

BIOCHEMISTRY

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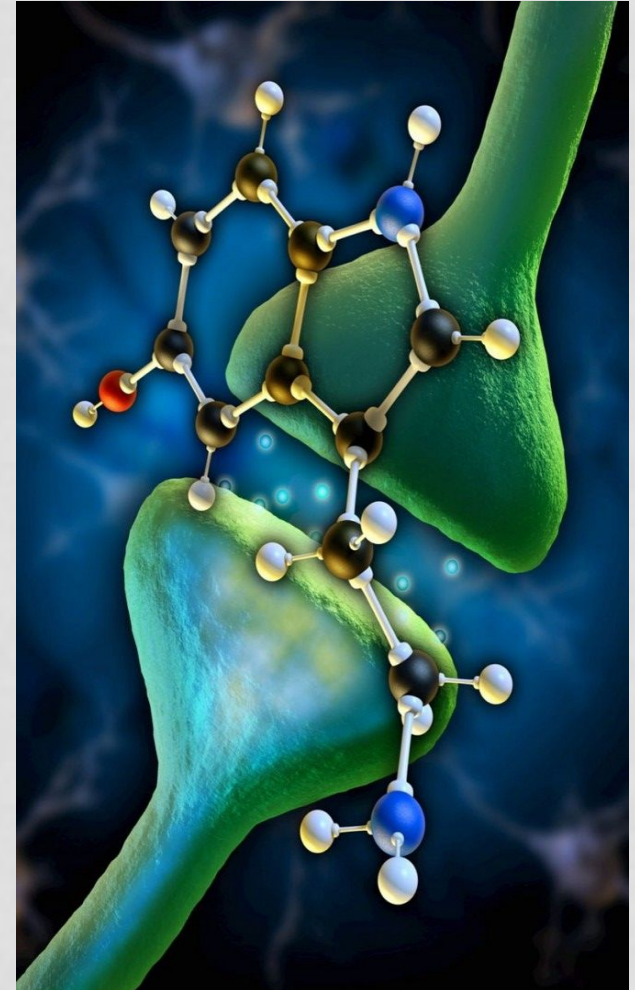


INTRODUCTION

Biochemistry is study of the chemical substances and processes that occur in plants, animals, and microorganisms and of the changes they undergo during development and life. It deals with the chemistry of life, and as such it draws on the techniques of analytical, organic, and physical chemistry, as well as those of physiologists.

The term *biochemistry* is synonymous with two somewhat older terms: *physiological chemistry* and *biological chemistry*. Those aspects of biochemistry that deal with the chemistry and function of very large molecules are often grouped under the term *molecular biology*.

Biochemistry is a young science, having been known under that term only since about 1900.



HISTORICAL BACKGROUND

It all started with the work of **Robert Boyle** in the period from about 1650 to 1780. Boyle questioned the basis of the chemical theory of his day and taught that the proper object of chemistry was to determine the composition of substances. His contemporary **John Mayow** observed the analogy between the respiration of an animal and the burning, or oxidation, of organic matter in air. Then, when **Lavoisier** carried out his studies on chemical oxidation and he showed the similarity between chemical oxidation and the respiratory process.



Robert Boyle

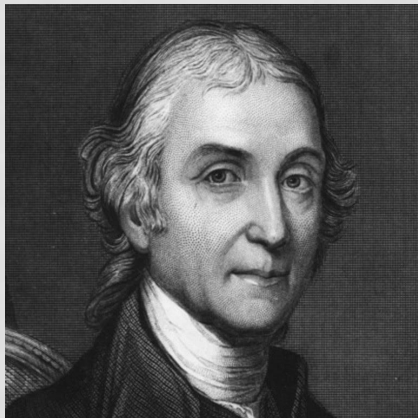


John Mayow



Antoine-Laurent Lavoisier

Photosynthesis was another biological phenomenon that occupied the attention of the chemists of the late 18th century. The demonstration, through the combined work of **Joseph Priestley**, **Jan Ingenhousz**, and **Jean Senebier**, that photosynthesis is essentially the reverse of respiration was a milestone in the development of biochemical thought.



