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Conceptual advances in organized solutions: a milestone in the physical chemistry of biological organization

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Abstract - Ideal dilute solutions, electrolyte solutions, regular solutions, regular polymer solutions and fused salts have been considered widely different systems. Yet an idealization of completely random mixing by thermal motion is adequate in these systems. In this respect these solutions are similar. Such recognition yielded a new concept, i.e., "Organized So lutions". From the comparison of characteristic properties of randomly mixed solutions and organized solutions, another new concept "Ideal Organized Solution" was evolved and further the conditions for the self-organization were derived. In idealized organized solution (system), such as lecithin-water, 1. random mixing region is negligibly small, 2. hydrated organized phase separation or organized aggregate formation occurs above the saturation concentration of singly dispersed species, and 3. self-organization of solute molecules occurs due to the association of strong solvent-phobic groups and the orientation of solvent-philic groups to depress the Gibbs energy of the system. At the saturation concentration Gibbs energy decrease due to maximum 'disorder' and Gibbs energy increase due to the dispersion of solvent-phobic groups just balance. Biological organization has been considered at variance with the second law of thermodynamics. The quality factor by Manfred Eigen and the dissipative structures by Ilya Prigogine were introduced in order to explain biological organization. In this paper, however, self-organization in amphiphile system was explained as a natural consequence of thermodynamics. Self-organization of proteins and lipids may be similarly understandable.

INTRODUCTION

Ideal dilute solutions, electrolyte solutions, regular solutions, regular polymer solutions and fused salts greatly differ from each other depending on the types of solvents from hydrocarbon to water and on the nature of interactional forces from Coulombic to London dispersion. These solutions have been considered widely different systems. Yet an idealization of completely random mixing by thermal motion is adequate in these systems. In this respect these solutions are similar. Such recognition seems a meaningful concept itself and served to recognize organized systems (1).

These random mixing solutions, however, represent exceptions among many cases which are encountered in the real world of many biologically and technologically important systems, such as amphiphile systems, lyotropic liquid crystals, solubilized solutions, functional polymer solutions, biological systems, etc. Randomly mixed solutions and organized solutions are summarized in TABLE 1.

TABLE 1 Disorganized and Organized Solutions.

Disorganized solutions (Randomly mixed solution)	Organized solutions (Dilute random mixing solution + Organized phase or particles)
Ideal dilute solutions	Amphiphile solutions(systems)
Electrolyte solutions	Vesicles, Liposomes
Regular solutions	Lyotropic Liquid Crystals
Regular polmer solutions	Solubilized solutions
Fused salts	Amphipathic polymer solutions (Protein solutions)
Inorganic, Unnatural	Biological, Functional, Natural

Solutions shown on the left hand side of TABLE 1 are randomly mixed solutions. An idealization of complete random mixing was adequate in these solutions and well systematized by respective noted scientists(2-5). Solutions enumerated on the right hand side of the TABLE 1 are difficult and complicated systems that deep insight into variety phenomena and creative thinking are very important in order to understand them. These solutions again appear greatly different from each other. Actually they have been neither coherently interpreted nor systematized over almost whole period of physical science. Since the orientation and organization by solute molecules are common characteristics, these solutions were designated as organized solutions(systems) (1,6). Based on such recognition, a first step to interpret them by the generalization through adequate simplification of these complicated systems has been undertaken. As the results several characteristics of organized solutions were clarified(1).

CHARACTERISTICS OF ORGANIZED SOLUTIONS

1. Saturation concentration of singly dispersed solute species is very small. Insolubility of solute in solvent is an important necessary condition to form an organized solution. Solute molecule should be amphipathic and at the same time amphiphobic for water and oil(lipid or hydrocarbon). While in randomly mixed solution, solvent and solute species dissolve each other.

2. Solvated solute is a real solute species. Melting point of anhydrous solute is dramatically depressed by the formation of hydrated solute species.

3. Liquid state of solvated solute is an important condition. Solvent dissolves into organized solute aggregate because it is in a liquid state. Liquid (crystalline) state may be also an important condition to avoid crystal growth which might lead to serious consequenses in biological organization.

4. Swelling of solvents in organized solute phase is large or infinite. Remarkable solvent power is due to the organization and association of solute molecules. Infinite swelling implies micellar dispersion of solute aggregates in solvent, and finite swelling means solvated phase separation.

5. Organized solution is a mixture of solvent molecules and organized aggregates. Critical point markedly deviates to solvent axis. While solvent and solute mix molecularly in disorganized solution. Critical point is roughly 1/2 on volume fraction basis.

6. Activity stays nearly constant with the concentration above the very small saturation concentration of singly dispersed species in organized micellar solutions, and it is constant above the phase separation (finite swelling of solvent into solute phase).

7. Large amounts of water and hydrocarbon can be swelled in an organized amphiphile phase when the hydrophile-lipophile property of the amphiphile aggregate is at balance in water/amphiphile/oil system; thus a continuous change of media from water to hydrocarbon via amphiphile phase can be achieved in balanced amphiphile solutions(7). On the contrary, the mutual solubility is very limited in water and oil system, i.e., random mixing region is very narrow and there exists a wide immiscibility gap.

