ELSEVIER

Biophysical Chemistry 114 (2005) 95–101

Biophysical Chemistry

http://www.elsevier.com/locate/biophyschem

Energy of an ion crossing a low dielectric membrane: the role of dispersion self-free energy

M. Boström[a,*], B.W. Ninham[b,c]

[a]Department of Physics and Measurement Technology, Linköping University SE-581 83 Linköping, Sweden
[b]Research School of Physical Sciences and Engineering, Australian National University Canberra 0200, Australia
[c]Institute of Physical and Theoretical Chemistry, University of Regensburg, D-93040 Regensburg, Germany

Received 25 August 2004; received in revised form 28 October 2004; accepted 5 November 2004

Abstract

The Born charging equation predicts that the permeability of a cell membrane to ions by the solubility-diffusion mechanism depends on the ionic radius and on the dielectric constant of the membrane. However, experiments, for example, on red blood cells and on lysosome membranes, show that the permeability depends strongly on the choice of salt anion in a way that cannot be accommodated by differences in ionic size. We demonstrate that one step towards understanding this ion specificity is to take account of the previously ignored dispersion self-free energy of the ion. This is the quantum electrodynamic analogue of the (electrostatic) Born self-energy of an ion. We show that the dispersion self-free energy contribution can be and often is of the same order of magnitude as the Born contribution. To understand the observed specificity, it is essential to take into account of both ionic size and ionic polarizability. In parallel and to reinforce these observations, we also give simple estimates for how self-free energy changes that occur when an ion moves into the air–water interface region (which has a density profile for water molecules) can influence the surface tension of salt solutions. Consistency can be found between the Hofmeister sequences observed in ion permeation and in surface tension of electrolytes when these previously ignored self-free energies are included properly.

Keywords: Ion permeation; Membrane permeability; Dispersion self-energy; Born self-energy

1. Introduction

From a physicochemical point of view, the cell membrane constitutes a region of low polarizability that acts as a barrier to the passage of ions between two aqueous solutions. Two different mechanisms are often used to describe ion permeation of cell membranes. In the first, ions traverse the membrane through pores. In the second, ions partition into the membrane phase and diffuse across the membrane. We will here only consider the second mechanism. Anions are frequently supposed to move across membranes via this solubility-diffusion mechanism. The permeation of an ion across a membrane depends directly on the Gibbs free energy change in transferring the ion from aqueous phase to membrane phase. The leading term in the free energy of an ion in a given medium is the electrostatic Born self-energy (or the "energy of charging") [1,2]. For thin membranes, Parsegian demonstrated that there is an important correction to the Born self-energy from the image energy when the ion sits in the interior of the membrane [1]. This purely electrostatic model [1] predicts that the only ionic properties that influence the permeability are the ionic charge and the ionic radius. According to this model, all monovalent anions with similar radii should permeate equally well. However, experiments reveal a much more complicated and interesting picture. The permeability of rat liver lysosome to anions follows a Hofmeister series for different anions, decreasing in the order thiocyanate, nitrate, iodide>bromide>chloride>sulfate [3]. The permeation through phospholipid bilayers follows

---

* Corresponding author. Tel.: +46 1328 8958; fax: +46 1313 7568.
E-mail address: mabos@ifm.liu.se (M. Boström).

0301-4622/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.bpc.2004.11.003

exactly the same series [2,4,5]. The influence on cell water in human red blood cells from different anions of the background salt also follows the same trend [6]. The observed Hofmeister series is not only observed in ion permeation but is in fact much more general [7]. It has been seen, for example, in membrane biology [8,9], surfactant self-assembly [10], activity coefficients of electrolytes [11], and cutting efficiency of DNA [12].

It is then clear that an electrostatic mechanism cannot provide the complete story. We demonstrate here that an extension of theory that seems important to an understanding of this ion specificity is via inclusion of the previously ignored dispersion self-free energy of the ion. This is the quantum electrodynamic analogue of the electrostatic Born self-energy of an ion. The source of this energetic contribution lies in the fact that ions have polarizabilities different from the surrounding medium in which they are immersed.

We first give the basic theory of self-free energies of polarizable particles (Section 2) and then proceed to discuss different effects (including self-free energies) that influence anion permeation through thin membranes. We also compare with general trends observed in experiments (Section 3). In Section 4, we deviate slightly from the main topic of this article to reinforce our claims. We examine how the same conceptual framework also provides a mechanism that can explain the Hofmeister sequence observed in experiments that measure the surface tensions of salt solutions. Having established the very important role for both electrostatic and dispersion self-free energy changes when an ion moves from one media to another, we end finally with some conclusions (Section 5).

