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The hydrophobic effect Gibbs energy

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Abstract

A new method of experimental determination of thermodynamic functions of the hydrophobic effect is proposed. It is based on regarding the thermodynamic functions of hydration as the sum of thermodynamic functions of nonspecific hydration, specific hydration and the hydrophobic effect. In addition to the previously developed method to determine the hydrophobic effect enthalpies, we present a new method to calculate the hydrophobic effect Gibbs energies. The hydrophobic effect Gibbs energies of noble and simple substance gases, alkanes, arenes, and their halogenated derivatives are determined. For all the compounds studied, the hydrophobic effect Gibbs energy is found to be positive. From the values of the Gibbs energies and the enthalpies of the hydrophobic effect, the entropies of the hydrophobic effect are calculated. They are found to be negative for all the compounds. An excellent linear correlation between the hydrophobic effect Gibbs energy and McGowan characteristic molecular volume of the solute is found. The method was applied to a large molecule of fullerene C_{60}. The hydrophobic effect Gibbs energy of fullerene does not deviate from the linear dependence observed for small solutes.

Keywords: Hydrophobic effect; Hydrophobicity; Hydration; Solvation; Gibbs energy

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1. Introduction

Hydrophobicity is an important factor that plays a significant role in various chemical, physical and biological processes [1–3]. It determines the stability of biological membranes, globular proteins, micelles, and governs the distribution of compounds in live organisms [4–7]. Although the hydrophobic effect is a well-known and extensively studied phenomenon it still is not thoroughly explained.

The studies of the hydrophobicity can be based on the analysis of thermodynamic functions of solution in water either focus on the solvent-induced interactions between apolar molecules or moieties in water. The following anomalies of thermodynamic functions are observed for the hydrophobic solutes in water: 1) large positive values of the Gibbs energy of hydration, dissolution in water, and transfer from an apolar solvent to water over a wide temperature range; 2) large negative entropies of hydration at 298 K rapidly growing up as the temperature increases; 3) large positive heat capacities of hydration [8]. In most of the studies (this includes simulation and scaled particles theory studies) these thermodynamic functions (Gibbs energy, enthalpy, entropy, and heat capacity) are considered directly. However, some researchers try to determine the contribution of the hydrophobic effect to the thermodynamic functions of hydration. This contribution is considered as the measure of the “special” properties of water in comparison with the other solvents.

The differences between the thermodynamic functions of hydration and solvation in a reference solvent are often used as the quantitative characteristics of the hydrophobic effect. The reference solvent is supposed to model water “in the absence of hydrophobicity”. For example, thermodynamic functions of transfer from liquid alkane into water are sometimes meant to be thermodynamic functions of the hydrophobic effect [9]. The most widely used parameter of hydrophobicity, the octanol–water partition coefficient (log *P*) [10], is related to the Gibbs energy of transfer from octanol into water phase. In these approaches it is tacitly assumed that the partial molar thermodynamic functions

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of nonspecific solvation in the reference solvent and in "water in the absence of hydrophobicity" are equal. If we use transfer function as the measure of hydrophobicity, we should agree that there is no difference in thermodynamic functions of solvation for the same solute in different solvents when no specific interactions occur. Such assumption is not correct. For example, enthalpies of transfer of hexane from its own neat phase into DMF [11] and DMSO [12] amount, respectively, to 8.5 kJ mol^{-1} and 13.9 kJ mol^{-1}.

For amino acids, tens of hydrophobicity scales exist [13,14]. In some of them, thermodynamic functions of transfer from different organic solvents into water are utilized as well.

It was also proposed [15] to estimate the hydrophobic effect contribution from the temperature dependence of thermodynamic functions of hydration of the hydrophobic compounds. The main idea is that the hydrophobic effect contribution decreases as the temperature increases, and disappears at a certain temperature. Other contributions to the enthalpy and entropy of hydration are supposed to be nearly independent from the temperature.

In Silveston and Kronberg study [16] the functions of transfer from poly(dimethylsiloxane) into water obtained from HPLC measurements were split into the "hydrophobic" and "nonhydrophobic" parts using the temperature dependence of these functions. The Gibbs energy of structuring of water around an apolar molecule (the "hydrophobic" part) was found to be negative.

Abraham suggested [17–19] that the hydrophobic effect contribution is absent in thermodynamic functions of hydration of noble gases. He showed that a linear dependence of the Gibbs energies and enthalpies of solvation for noble gases and alkanes from their molecular radius R is observed in many different solvents, but not in water. In Abraham works, thermodynamic functions of the hydrophobic effect of alkanes are considered as the differences between their experimental thermodynamic functions and thermodynamic functions of a hypothetic noble gas with the same R. However, the assumption regarding zero values of these functions for noble gases was not proven.

