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# Can Polyoxometalates be considered as super-chaotropic ions?

Carlos Drummond<sup>a,b</sup>, Leonor Pérez-Fuentes<sup>c</sup>, Delfi Bastos-González\*<sup>c</sup>

<sup>a</sup> CNRS, Centre de Recherche Paul Pascal (CRPP), UPR 8641, F3300, Pessac, France

<sup>b</sup> Université Bordeaux, CRPP, F-33600 Pessac, France

<sup>c</sup> Biocolloid and Fluid Physics Group, Department of Applied Physics

University of Granada, Av. Fuentenueva S/N, 18071 Granada (Spain)

e-mail: [dbastos@ugr.es](mailto:dbastos@ugr.es)

## Abstract

In this work we have studied the influence of different anionic species, including typical Hofmeister ions (citrate<sup>3-</sup> and SCN<sup>-</sup>), hydrophobic ions (tetraphenyl borate, Ph<sub>4</sub>B<sup>-</sup>) and polyoxometallic clusters (Keggin-type POM, PW<sup>3-</sup>), on the electrophoretic mobility of colloidal particles of different nature, charge and wettability. We focused the attention on the adsorption properties of PW<sup>3-</sup> in comparison with Ph<sub>4</sub>B<sup>-</sup> because both species have previously been termed as super-chaotropes. However, their different structural properties make it difficult to reconcile the same classification for both anions. We found that the influence of Ph<sub>4</sub>B<sup>-</sup> is alike and surpasses the characteristic effect of chaotropic anions (SCN<sup>-</sup>), in particular interacting more strongly with hydrophobic interfaces. On the contrary, we observed clear POM adsorption on the different particles investigated, regardless of their charge or wettability. These observations are complemented by direct adsorption measurement combining Quartz Crystal Microbalance and Atomic Force Microscopy, confirming the strong and irreversible self-assembly of POM on different substrates. Our results indicate that polyoxometallic anionic clusters should better be described as small colloids instead of as large anions. The exceptional adsorption properties of POMs clusters on any kind of interface suggest that their behavior goes beyond the classical Hofmeister effects and, therefore, these species should not be included in the Hofmeister series as super-chaotropic anions.

## Introduction

Most of the relevant interactions of macromolecules or colloids in water occur in presence of ions. The type and amount of ions in solution can modulate the macromolecular interaction, which can even be changed from attractive to repulsive, modifying their conformation, stability and activity.<sup>1,2</sup> The importance of these ion-specific interactions, whose origin is far more complex than the pure ionic valence, have attracted the attention of many groups. The first researcher that studied in a systematic way the influence of different ions in the interaction of proteins was Franz Hofmeister. For this reason, the Specific Ion Effects (SIE) are customarily known as Hofmeister Effects (HE) and the classification of the ions in systematic sequences refers as Hofmeister series (HS) or lyotropic series. After these initial studies, researchers have found a plethora of interacting systems and properties where SIE or HE manifest.<sup>3</sup> In addition, a number of ions have been added and classified into the HS during the last years. Figure 1 shows an up-to-date representative direct HS for anions; as SIE are typically more marked for anions than for cations, the specific effect of negatively charged ions has been investigated to a larger extent.

Nowadays, it is widely accepted that ionic hydration is an important parameter determining ionic specificity.<sup>1,4,5</sup> In accordance, the classification of the ions in the HS of Figure 1 is related with their degree of hydration.  $\text{Na}^+$  and  $\text{Cl}^-$  are usually considered as indifferent ions in the HE. Anions on the right of  $\text{Cl}^-$  are less hydrated than  $\text{Cl}^-$  and are known as chaotropes and anions on the left of  $\text{Cl}^-$  are more hydrated than  $\text{Cl}^-$  and are known as kosmotropes. Originally, the terms kosmotrope and chaotrope were related with the capability of the ions to modify the structural arrangement of water, but these ideas are still controversial (see the analysis of E. Leontidis<sup>5</sup> about these terms). However, kosmotrope and chaotrope terms are widely used in the studies of HE; we apply them exclusively in relation with the ionic hydration degree. In this sense, kosmotropicity is associated with a highly hydrated ion while chaotropicity is related with a poorly hydrated one. It has also been shown that the ionic character is strongly associated with the  $B$ -coefficient of the linear term in the Jones-Dole viscosity equation; larger positive  $B$  values are typically observed for more kosmotropic ions, while negative  $B$  values point to chaotropicity.<sup>6,7</sup> On the contrary, attempts to classify the kosmotropic or chaotropic character of the ions only considering their size and/or polarizability has been unsuccessful. For example, the halide sequence  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$  and  $\text{I}^-$  (from more kosmotropic

to more chaotropic) can be suitably explained considering both size and polarizability parameters. However, if the corresponding halate ions ( $\text{ClO}_3^-$ ,  $\text{BrO}_3^-$  and  $\text{IO}_3^-$ ) are considered, ionic size and polarizability cannot explain accurately their position in the HS;  $\text{BrO}_3^-$  and  $\text{IO}_3^-$  have clearly shown a kosmotropic character.<sup>1,8,9</sup>

It has been increasingly acknowledged that ions are not the only players in SIE. Ion-specific effects deal with macromolecules, substrates or interfaces which exert some influence on the surrounding water. Thus, the effects of hydration or wettability of the interface and their interplay with the ionic environment should be considered in a comprehensive description of HE. In this sense, SIE have been qualitatively explained taking into account that chaotropic ions tend to accumulate on poorly hydrated (hydrophobic) surfaces while they are excluded from the highly hydrated (hydrophilic) ones. Conversely, kosmotropic ions tend to accumulate on hydrophilic surfaces while they are excluded from the hydrophobic ones.<sup>1,2,5,10,11,12</sup> Figure 2 shows a representation of this accumulation/exclusion mechanism, which reinforces the importance of the water structure around both, ions and surfaces, to explain HE. However, the difficulty of properly describe and introduce the terms of hydration into a theoretical model (in particular for the interfaces) has hindered the emergence of a general theory able to explain HE.