2. Basic theory

By the abbreviation “dispersion” energy, we mean the totality of many body electrodynamic fluctuation energies of interaction between an ion and the surrounding medium. If the medium was a dilute gas, this would comprise just contributions from Keesom (dipole–dipole), Debye (dipole–induced dipole), and London dispersion (induced dipole–induced dipole) interactions [13].

We first demonstrate that this previously ignored dispersion self-free energy contribution for large polarizable anions is often of the same order of magnitude as the electrostatic Born contribution. To do so, consider a model membrane made up of an isotropic film of hydrocarbon with a dielectric susceptibility function $\varepsilon_1(i\omega_n)$ and the aqueous phases (water) to be homogeneous media with dielectric functions $\varepsilon_2(i\omega_n)$. Here, $i\omega_n$ is a discrete frequency (on the imaginary axis for technical reasons) that is used later in the calculation of the dispersion self-free energy. The electrostatic contribution to the change in free energy when an ion (with charge e and radius a) is transferred from aqueous phase to the center of the membrane is given by [1]

$$G^{el} = \frac{e^2}{8\pi\varepsilon_0 a}\left(\frac{1}{\varepsilon_1(0)} - \frac{1}{\varepsilon_2(0)}\right) - \frac{e^2}{4\pi\varepsilon_0\varepsilon_1(0)d}\ln\left[\frac{2\varepsilon_2(0)}{\varepsilon_1(0)+\varepsilon_2(0)}\right], \tag{1}$$

where ε_0 is the permittivity of vacuum, and d is the thickness of the membrane.

The concept of dispersion self-energy in atomic systems was developed by Mahanty and Ninham [13]. It is a quantum electrodynamic dipolar polarization analogue of the Born electrostatic energy of a charged particle. This dispersion self-energy has been neglected in the theory of ion permeation. This is clearly inconsistent as both the electrostatic (classical and zero frequency) and finite frequency (electromagnetic fluctuation) interactions are part and parcel of the same physical framework and must be considered on an equal footing. We will here give the finite temperature result for isotropic ions in aqueous phase and in the membrane. It is straightforward to extend the result of Mahanty and Ninham to take into account the effect of surrounding media and finite temperature T. The contribution from dispersion self-free energy to the free energy of transfer between the two phases is

$$G^{\mathrm{disp}} = \frac{4k_{\mathrm{B}}T}{\sqrt{\pi}}\sum_{n=0}^{\infty}{}'\left[\frac{\alpha_1^*(i\omega_n)}{a_1^3\varepsilon_1(i\omega_n)} - \frac{\alpha_2^*(i\omega_n)}{a_2^3\varepsilon_2(i\omega_n)}\right], \tag{2}$$

where k_{B} is Boltzmann’s constant, a_i and a_i^* $(i\omega_n)$ are the ion radius and excess ionic polarizability in media i. We stress that both radius and excess ionic polarizability in principle will be different in different phases. Here, we approximate them with the result for water. This should lead to a small underestimate of the dispersion self-free energy change. However, we are, here, mainly interested in the general result and principles. It is the bare ionic radius that should be used in these calculations rather than the hydrated radius (the radius for the dispersion self-free energy involves a reasonable assumption of a Gaussion spread in the wave functions and polarization). This is so since the dispersion self-free energy obtains its main contributions from visible and ultraviolet frequencies. This depends on electronic densities, which are not affected much by orientation of dipoles or hydrogen bonding of water around the ion. The self-free energy change is obtained as a summation over discrete frequencies (ω_n=$2\pi k_{\mathrm{B}}Tn/\hbar$), and the prime indicates that the n=0 term carries a weight of 1/2.

We use the approximate excess polarizabilities for Cl^-, Br^-, and I^- given by Kunz et al. [11]. We model the ionic excess polarizability with a single adsorption frequency (ω_I) for each species using the London approximation,

$$\alpha^*(i\omega_n) = \frac{\alpha^*(0)}{1+\omega^2/\omega_I^2}. \tag{3}$$

The excess polarizability is the difference between the polarizability of the ion and the surrounding media (it can be either positive or negative, and it will be different for different ions, for example, larger for iodide than for chloride). Kunz et al. gave two sets of values for the static excess polarizabilities and adsorption frequencies. One set comprised the "expected" values taken from the literature, and the other was the "adjusted" values that they found could accommodate the experimental osmotic coefficients of a large number of different salt solutions. Since data for the properties of ions in water (polarizabilities, adsorption frequencies, and radii) are not yet well known and the two sets give quite different results, we will present results using both "expected" and "adjusted" values. The main point is that we observe in both extreme cases large effects from inclusion of ionic dispersion self-free energy. Further experimental results and molecular simulations are required to obtain more accurate knowledge of the ionic polarizabilities.

