

SHORT COMMUNICATION

## Comment on “Molecular Dynamics Simulations of Zinc Ions in Water Using CHARMM”

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**Abstract** In the recent paper by Obst and Bradaczek [1], which compares two sets of force field parameters for divalent zinc, several errors were made. Clarifying these errors leads to another interpretation of their simulation results, which, in contrast to their original conclusions, substantiates the parameter set for zinc ion developed by Stote and Karplus [2].

**Keywords** Molecular dynamics simulation, Zinc, CHARMM, Ions, Solvation

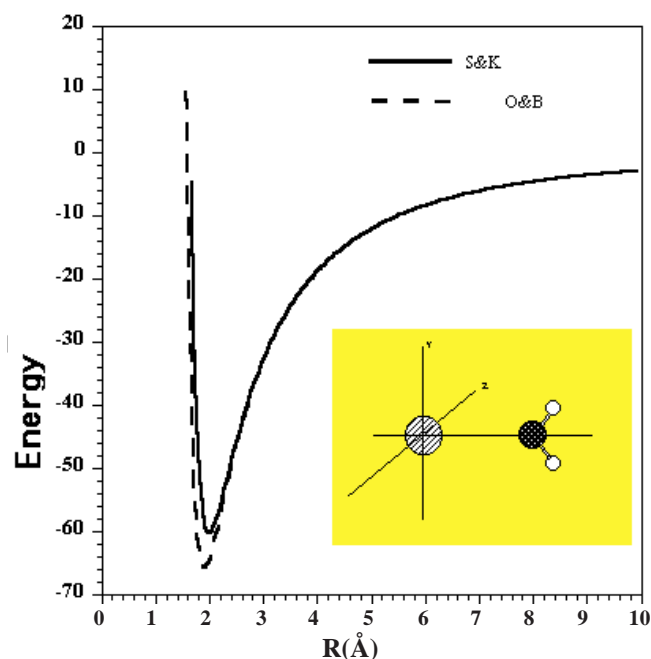
### Comment

In a recent paper [1], Obst and Bradaczek compare two sets of force field parameters for divalent zinc; one set of parameters was obtained from the QUANTA program [3] and the second set was derived from the parameters published by Stote and Karplus [2]. Using these parameter sets, simulations of the Zn<sup>2+</sup> ion solvated in water were done using the CHARMM program [4]. From their simulations, properties such as the radial distribution function, the coordination number and the diffusion coefficients were calculated.

Obst and Bradaczek claim that the calculated radial distribution function was in better agreement with the experimental data when using the ‘original’ CHARMM22 zinc ion parameters distributed by MSI than when using the ‘optimised’ parameters published by Stote and Karplus. In Table 1 of their paper, they present the two parameter sets

used in their calculations, the so-called MSI parameter set and the parameter set “modified by Stote and Karplus” [2]. From this Table, it is evident that errors were made in converting between the parameters published by Stote and Karplus and the parameters used by them in their simulations. The parameters presented in Table 1 of their paper for the zinc ion are  $r_{\min}=0.975\text{\AA}$  and  $E_{\min}=0.250\text{kcal/mol}$  for the Lennard-Jones 6-12 potential and  $q=+2.0$  for the point charge. In the paper by Stote and Karplus, the parameters for zinc ion are given as  $\sigma=1.95\text{\AA}$ ,  $\epsilon=0.250\text{kcal/mol}$  and  $q=+2.0$ . In converting  $\sigma$  to  $r_{\min}$ , Obst and Bradaczek divided  $\sigma$  by 2 to arrive at the  $r_{\min}$  given in Table 1 of their paper. This conversion is incorrect; the correct relationship between  $r_{\min}$  and  $\sigma$  is  $r_{\min}=2^{1/6}\sigma$ , which is obtained by solving for  $r$  in terms of  $\sigma$  at the minimum of the Lennard-Jones potential. Also, in the CHARMM parameter files, the Lennard-Jones parameters are given as  $\epsilon$ , which is equivalent to  $E_{\min}$ , and  $r_{\min}/2$  rather than  $r_{\min}$  [4,5]. Therefore, the parameters used by them and referred to as those “modified by Stote and Karplus” are not the parameters presented in the paper

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**Figure 1** Comparison of zinc-water interaction potentials calculated using the parameters of Stote and Karplus (S&K) and using those employed by Obst and Bradaczek (O&B) in their simulations of solvated zinc ion. The insert shows the orientation of the TIP3P water; the hydrogens are in the  $x$ - $y$  plane and  $R$  is the distance between the zinc ion and the oxygen atom

by Stote and Karplus [2]. In fact, the parameter set for zinc ion presented in the paper by Stote and Karplus is the one used in the program QUANTA. Thus, the simulations of Obst and Bradaczek [1] used another parameter set and the worse results substantiate the parameter set developed by Stote and Karplus.

An additional point concerns the observed changes in water geometry reported by Obst and Bradaczek [1]. During MD

simulations, the SHAKE algorithm [6] is usually invoked to fix bond lengths between hydrogens and heavy atoms; hence changes in water geometry cannot occur while SHAKE is enabled. In the study by Obst and Bradaczek [1], the SHAKE algorithm was called after an energy minimization and prior to the molecular dynamics simulation, so the constraints for SHAKE were taken from the non-standard geometries of the energy minimized water molecules rather than from the standard values for TIP3P water [7]. The molecular dynamics simulations with SHAKE were then run using these constraints; each water molecule had slightly different SHAKE constraints. The observed distortions of the geometry of water molecules from the first hydration shell are, then, the result of the minimization procedure and reflect the influence of the zinc ion on its nearest neighbour water molecules. The distortions in first shell water molecules were small; moreover, these water molecules did not exchange during the course of the 1 ns simulation. The results of the MD simulations are, therefore, not expected to differ significantly from what would have been observed if the water geometry had been fixed before minimization.

## References

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[a] In the parameter files distributed with the QUANTA program, the columns of nonbond parameters are labeled as  $E_{\min}$  and  $R_{\min}$ , however, the values actually are  $E_{\min}$  and  $R_{\min}/2$ .