

**75-th ANNIVERSARY
of the
NENCKI INSTITUTE
OF EXPERIMENTAL BIOLOGY**



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Pictures on the previous page:

Upper picture: Warsaw, 8 Śniadeckich St. (the house with the gate). Building of the Nencki Institute before Second World War.
Lower picture: Warsaw, 3 Pasteur St. Present building of the Nencki Institute.

Address of the President of Polish Academy of Sciences. The Nencki Institute of Experimental Biology - 75 years in the service of science

The Nencki Institute of Experimental Biology was founded by uniting into a new entity of two previously existing research units of the Warsaw Scientific Society: Department of Physiology and Department of General Biology. The first of them was headed by Kazimierz Białaszewicz and the second by Romuald Minkiewicz. However, apart from this encyclopedic information, some more significant features of this event should be emphasized.

The history of founding and development of the Nencki Institute of Experimental Biology reflects the Poland's history of the XX-th century, the history of noble efforts as well as difficult and sometimes tragic events. First of all, the date of its founding significantly coincides with the regaining of independence and establishing of the II Republic of Poland, after the First World War. Despite numerous efforts, all endeavours to create the Polish biological research centre in Warsaw, undertaken since 1901, did not succeed until Poland was reborn. The obstacles encountered when the goal of establishing the new Marcei Nencki Institute on the Polish territories under Russian and later German occupation was pursued, were described by Romuald Minkiewicz. In the first volume of the journal "Polish Science", which appeared when the German administration and military forces were still present in Warsaw, Minkiewicz published a paper under an ominous title: "For the Polish scientific endeavours". Its first sentence summarized the author's central idea: "Polish scientific needs in all particular fields and fractions of science are numerous, various and urgent; however, something more general and universal distinguishes itself over them all, something which is the essence and core of our needs and which equally concerns all branches of science and every single one of them: the need of founding of the Polish science".

In a footnote Romuald Minkiewicz wrote: "In a domain closer to me, the most important thing would be the founding of the separate Institute of Experimental Biology on a larger scale, where all laboratories devoted to experimental research of the organic life would concentrate. However, such an institute would have to be properly equipped and organized from the very beginning. As far a smaller scale undertakings are concerned, there should be founded immediately:

- central hydrobiological laboratory, with at least two aquatic stations: lake- and river-type (Vistula);
- laboratory of experimental zoology, with a wide program, including zoopsychology, etc."

Such goals and image of the future Nencki Institute were drawn by one of its founders. The Institute was to meet Polish needs in several fields of experimental biology.

When we look back from the perspective of its 75 years' history, we can state that those difficult and noble goals were certainly achieved. What more, they were achieved in spite of the tragic consequences of the Second World War, as a result of which most of its employees were killed, died due to hardships or were scattered all over the world and its property and scientific equipment were completely destroyed. So the question arises: how could this research centre, pursuing the example of scientific excellence of its namesake, succeed not only in being reborn, but also in growing and consolidating its scientific position in Poland and in the international science.

The strength of the Nencki Institute depends on setting certain standards of human relations, on its attitude to the scientific research, on promoting scientific ideas and methods, on international

collaboration and on imprinting its approach to science in the successive generations of researchers. The Institute was and remains a modern research centre, promoting new theories, hypotheses and methods. It is open for everyone, irrespective of nationality, sex, religion or political views, for everyone desiring to contribute to the scientific knowledge and ready to conform with the unwritten but obliging standards of the Institute's community.

In the day of such an important anniversary I wish my Institute that it would maintain all those noble traditions in the future.

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Leszek Kuźnicki

Address of the Director of the Nencki Institute of Experimental Biology

The Nencki Institute of Experimental Biology has some characteristics unique among scientific institutions in Poland. First of all it has an interdisciplinary character, employing specialists from all fields of biology and biomedical sciences as well as researchers of medical, physical, chemical and technical education. This heterogeneity enables the Institute to cover a broad spectrum of research activities, from psychology and behavioural sciences, through neurophysiology, electrophysiology and neurochemistry to cellular biology, biochemistry, bioenergetics and molecular genetics. Thus the Institute is competent and able to realize complex scientific projects dealing with important, basic biological problems that require simultaneous studies by different approaches. Examples of this are e.g. in coping with realization of such general research problems as mechanism of learning and memory, of motility processes in muscle and non-muscle systems, of aging, regeneration and repair processes on cellular and organismal levels, or of transduction of biological signals between and within cells.

Due to its achievements and high scientific reputation the Institute was also able to attract sufficient financial resources to acquire and collect through years a really excellent research equipment. Many pieces were unique in Poland or in Eastern European Region by the time of their instalment, and are still unique (e.g. the confocal microscope). This, taken together with the human potential, makes the Nencki Institute a true front-runner among Polish biological institutions.

As the oldest non-university biological research center in Poland the Institute is at the same time a very traditional, almost historical entity, what again points to its uniqueness.

Definitely, it is an honour to belong to the community of the Nencki Institute. But it is also a lot of pleasure and satisfaction. The Nencki Institute is the place one likes and the place one is from, whenever and wherever one is. Again, something special.

On the occasion of the 75th anniversary of the Nencki Institute these and similar thoughts were often mentioned. And although no firm conclusion or even analysis of the "Nencki phenomenon" was given - we all felt this "something". In my personal view, it is, at least partially, a felling of continuity, of certain moral obligation to follow our predecessors, and to stand up to tradition of high standards. There would be no Nencki Institute without these few Giants that made it up and Their Pupils that followed. But there would neither be the 75th anniversary without the actual, excellent and largely young staff of the Nencki Institute.

Maciej J. Nałęcz



MARCELL NENCKI

1847 - 1901

Marcell Nencki was born on January 15, 1847 at a small estate owned by his parents in the village Boczek near Sieradz, Poland, which however did not exist as an independent state at that period. At the age of 9 Nencki entered grammar school and then gymnasium in Piotrków Trybunalski, which he completed in 1863. In that year, as a 16 years old gymnasium student he joined the Polish uprising against Russia, one of the states partitioning Poland. When the insurgent army was defeated, Nencki had to leave his homeland and settled in Cracow (then under the Austro-Hungarian authority), where he enrolled into the Philosophical Faculty of the Jagiellonian University. However, since he did not feel safe in Cracow either, he soon moved to Jena and then to Berlin where he studied philosophy and classics. In Berlin Nencki became acquainted with two young physicians, Otto Schultzen and Bernhard Naunyn who soon became his close friends. Probably influenced by them, he became fascinated by natural sciences and in 1867 he enrolled in the Medical Faculty of the Berlin University with the aim to study chemical processes in living organisms. To acquire a more profound knowledge in chemistry, Nencki worked at the same time for two years at the "Gewerbeinstitut" under a well known organic chemist Adolf Bayer. Nencki completed his medical education in a short time. In 1870 he presented his thesis on "Oxidation of aromatic compounds in the animal body" (*Opera Omnia*, Vol. 1, 17, 1870) and obtained the degree of Medicine Doctor. In 1869, while still a student, he published, together with

Schultzen, the results of their research on urea formation (*Opera Omnia*, Vol. 1, 1, 1869) and in 1871 a paper on the structure of uric acid (*Opera Omnia*, Vol. 1, 3, 1871). He remained interested in these three problems till the end of his life. The outstanding quality of Nencki's research attracted considerable attention, and as early as 1872 he was offered the position of assistant in the Department of Pathology of the University in Bern. Here in Switzerland, his scientific career developed in a spectacular manner. In 1876 he was appointed associate professor and in 1877 full professor and head of the Chair of Physiological Chemistry, the first chair of that kind in Switzerland, founded especially for him.

Nencki continued his scientific and organizational activity and soon became a well established authority, developing and improving curricula of students of medicine and pharmacy as well as organizing social health services. His research and that of his increasingly numerous disciples and students gained him a world-wide renown.

However, in 1890, after 18 years of his fruitful activity in Bern, Nencki decided to leave his established position in Switzerland and accepted the invitation to organize, together with the Russian physiologist Ivan Petrovich Pavlov, the Institute of Experimental Medicine in Russia's capital St. Petersburg. This decision was probably influenced by exceptionally favourable conditions he was offered there for his scientific research, far exceeding anything he could ever hope to obtain in Switzerland. The future proved that he was right: the period of Nencki's activity in St. Petersburg (1891-1901) was the most successful in his scientific career. He was nominated director of the Department of Chemistry and Biochemistry, and special building to accommodate this Department was constructed strictly according to his instructions. His laboratories were equipped with most up-to-date scientific instruments available at those times. Another advantage of Nencki's position in Petersburg was the possibility of a close collaboration with Pavlov and the fact that a group of scientists from his former laboratory in Bern could join him in his new department. In this way investigations initiated by Nencki in Petersburg were largely a continuation of his previous work in Bern.

Unfortunately, this period of Nencki's most intense and fruitful scientific activity lasted no longer than a decade. He died prematurely on October 14, 1901 in St. Petersburg of stomach cancer at the age of 54. In compliance with his last will, his body was brought to Warsaw and buried at the Reformed Evangelical Cemetery.

It is not possible to present in this short outline a full picture of Nencki's scientific achievements. His lasting contribution to various fields of natural sciences is hard to overestimate. Nencki's research encompassed a wide range of topics in several disciplines ranging from organic chemistry and biochemistry through pharmacology to pathology and veterinary medicine. In most of them he had initiated lines of investigation which are often continued until now and sometimes contemporary theories confirm ideas formulated by Nencki far ahead of his times. The three main fields of Nencki's interest were organic chemistry, bacteriology and, last but not least, biochemistry. Biochemistry is a rather young discipline, its enormous progress being a matter of the last 50 years, and as a matter of fact one can regard Nencki as one of its pioneers, especially concerning his modern approach to biochemical research.

The three major problems which he began to study as a young man and which never ceased to interest him were urea formation, chemistry of purines (in particular of uric acid) and the oxidation of aromatic compounds. Very early Nencki came to the conclusion that urea was formed in the organism from amino acids rather than being preformed in a protein molecule, as it was generally believed at that time, and that urea synthesis is accompanied by binding of carbon dioxide. This concept was proven by Nencki experimentally. The addition of glycine and some other amino acids to dog's diet raised the amount of excreted urea.

Nencki's research carried out together with Pavlov demonstrated that liver was the main, if not the only, site of urea formation. These studies were also far ahead of their times. Nencki also pointed to the role of water not only in dissociation processes of various compounds in the animal body but also in syntheses which occur with the liberation of water molecules. Nencki proposed that the synthesis of long chain fatty acids proceeds stepwise, with a gradual condensation of two-carbon-atom fragments, whereas successive splitting off of two-carbon units occurs on oxidation of fats. The latter concept became the basis on which, many years later, Knoop formulated his classical theory of beta-oxidation of fatty acids. It was also Nencki who first suggested that acetylaldehyde could function as an active two-carbon unit, a concept which has much in common, at least in principle, with the present view on the role of acetyl-CoA.

One of Nencki's favourite problems, in which he remained interested during his whole scientific activity, was the metabolism of foreign compounds in the animal organism, in particular that of aromatic substances. These compounds can be used as "markers" in investigations of some biochemical processes. On the other hand, Nencki's observation that aromatic compounds became less toxic when oxidized was of fundamental importance for pharmacology.

Among Nencki's greatest achievements were his studies on the chemical structure of haemoglobin. This work was partly carried out in a cooperation-at-distance with a Polish biochemist Leon Marchlewski (1869-1946), Nencki's junior by about 20 years. Marchlewski worked first in Manchester and then in Cracow studying products of chlorophyll degradation. The two scientists succeeded, independently, in identification of the same compound among the degradation products of haemoglobin and chlorophyll, namely haemopyrrole. This finding pointed to a close chemical and structural similarity between the two substances and led Nencki and Marchlewski to far-going biological generalization concerning the common origin of animals and plants (see Excerpta 1). Thus, that branch of biochemistry which was later named "evolutionary biochemistry" has some of its roots in the Nencki's work.