The expected values for Cl^-, Br^-, and I^- are 2.1 (1.97×10^{16} rad/s), 3.17 (1.80×10^{16} rad/s), and 4.6 Å^3 (1.59×10^{16} rad/s) for the static excess polarizability (adsorption frequency) [11]. The adjusted values for Cl^-, Br^-, and I^- are 4.7, 6.1, and 6.1 Å^3 for the static excess polarizability [11]. The same adsorption frequencies were used in both cases, but they are by no means better known than the static polarizabilities. The ionic radii are also the same in both sets for these ions and are approximately 1.81, 1.96, and 2.2 Å for Cl^-, Br^-, and I^- [11]. Since all these ions have different radii, it may be argued that the effects obtained by inclusion of dispersion self-free energies can be obtained by adjusting the radii for the electrostatic contribution. However, also ions with very similar radii, such as iodide and chlorate, give different results. This is because they have very different polarizabilities. The main reason that one has to include dispersion self-free energies is of course that it is of the same order of magnitude as the main electrostatic term (and as the experimentally observed ion specificity). It is as fundamentally incorrect to omit this term as it would be to omit the Born energy.

The dielectric function of the aqueous phase (water) was obtained from tabulated optical data and the use of a Kramers–Kronig relationship (complemented with a high-frequency asymptote) [14]. The dielectric constant of water is 80. The dielectric function of the membrane is modeled with a single oscillator frequency [13]

$$\varepsilon_1(i\omega_n) = 1 + \frac{\varepsilon_1(0) - 1}{1 + \omega^2/\omega_{uv}^2}, \tag{4}$$

where we take the dielectric constant to be 2, and the resonance frequency $\omega_{uv}=10^{16}$ rad/s. In numerical examples, we will also consider model dielectric functions for octane and pentane obtained from Mahanty and Ninham [13]. This will demonstrate that the frequency-dependent membrane dielectric function has a strong influence on the dispersion self-free energy.

There will in general also be contributions from the dispersion interaction free energy. It is straightforward to extend the expression for the complete dispersion energy (that includes both self-energy and interaction energy) of an atom in a thin film given by Mahanty and Ninham (Eq. (4.105) of [13]) to include the effect of finite temperature. Thin membranes are typically around 20–100 Å thick. In the numerical examples, we will consider a 20 Å thick membrane. The reason for our choice of such a thin membrane is to demonstrate that, for all practical purposes, the effects of ionic dispersion interaction free energies are small. This modification within the membrane can be neglected as compared to the changes in bulk ionic dispersion self-free energy (dispersion interaction energies are simply the change in dispersion self-energy due to the presence of an interface, the precise analogy of image terms for the electrostatic component [13]). We have found that the contribution from dispersion interaction free energy of an ion in the film only influences the free energy in the close proximity of the interface. In the middle, it is quite negligible for any film with realistic thickness. However, as we will discuss later, ionic dispersion interaction energies acting on ions that are in the salt solution do play an important role. The image term given by Parsegian [1] gives a measurable effect in reducing the electrostatic energy in the center of the film by roughly 20%. For comparison, the dispersion self-free energy and electrostatic contributions to the transfer energy of the three anions considered are shown in Table 1. The large differences between the results found using the different sets of polarizabilities demonstrate that more accurate data for the polarizabilities and radii of ions in water and in different membranes are essential. However, the main point is that effects of ionic dispersion potentials cannot be ignored. They contribute almost as much as the main electrostatic contribution and clearly are as large as the experimentally observed ion-specific effects. In the following section, we will discuss some further complications that should be included in a more refined theoretical analysis.

Table 1
Different contributions to the transfer energy of three anions (Cl^-, Br^-, and I^-) are shown

	Cl^-	Br^-	I^-
F^{disp}(expected) [kJ/mol]	21.75	23.32	20.64
F^{disp}(adjusted) [kJ/mol]	48.67	44.88	27.37
$F^{electrostatic}$ [kJ/mol]	187.10	172.78	153.93
F^{total}(expected) [kJ/mol]	208.85	196.11	174.57
F^{total}(adjusted) [kJ/mol]	235.77	217.66	181.31

These contributions are the dispersion self-free-energy (using expected and adjusted polarizabilities), electrostatic transfer energy (Born+image), and the sum of electrostatic and dispersion self-free energies.

