SPECIAL ARTICLES

SOME PHYSICOCHEMICAL ASPECTS OF LIFE, MUTATION AND EVOLUTION[1]

THE conversion of non-living matter into living matter by growth and reproduction is generally considered one of the least comprehensible of natural phenomena. An attempt is made here to translate the mechanism of life into terms of better known and more readily grasped physicochemical concepts.

The chemist and physicist, starting with atoms and electrons, have been working upward into larger units, the molecules, and still larger units, the molecular groups, while biologists have been steadily working downward to smaller and still smaller hereditary units in the cell. These two groups of investigators have been approaching each other from opposite directions. It is no simple task to make a perfect joining of the two pathways.

Many of the difficulties arise from the fact that attention is not focused upon vital units sufficiently simple in their nature to be comprehended in both structure and behavior. Even the smallest cell or unicellular being is an exceedingly complicated structure. If we would form a precise mechanical picture of what occurs in life, we must dissect down through the layered structure of its matter, until we reach the simplest unit which can be regarded as living. The tiny ultimate vital units, from their ultramicroscopic domain, direct and dominate the material changes of life.

The principal *physical* units or groupings recognized at present in dealing with phenomena are shown in the table. Opposite each unit or group, is set, for convenient comparison, the biological unit of approximately corresponding order of size, though perhaps of greater order of complexity.

TABLE

Physical Units	Approximate Diameters	Biological Units
Electron positive	2×10^{-8} Å	
Electron negative	3.8×10^{-5} Å	
Atomic nucleus H	2×10^{-8} Å	
Atomic nucleus Au	4×10^{-7} Å	
Atoms	0.1–0.6 mμ	
Molecules	0.2–5 mμ	Moleculobiont (Hypothetical simplest life)
Molecular groups	0.5–10 mμ	
Primary colloidal particle	2–20 mμ	
Secondary colloidal particle	5–100 mμ	20–70 mμ Gene (*D. melanogaster*) 50 ± mμ Bacteriophage 2 ± μ Coccus
Microscropically visible particle	over 100 mμ	0.2–3.5 μ Chromosome (*D. melanogaster*) 5–15 μ Nucleus (*D. melanogaster*) 7–25 μ Cell (*D. melanogaster*)
Visible particle	over 50 μ	
Mass	over 1 mm	2.5 mm *Drosophila melanogaster*
Planet (Earth)	1.3×10^{4} km	Equivalents
Solar system	5×10^{9} km	1 Å $= 1 \times 10^{-7}$ mm
Star cluster	5×10^{3} lt. yr.	1 mμ $= 1 \times 10^{-6}$ mm
Galaxy	5×10^{4} lt. yr.	1 μ $= 1 \times 10^{-3}$ mm
Einsteinian universe	2×10^{9} lt. yr.	1 lt. yr. $= 9.4627 \times 10^{12}$ km

With the geneticists, cytologists and other biologists here assembled, there is no need to review the nature of chromosomes and genes, and their behavior in the mechanism of mitosis. All agree that in the normal reproduction cycle of the cell, each chromosome doubles its mass and divides into two equal parts, and each part enters one of the two daughter cells. The genetic evidence indicates that the chromosomes, which themselves bulk quite small in a microscopic field, are composed of very large numbers of particulate subunits, the genes. Calculations of the size of genes have shown that they must be of the order of very large organic molecules or of small organic molecular groups. Further, the evidence (especially from linkage and crossing-over) indicates that each of these chromosomal subunits actually reproduces itself *next* to itself. Genic reproduction is self-duplication *in situ.*

Since the addition, removal or modification of these subunits, the genes, produces marked and characteristic changes in the cell and in what develops from it, we are justified in regarding them as specific catalytic particles which direct chemical changes within their respective domains, and thus dominate developmental and life processes. It is the genes, within the gene-strings or chromosomes, which deter-

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mine whether a certain cell will develop into a flea, an elephant or a man.

