CHAPTER XVIII

THE CELL

PART I — MORPHOLOGY

Introduction. Living things are organizations of units called cells. Organs are composed of tissues which are composed of cells, which although of great variety of form yet exhibit evidences of a similar basic organization. All cells have many similar characteristics.

Some organisms consist of single cells or aggregations of similar cells, as, for example, the Protozoa and Protophyta. The gametophyte stage in plants begins life as a single cell, a spore. Metazoan animals and the sporophytes of plants begin life as a fertilized egg cell or zygote which develops into the adult organism. The word " cell " is a misnomer. Introduced first by Hooke in 1665, and applied by him to the microscopic box-like units forming cork tissue, the name has persisted, although today, and for nearly a century now, the word has connoted not an empty box but a small mass of living substance called protoplasm. In modern biological thought, *cell* and *protoplasm* are conceptions that should be thought of as merely two aspects of one phenomenon. In the present chapter, we shall consider the cell first from a morphological point of view.

Most cells possess many similar structures. In the center of the cell can be seen a small body, circular in outline and lighter in color. This is the nucleus; the portion outside the nucleus is the cytosome, and both are composed of protoplasm. The nucleus is visible in many living cells. Both cytosome and nucleus are optically so homogeneous that few details are revealed by a study of the living cell. But cytological technic enables us to extend our knowledge of these regions (Fig. 286).

Cytosome. The protoplasm constituting the cytosome is called cytoplasm. This is a translucent, somewhat jelly-like substance. Max Schultze described it as being a viscid fluid, *hyaloplasm*, containing microscopic granules called *microsomes.* Later workers studied its appearance after treatment with killing and fixing reagents, and Leydig, for example, stated that the hyaloplasm supported a fine network of fibrils which he called *spongioplasm.* Later, Bütschli in 1890 studied living protoplasm of Protozoa and described it as being composed of very small, different-sized globules, distributed in a liquid medium, the hyaloplasm of Schultze. Bütschli called the globules, *alveoli,* and his conception is known as the *alveolar theory.* According to this theory, protoplasm resembles an emulsion. It is pretty well agreed now that cytoplasm consists of viscous clear fluid — *hyaloplasm* — permeated in some cases by *granules* of different sizes, in other cases by *fibrils,* sometimes very fine, sometimes coarser, as in nerve fibers; and in still other cases by different sized globules or *alveoli.* In the interalveolar substance granules or *microsomes* are at times observed. Certain studies reveal evidence of granules changing to alveoli, or the reverse in certain cell activities. The granule is possibly an early stage in the formation of the alveolus.

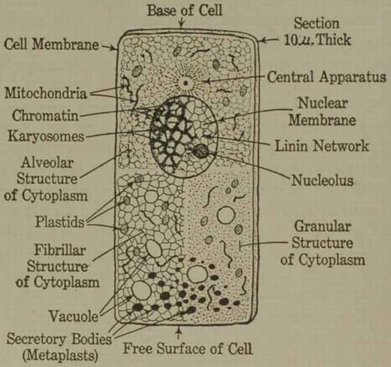


FIG. 286. — Diagram of a section of a cell illustrating general morphology of cells.

Special staining fibers called *mitochondria* have been found in most kinds of cells. These appear to be linear groupings of granules. They seem to be scattered granules in embryonic cells and a thread-like arrangement of granules, *i.e.*, fibrils in older differentiated cells. Their function is still problematical. They are regarded as permanent morphological structures of the cytosome. Some workers believe that they form the myofibrils of voluntary muscle fibers, and the neurofibrils of a nerve fiber; others state that they play an important part in inheritance and still others assign other functions to them. In the cytosome, at times, are found *chromidia*, which are masses of chromatin discharged from the nucleus.

In some cells, chiefly those of plants, are found special bodies called *plastids*. In the mesophyll of the leaf occur green *chloroplastids*, living, self-propagating bodies containing chlorophyll and therefore vital to the formation of starch. Non-living bodies or substances called *metaplasts* occur in cytoplasm. These are products of the cell's activity. A gland cell forms granules which are discharged from the cell in a liquid form called a secretion. Parenchyma cells in plants contain starch grains. Cells, chiefly those of protozoans and of plants, contain spaces called *vacuoles*. The contractile vacuoles of Amoeba and Paramecium are intracellular organs which, beginning as minute structures, increase in size, contract and repeat the same changes rhythmically. They are probably drainage reservoirs for liquid wastes of excretions which are discharged by contraction. The *fat cell* of animal adipose tissue is a large vacuole or droplet of oil surrounded by a thin pellicle of cytoplasm at one point of which is the nucleus of what was once a small stellate connective tissue cell. The vacuolated condition of plant cells is characteristic of them. The plant cell is inclosed in a box of cellulose, and the inner surface of this is lined with a thin layer of cytoplasm at one point of which may be the nucleus. Strands of protoplasm may form a crude network within the cellulose walls and the vacuolated spaces within this network are filled with cell sap.

Nucleus. The nucleus is such a characteristic structure that Schultze defined a cell as a mass of protoplasm containing a nucleus. It is now known that nuclear matter is protoplasm, differing somewhat chemically from that of the cytosome. The nucleus of plant cells was discovered in 1831 by Robert Brown, an Englishman, described by Humboldt as the "most famous of botanists." As a rule there is but one nucleus. No distinct nucleus can be demonstrated in Bacteria although staining methods indicate distributed nuclear material. Distinct nuclei are not seen in the cells of Blue-green Algae. Red blood cells of Mammals lose their nuclei after they are formed, and yet these cells remain functional. They later disintegrate without dividing. Certain Protozoa have a long beaded nucleus. Although most of the cells of the liver are uninucleated, some are found with two nuclei, and the giant cells of developing bone have many nuclei. In a certain type of white blood cell the nucleus may be in the form of irregular masses connected by small strands. The nucleus is inclosed in a nuclear membrane which disappears during cell division. The protoplasm of the nucleus consists of a liquid nucleoplasm or nuclear sap traversed by a network of *linin fibers.* Neither of these stains well with basic dyes such as haemotoxylin, and hence are called the achromatic parts of the nucleus. The colorless linin fibers support fine granules called *chromioles.* Where the fibers cross each other, little masses of chromioles are present, forming *karyosomes.* During cell division the chromioles fuse to form distinct aggregations or bodies called *chromosomes.* Chromosome substance has a great affinity for (basic) dyes, such as hematoxylin. On account of its staining property, this unique cell substance has received the name *chromatin.* Chromatin is a nucleo-protein compound containing nucleic acid. The intensity of staining with basic dyes depends on the proportion of nucleic acid present. Most nuclei possess a small body called the *nucleolus,* which is spherical in form and dense in appearance. It is not a chromatin body because it stains with acid or neutral dyes. Some cells have no nucleoli. The function of the nucleolus is not understood.

It is believed that the nucleus regulates the metabolic activity of the cells. An enucleated mass of cytoplasm may continue to function for a short time, but soon dies, for metabolic processes connected with feeding cannot take place. Such a piece continues to live until the supply of energy available is dissipated. A piece of cytoplasm containing a nucleus or part of a nucleus of adequate size does continue to function and will regenerate a new cell. Certain observations lead to the interpretation that the nucleus is directly concerned with secretory activities. It is pretty well agreed that there is a constant interaction between nucleus and cytosome. The organization termed the cell, therefore, has at least two different regional organizations *within it,* namely, that of the cytosome and that of the nucleus.

If one body cell of an organism contains a certain number of chromosomes, then every body cell contains a similar number and the body cells of any other animal or plant of that same species contains the same number of chromosomes. Chromosomes or chromioles are now thought to contain ultramicroscopic multimolecular masses of protein substance called *genes* which are the determiners of inherited characteristics, but function only in germ cells. That is, although the chromosomes of a liver or muscle cell, for example, are similar in this respect to those of a germ cell, yet the heredity function is inhibited in all cells except mature sex cells.

Centrosome. Near the nucleus, at the time of cell division, a small body called the *centrosome* appears in most animal cells, but rarely in plant cells. The centrosome is surrounded by a clear area of cytoplasm known as the *centrosphere.* From this clear area extend radiating protoplasmic strands, or spindle fibers, in all directions, thus constituting the *astrosphere.* The centrosome or centriole, the centrosphere and the astrosphere constitute the *central apparatus.* It is described as the dynamic center which organizes the apparatus, or mechanism, engaged in cell division.

