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# On calculations of the ion hydration free energy within the framework of the RISM approach

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The results of calculations of the hydration free energy for monovalent ions by the integral equation method within the framework of the RISM approach with different sets of parameters of the Lennard-Jones potential are presented. The main goal of the study is to choose the optimum potential model providing reliable and the most accurate description of ion hydration thermodynamics and the fit to experimental data. The accuracy of calculations of the hydration free energy was tested using five equations available in the literature and five sets of parameters of the Lennard-Jones potential. The proper choice of parameters of the Lennard-Jones potential plays a significant role in RISM calculations of thermodynamic properties, whereas the use of improved models in calculations of the hydration free energy does not always lead to more accurate results

**Key words:** integral equation method, ion hydration free energy, potential model.

In recent decades, improvement of traditional and elaboration of novel computational schemes for calculations of solvation effects[1,2] led to considerable progress in theoretical studies of ion solvation (hydration). Among widely used nonempirical methods of description of the equilibrium properties of liquid-phase systems, there is the integral equation method in the site-site or the RISM (Reference Interaction Site Model) approximation.[3] This approach allows one to take account of real functional groups, (intra)molecular geometry, and the atomic charge distribution and offers new prospects for the investigations of ion solvation on the molecular level. Unlike continuum models, such as the Born model or the Debye—Hückel theory, the site-site approximation enables description of systems with hydrogen bonds and solvophobic effects.[4] The state-of-the-art in RISM and its computational advantages over computer simulation have made this technique very attractive for chemistry, biochemistry, and molecular biology research. However, at present the RISM method is suitable only for qualitative description of the properties of molecular and ion-molecular systems due to inclusion of various assumptions and approximations.[5,6] In particular, the results of calculations depend on a potential model. Different models give different estimates of the structural characteristics and thermodynamic properties and, consequently, lead to different degree of agreement with experimental data. Therefore, a proper choice of potentials and their parameters plays an important role in the theory of solvation.

In this work we present the results of calculations of the hydration free energy for monovalent ions under ambient conditions. In this case, the potential model describes the ion—solvent (water) interactions by the sum of the Coulomb and Lennard-Jones potentials. We have tested and compared the available[7—18] sets of parameters of the Lennard-Jones potential. The aim of the present study was to choose an optimum potential model providing reliable and the most accurate description of ion hydration thermodynamics and the best fit to the experimental data obtained within the framework of the RISM approach. We analyzed the data for alkali metal ions and halide ions at infinite dilution. An infinitely dilute solution has been traditionally considered as a criterion for correctness of theoretical calculations with a given potential model. The hydration free energies (excess hydration chemical potential) were calculated using various expressions within the framework of the RISM approach.[19—23] This allowed us to choose the most appropriate potential model from the standpoint of thermodynamics of ion hydration.

## Calculation Procedure

As applied to molecular liquids, the site-site approach is based on the reference interaction site model.[3] It allows one to describe molecular and ion-molecular systems in terms of the statistically averaged site-site pair correlation functions (PCFs), which determine the probability density of the distribution of sites belonging to different particles in the system. Usually, the

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PCFs are calculated using the site-site Ornstein—Zernike equation.[3] The fundamentals of the RISM theory have been well documented;[1,3—6,24] therefore, we will only dwell on some key aspects necessary for understanding of this work.

In studies of ion-molecular systems, the site-site Ornstein—Zernike equation is as a rule used with the hypernetted chain (HNC) closure, which is used to describe systems with long-range interactions,

$$h_{\alpha\beta}^{xy}(r) + 1 \equiv g_{\alpha\beta}^{xy}(r) = \exp\{-\beta U_{\alpha\beta}^{xy}(r) + h_{\alpha\beta}^{xy}(r) - c_{\alpha\beta}^{xy}(r)\}, \quad (1)$$

