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THE ROCKEFELLER UNIVERSITY
JAN 13 1983
OFFICE OF THE PRESIDENT

January 10, 1983

Professor Joshua Lederberg, President
The Rockefeller University
1230 York Avenue
New York, New York 10021-6399

Dear Professor Lederberg:

Thank you for your note concerning my work at the old Institute. I had not seen Dr. Corner's history and do appreciate what he had to say in the sheet you sent.

I tend to think of my years there while Simon Flexner was Director as intellectually the most rewarding of my scientific life. Under him I found it a marvellous place to be and I am eternally grateful for the help he gave in what I was trying to do. The last years, culminating in my enforced leaving, seemed at the time tragic for they meant the abrupt loss of what had been built up for the future and led to the cessation of the crystal structure studies that had been the basis of my career. It took quite a time to realize that all this was in fact a blessing well disguised.

Ewald's "Fifty Years of X-Ray Diffraction" published 20 years ago contains "Reminiscences" in which there is a brief reference to our x-ray studies at the Institute. Some years ago I put together for the benefit of our children a few biographical notes that include a short account of my years in New York. I am enclosing a copy of the pertinent pages in case they present information not mentioned by Dr. Corner. If you read them, please bear in mind the rather special audience for which they were written.

Sincerely yours,

Ralph Wyckoff

Ralph W. G. Wyckoff

Excerpted from Private Notes of R.W.G. Wyckoff

visiting laboratories abroad. I began doing this after the return from Pasadena. An acquaintance had created with the Holland-America Line a Student Third Class Association to occupy the erstwhile steerage of its ships; I crossed several times under these auspices, making new friends among the chaperones and passengers and often traveling with them abroad. During these summer trips I came to know many German scientists, especially those at the Kaiser Wilhelm Institute in Dahlem. From the standpoint of my scientific work these were highly productive years, with steady progress being made in the complexity of crystals that could be successfully analyzed.

The next major change in my career was the result of a visit to my laboratory in 1925 by Lecomte du Noüy. He was sent from the Rockefeller Institute to spend a few weeks with me and decide whether or not the Institute should undertake x-ray work. He and his wife took an apartment near by and the three of us began a friendship which deepened with the years and lasted throughout their lives. Returning to New York he told Simon Flexner, Director of the Rockefeller Institute, that x-ray studies should be undertaken but that he did not want to interrupt his surface tension investigations to start them. Some time later I received from Dr. Flexner an offer to go to New York as an Associate Member of the Institute in charge of a new Subdivision of Biophysics. This offer was in many respects very tempting. Most of the important types of minerals had been investigated though there remained a generation of work in defining their structures more closely. By this time I had come to realize that my interests and abilities lay in exploring a new field rather than in filling out the body of one that had already been outlined. For me it was obvious that organic crystals were the next large group open to x-ray diffraction. Almost none had been analyzed but we were learning how to measure x-ray reflections with the needed accuracy and were devising ways to carry out calculations which would be arduous for even the simpler organic compounds. These substances could obviously be more appropriately studied in a medical institution than in one devoted to rocks.

And so at the beginning of 1927 I left the Geophysical Laboratory for the Rockefeller Institute for Medical Research. It opened for me a new and far richer life, leaving as my only lasting regret the fact that Dr. Day unforgivingly resented my going. I would have left Washington in any event for in accepting the Rockefeller opportunity I turned down the chance to return to Cornell as Professor of Chemistry.

Going to the Rockefeller was a new life in more ways than I could at the time appreciate. Before then the center of all my interests had been the investigation of inanimate Nature. In the future I would be increasingly concerned, almost involuntarily, with the world of living matter. In this I was of course following unconsciously the path that scientific thought had begun to take late in the 19th century. The material universe as our grandfathers could perceive it was infinitely simpler than the living and it was inevitable that first advances of modern science and perhaps one's own efforts should be in the direction of the non-living.

These advances were indeed so rapid and notable that it was easy to be completely absorbed in them and lose sight of science's limitations. A faith in its omnipotence began for many to replace a faith in religion and even the religious-minded tended to believe that through the advance of modern science answers could be found to all questions about external Nature and life itself. We were dealing with what seemed the ultimate composition of all matter, we were mastering more and more naturally occurring processes and using them to improve the conditions of human life, and we were controlling an increasing number of diseases afflicting man and his domesticated animals. It was natural to imagine that this progress would continue without limit if only science were given the necessary support. I now find it almost impossible to reclaim the euphoria that colored my thinking at the time I went to New York. My interests in things outside the laboratory prevented me from being caught up in the all-inclusive materialism that appealed to so many of my confreres but the scientific advances in which I was participating were so fascinating that there remained little time to meditate on their limits.