Cell Membrane. At the surface of liquids where they are in contact with air, a film is present, possessing the property known as surface tension. The existence of this film can be demonstrated by rubbing a needle with a little oil and laying it carefully on the surface of the water in a dish. The needle floats. If the film is broken, the needle sinks. The properties of the film depend on the nature of the medium of which it is the boundary. Cytoplasm is a semifluid substance. As such, the boundary of the cell is a surface membrane or film, probably possessing an aggregation of particles more dense than the rest of the cytoplasm. It appears to be rich in proteins and phosphatides. The cell membrane regulates the passage of oxygen and food compounds into the cytoplasm and also carbon dioxide and nitrogenous waste products out of the cytoplasm. Through it must pass also secretory products that perform useful work elsewhere. The exposed surface of some cells, as those forming the outer part of the ‘ skin ’ of the earthworm, have a thickened, tough external wall called a cuticle. The cytoplasm of plant cells (Fig. 287) secretes a box-like cellulose wall outside the real cell membrane. Not all cells have cell membranes. The histologic unit of voluntary muscle tissue is

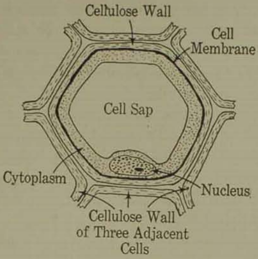


Fig. 287. — Diagram of a plant cell. From Sinnott, *Botany*, 2nd edition, McGraw-Hill Book Co. Reprinted by permission.

a cylindrical multi-nucleated mass of protoplasm. The protoplasm of one nuclear region is not separated by a membrane from the protoplasm of adjacent nuclear regions. Nevertheless, it is proper to call such a grouping a mass of cells. In such a case, the special arrangement in which cells are not separated from each other by a cell membrane is called a *syncytium*.

Shape of Cells (Fig. 288). Cells vary greatly in shape. In many cases single free cells are spherical — for the same physical reasons that determine the contour of a drop of water or jelly. The egg cells of many animals are little spheres. Some soft-walled cells in masses are irregularly polygonal in form with flattened sides much like the form of bubbles in a mass. The parenchyma tissue of plants is composed of cells of this form.

Some cells resemble bricks set on end and arranged side by side, as columnar epithelium, for example. Cells belonging to this general type are shaped like short columns or cubes. The epithelium that forms the walls of capillaries

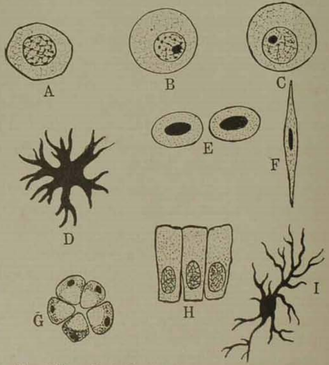


Fig. 288. — Variation in shape of cells. *A*, human egg cell; *B*, egg cell of cat; *C*, egg cell of sea-urchin; *D*, pigment cell from skin of frog; *E*, red blood cells of frog; *F*, smooth muscle cell; *G*, five pancreas cells; *H*, columnar shaped cells from intestine; *I*, nerve cell from brain.

consists of flat, thin cells with irregular outlines. The smooth muscle cell is long and spindle-shaped. One type of nerve cell has a stellate body with a long, attenuated process extending from the nucleated body part. We have already noted great variation in the form of Protozoa and Protophyta.

Size of Cells. For the most part cells are microscopic in size. Some single-celled animals can just be seen with the naked eye, and look like tiny white specks. However, most cells are very much smaller. 0.001 millimeter equals one *micron*, represented by the letter " μ." It has been claimed that most of our own cells are 5 μ in diameter. Yeast cells are about 7 μ in diameter. Human red blood cells are circular discs about 7 μ in diameter. The human egg cell is about 135 μ in diameter, while the human sperm cell is 50 μ long. Bacteriologists believe that there are bacteria so small that they cannot be seen with the microscope. Animals of different sizes have cells which are of about the same size; as, for example, the elephant and the mouse. The hen's egg is a single large cell, yet the shell and the white are not part of the cell, but merely associated with it. The egg cell nucleus and protoplasm is a tiny microscopical mass on the top of the yolk. The ostrich egg is still larger, but this is because there is so much more yolk present. The egg of the elephant, on the other hand, is microscopic in size. The human body contains millions of cells. It is a community containing more members than the population of the earth, and in health these units function as a perfect whole.

History of Ideas Concerning Cells. In the seventeenth century the compound microscope had come into use. An Englishman, Robert Hooke, examined many objects with this new and fascinating instrument. He cut cork into thin slices and studied them. He noted that cork was an assemblage of little box-like units, which he called *cells*. Contemporaries of his in other countries also studied thin preparations of plant tissues microscopically, and even drew diagrams of somewhat similar " cells," but overlooked their importance. In 1759 a German embryologist, Wolff, saw little " globules " in early embryos. Yet Bichât, the founder of histology (1771–1802), in spite of all his microscopical investigations, did not discuss cells. Oken, a somewhat fanciful philosopher, in 1805 stated that he could easily prove " that animals and plants were nothing but numerous aggregations of vesicles," but his mere statement carried no conviction. During the later years of the eighteenth century the idea was developing that animals and plants were, after all, composed of "globules."

During the early years of the nineteenth century the *cell* was more and more discussed in scientific papers, especially those dealing with plant structures. In 1831, Robert Brown ascertained that within each was an inner body, the nucleus. At this time in Germany, a botanist, Schleiden (Fig. 289 *A*), concluded that to understand plant structures it was necessary to know their development. Brown's discovery of the nucleus suggested to Schleiden that new cells originated from this. He worked along this line. Incidentally his ideas as to the development of new plant cells were erroneous. It was in 1838 that he happened to tell Theodore Schwann (Fig. 289 *B*) about his work. As a result Schwann exhibited some of his own preparations of animal tissues to Schleiden, who saw in them nuclei which resembled those of plant cells. Schwann was led to conclude that the units of animal tissues were very similar to those of plants.

Fig. 289 *A*. — Schleiden. From Locy, *Biology and Its Makers*. Courtesy Henry Holt & Co.

Although usually credited with being one of the founders of the *Cell Theory*, Locy considers that Schleiden's chief service consisted in suggesting the idea to Schwann, who further developed it, publishing a brief account of his views in 1838, and in 1839 a long and carefully planned and illustrated monograph. The title of this classic was "Microscopical Investigations on the Correspondence in Structure and Growth of Animals and Plants."

He said that the investigation indicated the identity of structure of plants and animals, as shown by their development, and concluded that "the elementary parts of all tissues are formed of cells in an

Fig. 289 *B*. — Schwann. From Locy, *Biology and Its Makers*. Courtesy of Henry Holt & Co.

analogous though very diversified manner." "The development of the proposition that there exists one general principle for the formation of all organic productions and that this principle is the formation of cells, as well as the conclusions which may be drawn from this proposition, may be comprised under the term, Cell Theory." Schwann was in many respects wrong in his understanding of the structure and development of cells, but he did succeed in establishing the idea of the cellular nature of plants and animals so that a great amount of critical work on the detailed structure of cells followed. It should be said here that although Schwann was led to his conclusions regarding the cellular nature of all organisms by a study of the nervous system, yet it was not until the latter part of the nineteenth century that it was finally accepted so that even the nervous system was included in the general law. The special application of this to the nervous system is known as the "*Neuron Theory*" — a neuron being a special name for a nerve cell.

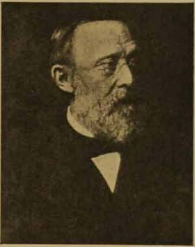


FIG. 290 *A*. — Virchow. From Locy, *Biology and Its Makers*, Courtesy of Henry Holt & Co.

It gradually became evident that the cell was the locus of physiological activities, and the physiology of an organ was to be explained by finding out the physiology of its cells. The importance of the cell in embryology was recognized and that science advanced greatly. The greater importance of the cell in heredity was made clear, and much work along this line is continuing at present. In 1861, when Schultze made his great generalization, he emphasized the fact that cells are masses of protoplasm, each containing a special mass of protoplasm — the nucleus. In 1855 it was accepted that new cells could arise only from preceding cells. Cells would not arise *de novo*. Virchow (Fig. 290 *A*) introduced a now famous phrase, "*Omnis cellula a cellula*." Wilson says with regard to the Cell Theory that "No other biological generalization save only the theory of organic evolution has accomplished more for the unification of knowledge."