One should also mention Nencki's important contribution to a campaign against rinderpest, a dangerous cattle disease that spread over the southern provinces of the Russian empire. Nencki and a group of his coworkers spent several months in the Caucasian region and succeeded in raising an antiserum which was effective when applied to sick animals and also as a prophylactic measure.

Although Nencki worked throughout his lifetime outside Poland, he maintained close relations with his country. He visited it quite frequently and became a member of several Polish scientific societies, including the Polish Academy of Sciences and Letters. He became Doctor Honoris Causa of the Jagiellonian University, and in 1900, at the Meeting of Physicians and Naturalists in Cracow, he delivered his famous lecture on the "aims" of biological chemistry, the presentation which is recognized as his scientific testament (see Excerpta 2). The immense scientific heritage of Nencki was edited in 1904 by his coworkers N. Sieber and J. Zaleski as *Opera Omnia*. Soon after Nencki's death his coworkers put forward an idea of building in Warsaw a scientific institute that would bear his name. This was fulfilled only in 1918 when the Nencki Institute of Experimental Biology was founded.

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Włodzimierz Niemierko

and Stella Niemierko

On the biological relation between the leaf pigment and the blood pigment (*excerpta*)

(*Gazeta Lekarska*, Vol.XVII, No. 23, Warszawa, 1897)

by Professor Marcei Nencki

(Read at the Conference of the Chemical Society, Warsaw, 1896)

...I would like to make some comments on the biological significance of the discovery recently made by Schunck and Marchlewski that a derivative of chlorophyll phylloporphyrin, and haematoporphyrin obtained by myself and N. Sieber are in an extremely close genetic relationship. According to those authors, phylloporphyrin $C_{16}H_{18}N_2O$ is probably related to haematoporphyrin $C_{16}H_{18}N_2O_3$ in a similar way as, e.g., anthra purpurin to oxyanthraquinone, i.e. the two compounds are one and the same substance at different stages of oxidation. The spectra of the two pigments dissolved in ether, acidic or alkaline fluid, as well as the spectra of their zinc salts, are almost identical; the only difference consists in that the bands of haematoporphyrin are slightly shifted to the red side of the spectrum. This analogy of the spectra also includes the ultraviolet part, as it could be seen in the photographs made by Tschirch with the use of a quartz spectrograph. Both substances dissolved in a neutral fluid are of the same colour and both are fluorescent; when dissolved in ether and left in sealed tubes in dispersed light, they lose the colour completely after a few months.

It is interesting to note a similarity between the chemical properties of haemin and phyllotaonin because they are derivatives of the pigments with which we are now dealing. By acting on haemoglobin with hydrogen chloride, hydrogen bromide or acetic acid the respective haemins $C_{32}H_{31}O_3N_4FeCl$, $C_{32}H_{31}O_3N_4FeBr$, $C_{32}H_{31}O_3N_4FeOCOCH_3$ are obtained, i.e. esters of haematin from which haematin ($C_{32}H_{31}O_3N_4FeOH$) is formed by saponification. A similar facility of ester formation is also the property of phyllotaonin. ... Haematin, or rather haemochromogen, in combination with various proteins form blood haemoglobins of different kinds. Bertin-Sans and Moitessier recently reported that they had obtained methaemoglobin from protein and haemoglobin in alkaline solution. By acting on methemoglobin with ammonium sulphide they obtained haemoglobin, and from the latter, oxyhaemoglobin. Unfortunately, what was missing in their reports and what could be the most important argument for the validity of their opinion was their omission to state that they obtained the crystals of the respective haemoglobins. On the other hand, Küster achieved a rather far-reaching degradation of haematin to less complex compounds. By acting on haematin with chromic acid dissolved in acetic acid, he obtained two nitrogen-free acids of rather simple composition $C_6H_{10}O_5$ and $C_8H_{10}O_6$. It should be expected that the structure of these acids will soon be established.

So far we do not know in what way and with what substances chlorophyll is combined in plant cells. Neither is the chemical relationship between chlorophyll and phylloporphyrin as simple as that between haematin and haematoporphyrin. The discovery of Schunck and Marchlewski is, therefore, of extreme significance for biological chemistry as it sheds some light on the earliest periods of the history of development of the organic world, and simultaneously they point to a common origin of the animal and plant kingdoms. The theory of Darwin on the origin of species is based on the variations of form due to the effect of various life conditions in the struggle for existence. The differences between the organisms depend, however, not only on the diverse form and structure of their organs but also on the differences in the chemical composition of those compounds of which their living cells are composed. It is on the properties of those compounds that the character of their metabolism depends which affects the form of the cells and the formation from them of particular organs. In other words, the form of cell groups composing an organ is dependent on the type of metabolism which had been evolved by the organisms in the course of the struggle for existence under varying life conditions. With the changes of life conditions not only the form of the cells becomes altered but simultaneously so does their chemical composition and metabolism. Therefore, for a more precise understanding of the history of development of the world of organisms it is essential not only to compare the morphological properties of the cells but also their chemical composition and their metabolism. For that reason the studies of Schunck and Marchlewski which show the relationship between the blood pigment and the leaf pigment, substances differing so widely in their physiological significance, have an unquestionable scientific value.

Owing to the bacteriological research performed during the last twenty years our knowledge about unicellular organisms and their metabolism is much more complete and, therefore, we now take a different view on life phenomena of the more complex beings of the animal and the plant worlds. Studies of Vinogradski have shown that nitrifying bacteria containing no chlorophyll contribute to the formation of complex organic compounds from carbon dioxide, ammonia and inorganic salts. ... Other bacterial species develop and multiply using carbon hydrates or ammonium salts of organic acids having a rather simple structure, e.g. malic, tartaric or citric acids. Complex proteins which provide nourishment for animals are also consumed by many bacteria. In such cases the bacteria take up the necessary oxygen from air or from the substrate. Thus, in the organisms devoid of chlorophyll or haemoglobin we observe a great diversity in the types of metabolism which may be similar to either that of animals or that of plants. However, we find here all kinds of intermediate forms among which anaerobiosis, a characteristic feature of all fermentative processes, deserves special attention. It should be pointed out that the chemical composition of microbes varies not only between different forms of these organisms but even within one and the same form depending on external conditions of life. Also, the variability of morphological features of microbes is so great as in no other class of organic beings. ... Hundreds of similar examples could be mentioned and all of them would testify that the formation of still new kinds of bacteria occurs much easier than in higher organisms which originated at a later time. We have the right to assume that the most simple organisms which form their body from the compounds so relatively simple as carbonic acid, water and ammonia, belong to the most ancient inhabitants of our planet... According to the more recent research of Engelmann, there are also bacteria, called by him Purpurbacterien (*Purpurobacteria*) whose protoplasm is coloured by a red pigment, bacteriopurpurin, and which produce oxygen on illumination in a similar way as green plants.

...Just as, on the one hand, there are chlorophyll-free plants, so, on the other hand, whole classes of animals without red blood are also known. For insects whose tissues are supplied with oxygen directly from the air by means of tracheae, haemoglobin is of course unnecessary as a mediator to provide the

tissues with oxygen ... In many *Cephalopoda*, *Gastropoda* and *Crustacea* the system of blood vessels contains a soluble proteinaceous substance, haemocyanin which turns blue in air and which is supposed to take some part in the respiration. ...

Thus, we have seen how numerous are in the organic world examples of synthesis of organic substances from carbon dioxide without the participation of haemoglobin. Furthermore, we see that in the most perfect representatives of the animal and plant kingdoms - plants with green leaves and animals with red blood - the corresponding pigments, i.e. chlorophyll and haemoglobin, are of a common origin. We have inherited the view that the relation between the world of plants and that of animals is such that one without the other is almost unable to exist. I would like to express a different opinion. I believe that there was a time when the animal kingdom, with the exception of unicellular organisms did not exist. The role in nature economics concerned with processes of putrefication and slow combustion was fulfilled by microorganisms, the function now taken over by animals.

It seems premature to draw further conclusions but I considered it useful to express my ideas and simultaneously to call the chemists attention to the fascinating and worthy of investigation field of research. The analysis of haemoglobin and chlorophyll is nearly complete. Thus, further studies in this field of knowledge should be aimed towards investigation of the structure of these substances by means of synthesis. It seems clear that this is the way leading to new ideas...

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 Revised by *Anna Olszańska*

On the aims of biological chemistry (*excerpta*)

(Przegląd Lekarski, No. 31, Kraków, 1900)

by **Professor Marcei Nencki**

(Lecture delivered at the 9th Meeting of Polish Physicians and Naturalists, Cracow 1900)

If someone has devoted over 30 years of one's life to scientific work in a certain direction, as I did, then unwillingly, the idea emerges that the time which is still left is short and that one should consider one's strength, on one hand, and the tasks on the other, so that the moments still remaining be utilized in the best way, and the skills acquired in laboratory techniques and the resources be not dispersed but reasonably concentrated; *Carpe diem* - tells me my scientific conscience.

When I realize what, at the beginning of my scientific activity, appeared to me as a distant goal difficult to attain, and compare it with what, after 30 years, has been already achieved, then I can say with Goethe: "*Wonach ich mich in der Jugend sehnte, davon habe ich in Alter die Fülle*" (What in my youth I have sought, of that in old age I have plenty). The synthesis of products of catabolism, such as,

e.g. xanthine substances, uric acid and other substances, synthesis of sugars, degradation of proteins to crystalline products, whose chemical structure is mostly known, crystalline proteins etc., all this has been already accomplished. In the course of time, that which seemed almost impossible to know fell into our hands; but moving still forward, we have other desires more difficult to accomplish. I have no doubt that these aims will be attained by the new scientific generation and that our successors will again set themselves goals which we are even unable to imagine. Many new branches of science have appeared: bacteriology, serotherapeutic, etc. ... Numerous new facts on metabolism and life phenomena, in general, became known, they concern metabolism of unicellular and complex organisms. If the results obtained so far encourage us to study more and more difficult problems of life, then it would be worthy to realize which is the ultimate aim of investigations in the field of biological chemistry.

The aim of biological chemistry is not only to gain knowledge of the chemical structure of unicellular and multicellular organisms but also of their metabolism. Here, on every step the question arises how it really happens that a living cell is formed, feeds, grows, multiplies and at the end, sooner or later, inevitably dies - and in the dead cell we find exactly the same components as in the living one ... When alive this living cell is composed of water, proteins, carbohydrates, fats, extractable substances and inorganic compounds, the same components and in the same proportions will be found in this organism it is dead. Well, what had happened? How is the matter changed on transition of the living cell into a dead one? This question recurs at each step of our studies, and its elucidation is the ultimate aim of biological sciences.

Is it possible that this aim would be reached? Or, as it is sometimes argued, *semper ignorabimus* (we shall for ever ignore).

I can say in advance that everyone working in the field of biology strives consciously or unconsciously to achieve this aim. ... In fluids and excreta of living organisms there occur labile proteins. Many of them are able to disintegrate other complex molecules to less complex ones. Such proteins we call the hydrolysing enzymes. Others (in the presence of oxygen) are able to transfer oxygen to other molecules. Such enzymes are called "oxidases". The functions of other proteins which occur chiefly in living cells, but not in their excreta, are even more complicated. Recently, pressing the yeast cells, Büchner obtained a protein-rich juice which, in 40% solution of sugar, was able to carry out an alcoholic fermentation, i.e. it transformed sugar into alcohol and carbonic acid. ... Wiener has stated that the juice extracted from the cells of bovine liver forms uric acid, and a similar juice from kidney cells destroys uric acid. ... Some authors consider such processes as driven by specific enzymes, whereas other assign them to the living protoplasm in solution. It is very difficult to differentiate precisely between these concepts. It seems possible that further studies shall elucidate whether the living protoplasm is a mixture of various enzymes or whether the protoplasm is itself one whole molecule which is able to perform various functions. ... I draw attention to the fact of supreme importance that in such solutions extracted from living cells processes occur which we have so far considered as an exclusive property of the living matter. Here it is difficult to establish what is dead and what is living..

