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PROPERTIES OF DOMAINS IN HETEROGENEOUS SYSTEMS FROM THERMODYNAMIC FUNCTIONS OF SOLUTION

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ABSTRACT

This article shows that we can find properties of specific domains in heterogeneous systems by using suitable molecular probes combined with the application of solution theory. The thermodynamic functions that can be found in this way include free energy, entropy, enthalpy, compressibility and thermal expansion. The deduced molecular parameters include the molecular polarizability, the cohesive interaction between close neighbors and number of nearest neighbors involved in the interactions of each individual. In addition it is possible to obtain the temperatures and energies of the phase transitions of the domain probed.

INTRODUCTION

Being interested in the factors which determine the equilibrium solute concentrations in membranes we measured solubilities in phospholipid bilayers [1] [2]. Ambiguities resulted in most cases because phospholipid membranes are heterogeneous, having hydrophilic heads and paraffinic hydrophobic tails. The number of independent measurements was not sufficient to measure the distribution of the dissolved solute between the phases mentioned [3]. Unusual in this respect are the noble gases which dissolve preferentially into the hydrophobic region of the membrane[2]. Because these solutes are simple in structure and behaviour we were able to develop a quantitative relationship between solubilities and molecular parameters[4]. The combination of a specific adsorption and a quantitative theoretical connection between probe solubility and its molecular properties can therefore be used to analyze heterogeneous systems which have several interconnected different domains. Our main interest is in the characteristics of biological membranes where we want to deduce the behaviour of the many microdomains which influence the behaviour of whole membrane. The thermodynamic behaviour cannot be deduced by direct calorimetry which gives only an integrated result affected by the collective contribution of the individual domains. The method may prove useful also in the analysis of many polymeric systems, of soaps and of various biological systems where attention must be paid to the thermodynamic characteristics of domains in a complex system. In this article we review the existing results and explore which generalizations are needed when extension to systems with many domains is made.

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THEORY AND METHOD

Solubility measurements are best carried out under conditions where comparisons between diffenent solutes or solvents can be made. A suitable reference system for measurements of solubilities is the gas phase. At a given temperature, pressure and concentration all gases have identical chemical potentials. We can therefore compare the behaviour of solutes under iso-chemical potential conditions. This chemical potential is also their chemical potential inside the solution probed. The chemical potential of a solute in solution is the result of a combination of the standard chemical potential and the concentration dependent part of the chemical potential:

$$\mu = \mu^{o} + RT \ln C \qquad (1)$$

Two consequences which are of importance to us follow from this equation; the standard chemical potential of a solute in solution can be determined by finding the concentration C of the gas dissolved if the concentration of the gas phase is known, the standard chemical potentials of two solutes can be compared if these two solutes are measured at the same chemical potential. The different standard chemical potentials are compensated by the concentration dependent part of the chemical potential so that the solute with lower standard chemical potential is the one that has the higher concentration in the condensed phase. Partial entropies and enthalpies can be found by measuring the effect of temperature on the solubility.

From a thermodynamical point of view we are allowed to consider the process of solubility as consisting of two independent processes, a creation of a hole in the solvent medium and an adsorption of the solute into the created hole[5]. This kind of calculation leads to the following equations:

$$\Delta\mu^{o} = N(f_{11} - f_{s1}) + RT \ln(RT/V_1) \qquad (2)$$

$$\Delta H^{o} = N(\varepsilon_{11} - \varepsilon_{s1}) - RT \qquad (3)$$

$$\Delta S^{o} = N(\sigma_{11} - \sigma_{s1}) - R(1 + \ln(RT/V_1)) \qquad (4)$$

where subscripts 11 denote quantities related to hole creation and the quantities which are denoted by the subscript s1 refer to the process of solute adsorption. Thus f_{11}, ε_{11}, σ_{11} refer to the free energy, energy and entropy of hole creation and f_{s1}, ε_{s1}, σ_{s1} are free energy, energy and entropy of solute adsorption to the hole. N is Avogadro's number. It was shown that the 11 parameters depend solely on the features of the solvent and the only effect that a solute has is on the size of the hole i.e the size of a hole can never be smaller than that of the solute[6].