Mastroianni et al. [20] and Somsen et al. [21,22] proposed another method to estimate the hydrophobic effect enthalpy from the data on solvation enthalpies in binary water-organic solvent mixtures. In this method, the preferential solvation phenomenon and the specific interactions between water and organic cosolvent are both neglected. In a series of works [23–25] Jozwiak and Piekarski made an attempt to take these effects into account by adding a correction term ΔH^*, but an ideal behavior ($\Delta H^*=0$) of DMF–water mixtures is still presumed.

In a number of works [26,27] another attempt to evaluate the hydrophobic effect thermodynamic parameters was made. Thermodynamic functions of hydration for the solutes A not interacting specifically with water ($\Delta_{\mathrm{hydr}}\mathrm{H}^{\mathrm{A}}$ and $\Delta_{\mathrm{hydr}}G^{\mathrm{A}}$) are regarded as the sum of the nonspecific hydration thermodynamic functions and the hydrophobic effect thermodynamic functions. The nonspecific hydration enthalpies and Gibbs energies had been determined from a linear dependence between the enthalpy of solvation or the Gibbs energy of solvation of A in a series of solvents ($\Delta_{\mathrm{solv}}G^{\mathrm{A/S}}$ or $\Delta_{\mathrm{solv}}H^{\mathrm{A/S}}$) and the corrected Hildebrand solubility parameter of solvent S. The difference between the experimental values of $\Delta_{\mathrm{hydr}}H^{\mathrm{A}}$ or $\Delta_{\mathrm{hydr}}G^{\mathrm{A}}$ and the values interpolated from the linear dependence was meant to be the hydrophobic effect enthalpy or Gibbs energy. There are two severe problems in this method. First, no linear dependence between $\Delta_{\mathrm{solv}}G^{\mathrm{A/S}}$ ($\Delta_{\mathrm{solv}}H^{\mathrm{A/S}}$) and the corrected Hildebrand solubility parameter is observed for a large number of apolar compounds A. Second, a large amount of experimental data is required to plot the correlation line.

In our recent work [28] we developed a method to determine the enthalpy of the hydrophobic effect that uses the same principle of additivity of contributions from different types of interactions to the enthalpy of hydration. However, it is free of the imperfections described above because it is based on a completely different method to evaluate the nonspecific hydration enthalpy.

We determined the hydrophobic effect enthalpy for noble and simple substance gases, alkanes, aromatic hydrocarbons and normal aliphatic alcohols. For inert gases and alkanes it was found to be negative. This result agrees well with the classic interpretation of the hydrophobic effect as the strengthening of the hydrogen bonds network around apolar molecules [15,29,30]. For aromatic hydrocarbons, the hydrophobic effect enthalpy is positive and grows up with the size of the hydrocarbon. The hydrophobic effect enthalpies for the aliphatic alcohols (-10.0 ± 0.9 kJ mol^{-1}) were found to be close to those of alkanes (-10.7 ± 1.5 kJ mol^{-1}).

Over the last decade, a lot of theoretical examinations of the hydrophobic effect were made. In simulation and SPT studies [31–33] the hydrophobic and non-hydrophobic contributions to the thermodynamic functions of hydration are not separated. Therefore, we do not discuss the results of these works in our paper.

In our opinion, the quantitative measure of the hydrophobicity is necessary to understand the hydrophobicity phenomenon. The main purpose of this work is to develop a new method to evaluate the hydrophobic effect Gibbs energies.

2. Methodology

The Gibbs energy of solvation $\Delta_{\mathrm{solv}}G^{\mathrm{A/S}}$ is the Gibbs energy of isothermal transfer of solute A from the gas phase to an infinitely diluted solution in solvent S. In the present work, the standard states we use are as follows: 298.15 K temperature, 1 bar fugacity of gaseous A and the hypothetical ideal unit molar fraction solution. Most of the literature values of the Gibbs energies of solvation are given for the same standard states. It should be noted that the choice of the standard states for the analysis of thermodynamic quantities is a matter of discussion. Ben-Naim standard state [34] (1 M ideal solution and 1 M ideal gas) is commonly used too. According to our calculation procedure, neither the specific hydration Gibbs energy nor the hydrophobic effect Gibbs energy does not depend on choice of the standard state for the solute. The Gibbs energy of solution $\Delta_{\mathrm{soln}}G^{\mathrm{A/S}}$ is the Gibbs energy change for transfer of 1 mole of solute A from its standard state (solid, liquid, or vapor) to an infinitely diluted solution in solvent S at