ORIGINAL PAPER

Molecular simulations of intermediate and long alkanes adsorbed on graphite: Tuning of non-bond interactions

Lucyna Firlej · Bogdan Kuchta · Michael W. Roth · Carlos Wexler

Abstract The interplay between the torsional potential energy and the scaling of the 1-4 van der Waals and Coulomb interactions determines the stiffness of flexible molecules. In this paper we demonstrate for the first time that the precise value of the nonbond scaling factor (SF)—often a value assumed without justification—has a significant effect on the critical properties and mechanisms of systems undergoing a phase transition, and that, for accurate simulations, this scaling factor is highly dependent on the system under consideration. In particular, by analyzing the melting of n-alkanes (hexane C6, dodecane C12, tetracosane C24) on graphite, we show that the SF is not constant over varying alkane chain lengths when the structural correlated transformations are concerned. Instead, monotonic decrease of SF with the molecular length drives a cross-over between two distinct mechanisms for melting in such systems. In a broad sense we show that the choice for SF in any simulation containing adsorbed or correlated long molecules needs to be carefully considered.

L. Firlej · B. Kuchta · C. Wexler
Department of Physics and Astronomy, University of Missouri,
Columbia, MO 65211, USA

M. W. Roth (✉)
Department of Physics, University of Northern Iowa,
Cedar Falls, IA 50614, USA
e-mail: rothm@uni.edu

B. Kuchta
Université Aix-Marseille 1, Laboratoire Chimie Provence,
Marseille, France

L. Firlej
Université Montpellier 2, Laboratoire des Colloides,
Verres et Nanomatériaux,
Montpellier, France

Introduction

During the last half century computational physics has grown in scope and importance to a point where it became a third part added to the traditional divisions of experimental and theoretical physics. Computer simulations have brought remarkable insight into the behavior exhibited by complex systems with large numbers of degrees of freedom. Recent advances in computer power and algorithms have facilitated detailed simulations of systems comprised of thousands to millions of atoms, for periods of ns to μs, permitting detailed pictures of diverse phenomena, ranging from simple atomic processes to complex behavior of biological macromolecules.

The integrity of the results of computer simulations of any real system depends, however, on the quality of the force fields in the theoretical model. This becomes critically important when modeling large systems of flexible molecules, such as biomolecules (especially proteins or lipids) or polymers, for which alkanes are prototypes. In such systems, correlations between internal and external degrees of freedom determine the local conformational stability of molecules (*i.e.*, folding). Conversely, the same correlations affect intermolecular correlated processes (*e.g.*, phase transitions). Being able to correctly account for the energy and ordering of conformations is essential if force field methods are to be considered as predictive.

Recently, a number of auto-assemblies for alkanes on graphite have been studied by molecular dynamics (MD) methods [1–8]. Two important conclusions emerged from

comparative analyses of those studies. First, an all-atom representation of the molecules was always necessary to reproduce the intricacies between structural and melting properties of the systems [4, 7]. Second, it is of extreme importance to model correctly the internal non-bonded interactions because they are the ones that define the molecular stiffness and hence the ability of molecules to deform [3]. The relative stability of a particular conformation of a given molecule is determined by a balance between the torsional energy and the nonbonded energy terms (electrostatic, van der Waals and repulsive). When the conformational changes are involved in thermodynamic phenomena (such as phase transitions), the necessary precision of the interaction model is even more demanding, as it has to reproduce correctly the whole distribution of instantaneous configurations. This requirement is usually satisfied by a parameterization of the force fields. However, in spite of the enormous progress made in recent years, uncertainties in the non-bonded internal energy components and electrostatic interactions (including the polarization energy) still persist.

Fitting force-field parameters is an elaborate task. All of the most popular modern force fields (OPLS-AA [9]; CHARMM22 [10]; AMBER-94 [11]) define several parameters that attempt to quantify the relative contribution of different internal and intermolecular energy terms to the total energy of the systems. Certainly, it is always desirable for parameters to be transferable and applicable to a wide class of molecules—in practice this is quite difficult to attain. Although ab initio electronic calculations have become the primary source of energies which are used to fit force field parameters, the resulting force fields are not perfect in the sense that they often fail to reproduce some properties of the modeled object. Since ab initio calculations used for the derivation of parameters are performed in the gas phase, intermolecular correlations occurring in dense (liquid or solid) phases are not included.