Joseph Priestley



Jan Ingenhousz



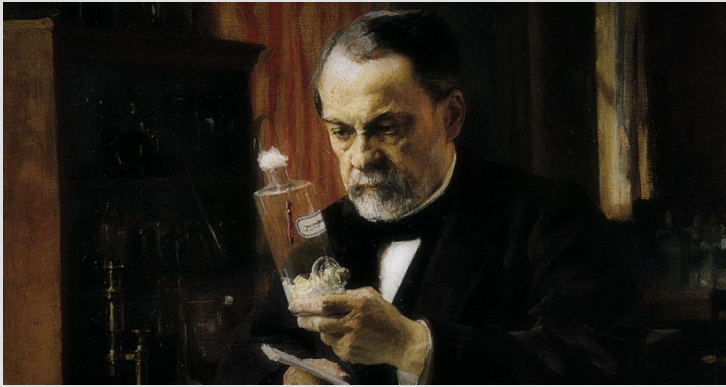
Jean Senebier



Friedrich Wöhler

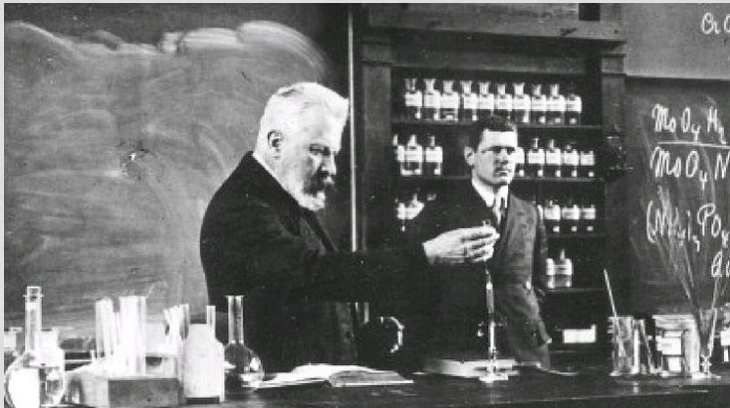
The first laboratory synthesis of an organic compound, urea, was carried out by **Friedrich Wöhler** in 1828.

Justus von Liebig established at Giessen a great teaching and research laboratory. Besides putting the study of organic chemistry on a firm basis, Liebig described the great chemical cycles in nature.



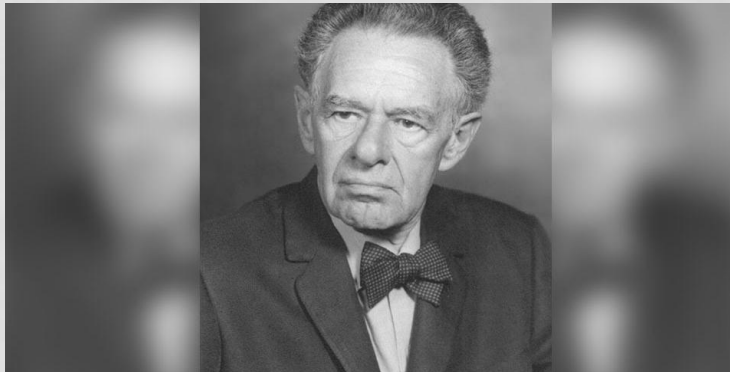
Louis Pasteur

In the 1860s **Louis Pasteur** proved that various yeasts and bacteria were responsible for “ferments,” substances that caused fermentation and, in some cases, disease. He also demonstrated the usefulness of chemical methods in studying these tiny organisms and was the founder of what came to be called bacteriology.



Eduard Buchner

Later, in 1877, Pasteur’s ferments were designated as enzymes, and, in 1897, the German chemist **E. Buchner** clearly showed that fermentation could occur in a press juice of yeast, devoid of living cells.



Fritz Albert Lipmann.

In 1940 **F.A. Lipmann** proposed that ATP is the common form of energy exchange in many cells, a concept now thoroughly documented. ATP has been shown also to be a primary energy source for muscular contraction.

The use of radioactive isotopes of chemical elements to trace the pathway of substances in the animal body was initiated in 1935 by two U.S. chemists, **R. Schoenheimer** and **D. Rittenberg**.

In 1869 a substance was isolated from the nuclei of pus cells and was called nucleic acid, which later proved to be deoxyribonucleic acid (DNA), but it was not until 1944 that the significance of DNA as genetic material was revealed, when bacterial DNA was shown to change the genetic matter of other bacterial cells. Within a decade of that discovery, the double helix structure of DNA was proposed by **Watson and Crick**, providing a firm basis for understanding how DNA is involved in cell division and in maintaining genetic characteristics.



Rudolf Schoenheimer



Watson and Crick

AREAS OF STUDY

- **Chemical composition of living matter**

In general, the bulk of the organic matter of a cell may be classified as *protein*, *carbohydrate*, and *fat*, or *lipid*. *Nucleic acids* and various other organic derivatives are also important constituents.

Proteins are fundamental to life, not only as structural elements (e.g., collagen) and to provide defense (as antibodies) against invading destructive forces but also because the essential biocatalysts are proteins.

Carbohydrates include such substances as sugars, starch, and cellulose.

