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## ARTICLE

# Adsorption of potentially toxic metals on negatively charged liposomes: Equilibrium isotherms and quantitatively modeling

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Y. Yu<sup>a</sup>, X. Liu<sup>b</sup>, W. Gong<sup>b</sup>, G. Liu<sup>b</sup>, D. Cheng<sup>b</sup>, H. Bao<sup>a</sup> and D. Gao<sup>b</sup>

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We investigated the adsorption behaviour of ten potentially toxic metals (Ni, Co, Cd, Fe, Ba, Sr, Cr, Hg, Ag and Zn) on negatively charged liposome vesicles composed of phosphatidyl choline (PC), phosphatidyl glycerol (PG) and cholesterol. The adsorption data for selected metal ions closely fit the Freundlich isotherm. Most metal ions (except Cr<sup>3+</sup> and Cd<sup>2+</sup>) were strongly adsorbed by liposomes ( $n > 1$ ) and the ionic covalent index significantly affected the Freundlich adsorption intensity. We used multivariate statistical methods, including principal components analysis regression and partial least squares regression, to elucidate the adsorption relationships between 18 physical and chemical properties and their respective Freundlich isotherm constants ( $K_F$ ). The cross-validated correlation coefficient ( $Q^2_{cum}$ ) and correlation coefficient ( $R^2_Y$ ) of the model were 0.76 and 0.91, respectively. High  $Q^2_{cum}$  and  $R^2_Y$  values indicated that the predictive model was both precise and robust. According to the VIP value, parameters like ionic polarisation, ion charge and ionisation potential played crucial roles in predicting  $K_F$ .

## Introduction

Potentially toxic metal pollution is becoming a worldwide environmental issue due to its increasingly negative impacts on human health<sup>1-4</sup>. Many studies<sup>5-7</sup> using animal and cell cultures to assess the toxicity of metallic elements have demonstrated a connection between metal exposure and the onset of various diseases. Understanding biological processes at the membrane level is imperative because toxic metals must first interface with cell membranes before further interaction can occur<sup>8, 9</sup>. Nevertheless, studying a specific process on natural membranes is extremely challenging due to the complex composition and dynamic environment of membranes<sup>10</sup>. One attractive solution is to use a biomembrane mimetic system in lieu of a natural membrane structure<sup>11-13</sup>. Liposome vesicles, with their artificial spherical lipid bilayer structure, are the most widespread kind of mimic biological membrane due to its self-assembled and well-known composition<sup>14</sup>. In most studies, the main component of liposome membrane is phosphatidyl choline (PC)<sup>15-18</sup>, which is zwitterionic lipid abundant in natural membranes. Usually, phosphatidyl glycerol (PG), a negatively charged lipid that results in a negatively charged liposome vesicle, and cholesterol are added to improve the stability and permeability of liposome vesicles<sup>14, 17, 19, 20</sup>. In this study we used negatively charged liposome vesicles as the adsorbent in part because oppositely charged particles should interact more strongly<sup>17</sup>.

Most relevant investigations have sought to describe binding characters and the corresponding changes on membranes<sup>17, 21, 22</sup>, while the adsorption is in fact a major cause of toxic metal accumulation<sup>23, 24</sup>. Therefore, studying the adsorption process is vital to understanding of how toxic metals bond with and transport across membranes. Previous studies have demonstrated that metal ions are adsorbed by the membrane according to specific molecular interactions that depend on the metal ion species and liposome composition<sup>25-27</sup>. Alkaline and alkaline-earth metal ions have been frequently investigated<sup>19, 25, 28, 29</sup>, but interactions between toxic metal ions and liposome vesicles remain poorly understood.

Due to financial and practical limitations, investigating the adsorption of every species of metal ion is impossible. Thus, developing an efficient method to predict the adsorption behaviour of untested metallic ions is desirable<sup>30</sup>. One approach to estimating the potential hazards of chemicals is to develop mathematical models, e.g. quantitative structure activity relationship (QSAR) models<sup>31, 32</sup>. In past decades, these have been employed successfully in the drug discovery and activity prediction fields<sup>33-35</sup>.