Aspects of the Cell Doctrine. Thomson says "that the cell doctrine has three aspects: (1) Morphological, *i.e.*, that all plants and animals are composed of cells; (2) Embryological, *i.e.*, every organism begins life as a single cell; (3) Physiological, *i.e.*, the functions of higher organisms are expressible in terms of the activities of their cells." "Each cell," said Schleiden in 1838, "leads a double life, one pertaining to its own development, which is independent, and a second as an integral part of plant or animal." Schwann expressed this idea in these words, "The whole organism subsists only by means of the reciprocal action of the single elementary parts." Virchow, in 1859, said, "Every animal appears as the sum of vital units, each one of which bears with it the characteristics of life." Thomson has put it thus, "These conclusions combine in impressing us with the unity of organic nature, for although a plant cell is often very different from an animal cell, and one animal or vegetable cell may be very different from another in the same or another body, yet the points of agreement in structure, in development and in function are at least as striking as the observable differences, and often more striking."

Vitalism and Mechanism. Protoplasm or cell substance is not merely a mixture of complex materials. Brucke, in 1861, stated, "We must ascribe to living cells, in addition to the molecular structure of organic compounds which they contain, still another and otherwise complicated structure (property or characteristic); and this is what we designate by the term organization." Inseparably connected with the physical and chemical structure of protoplasm is the functioning of protoplasm. Inseparably connected with the societies of cells must be an integrative activity of whole mass as a unit. This organization cannot be dissected; it cannot be seen with the aid of a microscope. It is not material in the ordinary sense of the word. This has led to the development of two general ideas or schools of thought — *Vitalism and Mechanism.* The vitalist says that life is *more* than mere physical and chemical reactions, as claimed by the mechanist, and that we have not yet been able to elucidate what life is. Many mechanists, on the other hand, have a tendency to present explanations of life processes in terms far too simple to unknown complexities. One result, however, of the vitalistic idea is to stifle investigation. The mechanistic position has done more to stimulate research, and many valuable discoveries have, as a consequence, been made.

The truth of the matter probably lies in the *direction* of mechanism. Investigators in physics and chemistry know very well that all the knowledge they possess *today* concerning matter and force is incomplete. Nature is still, to a great extent, *unknown* to them, but they are making new discoveries constantly. The biological mechanist, who confidently asserts that life processes are merely exhibitions of phenomena taking place according to known laws of physics and chemistry, is open to criticism fully as much as the vitalist. The salvation of the mechanist is that he keeps busily at work. When the mechanist arrives at a barrier, he changes the method of attack. Some idea of the nature of chemical and physical explorations in the field of cell physiology is presented in the following section.

FIG. 290 *B*. — Schultze. From Locy, *Biology and Its Makers*. Courtesy of Henry Holt & Co.

PART II — CHEMISTRY AND PHYSICS OF PROTOPLASM

Introduction. Cells are morphological units. They are also protoplasmic organizations of complex compounds in which actions and reactions occur and recur during life. Prior to 1828 it was customary to regard matter as occurring in two forms — inorganic and organic. In the year just referred to, Wöhler was able to *make* urea, a characteristic organic compound. He synthesized it from inorganic compounds. This experiment broke down the barrier separating organic from inorganic chemistry and indicated the chemical relationship of all existing substances. About 1860 Schultze (Fig. 290 *B*) came to the conclusion that the living matter of plants and animals was essentially similar. He arrived at this conclusion from a study of the *appearance* of this substance. An eminent English zoologist, Professor T. H. Huxley (Fig. 290 *C*), in an address in Edinburgh in 1868, referred to protoplasm as the "Physical Basis of Life."

FIG. 290 *C*. — T. H. Huxley.

The chemist has determined that the inorganic world, *i.e.*, lifeless matter, consists of compounds of some ninety chemical elements. Chemical examination of protoplasm reveals the fact that it is composed of a *certain few* of these elements. The living world is but a *phase* of the great world of matter and energy. The astronomer studies the turbulent 'flames' of the sun; the geologist notes continental elevations, the erosion of mountain valleys; the biologist, the germination of a seed, the busy activity of a honey bee or the division of a cell. All are manifestations of matter in motion. The laws of conservation of matter and of energy apply to the whole knowable universe. Moreover, there is no complete discontinuity in the numberless transformations of matter from the simple to the very complex, from the inorganic to the organic, or from the most complicated compounds of protoplasm back to the elements found in it. It is all *one* world.

Physical Appearance. In the description of the morphology of the cell, attention was called to the physical appearance of cell substance — protoplasm. To this may be added that it is translucent and nearly colorless, sticky, viscous, cohesive, heavier than water; jelly-like in some cases, more fluid-like in others.

Chemical Elements in Protoplasm

Chemical analysis reveals the following elements occurring in protoplasm: Carbon, Hydrogen, Oxygen, Nitrogen, Sulphur, Phosphorus, Sodium, Calcium, Potassium, Magnesium, Chlorine, Iron, Manganese, Iodine, Silicon, Copper and at times traces of others. A study of each of these reveals interesting facts.

Carbon. The greater part of protoplasm by weight is carbon. The primary materials of protoplasm are carbon compounds. They are combustible, they unite with oxygen to form carbon dioxide and water and at the same time liberate energy. In the inorganic world carbon combined with oxygen produces carbon dioxide and liberates energy. Carbon dioxide of the atmosphere is utilized by plants in the reorganization of oxidizable carbon compounds.

Hydrogen exists as part of water and other compounds of protoplasm. Hydrogen ions are constantly liberated in protoplasmic activities and tend to effect an acid condition which is as constantly neutralized. The presence of hydrogen ions affects greatly many of the chemical reactions characteristic of living things. In fact, evidences indicate that the transfer of energy in biological oxidations is mediated by hydrogen transfer.

Oxygen has a unique place among all the protoplasmic elements. Oxidation reduction is one of the commonest features of protoplasmic activity; it releases the energy for life processes.

Nitrogen is absolutely essential to protoplasmic formation. It forms 79 per cent of the atmosphere, but is not available to any great extent to the living world. The transfer from the non-living to the living world is by way of nitrates taken from soil water by roots of plants.

The above-named elements are 'the big four' of protoplasmic compounds. But since elements occur in definite chemical compounds, quite characteristic of protoplasm, it is more instructive to study these.

The physiologist, Verworn, advanced the theory that protoplasm was one exceedingly complex but unstable chemical compound of all or most of the above-named elements. He called this gigantic molecule a *biogen*. Sir Michael Foster, however, expressed the prevailing view when he described it as a mixture of molecules, between which temporary combinations or associations are constantly taking place, and as constantly parting company to combine elsewhere and otherwise. "It is a complex whirl, an intricate dance of composition — the renewal of the protoplasm is but the continuance of the dance, its functions and actions the transfer of figures," — *i.e.*, analogous to a dance in which different groupings are made and broken.

The Compounds in Protoplasm

These are (1) water, (2) salts and inorganic elements, (3) proteins, (4) carbohydrates, (5) lipoids and fats, (6) enzymes, (7) hormones, (8) vitamins, (9) gases.

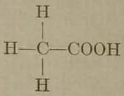
Water. Life probably arose in an aqueous medium. About 70% of protoplasm is water. Mammalian muscle contains about 75%, bone 25% and the jellyfish has been described as animated seawater. Water is the medium in which protoplasmic transformations take place. Extreme dehydration or loss of water usually means death. The other compounds of protoplasm are dissolved in it. Transportation of material to and from the cells of metazoans occurs in aqueous solutions. Solutions carry electrical currents; aid in speeding up chemical reactions; have high specific heat and so absorb and dissipate the heat of chemical reactions that might injure the cell. Dissociation of compounds easily occurs in them. We shall presently describe many physico-chemical processes, necessary to life, that occur in a water medium.

Inorganic Salts. These are usually chlorides, sulfates, carbonates and phosphates of calcium, sodium, potassium and magnesium. The salt solutions of protoplasm resemble those of the sea. They do not occur in the same amounts as in sea water, but the proportions present suggest that the sea water is similar to the salt solutions of living matter. Matthews says, " It has been suggested that it was in some slowly drying volcanic pool, that living matter first appeared." " We are the children of the sun and the sea." Salts enter into combination with compounds presently to be described. They play an active part in the chemistry and physics of the living process.

Proteins. Proteins are complex compounds of carbon, hydrogen, oxygen, and nitrogen, and in some cases also phosphorus and sulphur. They constitute the greater part of protoplasm after dehydration. They are combinations of peculiar elementary compounds known as amino-acids. An amino-acid has been described as containing a central carbon atom with four valences and associated — *first*, with a hydrogen atom; *second*, with a carboxyl group, COOH; *third*, another hydrogen atom; *fourth*, an amino group, NH_2. The latter suggests a relation to ammonia, an inorganic compound. Ammonia is one of the disintegration products of proteins, accomplished by decay bacteria. Ammonia solutions in the soil are eventually changed by bacteria to nitrates which are absorbed by plant roots and made into amino-acids and proteins by plant cells.

