The Academy and the Biological Sciences

The Academy has played a major role in promoting research projects in the humanities and applied physics. Its influence on biological research has been less direct. By electing the Board of Directors of the *Carlsberg Foundation*, it has, however, influenced the biological sciences in a decisive way. Up to the Second World War the development of biochemistry in Denmark was more or less synonymous with the research carried out at the *Carlsberg Laboratory*. Also, genetics and cell biology in this country owe a great deal to that laboratory.

The Laboratory consists of two sections, a Department of Chemistry and a Department of Physiology, which happen to have had men of great talent as leaders. The Foundation chooses from among its own Board members three natural scientists who, together with two adjunct members, consitute the Board of Trustees of the Carlsberg Laboratory. Although connected with a large industrial enterprise, research in the Carlsberg Laboratories has largely been of a basic and fundamental nature; but applied research has also been carried out. All the heads of departments of the Carlsberg Laboratory throughout its existence have been members of the Academy.

There are two periods in which biological

research has flourished in Denmark, these being the second half of the 17th century and, some 300 years later, in the present century.

ANATOMISTS

The first period of biological research in Denmark, which occurred before the founding of the Academy but should nevertheless be mentioned, was dominated by the scholars THOMAS BARTHOLIN (1616–1680) and NIELS STENSEN (NICOLAUS STENO) (1638–1686). In 1652 Bartholin described the human thoracic duct, and in 1654 the lymph vessels, to which he gave the name *vasa lymphatica*. This original discovery was made simultaneously by OLOF RUDBECK in Uppsala. Bartholin wrote a textbook of anatomy that appeared in 30 editions in a number of European languages; and in 1663 he published a second edition of MALPIGHI's treatise from 1661, *De pulmonibus*, in which Malpighi reported the discovery of the capillaries. This demonstrates the close contact which existed between Danish biologists and distinguished scholars abroad. Stensen discovered the duct of the parotid gland (*ductus Stenonianus*) and described the histological structure of muscle tissue. He rapidly became known throughout Europe and was appointed court physician in Florence (to Fernando II and Cosimo III). He correctly interpreted fossils of marine animals as being evidence that an area of land had earlier been covered by sea, and he is considered to be one of the founders of geology and palaeontology. His work *De solido*

appeared in an English translation in 1671. In 1675 he converted to Catholicism and relinquished all his scientific pursuits.

Of the 19th century, ADOLPH HANNOVER (1814–1894) was the most distinguished anatomist in Denmark.About the year 1842, after studying with Johannes Müller in Berlin, he published his *Mikroskopiske undersøgelser af nervesystemet* (Microscopical investigations of the nervous system). He introduced the method of using a chromic acid solution as a fixative. Hannover found that this preserved both the outer and inner structure of a tissue as well as hardening it to the right degree for sectioning. Furthermore, he recognized that the nerve fibres of the brain originate from cells in the brain. Later he carried out research on cancer and introduced epithelioma as a concept. For various reasons, he never held a chair in anatomy and his membership of the Academy was therefore of importance to him. L. L. JACOBSON (1783–1843), who was both an anatomist and a practising physician, discovered the sense organ *organon vomeronasale* in the nasal cavity of plant-eating vertebrates. He also described the renal portal vein system of some vertebrates and demonstrated the presence of kidney-like structures in invertebrates.

Among later anatomists, LÁRUS EINARSON (1902–1969) is known for his investigations into nerve cells and for the invention of gallocyanine staining. He developed micro-spectrophotometric methods of studying the nuclei of nerve cells.

PHYSIOLOGISTS

Several distinguished physiologists have been members of the Academy. The first, P. L. PANUM (1820–1885), established the Danish school of experimental physiology around 1860, after having studied with Claude Bernard in Paris. He is probably best known for his epidemiological studies of measles. He studied an epidemic on the Faroe Islands, where measles had not previously occurred, to determine its incubation time. Panum's most important pupil was CHRISTIAN BOHR (1855–1911), who studied with Carl Ludwig in Leipzig and became one of the leading pulmonary physiologists of his time. He discovered, in 1904, the effect of CO_2 on the oxygen binding curve of haemoglobin (the Bohr effect) and developed methods of determining respiratory "dead space". In studies of oxygen transport from alveolar air to lung capillary blood, it was necessary to know the average oxygen pressure in the blood during passage through the lungs. For this purpose Bohr developed a method of integration (the Bohr integration) and formulated the first mathematical model of gas exchange between blood and alveoli. His innate understanding of physics made him a pioneer in the rational description of physiological phenomena. He came to the conclusion (which later proved to be erroneous) that oxygen was transported into the blood of the lung by an active process. His treatment of the problem was so precise that his papers on gas exchange in the lungs are still being discussed.