Beyond adsorption conditions and adsorbent species, metal ionic properties also affect adsorption processes in aqueous solutions. Properties such as electrochemical potential ( $\Delta E_0$ ), covalent index ( $X_m^2r$ ), log of the first hydrolysis constant ( $\log K_{OH}$ ), and ionic radius ( $r$ ) have been identified as influential factors in predicting metal and metalloid toxicity and

biosorption capacity<sup>30, 36, 37</sup>. However, these studies were restricted by the use of bivariate linear correlation tests such as ordinary least squares regression. Considering the great number of variables examined, known models are subject to misinterpretation<sup>38</sup>. Consequently, their conclusions might be misleading, and therefore, a more reliable model is required. In this study, principal components analysis (PCA) regression<sup>39</sup> and partial least squares regression (PLS), two multivariate methods that can cope with numerous and strongly collinear variables<sup>40-42</sup>.

The primary goal of this research was to examine the potential application of mimic biomembrane materials and to develop a quantitative detection method for multiple metal ions. We used liposome vesicles, a mimetic membrane structure, to investigate the adsorption of 10 potentially toxic metal ions. Considering the diversity of metal properties, the selected metal ions covered main-group elements and transition metals, mono-, di- and trivalence metals, including Ba<sup>2+</sup>, Sr<sup>2+</sup>, Ni<sup>2+</sup>, Co<sup>2+</sup>, Cd<sup>2+</sup>, Fe<sup>3+</sup>, Cr<sup>3+</sup>, Hg<sup>2+</sup>, Ag<sup>+</sup> and Zn<sup>2+</sup>. The liposome vesicles were made of egg phosphatidyl choline (ePC), dipalmitoyl phosphatidyl glycerol (DPPG) and cholesterol. The adsorption data of each metal ion matched the Freundlich experimental adsorption equilibrium. We developed a quantitative model of metal ion physical and chemical properties relative to the Freundlich constant,  $K_F$ , using PCA and PLS. The value of this new model lies in understanding and predicting the adsorption behaviour of ions on liposome vesicles.

## Materials and methods

### Chemicals and reagents

Egg phosphatidyl choline (ePC), dipalmitoyl- phosphatidyl glycerol (1, 2-dipalmitoyl-sn-glycero-3-phospho-(1'-rac-glycerol) DPPG) were purchased from Shanghai Advanced Vehicle Technology L-t.d. Co. Sodium dihydrogen phosphate NaH<sub>2</sub>PO<sub>4</sub>, disodium hydrogen phosphate Na<sub>2</sub>HPO<sub>4</sub>, cholesterol, chloroform and methanol were purchased from Sino pharm. FeCl<sub>3</sub>, Co(NO<sub>3</sub>)<sub>2</sub>, CdCl<sub>2</sub>, Ni(NO<sub>3</sub>)<sub>2</sub>, Ba(NO<sub>3</sub>)<sub>2</sub>, AgNO<sub>3</sub>, Sr(NO<sub>3</sub>)<sub>2</sub>, HgCl<sub>2</sub>, ZnSO<sub>4</sub>, and Cr(NO<sub>3</sub>)<sub>3</sub> were used to prepare stock solutions with deionised water. Ultrafiltration membrane were purchased from Pall Corporation.

### Preparation and characterisation of liposome vesicles

Liposome vesicles were prepared by solvent evaporation method<sup>15</sup>, wherein 100 mg ePC, 40 mg cholesterol and 10 mg DPPG were dissolved in 5mL of a chloroform/methanol solvent mixture (2:1 v/v) in a round bottom flask. Next, we attached the flask to a rotary evaporator and immersed it in a water bath. The resulting solution was dried and yielded a dry lipid film deposited on the wall of the flask. Next, we placed the open flask in a vacuum for at least 1 h to remove any traces of organic solvent. After this step, the lipids were hydrated by adding 5 mL phosphate-buffered solution (PBS; 10mM phosphate; pH 7.5) to the flask, attaching the flask to the evaporator and rotating it until all the lipids were removed from the wall of the flask. This

yielded a homogeneous milky-white suspension of multilamellar large vesicles (MLVs) with no visible particles.

