Introduction to Biochemistry

The term introduced by a German chemist *Carl Neuberg* in 1903. Biochemistry may be defined as a science "*Biochemistry (bios = life) was first concerned with the chemical nature and chemical behavior of the living matter*". Biochemistry is, literally, the study of the chemistry of life. Although it overlaps other disciplines, including cell biology, genetics, immunology, microbiology, pharmacology, and physiology, biochemistry is largely concerned with a limited number of issues:

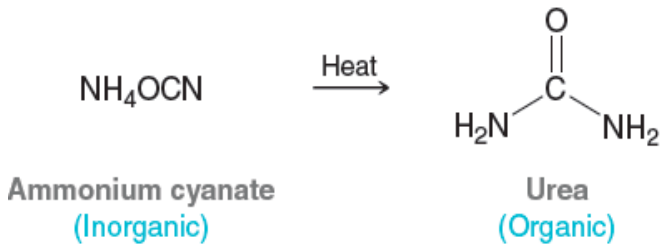
- *What are the chemical and three-dimensional structures of biological molecules?*
- *How do biological molecules interact with one another?*
- *How does the cell synthesize and degrade biological molecules?*
- *How is energy conserved and used by the cell?*
- *What are the mechanisms for organizing biological molecules and coordinating their activities?*
- *How is genetic information stored, transmitted, and expressed?*

Biochemistry, like other modern sciences, relies on sophisticated instruments to dissect the architecture and operation of systems that are inaccessible to the human senses. In addition to the chemist's tools for separating, quantifying, and otherwise analyzing biological materials, biochemists take advantage of the uniquely biological aspects of their subject by examining the evolutionary histories of organisms, metabolic systems, and individual molecules. In addition to its obvious implications for human health, biochemistry reveals the workings of the natural world, allowing us to understand and appreciate the unique and mysterious condition that we call life.

Historical Background

Biochemistry has emerged as an independent science only within the past 100 years but the groundwork for the emergence of biochemistry as a modern science was prepared in earlier centuries. The period before 1900 saw rapid advances in the understanding of basic chemical principles such as reaction kinetics and the atomic composition of molecules. Many chemicals produced in living organisms had been identified by the end of the 19th century. Since then, biochemistry has become an organized discipline and biochemists have elucidated many of the chemical processes of life. The growth of biochemistry and its influence on other disciplines will continue in the 21st century.

In 1828, *Friedrich Wohler* synthesized the organic compound urea by heating the inorganic compound ammonium cyanate.



This experiment showed for the first time that compounds found exclusively in living organisms could be synthesized from common inorganic substances. Today we understand that the synthesis and degradation of biological substances obey the same chemical and physical laws as those that predominate outside of biology. No special or "*vitalistic*" processes are required to explain life at the molecular level. Many scientists date the *beginnings of biochemistry* to Wohler's synthesis of urea, although it would

be another *75 years before the first biochemistry departments were established at universities*.

Louis Pasteur (1822–1895) is best known as the *founder of microbiology* and an active promoter of *germ theory*. But Pasteur also made many contributions to biochemistry including the discovery of stereoisomers.

Two major breakthroughs in the history of biochemistry are especially notable—*the discovery of the roles of enzymes* as catalysts and the *role of nucleic acids as information-carrying molecules*. The very large size of proteins and nucleic acids made their initial characterization difficult using the techniques available in the early part of the 20th century. With the development of modern technology we now know a great deal about how the structures of proteins and nucleic acids are related to their biological functions.

The first breakthrough—identification of enzymes as the catalysts of biological reactions—resulted in part from the research of *Eduard Buchner*. In 1897 *Buchner showed that extracts of yeast cells could catalyze the fermentation of the sugar glucose to alcohol and carbon dioxide.* Previously, scientists believed that only living cells could catalyze such complex biological reactions.

The nature of biological catalysts was explored by Buchner's contemporary, *Emil Fischer*. Fischer studied the catalytic effect of yeast enzymes on the hydrolysis (breakdown by water) of sucrose (table sugar). He proposed that during catalysis an enzyme and its reactant, or substrate, combine to form an intermediate compound. He also proposed that only a molecule with a suitable structure can serve as a substrate for a given

enzyme. Fischer described enzymes as rigid templates, or locks, and substrates as matching keys. Researchers soon realized that almost all the reactions of life are catalyzed by enzymes and a modified lock-and-key theory of enzyme action remains a central tenet of modern biochemistry.