3. Different effects that influence anion permeation and comparison with experiments

In this section, we discuss how self-free energies influence ion permeation occurring via the solubility-diffusion mechanism. We will also consider some additional effects that complicate the theoretical analysis of ion permeation across membranes and make a qualitative comparison with trends in some experiments.

The permeability of a (hydrocarbon) membrane to ions is directly related to the Gibbs free energy of transfer (it is proportional to $\exp[-G/k_{\mathrm{B}}T]$). At a fixed bulk concentration, the experimental flux of anions across rat liver lysosome membranes decreases in the order thiocyanate, nitrate, iodide>bromide>chloride>sulfate [3]. The same order has been found in permeation of anions across different lipid bilayer membranes [5,15]. The experimental results support diffusion as a mechanism for anion transfer in these cases, and the transfer self-free-energy should increase in the order iodide<bromide<chloride. This is exactly the same trend that we find theoretically. However, it is important to stress that the results given in the previous section are not yet good enough to compare with experiments in quantitative detail.

One complication is the fact that the radii used for the electrostatic and electrodynamic dispersion self-free energy contributions are not treated in a consistent way. Different groups have taken opposite points of view on which radii should be used for the electrostatic contribution. Some have argued that one should use hydrated radii [5], and others the bare ion radii [16,17]. This conceptually important problem is not with dispersion forces or dispersion self-energies but with the electrostatic contribution. Pauling radii usually used in electrolytes are deduced from crystal radii, assuming a hard core model for ions, or else they are arbitrarily "hydrated" fitting radii (fitted, say, to activity coefficients at low concentrations). In fact, the radius is always of quantum mechanical origin, and one needs to take into account of the Gaussian spread of the polarizability derived rigorously from quantum mechanics. Mahanty and Ninham [13] accounted for this in their work on the dispersion self-energy, and we will, in the near future, come back to how this also needs to be taken into account for the electrostatic contributions. Here, we will mainly focus on the electrodynamic dispersion contributions.

3.1. Membrane-induced surface potential effects

Before we compare with general trends from experiments, we first discuss a few other effects that influence ion permeation. It is essential to note that self-free energies are clearly not the entire story. Chloride, cation, and water molecule permeabilization across human red blood cell membranes depends strongly on the choice of anions of the background salt solution [6,18–24]. The permeability of radiolabeled albumin across bovine pulmonary arterial endothelial monolayers also depends on the choice of anions in background salt solution [25]. These effects cannot be explained as self-energy effects since they depend on other species. As discussed recently by Boström et al. [26], ionic dispersion potentials acting between ions in salt solution and a membrane surface can give rise to a substantial and highly ion-specific membrane potentials at physiological concentrations (say, around 0.1 M and above). This leads to an ion-specific electric field inside the membrane and an ion-specific membrane potential ($\Delta\phi$). The contribution from the membrane potential to the total (Gibbs) free energy is

$$\Delta G = -q\Delta\phi,$$

where q is the ion charge. This should be accounted for in a detailed investigation of ion permeation.

3.2. Effects of ion concentration near a membrane surface

In a series of papers Wieth et al. investigated the effect of salt on the permeability of human red blood cells. They found that, under normal conditions, the human red blood cell "prefers" Cl^- over K^+ by a factor of 10^6. With 0.12 M chloride anions replaced with salicylate anions, the human red blood cell "prefers" K^+ over Cl^- by a factor of 2! This is inexplicable via electrostatic theories. We propose that one reason for this is that salicylate anions are attracted (much more than chloride anions) towards the cell membrane by ionic dispersion potentials. This adsorption gives rise to an electrostatic potential that favors potassium ions near the interface, while the surface chloride concentration will be much reduced. In other words, the "effective charge" of the red cell may change sign when the anion of the background salt is changed. An unknown referee has suggested that the dielectric constant might increase towards the edges of a membrane. This would probably not influence much the self-energy in the membrane, which is the focus of this paper (at least not in the middle of the membrane), but it would increase the ionic dispersion potential attracting ions in solution towards the solution–membrane interface.