In my opinion, it is, and for a time will be, rather a matter of convention whether such manifestations should be called the function of enzymes, or of the living protoplasm, or of the living protein, or life itself. Gentlemen, you can imagine how immense perspectives extend for studies in this direction and how deep a sorrow overwhelms someone who has to leave the field of work when he sees so important tasks awaiting the generations to come.

... As a clear-headed investigator I felt it my duty to warn against premature conclusions and, first of all, generalization. In natural sciences, in general, and in biological sciences in particular, one

should never formulate a general law on the basis of a few or a dozen well-documented facts. ... It is now impossible even to dream that it could be possible to create in our laboratories even a most simple unicellular organism, but such a conviction constitutes in itself some progress because it proves that we realize the difficulties we encounter in our studies. Now our aim is to obtain, in an artificial way, such "labile" proteins which would have the properties of enzymes. This task also appears to us as one which could be fulfilled only in a distant future. However, even here it is difficult to prophesize. Persistent studies in this field of a vast number of scientists over the whole civilized world may lead to earlier attainment of this goal. Progress in biology is also dependent on the progress in other experimental sciences such as physics, chemistry and morphology. The main aim of biological chemistry is the elucidation of the phenomenon of life which can be most easily studied on unicellular organisms. This aim, however, not the only one. Elucidation of life phenomenon in more complex organisms is also our goal, this is an enormous, almost unlimited, area. Here we strive to gain knowledge of the special function of each organ, to elucidate how far the cells forming an organ are dependent on the whole organism and how far they possess some individual independence.

... There is an infinite number of problems to be solved, and a single investigator, after having worked his whole life, cannot repeat the words of Seneca *Si quis totam diem currens parvenit ad vesperum, satis est* (when someone running the whole day long comes to the evening, that is enough) because he knows that generations after generations have to go on and continue the work, and they will never see the end of the investigations. But our knowledge will become still wider and deeper and its advantage for practice, especially medicine, will be increasingly great.

Translated from Polish by *Stella Niemierko*
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Nencki Institute of Experimental Biology: foundation, restoration, further development

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A few years after the failure of the Polish Uprising in 1863, the tsar's regime closed all educational and scientific institutions in which lectures in Polish were held, including the "Main School" - a Polish University in Warsaw. The Imperial University was opened in Warsaw instead, with lectures in Russian, where no new positions were offered for Polish professors. Polish society began a long period of struggle for restoration of the national scientific and educational institutions in Warsaw. The efforts leading to the foundation of the Nencki Institute were an important part of the struggle.

Soon after the death of Marcei Nencki in 1901, some of his pupils and associates from the Berne University and the Institute of Experimental Medicine in St. Petersburg, decided to establish in his honor a "Society for Exact and Applied Sciences" in Warsaw. The tsar's autocratic regime refused to permit the founding of such a society. It was only after the revolutionary events of 1905 that the permission to form the "Association of Polish Scientists" was granted. Next, in 1907, the official approval was received for registration of the Warsaw Scientific Society.

The main purpose of the Warsaw Scientific Society was to establish research laboratories in various branches of science. The founding of the Marcei Nencki Institute of Biology constituted an integral part of this program and was stipulated in bye-laws of the Society approved in 1911. Generous donations, the largest one from Nadiezhda Sieber-Shumova, long-time Nencki's associate, provided the necessary funds. An Organizing Committee for the establishment of the Institute was appointed by the Warsaw Scientific Society. In 1913 General Assembly of the Society confirmed the Institute's statutes. However, it was only after Poland regained independence in 1918 that the organizational work was resumed by the directors of the Warsaw Scientific Society's laboratories of experimental biology. From their initiative, an autonomous organization was formed under the name of "Marcei Nencki Institute of Experimental Biology". Initially the Institute consisted of the Department of Neurobiology existing since 1911, the Department of Physiology organized in 1913, and the Department of General Biology opened in 1918 (Table I).

During the period of 1918-1939, the Nencki Institute was a part of the Warsaw Scientific Society, but from the very beginning it constituted an important unit of the scientific policy of the Polish government as well. One of the aims was to bring together those numerous Polish scientists who had been dispersed all over the world. In an effort to create research facilities, the Geological Institute and the State Institute of Hygiene in Warsaw as well as the Agricultural Institute at Puławy were established almost simultaneously, and some others followed later. The Nencki Institute, formally a private institution, was supported primarily by the Ministry of Education, receiving also special purpose grants from the Ministry of Agriculture and State Lands, the Ministry of Trade and Industry, and the National Culture Fund.

TABLE I

Heads of Departments and Stations of the Nencki Institute during inter-war period

E. Flatau	Department of Neurobiology	1911 - 1923
K. Białaszewicz	Department of Physiology	1916 - 1939
R. Minkiewicz	Department of General Biology	1918 - 1939
A. Lityński	Hydrobiological Station on the Wigry Lake	1920 - 1939
J. Eismond	Department of Experimental Embryology	1922 - 1926
J. Dembowski	Department of Experimental Morphology	1927 - 1934
J. Szaława-Neyman	Department of Biometry	1928 - 1937
M. Bogucki	Maritime Station on the Hel Peninsula	1932 - 1939
K. Orzechowski	Department of Neurobiology	1935 - 1939
J. Wiszniewski	The Biological Station in Polesie	1937 - 1939

The main aim of the Institute was research and dissemination of experimental methods amongst biological scientists in Poland. It was very fortunate that Kazimierz Białaszewicz, a gifted experimenter and organizer, was the first Director of the Institute and Head of the Department of Physiology. He played a leading role in the research and organizing activity of the Institute during the whole inter-war period. In 1920 he was also appointed a professor of Animal Physiology at the Faculty of Natural Sciences of the Warsaw University. The research work of the two units was conducted in the Department of Physiology of the Nencki Institute and students were encouraged to conduct experiments using facilities of the Institute. Research concerned comparative physiology and biochemistry. The main scientific interests of Białaszewicz were the role of osmotic pressure in the embryonic development in frog and chicken and also mineral metabolism in higher vertebrates (Niemierko 1987). His theory, based on experimental findings, was that intense degradation of protein during starvation is the characteristic feature of metabolism in poikilothermic animals. Białaszewicz improved several analytical methods, invented an original method for studying absorption in the alimentary tract, and made significant contribution to the methodology of studies on the physiological changes accompanying physical work in humans. In the early Thirties he introduced neurophysiological research into the Department of Physiology of the Nencki Institute. Liliana Lubińska started her work on the peripheral nervous system and Jerzy Konorski and Stefan Miller conducted experiments on transformation of instrumental reflexes in dogs.

The permanent staff of the Department of Physiology and of the whole Nencki Institute was scarce during the whole inter-war period. The main achievements were accomplished by the intensive research work of young scientists, who were granted for a few years the use of the Institute's facilities, library and the guidance of the senior staff. This way Białaszewicz formed a scientific school of physiology and comparative biochemistry which had a great impact on the development of biology in Poland. Fifteen pupils and coworkers of Białaszewicz were appointed professors after World War II at Polish academic schools and scientific institutions.

Another branch of the Institute was the Department of General Biology (Table I), where environmental adaptation mechanisms of animals were studied. Different approaches were used including psychophysiological and neurophysiological methods. Romuald Minkiewicz, head of the Department, investigated perception of various aspects of visual stimuli (color, shape, motion) and their recognition in amphibians, as well as excitability and transmission in the nerves. He conducted also ethological studies, in particular on insects (Chmurzyński 1966).

Ethological, physiological and morphological studies were conducted in the Department of Experimental Morphology. Jan Dembowski investigated behaviour of the caddis fly larvae and of the earthworms, but his main object of experiments was the protozoan *Paramecium caudatum*. Food preferences and intake, locomotory responses depending on the angle of reflection from a solid obstacle, the role of the location of the center of gravity for orientation in space, plasticity of the geotactic response were investigated (Kuźnicki 1964). Stanisława Dembowska published her classical papers on regeneration of another protozoan, *Stylonychia metilus*.

Experimental neurosurgery and histopathology were the subjects of investigation at the Department of Neurobiology. Staining of living cells and histochemistry were the main methods used in the Department of Experimental Embryology.

Thus, research in these departments focused on current problems of physiology, biochemistry and developmental biology. An important decision was to organize the Department of Biometry in close co-operation with the Warsaw Agricultural University. The aim of the Department was applications of mathematical statistics in different branches of biology, agriculture and economics. Initially, this Department was placed in Chief Census Bureau of Poland. A series of publications by Jerzy Sława-Neyman in collaboration with the eminent British mathematician Egon S. Pearson on the theory of verification of statistical hypotheses had a great impact on the world science (Bartoszyński and Klonecki 1977).

New branches of the Institute were formed consecutively. The Hydrobiological Station on the Wigry Lake was temporarily accommodated in very modest conditions but in 1928 moved to its own new buildings. The research plan was very ambitious, comprising studies of fauna and flora as well as physico-chemical studies on thermal stratification of the lakes and their oxygen balance. The Station's contribution to the foundation of the modern natural classification of fresh-water reservoirs is substantial. Many zoologists, ecologists and hydrobiologists from all over Poland participated in this work. The Station organized the field exercises in biology and fishery for students and other persons.

In 1932 the Ministry of Religious Creeds and Public Education in collaboration with the Ministry of Trade and Industry, entrusted the Institute with the task of organizing a Maritime Station on the Hel Peninsula. The Station conducted hydrographic and physiological research and also algological and parasitological studies. Mieczysław Bogucki investigated adaptation of animals to changes in osmotic pressure and also reproductive and developmental biology of the medusa *Aurelia aurita* from Baltic Sea (Editor 1967). In addition, a series of projects concerning marine biology, reserves of sea fish and various fishing methods were soon initiated. Bogucki was regularly a member of the Polish delegations which participated in annual conferences of the International Council on Maritime Research.

In 1929 the Institute organized an expedition to the district of Polesie to study of the hydrobiological conditions in the Pripet Marshes. However, the Biological Station was open there only in 1937.

Owing to the Stations, the origins of hydrobiology and marine research in Poland are linked to the Nencki Institute.

Publishing activity was another domain in which the Institute was successful. Already in 1926 "Archiwum Hydrobiologii i Rybactwa" (Archives of Hydrobiology and Fishing) and in 1928 "Acta Biologiae Experimentalis" were founded. From the very beginning they attempted to present Polish biological research to the world. The scientific journals of the Nencki Institute were exchanged for the journals of many foreign scientific institutions and the Institute's achievements were recognized in the international world of science.

Thanks to the funds for buying books and the exchange of publications, the Institute's library expanded rapidly from a total of 695 volumes in 1920, to 22,530 volumes of books and periodicals in

1935. It was run on an open basis; scientists from other research centers and students had a free access. Konorski noted in his autobiography (Konorski 1974) that in their student days he and Miller, thanks to the Nencki Institute's library, had an access to the writings of Pavlov, which started their interest in the research on conditioned reflexes.

A very important line of the Institute's activity was lecturing, publishing books and brochures. "The Natural History of a Protozoan" by J. Dembowski, which first appeared in 1924, was a classic in Polish popular science. Members of the Institute participated in preparing university textbooks. Many scientific publications of world significance were also translated and published in Polish. Konorski and Miller translated some Pavlov's lectures and writings of C. Sherrington and E. Adrian.

The devastation of Poland during World War II was immediately felt by the Nencki Institute when the Nazis invaded in September 1939. The Physiology Department on 15 Wawelska Street was destroyed by artillery fire, and laboratories located on 8 Śniadeckich Street received a direct hit of the air bomb. Part of the Institute's library was lost; the remainder was either dispatched to Germany or burnt during occupation. Only a few dozen volumes remained of the 30,000 volume collection. Attempts to extricate equipment, library volumes, laboratory notes, and manuscripts were futile, and all that remained after the invasion was destroyed or lost during the long occupation.