It was Bohr's pupil, AUGUST KROGH (1874–

1949), who in the last year of Bohr's life proved that gas transport in the lungs occurs by passive diffusion. Krogh became one of the leading figures in physiology and his fields of activity were extremely wide ranging; among his achievements were the determination of cardiac output by means of acetylene, and investigations of capillary function. He formulated the concept – since called the Krogh cylinder – explaining the functional unit in solute exchange between blood and tissue and in 1920 was awarded the Nobel prize for this work on capillary physiology. Later, Krogh studied osmoregulation in marine animals and comparative respiratory mechanisms. In his later years his interests shifted from passive diffusion processes to energy-dependent transport of ions and molecules, and he became a pioneer in this field. In 1946 Krogh delivered the Croonian Lecture to The Royal Society; in this succinct account he summarized the results of his transport studies. In his final years Krogh once more changed his field of research, this time to the study of the metabolism of insect flight. Krogh made important contributions in fields ranging from plankton biology to the physiology of the blue whale. In 1948 he resigned his membership of the Academy in protest against an election policy which he considered too conservative. T. Weis-Fogh (1922–1975), who was the last of Krogh's many pupils, studied the physiology of insect flight, in particular the metabolic state before and during flight in the locust. He contributed to our understanding of the formation of insect cuticle and the molecular basis of the elasticity of resilin and elastin. Weis-

Fogh held a chair in zoology at Cambridge University from 1966 until his untimely death in 1975.

Einar Lundsgaard (1899–1968) discovered that muscle contraction does not require the production of lactic acid, as had been assumed by Otto Meyerhof and A. V. Hill, but that the contraction takes place by means of energy stored in phosphate bonds. These investigations, which started with the discovery that iodo-acetic acid prevents the production of lactic acid, but not the contraction itself, revealed that creatine-phosphate was the energy donor (although this was later placed secondary to adenosine triphosphate (ATP), both of which are produced by energy-coupled processes). Lundsgaard also discovered that alcohol conversion is a function exclusive to the liver. Quite early in his career (1939) he demonstrated that the main effect of insulin on blood glucose concentration is secondary to an action on the membrane transport of glucose in muscle cells.

Emil Christian Hansen (1842–1909) worked in the Department of Physiology at the Carlsberg Laboratory, where he developed a method of cultivating yeast from a single cell, now an important technology in the production of beer of constant quality.

Erik Zeuthen (1914–1980) became head of another Carlsberg research institute, *The Biological Institute of the Carlsberg Foundation*, where he succeeded Albert Fischer (1891–1956), known as one of the pioneers of tissue culture. Zeuthen developed a technique for synchronization of cell growth by means of heat shock. The protozoa *Te-*

trahymena pyriformis was the preferred test object in his studies of the biochemistry of cell division.

BIOCHEMISTS

The development of biochemistry in Denmark is closely connected with the research carried out at the Carlsberg Laboratory. After the establishment of the Laboratory in 1875, the Department of Chemistry was headed by JOHAN KJELDAHL (1849–1900), who developed a method for determination of nitrogen in organic material which is still utilized. Kjeldahl was followed by S. P. L. SØRENSEN (1868–1939), who studied the chemistry of proteins. He synthesized ornithine and proline, and elucidated the composition of arginine. He also developed the technique of formol titration as the first practical method for studying proteolytic cleavage. In 1909 he introduced the concept of pH, as an expression of hydrogen ion concentration; and he demonstrated the significance of pH in enzymatic processes. A number of his buffer solutions became standard requisites in many laboratories. Sørensen was a distinguished pioneer of protein chemistry and, toward the end of his life, he became president of the Academy. He was succeeded at the laboratory by K. LINDERSTRØM-LANG (1896–1959), likewise a protein chemist. Lang contributed both theoretically and experimentally to the understanding of the nature of proteins in solution, and he established the concepts of primary, secondary and tertiary structure of proteins. In cell physiology he developed micro-