where $g_{\alpha\beta}^{xy}$ is the PCF of the sites α and β belonging to the molecules $x$ and $y$, respectively; $\beta = 1/k_BT$ ($k_B$ is the Boltzmann constant); $U_{\alpha\beta}^{xy}(r) = \phi_{\alpha\beta}^{xy}(r) + \Phi_{\alpha\beta}^{xy}(r)$ is the site-site interaction potential (sum of the short-range and long-range parts). In particular, the potential of the ion—solvent interaction is given by the sum of the Lennard-Jones potential and the Coulomb term

$$U_{\alpha\beta}(r) = 4\varepsilon_{\alpha\beta}\left(\left[\frac{\sigma_{\alpha\beta}}{r}\right]^{12} - \left[\frac{\sigma_{\alpha\beta}}{r}\right]^{6}\right) + \frac{q_\alpha q_\beta}{r}, \quad (2)$$

where $\varepsilon_{\alpha\beta}$ is the depth of the potential well and $\sigma_{\alpha\beta}$ are the standard Lennard-Jones diameters. The parameters $\varepsilon_{\alpha\beta}$ and $\sigma_{\alpha\beta}$ obey the combination rules $\varepsilon_{\alpha\beta} = (\varepsilon_{\alpha\alpha}\varepsilon_{\beta\beta})^{0.5}$ and $\sigma_{\alpha\beta} = (\sigma_{\alpha\beta} + \sigma_{\beta\alpha})/2$.

The site-site PCFs $g_{\alpha\beta}^{xy}(r)$ with allowance for the molecular geometry determined by the intramolecular correlation functions $s_{\alpha\beta}(r)$ provide complete information on the local microscopic structure of the solution and the hydrated complex. In particular, ion hydration is described by the functions $g_{IW}(r)$, which allow one to determine all thermodynamic properties of a given process (the Gibbs energy of hydration, hydration free energy, *etc.*).[10,15] Spherical symmetry of monatomic ions allows one to derive analytical expressions for the ion hydration free energy.

In the RISM approach, the free energy of hydration (Δμ) is a functional of the site-site PCFs and the equation for $\Delta\mu_{HNC}$ in the HNC approximation has the simplest form.[19] However, the accuracy of calculations[25] of thermodynamic properties in this approximation is insufficient owing to a large overestimation of the heights of the PCF peaks responsible for hydrogen bonds. Improved expressions for $\Delta\mu_{HNC}$ in different approximations were proposed. For instance, the empirical repulsive bridge (RB) approximation[20] makes it possible to considerably decrease the amplitude of the ion—hydrogen PCF while the Gaussian fluctuation (GF) approximation[21] implies a Gaussian distribution of positions of solvent molecules. There are also the PW model[22] with a correction for the mutual orientation of solvent molecules around the solute and the PWC model[23] including semiempirical corrections for the partial molar volume of solute and for the number of OH groups in the hydrated solute molecule. The ion hydration free energies we have calculated in the approximations mentioned above are denoted as $\Delta\mu_{HNC}$, $\Delta\mu_{RB}$, $\Delta\mu_{GF}$, $\Delta\mu_{PW}$, and $\Delta\mu_{PWC}$. Modifications of the equation for $\Delta\mu_{HNC}$ represent attempts to improve agreement between the results of calculations and experimental data. They were repeatedly used in studies on the thermodynamic characteristics of ion hydration.[19—23,26—31] But, as we will show in the following, the use of a modified equation for the calculations of Δμ does not always give better results if the quality of the potential model intrinsic to the integral equation method is ignored.

**The model and details of calculations.** Calculations were carried out for the model systems $Cat^+—H_2O$ ($Cat^+ = Li^+, Na^+, K^+, Rb^+, Cs^+$) and $An^-—H_2O$ ($An^- = F^-, Cl^-, Br^-, I^-$) at infinite dilution ($\rho = 0.997$ g cm$^{-3}$). Water was described using the MSPC/E model[26] (modified SPC/E model[32]). The modification consists in augmentation of the Lennard-Jones potential with a term to describe the repulsive interaction between O and H atoms of the water molecule (initial SPC/E model of water was free from this term). The MSPC/E model quite correctly describes the structural and thermodynamic properties of water.[26,29,33]