3.3. Ion-specific membrane charge effects

To rehearse the arguments so far, we have mentioned three effects that should be considered if we are to understand ion-specific permeation. These are ionic self-energy, membrane potential, and the surface concentration of ions. Another very important factor is the fact that ions influence pH and charges of membrane-bound proteins in a highly specific way. It has been observed experimentally that nitrate anions have a larger affinity for hemoglobin than chloride. The membrane-bound protein hemoglobin, not only buffers the human red blood cell, but also regulates the charge. To put this in other words, the charge of the human red blood cell membrane will be different in different salt solutions. This is because both the pH of the salt solution and the ionic distributions (including the hydronium ions that regulate the charge) at the protein surface depend on the choice of background salt. In this connection, Baglioni et al. (to be published) in Florence have recently demonstrated that, under certain circumstances, one could replace 0.5 M NaCl with 0.1 M NaSCN and get the same pH in a cytochrome *c* solution. The buffer capacity of a protein solution increased with increasing salt concentration and with increasing ionic polarizability. Similar effects must clearly also be present in the human red blood cell. We will explore this effect elsewhere, but it is important to stress that the charge of membranes with embedded proteins will be ion-specific for this reason. This circumstance then gives rise to further ion specificity for the membrane permeation of anions. There may also be ion-induced conformational changes in membranes [27]. Gurau et al. [27] presented experimental surface potentials with trends that conform nicely with the theoretical result presented by us recently [26] and new experimental results that provide experimental support for the view that the observed Hofmeister series usually has less to do with bulk water structure than with ion–surface interactions. There can be different situations where different effects (self-free energies, surface potential, surface concentration of ions, membrane charge, and ion-induced changes in the membrane) can be the more important one(s).

3.4. Qualitative comparison with experiments

We will now discuss the experimental results of Paula et al. [5] in some details. They fitted their experimental permeation with one ion-specific term and used a common hydrated ionic radius for the Born self-energy of chloride, bromide, and iodide. Their calculations were based on few assumptions concerning the prefactors for the ion permeation and left some uncertainty about how accurate their transfer free energies are. However, in the light of the limitations that our theoretical results have (in detailed ionic properties), we should be quite happy if we can compare with the general trends. Paula et al. found a common electrostatic contribution of 79.09 kJ/mol for all three anions. They then further estimated a "hydrophobic" contribution to be −29.02 kJ/mol and some kind of effective dipole potential contribution to be −23.15 kJ/mol (this dipole potential depends on surface potentials but also on charges of embedded charge groups). They then added an additional ion-specific term (of unknown origin) of 10, 5, and 0.5 kJ/mol for Cl^-, Br^-, and I^-. Clearly, the differences in our calculated transfer energies between different anions (from the results presented in Table 1) are all larger than what Paula et al. used. We find, for instance, that, using the "expected" polarizabilities for chloride and bromide, the difference in transfer energy for these two anions are 12.7 kJ/mol if the total contribution is included, while it is 14.3 kJ/mol if only the electrostatic contribution is included. These values of course depend strongly on the ionic radii, ionic polarizabilities, and dielectric properties assigned to the membrane.

The total transfer energies of individual anions that we obtained here are much too large as compared to the results obtained by Paula et al. This provides strong motivation for us to come back in a later publication to a consistent treatment for the spread of the polarizability and evaluation of dispersion and electrostatic contributions consistently and together (it is not only important to do the electrostatic contribution properly as was done for the dispersion contribution, but they have to be treated together). Here, we focus on the contribution from dispersion self-free energies that are exactly of the right order of magnitude when compared to experimental ion specificity. What we will demonstrate is that this contribution is important but that there is need to improve our knowledge of ion polarizabilities and ion radii in different phases. There is reasonably large spread in these parameters between results used, calculated, or estimated by different groups. We will fix the radii at the values given in Section 2 and consider how the dispersion self-free energy differs when different polarizabilities and membrane dielectric properties are used. Using the polarizabilities suggested by Tavares et al. [9] for ions in water, we find a dispersion contribution of 13.4 kJ/mol for chloride and 12.3 kJ/mol for bromide in the model membrane. If we instead use these model polarizabilities together with the model dielectric functions for octane and pentane [13], we find 6.3 and 10.1 kJ/mol for chloride and 5.7 and 9.5 kJ/mol for bromide. The model polarizabilities calculated by Netz [28] for ions in air and water have, in our opinion, too low resonance frequencies. We still use these values (with properties in membrane replaced by those in air) to see how changes in frequency dependence of ions in different phases may potentially have a strong influence. In the model membrane, we then find a contribution from dispersion transfer self-free energy of 7.5 kJ/mol for chloride, and, for bromide, it is even an energy gain of −15.1 kJ/mol. Different simulations have suggested that the static polarizability of chloride in water should be around 4 Å^3. If we use this value both in water and membrane, together with a typical resonance frequency of 10^{16} rad/s, we find a dispersion self-free energy of 17.4 for the model membrane, 12.6 kJ/mol with a "pentane membrane," and 8.2 kJ/mol with an "octane membrane." The upshot is that however we vary ionic and membrane parameter within a wide range, dispersion self-free energies are important and cannot be ignored, but better knowledge of the properties of ions in different phases and of the dielectric properties of membranes is essential. At the present stage, with or without contributions from dispersion self-free energy, theory is still not accurate enough for detailed comparison with experiments. The only thing we can honestly conclude is that dispersion self-free energies are important and that they do give the right trends when compared to experiment.