methods, including the Cartesian diver method for the measurement of respiration in individual cells. Numerous distinguished guests were received at his laboratory, many of them from abroad, particularly from the USA during Lang's later years. By means of his ultramicromethods, enzymatic processes could be determined quantitatively in microscopically small amounts of tissue. In addition, Lang had an unusual flair for the mathematical analysis of biochemical conditions. Among biochemists from outside the Carlsberg Institute, Henrik Dam (1895–1974) was awarded the Nobel Prize for his discovery of vitamin K in 1940.

GENETICISTS

Wilhelm Johannsen (1857–1927) received his scientific training under Kjeldahl and Wilhelm Pfeffer (Leipzig). Although he was a professor of plant physiology, Johannsen's interest lay in genetics. In a series of fundamental experiments on the inheritance of seed size in beans, employing rigorous statistical methods, Johannsen clarified the difference between inherited and environmentally produced variation. He found that selection for size within "pure lines" obtained by strict self-fertilization was without effect on the offspring. Two lines differing only slightly in size would retain this slight difference generation after generation. After crossing the two lines they could be reestablished in the progeny by selection. His work *Elemente der exakten Erblichkeitslehre* established the concepts of the genotype and phenotype as well as the term

gene. This book formed the theoretical basis for the development of genetics in this century.

ØJVIND WINGE (1886–1964) formulated the theory of speciation in plants through polyploid evolution by means of species hybridization followed by doubling of the chromosome number of the hybrid. This work and his experimental cytogenetic investigations initiated extensive research into chromosome cytology and cytogenetics in Denmark. Winge can claim to be the founder of chromosome pathocytology through his discovery of chromosome abnormalities associated with plant and animal tumours, and is known as the father of yeast genetics through establishment of the sexual cycle for yeast and carrying out of the first genetical work with this organism. His international reputation is attested by his membership of both the Royal Society and the National Academy of Sciences of the USA.

MOGENS WESTERGAARD (1912–1975) was the intellectual successor of Johannsen and Winge. He discovered that the male sex in *Melandrium album* (white campion) is determined by the presence of a Y-chromosome – an important step in the development of cytogenetics. Westergaard worked on chemical mutagenesis and used the back mutation test to establish the allele-specific pattern of back mutation. He later used electron microscopy to study the importance of the synaptonemal complex in crossover mechanisms. He, too, was a member of the National Academy of Sciences of the USA; through his contacts with leading laboratories abroad he played a large part in the development of molecular biology in Denmark.

Carl Syrach-Larsen (1898–1979), a pupil of Ø. Winge, was the founder of the genetical school of forest tree breeding and established the first seed orchards for forest trees in Denmark. His concepts made a major impact on the development of such seed orchards in other countries.

PATHOLOGISTS AND MICROBIOLOGISTS

The best known of Danish pathologists, Johannes Fibiger (1867–1928), was awarded the Nobel prize in 1926 for his investigations of the *Spiroptera carcinoma*, an example of a cancer produced exogenously. The finding was based on an accidental observation on rats, being used for other purposes, which developed cancer of the stomach. The tumours contained a nematode (*Spiroptera neoplastica*) with which the rats had been infected by eating cockroaches, the host of this nematode. His work on exogenously produced cancer was a great stimulus for this branch of cancer study; and in 1949 an experimental cancer research institute was set up in Copenhagen bearing Fibiger's name. Bernhard Bang (1848–1932) was a professor at the Royal Veterinary and Agricultural University. His name is associated with the bacteria that gives rise to contagious abortion in cattle. He described this microorganism (*Brucella abortus* Bang) , which produces undulant fever in man. Bang is also known for his fight against tuberculosis in domestic animals, based on the principle of ridding the

stocks of tuberculosis by isolation of the infected cattle under continual tuberculin control. GUNNAR TEILUM (1902–1980) classified and systematized tumours of the testicles and ovaries.