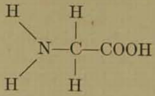
The initial organization of amino-acids and proteins is accomplished chiefly by plants, although animals possess this power to a limited degree. Animals secure their proteins almost entirely from their plant food.

The formula for acetic acid is CH_3COOH. This may be pictured as follows:

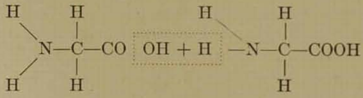


$$\begin{array}{ccc} & \text{H} & \\ & | & \\ \text{H}- & \text{C} & -\text{COOH} \\ & | & \\ & \text{H} & \end{array}$$

By substituting an NH_2 group for one of the H atoms, the result is:



This can be written $NH_2 \cdot CH_2 \cdot COOH$. But this is one of the eighteen or twenty known amino-acids. It is called *glycocoll* or *glycine*. Amino-acids combine to form more complicated compounds called proteins. As depicted in the formula for glycine, an NH_2 group is shown at one side of the carbon atom and opposite it, a carboxyl group, COOH. When amino-acids combine, there is a tendency for an OH part of the carboxyl group of one acid to unite with one of the H atoms of the amino group of another acid to form water, and also for the two acids to combine at that point. In other words, it is a linkage between the carboxyl group of one acid with the amino group of another. A simple illustration of this is shown below; two glycocoll molecules take part in the reaction:



The dotted rectangle shows what takes place. The resulting compound may be written thus: $NH_2 \cdot CH_2 \cdot CO \cdot NH \cdot CH_2 \cdot COOH + H_2O$. This very simple amino-acid may be called *glycine-glycine*. The formula of *alanine*, another amino-acid, is $NH_2 \cdot CH_3 \cdot CH \cdot COOH$; and the formula of *valine* is $CH_3 \cdot CH_3 \cdot CH \cdot CH \cdot NH_2 \cdot COOH$. The amino-acids *known* to play a part in the formation of most proteins occurring in living things are: 1. Glycine; 2. Alanine; 3. Valine; 4. Leucine; 5. Isoleucine; 6. Caprine; 7. Phenylalanine; 8. Tyrosine; 9. Serine; 10. Cystine; 11. Aspartic acid; 12. Glutamic acid; 13. Arginine; 14. Lysine; 15. Histidine; 16. Proline; 17. Oxyproline; 18. Tryptophane. They have been isolated from proteins. Animals feed on highly organized proteins. Enzymes in the digestive tract disintegrate these into simpler compounds, probably amino-acids, which pass into the circulation and thus reach the cells of the various tissues. Within the cell the amino-acids are reorganized into the proteins of that cell. There are *many* kinds of proteins. For example, about one fifth of muscle substance is the protein, myosin; and about ten per cent of the white of egg is egg albumen; casein occurs in milk; gluten in wheat flour; legumen in peas and beans; zein in corn. Proteins have great molecular weight. For example, the molecular weight of egg albumen has been estimated to be 33,800; of gelatin, 123,000; of casein to be 192,000. The molecule is extremely complex. This is faintly indicated by the formula for hemoglobin, said to be $C_{758}H_{1203}N_{195}S_3FeO_{218}$. Amino-acids may combine with acids or bases. Glycocoll combines with hydrochloric acid to form glycocoll hydrochloride or with potassium to form potassium glycocollate. This property is of great moment in vital activities. Some proteins lack certain amino-acids, few contain all. If the food of an animal lacks just one amino-acid which normally takes part in the organization of that animal's protoplasm, then that food is deficient. Ordinary diet is so diverse that it probably contains all the amino-acids *we* need. In times of famine, when food variety is greatly restricted, the deficiency in necessary amino-acids may be as serious as the lack in quantity of food.

The protoplasm of the tissues of different animals, although in many respects similar, differs in details. One might think that the blood of mammals is quite identical in all respects. This is not true, for even a small amount of blood (5 cc.), of one animal introduced into the blood stream of another species of animal acts as a poison to the recipient. Biochemists conclude that there is a vast number of different protein compounds in animals and plants. The possible permutations and combinations of the amino-acids are beyond human comprehension. Proteins are used chiefly for the reconstruction of protoplasm destroyed in cell activity. During the development of an organism, additional protoplasm is needed for the increase in cell population, for the tissues and organs so that an intense production of proteins occurs then.

The presence of NH_2 groups tends toward a basic condition while the COOH group tends toward the acid condition. In living matter there is a constant slight transition back and forth between the slightly acid and the alkaline condition with a tendency toward the slightly alkaline. The peculiar structure of the amino-acids is adapted to the characteristic chemistry of the living process.

Only plants can construct amino-acids and so eventually proteins from inorganic compounds. Animals are dependent upon plants. Plant proteins are made over into the peculiar protein of the particular kind of animal feeding on these plants.

Carbohydrates. These are compounds of carbon, hydrogen and oxygen, in which the last two occur in the same proportions as in water. One of the great basic operations of plant life is the manufacture of carbohydrates from carbon dioxide and water. There are many combinations of the carbohydrates. Three of these will be discussed. The formula of one group is $C_6H_{12}O_6$. But different arrangements of atoms in such a molecule are possible and so there are a number of different compounds having the molecular formula, $C_6H_{12}O_6$, each having its own properties and its own peculiar physiological behavior. One of these types is called glucose and another is fructose. It is said that such a hexose sugar as glucose is the primary fuel used in all protoplasmic activities. It contains potential energy. It was formed in light and the energy of the light is locked up in it. Within the organism, combination with oxygen releases this energy. This type of sugar is in solution in the protoplasm of the cell. When a molecule of glucose and one of fructose are united with the loss of one molecule of water, another type, $C_{12}H_{22}O_{11}$, *cane sugar,* is formed. This is present in varying quantities in plants, particularly in the stem of the sugar cane and in the fleshy root of the sugar beet. When cane sugar is eaten by man, it is *digested* into glucose, $C_6H_{12}O_6$, in which form it circulates to the tissues. Cane sugar solution acts as a poison when injected directly into the blood. Another carbohydrate type of compound is *starch.* Its formula is a *multiple of* $C_6H_{10}O_5$. Common examples are wheat flour, potato, tapioca and corn starch. It is in the form of starch that carbohydrates are stored as reserve fuel supply in plants, to be used in further life processes. Surrounding the embryo in the seed is starch, to be used by the embryo during germination. Animals do not store up any great amount of carbohydrate fuel. Some animal starch or glycogen is temporarily stored in the liver and less in the muscles. It is present in considerable quantity in digestive glands of oysters. The cellulose of plant cells is a carbohydrate compound, not easily digested by most animals, although the goat is an exception to this rule. Gums, such as gum arabic, are also carbohydrate compounds made by plants.

Fats. They are storage compounds, reservoirs of energy, and are present in many plants and animals. They are synthetic products of cell activity. Protoplasm contains *fat-like* compounds called phosphatides. While fat is a compound of carbon, hydrogen and oxygen, as, for example, butter, $C_{51}H_{98}O_6$, the phosphatides consist of fat combined with phosphoric acid and an organic base, a derivative of ammonia. They probably exert an influence on the permeability of the cell membrane, a matter of fundamental importance in cell life. Fats deposited in tissues are derived principally from fats or carbohydrates ingested. There is some indication that part of the protein molecule can be converted into fat. Fat can also be converted by the living organism into sugar. This possibility of transformation is one illustration of the unique property of protoplasm. Fat has twice the heating or energy value of sugar and is burned for this purpose in the body. The diet of Eskimos is almost entirely meat, *i.e.*, proteins and fats. In plants, fat is stored in seeds such as those of the peanut, cocoanut, cotton and flax plant. In animals it is stored in a type of connective tissue called adipose tissue.

Physical Chemistry of Protoplasm

Colloids. Protoplasm is a colloid. The name *colloid* was introduced in 1861 by Graham. It is derived from a Greek word meaning ' glue.' Glue is derived from gelatin and gelatin is a protein and also a colloid. Colloid is not a name for a special chemical compound but for a *state of matter*. If small particles of gold are shaken up in water, they settle to the bottom in a short time. If they are divided into *very small* particles, these will remain suspended for a time, but *may* gradually settle. Such a combination of water and gold is called colloidal gold. Any active portion of the world studied by itself is called a *system*. If it is alike in every part, it is a *homogeneous* system. Gold is a homogeneous system. A system composed of unlike parts is *heterogeneous*. Colloidal gold is a heterogeneous system. A heterogeneous system can be separated into its constituent parts or phases. Colloidal gold has two phases: first, the *continuous* phase, *i.e.*, water; second, distributed throughout this are the fine gold particles, the *dispersed phase*. A colloid is unlike a solution of water and sugar or sodium chloride. In the latter case the solvent, water, separates the sugar or salt into individual *molecules* or *ions* which are evenly distributed through the water. Such a solution is crystalloidal. Crystalloids in solution diffuse through membranes quite easily and can be recovered as crystals from the solvent. In colloidal solutions the dispersed phase consists of fine particles which are multimolecular and small enough to remain suspended but too large to diffuse through membranes.