4. Towards consistency between ion permeation, solvation energies, and the surface tension of electrolytes

To reinforce the inferences of the previous section, we here briefly describe how an understanding of the air–water interface emerges when one realizes that the interfacial region in some sense can be considered as a very thin "membrane" with different dielectric properties than those of bulk water. There has been controversy in the literature on the true origin of the ion-specific surface tension of salt solutions, which remained unexplained. We have demonstrated earlier that inclusion of ionic dispersion potentials acting between ions and the air–water interface gives surface tension changes with added salt of the right order of magnitude [8]. However, the calculations gave an incorrect Hofmeister series [11]. Jungwirth and Tobias demonstrated that simulations that include static ion polarizabilities give the right Hofmeister series, but the values obtained were a factor of 2 too large (and calculated surface tension and freezing temperature of pure water were incorrect) [29]. We have recently demonstrated how it is possible to better unravel this problem—by inclusion of dispersion self-energies, exactly as for our membrane problem (Boström et al., submitted for publication). We will here summarize the essential features of that work since it demonstrates that one can find consistency between the ion-specific surface tension of electrolytes, solvation energies, and membrane permeation.

To proceed, in the air–water interfacial region towards the interface, there is a transition region, around 6 Å thick, with increasing concentration of dissolved gas and decreasing concentration of water molecules. This means that the self-energy of the ion will increase as it goes towards the interface (there will also be some influence of the anisotropic ordering of water). While the solvation energy of ion pairs is well known, it is less well described for single ions. We used, for demonstrational purposes, the results given by us elsewhere [17]. The solvation energies of Na^+, F^-, Cl^-, Br^-, and I^- can then be estimated to be around 407.6, 502.7, 361.8, 334.3, and 209.5 kJ/mol (of these solvation energies, around 10–30% comes from dispersion self-free energies). We have demonstrated elsewhere how the profile of water near the air–water interface gives rise to a distance-dependent change in the free energy of ions near the interface. This gives rise to a repulsive force acting on the anions going in the sequence $F^- > Cl^- > Br^- > I^-$. This correlates perfectly with the observed Hofmeister series observed in experiments on surface tension of electrolytes. One can then demonstrate that inclusion of ionic dispersion potentials further improves the agreement with experiments. We find exactly the right magnitude for surface tension changes with added salt (and also for surface potentials) when both self-free energy changes and ionic dispersion potentials are accounted for. More importantly, we demonstrated that it is the inclusion of solvation energies that is the origin of the observed Hofmeister sequence in interfacial tensions. This is interesting and demonstrates that a more accurate investigation of the air–water interface has to take into account how the dielectric properties of water changes near the interface and how the ion self-free energy changes when the ion moves towards the interface. We have recently submitted the result of such investigation to Langmuir, but we would like to emphasize again that it is the inclusion of self-free energy effects (electrostatic and dispersion) that give consistency between experimental results observed for ion permeation across membranes and for the surface tension of electrolytes.

In cases where ions go from one phase to another (as they do in ion permeation, at air–water interface, and at bubble surfaces), the change in water and dissolved gas densities will give important self-free energy contributions. In other cases, these effects will be much smaller, and specific ion effects are then dominated by ionic dispersion (interaction) potentials. However, it is in general important to also consider possible changes in self-free energies as ion approaches any interface. Some proteins are, for instance, known to "bind" water (i.e., have a slightly larger water density than the surrounding solution), in other cases, for example, near some "active sites" on proteins, water seems to be expelled.

