SOME CONSIDERATIONS ON MATHEMATICAL MOLECULAR BIOPHYSICS

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The possibility of a single molecule or of a few molecules controlling the basic metabolic reactions in a cell is discussed from the molecular-kinetic point of view. For such a control by a single molecule to be possible, it is necessary to assume a chain reaction, consisting of at least two steps.

Hitherto the development of mathematical biophysics has been based almost exclusively on "macroscopic" concepts of classical physics. Diffusion phenomena, plastic deformations, and other phenomena important for mathematical biophysics, are treated from the point of view of a continuum. Different metabolic reactions are considered as given, and although definite assumptions are made and studied about the interrelations of such reactions, nevertheless these assumptions are of such a nature as not to involve any molecular or atomic considerations.

It is very significant that even with this limitation to the domain of the classical physics of the continuum, mathematical biophysics has made considerable progress in quantitatively describing a large array of biological phenomena. Nevertheless it has been clear from the very beginning of mathematical biophysics, that eventually an extension into the domain of molecular or atomic physics will have to be made (Rashevsky, 1934). Even long before the development of mathematical biophysics proper, a number of biological observations have been pointing to the importance for biology of atomic physics, and have turned the attention of noted quantum physicists to biological phenomena (Jordan, 1939). Observations on the killing of unicellular organisms by different radiations indicate that sometimes a single X-ray quantum, or a single α-particle hitting a cell are capable of causing its death. Although for a biologist even a large cell is still a "microscopic" object, from the point of view of molecular physics an average cell is decidedly "matter in bulk", and at first sight it might look puzzling as to how a single molecule coming from outside can totally upset a mechanism composed of some $10^{14}$ other molecules, a
mechanism known to follow in many respects the laws of the physics of the continuum.

Another set of biological facts, falling into a similar category is supplied by observations on the extreme sensitivity of some sense organs, particularly that of smell. The number of molecules leaving some solid aromatic substances is very small in itself. If we consider the amazing sensitivity of the sense of smell of some animals, we may wonder whether only a few molecules may not be responsible here for setting into operation a complex macroscopic mechanism of sensation.

A still different field of biology leading us to the same questions is the study of some vitamins and hormones. Even now in many cases biological tests are the only ones that are sensitive enough to reveal the presence of those substances, the most refined physicochemical methods still failing. The more or less tacit assumption is frequently made, that surface action may account for the strong activities of small quantities of such substances, a very small volume concentration being sufficient to form monomolecular surface layers, which affect the surface properties of cells. In some cases however, a simple calculation shows that the concentrations of the active substances are so small, as to be quite insufficient to cover any appreciable area of a cell surface.

Phenomena of immunization, sensitization and allergy also raise questions of the same kind.

It is therefore indicated to investigate first in its general aspects the problem of how such effects may be brought about, and to ask ourselves whether such phenomena do present any particular difficulties from the point of view of molecular kinetics.

The problem consists of two parts. First there is the question of the atomic mechanism of catalytic interactions. To this field some contributions have already been made by quantum mechanics, and important further progress is undoubtedly still to come. Second — there is the purely kinetic problem, as to the conditions permitting the above mentioned atomic mechanism to come into action. In order for a molecule A to affect catalytically other molecules $B_1, B_2 \ldots$ etc., it is necessary that a relatively close contact between the molecule A and the molecules $B_1, B_2 \ldots$ etc. should be established for at least a short time. All atomic forces, decrease very rapidly with increasing distance, and any distant actions are out of question.

Consider, for the sake of definiteness, a reaction in which a molecule $B$ breaks up into molecules $C$ and $D$. Let the rate of breakdown of $B$ be $q \text{ gm} \cdot \text{cm}^{-3} \text{ sec}^{-1}$. Denoting the molecular weight of $B$ by $M$, Avogadro's number by $N$ and the volume of the cell by $V$, we find that