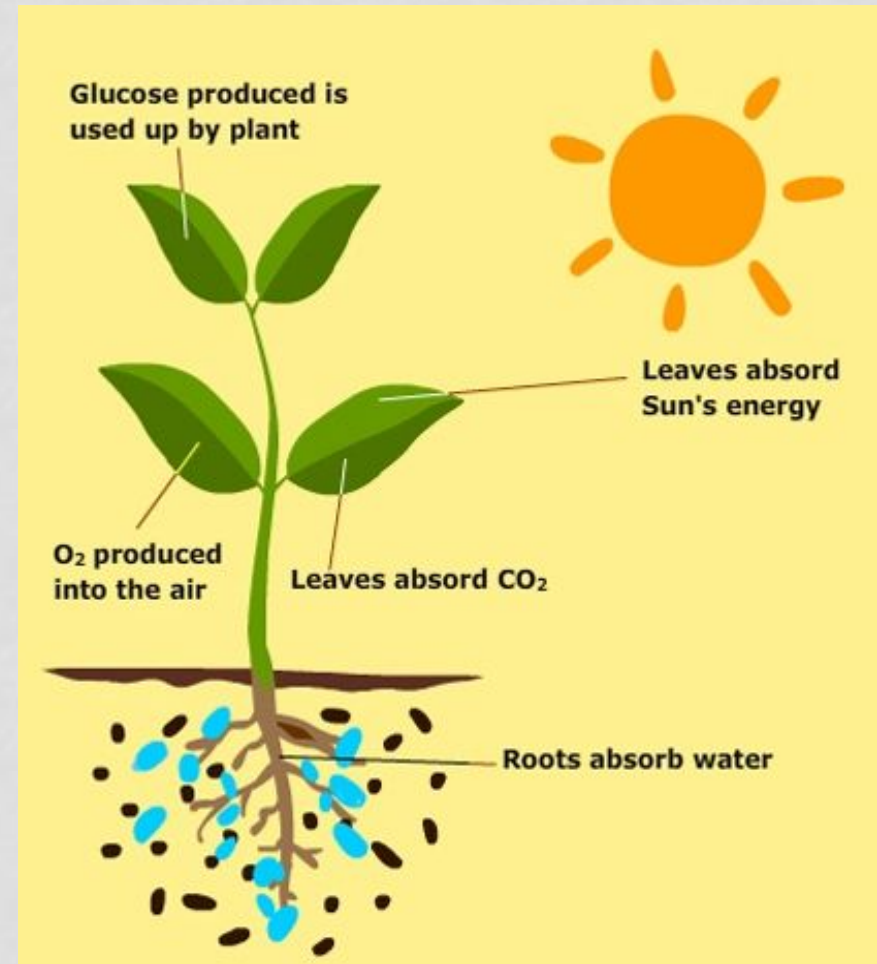
Fats, or lipids, constitute a heterogeneous group of organic chemicals that can be extracted from biological material by nonpolar solvents such as ethanol, ether, and benzene. The liver is the main site of fat metabolism. The control of fat absorption is known to depend upon a combination action of secretions of the pancreas and bile salts.

Nucleic acids are large, complex compounds of very high molecular weight present in the cells of all organisms and in viruses. They are of great importance in the synthesis of proteins and in the transmission of hereditary information from one generation to the next.

• **NUTRITION**

All animals require organic material in their diet, in addition to water and minerals. This organic matter must be sufficient in quantity to satisfy the caloric, or energy, requirements of the animals. Within certain limits, carbohydrate, fat, and protein may be used interchangeably for this purpose. Certain essential fatty acids, about ten different amino acids, and vitamins are required by many higher animals.

That plants differ from animals in requiring no preformed organic material. The ability of green plants to make all their cellular material from simple substances—carbon dioxide, water, salts, and a source of nitrogen such as ammonia or nitrate—was termed **photosynthesis**.