According to Eq. (2), ion-water interactions are represented by the sum of the Lennard-Jones and Coulomb potentials responsible for the short- and long-range interactions, respectively. Some sets of parameters of the Lennard-Jones potential are known. The sets of parameters for cation—water[7] and anion—water interactions[8—10] are most widely used. They are included in the Optimized Potentials for Liquid Simulations (OPLS) force field.[34] For brevity, in the text below they are denoted as "set *1*". Yet another popular set of parameters[12—16] is denoted as "set *2*". Recently, some other parameterization schemes for the Lennard-Jones potential were proposed.[11,17,18] These sets of parameters are denoted below as "set *3*", "set *4*", and "set *5*", respectively. Note that the set *5* has no parameters for the $Rb^+$ ion. The sets *3*—*5* differ from one another in $\varepsilon_{\alpha\beta}$ and $\sigma_{\alpha\beta}$ due to the choice of the parameterization scheme of the Lennard-Jones potential.[18] This procedure specifies the functional form of the potential including some fitting parameters that are chosen by comparing the results of test calculations and the experimental structural parameters and thermodynamic properties of monatomic and molecular liquids.

The Ornstein—Zernike integral equations were numerically solved within the framework of the RISM approach by an iterative procedure using a multigrid technique,[35] which implies discretization of solution using an iterative algorithm on different grid spacing, which allows one to significantly accelerate calculations.[35,36] In this work, calculations were performed to an accuracy of $10^{-4}$.

## Results and Discussion

Figure 1 presents the PCFs $g_{Cat+O}(r)$ and $g_{An-O}(r)$ calculated using the set *4*. The pair correlation functions calculated with other sets of parameters of the Lennard-Jones potential are similar in shape, being slightly different in peak heights and positions. From the plots in Fig. 1 it follows that the heights of the main peaks and the depths of the first minima of these PCFs considerably decrease in the series $Li^+ \rightarrow Na^+ \rightarrow K^+ \rightarrow Rb^+ \rightarrow Cs^+$ and $F^- \rightarrow Cl^- \rightarrow Br^- \rightarrow I^-$. The maxima and minima are shifted toward larger $r$ while the peaks are broadened. A similar behavior of the PCFs was obtained from the molecular dynamics calculations of these systems.[37,38]

The hydration free energies Δμ of monovalent ions calculated using the HNC, RB, GF, PW, and PWC models with the parameter sets *1*—*5*, as well as the experimental data[39,40] are listed in Tables 1 and 2.