In most non-polar organic systems, electrostatic terms have a negligible impact [11, 12] and are usually totally ignored [13, 14]. However, ab initio calculations indicate significant charge separation within a C-H bond (0.3-0.6 D). The optimized parameters for liquid simulations-all atoms representation (OPLS-AA) force field tries to account for that, introducing partial charges specific to atoms involved in a given chemical bond. These non-negligible bond dipoles noticeably affect the interaction energies when two molecules approach each other, becoming more important as molecules become less symmetrical.

The modeling of the internal non-bonded interactions is much less obvious: in particular, how to correctly account the 1-4 interactions (atoms separated by three bonds) that are partially included in the dihedral torsion term, *i.e.*, how to avoid double-counting those. This is crucial since, as will

be shown later in the paper, the interplay between the torsional potential and the scaling of 1-4 van der Waals (vdW) and 1-4 Coulomb interactions determines the internal (conformational) stiffness of the molecule and its ability to deform in a very sensitive way. To deal with this possible over counting, the CHARMM [10] force field introduces a scaling parameter which allows one to reduce the strength of the 1-4 electrostatic and vdW interactions. At present, there is no physical justification to choose a particular value for such parameter. Nevertheless, in most large scale MD computations and their associated force fields (AMBER [11]; YAMBER [15]; NAMD [16]) used for simulations of soft molecules (polymers and proteins) its value is arbitrarily fixed.

A possible way to characterize the behavior of adjustable parameters is to check how different components of the force field affect the kinetic and thermodynamic quantities that can be extracted from numerical simulations. In this paper we present what is, to the best of our knowledge, the first attempt to gain an understanding of the 1-4 scaling influence on physical properties, as implemented in NAMD code that uses a CHARMM force field. Because of the complexity of proteins, we have chosen to focus first on much simpler physical systems: n-alkanes. We base our analysis looking at the ability of interaction models that differ by scaling parameter to reproduce two aspects of experimentally determined physical properties of monolayers of alkanes adsorbed on graphite: temperatures of melting, and the mechanism of the transition. The valid range of scaling is tested by comparing the optimal scaling parameter determined for three alkanes of different length: hexane C_6H_{14} ($l \sim 6.4$ Å), dodecane $C_{12}H_{26}$ ($l \sim 13$ Å) and tetracosane $C_{24}H_{50}$ ($l \sim 28$ Å).

Numerical aspects

Large scale molecular dynamics (*NVT* ensemble, all atom representation) simulations were performed within the NAMD [16] package. The simulation box contained on the order of 50,000 atoms (adsorbate + substrate). The optimizations and parallelization of NAMD permitted us to offset the extra computation time cost of the explicit hydrogen inclusion. However, the simulations still required very long runs (~0.1 μs) which used on the order of 10 CPU years per alkane.

The interaction model applied in this paper uses the CHARMM22 [10] format and parameters. Non-bonded interactions include an electrostatic interaction, a two-body atom-atom Lennard-Jones interaction between different molecules, and atom-substrate pair interactions. The internal degrees of freedom include the three-body bond angle

bending and four-body dihedral torsions. The values of potential parameters are listed in a previous paper [4].

The CHARMM22 [10] force field offers several options of exclusion and scaling policies for non-bonded interactions. In the present study, the exclusion/scaling options have been fixed as follows: any one of the 1-2, 1-3, and 1-4 intramolecular energy components can be scaled. In the case of the so called scaled 1-4 exclusion option, the 1-4 electrostatic interaction is modified by a SF (0< SF <1) and 1-4 van der Waals energy is rescaled down using a (slightly) modified 6-12 interaction parameter defined in the CHARMM2 force field. This scaling option was applied in our calculation. At the same time the interactions between pairs 1-2 and 1-3 are totally excluded from non-bonded terms. We will show that any modification of electrostatic SF dramatically affects the physical properties of alkanes and modifies the balance between the torsional and non-bonded energies.