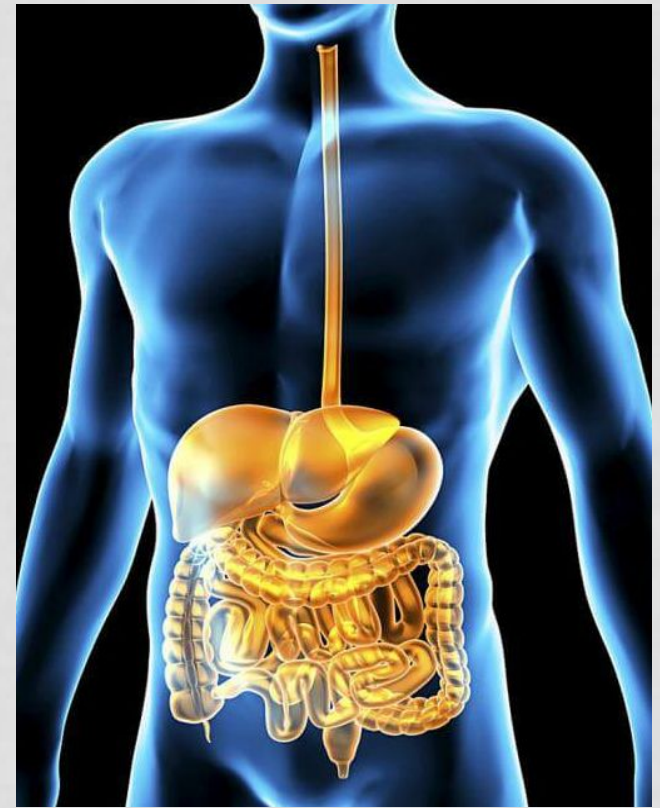


• **DIGESTION**

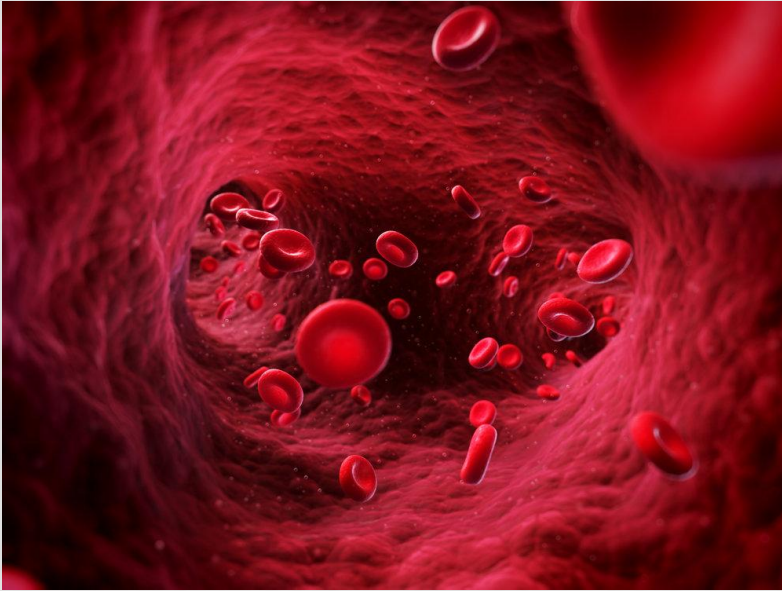
The organic food of animals, including man, consists in part of large molecules. In the digestive tracts of higher animals, these molecules are hydrolyzed, or broken down, to their component building blocks. Proteins are converted to mixtures of amino acids, and polysaccharides are converted to monosaccharides. The hydrolysis of food material is necessary also to convert solid material into soluble substances suitable for absorption. Pepsin and trypsin, the proteolytic enzymes of gastric and pancreatic juice, respectively, continue to be intensively investigated.

The products of enzymatic action on the food of an animal are absorbed through the walls of the intestines and distributed to the body by blood and lymph.

In the case of the secretion of hydrochloric acid into gastric juice, it has been shown that active secretion is dependent on an adequate oxygen supply (i.e., on the respiratory metabolism of the tissue), and the same holds for absorption of salts by plant roots. The energy released during the tissue oxidation must be harnessed in some way to provide the energy necessary for the absorption or secretion.



• BLOOD



One of the animal tissues that has always excited special curiosity is **blood**.

The blood **pigment hemoglobin** has been intensively studied. Hemoglobin is confined within the blood corpuscles and carries oxygen from the lungs to the tissues. It combines with oxygen in the lungs, where the oxygen concentration is high, and releases the oxygen in the tissues, where the oxygen concentration is low.

The proteins of blood plasma also have been extensively investigated. The gamma-globulin fraction of the plasma proteins contains the antibodies of the blood and is of practical value as an immunizing agent. An animal develops resistance to disease largely by antibody production.

Antibodies are proteins with the ability to combine with an antigen. When this agent is a component of a disease-causing bacterium, the antibody can protect an organism from infection by that bacterium. The chemical study of antigens and antibodies and their interrelationship is known as immunochemistry.