RESULTS AND DISCUSSION

Three aspects of description are of interest. First there is a characterization of the system in terms of molecular configurations and intermolecular forces. Second there is the statistical mechanical characterization and third there is the development of the macroscopic consequences of statistical mechanics which constitute the subject matter of thermodynamics. Using the available data we show the conclusions which can be arrived at from solubility measurements and that these conclusions span the three levels of understanding mentioned above.

Extrapolation to systems where there are negligible solute-solvent interactions furnish f_{11}, ε_{11} and σ_{11} values of the thermodynamic parameters which characterize the formation of a hole in the solvent medium. An example to a characterization of a domain in a heterogeneous system by this method is the deduction of the f_{11}, ε_{11} and σ_{11} parameters characterizing the hydrophobic region of the phospholipid membrane of dimyritoylphosphatidylcholine (DMPC) from solubility measurements of noble gases. The extrapolation is depicted in Fig. 1 and the thermodynamic parameters of the hydrophobic region are given in Table 1. It can be shown that the same values will be obtained for the given parameters if we will measure the solubility of other small solute molecules in the hydrophobic region [7] . However, when larger solutes are used we expect the value of the derived parameters to deviate.

A starting point in any statistical mechanical discussion is the construction of a partition function. The partition function includes the contributions by the solute and the solvent and each term has the form:

$Z = z_{trans} z_{rot} z_{vib} z_{inter.\ rot}$ where the subscripts represent respectively translational, rotational, vibrational and internal rotational degrees of freedom . The partition functions are related to the free energy by the relation $F = -kT \ln Z$. The fact that hydrocarbons have internal degrees of freedom which the noble gases do not have and the fact that the interactions with the solvent follow the same law of force in both cases were used to deduce structural and functional elements of phospholipid membranes [8]. Information on the characteristics of the different partition functions and therefore of contribution coming from the different degrees of freedom was furnished by the solubility measurements mentioned. These conclusions, which are given in Fig. 2, are in line with the results that were obtained from NMR and ESR measurements [9].

Statistical mechanics bridges between thermodynamics and the atomic picture of matter and this is usually done through the use of the Boltzmann term to express the distribution of molecular states available to the system under the specified conditions. Since the partition function reflects independent contributions of the different degrees of freedom it follows that we need a Boltzmann term for each of the partitions functions: z_{trans}, z_{vib} etc. The distribution which the Boltzmann terms represent is rather sharp for macroscopic systems which means that we can use the macroscopic value as representing energies of interaction of the most probable distribution. These energies derived from thermodynamic functions of solution can be used to find the molecular energies of the domain. The derivation is based on the following properties of the energies of interaction: 1) The total energetic contribution is an additive function of the different kinds of possible interactions ionic dipole, London, induced dipole,etc. 2)The contribution of each solvent molecule is independent of the other solvent molecules 3) Solvent and solute parameters multiply each other to give the total adhesive interaction energy between the two (e.g the coulombic interaction energy is obtained by multiplying the charge on the solvent by the charge on the solute, the London interaction energy is a multiplication of the molecular polarizations of solvent and solute. Using these properties it is possible to construct selectivity sets and to obtain from the sets the contribution of the solvent by plotting the adhesive parameters sl vs. the solute contributions. This gives the solvent contribution as the slope of a linear dependence. Some physical parameters of the hydrophobic region of the DMPC membrane which were obtained by the method outlined above are depicted in Table 1.

The method which is described in this article depends on a selective adsorption of probes to domains in the heterogeneous system on the one hand and on using probes whose adorption is easy to interpret. These two conditions cannot be fulfilled simultaneously in all cases of interest. We recommend the use of photolabile probes in these occasions. It is possible to dissolve such probes and then to fix them to the adsorbing system. The distribution of the probe in the different domains can then be found by simple analysis.

It is of interest to note that solubility measurements are sensitive enough to be used for the detection of phase transitions in domains of heterogeneous systems. Examples of the use of solubilities and their temperature dependences for such evaluations of DMPC bilayers appear in the literature [10] [13].