Each batch of liposome vesicles was sized using a laser particle size analyser (Microtrac S3500, Microtrac Inc, USA). The settings for which were as follows: flow rate 50%; runtime 30s; each sample was run twice and then averaged; type of particle: reflection; shape of particle: regular.

### Adsorption of metal ions

Each type of metal ion solution was derived from dissolved salts, producing a stock solution with deionised water. The experiment proceeded in same process order each time. First, we added stock and buffer solutions (PBS; 10mM phosphate; pH 7.5) to a glass cuvette and then added the liposome suspension. The initial metal concentrations were ranged from 0.5 to 12 mg/L due to the hydrolysis of some metal ions, for instance Cr<sup>3+</sup> and Fe<sup>3+</sup>. Finally, we adjusted the pH to the expected value of 7.5. The solution was shaken at 180 rpm for 12 h in the dark until it reached an equilibrium at temperature (25 ± 2 °C). Before metal concentration analysis, free metal ions were separated by ultracentrifugation at 14,000×g (12,210 rpm) for 60 min, and metal concentration was measured by inductively coupled plasma atomic emission spectrometry (ICP-AES, SPECTRO ARCOS EOP). The quantity of adsorbed metal ions in the liposome vesicle can be expressed as

$$Q_e = \frac{C_i - C_e}{S} \quad (1)$$

Where,  $Q_e$ ,  $C_i$ ,  $C_e$  and  $S$  are the adsorbed metal ions (mg/g), the initial concentration (mg/L), the equilibrium concentration of metal ions (mg/L) and the liposome mass (mg), respectively.

### Model development

Freundlich isotherm are readily available and easily adopted for correlating metal adsorption equilibria<sup>23, 37</sup>. The Freundlich isotherm model is empirical equation, as follow:

$$Q_e = K_F C_e^{1/n} \quad (2)$$

Where  $K_F$  and  $n$  are Freundlich constants, and  $K_F$  is the Freundlich isotherm constant related to adsorption capacity. The Freundlich equation is an isotherm model indicating the adsorbent surface to be heterogeneous<sup>43</sup>.

The Freundlich adsorption constants ( $K_F$ ) were regarded as independent variables and were and correlated with various ionic properties. Eighteen metal ion variables (in Table 1) were selected for analysis<sup>30, 36, 37, 44</sup>. Polarisation force parameters and other similar polarisation force parameters were calculated according their respective definition.

**Table 1** Physical and chemical properties of metal ions

Property	Symbol
Atomic number	AN
Ionic radius	r
Electrochemical potential	$\Delta E_0$
Electronegativity	$X_m$
Log of the first hydrolysis constants	$ \log K_{OH} $
Covalent index	$X_{mr}^2$

Ion charge	Z
Atomic weight	AW
Softness index	$\sigma_p$
Atomic radius	AR
Ionization potential	$\Delta IP$
Polarization force parameters	$Z^2/r, Z/r, Z/r^2$
Similar polarization force parameters	$Z/AR, Z/AR^2$
Electron density	AR/AW
Atomic ionization potential	AN/ $\Delta IP$

We performed multivariate data analyses (MVAs) using ORIGIN 8.0 (Origin Lab), MINITAB 15 (Minitab Inc.) and SIMCA software (Simca-P+ Version 11.5, DEMO, Umetri AB). No data need to be normalised or scaled to unit variance before MVA. We implemented the PLS procedure based on the default options, including a significant level limit of 0.05, seven cross-validation rounds and a 95% confidence level for each of the parameters. In PCA regression and PLS, the original set of correlated variables was transformed to a set of orthogonal variables, known as “principal components” and “latent variables” respectively.

