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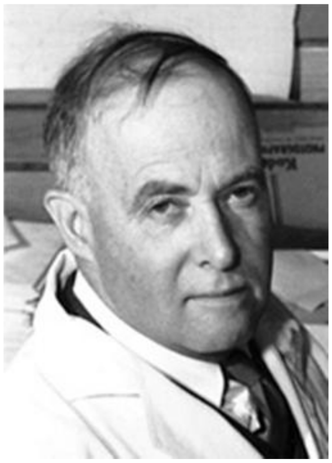
Nobel Prize in Chemistry 1946



James Batcheller Sumner **John Howard Northrop** **Wendell Meredith Stanley**

The Nobel Prize in Chemistry 1946 was divided, one half awarded to James Batcheller Sumner *"for his discovery that enzymes can be crystallized"*, the other half jointly to John Howard Northrop and Wendell Meredith Stanley *"for their preparation of enzymes and virus proteins in a pure form"*.

RESEARCH INFORMATION:

In 1897 Eduard Buchner, the German research worker, discovered that sugar can be made to ferment, not only with ordinary yeast, but also with the help of the expressed juices of yeast which contain none of the cells of the *Saccharomyces*. The discovery was considered so important that in 1907 Buchner was awarded the Nobel Prize for Chemistry.

Why was this apparently somewhat trivial experiment considered to be of such significance? The answer to this question is self-evident, if the development within the research work directed on the elucidation of the chemical nature of the vital processes is followed. Here, as in other fields of research, progress has taken place step by step, and the conquest of new fields has often been very laborious. But there, more than in most fields, a tendency has showed itself to consider the unexplained as inexplicable - which is actually not strange where problems of life and the vital processes are concerned. Thus ordinary

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yeast consists of living cells, and fermentation was considered by the majority of research workers - among them Pasteur - to be a manifestation of life, i.e. to be inextricably associated with the vital processes in these cells. Buchner's discovery showed that this was not the case. It may be said that thereby, at a blow, an important class of vital processes was removed from the cells into the chemists' laboratories, to be studied there by the chemists' methods. It proved, too, that, apart from fermentation, combustion and respiration, the splitting up of protein substances, fats and carbohydrates, and many other similar reactions which characterise the living cell, could be imitated in the test tube without any cooperation at all from the cells, and that on the whole the same laws held for these reactions as for ordinary chemical processes. But - and this is a very important reservation - this was only possible if extracts or expressed juices of such cells were added to the solution in the test tube. It was then natural to assume that these cell juices or cell extracts contained some substance which had the capacity of initiating and maintaining the reactions and guiding them into the paths they follow in the cell. These unknown active substances were called enzymes or ferments, and the investigation of their effects became one of the principal problems of chemistry during the first decades of this century, which for the rest it still is.

The important question of the nature of the enzymes remained unsolved, however, in spite of the energetic efforts of the research workers. It is manifestly a question of substances of complicated structures, which are present in such extremely small amounts that they, so to speak, slip through the fingers when one tries to grasp them. It is really remarkable to see how far it was possible to get in the study of the effects of the enzymes and the course of the enzymatic reactions, without knowing anything definite about the nature of these very active substances, nay, even without even being quite clear that they were substances which could be isolated in the pure form at all.

In 1926, however, in connection with his studies of a special enzyme "urease", James B. Sumner of Cornell University, Ithaca, U.S.A. succeeded in producing crystals which exhibited strikingly great activity. The basic material was the bean of a South American

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plant, *Canavalia ensiformis*, in America called the "jack bean", and the crystals had an activity that was about 700 times as great as that of bean flour. What was still more important was that it was possible to dissolve the substance and re-crystallize it several times without its activity being affected. The crystals proved to consist of a protein substance. Sumner expressed the opinion that in reality this protein substance *was* the pure enzyme.

As is so often the case with important discoveries, this result will probably to a certain degree have "been in the air", in that at the time it had been assumed in many quarters that the enzymes were protein substances of quite a special nature. On the other hand, Willstätter, the German chemist and Nobel Prize winner, had carried out far-reaching purifying experiments with enzymes and had arrived at results which caused him to doubt whether it was a question of protein substances or carbohydrates at all. We know now that this was due to the fact that Willstätter's purifying methods yielded solutions which were all too weak for it to be possible for chemical reactions to give a definite result.

For the chemist crystallization is the final goal in the preparation of a substance in pure form. Even though crystallizability is not such a reliable criterion of purity in the case of protein substances as in that of simpler substances, nevertheless Sumner's results have now been accepted as verified and thus also accepted as the pioneer work which first convinced research workers that the enzymes are substances which can be purified and isolated in tangible quantities. Thereby the foundation was laid for a more detailed penetration of the chemical nature of these substances, on which an understanding of the reactions taking place in living cells must finally depend.

Sumner's pioneer work was not immediately followed by similar work in other quarters, which might perhaps have been expected. About three years after Sumner's work had been published, however, Dr John Northrop of the Rockefeller Institute at Princeton began to work on the purification of the protein-splitting enzymes met with in the digestive apparatus and gradually succeeded in obtaining a number of them in crystallized form, e.g. the pepsin met with in the gastric juice and the trypsin and chymotrypsin in the pancreas.