There are a number of types. In the first place, a *sol* is a colloid in which the particles are *ultramicroscopic* in size and there is a relatively wide range of movement between the dispersed particles, *i.e.*, sols are fluid-like in nature; they have little viscosity. On the other hand, a *gel* is that condition in which there is little range of movement between the dispersed particles; gels are very viscous and form a jelly. Some colloids can change from the sol to the gel state and back again. Gelatin is an example of this. If the temperature is raised, it becomes a *sol*, while if the temperature is lowered, it becomes a *gel*. This is an illustration of a reversible reaction quite characteristic of protein colloids. The contraction and relaxation of muscle is possibly of this nature, *i.e.*, the change from a sol to a gel and the reverse. Mast explains *amoeboid* movement in this way. On the other hand, the clotting of blood is an example of an irreversible reaction, a change from the sol state to a permanent gel state.

Various conditions of sols have been distinguished. First: Suspensions, in which the minute bodies separate out by gravity if allowed to stand. Smoke is an example of this. The dispersed phase consists of minute particles of carbon distributed in air, the continuous phase. Second: Suspensoids in which *ultramicroscopic* bodies are dispersed in a fluid medium. They do *not* settle out. They do not gel and are easily precipitated by salts. Third: Emulsions are sols in which the dispersed phase consists of minute particles of liquid in a liquid continuous phase. The two liquids do not mix. Cream contains minute droplets of oil dispersed in water, while butter is another type of emulsion in which the minute droplets of water are dispersed in butter fat (oil). Fourth: An emulsoid is a sol resembling an emulsion but more viscous and may become semi-solid or even a gel. In the gel state it contains considerable water and will not gel if too much water is present. *Proteins are emulsoid gels.* They dissolve easily and have a great affinity for water. We have already noted how gelatin can be changed from sol to gel, or gel to sol. White of egg (albumen), on the other hand, coagulates on heating, *i.e.*, forms an irreversible gel. Starch forms a gummy paste when heated carefully in water and is then an emulsoid. Suspensoid states grade into the emulsoid states. The alveolar theory of the physical nature of protoplasm developed by Bütschli agrees with the conception that protoplasm is an emulsoid gel. It is perhaps more correct to say that several emulsoids occur in protoplasm in the same aqueous medium. Protoplasm is a polyphase colloidal solution. The same water holds in solution many crystalloids, such as NaCl, KCl, Na_2SO_4, Na_2CO_3, as well as sugars. The phosphatides are emulsoids.

The thousandth part of a micron is called a submicron and is represented by the letters '$\mu\mu$.' A submicron is a millionth of a millimeter. It is possible with the aid of the ultra-microscope to estimate the size of colloidal particles. It is estimated that particles, *i.e.*, molecules or ions, in true solution (crystalloidal) are never larger than 0.1 $\mu\mu$. Colloidal gold particles have a diameter of *about* 1 $\mu\mu$. It is thought that each suspended particle consists of hundreds of gold molecules. In emulsions of oil and water the oil particles are probably about 1000 $\mu\mu$ in diameter.

Brownian Movement. A suspensoid consists of ultramicroscopic particles that bear electric charges of the same sign and hence repel each other in their movements in the solution. This is true also of the dispersed phase of an emulsoid. In 1827, Brown, who later discovered the nucleus in plant cells, saw a movement of microscopical bodies in a suspension. The particles danced around a fixed point, first here, then there. This is known as the *Brownian Movement.* It can be observed under ordinary microscopic magnification in finely powdered carmine rubbed in water. The rate of movement increases with the decrease in size of the particles, and with the increase in temperature. The movements of fine suspensions, seen with the ultramicroscope, are considered to be identical with the " Brownian " movements. It is not ordinarily visible in protoplasm until this is made fluid, from which it has been concluded that protoplasm is usually in the gel state. If the electric charges of the dispersed phase are removed by the introduction of ions having opposite electric charges, then the dispersed particles settle or a gel may form.

Ionization. Some substances called *electrolytes,* dissolved in water, conduct an electric current, — for example, sodium chloride — while others, such as sugar, do not. It has been found that the molecules of substances which *do* conduct the electric current separate when in solution into portions called *ions*. Moreover, ions carry either positive or negative charges of electricity. The positively charged ions are called *cations;* the negatively charged are *anions*. Such solutions are known as *electrolytes*. If electrodes connected with a battery are placed in such a solution, then it is found that the positively charged ions (cations) collect at the cathode (−) and the negatively charged ions (anions) collect at the anode (+). The word *cation* means ' going down ' and *anion*, ' going up.' Not all the molecules of an electrolyte necessarily ionize. But let us illustrate what takes place in the electrolytes found in protoplasm. Hydrochloric acid, if present, forms H^+ (cation) and Cl^- (anion) ions; Sodium chloride, Na^+ and Cl^- ions; H^+ ions are formed if acids are present; OH^- ions when bases occur. Sodium, potassium and calcium salts have Na^+, K^+ and Ca^{++} ions. Ammonium salts have an NH_4^+ ion and nitrates have an NO_3^- ion, sulphates have an SO_4^- ion. It is evident that ions may be more than simple atoms. The degree of dissociation is related to the degree of dilution. If complete dissociation of NaCl took place, the number of particles in solution would be twice the number of molecules of salt added at the beginning of the experiment. Ordinarily dissociation approaches this point but does not reach it. Sugar does not form ions in solution and is therefore an example of a nonelectrolyte. It is now believed that even proteins may ionize — for example, an unattached carboxyl group may give off a positively charged H^+ (cation) while the remainder of the great molecule will bear a negative charge, *i.e.*, act as an anion. Ionization of living matter aids in the formation of an endless variety of combinations and disintegrations so characteristic of cell life. Some investigators say that the electrical charges carried by the ions of salts in solution contribute vital qualities to the colloidal proteins and phosphatides. Every functional activity of cells is accompanied by electrical discharges which indicate that electric phenomena are concerned in cell processes.

Hydrogen-Ion Concentration. Some solutions are acid and others are alkaline. It has been found that acidity is due to an excess of free hydrogen ions, and alkalinity to an excess of hydroxyl (OH) ions. Accurate methods are now available for determining the reaction of fluids. The degree of acidity or alkalinity is expressed in terms of the hydrogen-ion concentration, *i.e.*, designated by the symbol "pH." A pH of 7.0 means a neutral solution. Babor says: "The essential reaction of neutralization is the union of the hydrogen and hydroxyl ions to form water."[1] A number smaller than pH 7, as, for example, pH 5, means an acid condition, while a number greater than pH 7, as, for example, pH 8, means alkalinity. A normal solution of an acid would be pH 0; while a pH of 14.0 would represent a normal solution of an alkali. The range for protoplasm is said to be from 5.5 to 9.5. The fluids of the human body to which the cells are adjusted are slightly alkaline, *i.e.*, pH 7.3^+, and the slightest departure from this 'equilibrium' is of serious moment. pH has an important bearing on the relation of the dissolved salts to proteins and phosphatides.

Cell Membrane. Most cells are separated from each other by, or enclosed in, a *membrane* which holds intact the physico-chemical system within. The cellulose wall of plant cells is *not* their cell membrane. In this case the membrane is the superficial film of protoplasm just within the inner cellulose surface. Substances necessary for intracellular vital processes must pass in and out through the cell membrane so that the physiological importance of the latter is evident. It is composed largely of proteins and phosphatides. It is a film of somewhat condensed protoplasm. The following physical phenomena play a large part in membrane physiology.