EVOLUTION OF A NEW CONCEPT "IDEAL ORGANIZED SOLUTION"

The ideal solution has been considered, I think, to represent an idealized case of all types of solutions. After the comparison between random mixing solutions and organized solutions, I trust everyone in this assemblage will agree that it is an idealized case of randomly mixed solutions, but not for organized solutions. Organized solution is entirely different. There is a need to introduce a new concept for organized solutions. "Ideal organized solution" offers advantages similar to those furnished by the concept of the ideal (dilute) solution. Just as the properties of the ideal, ideal dilute and regular solutions suffice to describe the behavior of randomly mixed solutions as a limiting case, so does the ideal organized solution suffice to describe the characteristics of organized solutions. Namely; 1. Random mixing (singly dispersed) region is negligibly small. This region may be treated as "Ideal dilute Solution". 2. Self-organization of solute molecules above the saturation concentration of molecular dispersion due to the strong

solvent-phobic group(s) and solvent-philic goup(s). This region may be treated as "pseudo-phase dispersed solution" or "two phase system (dilute solution + organized phase)" depending on the aggregation number. The big difference between the two idealized solutions may be; ideal (dilute) solution was readily conceivable, whereas "ideal organized solution(system)" has not been conceived so far.

IDEALIZED LIMITING BEHAVIOR OF ORGANIZED SOLUTIONS AND THE CONDITIONS FOR SELF-ORGANIZATION

Peacocke said"The application of thermodynamic and kinetic principles to the study of the existence and evolution of something as complex as living organisms, - - -, exemplified repeatedly the need to stretch the characteristic concepts of thermodynamics and kinetics - - -. At many points entirely new concepts had to be devised, e.g. that of dissipative structures - - of the Brussels school(8) and of 'selection' and the 'quality factor' - - - - by Eigen and his colleagues(9)" in his book(10). However, self-organization is understandable with equilibrium thermodynamics, provided solute molecules satisfy the conditions of organized solutions.

1. Negligibly small ideal dilute (random mixing) region.

Due to the strong hydro-phobicity of solute the saturation concentration of singly dispersed species in water is negligibly small, e.g., lecithin, 4.7×10^{-10} mol/l.(11). This is a very important condition for self-organization. Raoult's law holds for solvent up to this very small concentration.

$$a_1 = f_1/f_1^\circ = p_1/p_1^\circ = x_1 \tag{1}$$

where a_1 is the relative activity of 1st component relative to pure liquid state, f the fugacity, p the partial pressure and x the mole fraction. Several corollaries follow from this relation.

$$(\partial \ln a_1/\partial \ln x_1)_T = 1 \tag{2}$$

from the Gibbs-Duhem equation

$$(\partial \ln a_2/\partial \ln x_2)_T = 1 \tag{3}$$

Upon integration this equation yields

$$p_2/p_2^\circ = a_2 = \gamma_2 x_2. \tag{4}$$

Namely, Henry's law holds for solute. a_2 is the relative activity of 2nd component relative to the coexisting solvated solute phase. Accordingly, a_2 increases linearly from 0 to 1 in a very small concentration range. Nonionic surfactant solution above and below the cloud point is a good example. Based on the accurate and elaborate water vapor pressure data(12), these conclusions were confirmed(13).

2. Non-existence of randomly mixed state above the saturation concentration of singly dispersed species.

Relative activity of solute in random mixing solution is expressed

$$\ln a_2 = \ln x_2 + B\phi_1^2/RT \tag{5}$$

where a_2 is the relative activity of hydrated solute, x_2 the mole fraction of hydrated solute, ϕ_1 the volume fraction of free water, B the energy of mixing hydrated solute with water, i.e., mixing of hydrocarbon portion with water. The activity coefficient of solute , $\gamma_2 = a_2/x_2$ is very large, for example 10^{11} in the case of lecithin in water due to the strong hydrophobic property. The solvated solute phase is taken as a standard state. Above this concentration the hypothetical activity and Gibbs energy of randomly mixed solute increase so much as illustrated in Figure 1.

The change of activity of solute with concentration in hypothetical random mixing solution and that of phase separation are compared. Certainly the entropy of imaginary randomly mixed solution is larger, but the Gibbs energy increases by random mixing. Namely, random mixing above the saturation concentration contradicts the law of thermodynamics(14) and such disordered state does not exist.