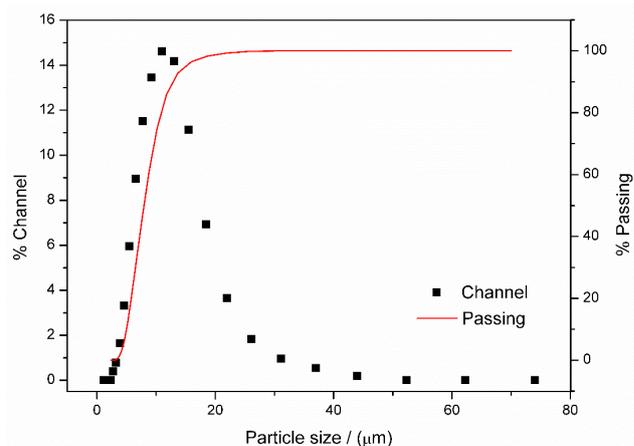
The large number of physical and chemical metal properties measured required that important information be extracted from intercorrelated data tables. We employed PCA to classify 18 physical and chemical properties and to reduce of the number of variables. The central principle of PCA is to reduce the dimensionality of a data set consisting of a large number of interrelated variables, while retaining as much as possible the variable present in the data set. This goal is achieved by transforming the whole data set into a new set of variable (PCs). PCs are uncorrelated, so that the first few retain most of the variation presented in all of the original variables.<sup>45</sup> To explore the relationship between principal components and dependences, PCA and multi-linear regression can be combined, this method is known as PCA regression. Not all PCs contribute significantly to the final regression equation.

In PLS analysis, a model including all physical and chemical properties of metal ions is firstly calculated, and any variable with a variable importance in the projection (VIP) value < 0.5 is eliminated, resulting in a new PLS regression model. In a PLS model, the VIP is a parameter that shows the relative importance of a variable. This procedure is repeated until only the variables with a VIP > 0.5 remained in the model<sup>38</sup>.

## Result and discussion

### Particle size

The volume average diameter of liposome vesicles was around 10 $\mu\text{m}$  (Fig. 1), which is in line with both the area average diameter and average number diameter. Strictly controlling the preparation process ensured the range of diameter among liposome vesicles batches remained constant.



**Fig. 1** The particle size distribution of liposome vesicles. Black dot line is a frequency distribution (% channel) and red line is a cumulative distribution (% passing).

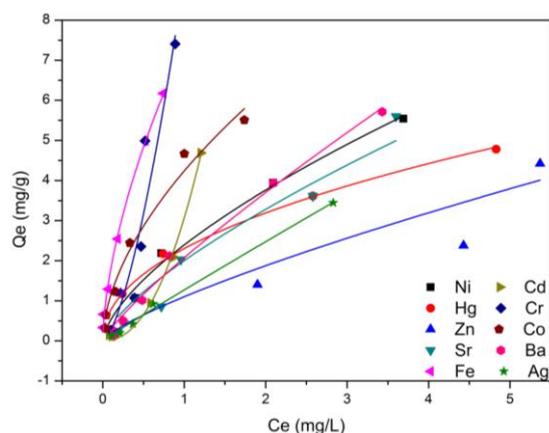
### Adsorption isotherms

Metal adsorption equilibrium data fit the Freundlich isotherm model relatively well. Eight metal ions (all except  $\text{Zn}^{2+}$  and  $\text{Cr}^{3+}$ ) were highly correlated ( $R^2 > 0.9$ ) with the Freundlich isotherm. Metal ion adsorption data and Freundlich model fitting data are shown in Fig. 2. The Freundlich constants were shown in Table 2,  $K_F$  stands for the adsorption capacity and  $n$  is a measure of adsorption intensity, which varies with the heterogeneity of the material being examined<sup>43</sup>.  $\text{Cr}^{3+}$  had the highest  $K_F$  value but a relatively lower  $n$  value.  $\text{Cd}^{2+}$  and  $\text{Cr}^{3+}$  displayed concave-upward isotherms ( $n < 1$ ) and are classified as solvent affinity isotherms, indicating that their marginal sorption energy will increase with increasing surface concentration<sup>46</sup>, while the other eight metals have isotherm with convex tendency ( $n > 1$ ).  $\text{Hg}^{2+}$  had the highest  $n$  value, indicating that it has a higher affinity to liposome vesicle functional groups than other ions.  $\text{Fe}^{3+}$ ,  $\text{Co}^{2+}$  and  $\text{Ni}^{2+}$  all had similar  $n$  values, indicating that their respective adsorption intensities on liposomes are similar. However, high affinity is not analogous to having a high  $K_F$  value (high adsorption capacity).  $K_F$  is governed by properties such as the size distribution of metal ions and adsorbents, the specific surface area and the surface functional groups of adsorbents<sup>46</sup>.