Pasteur's work on infectious diseases led to the initiation of prophylaxis, which resulted in great advances in microbiology. The first director of the Danish State Serum Institute, THORVALD MADSEN (1870–1957), developed quantitative methods for evaluating the antibody-antigen relationship and carried out reaction-kinetic investigations concerning the attenuation of toxins. He was president of the Permanent Standards Committee of the League of Nations and was president of its Committee on Hygiene. FRITZ KAUFFMANN (1899–1978), who came to Denmark from the Kaiser Wilhelm Institute, Berlin, in 1933, classified the types of Salmonella bacteria. Two other scientists have been of importance in basic and applied microbiology: S. ORLA-JENSEN (1870-1949) systematized lactic acid bacteria, and C. O. JENSEN (1864–1934) investigated the relationship between human and bovine tuberculosis.

ZOOLOGISTS

Although the 18th century was not a particularly outstanding period for Danish biological research, three zoologists deserve mention. All of them greatly extended our knowledge of new species. They were: O. F. MÜLLER (1730–1784), J. F. FABRICIUS (1745–1808) and OTTO FABRICIUS (1744–1822). The latter, who was at the same time a

clergyman and afterwards a bishop, provided knowledge of arctic fauna through his treatise *Fauna Groenlandica*. O. F. Müller developed our knowledge of small, mainly aquatic animals and plants by describing a large number of species from fresh and salt water. J. F. Fabricius, in 1776, published the most important entomological work in Denmark, *Philosophia entomologica*, containing some 10,000 descriptions of new species.

In the years 1845–1847 the corvette *Galathea* circumnavigated the globe, and the marine animals collected during the voyage were later deposited in the Zoological Museum in Copenhagen. The Academy was involved in the planning of this expedition, but it was carried out at the expense of the state which invested an impressive sum of money in this enterprise.

At the suggestion of the Academy, Peter Wilhelm Lund (1801–1880) travelled to Brazil in the 1820's to carry out investigations on the vegetation. Having returned to Brazil in 1835, he studied the stalactite caves of Lagoa Santa, where he excavated and exposed 150 species of mammals, among them a giant armadillo and a giant sloth, that were 'conserved' in these natural conditions. The *Galathea* expedition took home to Denmark many of Lund's finds; and although the British Museum wished to purchase them for a large sum of money, the collections remained in Denmark. Lund himself never returned to his native country, but stayed in Brazil where he is considered one of the founders of Brazilian zoological research.

Japetus Steenstrup (1813–1897) and J. C.

Schiødte (1815–1884) were the leading zoologists in Denmark in the 19th century. Although Steenstrup, like many other scientists in those days, never completed a formal university training, he became university professor in zoology. He is particularly well-known for his studies in quaternary zoology, in which he identified bones from peat-bogs and archaeological sites, making possible the ordering of the finds in a chronological system. He pointed out how the various layers of plant remnants in the bogs provide information as to successive conditions prevailing in nature through the ages, furnishing evidence on flora and fauna immigration. He became a founder of bog-geology and vegetational history and demonstrated, for the Danish region, four periods of afforestation: the aspen-, the pine-, the oak-, and the alder- (later beech-) periods – a sequence which is still held valid. He coined the term *køkkenmødding* for the Stone Age refuse dumps, a Danish word which has been incorporated into the English language as 'kitchen middens'. Steenstrup contributed to zoological systematics, and his studies of cephalopods in many ways represented an important contribution (which has recently been published in English, 1962). Being a very active and popular person, he was an influential member of the Academy and was instrumental in the creation of the Carlsberg Foundation. The collaborative work between archaeologists and zoologists was supported by the Academy which in 1848 appointed the first 'Kitchen Midden' commission. In 1893 and 1937, two similar commissions were formed – in both cases with considerable support

from the Carlsberg Foundation and with several members of the Academy as participants.

His contemporary, J. C. Schiødte, continued the entomological research of earlier times and made extensive contributions to the characterization of beetles and their larvae. At the age of 25 he published his first extensive work, '*Genera and Species of Danish Beetles*', dealing with ground-beetles and water-beetles. His life-long occupation with beetle taxonomy resulted in a series of papers published between 1861 and 1884 under the collective title, *De Metamorphosi Eleutheratorum Observationes*, a work which has proved of fundamental importance by its elucidation of the variations within every single character and by showing which characters are of systematic significance. Freshwater biology was introduced by C. Wesenberg Lund (1867–1955), who published *Plankton Investigations of the Danish Lakes I–II* at the turn of the century.