Recently, other type of ions, called super-chaotropes, has been added to the HS. These ions have similar effects than regular chaotropic ions, but to a much greater extent; for this reason, they have been located in extreme positions of the HS (see Figure 1). Examples of these ions are the tetraphenylborate ( $\text{Ph}_4\text{B}^-$ ) (see Figure 3a) anion or the tetraphenylarsonium ( $\text{Ph}_4\text{As}^+$ ) cation. Different studies have demonstrated how these ions strongly accumulate on hydrophobic surfaces while they are excluded from the hydrophilic ones, and how this accumulation augments as the hydrophobic character of the surface increases.<sup>2,8,13,14</sup> This behavior, which parallels and goes beyond what is regularly observed for inorganic ions in the original HS (e.g.  $\text{SCN}^-$  or  $\text{ClO}_4^-$ ), has motivated labeling the tetraphenyl ions as super-chaotropic. These ions has also been called “soft matter disruptors”, due to their manifest ability to disrupt the structure and phase transitions of many soft matter systems.<sup>15</sup> The inclusion of big hydrophobic monovalent charged ions in the HS reinforces the idea of the fundamental role that the solvent ion-interface interaction plays in the origin of the IES, and their connection with the hydrophobic interaction.<sup>2</sup> For monovalent ions, ion hydration and the

hydrophobic/hydrophilic character of the surfaces are essential to define the accumulation or exclusion of the ions from the interfaces and, hence, to determine their position in the HS.

Other type of anionic species called polyoxometalates, POMs, have been recently classified as super-chaotropes and introduced in the HS.<sup>16</sup> These charged metal-oxide clusters are characterized by high valences (three and higher) and very well defined molecular structures (see Figure 3b). POMs have found numerous applications in different fields as catalysis, lithography, medicine, etc. where their interaction with the interfaces plays a fundamental role.<sup>17</sup> Naskar et al. were the firsts to classify these species as super-chaotropes by studying the interaction of several POMs with nonionic surfactants.<sup>16</sup> They concluded that POMs have a tendency to adsorb on hydrophilic surfaces. More recently, part of these authors extend the study to estimate the super-chaotropic character of different type and charged POMs anions according to their affinity for polar surfaces,<sup>18</sup> although no adsorption in water-alkane interfaces was observed. A somehow different conclusion was reached by Kobayashi et al.,<sup>19</sup> who studied the interaction of POMs with different charges (3<sup>-</sup>, 4<sup>-</sup> and 6<sup>-</sup>) and several lipid monolayers to analyze the interplay between the electrostatics and hydrophobic interactions. They found that when working with the compressed lipid monolayers (hydrophobic environment) the chaotropic nature of the POMs was manifested. Chaumont et al. carried out molecular dynamic simulations of POMs with chloroform, ionic liquids and graphite and they observed that these anions tend to accumulate to some extent at the interface of the different liquids and surfaces.<sup>20</sup> These studies clearly show that POMs have interfacial activity, and seem to adsorb or accumulate on both hydrophobic and hydrophilic surfaces. However, these results related to the interaction of POMs with surfaces would be in contradiction with the definition of super-chaotrope ion proposed above for the tetraphenyl ions. This is, super-chaotrope ions should strongly accumulate on hydrophobic surfaces but they should be excluded from the hydrophilic ones, a tendency that is also observed for the monovalent chaotropic inorganic ions that belongs to HS (e.g. SCN<sup>-</sup> or ClO<sub>4</sub><sup>-</sup>).

In a different perspective, K. Assaf and W. Nau support in a recent paper that the chaotropic effect is a generic driving force for supramolecular assembly, “orthogonal” to the hydrophobic effect.<sup>21</sup> In their description, the chaotropic effect would be the force responsible for the strong interaction that very large anionic groups like dodecaborate,

$B_{12}X_{12}^{2-}$  and  $B_{12}X_{11}Y^{2-}$  ( $X= H, Cl, Br, I$  and  $Y= SH$ ), or POMs show with hydrophobic interfaces. In accordance, these groups should be classified as super-chaotropic ions. For these authors, the classification of ions as kosmotropic, chaotropic or super-chaotropic depends on hydration parameters previously proposed by Marcus.<sup>6,22</sup> In this sense, super-chaotropic ions are characterized by enthalpically driven processes with a negative entropic contribution. These super-chaotropic anions would be introduced in the extended HS between chaotropic and hydrophobic ions (e.g.  $Ph_4B^-$ ), which should not be considered as super-chaotropic.

As previously commented, the classification of the inorganic ions belonging to Hofmeister series are related to their hydration degree. Considering hydration parameters,  $Ph_4B^-$  is a hydrophobic anion, poorly hydrated, and its behavior matches the tendency observed for chaotropic ions. On the contrary,  $PW^{3-}$  is considered a hydrophilic ion,<sup>5</sup> highly hydrated and, hence, its behavior should be akin to that showed for kosmotropic ions.

These different views indicates that there is not a clear and unified concept about the meaning of super-chaotropic ion, or even of the Hofmeister series. This lack of consensus generates more confusion when it comes to understanding specific ion effects, which are already extremely complex, obstructing the development of a long-awaited general theory capable of explaining HE. It seems reasonable to explore the rationality of expanding the Hofmeister series to any type of ionic species; are all ionic effects Hofmeister effects? This study aims to contribute to the clarification of these concepts and to deepen in the origin of such phenomena.

The goal of this work is to study the electrokinetic behavior of several interfaces with different hydrophobic/hydrophilic character in presence of a typical Kegging POM,  $PW_{12}O_{40}^{3-}$  ( $PW^{3-}$ ).  $PW^{3-}$  contains a central phosphorus atom bonded to four oxygen atoms in tetrahedral configuration. These oxygen atoms are shared with 4  $W_3O_{13}$  groups (Figure 3b) arranged around the P-centred tetrahedron. Thus, the cluster has a quasi-spherical structure of ca. 0.8 nm.<sup>23,24</sup> Similarly to other heteropolyacids, 12-tungstophosphoric acid ( $H_3PW_{12}O_{40}$ ) is an extremely strong acid; thus, complete deprotonation of the anionic cluster will occur, even at very acidic conditions.<sup>25</sup> The results obtained with  $PW^{3-}$  are compared with those obtained in presence of the tetraphenyl anion,  $Ph_4B^-$ , a large hydrophobic anion (radii ca. 0.5 nm) with four phenyl rings bonded to a central boron

atom (fig. 3a),<sup>13</sup> and with archetypal chaotropic ( $\text{SCN}^-$ ) and kosmotropic ( $\text{citrate}^{3-}$ ) anions. In addition, Quartz Cristal Microbalance and Atomic Force Microscopy were used to reinforce the conclusions. All these results allow us to explore the role of the hydrophobicity of an interface in the ion-surface interaction and to revisit the concept of super-chaotropic anions.