Losses in human life were the heaviest blow to the Institute. Some members of the Institute were killed in action at the front, some were murdered by the Nazis, some fell in the Warsaw Uprising. Those who survived participated in the clandestine teaching organized during occupation. Professor Białaszewicz organized small scientific meetings of the Polish Physiological Society in his apartment. Only a few members of the Institute had the possibility of continuing their research work, among whom were Konorski and Lubińska, who left Warsaw for Białystok and thanks to colleagues from the Pavlov Laboratories, they eventually reached Leningrad. During the war they worked in the Center of Primates Research in Sukhumi, where Konorski became head of the Physiology Department.

In 1945, on their way back to Poland Jerzy Konorski and Liliana Lubińska met in Moscow with Jan and Stanisława Dembowski and then in Warsaw with Włodzimierz and Stella Niemierko. It was full agreement among them that the Nencki Institute should be reconstructed and, as Warsaw was completely destroyed, chose Łódź for its temporary site. Those six pre-war members of the Nencki Institute contributed prominently to its reconstruction. Organization work started in a four-room apartment, but in 1946 the Institute received from the City Council a building on 66 Południowa Street, where satisfactory space was available. W. Niemierko headed the Department of Biochemistry, J. Konorski the Department of Neurophysiology and J. Dembowski the Department of Biology. In accordance with the Institute's tradition they combined their duties with chairs in the Łódź University, teaching students and recruiting the most promising of them to the Institute.

This post-war generation of scientists grew rapidly. Young and old, everybody strived to compensate for the lost years of war. Professors reconstructed their manuscripts written earlier and lost during the war. The first editions of the "Animal Psychology" and of the "Ape Psychology" by J. Dembowski appeared in 1946. In the following years these books were translated and edited in German, Italian and Russian. In 1948 Konorski published a monograph "Conditioned Reflexes and Neuron Organization". The theoretical significance of this book for contemporary neurobiology has been fully appreciated only from a time distance (Mowrer 1976). The first post-war issues of both journals edited by the Nencki Institute appeared in 1947. In 1948, when the reconstructed Institute celebrated its 30th anniversary of foundation, the scientific staff counted only 36 members. Although not very large, the Institute once again had become a scientific center vibrating with life and energy.

Table II shows the main steps of further expansion of the Institute. A Hydrobiological Station was opened in Mikołajki, in the middle of Masurian Lakes area. At the same time the Institute organized a Department of Animal Ecology in Warsaw, which, however, soon transformed into the independent Institute of Ecology. It was replaced by the Department of Experimental Hydrobiology headed by Romuald Klekowski. The organization of the Polish Academy of Sciences in 1952, the election of Jan Dembowski as the first President of the Academy, and the incorporation of the Nencki Institute to the Academy as one of its four initial research centers, accelerated the erection of the new facilities for the Nencki Institute in Warsaw.

The Institute's return to Warsaw, where for the first time it occupied premises suited to its needs, contributed to its rapid development. The whole scientific staff moved to Warsaw as well. They were joined here by new colleagues recruited mostly among young graduates of the Warsaw University. A new Department of Experimental Psychology headed by Eugeniusz Geblewicz was founded. The reconstruction of the Nencki Institute was concluded in 1956, when the Institute was granted the rights to confer scientific degrees.

The development of the Institute survived some occasional interruptions. Members of the Institute twice experienced application of authoritarian methods in science. First, at the beginning of the Fifties, when an influential group of people, who doctrinally interpreted some Pavlov's writings, started sharp criticism of Konorski's views on the mechanisms of conditioning expressed in his book edited in Cambridge. High prestige of professor Jan Dembowski, the first director of the revived Nencki Institute, helped to reduce the attacks. Second, in the Sixties, important branches of the Institute, the Hydrobiological Station and the Department of Experimental Psychology, were removed from the Institute by the arbitrary decision of the Biological Section of the Academy. In addition, a substantial part of the Institute's space had been allocated to other institutions, financial support was drastically cut off, and the number of positions in the Nencki Institute steadily reduced. The government's edict precluding the possibility of combining research positions in the institutes and teaching positions in the Universities severed traditional contacts of the Nencki Institute with students.

The violent attacks against Konorski by no means had only personal character. They attempted to disprove directions of research and achievements of the Department of Neurophysiology, which aimed

TABLE II

Stages of the Nencki Institute development during post-war period	
1946	Department of Biochemistry and Department of Neurophysiology
1947	Department of Biology
1951	Hydrobiological Station in Mikołajki (till 1961)
1951	Department of Animal Ecology (till 1952)
1952	Department of Experimental Hydrobiology (till 1974)
1955	Department of Experimental Psychology (till 1961)
1956	The rights to confer advanced scientific degrees
1968	The first Antarctic Expedition
1968	Opening of the post-graduate courses
1970-1972	New by-laws and changes of internal organization
1971	Founding of the country-wide program of research
1973	Laboratory of Electron Microscopy
1975	Laboratory of Data Processing
1988	Laboratory of Cell and Tissue Culture

to test the set of working hypotheses advanced in the "Conditioned Reflexes and Neural Organization". The main problems under investigation concerned the neural models of instrumental responses and the role of conditioned inhibition in the transformations of conditioned responding. The role of the prefrontal cortex in learning and performance of a variety of tasks based on short- and long-term memory in dogs, cats and rats received world-wide recognition. Plastic changes of inborn reflexes, problem of their instrumentalization and the role of somatosensory and motor cortices in programming and execution of motor manipulatory and locomotory reactions were also intensively studied (Konorski 1968, Żernicki 1985).

The difficulties that the Institute confronted in the Sixties were related to the controversy concerning directions of further development of biochemical research in Poland. Shortening of space and resources was a real danger for the new lines of research growing within the Department of Biochemistry. Initially, insect biochemistry played a dominating role with special emphasis on the lipid metabolism, biosynthesis of phospholipids, oxidative phosphorylation in mitochondria, biosynthesis of nucleic acids and the role of folic acid (Niemierko 1963, Zielińska 1987). Gradually, the research developed into three directions: mitochondrial energy metabolism and the enzyme systems involved in one-carbon pathways in the cell, acetylcholinesterase activity and axoplasmic flow, and muscle biochemistry (Grzelakowska-Sztabert 1972).

Close collaboration of the two laboratories, one headed by Stella Niemierko in the Department of Biochemistry and the other by Liliana Lubińska in the Department of Neurophysiology, resulted in effective development of neuro-biochemistry in the Nencki Institute (Kaczmarek and Oderfeld-Nowak 1993). The greatest achievement was the discovery of the relatively fast bidirectional transport of the axon elements (Niemierko 1991, Zelená 1991).

Muscle biochemistry had a long tradition in the Nencki Institute but modern research in the area stems from the interest in ATP and calcium binding properties of G-actin and in the functional properties of troponin complex. The team headed by Witold Drabikowski, who organized the Department of Biochemistry of Nervous System and Muscle in 1970, was mainly responsible for the rapid growth of this direction of research in the Institute (Perry 1984).

The introduction of new methods and modern directions of research were important factors contributing to the progress of research in all departments of the Institute. The First International Congress of Protozoology in 1963 entrusted the Nencki Institute with founding and editing a new international journal, *Acta Protozoologica*. The Department of Hydrobiology joined the international research on biological productivity concentrating on the study of energy budgets of animal species. The other initiative was a participation in biological antarctic expeditions, the first one in 1968 and the second in 1971-1972, organized by the Arctic and Antarctic Institute in Leningrad. The opening of post-graduate courses in the Autumn of 1968 brought a new group of young people into the Institute.

In 1971 a new form of organization of research was introduced in Poland. Instead of financing each institute or academic school independently, the funds were given for large programs of research proposed and co-ordinate by leading centers in the field. The research proposed in the programs was conducted by selected laboratories from different institutions. As one of the first in Poland, the project "Structure and Functioning of the Nervous System" was established and its co-ordination was entrusted to the Nencki Institute. Next year another project also co-ordinate by the Nencki Institute, "Morphophysiology and Biochemistry of the Cell and Subcellular Structures" was started. Results of the research were reported on annual conferences and peer review was introduced.

The new system of financing increased the Institute's influence on the directions of bio-medical research in Poland and strengthened ties with many research centers, especially with the Institute of

Pharmacology (Cracow), the Center for Experimental and Clinical Medicine (Warsaw), the Institute of Animal Physiology and Nutrition (Jabłonna), the Jagiellonian and other Universities, and with nearly all Medical Academies in Poland (Zieliński 1978, Kossut 1991).

The change of research organization accelerated processes of transformation in the Institute. The departments became more homogeneous. By earlier mutual agreement, the Department of Energetics and Biological Production of the Nencki Institute was transferred to the Institute of Ecology of the Polish Academy of Sciences. The present structure of the Nencki Institute consisting of four departments (Department of Cellular Biochemistry, Department of Muscle Biochemistry, Department of Cell Biology and Department of Neurophysiology) subdivided further to laboratories was established. In accordance with the new needs, the independent Laboratories of Electron Microscopy, of Data Processing, and of Cell and Tissue Culture were organized. Dissemination of modern methods was stimulated by methodical courses, seminars and common projects. Many scientists from other institutions have taken advantage of the Nencki Institute's facilities.

To keep pace with the trends of the world's science, the new central project "Physiological and biochemical regulatory mechanisms of cell and organism" was proposed and then co-ordinate by the Nencki Institute in the years 1985-1990. Its aim was to study biochemical and physiological mechanisms of cellular interactions as a basis of functioning of more complex systems, particularly the brain - the most complex system created in the process of evolution.

In 1991 the system of individual grants was introduced. It appears that the Nencki Institute succeeded also within this system of research support, which is especially suitable for young scientists backed by the knowledge, equipment and facilities accumulated in the Institute.

It is necessary to acknowledge the role played by the Nencki Institute in the founding of other research centers in Poland. The pre-war Maritime Station of the Nencki Institute moved at the turn of 1938-1939 from Hel to specially erected buildings in Gdynia. After World War II it became the Sea Fisheries Institute with Mieczysław Bogucki as the first director. Three units of the Nencki Institute became the basis of establishment and development of the Institute of Ecology of the Polish Academy of Sciences: Department of Animal Ecology in 1952, Hydrobiological Station in Mikołajki in 1961, and Department of Energetics and Biological Production in 1974. The Research Center for the Biology of Antarctic of the Polish Academy of Sciences was established in 1992. It is headed by Stanisław Rakusa-Suszczewski, who was trained in the Nencki Institute and participated in the first antarctic expedition in 1968. A newly organized Research Center for Maritime Biology of the Polish Academy of Science in Gdynia has its roots in the Nencki Institute as well.

The Institute has contributed significantly to international co-operation of scientists. For 75 years the Institute maintained numerous links based on personal and institutional contacts with many research centers. From 1956 to 1982, the Nencki Institute played an important role in West - East dialogue of scientists (Brennan and Zieliński 1981). Many eminent scholars participated in the Departments' seminars, conferences and symposia organized by the Institute. Foreign researchers conducted experiments in Institutes' laboratories and some of them obtained their doctor degrees in the Nencki Institute. Several of our initiatives concerning international co-operation were taken up by foreign scientists and gave rise to new publications and new organizations.

The Nencki Institute succeeded in retaining certain important features: an interdisciplinary research program, an interest in modern methods and open character of its laboratories, a variety of approaches to form new lines of research and develop new generations of researchers, attempts to stimulate and integrate efforts of bio-medical research in Poland, and vivid contacts with research centers West and East.