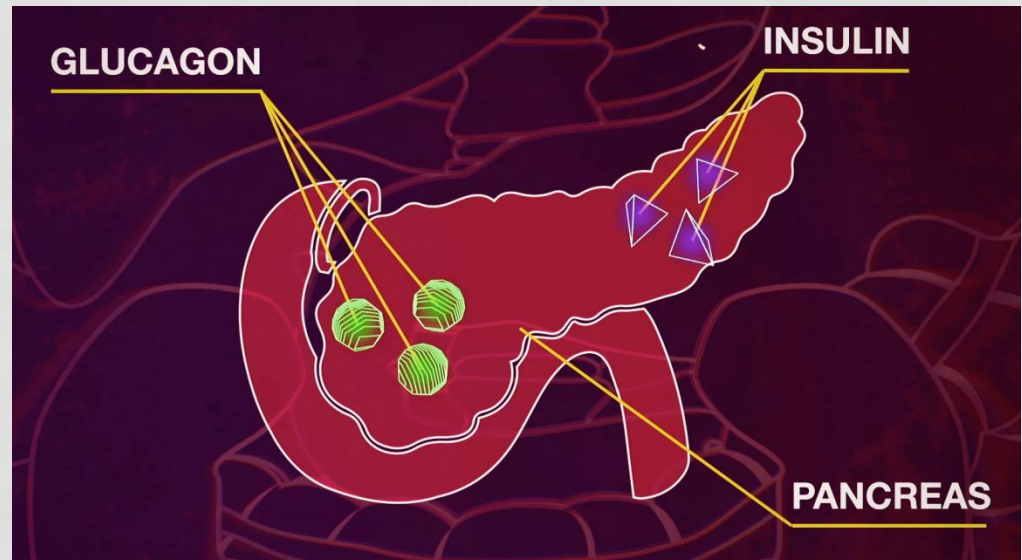
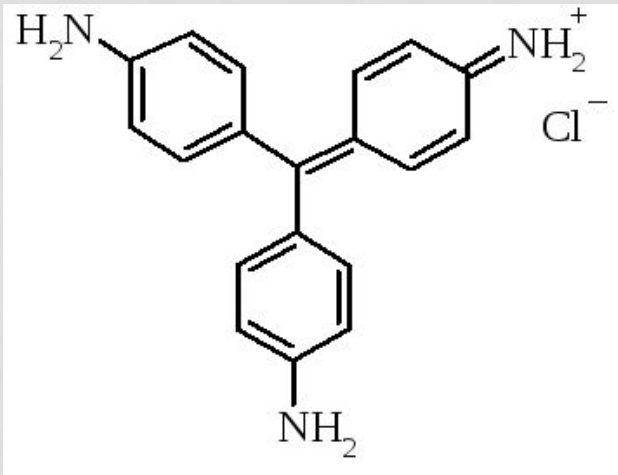


• METABOLISMS AND HORMONES

The cell is the site of a constant, complex, and orderly set of chemical changes collectively called **metabolism**.

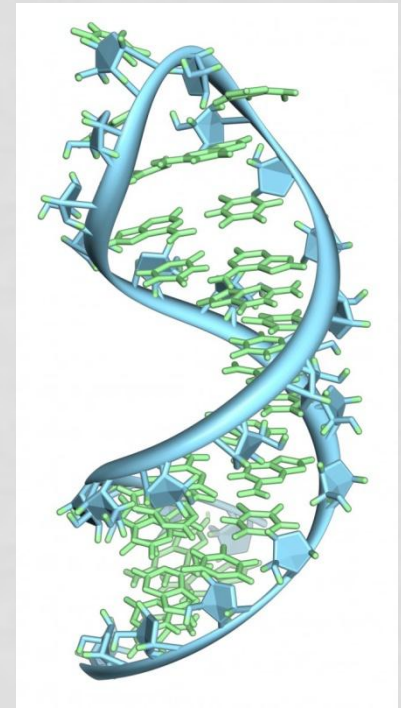
Hormones, which may be regarded as regulators of metabolism, are investigated at three levels, to determine their physiological effects, their chemical structure, and the chemical mechanisms whereby they operate. The chemical structures of thyroxine and adrenaline are known. The hormones of the pancreas—insulin and glucagon—and the hormones of the hypophysis are **peptides**. The chemical structures of the plant hormones, auxin and gibberellic acid, which act as growth-controlling agents in plants, are also known.

It seems likely that different hormones exert their effects in different ways. Some may act by affecting the permeability of membranes; others appear to control the synthesis of certain enzymes.