## Methods

### Reagents and proteins

All the salts in this study were of analytical grade and used as received. Sodium phosphotungstate hydrate,  $\text{Na}_3\text{PW}_{12}\text{O}_{40}$ , (purity  $\geq 99.9\%$ ) and sodium tetraphenylborate,  $\text{NaThB}_4$ , (purity  $\geq 99.5\%$ ) were purchased from Sigma-Aldrich; sodium citrate,  $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7$ , was obtained from Scharlau. Proteins from Sigma Aldrich: Bovine Serum Albumin (BSA) (purity  $\geq 98\%$ ),  $\beta$ -lactoglobulin (purity  $\geq 90\%$ , mixture of A and B genetic variants) and  $\beta$ -casein (purity  $\geq 98\%$ ). Olive oil was obtained from Sigma Aldrich. Epikuron 145 V, was kindly provided by CargillIbérica SL. Protasan® Cl 113, and medium-molecular-weight chitosan chloride salt with a deacetylation degree of 85%, was supplied from FMC Biopolymer Novamatrix (Norway). Several buffers of ionic strength lower than 2 mM were used for particle synthesis: the solution with pH 4 was buffered with acetic acid. In each case, the pH was adjusted by adding NaOH. In addition, we used a buffered solution at pH 7 with bis-Tris in order to dissolve the  $\beta$ -casein protein. The pH of this solution was adjusted by adding HCl; the ionic strength of the solution was 2.4 mM. Non-buffered solution at pH 3 was prepared by adding dilute HCl to deionized water. Deionized Milli-Q water was used throughout.

### Nanoparticles

Eight different types of colloidal surfaces were used in this work. Two polystyrene latexes prepared by the emulsion polymerization method in absence of surfactants were used as hydrophobic particles. One of them carried a negative charge on the surface due to the presence of sulfonate groups ( $d=138\pm 7$  nm),<sup>26</sup> and the other one had positive charge coming from amine groups ( $d=475\pm 4$  nm).<sup>27</sup> The electrophoretic mobility of the positively charged latex was larger than  $3.10^{-8} \text{ m}^2\text{V}^{-1}\text{s}^{-1}$  for pH values between 3 and 10. Both latexes were supplied by IKERLAT polymers. Negatively charged monodisperse silica hydrophilic particles ( $d=150\pm 9$  nm), were prepared by a seeded-growth protocol.<sup>28</sup> Positively charged chitosan nanocapsules ( $d=281\pm 6$  nm), with isoelectric point ca. pH



7.5, were synthesized as described before.<sup>29</sup> As intermediate positive hydrophobic system, modified silica particles were obtained by silanization of silica particles by using 3-aminopropyltriethoxysilane (APTES), which provides amine groups to the surface. All the details concerning particle synthesis and characterization can be found in the corresponding references. The other three surfaces were obtained by adsorbing BSA,  $\beta$ -lactoglobulin and  $\beta$ -casein onto the negative latex. Briefly, each protein was added to an aqueous solution at the desired pH containing latex particles with a total polystyrene area of 0.3 m<sup>2</sup>. The protein concentration used was high enough to guarantee a maximum coating. Incubation was carried out at 25°C for 21 h. Then, samples were centrifuged at 25.000  $\times$  g for 30 min, and the pellets were re-dispersed and stored at the desired pH. More details can be found elsewhere.<sup>14,30</sup>

### **Electrophoretic mobility**

The measurements of electrophoretic mobility were carried out using a Zetasizer Nano Z device (Malvern Instruments). The particles were diluted to a concentration of around 10<sup>10</sup> particles per cm<sup>3</sup>. The reported data were the average of three measurements; the standard deviation was always lower than 5%. Mobility-based isotherms were measured for the different particle-ion combinations; the low-salt limit equals the electrophoretic mobility of bare particles at pH 3. All the mobility measurements were performed at pH 3 (adjusted by addition of HCl in absence of buffer) except for the case of sodium citrate; in this case the pH was a function of salt concentration.

### **Quartz Crystal Microbalance with dissipation monitoring, QCM-D**

The adsorption of POM on silica was measured in a commercial quartz crystal microbalance (QCM-D E1, Q-Sense). The principles of the technique have been extensively described in the literature.<sup>31</sup> Briefly, the resonance frequency  $f$  of a quartz resonator is measured; a change in the effective mass of the resonator due to material adsorption translates into a variation in the resonance frequency,  $\Delta f$ . In addition, the damping of the oscillation of the crystal was measured, and used to calculate the “dissipation factor”,  $D$  (inverse of the quality factor of the resonance peak).<sup>32</sup> The measured  $\Delta f$  and  $\Delta D$  can be related to the thickness and viscoelastic properties of the material adsorbed on the quartz crystal by using adequate models.<sup>31</sup> We used 5.0 MHz quartz resonators with gold electrodes, which were coated with silica thin layers. At the

beginning of each experiment the resonator was placed in the cell and immersed in Milli-Q water at pH 3 for at least 30 minutes, until a stable baseline was established.  $\text{PW}^{3-}$  adsorption was determined by measuring the response of the odd harmonics ( $n=3$  to  $n=13$ ) of the coated quartz crystals.

### **Atomic Force Microscopy, AFM**

Morphology of  $\text{PW}^{3-}$  films irreversibly adsorbed on mica was measured by Atomic Force Microscopy in tapping mode (Multimode, Bruker) using Si tips (Bruker, RTESP-300).  $\text{PW}^{3-}$  adsorption was performed by immersion of freshly cleaved mica in  $\text{PW}^{3-}$  solutions of variable concentration for 12 h, and rinsing with water at pH 3 to remove the non-adsorbed excess material.

### **Results and Discussion**

Electrophoretic mobility ( $\mu_e$ ) measurements have proved to be very useful to analyze the accumulation (adsorption) or exclusion of ions at interfaces. For this reason, we have carried out  $\mu_e$  experiments with different type of surfaces varying their degree of hydrophobicity/hydrophilicity.

We have measured  $\mu_e$  as a function of  $\text{Na}_3\text{PW}_{12}\text{O}_{40}$  concentration for three different positively charged particles: hydrophobic cationic latex, hydrophilic chitosan particles and intermediate hydrophobic/hydrophilic silica- $\text{NH}_2$  particles, which were described in the previous section. All the measurements were carried out at pH 3 to ensure the stability of POMs clusters in water.<sup>16</sup> As can be observed in Figure 4a,  $\mu_e$  goes from positive to negative values as the concentration of  $\text{PW}^{3-}$  increases for the three systems. Because all the particles are positively charged ( $\text{PW}^{3-}$  is acting as counterion) the change in the sign of the mobility signals a significant charge reversal due to POM accumulation on the particles. It is noteworthy that this reversal is observed at very low POM concentrations ( $10^{-4}$  M or below) and that very large negative  $\mu_e$  values are reached. Thus,  $\text{PW}^{3-}$  clusters strongly accumulate on the surface of the different particles independently of their wettability. However, comparing the results obtained with the different particles, the adsorption seems stronger for the most and intermediate hydrophobic particles (latex and Silica- $\text{NH}_2$ ) as the charge inversion begins at  $10^{-6}$  M ( $I= 6.10^{-6}$  M) of POM while for the most hydrophilic chitosan particles it is completed ca.  $10^{-5}$  M.