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Past and present of the Department of Neurophysiology in the Nencki Institute

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The Department of Neurophysiology was founded in the Nencki Institute in 1946. At that time the Institute was located in Łódź, since Warsaw had been destroyed during the war. The founders of the Department were Jerzy Konorski and Liliana Lubińska, the pre-war Institute's workers. Konorski, the head of the Department, was a pioneer in investigations on instrumental conditioning. Within a few years he was joined by a group of about 15, mostly very young collaborators: a second generation of the Department's workers. The first Konorski's associates were: Zofia Afelt, Stefan Brutkowski, Elżbieta Fonberg, Włodzimierz Kozak, Waclawa Ławicka, Irena Łukaszewska, Irena Stępień, Genowefa Szwejkowska (a pre-war Institute's worker), Wanda Wyrwicka and Andrzej Zbrożyna. Their research was mainly devoted to various aspects of conditioning in dogs. This fitted the name of the Department since according to Pavlovian tradition, the conditioned-reflex investigations represent a part of physiological research.

In the middle fifties the Institute moved back to Warsaw, to a new, large building. About the same time the iron curtain was cracked in Poland and our west frontier became more open. Simultaneously the east frontier also became easier to cross. We began travelling frequently and many foreign scientists visited us. In consequence, the Department gradually lost its monolithic, conditioned-reflex profile, reacting rapidly to new tendencies in the international neuroscience. Visual, motor, psychophysiological and developmental investigations were introduced. In addition, the ethological group and later on the Laboratory of Neurochemistry (headed by Stella Niemierko, a pre-war Institute's worker) joined us from other departments of the Institute.

In the early seventies Polish authorities offered more money for science and for the second time after the war many new positions became available in the Institute. Konorski's pupils were joined by about 20 young researchers: a third generation of workers appeared in the Department. Some of them (Anna Grabowska, Małgorzata Kossut, Andrzej Wróbel, Jolanta Zagrodzka) are at present the heads of laboratories in the Department.

In 1973 Jerzy Konorski died and I succeeded him as the head of the Department. It was rather difficult to succeed a great leader and to direct the Department which was rapidly changing. However, I was fortunate to receive the help of several colleagues. I especially owe much to Irena Stępień and later to Jolanta Zagrodzka. I have also received important encouragement from two distinguished foreign colleagues, Jerzy Rose and Eliot Stellar.

Although large, the Department has remained well integrated. Our common roots are certainly one of the important reasons of integration. The Department's Wednesday seminars are excellent forum for discussion of our results. Last but not least we help each other in many respects. For example, Anna Kosmal is always ready to help in neuroanatomy and Kazimierz Zieliński in statistics.

We are fortunate that our Department is a part of the Nencki Institute. First, the development of various biological techniques in the Department make important contacts with three remaining Institute's departments: the Department of Cellular Biochemistry, the Department of Muscle Biochemistry and the Department of Cell Biology. Second, the Institute provides outstanding facilities for our work. In particular, we have an excellent animal house (headed by Maria Walkowska, previous Department's member) and library with almost all neuroscience journals.

The Department has always maintained vivid contacts with other neuroscience laboratories in Poland. Moreover, in some fields it has played an integrative role, e.g., we coordinated a number of large neuroscience programs in Poland. We have maintained particularly close cooperation with the Department of Neurosurgery, Medical Research Centre (headed by Lucjan Stępień, who was also the member of our Department, and later by Eugeniusz Mempel), the Department of Bionics, Institute of Biocybernetics and Biomedical Engineering (headed by Ryszard Gawroński and later by Wojciech Zmysłowski), the Department of Anatomy, Medical Academy in Gdańsk (headed by Olgierd Narkiewicz) and the Department of Animal Physiology, University of Łódź (headed by Andrzej Romaniuk).

We have also been collaborating with many foreign laboratories. About 250 foreign guests presented their results in the Department, some of them visit us every few years. We had about 50 foreign visitors, from East and West, working in the Department for at least three months. Some of our long-term and/or frequent visitors influenced strongly our work. Among these are: Jim Brennan, Ivan Divac, George Gerstein, Paweł Hnik, Adrian Morrison, Tomasz Radil, Guy Santibanez and Jeffrey Wilson. We also owe a lot to some other foreign friends: Giorgio Bignami, Roberst Brush, Jan Bureš, Pierre Buser, Robert W. Doty, Giuseppe Moruzzi, Giancarlo Pepeu, Steve Rose, Pavel Simonov, Jim Sprague, Michael Stewart, Holger Ursin and Clinton Woolsey. Many collaborations and the participation of many our workers in the international conferences were sponsored by international organizations, in particular by IBRO and the European Training Programme in Brain and Behaviour Research. The Department publishes a well established international journal *Acta Neurobiologiae Experimentalis* (until 1970, its title was *Acta Biologiae Experimentalis*).

We have very close relations with the Laboratory of Neuropsychology in Bethesda and the Institute of Neurological Sciences in Philadelphia. A number of NIH projects with these institutions (in Bethesda the project officers were H. Enger Rosvold, Patricia Goldman-Rakic and Mortimer Mishkin, and in Philadelphia, William Chambers and Eliot Stellar) had an important mutual impact. In the years 1958-1988 working conferences were organized every three years by our Department, the Institute of Higher Nervous Activity and Neurophysiology in Moscow and the Institute of Physiology in Prague. Jerzy Konorski, Ezras Asratyan and Ernest Gutmann were the organizers of the first conference held in Poland.

The Department is a place where Western and Eastern neuroscientists meet frequently. This particularly happens during international symposia organized by the Department. A good example is "The Warsaw colloquium on instrumental conditioning and brain research" (see Żernicki and Zieliński 1979), where half of the participants were from Eastern and half from Western countries. Many of our workers moved abroad for various reasons, not only scientific, but also political, personal and financial as the funds for conducting research are scarce and the wages of scientists ridiculously low in Poland. The majority of these colleagues remained scientifically active and stay in close contact with us. These are: Marek Celiński, Jan Bruner, Jolanta Chmielowska, Bogdan Dreher, Bella Harutiunian-Kozak, Krystyna Jabłonowska-Ciesielski, Elżbieta Jankowska, Paweł Jastreboff, Lech Kiedrowski, Ewa Kostarczyk, Włodzimierz Kozak, Grażyna Markow-Rajkowska, Alicja Markowska, Zygmunt Pizło,

Anna Potempska, Janusz Rajkowski, Ewa Rożkowska-Ruttiman, Stanisław Sobótka, Stefan Sołtysik, Bolek Srebro, Iwona Stępniewska, Jolanta Ułas, Klaudiusz Weiss, Andrzej Wieraszko, Wanda Wyrwicka and Andrzej Zbrożyna. At the 75th anniversary of the Institute we were not in the position to invite our numerous foreign friends because of financial limitations. However, we invited previous members of the Institute and many of them could attend the anniversary conference.

A number of Department's workers died. It was particularly difficult to accept the death of these who left as young persons. These were Stefan Brutkowski, Jadwiga Dąbrowska and Renard Korczyński.

The Department has obtained important results in the majority of fields of neuroscience, but it is concentrated on various aspects of neural plasticity (learning and memory, development driven by sensory stimulation, recovery of function after brain damage). It is beyond the scope of this article to review systematically the Department's achievements. I will only mention some representative results, characterizing the past and the present lines of research. Many of our papers were published in *Acta Neurobiologiae Experimentalis*; some are in the proceedings of symposia organized by the Department (Konorski et al. 1972, Doty et al. 1973/1974, Żernicki and Zieliński 1979/1980, Oderfeld-Nowak et al. 1990). Some of our results were described in detail in Konorski's monograph (1967) and in review papers (Brutkowski 1965, Konorski 1968, Fonberg 1986, Żernicki 1986, 1991, Kossut 1992).

Conditioning. Konorski (1948) presented a concept of neuronal plasticity and a concept that the mechanism of conditioned reflexes is based on the Sherringtonian principles of functioning of the central nervous system. Konorski and Szwejkowska (1952) described the principle of the primacy of the first conditioned-reflex training. Wyrwicka (1952) provided evidence that there are double connections linking the "center" of the conditioned stimulus with the "center" of the instrumental motor act; one of them is indirect, through the drive "center". Tarnecki (1962) demonstrated that it is easy to instrumentalize a movement elicited by electrical stimulation of the sensory cortex but not the motor cortex. Sołtysik and Kowalska (1960) determined the relations between classical and instrumental components in defensive conditioning. Górska and Jankowska (1961) found that proprioceptive feedback plays a minimal role in the instrumental conditioned reflex. Walasek et al. (in press) found a bidirectional effect of novel stimuli on the bar pressing response in rats. Łukaszewska and Niewiadomska (in press) found that discrimination learning is better in spontaneously hypertensive rats than in normotensive controls. Dobrzańska (1978) described social learning in ants and Godzińska et al. (1992) rapid escape learning in bumblebees.

Prefrontal cortex. It was found that after prefrontal lesions in dogs the inhibitory conditioned reflexes are disinhibited (Brutkowski et al. 1956, Dąbrowska 1972, Brennan et al. 1976). Zieliński (1972) showed that the short-latency avoidance responses are severely impaired in prefrontal cats. Stępień (1974) found that in prefrontal dogs the response to the conditioned stimulus location is enhanced. Dreher and Żernicki (1969) described the impairment of habituation of the ocular orienting reflex in prefrontal cats. Ławicka and Konorski (1959) and Stasiak and Ławicka (1990) found, respectively, that following prefrontal lesions in dogs the delayed responses and responses in the Konorski Test for short-term memory are impaired. Kosmal and associates (Kosmal 1981, Markow-Rajkowska and Kosmal 1987) described the distribution of afferents to frontal cortex in dogs.

Memory. Konorski (1967) presented a concept of gnostic units. Budohoska et al. (1973) described different mechanisms for immediate and short-term memory in man. Łukaszewska (1985) determined properties of the short-term memory of a visual change in rats. Nikolaev et al. (1992) documented increased expression of the c-fos mRNA in rat brain in learning-related phenomena and Kaczmarek (1993) formulated a hypothesis that gene regulatory regions play an important role in the integration of information during long-term memory formation.

Limbic system. Fonberg (1958) presented a concept on the role of fear in neurotic states. Fonberg and associates (see Fonberg 1986) discovered the inhibitory and excitatory role of two antagonistic parts of amygdala in motivation, emotional disorders and conditioned responses. Zagrodzka and Fonberg (1978) determined neural mechanism of the predatory behavior in cats. Kostarczyk and Fonberg (1982) determined the role of autonomic changes in the mechanisms of alimentary and social rewards in dogs. Werka and Marek (1990) found that amygdala is strongly involved in the control of post-stress analgesia. Srebro et al. (1973) showed that the destruction of specific septal nuclei evoked the degeneration of cholinergic fibers in the hippocampus.

Sensory systems. Using behavioural and electrophysiological methods Grabowska (1983) and Sobótka et al. (1984) showed in man that visual information is differently processed and stored in the left and right hemispheres. Walerjan and Tarnecki (1991) developed a new mapping technique for analysis of cerebral electrical activity in man. Harutiunian et al. (1970) and Turlejski (1975) described visual single unit responses in the tecto-pretectal region and in the lateral suprasylvian cortex, respectively, in the awake cat's cerebrum. Dec et al. (1978) described visual responses in cat's isolated midbrain. Wróbel (1982) proposed a new model for the circuitry of the lateral geniculate body and Wróbel et al. (1994) found the specific activity within beta frequency band (about 20 Hz) appearing in the cat's visual cortex and lateral geniculate nucleus during attentive visual behaviour. Dobrzecka et al. (1965) found direct sensori-motor pathway in dog's cerebral cortex for the "specific tactile stimulus". Chmielowska et al. (1986) mapped the vibrissal projections to the first somatosensory cortex of mice with 2-deoxyglucose and with this technique Kossut and Siucińska (1993) discovered reversible changes in the cortical body maps of vibrissal receptors resulting from classical conditioning training that involved stimulation of vibrissae. Korda (1974) described critical factors determining parental behavior in dogs. Chmurzyński (1964) identified mechanisms underlying stages of spatial orientation in the digger wasp *Bembix rostrata*.