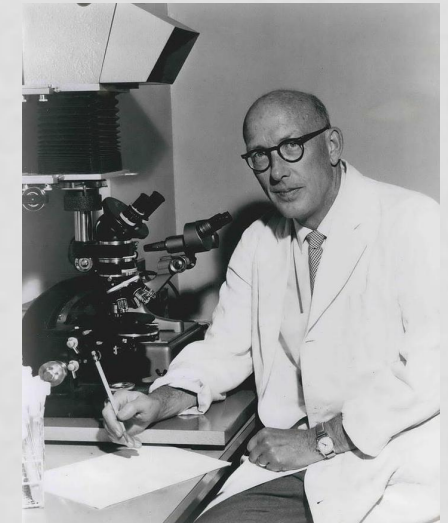


• GENES

Genetic studies have shown that the hereditary characteristics of a species are maintained and transmitted by the self-duplicating units known as genes, which are composed of nucleic acids and located in the chromosomes of the nucleus. Thus, the capacity of a protein to behave as an enzyme is determined by the chemical constitution of the gene (DNA) that directs the synthesis of the protein. The first successful experiments, devised by the Nobel Prize winners **George W. Beadle** and **Edward L. Tatum**, involved the bread mold *Neurospora crassa*; the two men were able to collect a variety of strains that differed from the parent strain in nutritional requirements. It was then shown that such a mutant had lost an enzyme essential for the synthesis of the amino acid in question.



George W. Beadle



Edward L. Tatum

• **EVOLUTION AND ORIGIN OF LIFE**

The exploration of space beginning in the mid-20th century intensified speculation about the possibility of life on other planets. At the same time, man was beginning to understand some of the intimate chemical mechanisms used for the transmission of hereditary characteristics. It was possible, by studying protein structure in different species, to see how the amino acid sequences of functional proteins (e.g., hemoglobin and cytochrome) have been altered during phylogeny (the development of species). It was natural, therefore, that biochemists should look upon the problem of the origin of life as a practical one. The synthesis of a living cell from inanimate material was not regarded as an impossible task for the future.

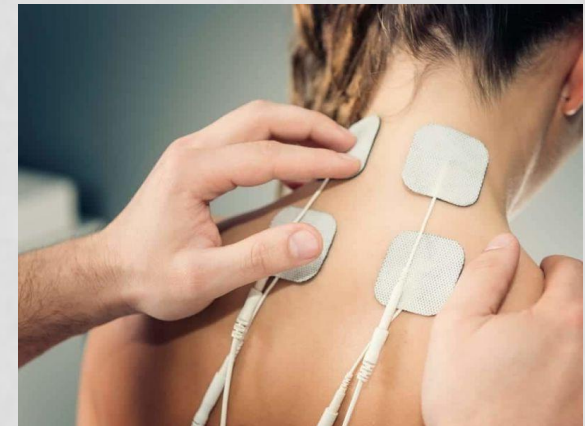


• **APPLIED BIOCHEMISTRY**

The clinical chemistry laboratory now has become a major investigative arm of the physician in the diagnosis and treatment of disease and is an indispensable unit of every hospital. Many specialized and sophisticated methods have been introduced, and machines have been developed for the simultaneous automated analysis of many different blood constituents in order to cope with increasing medical needs.

Analytical biochemical methods have also been applied in the food industry to develop crops superior in nutritive value and capable of retaining nutrients during the processing and preservation of food.

Biochemical techniques have been fundamental in the development of new drugs. The testing of potentially useful drugs includes studies on experimental animals and man to observe the desired effects and also to detect possible toxic manifestations; such studies depend heavily on many of the clinical biochemistry techniques already described. Biochemical advances in the knowledge of the action of natural hormones and antibiotics promise to aid further in the development of specific pharmaceuticals.

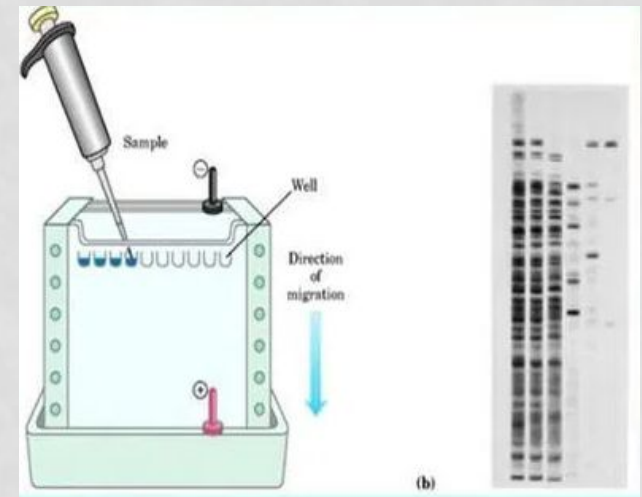
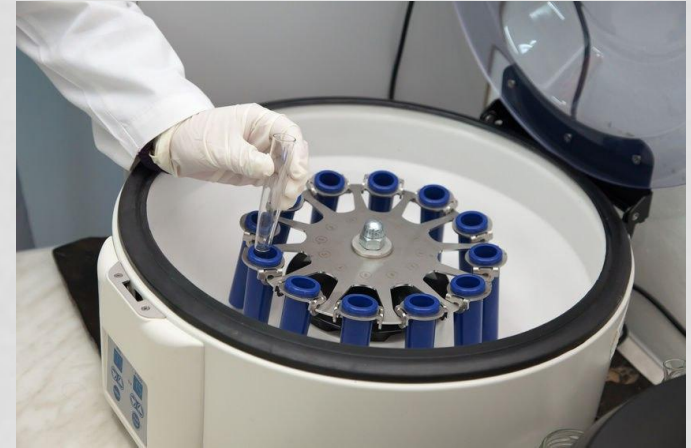


