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Origin of Life by Structural Fluctuation of Molecules : Generation of Metabolic Systems Induced by the Stochastic Nature of Polypeptides

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Summary——The first step for origin of life from matter is to generate irreversible systems to supply molecules and energy in primordial sea. The generation mechanisms of such metabolic systems are proposed based on the stochastic nature of various polypeptides in water.

Mechanism of enzymatic reactions and substrate induced generation of primitive enzymes are proposed based on the same stochastic processes.

Key Words: Metabolic System, Liposome, Stochastic Process, Origin of Life

Abstract

Life is a complex system composed of several functions, and the origin of life should be investigated on the generation of systems rather than the generation of specific biopolymers. The most essential system of life is the metabolic systems which supply molecules and energy necessary to keep and reproduce the whole life systems. The question is how to make such irreversible systems from the almost equilibrium primordial sea. To solve the question, a biophysical approach is proposed based on the stochastic structure of polypeptides or proteins and liposome like structures in water without any biological properties or functions.

Substrates induced generation of enzymes is favorable for the initial generation step of metabolic systems.

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1. Stochastic nature of protein structures and their fluctuations

Main frames of most proteins, especially enzymes, are composed of several α-helices or β-form structures cooperatively generated by many hydrogen bonds. Furthermore, the overall structures of proteins are supported by several kinds of weak secondary bonds like hydrogen bonds and hydrophobic bonds between side chains.

However, α-helical structures of poly-L-glutamic acid and that of copolymers of L-glutamic acid and L-alanine studied by deuterium-hydrogen exchange experiments, indicate that α-helical structures of polypeptides are not stable but fluctuate randomly at various environmental conditions. Similar stochastic nature of lysozyme structure ware observed by deuterium-hydrogen exchange experiments at various environmental conditions[1].

To discuss the stability and change of these stochastic structures of proteins in aqueous solution, the simple statistical thermodynamic model was proposed based on the equivalent and uniform lattice structure[2]. The model include 4 molecular parameters, total number of lattice points N_0, entropy of chain α increased by the loss of a bond in a lattice point, the equivalent bond energy ε irrespective of their positions or species. Similarly, the equivalent energy loss J is assumed for any two nearest neighbor bonds that are in different states. The equivalent entropy of chains α is produced when every bond breaks.

To estimate the values of these 4 molecular parameters, least square analysis was applied[3] to the sharp heat absorption or specific heat measured by Tsong[4] and Privalov[5] for typical globular proteins or enzymes (molecular weight 13600~25200).

These results suggest that most of the energy needed for enzymatic reactions are supplied from the conformational change or fluctuation of the complex form between enzymes and substrates.

2. Mechanism of enzymatic reactions and substrate induced generation of primitive enzymes

Several important features are revealed for many contemporary enzymes. 1) Most enzymatic reactions are performed near room temperature without any high energy source. 2) The size of most enzymes are larger than their substrates, and binding site of substrates S on enzyme E are clefts or pockets originally generated in the stochastic structures of enzymes. 3) The reactions are usually reversible and have been well expressed by Michaelis-Menton equation which assumes the intermediate complexes ES or E(P+P'),

$$\begin{array}{ccccccccc} & k+1 & & k+2 & & k+3 & & k+4 & \\ E+S & \Leftrightarrow & ES & \Leftrightarrow & E(P+P') & \Leftrightarrow & EP+ & \Leftrightarrow & E+P+P' \\ & k-1 & & k-2 & & k-3 & & k-4 & \end{array} \qquad (1)$$

Note that the reaction schemes expressed by (1) are composed of two parts. The second reaction between ES and E(P+P') indicates the reaction only within complexes at the equilibrium condition of temperature T and pressure p. The other three reactions in the scheme (1) depend mainly on the concentrations of small molecules S, P and P' in the solution.

To discuss the molecular mechanism of these enzymatic reactions, the same “equivalent and uniform” lattice model is applied for both E and ES complexes. That is, all the molecular parameters unchanged, but only the total lattice points N_0 depend on molecular weights of enzyme E and ES complexes, MW_E and MW_{ES}. Then, the mechanisms of reaction from S to P and P' and its reverse reaction are expressed as follow.

Suppose a small S molecule (MW_S) interacts with an stochastic enzyme E and make ES complex in a cleft or a pocket of the enzyme E, most of the additional lattice points $\Delta N_0 = \gamma MW_S$ should be distributed near the contact surface between E and S molecules. Then, Gibbs free energy of the ES complex is given by changing N_0 to $N_{ES} = \gamma MW_{ES}$.

The most probable structural state of ES complex, $X(ES)_m$, is always larger than $X(E)_m$. The excess number of secondary bonds generated by the ES complex formation at the same temperature T is given by $X(ES)_m \gamma MW_{ES} - X(E)_m \gamma MW_E > 0$. When most of the excess secondary bonds generated by ES complex formation are concertedly broken by the aids of overall structural fluctuation of the complex, the corresponding excess energy revealed by the secondary bonds formation $(X(ES)_m \gamma MW_{ES} - X(E)_m \gamma MW_E)\varepsilon$ should be available to cut the weak covalent bonds in substrate S. The probability to make such concerted energy transfer should depend on the molecular shape and arrangements in the contact surface area between E and S molecules.

When S is a long molecule, the cleft is better than the pocket for the contact surface area between E and S, because it generates the additional secondary bonds at the surface of S molecule. Then, if the covalent bond energy to cut S molecule into P and P' molecules is comparable to the above value, the reactions from ES to E(P+P') and its inverse reaction are possible by the aids of structural fluctuations of the large E molecule at a certain equilibrium temperature T and pressure p.

The separation of ES complex produces sufficient energy to break a weak covalent bond in the complex. Especially breaking a covalent bond in the small substrate S is more probable than that in the large E molecule, because the separation of smaller products P

and P' from larger E molecule is easier than the separation of the original large substrate S molecule.

The inverse reaction, from E+P+P' to E+S, is possible when concentrations of P and P' molecules are large enough to make much E(P+P') complexes than to make ES complexes.

The stability of the complex should be increased by the entropy decrease near binding sites of the complex. In this case, formation of the complex increases the probability to make a weak covalent bond between P and P', or to dissociate the deformed EP complex without any chemical changes.

Anyway, interaction between larger polypeptides like E molecules and small molecules promotes the generation or degeneration of rather weak chemical bonds in small molecules using the concerted energy transfer of secondary bonds between them. When molecular size of polypeptides are much larger than small molecule, the probability to make concerted energy transfer from polypeptides to small molecules should be increased compared to the opposite direction. Because the conformational changes of many polypeptides are very cooperative as is shown in the denaturation of many proteins.

Similar energy transfer from secondary bonds to a weak covalent bond are expected between almost the same size of polypeptides, though its probability should be smaller than the case of ordinary sizes of E and S molecules. When several aminoacids are associated on a polypeptide, the generation of oligo-peptides is possible though the probability is small compared to the case of ordinary enzymatic reactions. Though the generation probability of each oligo-peptide should be very small, accumulated oligo-peptides accelerate the generation of proper enzymes.

When the concentrations of substrates and aminoacids or oligopeptides in liposomes are large enough to generate new enzymes, the generations of long metabolic systems are possible.

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