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Using surface tension data to predict differences in surface and bulk concentrations of nonelectrolytes in water

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Abstract

Recently, we developed a quantitative interpretation of surface tension increments (STI) of salts, acids, and bases in terms of the solute (or salt ion) partitioning model (SPM). Here, we obtain an analogous SPM-based interpretation of surface tension increments of nonelectrolytes, which yields local-bulk partition coefficients (K_p) quantifying the accumulation or exclusion of these solutes in the local region near the air-water surface, and the amount of water per unit area of that region (b_1^s). Sucrose exhibits the largest positive STI (approximately $1.4 \text{ ergs cm}^{-2} \text{ Osm}^{-1}$). Assuming that $K_p = 0$ for sucrose (i.e. that it is completely excluded from the surface of water), these STI provide a minimum estimate of b_1^s of $0.20 \text{ H}_2\text{O}/\text{\AA}^2$, or a minimum thickness of the surface region of approximately two layers of water at bulk density. This is the same value as obtained previously from analysis of surface tension and hydrocarbon solubility increments of Na_2SO_4 and also for the interaction of glycine betaine with anionic carboxylate surface, indicating that this quantity is not a function of the type of solute or surface investigated and therefore that it may represent the molecular thickness of the region. Partition coefficients of other nonelectrolytes investigated range from moderately excluded (e.g. urea) to moderately accumulated (e.g. glycerol, ethylene glycol); strongly accumulated surface active solutes (e.g. mono-substituted alcohols) were not included in this analysis. Partition coefficients for many salt ions obtained from STI and hydrocarbon solubility increments fall in a rank order which corresponds to the Hofmeister series for protein folding and protein solubility, indicating a common pattern of accumulation or exclusion of salt ions at the air-water surface and nonpolar surfaces of dissolved hydrocarbons and proteins; no such patterns are observed for nonelectrolytes.

1 Introduction

At moderate to high concentration ($\geq 0.1 \text{ M}$), salts and uncharged solutes exert a wide range of effects on protein processes such as folding, assembly, and precipitation.^{1–4} In general, effects of salt anions and cations and of other solutes fall into regular series (called the Hofmeister series for salt ions). At one end of these series are nonelectrolytes (e.g. urea, formamide), anions (e.g. thiocyanate), and cations (e.g. guanidinium) that destabilize folded proteins and α helices, weaken protein assemblies, and increase protein solubility (cf. Fig. 1). At the other end of these series are nonelectrolytes (including osmolytes glycine betaine and trimethylamine oxide) and ions (e.g. sulfates, carboxylates, phosphates) that stabilize folded proteins and favor binding and assembly of protein subunits. In the middle of these series are nonelectrolytes and ions (e.g. glycerol, chloride, potassium) that do not exert large specific effects on most protein processes. The thermodynamic description of nonelectrolyte solute effects, as well as that of

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Hofmeister, osmotic, and Coulombic effects of electrolytes, on biopolymer processes is most fundamentally based on preferential interaction coefficients which quantify the thermodynamic consequence of the local accumulation or exclusion of the solute from the vicinity of the hydrated biopolymer surface as a function of solute concentration.^{3,4} Preferential interactions of solutes and of individual salt ions with biopolymer surfaces have previously been characterized by a solute-partitioning model, in which a partition coefficient quantifies the distribution of an uncharged solute or an ion between the bulk water and a local environment (i.e. water of hydration) at the surface of a biopolymer.⁵⁻⁷ The goal of the present study is to apply an analogous partitioning model to interpret solute effects on the surface tension of water and thereby obtain partition coefficients quantifying the accumulation or exclusion of these solutes from the surface of water.

Qualitatively, it had long been recognized that the ordering of salt effects on surface tension and on the “salting out” of model compounds was generally the same as that observed for the effects of salts on protein processes.^{2,8,9} We recently quantified the extent of Hofmeister cation and anion exclusion from (or in a few cases, accumulation at) nonpolar surfaces of hydrocarbon model compounds and compared the obtained partition coefficients to those determined for cations and anions at the air-water interface.¹⁰⁻¹² Both the amount of water per unit area in the surface region ($\sim 0.2 \text{ H}_2\text{O } \text{\AA}^{-2}$) and partition coefficients for many electrolyte ions are very similar for air-water and hydrocarbon-water interfaces. Does a similar series exist for nonelectrolyte solutes, and what quantitative information can be gleaned from the effects of nonelectrolyte solutes on surface tension?

