Current Opinion in Colloid & Interface Science 23 (2016) 10–18

Contents lists available at ScienceDirect

Current Opinion in Colloid & Interface Science

journal homepage: www.elsevier.com/locate/cocis

Reversed Hofmeister series—The rule rather than the exception

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ARTICLE INFO

Article history:
Received 20 January 2016
Accepted 29 April 2016
Available online 14 May 2016

Keywords:
Hofmeister series
Reversal
Surface charge
Salt concentration
Hydrophobicity
pH
Poisson–Boltzmann theory
Molecular dynamics simulations
AFM

ABSTRACT

Over recent years, the supposedly universal Hofmeister series has been replaced by a diverse spectrum of direct, partially altered and reversed series. This review aims to provide a detailed understanding of the full spectrum by combining results from molecular dynamics simulations, Poisson–Boltzmann theory and AFM experiments. Primary insight into the origin of the Hofmeister series and its reversal is gained from simulation-derived ion–surface interaction potentials at surfaces containing non-polar, polar and charged functional groups for halide anions and alkali cations. In a second step, the detailed microscopic interactions of ions, water and functional surface groups are incorporated into Poisson–Boltzmann theory. This allows us to quantify ion-specific binding affinities to surface groups of varying polarity and charge, and to provide a connection to the experimentally measured long-ranged electrostatic forces that stabilize colloids, proteins and other particles against precipitation. Based on the stabilizing efficiency, the direct Hofmeister series is obtained for negatively charged hydrophobic surfaces. Hofmeister series reversal is induced by changing the sign of the surface charge from negative to positive, by changing the nature of the functional surface groups from hydrophobic to hydrophilic, by increasing the salt concentration, or by changing the pH. The resulting diverse spectrum reflects that alterations of Hofmeister series are the rule rather than the exception and originate from the variation of ion-surface interactions upon changing surface properties.

1. Introduction

Most processes in electrolyte solutions depend not only on the salt concentration or valency of the ions but also on ion type. These ion specific effects are ubiquitous and appear in a large variety of physical properties such as osmotic coefficients, solubility of gasses and colloids, protein precipitation and crystallization, catalysis of chemical reactions or enzyme activity [1], suggesting a common origin of these vastly different phenomena [2•,3–6,7•,8,9•]. In most cases, anions and cations can be ranked reproducibly in a Hofmeister series according to their influence on these macroscopic properties [10]. Due to the widespread applicability and robustness of the same series in bulk, as characterized for example by the ionic solvation free energy, ion specific effects have traditionally been attributed to changes that ions provoke in the surrounding water. However, this simple explanation and the universality of the Hofmeister series have been called into question based on two important observations: First, recent experiments have demonstrated that ions do not perturb the water hydrogen bonding network beyond their first hydration shell [11–13]. Therefore, it is unlikely that the series originates solely from structuring effects of water induced by ions. Consequently, direct ion-macromolecule interactions are more important for ion specific phenomena than bulk ion properties [14,15•,16]. Secondly, over the past years a diverse spectrum of direct, altered and reversed Hofmeister series has been discovered that is not mirrored by a similar modification of the bulk series. Dependent on parameters like surface charge, surface polarity, temperature, salt concentration, pH, and buffer type the ordering of the ions within the series can be changed [17•,18,19••,20•,21,22,23••]. To give a few explicit examples, the aggregation of negatively charged proteins and colloids follows the usual direct Hofmeister series while cationic proteins [19••,24,25,26•] and cationic colloids [27••,28] show the opposite ordering. In colloidal systems, which allow to independently control surface polarity and surface charge, yet another reversal occurs when changing the surface properties of the particles from hydrophobic to hydrophilic [27••,28,29]. Finally, Hofmeister series reversal by pH has also been observed for surfaces containing dissociable functional groups [23••,30••,31,32,33•].

This lack of universality of the Hofmeister series has changed our current understanding of the series origin. By now, we know that ion specific effects are caused by ion accumulation or depletion from the solute/water interface [34]. Therefore, it is not surprising that the ion–surface affinity, and therefore the ranking in the Hofmeister series,

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http://dx.doi.org/10.1016/j.cocis.2016.04.003
1359-0294/

changes if surface properties like hydrophobicity, charge, or chemical structure of surface groups are varied [35,36]. However, the detailed mechanism by which ions are attracted to or repelled from interfaces is complex and results from the competition of direct ion–surface and indirect hydration-related interactions [37]. For simple non-polar surfaces like the air/water interface or the interface between water and a hydrophobic solid or liquid, the adsorption propensity of large anions such as iodide [38,39] can be rationalized in terms of hydrophobic solvation theory adapted to interfaces [40,41•,42,43••]. Some theories discuss the enhanced surface affinity also in terms of the ion polarizability [42,44], which is proportional to the ion volume and thus scales similarly as the hydrophobic solvation contribution. Ion accumulation and depletion at interfaces can be captured by simplified ion-surface interactions, which allow us a global analysis of interfacial ionic distributions and ion specific behavior [45]. However, a general theory that quantifies ion–surface interactions and encompasses hydrophobic as well as hydrophilic surfaces is still missing, due to the complex interactions between surface groups, ions and water. An indispensable tool for gaining insight into the adsorption propensity of ions to different interfaces are all-atom molecular dynamics (MD) simulations in explicit water, which account for the subtle interplay of ion hydration in bulk and partial ion dehydration upon surface binding. Effective ion–surface interactions can be derived from these simulations [38,44,46••,47•] and incorporated into multiscale theories [44,46••,48•], thereby providing a link between the microscopic adsorption behavior of the ions and macroscopic, experimentally accessible quantities.