To epitomize the biological evidence, the genes are particles, of molecular order, which locally duplicate themselves from what is admittedly non-living matter, and which control and direct the material changes of development and life. Can we interpret such behavior in the light of our present chemical and physical knowledge? It seems to us that this can be done through the idea of catalytic synthesis.

Before considering the modern view of catalysis, let us first review some consequences of the structure of matter which make catalysis possible and specific. When electrons and protons combine to form atoms, when atoms combine to form molecules and when molecules combine to form larger groups, there are always left over some outwardly directed, unsatisfied fields of force. The residual forces of molecules exert powerful attractions or repulsions on particles which come within the range of attraction.

If we consider a single molecule, or a very small molecular group, A, it is obvious that the residual electrostatic or electromagnetic surface forces present to the milieu a mosaic which is highly specific in various directions. In Fig. 1 the specific nature of the surface of A is shown very diagrammatically by the convention of specific jaggedness in the outline. In consequence of its mosaic pattern, a particle may exhibit several different kinds of specific actions separately or simultaneously, on different portions of its periphery.

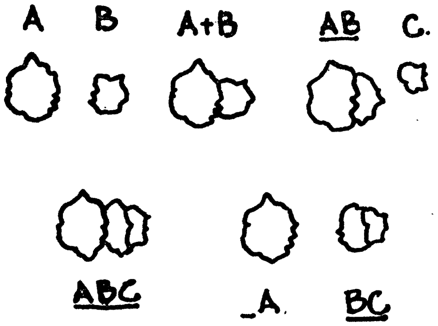

FIG. 1

Let us now imagine a simple molecule, B, approaching A, and the process of fixing itself at the surface. This will occur only if the surface charges presented by the approaching molecule bear a lock-and-key relation to those of the particle, and if the velocity of approach lies within critical limits.

As soon as the oppositely charged areas come within their critical distance, fixation occurs, as is diagramed $A+B$. Instantaneously thereafter occurs a mutual neutralization of forces and a complete reshuffling of all the internal and surface fields. The compound molecule, after the fixation, will present to the milieu a different configuration from what it presented before fixation. This is diagramed as AB. The former B portion might now be able to make other attachments previously not possible to it. The attachment of a second molecule, C, would once more cause a reshuffling of all the fields involved, as is diagramed ABC. Now, if the resulting bond between the two added molecules were stronger than the bond between the former A and B portions, then there might be released to the milieu a new type of duplex molecule, BC, while the fixation surface of A would be freed for renewed action.

Suppose now that we have a catalyst particle composed of several simple molecular subunits which we can diagram roughly as A in Fig. 2. Suppose that at some one of its faces the catalyst fixes or adsorbs the several subunits of which it is composed; that, because of the order of their fixation or because of the reshuffling of electronic fields which follows each addition, these component subunits form a new group identical with the fixation or catalyst group, and suppose, lastly, that the duplicate particles now separate or are separated. Each would be an exact duplicate of the other in catalytic and in self-duplicating behavior. Our original particle could properly be called an *autocatalytic catalyst.*

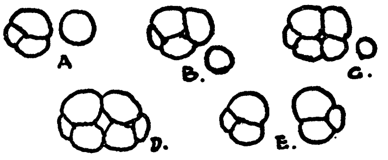

FIG. 2

As an example of a simple and well-known chemical process, analogous in a rudimentary way to the autocatalytic synthesis postulated above, one may mention the formation of crystals of the alums. If to pure cold water is added the salt potassium sulphate and the salt aluminium sulphate, a solution strongly supersaturated for the potential double salt, alum, may be obtained. But, in the absence of a fragment of a previously formed crystal of alum the supersaturated solution remains practically indefinitely without giving rise to alum crystals. However, if a tiny fragment of alum crystal is dropped in, or was present in the materials used, at its surface occurs an adsorption of the two separate salts together with a definite number of water units, the whole addition condensing into a very specific space lattice with repetitions of the unitary alum complex. Mechanical, or even thermal, agitation may break the bonds between the newly formed alum complexes and the parental crystal, so that a host of descendants may grow and reproduce in the nutrient solution.