TABLE 1

Physical properties and characteristic parameters of the hydrophobic region of the DMPC membrane from noble gas solubility data [10] [11] [12].

SOLVENT PARAMETERS

Nf_{11} KJ/mole	Ne_{11} KJ/mole	Ns_{11} J/(mole*degK)	Ts_{11}/e_{11}
14.53	31.21	55.00	0.53

PHYSICAL PROPERTIES

Dielectric constant	No. nearest neighbors	Cohesive energy density KJ/cm^3	Surface tension dyne/cm	Expansion to compressibility ratio (atm/K)(10^4)
2.01	6.2	1.23	41.1	41.00

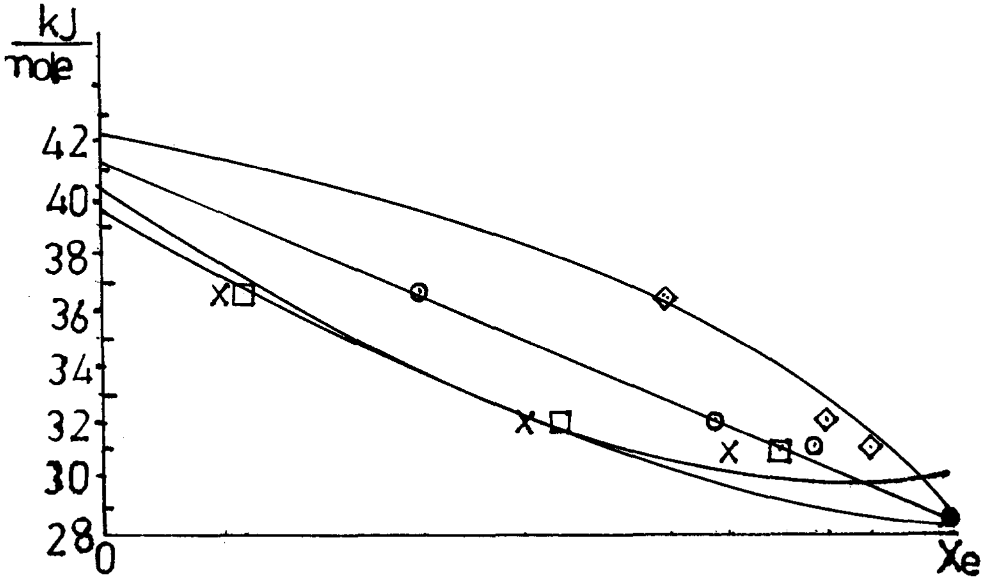

Fig. 1. Curves of free energies of solution of the noble gases in DMPC vs. molecular diameters ◇, force constants □ , energies of vaporization X and the square roots of the energies of vaporization of the solutes ⊙ extrapolate to the same value of f_{11}, the free energy of the hydrophobic region.

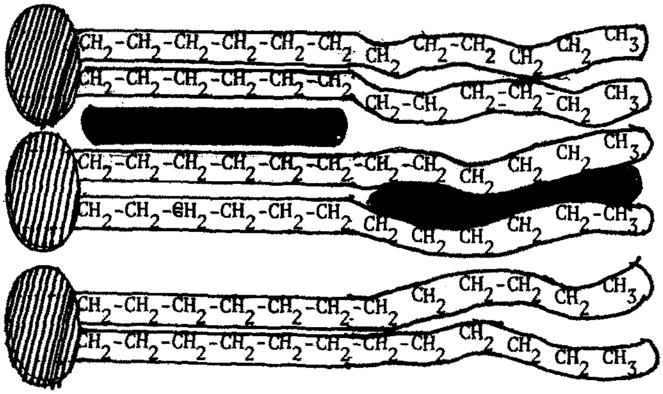

Fig. 2. Solubility measurements of paraffins and aliphatic alcohols (depicted in black) can be used to explore the ordering of the aliphatic chains of the hydrophobic region of a phospholipid bilayer [8].

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