At the Rockefeller Institute I had available the resources to put together an excellent laboratory, including the first instrument-making shop the Institute had ever had. Of greater value to me were the friendships that grew out of my continuing contacts with Lecomte du Noüy. He remained throughout his life the cherished elder brother whose help I valued and whose advice I sometimes followed. Of at least equal influence on my future was close contact with Alexis Carrel. He had brought Lecomte du Noüy to the Institute from his war hospital in Compiègne and though they worked independently, the association between the two was intimate. I found Carrel's highly rational way of thinking and his unlimited range of thought most congenial and I joined Lecomte du Noüy in this association. For a decade I lunched almost daily with Carrel and, except for his assistants, saw more of him than did anybody else in the Institute. These lunches were an education in themselves for at them everything that happened in the world was critically discussed and they were occasions for meeting the many well known persons who came to see him and his laboratory. I gained much from being thus with Carrel and developed for him a genuine affection. I do not know if that affection was to any extent reciprocated because his true feelings were never manifest behind the brittleness of his dominant intellect. To this day I cannot say if he was a man essentially devoid of feeling or one so inwardly shy that he feared to show it.

Carrel's often critical comments gained for him many enemies in the Institute and elsewhere. As might be expected where several prima donnas were brought together, the Institute abounded in cliques and petty jealousies and Carrel was the butt of many. I was made aware of this soon after coming to New York, being warned by one of his enemies that if I wished to be successful at the Institute I would have to renounce my connections with Carrel. Naturally I did not follow this advice, but my failure to do so was certainly an important factor in my final removal from the Institute. It is undoubtedly true that my close association with Carrel restricted the contacts I could have made with politically minded members of the Institute but a "career" as they understood it was never my objective and I shall always consider my years with Carrel among the pleasantest and most rewarding of my life. Neither before nor since have I found myself in so intellectually stimulating an environment.

By this time I was becoming more conscious of the problem of reconciling my accumulating scientific knowledge and my inherited religious attitude to life. I had had no difficulty in recognizing that faulty Church dogmas were the inevitable consequence of the imperfect knowledge of Nature that prevailed when they were formulated, but could never see how a scientific disproof of their literal truth had any bearing on the existence of the spiritual reality they sought to express. At the same time I could not accept the visionary assertions of many saintly persons as objective proof of such a reality. I thus became consciously aware of the fundamental problem to be faced by all modern men who are dissatisfied by the materialistic assertion that everything we can experience is fully explicable in terms of our physiology. This problem continues to obsess me.

Carrel, Lecomte du Noüy and I often discussed this problem and ways to come to grips with it. We were agreed that the only proof of the existence of a reality independent of the material world that could be scientifically satisfying would be an undebatable demonstration of events for which there was no material explanation. We disagreed with scientists who denied out of hand the possibility of the paranormal and critically reviewed much of the evidence in its favor, including Carrel's own experiments. I continue to be impressed by the evidence, but complete conviction still escapes me. Nevertheless I believe that serious investigation grows in importance as a materialism reputedly based on science finds broadening acceptance.

Lecomte du Noüy left the Rockefeller Institute and returned to Paris a few years after my coming to New York. His initial training and experience were not scientific and though he had spent time in Madame Curie's and Sir William Ramsay's laboratories and had done distinguished scientific work in Carrel's hospital in Compiègne during the war, many did not accept him as a bona fide scientist. He had been, like myself, an Associate Member of the Institute and when he was not made a permanent Member, he received a grant to establish a laboratory of biophysics at the Pasteur Institute. In Paris he continued with the help of his wife the important physicochemical studies of blood serum which he had begun in New York. I very much regretted his leaving but we continued to see them in France and in the United States until they died.

At the Rockefeller Institute my scientific interests shifted gradually from their earlier preoccupation with x-ray crystallography. This was partly because its developing problems were not ones that I felt particularly competent to solve but mainly because I was discovering aspects of biology that seemed to bear more directly on the underlying WHY of things. The greater complexity of organic crystals meant that the determination of their atomic positions required increasingly more accurate x-ray measurements and much more elaborate calculations. At the Institute we determined the structures of a number of simple organic crystals and used the shop I had developed to build apparatus for the eventual study of biologically important substances. Calculations became much more time-consuming as more complex crystals were studied and it became clear that new mathematical procedures were needed. Their application is now leading to the successful analysis of the huge molecules of proteins but this is a type of research that appeals to a different kind of person from those of us who were active in the early stages of crystal analysis.