We have also measured  $\mu_e$  for  $\text{PW}^{3-}$  acting as co-ions (Figure 4b), in presence of hydrophobic anionic latex and hydrophilic silica particles. We can see that the  $\mu_e$  augments (in absolute values) as the concentration of  $\text{PW}^{3-}$  increases, indicating that ions are adsorbing on the surface of the particles despite of the repulsive electrostatic interaction. This happens for the hydrophobic and hydrophilic particles, indicating again the high affinity that POMs ions show for both types of surfaces.

We have carried out similar  $\mu_e$  measurements for the different particles in presence of the hydrophobic  $\text{Ph}_4\text{B}^-$  ions; the results are displayed in Figure 5. For the positive surfaces, i.e.  $\text{Ph}_4\text{B}^-$  acting as counter-ions, clear charge reversal is observed only for the most hydrophobic particles, while for the intermediate and hydrophilic ones no reversal is found. Thus,  $\text{Ph}_4\text{B}^-$  ions accumulate on hydrophobic surfaces but are excluded from the hydrophilic ones. Thus, a good correlation between surface wettability and ionic adsorption is observed. In fact, for the intermediate and hydrophilic particles aggregation is observed at a sufficiently large  $\text{Ph}_4\text{B}^-$  concentration (due to the screened electrostatic repulsion) which is higher as the surface is more hydrophilic; no signs of re-stabilization or charge reversal were observed at large  $\text{Ph}_4\text{B}^-$  concentrations. These observations agree with previous studies, where we demonstrated that the driving force for the charge inversion in the hydrophobic particles and the mechanism preventing the charge inversion in hydrophilic particles is the hydrophobic effect.<sup>2</sup> For the negatively charged particles ( $\text{Ph}_4\text{B}^-$  acting as co-ions), we observed a small  $\mu_e$  increment at large  $\text{Ph}_4\text{B}^-$  concentrations for the hydrophobic latex, and for the silica particles

The results described above evidence the widespread ability of  $\text{PW}^{3-}$  to adsorb on different interfaces. This conclusion can be reinforced by exploring the behavior of a different set of particles in presence of  $\text{PW}^{3-}$ . We have recently reported a study where we explored how cationic latex particles covered with different proteins ( $\beta$ -lactoglobulin,  $\beta$ -casein and bovine serum albumin, BSA) interact with tetraphenyl hydrophobic ions.<sup>14</sup> Semi-empirical thermodynamic simulations showed that these proteins can be ranked by hydrophobicity as  $\beta$ -casein > BSA >  $\beta$ -lactoglobulin.<sup>14</sup> In that study we showed that the affinity of the organic ions paralleled the hydrophobicity of the proteins. In this work we have completed a similar study in presence of  $\text{PW}^{3-}$  ions. The results are displayed in Figure 6a. They are presented as a function of the ionic strength  $I$  ( $I=1/2 \sum c_i n_i^2$ , where  $n$  is the valence of each ion and  $c$  its molar concentration) to take into account the difference of charge of  $\text{PW}^{3-}$  and  $\text{Ph}_4\text{B}^-$ . As can be observed in the figure,  $\text{PW}^{3-}$  clusters interact

strongly with the three proteins, as reflected by the large charge inversions appearing at very low POM concentrations in all cases. More interestingly, the charge reversal concentration is rather independent of the degree of hydrophobicity of the protein (for the protein-coated particles). A more important POM adsorption appears for the more hydrophobic particles (bare latex and  $\beta$ -casein coated particles). These results can be compared with the behavior observed in presence of  $\text{Ph}_4\text{B}^-$  reported before (Fig. 6b)<sup>14</sup>: in this case, there is an important influence of the hydrophobicity of the particle nature on the electrokinetic results. While charge reversal is observed for the bare cationic latex particles and for the most hydrophobic protein-coated ( $\beta$ -casein) latex, no charge reversal and particle destabilization was found for the other protein-coated latex. Once again, these results show that the interaction of  $\text{PW}^{3-}$  is stronger than that of  $\text{Ph}_4\text{B}^-$ , independently of the nature of the interface considered. Moreover, comparing the same type of surfaces, the charge reversal ionic strength for the case of  $\text{PW}^{3-}$  is always at least two orders of magnitude lower than for  $\text{Ph}_4\text{B}^-$ .

We can go back now to the question outlined in the introduction, regarding the convenience of including large ionic clusters like  $\text{PW}^{3-}$  in the HS. To support the discussion, it is convenient to compare the behavior of the different ionic species ( $\text{PW}^{3-}$  and  $\text{Ph}_4\text{B}^-$ ) with widely accepted HS ions, the chaotropic  $\text{SCN}^-$  and the kosmotropic citrate<sup>3-</sup>. In Fig. 7 mobility results obtained with the most hydrophobic and hydrophilic positively charged systems (the cationic latex and the chitosan particles) are presented as a function of the ionic strength  $I$  to take into account the difference of charge of the electrolytes used. For the hydrophobic particles (Fig. 7a), charge reversal is observed for some of the ionic species. However, it can be observed that the ionic strength at which  $\mu_e$  goes to zero for  $\text{PW}^{3-}$  is significantly lower than for the other anionic species. Charge inversion is also observed in presence of the chaotropic thiocyanate and the hydrophobic  $\text{Ph}_4\text{B}^-$ , both monovalent anions. We have shown before that the charge reversal will be more important at  $\text{SCN}^-$  concentrations larger than the ones used in the present study.<sup>2</sup> These results would suggest that both  $\text{PW}^{3-}$  and  $\text{Ph}_4\text{B}^-$  can be labeled as “super-chaotropic”, given that they parallel and exceed the behavior observed in presence of  $\text{SCN}^-$ . Interestingly, for the case of the multivalent kosmotropic citrate the mobility vanishes at sufficiently large citrate concentrations, probably due to the large ionic strength, and it does not decrease at larger values of  $I$ , despite of the high negative valence that promotes the adsorption of this counterion on the cationic latex. As mentioned before,

the pH of the media depends on citrate concentration; however, this fact does not directly affect the mobility of the cationic latex.

A completely different scenario is observed for the cationic hydrophilic chitosan particles (Fig. 7b).  $PW^{3-}$  strongly adsorb on these particles, as reflected by the large charge inversion at very low  $I$ . In this case clear charge reversal is also observed in presence of the trivalent kosmotropic citrate. In agreement with previous studies, there is a significant tendency of this kosmotropic ion to accumulate on hydrophilic surfaces.<sup>1,11</sup> On the contrary,  $Ph_4B^-$  ion is excluded from the hydrophilic surface and no charge inversion is observed, as is also the case for the chaotropic  $SCN^-$ . As can be observed in Fig. 7b,  $PW^{3-}$  mimics and surpasses the behavior of the archetypical kosmotropic ion. Should then be concluded that in this case it act as a “super-kosmotropic”? (in agreement with its hydrophilic character).