Motor system. Afelt et al. (1975) and Górska et al. (1993) described postural and locomotor deficits in cats with spinal lesions. Using a new recording technique Błaszczuk and Dobrzecka (1989) determined principles of limb coordination in dogs. Kasicki et al. (1991) described two locomotor strips in cat's diencephalon. Czarkowska-Bauch (1990) found common spinal mechanism of the tactile placing and stumbling in cat. Kałużny and Tarnecki (1993) developed a new method for the analysis of dynamics of spike trains in neuronal networks of cat's cerebellum and red nucleus.

Development. Jabłonowska and Budohoska (1976), Kołtuska and Grabowska (1992) and Szeląg et al. (1992) provided evidence that brain lateralization develops in ontogenesis and can be influenced by individual experience. Wyrwicka (1959) and Ławicka (1989) described impairment of the detour behaviour and delayed response learning, respectively, in cage-reared animals. Zabłocka et al. (1980) found that in cats deprived visually in the early period of life, the role of the superior colliculus in visual learning is increased. Michalski et al. (1984) found that one of the ways in which visual deprivation affects neuronal responses is by altering the interneuronal connectivity in primary visual cortex. Głazewski et al. (1992) found a correlation between functional plasticity of the barrel cortex and the development of mature activity of voltage dependent calcium channels and NMDA receptors. Dobrzański (1971) described rapid manipulatory learning in young ants.

Recovery from brain damage. Ślósarska and Żernicki (1971) found that the sleep-waking cycle recovers in chronic pretrigeminal and cerveau isolé cats. Oderfeld-Nowak et al. (1984) found in rats that administration of exogenous gangliosides facilitates recovery from brain damage.

Peripheral nervous system. Lubińska, Niemierko and associates (Lubińska et al. 1963, Lubińska and Niemierko 1971) discovered bidirectional flow of the axoplasm. Skangiel-Kramaska and Niemierko (1975) found the soluble form of acetylcholinesterase in peripheral nerves.

TABLE I

Current research of the Department's members with Ph.D.

BŁASZCZYK Janusz	Long term potentiation, brain slices.
BUDOHOSKA Wanda	Hemispheric differences in visual perception in man.
CHMURZYŃSKI Jerzy	Spatial and sexual orientation in insects. General ethology. Biological roots of culture, esp. aesthetic phenomena.
CZARKOWSKA Julita	Segmental cutaneous reflexes. Hoffmann reflex in awake animals. Plasticity of the monosynaptic reflex.
DJAVADIAN Rouzanna	Connections of visual areas in cat. Serotonin in development.
DEC Krystyna	Electrophysiological investigations of the visual system in cats.
FONBERG Elżbieta	The role of amygdala and hypothalamus in alimentary and social behavior, aggression and experimental neuroses. Pharmacological investigations.
GODZIŃSKA Ewa	Ethological analysis of learning processes in social insects (ants and bumblebees).
GÓRSKA Teresa	Locomotion after spinal lesions.
GRABOWSKA Anna	Psychophysiology of vision in man. Neurosurgical patients. Hemispheric differences.
KACZMAREK Leszek	Molecular basis of neuronal plasticity. Learning and memory.
KAŁUŻNY Paweł	Computational neuroscience, neural networks, electrophysiology.
KASICKI Stefan	Locomotion, EMG and EEG investigations.
KOSMAL Anna	Neuroanatomical and histochemical investigations of the associative cortex and limbic system.
KOSSUT Małgorzata	Cortical plasticity in visual and somatosensory systems.
KOWALSKA Danuta	Cerebral structures involved in recognition memory.
ŁAWICKA Wacława	Prefrontal cortex. Short-term memory. Auditory targeting reflexes.
ŁUKASZEWSKA Irena	Learning and memory. Cholinergic system.
MICHALSKI Andrzej	Single neuron recording from the visual cortex.
NIEMIERKO Stella	Acetylcholinesterase in peripheral nerves and in CNS.
NIEWIADOMSKA Grażyna	Neurochemical and morphological correlates of the basal forebrain cholinergic system in adult and ageing brain.
NOWICKA Anna	Visual evoked potentials, interhemisphere transmission of information, hemispheric specialization.
ODERFELD-NOWAK B.	Biochemical aspects of recovery from brain damage; neuron-glia interactions; effects of gangliosides and neurotrophic factors.
SKANGIEL-KRAMSKA J.	Neurochemical correlates of brain plasticity. Neurotransmitter receptors. Quantitative autoradiography.
SKUP Małgorzata	Neuronal death and recovery after brain damage: mechanism of trophic responses. Neurogenesis in the adult brain.
STASIAK Maciej	Memory, behavioral tests; prefrontal and temporal cortex. Visual deprivation.
SZELAĞ Elżbieta	Time perception, speech disorders, hemispheric differences.
TARNECKI Remigiusz	Visuomotor coordination, electrophysiological investigations. Computer techniques in electrophysiology.
TURLEJSKI Krzysztof	Cortical development and plasticity. Serotonin in development. Evolution of the CNS.
WALASEK Grażyna	Interrelations between alimentary and defensive stimuli.
WERKA Tomasz	Functional recovery from cerebral lesions. The role of limbic system in defensive behavior.
WĘSIERSKA Małgorzata	Antagonism between fear and alimentary drive in the CER method. Conditioned inhibitor. Strategies of responding.
WRÓBEL Andrzej	Visual system, electrophysiological investigations.
ZABŁOCKA Teresa	Visual deprivation, behavioral investigations.
ZAGRODZKA Jolanta	Predatory and aggressive behavior in cats and rats; pharmacological and surgical manipulations.
ŻERNICKI Bogusław	Visual deprivation. Pretrigeminal preparation. Ocular-fixation reflex.
ZIELIŃSKI Kazimierz	Strategies of conditioning. Defensive conditioning. Stimulus control. Prefrontal cortex.

The current research interests of individual Department's members can be found in Table I. A few of these researchers and 15 not listed young fellows working for the Ph.D. constitute a fourth generation of researchers of the Department.

A large group of highly experienced and devoted technical workers contributed greatly to the progress of the Department. A few of them are: the late Antoni Rosiak, animal caretaker, the late engineer Józef Folga, the late Ewa Stajudowa, the managing editor of *Acta Neurobiologiae Experimentalis* and Maria Rauowicz, the retired worker of the surgery room.

At present 12 laboratories constitute the Department of Neurophysiology: Laboratory of Visual Perception (head, Bogusław Żernicki), Laboratory of Afferent Systems (head, Remigiusz Tarnecki), Laboratory of Psychophysiology (head, Anna Grabowska), Laboratory of Defensive Conditioned Reflexes (head, Kazimierz Zieliński), Laboratory of Cortical Plasticity (head, Małgorzata Kossut), Laboratory of the Limbic System (head Jolanta Zagrodzka), Laboratory of Motor Control (head, Teresa Górská), Laboratory of Neurochemistry (head, Barbara Oderfeld-Nowak), Laboratory of Ethology (head, Jerzy Chmurzyński), Laboratory of Neuroanatomy (head, Anna Kosmal), Laboratory of Visual System (head, Andrzej Wróbel) and Laboratory of Molecular Basis of Brain Plasticity (head, Jolanta Skangiel-Kramska). In addition, Tissue Culture Unit (head, Leszek Kaczmarek) is scientifically a part of the Department.

The Department is a large, interdisciplinary and active neuroscience center. The presence of various lines of neurobiological research in the Department as well as a large and experienced group of researchers in other Institute's departments form a fertile ground for cross-breeding of ideas and borrowing of techniques. The new generation of neuroscientists grows in this unique multidisciplinary environment that is most suitable for modern neuroscience.

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Department of Cell Biology.

Research on protozoa - an important element of history and present times in the Nencki Institute

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Research on protozoa aimed at explaining the basic vital phenomena of an eukariotic cell is one of the specialities of the Nencki Institute since 1918 until today. Jan Dembowski was the founder of this discipline when after his return from Vienna in 1918 he began to work in the Department of General Biology as senior assistant. All his experimental research was devoted to a ciliate *Paramecium caudatum*, beginning with the first paper dated 1922 and ending with the last one published in 1950. *Paramecium* was also a subject of one of the best books in the Polish popular scientific literature entitled "The natural history of a Protozoan, the introduction to the general biology" (1st ed. 1924, 5th ed. 1962).

In 1920 Dembowski's wife - Stanisława joined the Department of General Biology of the M. Nencki Institute, at first as a laboratory assistant, then as a junior assistant. Dembowska is recognized in the international scientific literature for her papers concerning regeneration of *Stylonychia mylitis* and of several marine *Hypotricha* published in years 1924-1938. Alongside her husband Stanisława Dembowska was the second pioneer of protozoological research in the Institute. In the twenties and thirties a number of valuable experimental research on biochemistry and physiology of protozoa was also carried out by other scientists, especially in the Department headed by Kazimierz Białaszewicz.

Both Jan and Stanisława Dembowski paid considerable attention to the education of their followers. Financial shortages and sometimes even poor working conditions in the Institute in the period of the II Polish Republic did not help them to succede in this. During his work in the Institute (in the years 1918-1934) Dembowski, being the head of the Department of Experimental Morphology (1927-1934), had two collaborators: Max Chejfec and Wanda Milicer. Chejfec died in the Vilnius ghetto, Milicer worked as a teacher after the Second World War.

The rapid development of protozoology since 1948 i.e. since the return of the Dembowski's family from Moscow, is related to their didactic activities as well as to the research and didactic activities of the Dembowski's students and followers. The post-war generation of the Dembowski's alumni who developed research in protozoology consisted of the Łódź and Warsaw groups. In the years 1948-1952 members of the first one were: Stanisław Dryl, Maria Brutkowska, Andrzej Grębecki, Włodzimierz Kinastowski, Leszek Kuźnicki, Irena Nowakowska. The Warsaw group was led by Stanisława Dembowska and developed a little later (1952-1956). It consisted of: Marek Doroszewski, Krystyna Golińska, Maria Jerka-Dziadosz. After the Institute's removal from Łódź to Warsaw both groups

merged with a numerous group of ethologists, who examined first of all insects and mammals. As a result of the merger ethologists and protozoologists were represented in equal proportions in the Department of General Biology of the Institute.

The academic year 1960/61 initiates a new stage in the development of the Department of General Biology. Jan Dembowski retires and Stanisława Dembowska dies at the beginning of 1961. Stanisław Dryl becomes the head of the Department. During the decade 1961-1971 the Department evolves towards a more homogeneous research profile which is reflected in the change of its name to the Department of Cell Biology (1971) at which time all ethologists transferred to the Department of Neurophysiology.

In the sixties the possibilities of long-term study visits to the West were opened up, which made it possible for Polish protozoologists to study and work in the eminent American, French and British research centers as well as to participate substantially in the international congresses, symposia and meetings. Also, a considerable widening of the scope of research is being noted. Until sixties only ciliates were studied experimentally and later also amoebas, flagellates and myxophyta attracted attention of our researchers.

Founding of the journal "Acta Protozoologica" which started to appear in 1963 was an important factor in initiating the international scientific cooperation. The initiator and first editor of the "Acta Protozoologica" was Zdzisław Raabe, professor of the Warsaw University. It was absolutely clear to him that the office of the journal's editor should be placed in the Nencki Institute, where the biggest and strongest group of protozoologists in the country worked. Although the journal publishes results of research of a narrow discipline, it made an international carrier, and belongs to the top ten of all scientific periodicals issued in Poland, having an impressive foreign distribution. Its editorial level meets the most demanding criteria.

Years 1971-1981 are the period of the most intense development, coinciding with employing of numerous young researchers in the Department of Cell Biology, as in the whole Institute. In recognition of an increasing international importance of the Polish protozoological research the M. Nencki Institute was entrusted with the task of organizing the VI International Congress of Protozoology. The congress took place in Warsaw from 5 to 11 July 1981. It was a scientific and organizational success and it distinguished itself with friendly atmosphere.

