces of living tissues as due to a selective ion permeability in the membranes combined with ionic gradients across them, particularly of the potassium ion. He brought extensive experimental support to this conception, and his name is sometimes linked with Bernstein in describing the hypothesis. He lived to see hypothesis grow to theory and then to generally recognized fact. At the end of his life, he was delighted to follow the modern forms of the theory, such as have been presented by Hodgkin and Huxley, Curtis and Cole, and other recent investigators. While recognizing the validity of Overton's views for the penetration of organic nonelectrolytes, he strongly insisted upon the necessity for a complementary "pore theory" to explain many of the known facts of permeability, particularly for ions.

Höber's crowning achievement while at Zürich was the production of his monograph entitled, *Physikalische Chemie der Zelle und der Gewebe*. The first edition, in 1902, was a thin volume of 300 pages. The book went through seven editions, growing finally to 900 pages in the 1926 issue. This work established his reputation as an international authority in the field that is often called "general physiology." Although widely consulted in Britain and America, it was never translated into English. It antedated by 13 years the first edition of *Principles of General Physiology*, published in England in 1915 by Sir William M. Bayliss. Somewhat similar in scope and manner of treatment these two monographs have had a great influence in extending basic studies in physiology.

It is interesting to note that the determination to write a monograph came to Höber while he was still a student at Erlangen. His uncle, Isadore Rosenthal, was professor of physiology there. Rosenthal put into his hands Nernst's *Lehrbuch für Physikalische Chemie*. The idea then grew in his mind that he must attempt to apply physicochemical principles to living cells. He established contact with Nernst and had his help in devising apparatus. He was also influenced by the writings of Claude Bernard, Virchow, Ehrlich, and Helmholtz. He greatly admired the work of Jacques Loeb and maintained correspondence with him.

In all of his scientific interests, Höber was ably assisted by his devoted wife, Josephine, neé Marx, who completed the study of medicine after their marriage in 1901. She was one of the first women physicians in Germany. She not only directed his household and raised their son, Johannes, and two daughters, Gabriele and Ursula, but carried on a medical practice at the same time that she collaborated in some of his experiments.

In 1909 Höber left Zürich to go to the Institute of Physiology in Kiel, directed by Hensen, codiscoverer of glycogen. His old boyhood friend, Albrecht Bethe, shortly succeeded Hensen, and Höber was advanced to a full professorship in 1912. He followed Bethe as director in 1915, when the latter was called to Frankfort. In spite of increasing administrative responsibilities, his scientific productivity continued. His laboratory became a rendezvous for a long succession of graduate students and younger colleagues. Many came from Japan, Russia, Scandinavia, and America in addition to the more numerous groups from Germany, Austria, and Switzerland. In his view they were his fellow-students, partners in a research team. He was accessible to all, democratic in attitude, generous with aid and counsel, always interested in their problems.

In his work with medical students Höber was an outstanding teacher, speaking clearly and simply, with a lively sense of humor, much beloved by them. For their instruction he produced, in 1919, the first edition of his *Lehrbuch der Physiologie des Menschen*, which went through eight editions and became a popular textbook throughout Germany. It continued to be used long after he left Germany, the final edition being printed in Switzerland in 1939.

In 1918 Höber joined Abderhalden and Bethe to form the famous triumvirate that edited *Pflügers Archiv* over many years (1918–34). In it were reported many studies done in his laboratory. In a single decade (1924–33) we find there a series of 30 papers dealing with permeability studies done on perfused frog kidneys. Höber's interest was not primarily in the special physiology of the kidney. He used this organ, rather, as a means to attack more fundamental problems of general physiology. In the same spirit he perfused other glands, such as the liver, studying the role of lipoid solubility, of molecular volume, and of electric charge in the penetration of various substances through the gland cell membranes.

In recollection of Höber's technical skill, we may mention his measurement of the internal electric conductivity of living cells (1910). With the aid of Walter Nernst, he modified the Wheatstone bridge by the introduction of condensers into two arms. At high frequencies of the oscillating current, cell suspensions introduced between the condenser plates caused increases in capacity that demonstrated a considerable internal conductivity. Höber concluded that a substantial fraction of the intracellular electrolytes are present in free solution, and not held in organic union, as had previously been believed.

