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Nobel Prize in Chemistry 1972


Christian B. Anfinsen


Stanford Moore


William H. Stein

The Nobel Prize in Chemistry 1972 was divided, one half awarded to Christian B. Anfinsen *"for his work on ribonuclease, especially concerning the connection between the amino acid sequence and the biologically active conformation"*, the other half jointly to Stanford Moore and William H. Stein *"for their contribution to the understanding of the connection between chemical structure and catalytic activity of the active centre of the ribonuclease molecule"*.

Information about winners:

Christian B. Anfinsen,
National Institutes of Health, Bethesda, MD, USA
Stanford Moore and **William H. Stein**,
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RESEARCH INFORMATION:

This year's Nobel Prize in Chemistry has been awarded to three scientists who have made fundamental contributions to enzyme chemistry. They have worked with the same enzyme, ribonuclease. **Anfinsen's** investigations have provided the answer to an important question concerning the way in which the active enzyme is formed in living cells. **Moore**

and **Stein** have elucidated important principles related to the biological activity of the enzyme.

Those properties we generally associate with the concept of life and with living organisms - such as reproductive ability, growth, motility and reaction to external stimuli - are nothing but outward manifestations of a very complicated network of coupled chemical reactions. The chemical reactions in living cells are accelerated (catalyzed) by specific proteins, called enzymes. Consequently, enzymes must in many respects be considered the key substances of life. This becomes rather obvious from consideration based on the most important results of biochemical genetics, summarized in "the central dogma of molecular biology":

DNA --> RNA --> enzyme

DNA (deoxyribonucleic acid) is the carrier of the traits of inheritance, and these become expressed by DNA controlling the synthesis of enzymes.

Like all proteins enzymes are built up from about 20 different amino acids, which are linked together in long chains through peptide bonds. The existence of several thousand enzymes with very different specific properties, despite these similarities in structure, depends on differences in the number and sequence of amino acids between the molecules of different proteins. We now know that the genetic information in the DNA of a cell nucleus is indeed used to determine the sequence of the amino acid residues making up the peptide chain. An active enzyme is, however, not a long string of amino acids joined together through peptide bonds, but the chain is in general folded into a globular (ball-like) shape. In principle, it is of course possible to fold a given chain in many ways but it has been shown that the active enzyme has a singular unique three-dimensional structure (conformation). An important question, is the source of the information required for the peptide chain of a given enzyme to assume its specific confromation. In investigations on the enzyme ribonuclease **Anfinsen** has shown that this information is inherent in the linear sequence of amino acid residues in the peptide chain, so that no further genetic information than that found in DNA is needed. The driving force is the tendency of each

system to assume a state of minimum energy. More precisely this can be expressed by saying that the conformation of the enzyme represents the thermodynamically most stable state in the intracellular environment.

The enzymes are large molecules (macromolecules). The way in which an enzyme accelerates a chemical reaction involves an interaction of the reacting substance (the substrate) with only a limited part of the enzyme molecule, its active site. Anfinsen, Moore and Stein have carried out investigations which supplement each other and have led to a complete elucidation of the sequence of amino acids in the enzyme ribonuclease. It soon became obvious, however, that this knowledge alone tells us very little about the structure of the active site. The three-dimensional structure may bring together in the active site groups which are far apart in the linear sequence. **Moore** and **Stein** however, made an observation with ribonuclease of great general significance, namely that groups in the active site often have an anomalously high reactivity. This increased reactivity was utilized by Moore and Stein for chemical modification of groups in the active site, and in this way the position of these groups in the sequence could be unambiguously determined. Through these investigations Moore and Stein could give a detailed picture of the active site of ribonuclease long before the three-dimensional structure of the enzyme had been determined.

In summary it may be said that Anfinsen, Moore and Stein in pioneering studies have illuminated some of the most important principles describing the relation between the chemical structure and catalytic activity of an enzyme.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1972/press.html