Mathias Thomsen (1896–1976) initiated the study of insect endocrinology in Denmark.

MARINE BIOLOGISTS

The studies in marine biology of the zoologist Otto Frederik Müller have already been mentioned. Naturally enough, this subject has been of great importance in Denmark, which is surrounded on all sides by sea. C. G. Johannes Petersen (1860–1928) introduced quantitative techniques in the investigation of the benthic animals and plants. He invented the socalled "Petersen Grab". Johannes Schmidt (1877–1933) investigated the relation

between environment and genotype of Atlantic races of cod and gained special recognition for his theories on the migration of the eel between Europe and the Sargasso Sea. He worked at the Department of Physiology of the Carlsberg Laboratory and organized and led a circumnavigation of the globe with the expeditionary ship *Dana* (1928–1930). The voyage was funded by the Carlsberg Foundation. Descriptions of the material collected were issued over a series of years in the form of *Dana Reports*, comprising some 90 volumes and a total of 8,000 pages. The expedition discovered a submarine mountain ridge in the Indian Ocean, subsequently named the Carlsberg Ridge.

Among more recent Danish marine biologists, mention should be made of GUNNAR THORSON (1906–1971) who demonstrated the absence of planktonic larvae in arctic regions and the deep sea. His most important research concerned invertebrates of the marine bed. ANTON FREDERIK BRUUN (1901–1961) was particularly involved in deep sea research, in part on an international level, and is known for his definition of zones in the deep sea. He was the leader of the 2nd Danish *Galathea* expedition around the world (in 1950–1952). Bruun was not a member of the Danish Academy but was internationally recognized, as reflected in his membership of the Academy of Sciences of the United States.

EUGENIUS WARMING (1841–1924) originally studied with P. W. Lund in Brazil. He founded the study of ecological botany in Denmark, carried out research on plant geography, and described plant communities. C. RAUNKIÆR (1860–1938) introduced the circle method for quantitative description of the plant composition in different types of landscape. He is probably best known for his classification of plants according to 'life form', depending on how they have adapted themselves to survival during unfavourable periods, and for the fact that this classification of plants is confirmed by their geographical and climatic areas of distribution.

Three quaternary botanists have contributed in significant ways to their field, N. HARTZ (1867–1937), KNUD JESSEN (1884–1971), and JOHANNES IVERSEN (1904–1971). Hartz, who was not a member of the Academy, discovered the Allerød oscillation, a warmer period during late glacial periods – later demonstrated all over the earth. Jessen carried on the work of Hartz. In 1928 he published *Stratigraphical and Paleontological Studies of Interglacial Fresh-water Deposits in Jutland and North-East Germany*, in which pollen-analysis was employed for the first time in Denmark, parallel with the identification of seeds and fruits. Jessen carried out a series of pollen-analytical datings of prehistoric finds and on the whole did a great amount of pioneering work: investigations on cereals and weeds in the past, pollen-analytical and geological investigations of interglacial and post-

glacial peat-bogs in Ireland. Finally, Johannes Iversen became internationally respected as a leading figure in vegetational history. He included the herbaceous plants in pollen-analysis and by this means produced a far more varied picture of, for example, late glacial vegetation and climate. He demonstrated a late climatic oscillation before the Allerød period (the Bølling oscillation, which later has been identified everywhere). His eminent knowledge of vegetational ecology is the background for his paper on Stone Age farming and clearing of forests *Landnam in Denmark's Stone Age*. In the early 1950's he hacked out a slash and burn clearing in Draved Forest in order to support his interpretation of pollen-diagrams. A part of the forest was burned down after felling of the large trees with flint axes, followed by sowing in the ashes and (later) by cropping by cattle.

P. Boysen Jensen (1884–1959) investigated the production of organic matter in woods and was one of the pioneers in the study of growth hormones in plants. He also made quantitative investigations into the light-requirements of various trees.

Much of the work carried out by Danish zoologists and botanists in the 19th century, and also in this century, has only slowly gained international recognition, because it was mainly published in Danish – in contrast to the contributions within the experimental biological sciences, physiology, biochemistry, and genetics which, from the beginning, have been internationally oriented.

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