**Table 2** Parameters of Freundlich isotherm

Metals	Freundlich isotherm constants		
	$K_F$	$n$	$R^2$
$\text{Ni}^{2+}$	2.40	1.53	0.99
$\text{Ba}^{2+}$	2.07	1.20	0.99
$\text{Sr}^{2+}$	2.00	1.40	0.98
$\text{Ag}^+$	1.27	1.04	0.99
$\text{Hg}^{2+}$	2.30	2.12	0.99
$\text{Co}^{2+}$	4.24	1.77	0.98
$\text{Fe}^{3+}$	7.36	1.64	0.99
$\text{Cd}^{2+}$	3.07	0.45	0.98
$\text{Zn}^{2+}$	1.10	1.40	0.80
$\text{Cr}^{3+}$	9.08	0.66	0.84

Liposome binding sites are thought to be oppositely charged phosphodiester trimethylammonium groups, which are located at the surface of liposome vesicles<sup>47</sup>. It was found that the electrostatic interaction determined portioning of the ionized species in membrane system<sup>48,49</sup>. That is the reason why metal particles could be adsorbed strongly by the negatively charged liposome vesicles. Most metal ions partially complex with  $\text{HPO}_4^{2-}$  in the buffer solution. While Fe, Hg and Cr tend to combine with  $\text{OH}^-$  and Ag remains free ion (for the species distribution of metals, see supporting information Table S1.). All the metal ions can be dissolved in aqueous solution in our concentration range. Mercury is characterised as a “soft” Lewis acid due to its high polarisability. It tends to form strong covalent bonds with soft Lewis bases, such as the liposomes in our study<sup>40</sup>.  $\text{Ni}^{2+}$  and  $\text{Co}^{2+}$  both have large covalent index ( $X_m^2r$ ) and polarisation parameters ( $Z^2/r$ ) and display a strong tendency to bind with liposomes, leading to higher  $n$  values. The borderline metal  $\text{Fe}^{3+}$  has a low  $X_m^2r$  value and a higher  $Z^2/r$  value, resulting in higher adsorption intensity.  $\text{Ba}^{2+}$  and  $\text{Sr}^{2+}$ , two typical hard Lewis acids, tend to bind weakly with liposomes via electrostatic attraction. Silver is another soft Lewis acid but has an extremely low  $Z^2/r$  value; hence the  $n$  value of  $\text{Ag}^+$  was just above 1. The tendency of  $\text{Zn}^{2+}$  to form covalent bonds is a low. Furthermore, a neutral aqueous solution will result in a decrease in  $\text{Cr}^{3+}$  concentration; however, other species, such as  $\text{Cr}(\text{OH})_2^+$ , saw increased because of their low  $|\log K_{\text{OH}}|$  values, and were also attracted to negatively charged functional liposomes<sup>50</sup>. The  $n$  value of  $\text{Cd}^{2+}$  is difficult to explain, but it may be due to  $\text{Cd}^{2+}$  interacting with liposomes via a different mechanism altogether. Further studies are required to address this issue. Besides, we have also proceed the Pb adsorption investigation but did not get detectable free Pb ions because of its great lipophilicity<sup>51</sup>.