The procedure proposed in this paper differs from that employed by the force field authors [9–11] where a sum of the dihedral terms and internal nonbonded energy should reproduce the torsional energy. Rather, we perform extensive tests where the SF is adjusted so as to give the most reasonable results for melting temperature and dynamics for alkanes of various lengths, as the scaling factor in this work affords the opportunity to balance the inter- and intramolecular components of the nonbonded energy terms. So, we do not aim at a complete re-parameterization of the applied force field; instead we choose the most arbitrarily adjustable potential parameter and tune it for optimal results in regimes outside those originally considered in the force field development: when the molecules are strongly correlated to each other or to a surface. Such types of physical situations are always encountered at the interfaces and in the vicinity of phase transitions and they are difficult to parameterize directly from ab initio gas phase calculations.

Results

Figure 1 shows the temperature dependence of the Lennard-Jones (LJ) intermolecular energy of the adsorbed alkane monolayers calculated assuming either a large effect with small scaling factor (SF=0.1) or small effect with large scaling factor (SF=0.9) of 1-4 nonbond interactions. Clearly, by scaling the 1-4 nonbond terms one shifts the position of the inflection point on energy curve that indicates the temperature of the melting transition. Additionally, the amplitude of this shift increases with the backbone length in a monotonic way and reaches a value of several tens of degrees for tetracosane, the longest alkane studied here. Furthermore, as will be discussed later, the

most interesting result induced by scaling 1-4 interactions is the change of the microscopic mechanism of melting. First, it should be recalled and emphasized that melting of alkanes layers adsorbed on graphite is quite different from the traditional picture of melting. Alkane molecules are neither isotropic nor rigid; for these reasons, as it has been shown and discussed in recent papers [1–8], the melting of solid layers is a cooperative process in which the molecular layer loses both inter- and intra-molecular order. Such a transformation is driven by a progressive deformation of the internal structure of molecules.

The rigidity of the molecular backbone may be characterized by its facility of gauche defect formation [7]. The apparent stiffness of molecules results from a competition between the internal forces and the external field, resulting from the interactions with neighboring molecules. Figure 2 shows the fraction of the gauche defects formed in a molecular backbone as a function of temperature, for different SFs meaning that: (i) The stiffness increases for higher SFs, implying that the electrostatic term of the interaction stabilizes the linear configuration of molecules and prevents the backbone destabilization; (ii) The strength of intermolecular forces that defines topological aspects of melting increases with the molecule length. Therefore, both components tend to stabilize the solid state of the layers and in simulations the observed temperature of melting, T_{melt}, is higher than the experimental one for high SFs. These shifts increase with alkane length and for tetracosane reaches the unrealistic value of 200 K for SF=1. On the other hand, if the 1-4 electrostatic interaction is almost totally suppressed (SF=0.1) the simulated layers become disordered easily via excessive chain deformation and melts at unrealistically low temperatures. Experimentally, the layers of shorter molecules melt with molecules much less deformed (stiffer), whereas in longer ones the deformation of the backbone appears to be the driving force of melting [1–8]. To reproduce this observation in computer simulations, the competition between the stiffness-defining components of energy should be correctly balanced. In this paper, we achieve this by scaling the 1-4 non-bonded terms (in CHARMM2).