METHODS IN BIOCHEMISTRY

- **Centrifugation and electrophoresis**

An important tool in biochemical research is the centrifuge, which through rapid spinning imposes high centrifugal forces on suspended particles, or even molecules in solution, and causes separations of such matter on the basis of differences in weight. Thus, red cells may be separated from plasma of blood, nuclei from mitochondria in cell homogenates, and one protein from another in complex mixtures.

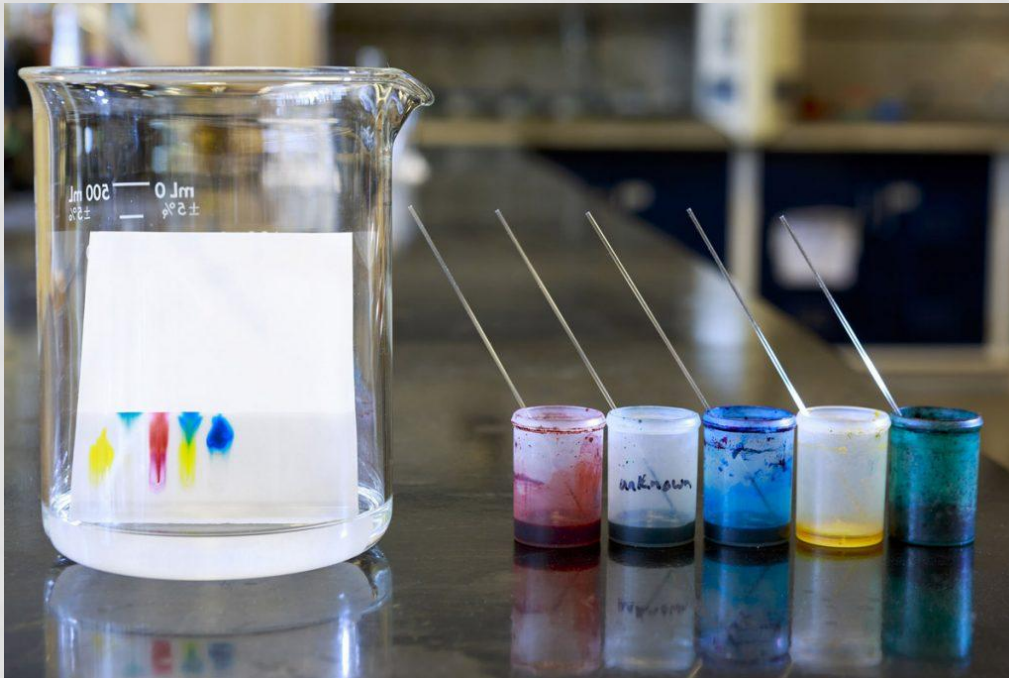
Another property of biological molecules that has been exploited for separation and analysis is their electrical charge. Amino acids and proteins possess net positive or negative charges according to the acidity of the solution in which they are dissolved. In an electric field, such molecules adopt different rates of migration toward positively (anode) or negatively (cathode) charged poles and permit separation. By appropriate colour reactions of the proteins and scanning of colour intensities, a number of proteins in a mixture may be measured. Separate proteins may be isolated and identified by electrophoresis, and the purity of a given protein may be determined.