In this review, we summarize our recent work and provide insight into the full spectrum of direct, reversed, and altered anionic and cationic Hofmeister series. In particular, we uncover the effects of surface charge, surface hydrophobicity and pH on the ordering of halide anions and alkali cations. First, detailed insight into the interplay of direct ion–surface interactions and the role of ion hydration is derived from all-atom MD simulations in explicit water at surfaces containing non-polar methyl (CH_3), polar hydroxide (OH), polar carboxyl (COOH), and charged carboxylate (COO^-) surface groups. Ion specific binding affinities to the different surface groups are quantified by calculation of the free energy profile or potential of mean force (PMF) underlying ion adsorption or depletion. For anions, a clear reversal of the surface affinity is observed if non-polar surface groups are replaced by polar or charged groups. For cations, a diverse spectrum of direct, reversed and partially reversed series based on single-ion binding affinities to non-polar, polar and charged groups is encountered, which makes cations less regular compared to anions. In a second step, the ion–surface interaction potentials are embedded into the Poisson–Boltzmann theory to yield the ranking of anions and cations based on macroscopic quantities. In particular, the long-ranged electrostatic forces, which stabilize solutes against precipitation due to van-der-Waals attraction, are quantified in different electrolyte solutions and compared to precise AFM measurements of forces between silica surfaces. Based on these forces, the direct Hofmeister series is obtained for negatively charged non-polar surfaces. Hofmeister series reversal or partial alterations are induced by changing the sign of the surface charge from negative to positive, by changing the nature of the functional surface groups from hydrophobic to hydrophilic, by increasing salt concentration, or by changing the pH for surfaces containing acidic surface groups. In all cases, Hofmeister series reversal emerges as a direct consequence of specific ion adsorption at the surface leading to enhancement or reduction of the effective surface charge and the associated electrostatic force of stabilization.

2. Methods

2.1. Simulations and Poisson–Boltzmann theory

2.1.1. Multiscale modeling approach

We use a two-step modeling approach that has been described in detail in refs. [33•,43••,46••]. Briefly, in the first step, explicit solvent molecular dynamics (MD) simulations are used to calculate single ion-surface interaction potentials for halide anions and alkali cations at surfaces containing hydrophobic methyl (CH_3), polar hydroxide (OH), polar carboxyl (COOH), and charged carboxylate (COO^-) surface groups. In the second step, these interaction potentials are imported into the Poisson–Boltzmann theory to calculate the ionic density profiles and the electrostatic potential at surfaces of arbitrary charge and for finite ion concentrations.

2.1.2. MD simulations

In the simulations the surface is a 3.5×3.46 nm^2 self-assembled monolayer (SAM) consisting of 56 $C_{20}H_{41}$ chains with different terminal groups. The simulation box has an extension of 9 nm in the *z*-direction and is filled with about 2700 SPC/E water molecules. The SAM is modeled with the GROMOS96 force field [49]. To ensure correct ion–water and ion–ion interactions, we use previously optimized force field parameters for anions and cations [50•] that reproduce thermodynamic solvation properties and yield accurate ion pairing properties as judged by comparison with experimental osmotic coefficient data [51]. The simulations are done at a temperature of 300 K and a pressure of $P_z = 1$ bar maintained by anisotropic pressure coupling, corresponding to the NAP_zT ensemble using the Gromacs simulation package [52]. Periodic boundary conditions are applied, long range Coulomb forces are calculated using the particle-mesh Ewald summation [53] and for the van-der-Waals interactions a cutoff radius of 1.2 nm is used. A single ion is placed into the water phase and its potential of mean force (PMF) is calculated by umbrella sampling [54] with a window spacing of 0.025 nm and 3–10 ns simulation time discarding the first 1 ns for equilibration. A time step of 2 fs and the weighted histogram analysis method [55] with force constant $k_z = 1000$ kJ/(mol nm^2) is used. For the charged surface, we use an additional two-dimensional harmonic potential with $k_BT/k_{x,y} = 0.0145$ nm^2 to laterally confine the ion above the charged group.

2.1.3. Poisson–Boltzmann modeling

In our multiscale modeling we consider two limiting scenarios for the surface charge density. In the first scenario, we assume evenly distributed charges and the chemical structure of the surface groups remains unchanged. In this scenario, we allow both polar hydroxide and non-polar methyl surface groups to carry a net charge. This corresponds to a situation where the charge is distributed evenly over the surface and can be realized experimentally by using back-gated semiconductors or self-assembled monolayers [56]. This distinction between surface polarity and surface charge corresponds to an idealized limit and allows us a successful classification in line with a broad range of different colloidal surfaces [27••,28]. In the second scenario, we model the pH dependent deprotonation of carboxylic surface groups. Thereby, we not only change the surface charge density but also the chemical structure of the surface group. Here, the surface acquires charges by deprotonation. Prominent examples are minerals with hydroxide surface groups and proteins with carboxyl surface groups [57]. To account for surfaces of varying hydrophobicity (scenario 1) or of varying degree of deprotonation (scenario 2), we use a molecular-scale approach, where the effective ion–surface interaction results from the weighted average of the potentials of the polar OH (V_i^{phil}) or non-polar CH_3-groups V_i^{phob} and the uncharged COOH (V_i^{COOH}) or charged COO^--groups ($V_i^{\mathrm{COO^-}}$) [43••]. The PB equation including the ion specific PMFs of anions and cations for two different surface groups then reads

$$\epsilon\epsilon_0 \frac{d^2}{dz^2}\Phi(z) = \sum_{i=\pm} q_i c_i(z) \tag{1}$$