2 Thermodynamic Analysis and Background

2.1 Analysis of Nonelectrolyte Solute Effects on Surface Tension Using the Solute Partitioning Model

Guggenheim developed a treatment of the thermodynamics of interfaces in which the vapor and liquid phases are separated by an interfacial layer (denoted by σ) of small but finite thickness.¹³ At constant temperature and pressure, the effect of an uncharged solute (component 2) on the surface tension (γ) of water (component 1) is obtained from the surface-phase analog of the Gibbs-Duhem equation:

$$d\gamma + \Gamma_1^\sigma d\mu_1 + \Gamma_2^\sigma d\mu_2 = 0, \quad (1)$$

where $\Gamma_1^\sigma = n_1^\sigma / A$ and $\Gamma_2^\sigma = n_2^\sigma / A$ are the total numbers of water and solute molecules (per unit surface area, A) in the surface phase and γ is the surface tension. Since the bulk (b) and surface phases are at equilibrium, changes in the chemical potentials μ_1 and μ_2 (Eq. 1) are related by the bulk-phase Gibbs-Duhem equation:

$$d\mu_1 = - \frac{n_2^b}{n_1^b} d\mu_2. \quad (2)$$

Therefore, from Eqs. 1 and 2,

$$d\gamma = \left[\Gamma_2^\sigma - \left(\frac{n_2^b}{n_1^b} \right) \Gamma_1^\sigma \right] d\mu_2. \quad (3)$$

where Γ_2^σ and Γ_1^σ individually depend on the location of the surface phase boundaries, but the quantity in brackets is independent of the size and location of the surface phase. Equation 3 is formally analogous to the Gibbs adsorption isotherm, where Γ_1^{Gibbs} and Γ_2^{Gibbs} are excesses (positive) or deficits (negative) of solvent and solute relative to the bulk. In Gibbs' analysis, individual values of the excess quantities Γ_1^{Gibbs} and Γ_2^{Gibbs} depend on the placement of the Gibbs dividing surface, but the term in brackets in Eq. 3 does not. Although Eq. 3 has the same form as the Gibbs equation, in the Guggenheim analysis, Γ_2^σ and Γ_1^σ cannot be negative.

Equating the mole ratio n_2/n_1 in each region (surface, bulk) to the corresponding molal concentration ratio $m_2/m_1^\bullet$, where m_2 is the solute molality and $m_1^\bullet$ is the molality of water (55.5 mol/kg), yields the following equation:

$$d\gamma = - \frac{RTn_1^\sigma}{m_1^\bullet A} (m_2^\sigma - m_2^b) d\ln a_2. \quad (4)$$

Equation 4 specifies the dependence of surface tension on solute activity, a_2 , in terms of the quantities n_1^σ/A (the number of water molecules in the surface region per unit area of surface) and $(m_2^\sigma/m_2^b - 1) \equiv K_{p,2} - 1$ where $K_{p,2}$ is the surface-bulk partition coefficient for the solute, defined as the molal concentration ratio ($K_{p,2} \equiv m_2^\sigma/m_2^b$). Ordinarily, the surface phase is negligibly small in comparison to the bulk so m_2^b can be accurately approximated by the overall solute molality, m_2 . Since

$$m_2 \frac{d\ln a_2}{dm_2} = \frac{d\ln a_2}{d\ln m_2} = 1 + \frac{d\ln f_2}{d\ln m_2} \equiv 1 + \varepsilon_2, \quad (5)$$

where f_2 is the bulk activity coefficient of the solute and $\varepsilon_2 \equiv d\ln f_2/d\ln m_2$, therefore

$$\frac{d\gamma}{dm_2} = - \frac{RT}{m_1^\bullet} \left(\frac{n_1^\sigma}{A} \right) (K_{p,2} - 1) (1 + \varepsilon_2). \quad (6)$$

The nonideality term, $1 + \varepsilon_2$, is directly evaluated from the concentration dependence of the osmolality (Osm) of the two-component solution; $1 + \varepsilon_2 = d\text{Osm}/dm_2$. Using this relationship, one obtains the result:

$$\frac{d\gamma}{d\text{Osm}} = - \frac{RT}{m_1^\bullet} \left(\frac{n_1^\sigma}{A} \right) (K_{p,2} - 1). \quad (7)$$

Equation 3 was obtained by Guggenheim and has been cited in various forms;^{13–16} however, nonelectrolyte solute effects on surface tension have not been interpreted previously by a solute partitioning model (SPM) as developed in Eqs. 4–7 in terms of a partition coefficient, $K_{p,2}$ that describes equilibrium partitioning of solute between bulk solution and water at the surface. By analogy with macroscopic partition coefficients, $K_{p,2} \equiv m_2^\sigma/m_2^b$ is expected to be relatively independent of solute concentration, except where nonideality effects for solute-solute interactions are very significant.⁷ The quantity n_1^σ/A is expected to decrease with increasing m_2^σ as a result of replacement of solvent by solute in the surface region; the analogous situation has been treated for biopolymer surfaces but is not expected to make a significant contribution

at the low solute concentrations and for the range of partition coefficients ($K_p \sim 0$ –4) discussed here.

