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A NOTE ON BIOTOPOLOGY OF REPRODUCTION.

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In a recent paper (*Bull. Math. Biophysics*, 20, 245, 1958), Robert Rosen applied topological considerations to the study of an organism as a whole. Those considerations have no direct relation to the principle of biotopological mapping. They rather represent a topological model of an organism, especially a model of the repair mechanisms which organisms possess for lost or impaired parts. In this note it is shown that the model introduced by Rosen may possibly be derived from the principle of biotopological mapping plus a proper definition of the primordial. Such a derivation may also provide a clue to a proper biotopological approach to the problem of multiplication of organisms.

In an interesting paper, published in this issue of the *Bulletin*, Robert Rosen (1958) outlined a novel topological approach to the theory of the organism. He defines the so-called (M, R)-systems in which certain components, the R-components, play the role of repair mechanisms for the other components, the M-components. Rosen proves a number of important theorems about such systems. Familiarity with his work is presupposed for the understanding of the following argument.

A somewhat weak point of Rosen's theory is the question as to what happens when an R_i-component is destroyed. Does it become re-established and if so, how? Or are the R_i-components not re-establishable? In the latter case we have a biologically somewhat unlikely situation. Catabolic processes must take place also in the R_i-components. Therefore after a while those components will cease to exist and the M_i-components will become not re-establishable. On the other hand, if for some reason or other the life span of the R_i-components is much greater than that of the M_i-components, in other words if they decay much more slowly, then the above situation may not appear to be quite so unlikely. We may perhaps associate some phenomena of aging with the decay of the R_i-components, inasmuch as it is known that with age the self-repairing ability of an organism in general decreases.

However, it would seem decidedly desirable to investigate different possibilities, namely, such where a re-establishment of the R_i-components takes place. The most interesting of such possibilities is to consider that some M_k system or several of them may play the role of R-systems with respect to some R_i-systems. This will impose certain conditions on the whole (M, R)-system, and the study of the resulting possibilities is likely to offer a fertile field for biotopological investigations.

Another possibility, which is probably the simplest one, is to assume that an R_i-component, if destroyed, becomes re-established automatically as long as the corresponding set θ_i of environmental outputs of M remains intact.

Regardless of the above, a very interesting aspect of Rosen's (M, R)-systems is that they may offer a clue to a possible biotopological treatment of the problem of reproduction. Hitherto in all our previous publications we considered reproduction just as another basic biological property, on par with any other property P_i. Yet somehow this seems to be inadequate, because reproduction seems to occupy a central position among the other properties. Reproduction causes the spread of life on earth, and all other biological activities of the organism seem to converge towards that result.

The theory of the (M, R)-systems has no connection with the principle of biotopological mapping. It is basically a topological *model* of the organism. Inasmuch as our aim is to discover fundamental general principles in biology, we should attempt to reduce any models, topological or otherwise, to the general principles. We shall now *very tentatively* suggest a possibility of deriving the (M, R)-systems from the principle of biotopological mapping combined with a proper *definition* of the primordial.

We already indicated (Rashevsky, 1958a) that the primordial organism may not be an actually existing one. We may go now a step further and say that the primordial need not be even an organism that ever existed. For our purposes it may perfectly well be an abstraction, defined as the smallest set of basic properties which still would be considered as an organism. According to a previous paper (Rashevsky, 1958a) a basic property P_i is the logically most inclusive set of all subproperties $P_{i\alpha}$. If we apply this point of view, then we can considerably reduce the cardinal number of the set of basic properties of a primordial. Essentially, as we already remarked elsewhere (Rashevsky, 1955, 1956b), the many properties of an organism are logically different aspects of *selection*. An organism, through its sense organs, selects the proper location and proper character of its food. Through either *molar* (Rashevsky, 1958a) or *molecular* movements P_M it continues the selection of the proper food. The digestive enzymes act *selectively* on certain substances and break them down in a *selective* manner. Thus the idea is naturally suggested to consider all the above-mentioned basic properties as subproperties of the more inclusive property P_{sel} of selection. Some of the subproperties and therefore P_{sel} itself would be inputs into the primordial, some—outputs. The next set of properties all deal with metabolic activities and may perhaps be all considered as subproperties of another basic property P_T which can be denoted as *transformation*. This transformation includes both production of enzymes and of waste products, and the proper arrangement of the selected molecules, obtained as a result of the operation of property P_{sel}, into a new organism. In line with Robert Rosen's views (1958), we shall consider the property P_T neither as input nor as output, but as a mapping of outputs on inputs, or as relations between inputs and outputs.

In line with this view the simplest organism recognizable as such would consist of two components. One, M, will have as outputs certain enzymes or enzymatic properties connected with the organism directly (if the organism consists of only one molecule). The effect of this output would be to produce by selection from the fragments of food, a set of molecules which can be used as building stones for the organism. The second component, R, would take those in as inputs and produce as output through synthetic processes a new organism.

The graph representing such an organism would be a simple open-branched structure with an additional environmental input into M and an output from M, as shown in Figure 1.