During the Congress I delivered the plenary lecture "Protozoology in Poland - Past and Present". The basic research staff of the 5 laboratories of the Department of Cell Biology of the Institute, as well as their research topics in 1982, are shown on the figures No. 1, 2, 3, 4, 5. During the VI Congress of Protozoology Polish scientists made 42 presentations of their results. More than half of those presentations concerned two sets of problems: 1) motile mechanisms (in ciliates, amoebas and cytoplasm), excitability and taxis; 2) morphogenesis and genetics of ciliates. These were the problems traditionally developed by our research staff since the establishing of the Institute. Obviously the scope of scientific trends, cultivated during the previous 75 years, was much wider.

Protozoa as the simplest eukariotic organisms are used in various research - from molecular genetics to ecological and environmental studies. Dangers to man and animals caused by pathogenic species of protista remain as yet unfended and demand further studies. All this makes me look optimistically in the future of protozoology in the Nencki Institute. I regard as temporary the difficulties concerning low interest in this discipline among university graduates. I believe that in the next decades the research on basic vital processes in those small, but intriguing objects will remain the speciality of the Nencki Institute.

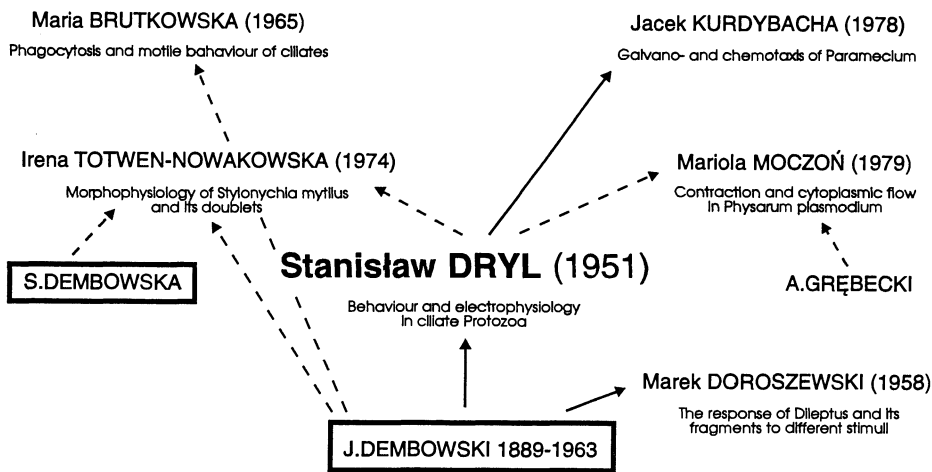


Fig. 1. The Laboratory of the Cell Membrane in 1981. Head: Stanisław Dryl. Main problem: behaviour, reactivity and electrophysiology of Ciliata.

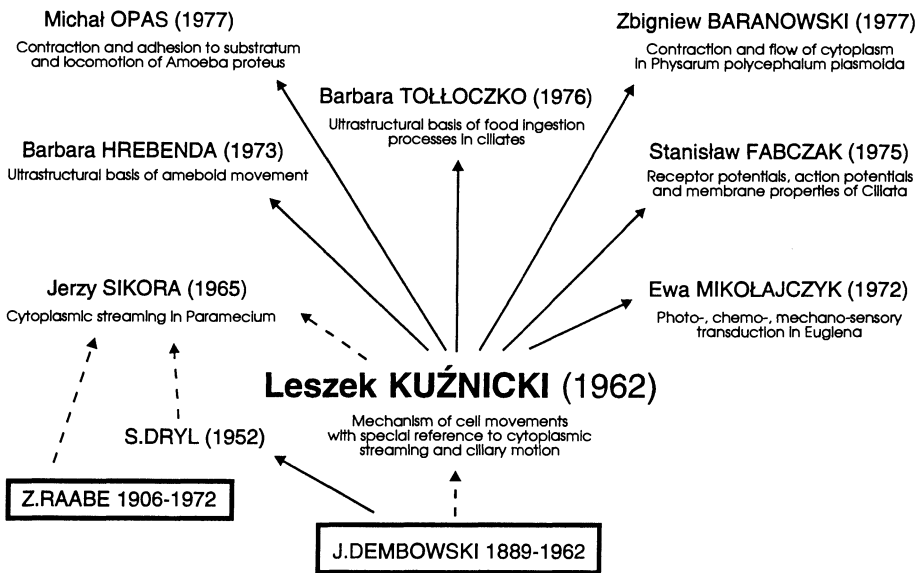


Fig. 2. The Laboratory of the Cell Movements in 1981. Head: Leszek Kuźnicki. Main problem: mechanism and ultrastructure of various types of primitive systems.

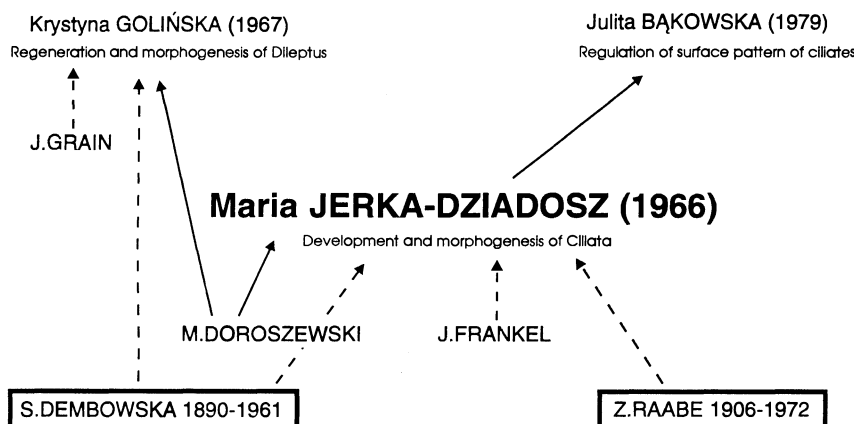


Fig. 3. The Laboratory of Regeneration and Morphogenesis of Protozoa in 1981. Head: Maria Jerka-Dziadosz. Main problem: development of ciliates.

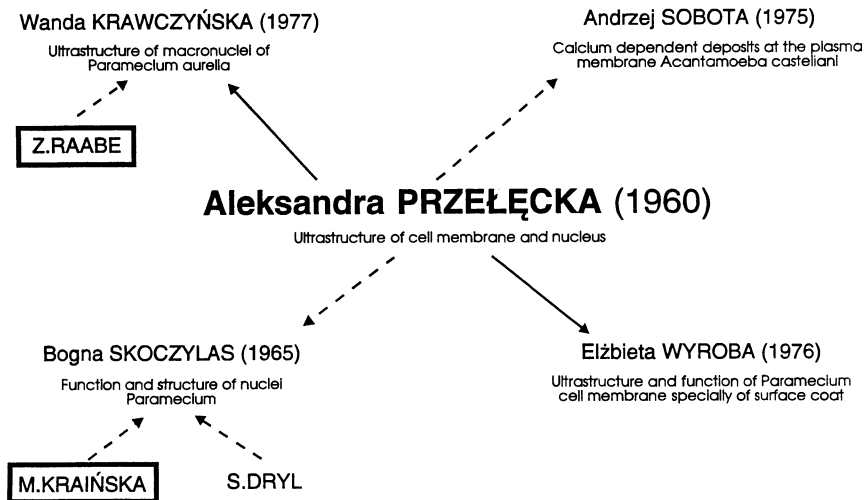


Fig. 4. The Laboratory of Cytochemistry of Cell Growth and Differentiation in 1981. Head Aleksandra Przełęcka. Main problem: ultrastructure and function of cell membrane and nucleus.

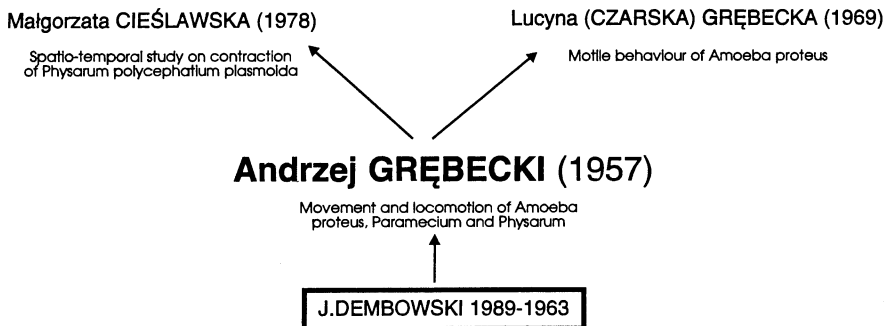


Fig. 5. The Laboratory of Morphodynamic of the Primitive Motile Systems in 1981. Head: Andrzej Grębecki. Main problem: mechanism of amoeboid motion of Amoeba proteus and Physarum polycephalum.

Paper presented at the Conference on 75-th Anniversary of the Nencki Institute

PRESENT ACTIVITY OF THE DEPARTMENT OF CELL BIOLOGY

Head: Stanisław Fabczak

LABORATORY OF PHYSIOLOGY OF THE CELL MEMBRANE

Head: Elżbieta Wyroba

The research is concentrated upon the signal transduction (chemo- and photo-) in unicellular eukaryotes (ciliates). Studies are focused on two major directions: (a) effect of beta - adrenergic agents and specific calcium channel blockers upon phagocytosis and motile responses in *Paramecium*, (b) mechanism of photosignal transduction in *Stentor* and *Blepharisma*. Protozoan cells are also used

as a tool for determination of the internalization of compounds acting as the photosensitizers in photodynamic therapy of tumors.

Current research activities: search for mechanism of beta - adrenergic stimulation of phagocytosis and ciliary reversal in *Paramecium*; studies on function of ion channels in ciliates; search for mechanism of internalization of compounds acting as the photosensitizers in photodynamic therapy of tumors; search for new approaches towards FURA-2 diffusion in cell and its use as an indicator of calcium level changes in mammalian cells and unicellular organisms; studies on mechanisms of light signal transduction and possible involvement of cyclic nucleotide cascaded and G-protein in phototransduction pathway in ciliates, *Stentor* and *Blepharisma*.

LABORATORY OF MORPHODYNAMICS OF THE PRIMITIVE MOTILE SYSTEMS

Head: Andrzej Grębecki

Cell motility research focused on the structural and functional aspects of locomotion, response to stimuli, endocytosis and surface movements of amoeboid cells. The free-living amoebae are used as experimental material; the application of tissue cells is pending. Principal methods: digital video-enhancement, micromanipulation, routine and confocal fluorescence microscopy.

Current research activities: localization of motor and steering effectors in amoeboid locomotion and response to stimuli; motor polarity of amoeboid cells and the impact of cell nucleus on its perseveration; dynamics of membrane-cytoskeleton association at the leading edge of amoeboid cells; lateral movements of the cell surface and submembraneous contractile layer during locomotion, endocytosis and capping.

LABORATORY OF PHYSIOLOGY OF CELL MOVEMENTS

Head: Leszek Kuźnicki

Ultrastructure and motile activity of ciliates and plasmodia of *Physarum polycephalum*. Ultrastructure of marine ciliates of suborder Tintinnine. Ion transport in ciliates. Respiration and motile behaviour of *Physarum polycephalum* in relation to cell cycle. Cytoplasmic streaming and its relation to cell cycle.

Current research activities: the main achievements of the laboratory during the last two years are: Finding that starvation evokes synchronous division of *Physarum polycephalum* mitochondria. The mitochondrial division, decrease in activity of the respiratory chain and maximum of its cyanide resistance occur at the same time. The contractile effects of local treatment of *Physarum* plasmodia strand with respiratory inhibitors allow to conclude that mechanical strain is involved in the system regulating the endogenous contraction-relaxation cycle.