5. Conclusions

The permeability of the membrane to ions is directly related to the Gibbs free energy of transfer (it is approximately proportional to $\exp[-G/k_BT]$). In the expression for the transfer Gibbs free energy, the dispersion part may well contribute almost one-third of the total energy. It is clear that it is fundamentally wrong to ignore this contribution as has been done. It may be a smaller effect for some anions and for some membranes, but the point is that it is essential to include the dispersion self-free energy in any realistic modeling of ion permeation. It has earlier been proven that the incorrect separation of electrostatic and electrodynamic forces in double-layer theory of colloid stability is one of the reasons why theory for more than 50 years failed to understand the ion specificity endemic in colloid science [7]. It is equally incorrect to ignore the electrodynamic dipolar polarization contributions to the self-free energy. We have demonstrated that highly ion-specific results follow when this defect in the theory is corrected. We have also highlighted the pressing need for more simulations and experiments that can provide better knowledge of the polarizabilities and radii of ions in solution, in membranes, and in air. In a more refined continuum theory, one ought to evaluate the dispersion and electrostatic self-energies together for a charged and polarizable particle. We will address this important point in a subsequent publication. Simulations that include the polarizability of ions [29–32] would appear to be a very promising avenue for future understanding of permeation of ions across membranes, especially when dispersion self-free energies in the future are included correctly. Including dispersion self-energy effects must clearly also be important in many other cases, such as for a correct understanding of ion exchange in micellar solutions [33,34].

Acknowledgements

M.B. is grateful for financial support from the Swedish Research Council. We are grateful to E. Fratini, B. Lonetti and P. Baglioni for kindly letting us refer their unpublished data.

References

[1] A. Parsegian, Energy of an ion crossing a low dielectric membrane: solutions to four relevant problems, Nature 221 (1969) 844–846.

[2] J.P. Dilger, S.G.A. McLaughlin, T.J. McIntosh, S.A. Simon, The dielectric constant of phospholipid bilayers and the permeability of membranes to ions, Science 206 (1979) 1196–1198.

[3] A.R. Klemm, K.L. Pell, L.M. Anderson, C.L. Andrew, J.B. Lloyd, Lysozyme membrane permeability to anions, Biochim. Biophys. Acta 1373 (1998) 17–26.

[4] S. McLaughlin, The electrostatic properties of membranes, Annu. Rev. Biophys. Biophys. Chem. 18 (1989) 113–136.

[5] S. Paula, A.G. Volkov, D.W. Deamer, Permeation of halide anions through phospholipid bilayers occurs by the solubility-diffusion mechanism, Biophys. J. 74 (1998) 319–327.

[6] J.A. Payne, C. Lytle, T.J. McManus, Foreign anion substitution for chloride in human red blood cells: effect of ionic and osmotic equilibria, Am. J. Physiol. 259 (1990) C819–C827.

[7] B.W. Ninham, V. Yaminsky, Ion binding and ion specificity: the Hofmeister effect and Onsager and Lifshitz theories, Langmuir 13 (1997) 2097–2108.

[8] (a) M. Boström, D.R.M. Williams, B.W. Ninham, Surface tension of electrolytes: specific ion effects explained by dispersion forces, Langmuir 17 (2001) 4475–4478;
  (b) M. Boström, D.R.M. Williams, B.W. Ninham, Ion specificity of micelles explained by ionic dispersion forces, Langmuir 18 (2002) 6010–6014;
  (c) M. Boström, V.S.J. Craig, R. Albion, D.R.M. Williams, B.W. Ninham, Hofmeister effects in pH measurements: role of added salt and co-ions, J. Phys. Chem., B 107 (2003) 2875–2878;
  (d) M. Boström, D.R.M. Williams, B.W. Ninham, Specific ion effects: role of salt and buffer in protonation of cytochrome *c*, Eur. Phys. J., E Soft Matter 13 (2004) 239–245.

[9] F.W. Tavares, D. Bratko, H.W. Blanch, J.M. Prausnitz, Ion-specific effects in the colloid–colloid or protein–protein potential of mean force: role of salt–macroion van der Waals interactions, J. Phys. Chem., B 208 (2004) 9228–9235.

[10] E. Leontidis, Hofmeister anion effects on surfactant self-assembly and the formation of mesoporous solids, Curr. Opin. Colloid Interface Sci. 7 (2002) 81–91.

[11] W. Kunz, P. Lo Nostro, B.W. Ninham, The present state of affairs with Hofmeister effects, Curr. Opin. Colloid Interface Sci. 9 (2004) 1–18.

[12] H.-K. Kim, E. Tuite, B. Norden, B.W. Ninham, Co-ion dependence of DNA nuclease activity suggests hydrophobic cavitation as a potential source of activation energy, Eur. Phys. J., E Soft Matter 4 (2001) 411–417.