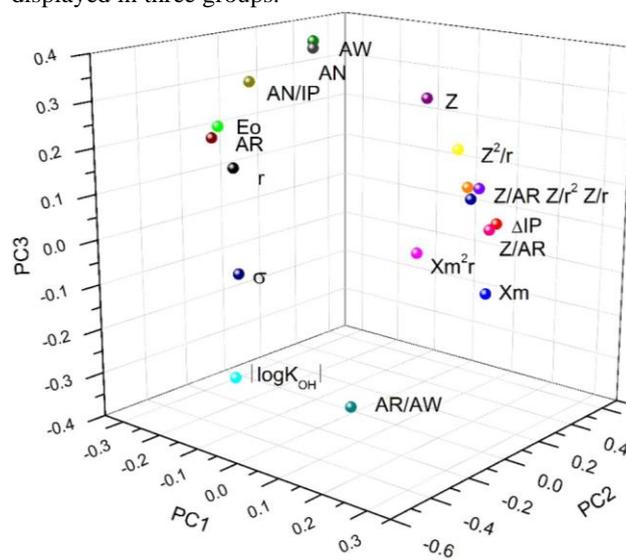
**Fig.2** Experimental adsorption for ten metal ions (data points), and corresponding fitted isotherm (line) (PBS buffer solution, 0.01M; pH, 7.5; adsorption time, 12h; temperature,  $25 \pm 2^\circ\text{C}$ ; shaken rate, 180 rpm).

## Multivariate data analysis

### PCA regression on eighteen physical and chemical properties

Only  $K_F$  was considered when correlating ionic property parameters. PCA allowed us to summarise the initial data (i.e. physical and chemical properties of metal ions) into a form more easily overviewed and used<sup>42, 45, 52</sup>.

PCs represent variation in the original data. PCA extracted nine PCs (with eigenvalues of 10.752, 4.31, 2.14, 0.26, 0.15, 0.10, 0.03, 0.03 and 0.01). Only three components had an eigenvalue larger than 1, and together, the first three components accounted for 96.8% of the inertia. Variable loading in the first three PCs shown in Fig. 3; the 18 physical and chemical properties are displayed in three groups.



**Fig.3** Loading of variables in first three principal components

Six variables, including  $\Delta\text{IP}$ ,  $Z^2/r$ ,  $Z/r^2$ ,  $Z/r$ ,  $Z/\text{AR}$  and  $Z/\text{AR}^2$ , had strong positive loadings in the first component.  $\Delta\text{IP}$  is the energy change in the ionisation process.  $Z^2/r$  was used as an index of both the ability of cations to form ionic bonds and the stability of the metal–ligand complex in aqueous solution.  $Z/r$  is an index of the tendency to form ionic bonds.  $Z/r^2$ ,  $Z/\text{AR}$  and  $Z/\text{AR}^2$  are all polarisation force parameters and are related to ionic bond stability during metal–ligand electrostatic interactions<sup>36, 44, 53</sup>. The ratio of atomic number to ionisation potential  $\text{AN}/\Delta\text{IP}$  and the Pauling ionic radius  $r$  contributed negatively to the first component. Hence, PC1 contains mostly information about ionic interaction, such as the tendency of forming ionic bonds and the strength of those bonds.

Parameters like  $E_0$ ,  $\text{AR}$ ,  $\text{AR}/\text{AW}$  and softness index,  $\sigma_p$ , dominated the second component and correlated negatively, while  $X_m$  and  $X_m^2r$  correlated positively.  $E_0$  is the absolute difference between the ion and its first stable reduced state. It reflects the ability of the ion to change its electronic state<sup>44</sup> and qualities, affecting interactions with ligands in aqueous solutions<sup>36</sup>.  $\text{AR}/\text{AW}$  is a measure of an ion’s electron density.  $\sigma_p$  separates metal ions into three groups according to their softness and quantifies electron donation ability. This index also reflects ionic interactions and the energy of an ion interacting electrostatically

with a ligand. Electronegativity ( $X_m$ ) reflects an ion's ability to attract electrons, while  $X_m^2r$  reflects the tendency to interact covalently with ligands, as opposed to ionically<sup>30, 36, 44, 54</sup>. Therefore, PC2 represented conditions surrounding the metal ions' electrons. A greater likelihood of forming covalent bonds and a higher affinity for electrons will result in increased PC2. Moreover, PC2 would decrease with increasing electron density and electron devotion ability.