The electrokinetic results described above show that the nature of the interaction of the organic tetraphenyl ions and the POM clusters with the interfaces are clearly different, a difference that goes beyond their dissimilar valence and hydration characteristics. POM adsorbs on the surfaces regardless of their nature, and always to a much larger extent than  $Ph_4B^-$ , which only adsorbs on hydrophobic surfaces (as commonly observed for chaotropic ions). Thus, our findings argue against recent propositions of classifying POM clusters in the conventional HS (Fig. 1) between classical chaotropic (e.g.  $SCN^-$  or  $ClO_4^-$ ) and hydrophobic  $Ph_4B^-$  anions; taking into account that POM interacts more strongly than  $Ph_4B^-$ , it would appear more reasonable to place the POM at the most extreme position of the HS. However, considering the significant interaction of POM with both hydrophobic and hydrophilic surfaces, should these anions be classified as super-chaotropes and at the same time as super-kosmotropes? A number of studies of POM interfacial activity and affinity for different surfaces have been published, as pointed out in the introduction. These results strongly suggest that attempts to allocate a particular place to  $PW^{3-}$  in the HS may in fact be deceptive. Under the light of these findings, even the description of POM clusters as conventional ions must be examined. This question was recently explored by Malinenko and coworkers,<sup>33</sup> who proposed a dual character (ion and nanocolloid) for Keggin POMs.

To further assess the interaction of  $PW^{3-}$  with hydrophilic surfaces, we used a Quartz Crystal Microbalance to investigate the adsorption of this species on silica. We found

substantial irreversible adsorption of  $\text{PW}^{3-}$ , despite of the electrostatic repulsion with the negatively charge silica. As can be observed in Figure 8, adsorption saturation is achieved at low POM concentrations; the saturation thickness seems coherent with the adsorption of a compact monolayer at the interface. In addition, only limited desorption was observed upon rinsing with pure water, evidencing the strength of the interaction and the irreversibility of the adsorption. It is of interest to examine the nature of the  $\text{PW}^{3-}$  adsorbed layer. For this purpose, we have measured height AFM micrographs of freshly cleaved hydrophilic mica surfaces exposed to  $\text{PW}^{3-}$  solutions of different concentrations, and abundantly rinsed with pH 3 water; typical results are presented in Figure 9. As can be observed in the AFM micrographs, ionic islands of different size are irreversibly adsorbed on mica. For  $\text{PW}^{3-}$  concentrations below 20 mM the thickness of the adsorbed islands was ca. 1 nm, in good agreement with the expected size of  $\text{PW}^{3-}$ .<sup>24</sup> Thicker (ca. 10 nm) and larger aggregates were observed on mica exposed to a 100mM  $\text{PW}^{3-}$  solution. It is remarkable that these multivalent ionic clusters adsorb on negatively charged mica despite of the electrostatic repulsion, indicating the presence of strong attractive inter-cluster forces. In addition, the formation of  $\text{PW}^{3-}$  islands many tens of nm in lateral size shows that inter-cluster interaction is promoting cluster adsorption;  $\text{PW}^{3-}$  self-assemblies and forms organized aggregates on surfaces. Analogous results were reported in earlier studies of  $\text{PW}^{3-}$  adsorption on mica (hydrophilic) and graphite (hydrophobic); similarly to our findings, these authors report irreversible  $\text{PW}^{3-}$  adsorption, regardless of the wettability of the surface.<sup>24,34,35</sup> Supramolecular POM cluster organization upon adsorption was also predicted in a molecular dynamic simulation study.<sup>20</sup>  $\text{PW}^{3-}$  multifaceted adsorption, together with the electrokinetic measurements described above, challenge the idea of portraying  $\text{PW}^{3-}$  as regular ions or its arrangement in the HS. It appears more realistic to describe this large, phosphotungstic anionic cluster as a dense nanoparticle, with interesting self-assembly behavior and interfacial activity. In this sense, two (related) questions must be addressed: the cause of the significant driving force for inter-cluster association, and the state of the ionic clusters in solution. Is the observed assembly a purely heterogeneous process, driven by the presence of the interfaces, or there exist inter-cluster association already in the aqueous solution? The self-assembly of different POMs in superstructures (at sufficiently large POM concentration) has been reported in the past, with the interaction between the counter-cations (e.g. proton) and the anionic clusters playing a significant stabilizing role.<sup>36</sup> In this direction, it was recently reported that  $\text{PW}^{3-}$  dissolved in acidic environment both as individual and associated

macroions at sufficiently large concentrations ( $> 20$  mM); the association seems to be promoted by proton-mediated hydrogen bonds.<sup>37</sup> Similarly, Malinenko and coworkers observed the presence of a fast and a slow relaxation modes in dynamic light scattering of  $PW^{3-}$  solutions, suggesting the presence of aggregates in solution.<sup>33</sup> Analogously, we observed the adsorption of larger aggregates from concentrated  $PW^{3-}$  solutions. However, we can not assure that large clusters were present in solution: the presence of interfaces allows the occurrence of heterogeneous processes, promoting cluster adsorption and association. Caution must be exerted before extrapolating the results obtained with  $PW^{3-}$  to other POMs. In particular, inter-cluster association will be influenced by their valence, as shown by Bera and Antonio in a recent study of concentrated solutions of  $\alpha$ -Keggin anions of different central atoms.<sup>38</sup>

## Conclusions

The ensemble of results reported in this work evidence the marked differences in the behavior of ions belonging to Hofmeister series and the Keggin type POM,  $PW^{3-}$ . We have shown that monovalent chaotropic or poorly hydrated anions (like  $SCN^-$  or  $Ph_4B^-$ ) clearly accumulate on hydrophobic interfaces while they are excluded from the hydrophilic ones. In these cases, the accumulation/exclusion mechanism proposed to explain HE or SIE can readily explain the obtained results. In addition, we have investigated a typical kosmotropic anion, citrate<sup>3-</sup>, highly hydrated and charged. We observed that the strong electrostatic interaction favors the accumulation of this anion on cationic hydrophobic and hydrophilic surfaces, with a much stronger preference for hydrophilic interfaces, as expected from a kosmotropic ion. In contrast, the Keggin POM,  $PW^{3-}$  showed an extraordinary accumulation at interfaces of different wettability. In this regard, the strong adsorption of these anionic clusters on hydrophilic surfaces does not appear to be compatible with the behavior expected for conventional chaotropic ions. The high charge and hydrophilicity of  $PW^{3-}$  also fail to explain its marked interfacial affinity in comparison with the kosmotropic citrate<sup>3-</sup> anion. In conclusion, our results point out that POMs anionic clusters should be treated as small soluble (thermodynamically stable) colloids, and they should not be included in the Hofmeister Series of ions.