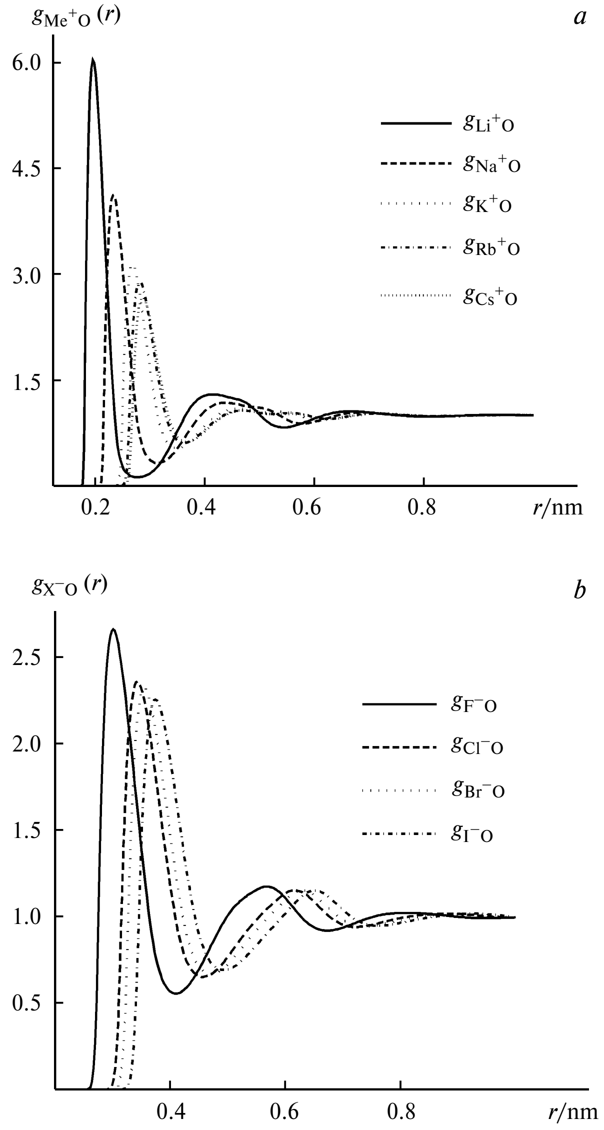

**Fig. 1.** Pair correlation functions $g_{Cat+O}(r)$ (*a*) and $g_{An-O}(r)$ (*b*) calculated using the set *4* of parameters of the Lennard-Jones potential.[17]

**Table 1.** Calculated and experimental hydration free energies of monovalent cations ($\Delta\mu$/kcal mol$^{-1}$)

| Parameter | $-\Delta\mu_{HNC}$ | $-\Delta\mu_{RB}$ | $-\Delta\mu_{GF}$ | $-\Delta\mu_{PW}$ | $-\Delta\mu_{PWC}$ | $-\Delta\mu_{exp}$[39] |
|---|---|---|---|---|---|---|
| | | | $Li^+$ | | | |
| *1* | 94.4 | 96.7 | 99.7 | 88.3 | 89.8 | |
| *2* | 101.8 | 103.9 | 107.8 | 95.3 | 96.0 | |
| *3* | 95.2 | 97.6 | 100.5 | 89.1 | 90.6 | 122.1 |
| *4* | 101.6 | 103.7 | 107.7 | 95.1 | 95.7 | |
| *5* | 102.8 | 105.0 | 108.7 | 96.2 | 97.1 | |
| | | | $Na^+$ | | | |
| *1* | 75.5 | 78.8 | 79.8 | 70.7 | 74.1 | |
| *2* | 75.3 | 78.8 | 79.6 | 70.6 | 73.7 | |
| *3* | 69.8 | 73.6 | 73.9 | 65.4 | 69.6 | 98.4 |
| *4* | 80.6 | 83.9 | 85.3 | 75.6 | 77.9 | |
| *5* | 81.4 | 84.5 | 85.9 | 76.2 | 79.0 | |
| | | | $K^+$ | | | |
| *1* | 57.1 | 62.1 | 61.2 | 53.6 | 59.9 | |
| *2* | 60.2 | 65.1 | 64.5 | 56.6 | 61.8 | |
| *3* | 51.2 | 56.8 | 55.4 | 48.1 | 55.6 | 80.6 |
| *4* | 65.5 | 70.3 | 70.0 | 61.7 | 65.7 | |
| *5* | 68.1 | 72.0 | 72.1 | 63.7 | 68.3 | |
| | | | $Rb^+$ | | | |
| *1* | 49.7 | 55.4 | 53.9 | 46.7 | 54.6 | |
| *2* | 56.6 | 62.0 | 60.9 | 53.3 | 59.2 | |
| *3* | 44.5 | 50.9 | 48.9 | 41.9 | 50.9 | 75.5 |
| *4* | 60.7 | 66.1 | 65.2 | 57.2 | 62.0 | |
| *5* | — | — | — | — | — | |
| | | | $Cs^+$ | | | |
| *1* | 37.5 | 44.9 | 42.2 | 35.5 | 46.3 | |
| *2* | 50.3 | 56.6 | 54.9 | 47.6 | 54.7 | |
| *3* | 35.3 | 43.0 | 40.2 | 33.5 | 44.9 | 67.8 |
| *4* | 55.6 | 61.1 | 60.0 | 52.4 | 58.5 | |
| *5* | 57.5 | 62.4 | 61.5 | 53.9 | 60.2 | |