Surface Tension, Absorption and Adsorption. Liquids possess a surface property known as surface tension. When some other substance (gas, liquid and solid) comes in contact with a liquid, the movement of its molecules will be restricted and the outer layer will thus acquire a more solid property, producing a surface film. Cell membranes possess the property of surface tension and the latter plays an important part in the *absorption* of water into the cell. It is evident that internal changes in cell protoplasm change the surface tension of the cell membrane and therefore change the amount of absorption of water, for example. This is constantly varying. Excess of hydrogen ions increases the attraction of proteins for water, while salts sometimes have the opposite effect. It is known that water which has a disagreeable odor may be puri-

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[1] For example a combination of solutions of NaOH and HCl becomes neutral when *all* the OH^- and H^+ ions unite to form H_2O. The other ions form NaCl.

fied by passing it through powdered charcoal. In certain cases a dye may be separated from its solute, water, by passing it through such a filter. The dye, methyl violet, is taken up by gelatin. This is not a case of *absorption*. In absorption the substance absorbed permeates the absorbing medium. Absorption occurs in cells. To a certain extent it is a diffusion. The illustrations just given are examples of a different physical phenomenon, namely, *adsorption*. The odoriferous particles in the water or those of the dye are condensed on the surface of the charcoal particles. The methyl violet is *adsorbed* on the surface of the fine particles of the dispersed phase of gelatin. The particles which *adsorb* do so because their surfaces possess unsatisfied free energy due in part to their surface tension properties. It can be seen that colloids are especially well fitted to display this property of adsorption on account of the relatively great surface area of the multitude of ultramicroscopic particles of the dispersed phase. To illustrate: a mass 6 cm. × 6 cm. × 6 cm. has an area of 216 sq. cm.; while if the same mass is separated into cubes 1 cm. × 1 cm. × 1 cm., the total surface area of all the smaller cubes is 1276 sq. cm. If the same mass were divided into millions of fine particles similar to those of a colloidal sol, it is evident that a still greater surface area would be presented. The degree of adsorption depends on the amount of surface presented, because at the surface there is free energy, which is the basis for the adsorption association. It is regarded as a sort of weak chemical union, but not of the usual type in which atoms or groups of atoms unite in definite proportions. Adsorption in a protoplasmic system, because it reduces the free energy, tends to produce a stable equilibrium — but in the living cell, static equilibrium is not attained but is constantly prevented by other forces.

Filtration. This has been described as the process by which a liquid is separated from a solid by passing it through a porous substance called a filter which retains the solid. It has been suggested that elimination of water from blood through the cells which form part of the excretory tubules of a vertebrate kidney is a filtration process. The pressure of the blood takes the place of gravity, which is the usual filtration force in the laboratory. Cell membranes exhibit the properties of a filter.

Diffusion. When certain dyes are added to water, small particles of dye dislodge themselves and move through the water until the entire mass of the dye is evenly distributed. If sugar crystals are added to water the same thing takes place. This process of even distribution of molecules of one substance between the molecules of another is known as diffusion. When substances are absorbed into cells, they also *diffuse* throughout the protoplasm. Nitrates diffuse through the cell membranes of the root-hair cells of plants — a matter of vital importance to plant and animal life.

Dialysis. If we place a quantity of egg albumen, salt and water in a parchment tube and suspend this in a beaker of water and later test the water, we will obtain positive tests for salt but not for albumen. The membrane is permeable to salt but not to albumen. This technic is used in separating proteins (colloids) from inorganic salts (crystalloids) when both are present in the same solution, since proteins as a rule are not diffusible through the parchment used.

The cell membrane exhibits this property of selective permeability, *i.e.*, dialysis, but the cell membrane has a far wider range of permeability properties than lifeless parchment membranes.

Osmotic Pressure. Membranes are known to differ in permeability. Some membranes will not permit dissolved substances to pass through them but will permit water or the solvent to do so. These are called semi-permeable membranes. If we tie a piece of such a membrane over the end of a thistle tube, fill the bowl of the tube with a strong solution of salt or sugar and immerse this in a vessel of water, we will find sometime later that liquid rises in the stem for some distance. Water has passed from the vessel through the membrane into the tube, diluting the solution, but the particles in solution do not pass through in the reverse direction or at most but very little. If we made the rising column of liquid press against a weight, we would have evidence of considerable force. Such a force is known as osmotic pressure. It is the diffusion pressure of dissolved substances. It therefore exists in solution, even though it is not demonstrated as in the illustration. It increases with the concentration and decreases with dilution. Not only molecules but ions present behave as molecules in determining its amount. Therefore it is a measure of molecular concentration although the ionization of the dissolved substance must be considered. A completely ionized substance such as sodium chloride would have twice the osmotic pressure as the same substance in molecular distribution in the solvent. With very strong membranes, columns of water 75 feet high have been raised by osmotic pressure. The movement of water is always toward the more concentrated solution. The osmotic pressure within the cells of the human body is equal to that of a 0.9% NaCl solution. The fluids bathing the cells have about the same osmotic pressure. The two are said to be isotonic. If the blood contains more concentrated salts than those of the cells, then it is said to be hypertonic. If less salts, its osmotic pressure is less and it is said to be hypotonic. If we place red blood cells in a hypotonic solution, the red cell swells and bursts. Endosmosis has occurred. If we place the cell in a hypertonic solution, water diffuses out and the cell shrinks. Exosmosis has occurred. The osmotic pressure of root-hair sap is hypertonic to soil water, hence endosmosis occurs. It is thought that variations in the osmotic equilibrium between the cells and their environment is a normal part of the physiological condition, but that the tendency is always toward an osmotic equilibrium. Cell membranes permit the passage of some substances through but not others. Cell colloids do not pass out through it. The condition of the membrane varies from time to time. Certain aspects of membrane permeability do not appear to be explained by what we know *now* about diffusion, dialysis and osmosis. Most of our present knowledge of these processes has been determined by the use of non-living membranes while the cell membrane is a living colloid. It appears to possess properties of which we know little at present. The great amount of research today as to the nature of the cell membrane indicates that biophysicists regard it as one of the keys to the understanding of vital processes.

Types of Reaction. A review of our study of the formation of proteins from amino-acids and the reverse of the process and also the synthesis of carbohydrates and disintegration of the same, all point to the fact that many kinds of reaction take place within the cell. The most complicated reactions take place with the greatest ease. In this factory everything is orderly. Different processes apparently occur in different parts of the factory at the same time. The physiological chemist has so far been more successful in *analyzing* complex proteins and has thrown light on just how disintegration of complex compounds takes place. He also knows *something* about the *manufacture* or synthesis of proteins from amino-acids and he has actually made them. Although these synthetic products resemble compound proteins, it is felt that they are not identical with natural proteins.

As yet the bio-chemist cannot readily imitate the greatest of all biological reactions — namely, the synthesis of carbohydrate from carbon dioxide and water by the energy of the sunlight in a field of chlorophyll. Balz appears to have succeeded in making sugars in the presence of MgO_2 (present in chlorophyll), but his process requires much more energy than does the natural process.

Among the types of reactions known to take place are:

1. *Hydrolysis:* In this case a molecule of water is added to a molecule of some other substance and then the combination is split into two molecules of some simpler compound. Cane sugar plus water is reduced to glucose and fructose as illustrated in the following equation: $C_{12}H_{22}O_{11} + H_2O = 2(C_6H_{12}O_6)$. This process, involving the taking up of water (*i.e.*, the loss of water), is called hydrolysis. Complex proteins taken in with food are by successive hydrolyses reduced to amino-acids in the intestine, and only these can be absorbed and circulate in the blood. In the day's work within the cell, hydrolysis occurs over and over again.

2. *Dehydration Synthesis:* This is the opposite process. Complex compounds rich in energy are built up from simpler compounds. For example, a molecule of glucose and one of fructose can unite with the liberation of one water molecule, resulting in cane sugar. In the discussion of amino-acids, the formation of glycine-glycine from amino-acids was of the same nature. Many reactions within the organism are of this sort.

3. *Oxidation:* The basic fuel supply or source of energy for the cell is a simple sugar like glucose. When a plant organizes sugar from CO_2 and H_2O, oxygen is liberated and energy stored. To release this energy it is evident that oxygen must again be combined with sugar. Such a combination or combustion by oxidation occurs in cells. Matthews says: "The discovery of the origin of the energy of living protoplasm in the combustion of carbon and hydrogen was one of the greatest and most fundamental discoveries of chemical biology." The pioneer in this work was that "benefactor of humanity," the chemist, Lavoisier, put to death by the proletariat of the French Revolution.

Enzymes. The above processes of hydrolysis, dehydration, synthesis and oxidation would take place very slowly in protoplasm if it were not for the presence of catalysts known as enzymes. Enzymes are organic catalysts, probably protein compounds and colloidal. They hasten chemical reactions in the cell. They act when present in but small quantities; they are not changed by the changes they bring about. Increase in temperature hastens the reaction up to a certain optimum which in warm-blooded animals is about the temperature of the body. If the temperature is increased beyond this, the enzyme is destroyed. Some enzymes are intracellular, some produced by cells are secreted from them and act outside. Pepsin powder sold by the druggist is dried extract of the gastric glands mixed with inert ingredients and yet the enzyme retains its hydrolytic power long after it has been separated from the living tissue. There are many enzymes and many kinds. They are specific, some acting in an acid medium, some in an alkaline medium, some acting on proteins, others on carbohydrates, others on fats. Some enzymes known to be present in the blood are prevented from acting by the presence of *anti-enzymes*. Coagulation of the blood while circulating in the body is prevented by the presence of an anti-enzyme. When bleeding occurs, the anti-enzyme is otherwise engaged, thus freeing the enzyme to initiate coagulation, which, as already stated, is a transition from a sol to an irreversible gel. Cells apparently possess enzymes that would, if allowed to act, disintegrate the compounds of the cell. Anti-enzymes prevent this. At death, the disintegration enzyme is released and the organ undergoes dissolution. This process is known as *autolysis*. The organization of protoplasmic systems carries along agents of dissolution which operate at death, even in the absence of bacteria, and so make possible the nitrogen cycle.