Another key property of enzyme catalysis is that biological reactions occur much faster than they would without a catalyst. In addition to speeding up the rates of reactions, enzyme catalysts produce very high yields with few, if any, by-products. In contrast, many catalyzed reactions in organic chemistry are considered acceptable with yields of 50% to 60%. Biochemical reactions must be more efficient because byproducts can be toxic to cells and their formation would waste precious energy.

The last half of the 20th century saw tremendous advances in the area of structural biology, especially the structure of proteins. The first protein structures were solved in the 1950s and 1960s by scientists at Cambridge University (United Kingdom) led by *John C. Kendrew* and *Max Perutz*. Since then, the three-dimensional structures of several thousand different proteins have been determined and our understanding of the complex biochemistry of proteins has increased enormously. These rapid advances were made possible by the availability of larger and faster computers and new software that could carry out the many calculations that used to be done by hand using simple calculators. Much of modern biochemistry relies on computers.

The second major breakthrough in the history of biochemistry—identification of nucleic acids as information molecules—came a half-century after Buchner's and Fischer's experiments. In 1944 *Oswald Avery*, *Colin MacLeod*, and *Maclyn McCarty* extracted deoxyribonucleic acid (DNA) from a pathogenic strain of the bacterium *Streptococcus pneumoniae* and mixed

the DNA with a nonpathogenic strain of the same organism. The nonpathogenic strain was permanently transformed into a pathogenic strain. This experiment provided the first conclusive evidence that DNA is the genetic material. In 1953 *James D. Watson* and Francis H. C. Crick deduced the three-dimensional structure of DNA. The structure of DNA immediately suggested to Watson and Crick a method whereby DNA could reproduce itself, or replicate, and thus transmit biological information to succeeding generations. Subsequent research showed that information encoded in DNA can be transcribed to ribonucleic acid (RNA) and then translated into protein.

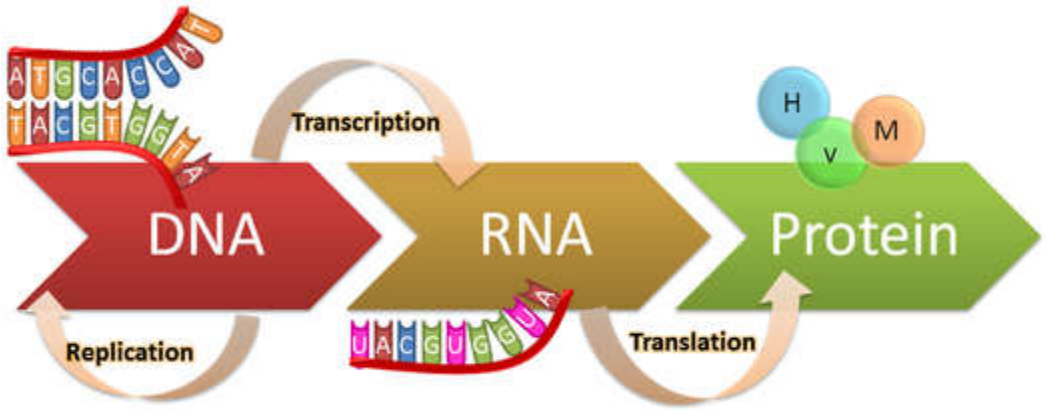


Fig 1. Central dogma of molecular biology

The study of genetics at the level of nucleic acid molecules is part of the discipline of molecular biology and molecular biology is part of the discipline of biochemistry. In order to understand how nucleic acids store and transmit genetic information, you must understand the structure of nucleic acids and their role in information flow. You will find that much of your study of biochemistry is devoted to considering how enzymes and nucleic acids are central to the chemistry of life.

As Crick predicted in 1958, the normal flow of information from nucleic acid to protein is not reversible. He referred to this unidirectional information flow from nucleic acid to protein as the *Central Dogma of Molecular Biology (Fig 1)*. The term "*Central Dogma*" is often misunderstood. Strictly speaking, it does not refer to the overall flow of information shown in the figure. Instead, it refers to the fact that once information in nucleic acids is transferred to protein it cannot flow backwards from protein to nucleic acids.