Logically, it could be possible to determine the correct SF directly from the calculations performed at the experimental T_{melt}. Figure 3 shows the intermolecular LJ energy calculated for each alkane at the experimental melting temperature (170 K, 283 K and 340 K for C6, C12 and C24, respectively) as a function of the SF. The optimal SFs determined as the inflection point at the curves in Fig. 3 are: SF≅0.45 for tetracosane, SF≅0.65 for dodecane and SF≅0.8 for hexane. For optimal SF, all observables of the system (LJ energy, and also order parameters, see Fig. 4) show a clear singularity at T_{melt}. Figure 5 shows the variation of the optimal SF as a function of the number of
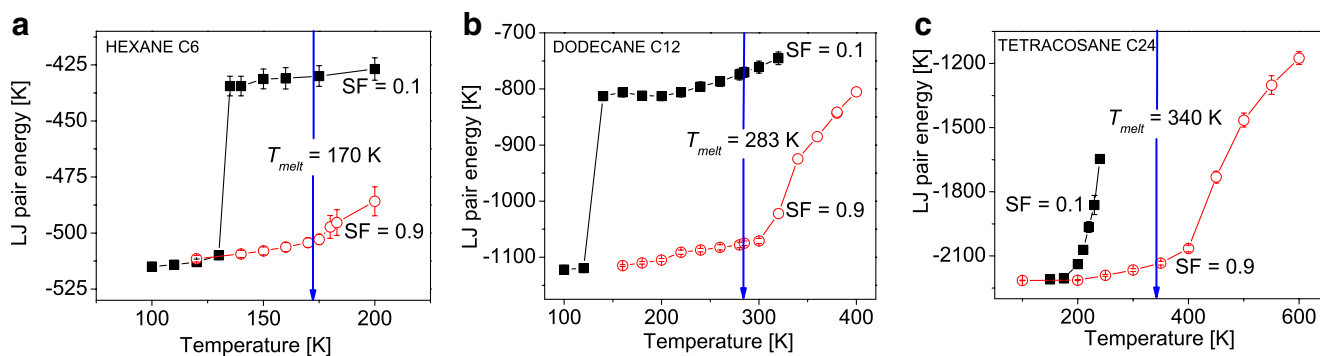
Fig. 1 LJ intermolecular energy as a function of temperature for two values of the scaling factor: SF=0.1 and SF=0.9 for (**a**) hexane, (**b**) dodecane and (**c**) tetracosane. The inflection point indicates the melting transition in each model situation. The arrows indicate the experimental melting temperatures T_{melt}

carbon atoms in the alkane chain. This dependence can be tentatively approximated, within the error bars, by a monotonically decaying function which permits the estimation of the SF for other alkanes. Verification of our conclusions for other alkanes will be possible when experimental melting of other alkanes becomes known.

Figure 3 illustrates another interesting feature: each alkane shows different sensitivity to the scaling procedure. For C6 at T_{melt} the LJ energy is not strongly dependent on the 1-4 SF. This is because in short alkanes ($n<10$) melting is not induced by the internal deformation of molecules; therefore the conformational intramolecular force terms are less coupled to intermolecular forces and do not play a significant role in the mechanism of melting. This conclusion is also supported by an analysis of the average bond length (calculated from the end-to-end length, see Fig. 6). The change in the average bond length reflects the change of the molecular conformation at melting. Hexane molecules are stiff and remain unfolded up to the melting temperature, where the gauche defects start to form at the molecules ends [17]. The process of melting in the layer is thus driven by the reduction of the molecules' footprint via

rolling of the alkane plane to the orientation perpendicular with respect to the substrate and, subsequently, the molecules promotion to the second layer [3, 4]. For long molecules, the deformation of the molecular backbone through gauche defect formation (in-chain melting) assures the reduction of the molecules' footprint prior to intermolecular disordering. If a similar mechanism were responsible for melting in shorter alkanes, the melting temperature would be much lower (Figs. 1 and 2). Therefore for C6 the experimental temperature of melting is reproduced in the simulation only if the SF is relatively large. As a consequence, C6 molecules remain stiff and not deformed until the melting temperature. In the case of C12 and C24, much smaller SFs are required to correctly describe the smaller molecular stiffness.