The data of Tables 1 and 2 show that all models systematically underestimate the $|\Delta\mu|$ values for cations irrespective of the set of parameters. At the same time, the absolute values of $\Delta\mu_{calc}$ for the anions may be either larger or smaller than the experimental values depending on the model and the set of parameters. A comparison of the theoretical values shows that the $\Delta\mu_{calc}$ values for anions are in better agreement with the experimental data for all models and parameters of the Lennard-Jones potential compared to the $\Delta\mu_{calc}$ values for cations. The best fit for both cations and anions was obtained with the set *4* and set *5*. The average relative deviation from experimental data for cations was at most 24.2 and 22.6%, respectively; for anions, one has 17.2 and 13.6%, respectively (*cf.* 47.6, 29.8, and 50.6% for cations and 22.6, 18.6, and 29% for anions obtained with the sets *1*, *2*, and *3*, respectively). In some cases, the $\Delta\mu_{calc}$ values obtained with the set *1* almost coincide with the experimental data (see Table 2, $\Delta\mu_{HNC}$ for the bromide ion and $\Delta\mu_{GF}$ for the chloride ion).

Now we will analyze which equation for the calculations of the ion hydration free energy with the sets *4* and *5* gives the best fit to the experimental data. To this end, we calculated the root-mean-square deviation (RMSD) of the difference $\Delta\mu_{exp} - \Delta\mu_{calc}$ (Fig. 2). From Fig. 2 it follows that the GF and RB models for cations and the GF and HNC models for anions give the best results. In particular, the RMSD of the difference $\Delta\mu_{exp} - \Delta\mu_{calc}$ calculated for cations (Fig. 2, *a*) is 12.6 (set *4*) and 10.6 (set *5*) kcal mol$^{-1}$ for the RB model and 11.5 (set *4*) and 12.1 (set *5*) kcal mol$^{-1}$ for the GF model. Thus, the RB and GF models give nearly equal errors in the estimation of the hydration free energy of cations. The RMSD of the difference $\Delta\mu_{exp} - \Delta\mu_{calc}$ calculated for anions (Fig. 2, *b*) is

**Table 2.** Calculated and experimental hydration free energies of monovalent anions ($\Delta\mu$/kcal mol$^{-1}$)

| Parameter | $-\Delta\mu_{HNC}$ | $-\Delta\mu_{RB}$ | $-\Delta\mu_{GF}$ | $-\Delta\mu_{PW}$ | $-\Delta\mu_{PWC}$ | $-\Delta\mu_{exp}$[39] |
|---|---|---|---|---|---|---|
| | | | $F^-$ | | | |
| *1* | 122.4 | 130.4 | 131.1 | 113.4 | 112.3 | |
| *2* | 112.0 | 119.8 | 119.3 | 103.8 | 103.9 | |
| *3* | 109.5 | 118.3 | 116.7 | 101.9 | 101.6 | 107.0 |
| *4* | 97.7 | 105.5 | 103.6 | 90.9 | 92.3 | |
| *5* | 102.7 | 110.9 | 109.1 | 95.4 | 96.3 | |
| | | | $Cl^-$ | | | |
| *1* | 73.2 | 84.4 | 78.3 | 68.9 | 73.4 | |
| *2* | 74.2 | 85.1 | 79.2 | 69.7 | 74.1 | |
| *3* | 80.0 | 92.1 | 85.6 | 75.4 | 78.1 | 78.1 |
| *4* | 72.3 | 82.4 | 77.1 | 67.8 | 72.7 | |
| *5* | 74.2 | 85.1 | 79.2 | 69.7 | 74.1 | |
| | | | $Br^-$ | | | |
| *1* | 69.0 | 80.5 | 74.0 | 65.0 | 70.3 | |
| *2* | 70.7 | 82.1 | 75.7 | 66.6 | 71.5 | |
| *3* | 73.7 | 86.9 | 79.4 | 69.9 | 73.5 | 69.2 |
| *4* | 67.0 | 78.0 | 71.9 | 63.1 | 68.8 | |
| *5* | 66.1 | 77.6 | 71.1 | 62.3 | 68.2 | |
| | | | $I^-$ | | | |
| *1* | 52.0 | 65.9 | 57.5 | 49.6 | 58.5 | |
| *2* | 56.1 | 69.7 | 61.5 | 53.4 | 61.2 | |
| *3* | 62.1 | 77.8 | 68.3 | 59.6 | 65.4 | 60.3 |
| *4* | 58.2 | 70.7 | 63.2 | 55.1 | 62.6 | |
| *5* | 55.7 | 68.5 | 60.9 | 52.9 | 60.9 | |