## Notes

The authors declare no competing financial interests.

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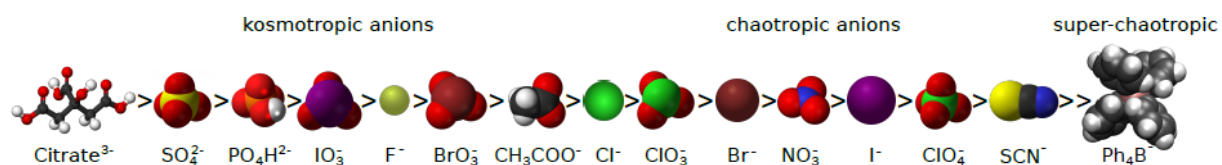


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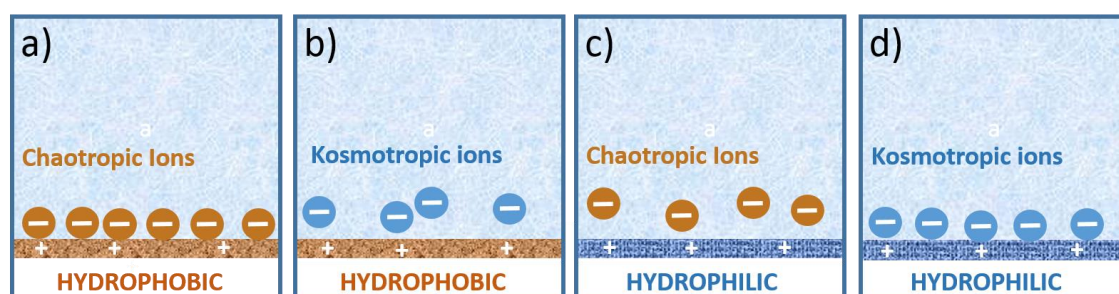
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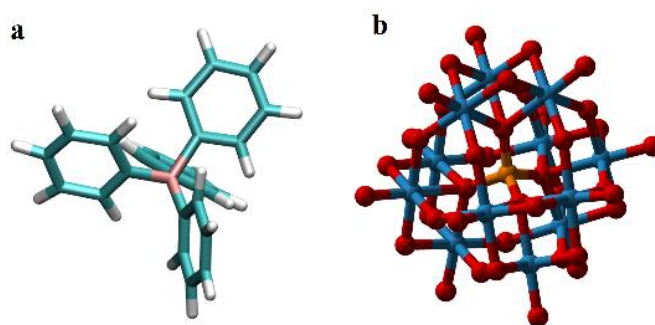




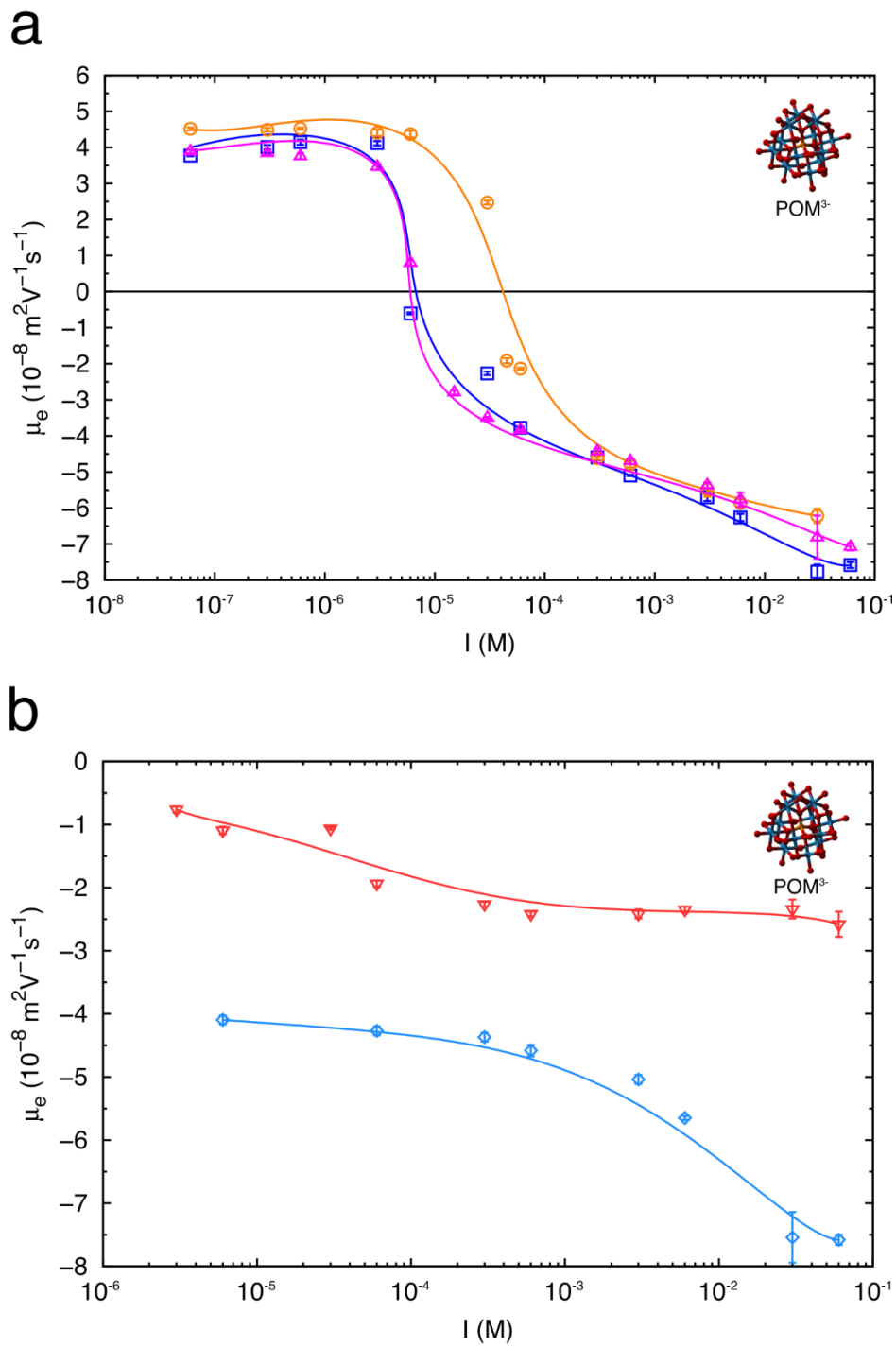
**Figure 1.** Extended Hofmeister series for anions