3 Results and Discussion

Shown in Table 1 are surface tension increments (STI) $d\Delta\gamma/dOsm$ for 13 nonelectrolyte solutions; a subset of the data is shown in Fig. 2. The STI presented in Table 1 were obtained at a constant temperature in the range 15–30°C. Although some temperature dependence of the slope $d\Delta\gamma/dOsm$ is expected from Eqs. 6–7 (the net effect of the direct dependence (RT) and any temperature dependence of $K_{p,2}$ or b_1^σ), within this temperature range, differences in experimental methods and technique appear to have more significant effects on $d\gamma/dm_2$ than differences in temperature. Reported molar and molal concentrations were converted to osmolality for convenient application of Eq. 7. Linear dependences of surface tension on osmolality (cf. Fig. 2) and on concentration (molar and molal) were observed for most nonelectrolytes investigated, and given the uncertainties, it was not possible to determine whether γ is more linear plotted against concentration or against osmolality.

The largest positive STI ($d\Delta\gamma/dOsm$) is observed for sucrose (+1.44 erg cm⁻² Osm⁻¹). At the same osmolality, acetamide depresses the surface tension by -3.84 erg/cm⁻². Between these two extremes, the following range, in order of decreasing STI, is observed: sucrose ~ mannitol > glucose > sarcosine > urea > glycerol > ethylene glycol > acetamide. Unfortunately, large differences in surface tension increments are sometimes observed for the same solute. As an extreme example of this variability, the STI for glycine betaine has been independently determined three times with vastly different results:^{17,20,27} 0.93 erg cm⁻² Osm⁻¹, 0.40 erg cm⁻² Osm⁻¹, and -0.16 erg cm⁻² Osm⁻¹. The source of this large discrepancy is unclear.

To obtain partition coefficients $K_{p,2}$ of nonelectrolyte solutes (Eq. 5; Table 2), we assume that the thickness of the surface water layer is independent of the concentration and nature of the solute and use the lower bound value of b_1^σ obtained by assuming that sucrose is completely excluded from the interfacial region (i.e. $K_p=0$). This value of b_1^σ (0.20 H₂O Å⁻²), which corresponds to approximately two layers of water at bulk density, is the same within uncertainty as the results obtained from surface tension and hydrocarbon solubility increments for Na₂SO₄, assuming complete exclusion of both sodium and sulfate ions from air-water and molecular hydrocarbon surfaces (b_1^σ and 0.18 H₂O Å⁻²) and is remarkably similar to the value obtained assuming complete exclusion of glycine betaine from carboxylate surface on biopolymers (~0.22 H₂O Å⁻²).³⁶ (Note that if a more excluded solute is characterized and set as the reference, b_1^σ will increase and all K_p values reported in Table 2 will shift, but the relative order of solute partitioning established by the following analysis will not be affected). The similar values of b_1^σ obtained for interfaces as disparate as nonpolar macroscopic air-water, molecular hydrocarbon-water and anionic carboxylate-water suggests that it is generally applicable as a molecular measure of hydration of aqueous surfaces. The hypothesis that this value of b_1^σ has molecular significance is supported by the fact that it is obtained for solutes/ions as dissimilar in size and charge as sucrose and Na⁺ and SO₄²⁻. Recent molecular dynamics simulations on the water hydrating the villin headpiece subdomain (HP36) indicate that the influence of the protein on water properties extends beyond the first hydration layer and that the thickness of this hydration layer is uniform, both features which are consistent with our results.³⁷

The partition coefficients obtained through application of Eq. 7 (or Eq. 6) are shown in Table 2. The most excluded solute is sucrose, with a K_p set to zero. Other large polyols are also highly excluded from the surface region (mannitol $K_p=0.1$, glucose $K_p=0.2$). Glycerol and ethylene glycol are both moderately accumulated in the surface region ($K_p=1.1$ and 2.6). In contrast to

the electrolyte case,^{10,11} there is no obvious correlation between the partitioning of nonelectrolyte solutes at the air-water surface and the observed effects of these solutes on protein processes, as noted previously.¹⁷ For example, urea, a protein denaturant, is slightly excluded from the air-water surface while trimethylamine oxide (TMAO), a protein stabilizer, is moderately accumulated. This is consistent with earlier hypotheses that interactions with polar or charged surface elements on biopolymers determine the relative effects of these solutes on biopolymer processes.^{17,36,38,39}