PC3 reflected various properties related to atomic size, and was significantly affected by atomic weight, atomic number and the ratio between the atomic radius and atomic weight. Larger, heavier atoms and those with greater charge should yield higher PC3 values.

**Table 3** The linear regression analysis of relationship between Freundlich constant  $K_F$  and three principal components

	Constant	PC1	PC2	PC3	$R^2$	$R^2_{adj}$
Model 1	3.49	0.66			0.65	0.61
Model 2	3.49	0.66	-0.19		0.68	0.59
Model 3	3.49	0.66	-0.19	0.64	0.80	0.70

Stepwise regression retained only PC1 in the final regression model. When PC2 was added (model 2), the correlation coefficient ( $R^2$ ) increased slightly, while  $R^2_{adj}$  declined (0.65–0.68 and 0.61–0.59, respectively). Thus, it is perhaps not surprising that PC1 was the most important component, as other studies<sup>18</sup> have proposed that the interaction of metal ions and liposomes involves electrostatic forcing. PC3 had a slightly positive effect on the adsorption quantitative model. In other words, the adsorption interaction of metal ions and liposomes is simpler when the metal ions are larger and heavier (Table 3).

### PLS on adsorption isotherm constants

In PLS, we applied leave-one-out cross-validation (LOOCV) in optimising the number of components and chose the model giving the lowest PRESS as the optimal predicting model. We also calculated the cross-validated correlation coefficient,  $Q^2$ , defined as  $1.0 - \text{PRESS}/\text{SS}$ <sup>45, 50</sup>, and performed CV-ANOVA to assess the statistical significance of PLS after developing each model. In general, models with  $Q^2_{cum} > 0.5$  are most acceptable.

$$PRESS = \sum_y (y_{predicted} - y_{observed})^2 \quad (1)$$

$$Q^2_{cum} = 1 - \frac{\sum_n (y_{predicted} - y_{observed})^2}{\sum_n (y_{predicted} - y_{mean})^2} \quad (2)$$

Based on the adsorption constant and 18 physical and chemical properties of metal ions, the PLS model with eight significant properties was obtained and presented as blow.

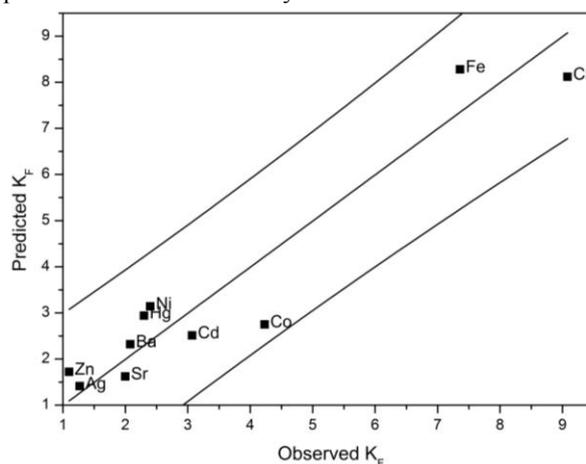
$$K_F = -8.7 + 4.9r + 4.4 \times 10^{-1} \Delta IP + 3.2 \times 10^{-1} \frac{Z^2}{r} + 3.3 \times 10^{-2} Z - 5.0 \times 10^{-2} \frac{Z}{r^2} - 2.6 \times 10^{-2} \frac{Z}{r} + 5.5 \times 10^{-1} \frac{Z}{AR} + 6.3 \times 10^{-1} \frac{Z}{AR^2} \quad (3)$$