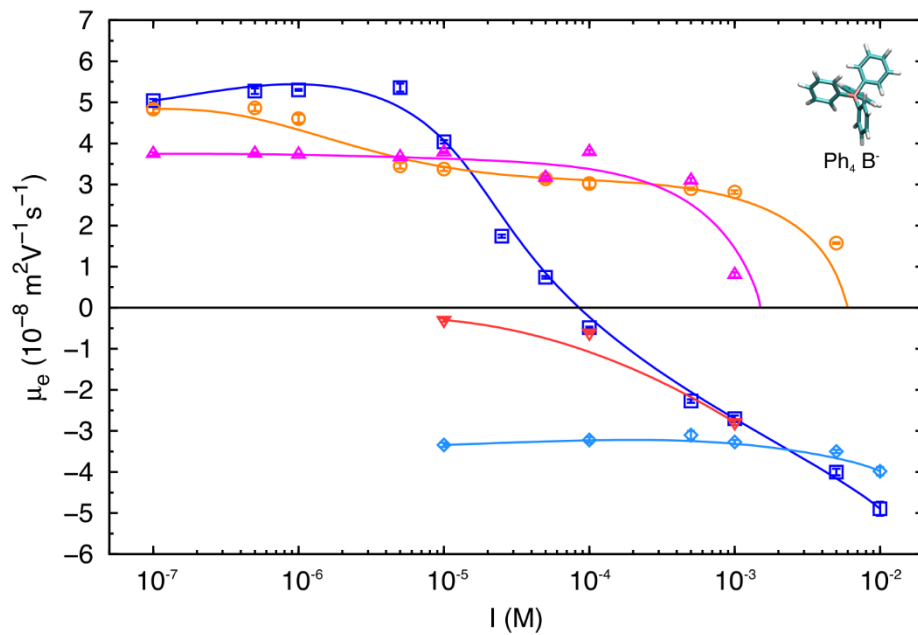
**Figure 2.** Schematic of the accumulation/exclusion mechanism of ions on interfaces. As an example we have considered positive surfaces, so that anions act as counter-ions. For simplicity, co-ions are not included. a) Accumulation of chaotropic (poorly hydrated) ions on hydrophobic interfaces. b) Exclusion of kosmotropic (highly hydrated) ions on hydrophobic interfaces. c) Exclusion of chaotropic ions on hydrophilic interfaces. d) Accumulation of kosmotropic ions on hydrophilic interfaces.



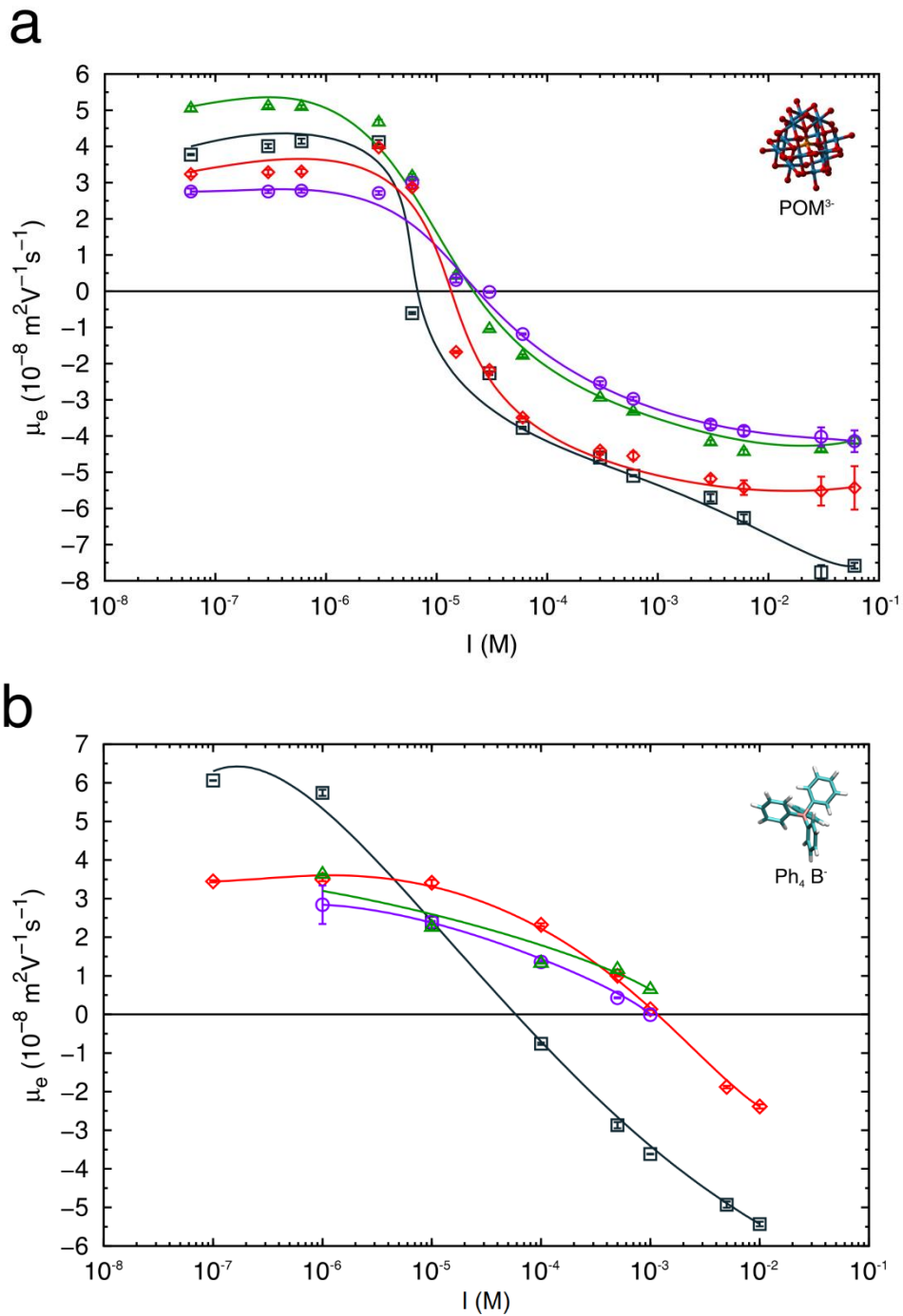
**Figure 3.** Chemical structure of a) Tetraphenyl borate ( $\text{Ph}_4\text{B}^-$ ) and b) Kegging POM ( $\text{PW}_{12}\text{O}_{40}^{3-}$ ) anions used in this work.