In Fig. 3, the partitioning free energy ΔG_p for each polyol investigated is plotted against the solvent accessible surface area (ASA^1) of that solute. For ethylene glycol, glycerol, glucose, and mannitol, there is an excellent correlation; ΔG_p increases linearly with ASA . Sucrose, assigned the value $K_p=0$, cannot be included in the fit, but by extrapolating to the ASA of sucrose, we obtain an estimated K_p of 0.005, completely consistent with the assigned value within the uncertainty. Additional STI data will be required to determine whether a linear extrapolation to sucrose (or beyond) is appropriate. All the polyols in Fig. 3 have similar ASA compositions: 40–50% hydrocarbon and 50–60% oxygen (entirely hydroxyl except for a small ASA contribution from ether oxygens on sucrose and glucose). The partitioning behavior of these polyols is presumably the combined result of the tendency of hydrocarbon ASA to partition into the surface layer and for oxygen (hydroxyl) ASA to partition into bulk water, but conformational entropy and ring strain for higher-order polyols (e.g. mannitol and sucrose) may also play a role. We are currently extending this analysis to alcohols and additional polyols and interpreting the partition coefficients in terms of the favorable interaction of polar functional groups, and unfavorable interaction of hydrocarbon groups, with water.

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¹The online SMILES (simplified molecular input line entry specification) translator at <http://cactus.nci.nih.gov/translate>⁴⁰ was used to generate pdb files of the solutes. The surface areas were calculated using Surface Racer 3.0,⁴¹ with a probe radius of 1.4 Å and accepted values of van der Waals radii (set 1⁴²)

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Fig. 1.

Solute and salt ion series: Positioned with regard to effects on protein folding.

Fig. 2.
Effects of nonelectrolytes on the surface tension of water.

Fig. 3. Correlation of polyol partitioning free energies with ASA. The polyols designated by black symbols were fit linearly, and this fit was extrapolated to the ASA of sucrose, in order to obtain an estimated K_p to compare to the assigned value of zero.

Table 1
Surface tension increments $d\gamma/dOsm$ for nonelectrolyte solutes

Solute	$d\gamma/dOsm$	reference(s)	$b_1(K_{p,3} - 1)$
sucrose	1.41 ± 0.10	17–19	-0.19 ± 0.01
	1.35 ± 0.05	20	-0.18 ± 0.01
	1.57 ± 0.17	18,19,21	-0.21 ± 0.02
mannitol	1.37 ± 0.49	21,22	-0.19 ± 0.07
glucose	1.09 ± 0.03	23,24	-0.15 ± 0.01
	1.28 ± 0.31	21,24	-0.17 ± 0.04
glycine	1.25 ± 0.04	25,26	-0.17 ± 0.01
	1.05 ± 0.03	26,27	-0.14 ± 0.01
alanine	0.98 ± 0.08	25,28–30	-0.13 ± 0.01
	0.60 ± 0.04	27–30	-0.08 ± 0.01
sarcosine	0.81 ± 0.11	17,31,32	-0.11 ± 0.02
glycine betaine	0.76 ± 0.11	17,31,32	-0.10 ± 0.01
	-0.16 ± 0.07	27,31,32	0.02 ± 0.01
urea	0.40 ± 0.07	20	-0.05 ± 0.01
	0.22 ± 0.03	17,33	-0.03 ± 0.01
	0.35 ± 0.07	22,34	-0.05 ± 0.01
glycerol	-0.21 ± 0.16	21,22	0.03 ± 0.02
proline	-0.26 ± 0.06	17,30,31	0.01 ± 0.01
	-0.47 ± 0.09	25,30,31	0.06 ± 0.01
TMAO	-0.99 ± 0.06^a	17	0.13 ± 0.01
ethylene glycol	-2.33 ± 0.07	21,22	0.31 ± 0.01
acetamide	-3.84 ± 0.09	21,35	0.52 ± 0.01

^aThe STI for this solute is reported as $d\gamma/dc_2$ at 1M.¹⁷ To our knowledge, density data and osmotic coefficients for this solute are not available, and so the application of Eq. 6 is approximate.

Table 2

STI-based partition coefficients for nonelectrolyte solutes at the air-water surface

Solute	K_p
sucrose	0.0 ± 0.1
mannitol	0.1 ± 0.1
glucose	0.2 ± 0.1
glycine	0.2 ± 0.1
sarcosine	0.4 ± 0.1
alanine	0.5 ± 0.2
glycine betaine	0.8 ± 0.3
urea	0.8 ± 0.1
glycerol	1.1 ± 0.1
proline	1.3 ± 0.1
TMAO	1.7 ± 0.1
ethylene glycol	2.6 ± 0.1
acetamide	3.7 ± 0.1