Such observations are of extreme importance: there is a crossover between two limits of scaling 1-4 non-bonded interactions which modifies the melting mechanism. Depending on the alkane length, it is a continuous crossover between melting induced by the lattice instability (short alkanes, $n<6$) to melting induced by instability of internal configurations of long molecules ($n\geq12$).
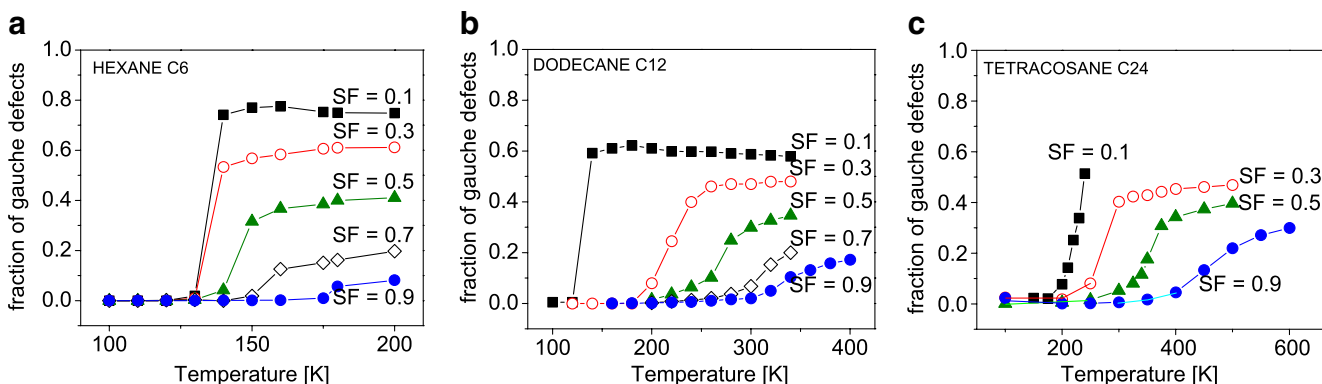

Fig. 2 Fraction of gauche defects formed within the molecular backbone at different SFs, as a function of temperature for (**a**) hexane, (**b**) dodecane and (**c**) tetracosane
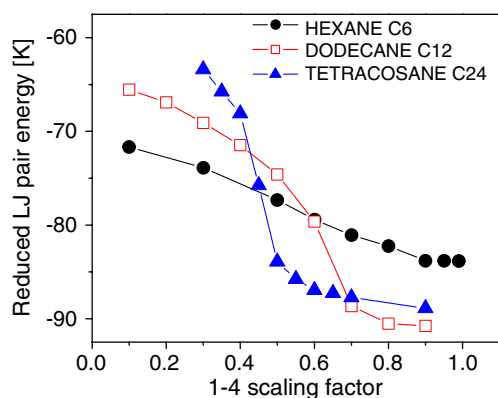
Fig. 3 LJ intermolecular energy as a function of 1-4 scaling factor. The calculations were done at the experimental temperatures of melting. For comparison, the values of LJ energy on the graph were normalized with respect to the number of carbons in the alkane chain

Fig. 5 Optimal scaling factor as a function of the number of carbons in the alkane backbone

From the point of view of computer modeling methodology, it is always desirable to have a set of force field parameters readily available that could be used for simulations of a broad range or even family of materials. Unfortunately, for the SF of the 1-4 non-bonded interactions there is no theoretical formula which would allow estimating its value *a priori*. Very often a conventional value of 0.4 or 0.5 has been used in studies, but it is the most poorly understood parameter in the CHARMM force field and therefore became the subject of the study reported in this work [11, 15]. Here, we have explicitly shown that the scaling of the 1-4 non-bonded interactions is strongly system-dependent, even within a group of molecules that differ only in length. We have observed that, in the case of alkanes the scaling factor decreases when the number of carbons in the molecular backbone increases. Our results allow the estimation of the optimal value of SF for any linear alkane. Extrapolating our results to longer alkanes,
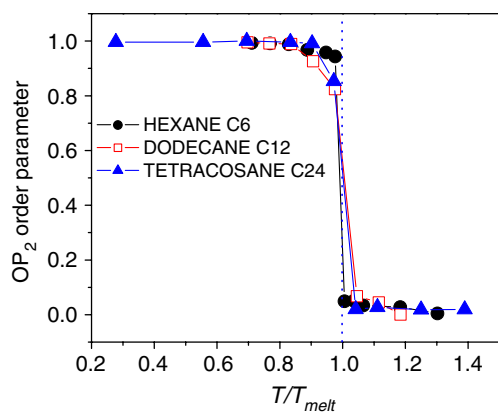
we estimate the SF approaches zero for alkanes with more than 50 carbons in the backbone. Such inference is consistent with the fact that the CHARMM force field, developed for modeling of large biological molecules was parameterized without any scaling of the internal electrostatic energy [10, 16].