Description of morphology and ultrastructure of marine ciliate *Cymatocylis convallaria* with special attention to paddle cilia being involved probably in trapping food particles.

A new method of quantitative estimation of *Paramecium bursaria* thigmotaxis was introduced. The thigmotaxis is defined as the rate constant of transition of cilia from motion into motionless state. It was found that endogenous factors appear to control the kinetics of cytoplasmic streaming in *Paramecium bursaria*. The change of streaming direction and its eventual arrest in a dividing cell is of importance in intracellular morphogenetic translocation of organelles. In that regard it seems that the major function of the reversal of the streaming direction is to move the dividing micronucleus into the right position in prospective daughter cells.

LABORATORY OF REGENERATION AND MORPHOGENESIS OF PROTOZOA

Head: Maria Jerka-Dziadosz

The research is concentrated upon structural aspects of cytoskeleton plasticity in experimentally modified morphogenesis. The function of nucleating centers for fibrillogenesis of cytoskeletal elements during the cell and life cycle in free living ciliates is analyzed. We study normal cells and mutants expressing cortical pattern modifications. Methods applied: cytological preparation, transmission and scanning electron microscopy and immunocytochemistry using specific antibodies directed against cytoskeletal proteins.

Current research activities: dynamics of filamentous and microtubular structures during cell fusion and during the development of nuclear apparatus in conjugation of *Tetrahymena*, *Dileptus* and *Paraurostyla*.

Phenotypic analysis of cortical pattern in mutants mlm/pl of *Paraurostyla*, *cro5* and *kin 241* of *Paramecium tetraurelia* with affected control of ciliary pattern formation, relations between affected pattern and cell cycle events.

LABORATORY OF CYTOCHEMISTRY OF CELL GROWTH AND DIFFERENTIATION

Head: Andrzej Sobota

The research is focused on participation and role of submembrane proteins, such as spectrin and annexins, in plasma membrane-cytoskeleton interactions. The immunocytochemical and biochemical studies allow to identify and localize the proteins in the cortex of cells which have different structural and functional organization of their surface layer. The involvement of the proteins in linkage of microfilaments to plasma membrane is studied in such physiological processes as capping and phagocytosis.

Current research activities: identification, immunofluorescent and immunoelectron microscopy localization of alpha-spectrin immunoanalog in protozoan organisms; Demonstration of the involvement of actin-binding proteins (spectrin, annexin I and II, vinculin) in linkage of microfilaments to EGF-receptors; only actin and spectrin accompany the EGF-receptors during their lateral translocation (capping).

Studies of calcium-sensitive interaction of annexin IV & VI with erythrocyte membrane as a model system of plasma membrane.

Visualization of annexin association with membrane - freeze etching and immunoelectron microscopy approaches.

Development and modification of the techniques of purification of monospecific antibodies.

Department of Muscle Biochemistry - the research profile

Head: Renata Dąbrowska

The Department of Muscle Biochemistry stems from the former Department of Nervous System and Muscle established in 1971 by Professor Witold Drabikowski. Presently it comprises four laboratories.

LABORATORY OF REGULATION OF CONTRACTILE PROCESSES

Head: Renata Dąbrowska

The research is concentrated on the molecular mechanisms of Ca^{2+} -dependent regulation of contraction-relaxation cycle in various types of muscle (skeletal and smooth) and motility phenomena in non-muscle cells. The main approach is to isolate the regulatory proteins, particularly those associated with actin filaments, and investigate their physico-chemical and structural properties, the Ca^{2+} -dependent effect on the enzymatic properties of actomyosin system and interaction with the contractile apparatus. Recent investigations are directed mainly to the role of caldesmon and calponin in actin-linked regulation (or modulation) of smooth muscle contraction and motile systems of non-muscle cells.

The main achievements of the laboratory in this field are:

- finding that the inhibitory proteins of actomyosin ATPase: troponin I and caldesmon affect contraction by immobilization of actin filament
- showing the participation of C-terminal amino acid residues of actin in its interaction with caldesmon
- evaluation of the secondary structure of caldesmon and calponin
- demonstration of the mutual exclusion of calponin and caldesmon from F-actin, suggesting that in vivo these two proteins are located in distinct classes of thin filaments
- proving that caldesmon is capable to dissociate G-actin-profilin (profilactin) complex and to polymerize released G-actin
- showing that caldesmon interacts with negatively charged phospholipids

LABORATORY OF BIOCHEMISTRY OF MUSCLE STRUCTURAL PROTEINS

Head: Hanna Strzelecka-Golaszewska

The research interest of this laboratory is in structure-function relationship in myosin and actin, the proteins involved in generation of force or movement in both muscle and non-muscle cells. Studies on myosin are concerned with structural rearrangements within the "head" portion of the molecule that may be relevant to the mechanism of force generation by actomyosin systems.

Studies on actin are aimed at identification of conformational transitions relevant to the mechanism of polymerization of the monomers into filaments, and at obtaining information on the role of various monomer-monomer contact sites in formation and stabilization of the polymer. Most recent achievements in this latter field include evaluation of the role of the C-terminal segment and of the

surface loop comprising residues 39-51 of actin in the polymerization of this protein, and demonstration of structural coupling between certain distant regions of the actin molecule.

LABORATORY OF CALCIUM BINDING PROTEINS

Head: Jacek Kuźnicki

The research has been concentrated on EF-hand binding proteins such as calmodulin, cerebral S-100 and calyculin. The studies has been focused on their biochemical properties (cation binding, conformational changes), distribution (tissues and cell specific) and function (interaction with target proteins). The aim of these studies is a characterization of calcium binding proteins as a potential markers of human diseases. At present, biochemical characterization of calyculin - its tissue and cell specific distribution and of target proteins is the primary project.

Recent achievements:

- Immunohistochemical and Western blotting experiments showed that calyculin is present mostly in fibroblasts and epithelial cells. In nervous system it was found in some populations of neurons, but not in glial cells.
- Analysis using calyculin antibodies showed higher amounts of calyculin in some pathological tissues (for instance in liver with biliaries cirrhosis).
- Studies on calyculin structure, particularly crosslinking experiments, revealed that calyculin exists in solution as a non-covalent dimer.
- Using iodinated calyculin, it was found that *in vitro* some proteins bound calyculin in a calcium dependent manner.

LABORATORY FOR MECHANISMS OF TRANSPORT THROUGH BIOMEMBRANES

Head: Maciej J. Nałęcz

The research is concentrated on various transport mechanisms through biomembranes, i.e. ion pumps, carriers and channels. Special emphasis is given to transport mechanisms and physiological role of carnitine in brain, to mitochondrial substrate carriers, to ATP-regulated potassium channels from various membranes and to ATPase from plasma membrane. Studies in the field of metabolic regulation, structure and function of biomembranes and role of protein kinase C in various cellular processes are also performed.

Within the current research activities are studies on the uptake of carnitine by nervous tissue (neurons in primary culture, neuroblastoma cells in culture), effects of carnitine and its derivatives on protein kinase C activity and cellular metabolism in brain, as well as studies on the identification and functional characterization of ATP-regulated potassium channels in liver and heart muscle mitochondria.

Department of Cellular Biochemistry

Head: Barbara Grzelakowska-Sztabert

LABORATORY OF BIOCHEMISTRY OF LIPIDS

Head: Renata Jasińska

The main interests of the laboratory cover the regulation of phospholipid biosynthesis, phospholipid transfer proteins and lipid-protein interaction.

Current research activities: transport and decarboxylation of pyrene-labelled phosphatidylserines of various fatty acid chain length; purification and kinetic properties of phosphatidylserine decarboxylase from rat liver mitochondria; regulation of base-exchange enzymes activity in cellular membranes; effect of exogenous phospholipids inserted into membranes on the activity of base-exchange enzymes and phosphatidylserine decarboxylase; regulation of phosphatidylethanolamine biosynthesis in regenerating rat liver; intracellular traffic of phospholipids.

LABORATORY OF BIOENERGETICS, BIOMEMBRANES AND METABOLIC REGULATIONS

Head: Lech Wojtczak

Research profile: energy coupling in mitochondria, mitochondrial metabolism, relationships between mitochondrial structure and function, transport of ions and metabolites in mitochondria, chemical and physical properties of biological membranes, metabolic control at the cellular and subcellular levels.

Current research activities: studies on proton permeability and electric capacitance of the inner mitochondrial membrane; determination of the role of passive proton fluxes in the control of resting state respiration of mitochondria; determination of the energy storage capacity of the mitochondrial protonmotive force; energetics of tumor mitochondria; interactions between the outer and inner mitochondrial membranes; regulation of monooxygenase activity in the liver cell by phosphorylation/dephosphorylation of cytochromes P-450.

LABORATORY OF LIPID SIGNALS TRANSDUCTION

Head: Jolanta Barańska

Major research interests: receptor families, receptor regulation of phospholipases, protein kinase C, spatial/temporal aspects of calcium signalling, crosstalk between signalling systems, membrane phospholipids.

Current research activities: investigations of the role of agonists and protein kinase C in phosphatidylserine biosynthesis in mammalian cells and in particular: studies on the effect of agonists and other agents changing the level of intracellular $[Ca^{2+}]_i$; on phosphatidylserine synthesis in glioma cells; search for the interaction of phosphatidylserine with protein kinase C in neuronal cells; determination of the participation of phosphatidylserine in phosphatidylcholine formation in slices originating from the different anatomical regions of rat brain; phosphatidylserine synthesis in rat liver microsomes - the role of Ca^{2+} , Mg^{2+} -ATPase in this process.

LABORATORY OF BIOSYNTHETIC PROCESSES

Head: Barbara Grzelakowska-Sztabert

The research activities of the laboratory are concentrated on several topics such as: metabolism of S-adenosylmethionine; role of polyamines in mouse kidney hypertrophy and hyperplasia; molecular mechanisms of cellular activation, especially the role of formation of transcription factors as one of the earliest nuclear responses to various stimuli; properties of thioredoxin reductase from rat liver mitochondria.

Current research activities: studies on the role of polyamines in the processes of hypertrophy and hyperplasia using mouse kidney models; HPLC determination of polyamine levels; studies on activation of transcription factors using gel shift assay in: a) aging cells stimulated to proliferation or apoptosis b) in young and old rat brain after functional activation; investigations of the regulation of mitochondrial disulfide reductase.

LABORATORY OF COMPARATIVE ENZYMOLOGY

Head: Wojciech Rode

Major research interests: different aspects of thymidylate biosynthesis: its enzymology, regulation and inhibition; thymidylate synthase and dihydrofolate reductase as targets in chemotherapy, including search for new drugs; drug resistance, specificity and mechanism of action.

Current research activities: search for new thymidylate synthase inhibitors; explanation of the mechanism of thymidylate synthase inhibition by N⁴-hydroxy-dCMP; purification and comparative studies of thymidylate synthases from the tapeworm, *Hymenolepis diminuta*, and from regenerating rat liver.

LABORATORY OF MOLECULAR BASIS OF MUSCLE CONTRACTION

Head: Anna Jakubiec-Puka

Major research interests: molecular mechanism of actin and myosin filament interactions and their modulation induced by the influence on kinase and phosphatase systems, and/or by other thick filament proteins; problem of reversible myocardial dysfunction and its connection with temporal modification of contractile proteins; adaptive response of the contractile apparatus of the striated muscle to altered innervation, function or length; attention is focused on changes in sarcomere organization, myosin isoforms and actin filament structure.

Current research activities: search for evidences of the influence of conformational changes of skeletal muscle myosin regulatory light chains on the structural organization of myosin head and its interaction with actin, and probable existence of cooperation between regulatory light chains and the protein C, search on the type-dependent response by the contractile apparatus to alteration in muscle function, innervation and length: a) isoforms of myosin heavy chains, b) properties of actin filament, c) quick reorganization of the contractile apparatus in the active muscle.