The quantitative model consisted of three latent variables (with eigenvalues of 7.31, 0.45 and 0.16, respectively) with the following model performance statistics:  $R^2_{X(cum)} = 0.99$ ;  $R^2_{Y(cum)} = 0.91$ ;  $Q^2_{(cum)} = 0.76$ . The  $Q^2_{(cum)}$  values (all  $> 0.5$ ) indicate good robustness and predictive ability. The CV-ANOVA results suggest that this model is highly significant, with a  $p$ -value of 0.001. As shown in Table 4, the VIP values of the polarisation force parameters, the ionisation potential and the ion charge were near or greater than 1, and were all important variables in the predictive model. Ionic radius was retained in the PLS model as well, illustrating its significant role in predicting the adsorption interaction of metal ions. Other parameters, similar polarisation force parameters or other forms of polarisation force are all supplements to  $Z^2/r$ .

**Table 4** The VIPs in the PLS model

Variables	VIP
$Z^2/r$	1.11
$\Delta IP$	1.01
$Z$	1.03
$r$	0.97
$Z/r$	0.98
$Z/AR$	0.96
$Z/r^2$	0.97
$Z/AR^2$	0.94

Based on the PLS model, we calculated the  $K_F$  values of test metal ions and plotted the predicted  $K_F$  values against the observed  $K_F$  (Fig. 4). Ten observed metal ion  $K_F$  values and 10  $K_F$  values predicted by the PLS adsorption model were all near the 1:1 line within the 95% confidence intervals. Thus, the predicted values from the PLS model fit the experimental data well. Furthermore, the high correlation coefficients ( $R^2 = 0.91$ ,  $p < 4.6 \times 10^{-6}$ ) between predicted and observed values confirmed the predictive model's accuracy.



**Fig. 4** Plot of the observed vs. predicted  $K_F$  values of ten metal ions

PLS is the regression extension of PCA. Using PLS allowed the data set to be efficiently modelled, and  $K_F$ , which is related

to the metal ionic adsorption capacity of liposome vesicles, to be predicted by metal ionic characteristics. Eight variables contributed to the adsorption model. Variables like  $Z^2/r$ ,  $Z$  and  $\Delta IP$  not only correlated positively with  $K_F$  but also played an important role in the predictive model ( $VIP > 1$ ). Metal ions with high polarisation force parameters should promote adsorption behaviour, which is consistent with the PCA regression model result. Stronger ionic binding strength and a greater tendency to form ionic bonds would also enhance the adsorption of metal ions on liposomes. As a measure of the electron affinity,  $\Delta IP$  correlated positively with the predictive equation, indicating that the electrophilic metal ions will facilitate adsorption. Because of the importance of electrostatic interactions between liposomes and metal ions<sup>48, 49</sup>,  $Z$  and  $r$  play a key role to describe the adsorption interaction. To some extent,  $Z/r$ ,  $Z^2/r$ ,  $Z/r^2$ ,  $Z/AR$  and  $Z/AR^2$  are just derived from this two parameters.

Unfortunately, the factors listed here were not sufficient to fully account for the adsorption process of toxic metals on liposome vesicles, most likely due to other contributing factors such as metal species and liposome composition. The predictive models enabled us to explain metal adsorption processes on liposome vesicles theoretically, and further studies are therefore required to provide experimental corroboration.

## Conclusions

In this paper, we used PCA regression and PLS analysis to develop a new quantitative model to predict the adsorption constant of metal ions on liposome vesicles by metal ionic properties. The adsorption equilibrium isotherms fit Freundlich isotherm models relatively well. Using this model, the Freundlich constant can be predicted accurately and conveniently. The model also allows us to estimate the possibility of liposome worked as metals detection material and encourages us to continue searching the liposome application potential.

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## Notes and references

<sup>a</sup> College of Chemistry, Beijing Normal University, Beijing, 100875, the People's Republic of China

<sup>b</sup> State Key Laboratory of Water Environment Simulation, School of Environment, Beijing Normal University, Beijing 100875, the People's Republic of China.

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