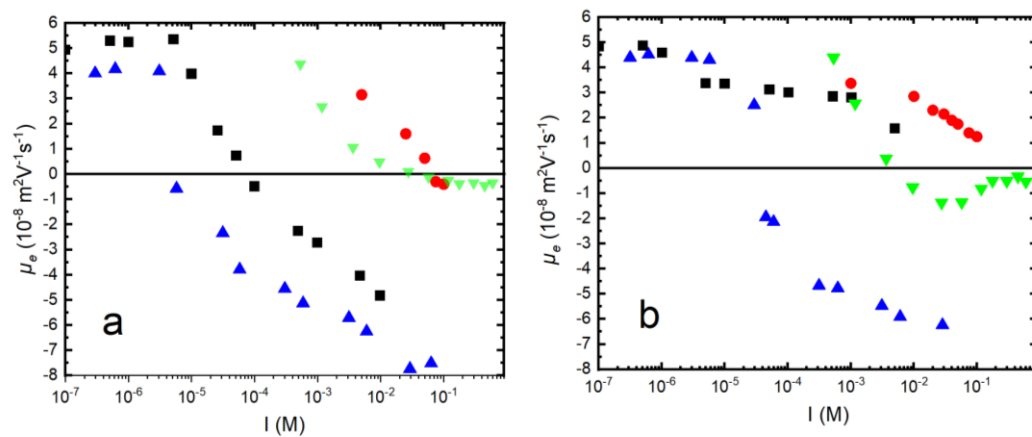
**Figure 4.** Electrophoretic mobility ( $\mu_e$ ) as a function of Ionic strength in presence of POM. (a) POM anions acting as counterions. ■ cationic latex, ▲ silica-NH<sub>2</sub> particles, ● chitosan particles. (b) POM acting as co-ion. ▼ silica particles, ◇ anionic latex.



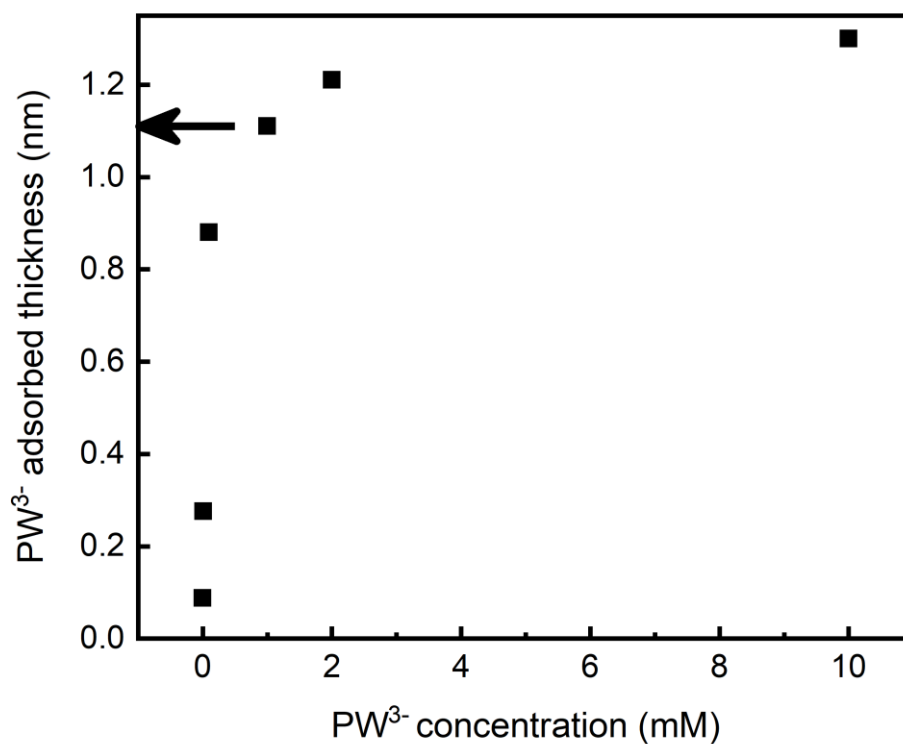
**Figure 5.** Electrophoretic mobility ( $\mu_e$ ) as a function of ionic strength in presence of  $\text{Ph}_4\text{B}^-$ . ■ cationic latex, ▲ silica-NH<sub>2</sub> particles, ● chitosan particles. ▼ silica particles, ◇ anionic latex.



**Figure 6.** Electrophoretic mobility ( $\mu_e$ ) as a function of ionic strength a) POM and b)  $\text{Ph}_4\text{B}^-$  anions (data taken from reference 11). ■ bare latex, ◇ latex with  $\beta$ -casein, ● latex with BSA, ▲ latex with  $\beta$ -lactoglobulin,

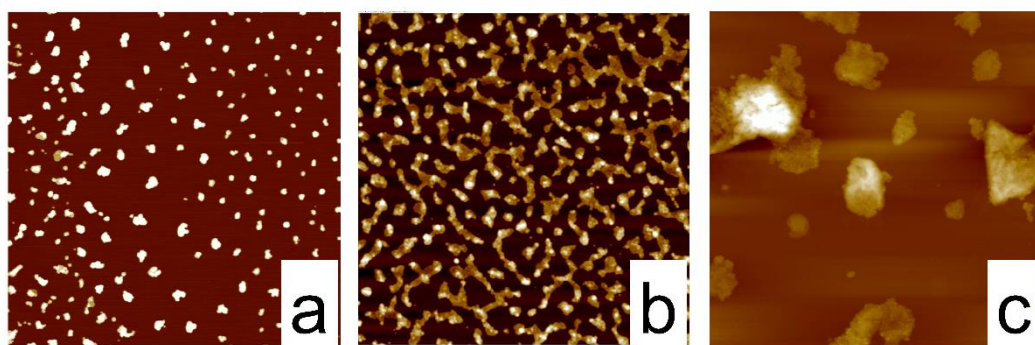


**Figure 7.** Electrophoretic mobility ( $\mu_e$ ) as a function of ionic strength for (a) hydrophobic latex and (b) hydrophilic chitosan particles. ●  $\text{SCN}^-$ , ▲  $\text{PW}^{3-}$ , ■  $\text{Ph}_4\text{B}^+$ , ▼  $\text{citrate}^{3-}$



**Figure 8.** Mean thickness of the adsorbed  $\text{PW}^{3-}$  layer on silica as a function of ion concentration in solution, measured by QCMD. The arrow indicates the final thickness of irreversibly adsorbed ions measured after rinsing with pH 3 water.





**Figure 9.**  $5 \times 5 \mu\text{m}^2$  tapping mode AFM micrographs of freshly cleaved mica surfaces exposed to  $\text{PW}^{3-}$  solutions of concentrations a) 1 mM, b) 10 mM and c) 100 mM for 12 hours, after rinsing with water at pH 3 and drying with nitrogen gas.