- **Chromatography and isotopes**

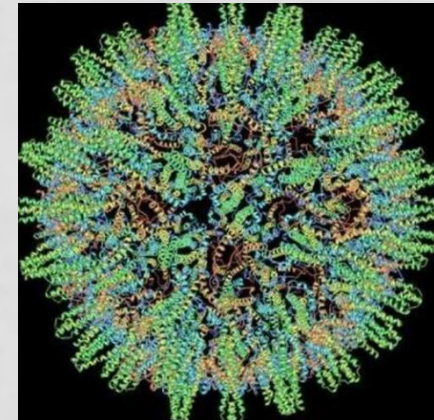
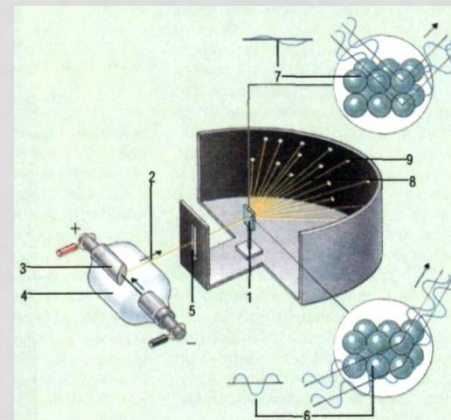
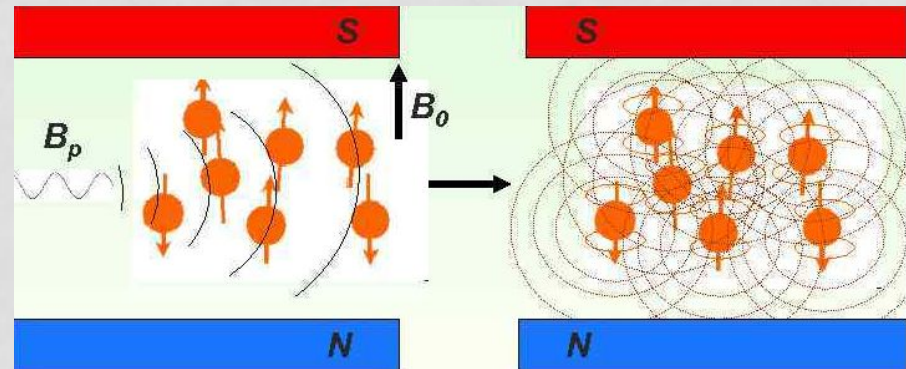
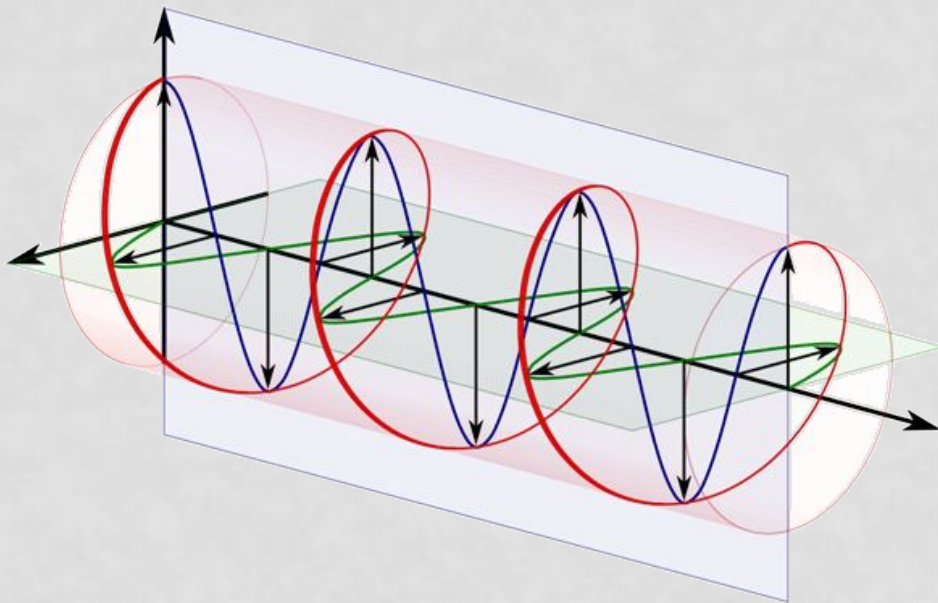
The different solubilities of substances in aqueous and organic solvents provide another basis for analysis. In contrast to electrophoresis, this method has been applied to a wide variety of biological compounds and has contributed enormously to research in biochemistry.

The general principle has been extended from filter paper strips to columns of other relatively inert media, permitting larger scale separation and identification of closely related biological substances. Particularly noteworthy has been the separation of amino acids by chromatography in columns of ion-exchange resins, permitting the determination of exact amino acid composition of proteins. Another technique of column chromatography is based on the relative rates of penetration of molecules into beads of a complex carbohydrate according to size of the molecules. Larger molecules are excluded relative to smaller molecules and emerge first from a column of such beads.



Perhaps the single most important technique in unravelling the complexities of metabolism has been the use of isotopes (heavy or radioactive elements) in labelling biological compounds and "tracing" their fate in metabolism. Measurement of the isotope-labelled compounds has required considerable technology in mass spectroscopy and radioactive detection devices.

A variety of other physical techniques, such as nuclear magnetic resonance, electron spin spectroscopy, circular dichroism, and X-ray crystallography, have become prominent tools in revealing the relation of chemical structure to biological function.



Thanks for attention!