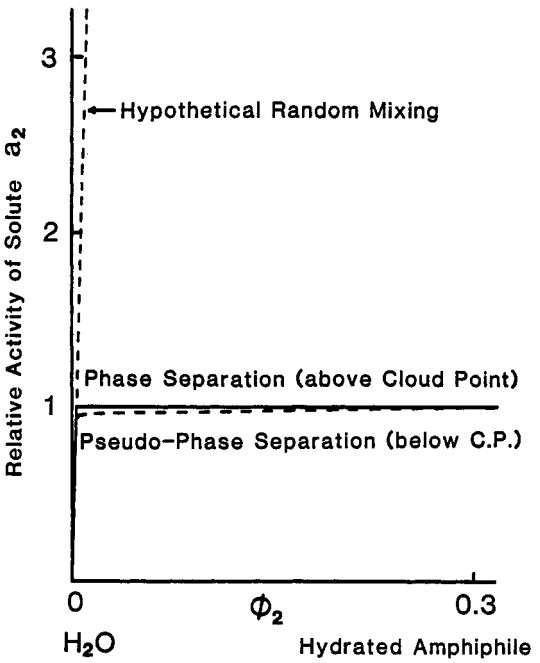

Fig.1. Schematic diagram of the change of relative activity of hydrated solute, a_2, with the concentration.

3. Self-Organization.

The association of hydrophobic groups starts due to the strong hydrophobic interaction at the concentration above which the hypothetical activity of singly dispersed species becomes larger than 1, i.e., larger than that of hydrated solute phase. In other words the depression of the partial molal Gibbs energy due to the mixing and that due to the association of hydrophobic groups just balance at the saturation concentration, so that the singly dispersed and aggregated solutes are in equilibrium. The Gibbs energy depression due to the association of hydrophobic groups is the main driving force of the biological organization of amphiphiles, lipids and proteins in aqueous solutions. On the other hand hydrophilic groups contribute for the orientation and organization of aggregates and to depress the interfacial free energy between organized aggregates and solvent. In oil medium situation of hydrophile and lipophile interaction is reversed.

4. Solvated solute phase is in self-organized state.

Solvated solute phase is in an equilibrium with dilute solution in most organized systems. Solute phase is not disorganized but in self-organized state. Numerous examples of organized hydrated solid may be found in text-books of biochemistry(15). Melting point of anhydrous solid is dramatically depressed by the formation of "lively" hydrated phase(16). Above the melting point hydrated solute phase further swells water(17). If the HLB of solute is shifted to more hydrophilic much more water will be swelled. Many biological substances are in liquid crystalline state at room temperature (18). There are many examples of organized liquid crystals composed of biological molecules(19-24); pertinent fact for biological organization.

5. Change of thermodynamic functions of mixing. (water + hydrated lecithin system as an example.)

The total molal entropy of mixing in random mixing region is given,

$$\Delta s_m = -R(x_1 \ln x_1 + x_2 \ln x_2) \qquad (6)$$

where x_1 is the mole fraction of water in solution and x_2 that of hydrated lecithin, $x_2 = 8 \times 10^{-12}$

Since the saturation concentration of solute is very small due to the large hydrophobic groups, partial molal entropy of mixing per mole of solute,

$$\Delta\bar{s}_2 = -R\ln x_2 \quad 51 \text{ e.u.} \tag{7}$$

is large. But the entropy of mixing of the system, eq.(6), is very small positive, 4×10^{-10} e.u., due to the very small saturation concentration, x_2.

Thus, organized solute phase and water form two phase solution with very small entropy increase and the organization is maintained. In biological system the aqueous solution will be saturated with various common molecules, such as lecithin, triglyceride etc. No more mixing may occur in such system that the entropy of the system scarecely increase.
The total molal Gibbs energy of mixing is given

$$\Delta G_m = RT(x_1 \ln x_1 + x_2 \ln x_2) + \Delta G(\text{hydration}) \tag{8}$$

Just like the entropy of mixing the first term is very small. Since an hydrated liquid lecithin, which is the state of lecithin in biological organization, was taken as the standard state, the Gibbs energy of hydration, second term in equation(8), is also very small. The entropy of mixing increases only a little and the Gibbs energy decreases only slightly in accordance with thermodynamics. Negligibly small saturation concentration of molecular solute is therefore, an important necessary condition for self-organization in many respects.

6. Criteria between organized phase separation and pseudo-phase dispersion.

Organized solution is a mixture of solvent molecules and organized solute aggregates. Since solvent is a small molecule, it is swelled or dissolves in the solvent-philic portion of the organized aggregates. The solubility of a solute in solvent is very small, but the solubility of solvent in the solute phase is large. If the energy of mixing of solvent with organized aggregate, ω, satisfies

$$2\omega < (1 + \bar{x}^{1/2})^2 \, kT \tag{9}$$

solvent molecules and the solute aggregates are mutually miscible and pseudo-phase dispersion occurs, where x is the ratio of the surfaces of the aggregated particle to solvent molecule. If the energy of mixing satisfies

$$2\omega > (1 + \bar{x}^{1/2})^2 \, kT \tag{10}$$

solvent and organized phase separation occurs.

7. Very small interfacial tension between separated phases.

In random mixing solution in which solubility is very small, such as water and hydrocarbon, the interfacial tension between separated phases is large. Although the solubility of self-organizing molecule in solvent is negligibly small, the interfacial tension between separated phases is very small due to the orientation and association of solvent-philic groups of organized phase. When the imaginary interfacial tension is negative, organized phase disperses forming organized aggregates.

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