[13] J. Mahanty, B.W. Ninham, Dispersion Forces, Academic, London, 1976.

[14] M. Boström, Bo E. Sernelius, Wetting problems for coatings on windshields, Appl. Surf. Sci. 142 (1999) 375–380.

[15] J. Gutknecht, J.S. Graves, D.C. Torsteson, Electrically silent anion transport through lipid bilayer membranes containing a long-chain secondary amine, J. Gen. Physiol. 71 (1978) 269–284.

[16] A.A. Rashin, B. Honig, Reevaluation of the Born model of ion hydration, J. Phys. Chem. 89 (1985) 5588–5593.

[17] M. Boström, B.W. Ninham, Contributions from dispersion and Born self-free energies of salt solutions, J. Phys. Chem., B 108 (2004) 12593–12595.

[18] G.F. Baker, P. Baker, Temperature dependence of the exchange of monovalent anions in human red cells, Biochim. Biophys. Acta 1285 (1996) 192–202.

[19] R. Serrani, D. Taborda, M. Zamero, J.L. Corch, Foreign anion substitution for chloride in neonatal human red cells. Effect on cellular volume, Arch. Physiol. Biochem. 103 (1995) 91–97.

[20] M. Dalmark, Chloride and water distribution in human red cells, J. Physiol. 250 (1975) 65–84.

[21] J.O. Wieth, Effect of some monovalent anions on chloride and sulphate permeability of human red cells, J. Physiol. 207 (1970) 581–609.

[22] M. Dalmark, J.O. Wieth, Temperature dependence of chloride, bromide, iodide, thiocyanate, and salicylate transport in human red cells, J. Physiol. 224 (1972) 583–610.

[23] J.O. Wieth, Effects of bicarbonate and thiocyanate on fluxes of Na and K, and on glucose metabolism of actively transporting human red cells, Acta Physiol. Scand. 75 (1969) 313–329.

[24] J. Funder, J.O. Wieth, Effects of some monovalent anions on fluxes of Na and K, and on glucose metabolism of ouabain treated human red cells, Acta Physiol. Scand. 71 (1967) 168–185.

[25] M.P. Griffin, Role for anions in pulmonary endothelian permeability, J. Appl. Physiol. 83 (1997) 615–622.

[26] M. Boström, D. Williams, P. Stewart, B.W. Ninham, Hofmeister effects in membrane biology: the role of dispersion potentials, Phys. Rev., E 68 (2003) 041902.

[27] M.C. Gurau, S.-M. Lim, E.T. Castellana, F. Albertorio, S. Kataoka, P.S. Cremer, On the mechanism of the Hofmeister effect, Am. Chem. Soc. 126 (2004) 10522–10523.

[28] R.R. Netz, Water and ions at interfaces, Curr. Opin. Colloid Interface Sci. 9 (2004) 192–197.

[29] P. Jungwirth, D.J. Tobias, Chloride anion on aqueous clusters, at the air–water interface, and in liquid water: solvent effects on the Cl^- polarizability, J. Phys. Chem., A 106 (2002) 379–383.

[30] (a) L. Perera, M.L. Berkowitz, Erratum: many-body effects in molecular dynamics simulations of Na+(H 20)n and Cl(H 2 0)n clusters, J. Chem. Phys. 99 (1993) 4236–4237;
  (b) I.-C. Yeh, L. Perera, M.L. Berkowitz, Photodetachment spectra of $Cl^-(H2O)_n$ clusters. Predictions and comparisons, Chem. Phys. Lett. 264 (1997) 31–38.

[31] L.X. Dang, A mechanism for ion transport across the water/dichloromethane interface: a molecular dynamics study using polarizable potential models, J. Phys. Chem., B 105 (2001) 804–809.

[32] A. Grossfield, P. Ren, J.W. Ponder, Ion solvation thermodynamics from simulation with a polarizable force field, J. Am. Chem. Soc. 125 (2003) 15671–15682.

[33] Z.-M. He, P.J. O'Connor, L.R. Romsted, D. Zannete, Specific counterion effects on indicator equilibria in micellar solutions of decyl phosphate and lauryl sulfate surfactants, J. Phys. Chem. 93 (1989) 4219–4226.

[34] F.H. Quina, M.J. Politi, I.M. Cuccovica, E. Baumgarten, S.M. Martins-Franchetti, H. Chaimovich, Ion exchange in micellar solutions: 4. "Buffered" systems, J. Phys. Chem. 84 (1980) 361–365.