Between 1925 and 1932 Höber served twice as dean of his medical school. In 1929, as president of the German Physiological Society, he paid his first visit to the United States, attending the XIII International Physiological Congress in Boston. After the congress he spent some time at the Marine Biological Laboratory at Woods Hole, a place to which he was later to return through many summers. As his final honor in Kiel, he served as rector of the University in 1930–31.

Although devoid of political connection and interest, Höber was forced at this time to oppose the rising tide of Nazism among the students. In the spring of 1931 a group of these students threw stench bombs into the church as the Reverend Otto Baumgarten, an outstanding Lutheran clergyman and pacifist and chaplain of the University, was conducting services. Fourteen Nazi students, caught by the police, were tried before a disciplinary court under Höber's chairmanship. Six were expelled from the University. There was general approval of the action, but Höber gained the bitter enmity of the Hitler group. Within a week after Hitler came to power, on 5 March 1933, Höber's laboratory was occupied by Nazi students. He was confined to his residence on the second floor of his Institute, with permission to go only to his study on the first floor. These restrictions were shortly lifted and he was able to resume lecturing at the beginning of the summer semester. His return to the lecture platform was greeted by an ovation from his students. But 4 months later, in September 1933, he was forced into retirement by the German Ministry of Education. Some vestige of German honor still moved the Nazi officials, for his pension was regularly paid until the time of Pearl Harbor.

Höber's plight became quickly known in England, where the press carried the story. He immediately received an invitation from the University of London. Leaving Germany at the end of September 1933, he worked for a few months with A. V. Hill, at University College. In the Spring of 1934 he received an invitation to join the staff of the Department of Physiology, School of Medicine, University of Pennsylvania, in association with H. C. Bazett and M. H. Jacobs. He and his wife soon reached America, accompanied by their daughter, Ursula, who continued her medical education at Pennsylvania, graduating in 1937. During the next few years Höber was able to assist the emigration to America of his son, Johannes, and his daughter, Gabriele, with their families. The time of stress and strain was finally over. In his last years he was happy in his circle of seven grandchildren.

In Philadelphia the Höbers created a new home and a new scientific life. Höber was able to resume his beloved teaching and research, with assistants financed by special grants. During the next 14 years he published 30 more papers, mostly in collaboration. In 1945, with David Hitchcock, John Bateman, David Goddard, and Wallace Fenn, he issued a symposium volume with the same title as that of his famous German monograph, *Physical Chemistry of Cells and Tissues* (Blakiston). He dedicated it to his wife "who inspired and encouraged me to create a renaissance of my previous book, and passed away too early to see it come to life." He here brought together his final summary of the various factors that determine the penetration of substances into cells and of the chemistry and physics of the plasma membrane. His basic faith in the importance of such analysis had never wavered, during half a century. He stated his conviction in the preface to this volume, as follows.

> It is not only possible, but of importance, to anchor physiology even deeper in physical chemistry than was done previously, *i.e.*, even closer to the fundamentals, on which our concepts of inorganic nature are erected . . . when one tries to segregate the elementary processes combined in the life of a cell and to analyze them with the new tools of modern physics, this attitude makes more discernible the great number of unsolved problems.

Soon after he reached America, I invited Höber to join the staff of the summer course in physiology at the Marine Biological Laboratory. He accepted at once and joined us with great interest and enthusiasm. His initial difficulties with spoken English could never mask his intense devotion to his scientific field and his mastery of it. He was soon speaking fluently, and his lecture hall was always crowded. He spent long hours with our students and was interested in every experiment that they did, recapturing in the new land his zeal for teaching. After the course his own experiments, with his wife's help, went actively forward. He was a veritable dynamo of intellectual power. He came back to Woods Hole last in 1949, at the age of 76, weakened in body and in mind by the passage of the years, but still eagerly attending the physiology lectures and engaging in scientific discussions.

Höber never returned to Germany, although he was often invited to do so. I went back to Kiel in 1947 and revisited the shattered city. The old laboratory is now a ruin, blasted by bombs that left only remnants of the walls. The basic science departments of the medical school of the University of Kiel have moved to new quarters. There a new Institute of Physiology has been created, named the "Rudolf Höber Haus," to perpetuate through the years the memory of the inspired teacher and investigator whose devotion gave us new insights into physiological function.