5.7 (set *4*) and 4.0 (set *5*) kcal mol$^{-1}$ for the HNC model and 2.6 (set *4*) and 1.5 (set *5*) kcal mol$^{-1}$ for the GF model. The errors in estimation of the hydration free energy of anions are an order of magnitude smaller than for cations. Thus, the GF and RB models for cations and the GF model for anions are the most accurate from the standpoint of description of the thermodynamics of ion hydration.

Figures 3 and 4 present the plots of the hydration free energies of cations and anions calculated using the equation for the GF model with the set *5 vs.* ionic radii (according to Pauling). For comparison, the experimental data[39] for all cations and anions,[40] as well as the results of alternative QM/MM (see Ref. 39) and RISM calculations[28,30] are also shown. Calculations using the HNC model were also performed[28] with the Lennard-Jones potential parameters[41] different from those used in our work. Calculations using the RB model with the set *1* were also reported.[30] From Figs 3 and 4 is follows that the $\Delta\mu_{calc}$ values obtined using the GF model and the set *5* better fit to the experimental data than those determined using other models and sets of parameters. Differences between the hydration free energies obtained from our RISM calculatons and those given in Refs 28 and 30 increase with an increase in the cation size and with a decrease in the anion size (see Figs 3 and 4).

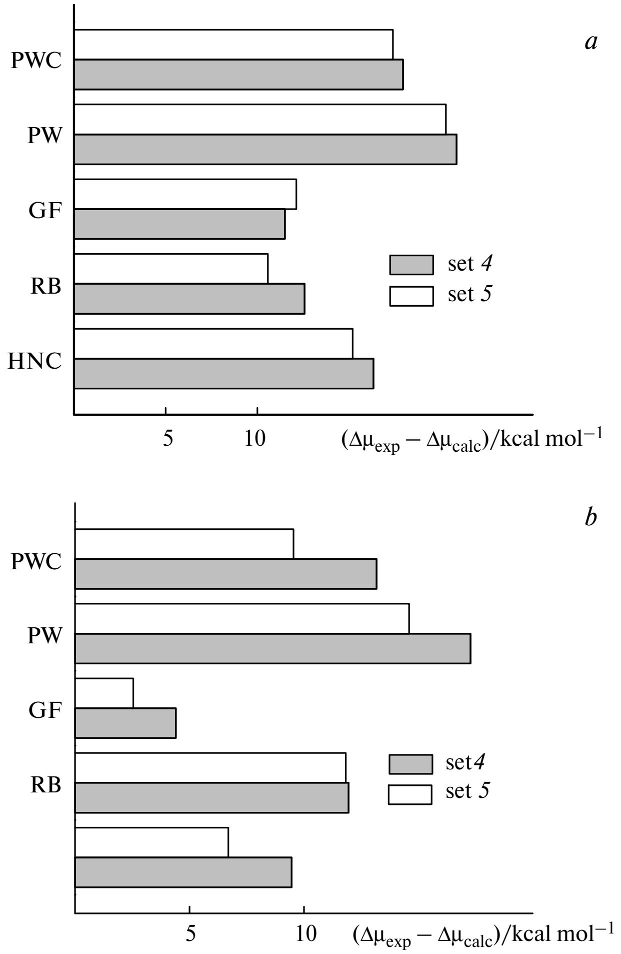

**Fig. 2.** Root-mean-square deviations of the difference $\Delta\mu_{exp} - \Delta\mu_{calc}$ obtained for cations (*a*) and anions (*b*) using the sets *4* and *5*. The $\Delta\mu_{calc}$ values were calculated using the equations for the HNC, RB, GF, PW, and PWC models.