We may remark that a virus molecule is not too dissimilar from the above scheme. The virus must either act directly as lytic agent on the cytoplasm of the host or send off small catalytic particles to do that. Its selectivity is well known. Once the building stones are obtained by lysis, the replication mechanism, presumably DNA, produces other virus molecules.

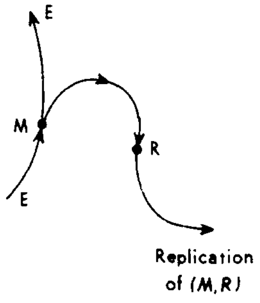

FIGURE 1

If we now apply either transformation rule A of the preceding paper (Rashevsky, 1958a) in its generalized form (Rashevsky, 1958b) or the rules $T^{(u)}$ ($u = 1, \ldots, 14$) discussed still earlier (Rashevsky, 1956b) to the primordial which we just suggested, we can obtain very complex structures. Formally the above transformation rules can be applied to an (**M**, **R**)-system, for it does not make any difference topologically whether the points represent biological properties or components. Instead of one output of M in the primordial, there will be now a number of "suboutputs," in which different components M_i will be specialized. The same holds about R. In effect we obtain an (**M**, **R**)-system.

Such an (**M**, **R**)-system differs, however, from the one introduced by Rosen, and discussed above, in one very essential feature: The components M_i are not merely repaired, but they multiply. There is, however, a close relation between repair of parts of an organism and the multiplication of its constituent cells. Multiplication does not occur, however, unless repair is needed. An explanation of this situation may lie in an assumption which we already made elsewhere (Rashevsky, 1948, Chapter XVIII) and which is almost inescapable, if we are to account for the cessation of growth of the whole organism after a certain time and yet understand the potentially unlimited cell multiplication which will go on in an excised piece of tissue of such an organism if the tissue is placed in a proper medium. We must assume that the different cells of an organism exert some kind of mutual inhibition on each other and that when the number of cells in the organ reaches a certain limit the inhibition becomes complete. The situation is *formally* not unlike that of mutually inhibiting neurons. When there are too many of them, the inhibition is complete.

With such an assumption, which may possibly eventually become a general principle, the (M, R)-system, obtained by a biotopological transformation from a proper primordial will behave just as discussed by R. Rosen (1958).

We now run, however, into another difficulty. The primordial reproduces itself, but the (M, R)-system obtained from it by a biotopological transformation only repairs its parts.

The solution of this difficulty is likely to lie in an extension or sharpening of the principle of biotopological mapping, to which we already alluded (Rashevsky, 1954). A complex higher organism is not obtained from a simple one by a single transformation but through a series of steps. The rule A of the previous paper (Rashevsky, 1958a) and the rules $T^{(u)}$ $(u = 1, \ldots, 14)$ presented elsewhere (Rashevsky, 1956b) give us the end result of the transformation. They do not tell anything about the steps in which it proceeds and which correspond to the steps of both phylogenetic and ontogenetic development. In *ontogenesis* an organism does not develop from a primordial but from an already rather complex, though unicellular, organism, the ovum. This does not contradict the principle of biotopological mapping, because if a simpler and a more complex organism both map continuously onto a primordial, then the more complex will map onto the simpler one. Hence we can introduce into the topological space or graph of an organism a subspace or partial graph, O, which represents the ovum, and from which the whole organism develops in successive steps. In terms of the (M, R)-system, O would be a subsystem. If we now assume that the subsystem O is the only one that is not inhibited, then all other components and subsystems will merely be re-established, while O will from time to time multiply and reproduce the whole organism.

As to the steps of the transformation from the representative space S_p of a primordial to the representative space S_0 of a complex organism, the most natural and simple thing to consider is that at first the more inclusive subproperties $P_{i\alpha}$ develop and later the less inclusive ones. Thus if $P_{i\alpha'} \subset P_{i\alpha}$, then $P_{i\alpha}$ will develop first. Since (Rashevsky, 1958a) any choice of $P_{i\alpha}$'s is permissible, *several* different situations are possible. We may have a series of organisms of increasing complexity, such that the set S_{i+k} of all subproperties of the more complex one includes the set S_i of the less complex one, thus $S_i \subset S_{i+k}$. Such a linear arrangement will, however, be a rather special one. More generally we shall find that for two organisms, i and k, of either the same or of different complexities

$$S_i \cap S_k \neq \emptyset; \qquad S_i \cup S_k \neq S_i; \qquad S_i \cup S_k \neq S_k; \tag{1}$$

which means that S_i and S_k have elements in common but neither is included in the other. The point at which the above relation holds may be reached at a certain degree of complexity prior to which the consecutive S_i's are included in each subsequent one. With increasing complexity, the cardinal number of the intersection $S_i \cap S_k$ may become smaller, and finally S_i and S_k may even become disjoined. They will both contain subproperties of the same basic properties P_i, but different subproperties.

A development of this type is not representable by a linear series or by a line. It corresponds to a branched tree, just as is the case in actual evolution.

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