Vitamins and Hormones. Although these substances are described in more detail elsewhere (page 429), yet they should be mentioned here as compounds which somehow are concerned with cell processes. They are products of cell manufacture, and are present in *very small* quantities. So far as we know, vitamins are of plant origin, but are as important for animal life as any other compounds. Animals, however, make hormones. In some cases the hormone is made by one part of the organism to be functional in another part. They have been called chemical messengers, bringing about integration of organ functions so that the entire assemblage of organs can act as an individual. They are an adjunct to the nervous system in this work.

Gases. Oxygen is necessary for cell metabolism. It is absorbed through the cell membrane and plays a part in reactions within the cell. A by-product of oxidation is carbon dioxide, which is excreted.

PART III — CELL PHYSIOLOGY

The structures described in the section on cell morphology, and the compounds and processes presented in the section on the physics and chemistry of protoplasm are concerned in cell physiology. The word *metabolism*, used by physiologists, refers to all the chemical reactions which take place in protoplasm. Metabolism is for convenience divided into two groups of processes, (*a*) *anabolism*, or those synthetic processes by which the complex protoplasmic compounds are built from simpler initial compounds and (*b*) *katabolism*, which refers to processes of analysis or destruction by which complex protoplasmic compounds are broken down into waste products. Both groups are concerned with cell physiology. The irritability of cells must be considered in any discussion of cell physiology.

Cells or *organisms* are going concerns, temporary organizations which maintain for a time a dynamic physico-chemical system in a universe of physico-chemical systems of a different sort. The organic physico-chemical system, be it cell or organism, possesses a property very seldom thought of, but very fundamental, namely, the property of *persistability*.

We noted in our study of protoplasm that within the cell there is a constant tendency toward the establishment of a static equilibrium and that this tendency is constantly checked. The cell is staggering as it were toward death from the moment of its origin. During life reactions are reversible — death comes when they are irreversible. The cell or the organism *tends* to continue its organization. The cell is an energy transformer, and since in maintaining its individuality it gives out energy constantly, it must acquire energy from without. The world acts on it and it reacts on the world. Physiology is therefore an analysis of how such a system is maintained under the conditions present.

Not only is there a general similarity in morphology among the many kinds of cells, but there is also a basic similarity in function; and yet over and above the underlying similarity there occurs specialization in structure and function. The physiologist finds in all the multiplicity of forms of cells in organisms, either simple or complex, unicellular or multicellular but a *few* kinds of physiological processes.

In discussing the physiology of a cell we are confronted with a difficulty due to the fact that in some cases, the organism is but a *single* cell; in other cases a *multicellular* individual consisting of a great many cells of different kinds. Long ago, Schleiden called attention to the fact that any one cell of a multicellular organism carried on a double life — first, activities which concerned itself as an individual entity; second, those activities that had to do with the part it played in the entire organization. It is this complex which renders difficult the discussion of cell physiology.

A single-celled organism such as the Amoeba is a "jack of all trades." It is an independent organism capable of maintaining existence. It performs the following functions: ingestion, secretion, digestion, respiration, circulation and metabolism which includes excretion. It adjusts itself through sensation, conduction and contraction, and it reproduces. And it has a limited control over nature.

On the other hand, the cells of Metazoa, and especially those of higher Metazoa, such as mammals, are specialists. Consideration of the physiology of such cells, involves the distinction between their basic activities common to all and special activities which distinguish one special type from another.

Basic Metabolism. In the first place every cell must be a *going concern*, capable of work necessitated by the fact that it is a system in the midst of other systems. Physiologists now recognize that a distinct part of every cell's life is concerned with its maintenance. This is known as basal metabolism. In basal metabolism a small amount of protein is used up and as constantly replaced. A certain amount of free energy is always present however.

Functional Metabolism. Physiologists have found that *over and above their basal metabolism, specialized cells* exhibit what is known as functional metabolism. Let us consider some of these special jobs.

(*a*) *Sensory cells.* These are said to possess the property of irritability. The protoplasm is in a state of somewhat stable equilibrium which is upset by sudden changes in the external medium. When its equilibrium is thus upset, the cell is said to have been stimulated and the external agent causing this is called a stimulus. Sensory cells in the retina are stimulated by sudden changes in color or intensity of light; the stimulus in the case of the sensory cells of the ear is a succession of sound waves. Such stimuli are physical and others of the same type are (*a*) sudden mechanical contacts with special sensory cells, (*b*) sudden changes of temperature which stimulate special sensory cells, (*c*) sudden changes in strength of electrical current. Stimuli are also chemical, such as the sudden presence of food in an empty stomach or of water or salts, etc.

(*b*) *Nerve cells* (Fig. 319). Adjustment of the organism as a whole may be necessary, involving organs of locomotion. The change brought about in the stimulated sensory cell is communicated to a nerve cell and upsets *its* equilibrium, initiating what is known as a nerve impulse, which is a change propagated over the long process of the nerve cell. The progress of the impulse is the functional metabolism of the nerve cell, which in turn upsets the chemical equilibrium, in a muscle cell, for example. The functional metabolism of a nerve cell is called *conduction.*

(*c*) *Muscle cell.*[1] The change in the muscle cell (Fig. 318) effected by the nerve impulse is evidenced by its functional metabolism, known as a *contraction.* The cell becomes shorter and thicker. The movement of a higher Vertebrate is not accomplished by the contraction of muscles alone, but these are connected with skeletal and other structures, forming a mechanism of moving levers, making locomotion possible.

The sensing, acquiring and ingestion of food requires the cooperation of sensory, nerve and muscle cells and many others also.

(*d*) *Gland cells.* Compound proteins, carbohydrates and fats eaten must be broken down into simpler compounds to be of use in basic and functional metabolism of all cells of the organism. The cells of many glands manufacture enzymes which do the work of *digestion.* The gland cells perform the special work of *secretion.* Digestion does not occur within the cells of metazoans but in tubes formed of cells. It is part of the functional metabolism of cells *lining* the digestive tract to form the container in which digestion takes place and another function is to absorb the digested products.

(*e*) *Cells of Respiratory Membranes.* The functional metabolism

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[1] In higher animals, the histologic unit of skeletal muscle is not a single cell but a multicellular syncytium of cells called a muscle fiber.

of these cells in part is to absorb oxygen and to hand this over to the blood. The functional metabolism of many other cells brings oxygen to the respiratory membranes.

(*f*) *Cells of the transport system.* Foods absorbed from the intestinal cavity and oxygen from the respiratory membranes pass into the *blood.* This is contained in a system of tubes and in many cases propelled by a muscular pump. Heart, arteries, veins and capillaries are composed of a multitude of various kinds of cells whose functional metabolism is the transportation of oxygen, amino-acids, glucose, fats, water, salts, vitamins and hormones throughout the body, *i.e.*, to bring them to *all* the cells of the body.

(*g*) *Cells of the excretory system.* Every cell excretes wastes of basic and functional metabolism. In a higher Vertebrate, such wastes find their way into the transport system. The functional metabolism of some cells, such as those of the kidney and urinary system, are concerned in eliminating some of these wastes from the body.

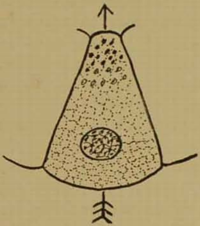

FIG. 291. — Diagram of a pancreas cell. Nucleus is near base. At this end, materials are absorbed. At the narrow end are indicated granules which are discharged as secretion. The arrow indicates *polarity*.

The functioning of secreting, digesting, circulating, respiratory systems furnish materials for basic and functional metabolism of *all cells.* A cell in the pancreas (Fig. 291), for example, secretes *trypsin,* which aids in the preparation of amino-acids which may be used in the metabolism of *that pancreas cell or any other cell.* Functional metabolism results in a greater energy exchange than is needed in basic metabolism. In every cell there is a period when only basic metabolism occurs. This is called its *resting* period. But basic metabolism must continue *during* functional metabolism. During the functional metabolism of a gland cell, the latter is elaborating compounds absorbed, especially protein compounds. During the metabolism of a muscle cell it is chiefly the carbohydrate glycogen that is involved. Very little energy exchange occurs during the metabolism of a nerve cell. Connected with the consideration of the functional metabolism of specialized cells is the significant fact that *the life of the organism as a whole is not the mere sum* *total of the activities of its various cells. Each cell is a part of an organization.* The persistence of the system as a whole depends on the cooperative work of all its units.