From the aforesaid it follows that the choice of parameters of the Lennard-Jones potential may significantly influence the results of calculations. This is clearly illustrated by the results of RISM calculations for cations with the RB model obtained in the present work and earlier[30] (see Fig. 3, inset). This model for cations is one of the most accurate models from the standpoint of description of the thermodynamics of ion hydration. A comparsion of our results with those obtained earlier[30] shows that the results of our calculations using another set of parameters of the Lennard-Jones potential are in better agreement with the experimental data than the published data[30] (see Fig. 3), especially for larger cations. Differences between the hydration free energies increase as the radius of the cation increases.

Thus, a proper choice of parameters of the Lennard-Jones potential plays a significant role in RISM calculations of thermodynamic characteristics of ion hydration,

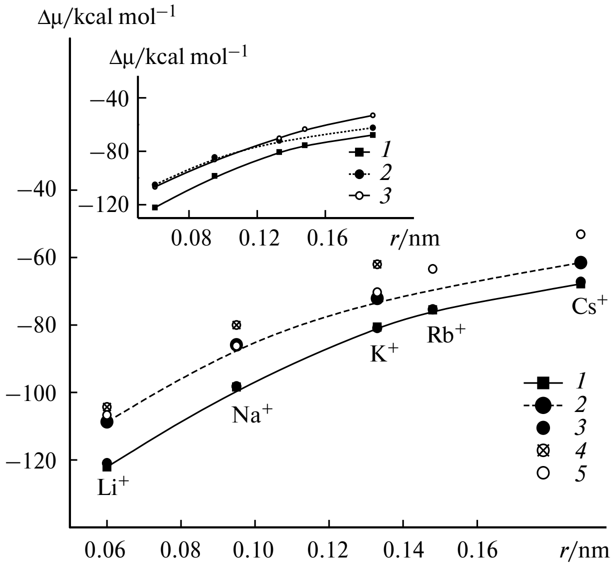

**Fig. 3.** Hydration free energies of cations plotted *vs.* their radii: experimental data[39] (*1*); calculations performed in this work using the GF model with the set *5* (*2*); results of QM/MM calculations[39] (*3*); alternative RISM calculations[28] with the HNC model and parameters of the Lennard-Jones potential[41] (*4*) and RISM calculations[30] with the RB model and the set *1* (*5*). Inset: experimental data[39] (*1*); results of calculations performed in this work using the RB model with set *5* (*2*); and alternative RISM calculations[30] using the RB model with the set *1* (*3*).

whereas the use of improved models, *e.g.*, PW or PWC, in calculations of the hydration free energy does not always give more accurate results.

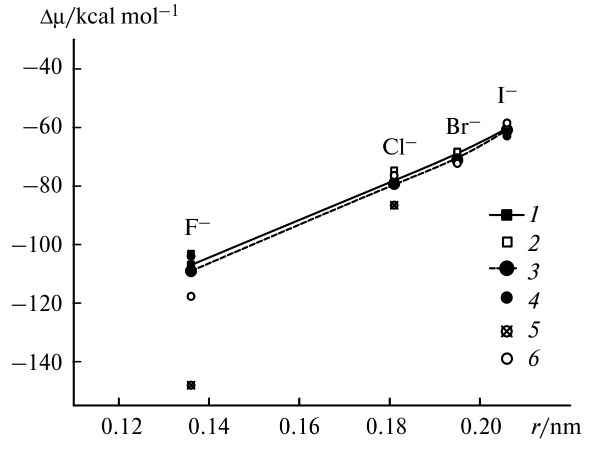

**Fig. 4.** Hydration free energies of anions plotted *vs.* their radii: experimental data[39,40] (denoted *1* and *2*, respectively); results of calculations performed in this work using the equation for the GF model with the set *5* (*3*); results of QM/MM calculations[39] (*4*), and results of alternative RISM calculations[28] with the HNC model and the parameters of the Lennard-Jones potential[41] (*5*) and results of RISM calculations[30] using the RB model and the set *1* (*6*).

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