Conclusions

The first important conclusion from this paper is the fact that the choice of SF within a given force field can profoundly modify our understanding of physical properties of highly correlated systems as seen in molecular simulations. The backbone torsional potential, 1-4 term scaling and the intermolecular interactions act collectively to determine the preferred conformational regions of the physical space and to define the melting transition temperature. We show that the variation of the SF affects both the energy barrier and the relative populations of trans

Fig. 4 OP$_2$ order parameter calculated for optimal scaling factors versus reduced temperature T/T_{melt}. $OP_2 = \sum_{i=1}^{N_m} \langle \cos 2\varphi_i \rangle / N_m$, where the sum runs over all N_m molecules in the simulation and $\phi_i \in [0, 180°]$ is the angle that the smallest moment of inertia axis for molecule i makes with the x-axis of the simulation box[4]
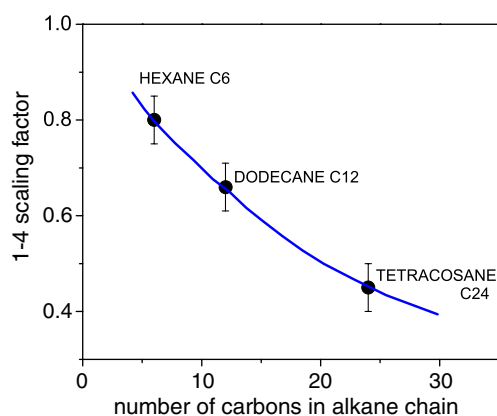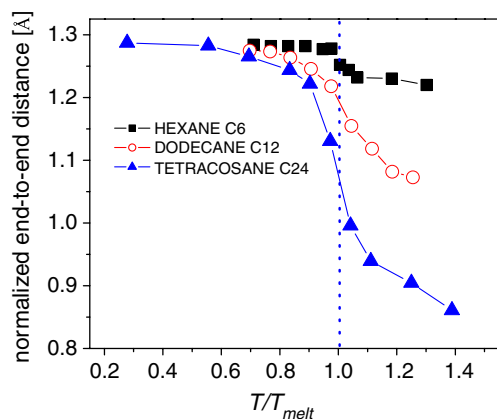

Fig. 6 Average end-to-end length of alkanes as a function of reduced temperature. Optimized scaling factors have been used in the calculations. The end-to-end distance was normalized with respect to the backbone number of C-C bonds

and gauche configurations of molecules. In consequence the mechanism of the melting is different when the scaling factor changes. When the SF is large (close to 1) the molecules are stiff and the melting of the adsorbed layer is induced by the molecules' promotion to the second layer. When SF decreases, the molecules are more flexible and the "footprint reduction" becomes the leading mechanism of the melting due to a higher probability of the gauche defect creation.

Properly adjusting the SF allowed us to easily modify the properties of alkanes adsorbed on graphite to reproduce the experimental properties of the melting transition. The results show that the initial force field parameters cannot be applied to quantitative simulations of the dense and correlated layer but they can be easily adapted to this particular situation. The fully correct procedure would involve a new fit of the rotational parameter to different scaling factors. However, there is no proof that such a procedure would give the force field parameters that are able to reproduce the dynamic properties of melting. Therefore, we have not attempted to find a new set of parameters and present our results as a voice in the long and difficult process of building more precise force fields applicable outside the gas phase.