I did not suddenly abandon my study of crystal structures but, as my interest in biological problems developed, concentrated on gaining limited x-ray data from proteins and on solving simple related structures. After examining urea and some of its derivatives, I turned to the amino acids which are the basic ingredients of all proteins. Corey, who had come some years before from Cornell to learn x-ray methods, and I undertook the study of glycine as the simplest amino acid. Considerable progress was made with this but at this moment Simon Flexner was replaced by Gasser as Institute Director and I was told that my appointment was being terminated. Corey took the glycine data to Pasadena and from there published the structures of this and other amino acids.

Hemoglobins were among the few proteins that had at the time been obtained pure and in crystalline form. I determined to try to get x-ray diffraction patterns from them and from some of the enzymes that had recently been crystallized. We did succeed in getting preliminary patterns, especially from hemoglobin and collagen, but only when my laboratory was about to be disbanded.

These preliminary successes did, however, lead to our building of ultracentrifuges. Svedberg with his big, oil-driven analytical instrument had recently shown that proteins were not structureless colloids but had very large molecules whose weights could be precisely measured. His ultracentrifuge was very expensive to build and operate and could handle only a small volume of liquid. Beams had shown how the air-driven rotors of Henriot and Huguenard could be employed to spin large, vacuum-enclosed objects. Working with Pickels, one of his students who had come to the laboratories of the Rockefeller Foundation, I built in my shop an air-driven analytical ultracentrifuge to characterize the proteins we were seeking to crystallize. We next constructed, using light metal <u>in vacuo</u> rotors like those with which Beams had been experimenting, an ultracentrifuge that would hold large volumes. With this I prepared in pure state the tobacco mosaic virus starting from infected plant juice supplied by Stanley. After this success I concentrated, purified and determined for the first time the molecular sizes of a number of plant and animal viruses.

There was much debate about the fundamental nature of viruses: were they living organisms of unusually small size or huge inanimate molecules? Hoping to throw light on this question we initiated experiments comparing the action of x-rays and other forms of radiation on them and on bacteria. The killing of bacteria was studied in especial detail in an effort to define the precise mechanism of the lethal action of x-rays and other types of radiation. In doing this I was brought into contact with French workers carrying out similar experiments. As a part of this program we photographed bacteria and cells with ultraviolet light to reveal those internal structures which could absorb these radiations and made motion pictures under the microscope to show how wide ranges of bacterial types grow and multiply. Some of these motion pictures are still, more than 40 years later, being shown in schools and colleges.

The smooth running of life at the Rockefeller Institute was suddenly interrupted when Simon Flexner was retired as its Director. In telling me that my appointment would not be renewed the new director, Herbert Gasser, stated that the type of research I was doing was medically inappropriate. Since this was when we were for the first time purifying viruses with our ultracentrifuges, the questionable nature of this explanation was apparent. The underlying reason seemed clearer when it became known that Alexis Carrel was soon to be retired and his large research installation disbanded. My ultracentrifugation of animal as well as plant viruses, carried out in collaboration with J. W. Beard, had been arousing violent opposition from Thomas Rivers, who later went to the extreme of spreading beyond the Institute the rumor that

I had stolen from the Rockefeller Foundation its plans for constructing ultracentrifuges. Having in hand definite written proof to the contrary, I was able to stop the rumors but Gasser never forgave and later refused to allow the National Institutes of Health to acquire for my use there my x-ray equipment which continued to lie idle in my old laboratory at the Institute.

In the meantime, with two more years before the expiration of my contract, the purification of plant viruses was proceeding so well that I transferred my ultracentrifuges to the Institute's Princeton branch where infected plants were being grown by Stanley and his associates. While these viruses were being characterized I isolated and purified papilloma and vaccinia viruses. I also concentrated and partially purified the virus of Western encephalomyelitis grown in chick embryos. The concentration of virus thus obtained was so great that Beard and I could show that formalinized vaccines from it were extraordinarily effective. It was this observation which made available to me a job at Lederle when my time at Princeton ended.

When I went to Lederle my relationa with Alexis Carrel were not interrupted. Hog cholera was one of the serious animal diseases with which the company was concerned and, wondering if a vaccine could be produced with hog tissue, I spent time in his laboratory learning to cultivate embryonic hog tissue but this was when Carrel was soon to be retired. Lindberg was working there at the time and as a consequence the three of us made tentative plans for establishing a new private laboratory. All was abandoned, however, when the war broke out in Europe and Carrel went to France never to return.