Northrop and his collaborators, among whom should be mentioned in the first place Kunitz, also made extremely comprehensive studies of the homogeneity and purity of these purified enzymes, and in that connection gave further proof of their nature as protein substances. Exceedingly interesting results were attained also in the isolation of some protein substances which appeared to be the mother substances of these enzymes. On the whole Northrop used his purified material for detailed chemical studies to a greater extent than did Sumner, and his contributions in the matter of working out the most satisfactory conditions for the crystallization of enzymes have been of the greatest importance for subsequent research workers.

This year's third Nobel Prize winner in Chemistry, Dr Wendell Stanley, first worked at the Rockefeller Institute in New York but moved in 1932 to the department of that Institute at Princeton. The problem which attracted his attention, namely the chemical nature of the viruses, was to a certain degree analogous to the problem of the enzyme just mentioned. As is well known, viruses are contagia which give rise to a large number of the best known illnesses in man, animals and plants, e.g. smallpox, infantile paralysis, influenza, foot-and-mouth disease, mosaic disease (on tobacco plants), etc. The virus particles are invisible in the microscope, and when Stanley began his work, they could only be identified by the symptoms of disease which they occasioned. Thus the problem was more difficult, inasmuch as the effect of the virus could not be as easily measured as that of an enzyme, where an exactly known chemical reaction can be employed. Stanley first tried to show the protein nature of viruses by studying how the virus of the tobacco mosaic disease was attacked by protein-splitting enzymes, but in 1934 he passed on to attempting to purify that virus by methods similar to those which Sumner and Northrop had employed so successfully for enzymes. In 1945, by using large quantities of infected tobacco leaves, he did succeed in producing small amounts of crystals which were extremely active, and which, after detailed investigation, proved to be the bearers of the virus's activity. Here, too, it was a matter of active protein substances. Subsequently it has been proved that nucleic acid also forms an important constituent of the latter.

It seems as though Stanley's discovery may take us another long step forward along the road towards a closer understanding of the chemical nature of the vital processes, for apart from the fact that in extremely small quantities they can give rise to diseases, the virus substances, like the bacteria, have the capacity to reproduce themselves. It was remarkable enough when Buchner found that certain of the functions of the living cell can be separated out from it and are to be found in the expressed juice, but it appears still more remarkable that the capacity to reproduce - this unique characteristic of life - can also be exhibited by certain molecules, thus by dead substances. It must be borne in mind, however, that, as far as we know now, this capacity is only possessed by the virus molecule when it is in contact with the living cell, and that probably the latter is materially responsible for the reproduction of the virus substance.

Investigations both by Stanley and by other research workers show that many kinds of viruses, e.g. the smallpox virus, are considerably more complicated in structure. It is conceivable that the "molecular virus" which Stanley isolated represents the simplest type in a long series of different kinds of viruses which gradually approach the living bacteria. An extraordinarily fascinating field is hereby opened up to research workers, and it is not improbable that development will lead to a closer scrutiny of the border-line between living and dead matter.

Even among scientists we sometimes hear the assumption expressed that the innermost secrets of the vital processes will always be hidden from us, that there is a wall through which we cannot penetrate. Today we do not know whether that be correct, but we know that this wall - if there is one - is considerably farther away than one had dared to believe earlier. That this is so is to an appreciable degree the result of the discoveries which have been rewarded with the 1946 Nobel Prize for Chemistry.

Doctor James Sumner. Your discovery of the possibility of crystallizing an enzyme was the first convincing proof that enzymes are proteins. It thus became possible, for the first time, to attack the problem of the chemical nature of these substances, so important in chemistry, biology and medicine. As is often the case with pioneer work, your results were not immediately accepted everywhere, but today they form a foundation for and have pointed the way to some of the most important work in biochemistry.

Doctor John Northrop. You and your collaborators have developed the crystallization of enzymes and other active proteins into an art, of which you are the masters. The conditions for successful work in this field were explored by you, and in the course of that work interesting relationships between enzymes and related proteins were discovered, which may ultimately afford a clue to a fuller understanding of the mode of action of these substances.

Doctor Wendell Stanley. We owe to you one of the most striking discoveries in modern chemistry and biology. The demonstration of the fact that a virus can be crystallized in the same way as many proteins and enzymes, and that it actually *is* a protein, at once opened up an almost unlimited field of research with fascinating possibilities. You have not only thrown open the portals to this domain, but you are yourself successfully exploring its possibilities, and rich fruits have already been harvested, thanks to your own work and that of your school.

Gentlemen. The fundamental problems which you have attacked and solved with such remarkable success are closely related, and the methods used have much in common. The more recent achievements have added to the significance of the earlier advances in this field. Your work and your discoveries deserve the gratitude of mankind. The award to you of the Nobel Prize in Chemistry for 1946 is an expression of this gratitude.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1946/press.html