(*h*) *Cells of the reproductive system.* The general effect of basic and functional metabolism is the persistence of this community of cells for a longer or shorter period. Both the constituent cells and the organism as a whole possess the property of *persistability.* But it is also a characteristic of unicellular or multicellular organisms that the dynamic system which they constitute has a limited period of existence. And yet the persistability property carries the particular *type* of organization beyond the period of its own individual existence. This remarkable phenomenon is accomplished by a special type of functional metabolism called reproduction. Cell division is an important feature in the development of plants and animals and in fact occurs all through the life period. In plants the power is restricted to the cambium and to formative cells in root tips and buds. In mature higher Vertebrates it occurs in all tissues with few exceptions, as, for example, in the cells of the nervous system. Cell division is so important in embryology and genetics that it will be considered in some detail.

Cell Division. The most intensive period of cell reproduction or division is during embryonic life. Yet it is not limited to this period. The cambium cells of ancient redwood trees are still continuing a process of cell divisions which began in the same trees, thirty centuries or more ago. Indeed, strange as it may seem, the cell divisions constantly taking place in one's own body are continuations of a process which was initiated unknown ages ago, back at the beginning of all life.

Amitosis. In a few cases, such as old tissues, some parasites and Protozoa, the nucleus, *appears* to divide by *simple* fission and this is followed by division of the cytoplasm. Probably most supposed cases of this sort are really of the type to be presently described. Most cells divide by a complicated and *Indirect* method. The former is now called Amitosis and the latter, indirect method, is known as *Mitosis.* Knowledge of this was gained between the years 1873 and 1882. In the latter year, Flemming suggested the name Mitosis for the process.

Mitosis. In mitosis several changes take place simultaneously in the cell. Therefore, a description is difficult. Moreover, the process is continuous, but for convenience of presentation it is divided into four successive phases. 1. *Prophase;* 2. *Metaphase;* 3. *Anaphase;* 4. *Telophase.* The following description is generalized, *i.e.*, it represents what is true of most cells. To understand it, a picture of a cell prior to mitosis, *i.e.*, a *resting cell*, must be studied. In this stage the cell wall is intact, and the nucleus in the interior has a nuclear membrane. A nucleolus may be present. Chromatin granules are clustered about the linin network, forming karyosomes where linin fibers cross each other.

1. *Prophase* (Fig. 292 — P^1–P^4). As mitosis begins the chromatin exhibits a greater affinity for certain dyes, showing that chemical changes are taking place. The chromatin granules assemble themselves to form a long thread, skein or spireme coiled somewhat intricately at first, but less so later on. The Greek word for *thread* is " mitos." In the meantime the nuclear wall and the nucleolus are disappearing. The centrosome outside the nucleus divides and each of these centrosomes moves away from the other. Around each centrosome appear radiating lines which form an aster (star). As the centrosomes diverge more or less slightly, fibers appear between them. The two centrosomes move away and down and around, each 90° from their starting place, so that they come to rest at opposite sides of the cell, 180° apart. An axis passing through them is at right angles to a plane which would pass through the original centrosome and through the center of the nucleus. The lines from the asters now extend in all directions out toward the cell wall. " Spindle " fibers extend across the cell between the two centrosomes. Spindle and asters are known

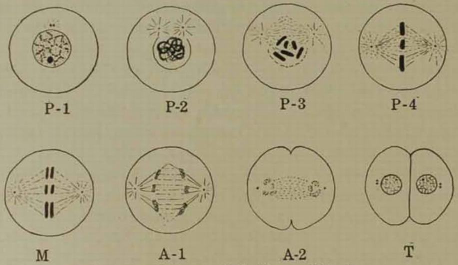

Fig. 292. — Indirect cell division or Mitosis.

as the *amphiaster*, or *achromatic* figure. What are these lines? Are they actual fibers or are they lines of force which have gathered protoplasmic granules along their course? The later behavior indicates that such physical properties as elasticity or tension are present. These spindle fibers penetrate in among the coils of the spireme. The *spireme* (chromatin thread) has divided into a number of pieces called *chromosomes* — the number being quite definite for each form of life. Thus in Hydra there are 12; in Lumbricus, 32; in Cambarus, 200; Anopheles, 6; in Drosophila, 8; Musca, 12; Rana, 26; Columba, 16; Equus, 60; Macacus, 48; Man, 48; Spirogyra, 24; Fucus, 64; Pinus, 24; Pisum, 14; Primrose, 36; Zea mays, 20; Allium, 16; Lilium, 24. Possession of a similar number of chromosomes does not mean genetic relationship because some plants and animals have the same number.

2. *Metaphase* (Fig. 292 — *M*). The chromosomes have moved into the equatorial plane which is at right angles to the axis joining the two centrosomes. This plane is that described above as passing through the original centrosome. Some of the fibers appear to be attached to the chromosomes. The chromosomes split longitudinally, each forming a pair. Careful examination indicates that *each chromosome* is *exactly halved.*

3. *Anaphase* (Fig. 292 — A^1–A^2). The members of each pair move away from each other and toward the nearest centrosome. The function of the anaphase is to provide each *daughter* cell with the same number of chromosomes possessed by the *mother* cell. Late in the anaphase a groove appears in the cell membrane where the equatorial plane coincides with it. In plant cells small granules appear on the spindle fibers just where this plane passes through them.

4. *Telophase* (Fig. 292 — *T*). This is the reconstruction of two new daughter nuclei and cells. The chromosome groups on each side pass over to their respective centrosomes, and then the spindle and aster fibers and chromosomes begin to disintegrate. The groove in the cytoplasm deepens and two daughter masses of cytoplasm are formed, each with its own cell wall. A new nuclear wall is formed in each and inside is nucleoplasm, linin network, chromioles and a reformed nucleolus. By this time the centrosomes in each may divide in preparation for the next division and then fade away to reappear when each daughter cell is about to

divide again. In the active cell division period of embryonic life, cells sometimes divide so rapidly for a time that they have no time to grow. That is, after repeated cell divisions of the fertilized egg, the embryo consists of hundreds of cells, each but a small part of the original size of the egg. There are many variations in the details of the process. For example, in higher plants there are no centrosomes; in some cells the formation of a spireme is omitted. In plant cells there is no constriction by cleavage of the cell wall when in the telophase, because the cell wall is of cellulose. A cellulose wall is built up in the equatorial plane, but it should be remembered that this new cellulose is not hard and rigid, but soft and fibrous.

What is the meaning of this complicated process? Apparently it is a most particular kind of division and the answer to the question seems to be that by mitosis *each daughter cell is insured an equal equipment of chromatin, the exact counterpart of that of the mother cell.* The bearing of this on heredity will be made plain later. What are the causes of cell divison? It has been found that reduction of the surface tension by chemical means causes certain eggs to divide; that the viscosity of the dividing cells increases up through the prophase and then decreases; also that the rate of oxidation increases and then decreases and that changes in electrical potential occur. But these are mere statements of observed physical and chemical changes which occur and which staining technique long before indicated. At present the causes of mitosis are not known.

Growth Metabolism. When a single cell divides into daughter cells, the latter are each half the size of the parent cell. Normally, they grow to the mature size. In the formation of spores, growth does not immediately take place, for the period of successive cell divisions results in smaller and smaller cells until the spore type is produced. In early cleavage stages of zygotes, the period is characterized by the production of smaller and smaller cells. But in *many* cases, cell division is followed by growth. This involves not only basic metabolism but also the formation of *more* protoplasm, hence the name growth metabolism. The energy stored is in excess of the energy dissipated. Growth metabolism is a distinct feature of development since development involves an ever greater increase in cell numbers. Growth involves increase in size, the formation of more cells, greater amounts of intercellular substances, more protoplasm. It also involves the differentiation from the somewhat spherical type of embryonic cell to all the cell varieties of the adult. Growth involves also the elaboration of an independent organization as development reaches it climax. During maturity, it has been found that the amount of nitrogenous compounds needed for basic metabolism averages about the same from day to day. The excess needed in functional metabolism is not so great as one might expect. But growth metabolism does demand an excess. In other words, the growing child needs actually more nitrogenous compounds than a grown person. It is from this material that the new cells are fashioned.

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