What has been said above is related to the second important conclusion of this work and that is the observation that electrostatic interactions may play a significant role for non-polar molecules and that the required value of the scaling factor is not constant within the alkane family. Application of a single and arbitrary SF leads to unrealistic mechanisms of the molecular deformation and eventually to melting mechanisms and temperatures very different from the experimental fact. Our work, however, raises the possibility that there could exist a function determining the SF value for families of molecules. The final verification of this dependence requires confrontation with more experimental data and, in particular, high quality experimental melting temperatures which are not presently available. A central unanswered, important question is how we should understand the physical basis of scaling of 1-4 interaction components in computer simulations. A simple explanation would relate it to the necessity of avoiding a double-counting of the interaction already included in the bond energies. It is interesting to note that the scaled energy is a relatively small part of the total system energy; however, it still plays an extremely important role in the systems' dynamics. Such an observation suggests that the usual treatment of electrostatic energy, limited only to the accounting for the static distribution of charges over the molecule may not, in fact, be correct. The first step to improve it would consist of an inclusion in the interaction model of the polarization energy and variable charges, depending on the conformation of the molecule. There are some reports indicating that both electrostatic and polarization energies may be of similar importance [17]. Such an effect can be important even in non-polar systems such as alkanes because of the large configurational fluctuations at melting which make instantaneous configurations of molecules highly asymmetric. Therefore application of charge distributions should be re-examined: the influence of polarization energy remains to be tested. This aspect is presently being studied and will be reported in the future.

References

1. Hansen FY, Criswell L, Fuhrmann D, Herwig KW, Diama A, Dimeo RM, Neumann DA, Volkmann UG, Taub H (2004) Phys Rev Lett 92:046103–046106
2. Hansen FY, Herwig KW, Matthies B, Taub H (1999) Phys Rev Lett 83:2362–2365
3. Wexler C, Firlej L, Kuchta B, Roth MW (2009) Langmuir Lett 25:6596–6598
4. Connolly MJ, Roth MW, Gray PA, Wexler C (2008) Langmuir 24:3228–3234
5. Taub H, Hansen FY, Herwig KW, Matthies B (1999) Inorg Mater 35:847–851
6. Pint CL, Roth MW, Wexler C (2006) Phys Rev B 73:085422–085431
7. Firlej L, Kuchta B, Roth MW, Connolly MJ, Wexler C (2008) Langmuir 24:12392–12397
8. Roth MW, Pint CL, Wexler C (2005) Phys Rev B 71:155427–155439
9. Jorgensen WL, Maxwell DS, Tirado-Rives JJ (1996) Am Chem Soc 118:11225–11236
10. MacKerell AD Jr, Bashford D, Bellott M, Dunbrack RL Jr, Evanseck JD, Field MJ, Fischer S, Gao J, Guo H, Ha S, Joseph-McCarthy D, Kuchnir L, Kuczera K, Lau FTK, Mattos C, Michnick S, Ngo T, Nguyen DT, Prodhom B, Reiher WE III, Roux B, Schlenkrich M, Smith JC, Stote R, Straub J, Watanabe M, Wiorkiewicz-Kuczera J, Yin D, Karplus M (1998) J Phys Chem B 102:3586–3616
11. Cornell WD, Cieplak P, Bayly CI, Gould IR, Merz KM, Ferguson DM, Spellmeyer DC, Fox T, Caldwell JW, Kollman PA (1995) J Am Chem Soc 117:5179–5197
12. Song W, Rossky PJ, Maroncelli M (2003) J Chem Phys 119:9145–9162
13. Sprik M, Ursula R, Klein M (1999) Mol Phys 97:355–374
14. Borofin O, Smith GD, Bedrov D (2002) J Phys Chem B 106:9912–9922
15. Krieger E, Darden T, Nabuurs SB, Finkelstein A, Vriend G (2004) Proteins 57:678–683
16. Phillips JC, Braun R, Wang W, Gumbart J, Tajkhorshid E, Villa E, Chipot C, Skeel RD, Kale L, Schulten K (2005) J Comput Chem 26:1781–1802
17. Rasmussen TD, Ren P, Ponder JW, Jansen F (2007) Int J Quant Chem 107:1390–1395