We do not contend that an alum crystal constitutes simple life, although there may be some who would do so. In vital units the building stones of the finer structure are not potassium, aluminium and sulphanion, but are carbon, nitrogen, phosphorus, etc., which are united in a unit complex which is far more voluminous and involved than alum is. Besides this difference in constituents, or more probably because of it, the units properly called vital are more flexible in their bonding and more diversified in the activities carried on at the catalytic surfaces.

The simplest living units of which we have indisputable evidence are the genes. The forces governing the reproduction of each gene are known to be *within* the individual gene. In evidence of this we need cite here only the well-known fact that in a heterozygote, each gene of the allelomorphic pair picks out of the common milieu exactly those constituents which lead to its own particular formation. Furthermore, this specific formation occurs nowhere else in the cell except precisely at the locus occupied by each particular allelomorph. All these properties conform to our postulated autocatalytic reproduction.

We would like to point out one more property of genes which has its analogue in a rudimentary way in the alum crystal. The growth rates of the genes of a given cell are remarkable in their uniformity. This holds true not only for a given temperature but throughout the great range of temperatures to which some organisms are adapted. If a particular gene did not keep step with the others it would either overreproduce or else fail to reproduce in time to be included in the daughter cells with the other genes.

Not simply this uniformity in temperature characteristics, but a considerable number of other properties, for example, the universal synthesis of the substance called chromatin, which envelops the genes or the string of genes, and the remarkable similarity in chemical constitution of nuclear materials as revealed by the exceedingly crude methods of chemical analysis now available, all point to one striking conclusion. This conclusion is that the genes may all be viewed as simple variants of one fundamental structure. We may suppose that their power of autocatalytic synthesis is the outcome of the possession of a common pattern of structure, and that the different allelomorphs, or indeed the different genes in a given cell or even the different genes in apparently very widely separated forms, are the same except for differences in the fringe of the gene, in its side chains and in localized additions or substitutions.

To return to our oversimplified analogy in the alum crystal: it is remarkable that alum crystals retain their specific structure through a host of substitutions of materials, or "mutations." Thus, rubidium, caesium and even ammonium can be substituted for the potassium; iron, manganese, etc., can be utilized instead of the aluminium; selanion (SeO_4), etc., instead of the sulphanion. The most essential characteristic of an alum crystal seems to be the particular strain set up in the local ether when alum crystals originated. It is the *structure,* the particular space-lattice present, that matters, and the points in that lattice can be taken by any materials whose outwardly directed fields of force are flexible enough to adapt themselves to the particular "set" that is in the local ether.

Although the gene is the simplest vital unit definitely known, it is possible that in some cases the gene is itself an aggregate of simpler autocatalytic units which have been called "gene elements," or "genels." The hypothetical lower limit of vital units is in the molecular order, for nothing simpler than a molecule, for example an atom, depends for its *increase* in numbers upon forces contained only within the unit itself.

The question arises: is there in nature any free-living unit of the grade of organization and properties of the gene? It has been suggested that in the bacteriophage and similar ultrafilterables we are dealing with living beings (bionts) which either are actually of this degree of simplicity or approach it closely.

Considering briefly the bearing of these ideas on the origin of life—a very speculative endeavor—it would seem that no biont as complex in its order of aggregation as a cell, or even a bacterium, could have been an initial form of life. The structure of a cell is a box-within-box series of units, of successively simpler orders of aggregation, and it seems reasonable to suppose that the simplest of these units was the first to appear in evolution. Life began, then, in the molecular order of complexity with an autocatalytic molecule of definite structure and less definite constituents. We will make no further comment on the sequence of evolutionary steps, although we have done so in a paper that has just appeared in the second volume of "Colloidal Chemistry, Theoretical and Applied,"[2] to which those interested may be referred.

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[2] Edited by J. Alexander, The Chemical Catalog Co., 1928.