Electronic Supplementary Information

for

Adsorption Mechanism of Single Amino Acid and Surfactant Molecules to Au {111} Surfaces in Aqueous Solution: Design Rules for Metal-Binding Molecules

by

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Details on Interatomic Potentials and Computed Adsorption Energies Using Two Independent Force Fields (CHARMM-METAL and CVFF-METAL)

In addition to the CHARMM22[32]–METAL[22] force field (Figure 1), we employed the CVFF[33]-METAL[22] force field for further validation of computed adsorption energies (Figure S1). The biomolecular force field CHARMM has been thoroughly validated with respect to molecular conformations and cohesive energies,[32] whereas the biomolecular force field CVFF[33] is a decade older and the quality of parameters is not as high, in part related to the availability of much less powerful computational resources at the time of development. The two combined biomolecular-metal force fields yield very similar results after some important differences are explained (Figure S1). These are: (1) The CVFF force field overestimates cohesive energies for aromatic molecules by 80% compared to experiment which results in overestimates of adsorption energies of aromatic molecules of similar magnitude (Trp, Tyr, Phe, His, PPh_3). (2) The CVFF force field underestimates the polarizability of the sulfur atom in Met (and Cys) to be lower than that of oxygen which results in underestimated (non-covalent) adsorption energies. (3) We employed estimated parameters for hydrocarbon chains of hexadecyltrimethylammonium bromide (CTAB) and hexadecylammonium chloride (HDAC) in CHARMM. After adjustment for these three major shortcomings, the two force fields CHARMM-METAL and CVFF-METAL perform similar within statistical error.

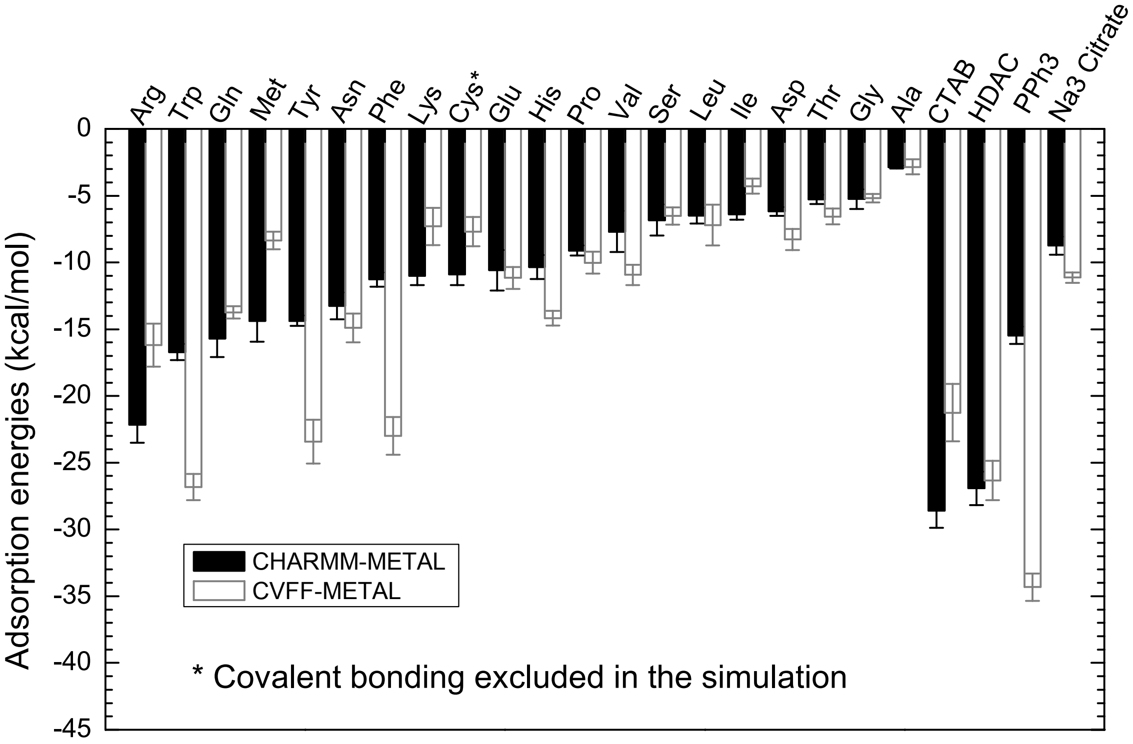

Figure S1. Computed energy of adsorption of single amino acid and surfactant molecules on the even Au {111} surface in dilute aqueous solution at pH = 7. Values for the CHARMM-METAL force field (as in Figure 1) and for the older, less rigorously validated CVFF-METAL force field are shown. The adsorption energy of aromatic residues (PPh3, Tyr, Trp, Phe, His) is lower in CVFF-METAL in proportion to excessive cohesive energies. The adsorption energy of Met is underestimated in CVFF-METAL due an underestimated polarizability of the sulfur atom (lower than oxygen). Adsorption energies of other residues are similar within statistical uncertainty. Every data point represents an average over up to ten independent simulations of 1 ns.

Differences between computed adsorption energies using the CHARMM22[32]–METAL[22] force field and the older CVFF[33]-METAL[22] force field can be explained on the basis of the energy expression:

$$\begin{aligned} E_{pot} = & \sum_{ij\text{ bonded}} K_{r,ij}(r_{ij}-r_{0,ij})^2 + \sum_{ijk\text{ bonded}} K_{\theta,ijk}(\theta_{ijk}-\theta_{0,ijk})^2 \left(+ \sum_{ijk\text{ bonded}} K_{S,ijk}(S_{ijk}-S_{0,ijk})^2 \right) \\ & + \sum_{ijkl\text{ bonded}} V_{\phi,ijkl}[1+\cos(n\phi_{ijkl}-\phi_{0,ijkl})] + \sum_{ijkl\text{ bonded}} K_{\chi,ijkl}[1+\cos(n\chi_{ijkl}-\chi_{0,ijkl})] \qquad \text{(S1)} \\ & + \frac{1}{4\pi\varepsilon_0\varepsilon_r} \sum_{\substack{ij\text{ nonbonded} \\ (1,2\text{ and }1,3\text{ excl})}} \frac{q_i q_j}{r_{ij}} + \sum_{\substack{ij\text{ nonbonded} \\ (1,2\text{ and }1,3\text{ excl})}} \varepsilon_{ij}\left[\left(\frac{r_{0,ij}}{r_{ij}}\right)^{12} - 2\left(\frac{r_{0,ij}}{r_{ij}}\right)^{6}\right] \end{aligned}$$

Equation (S1) contains additive contributions from quadratic bond stretching, quadratic angle bending, an Urey-Bradley term (only present in CHARMM, shown in brackets), a torsion potential, an out-of-plane term, the Coulomb energy, and a 12-6 van-der-Waals potential. The differences between CHARMM and CVFF are (i) an additional Urey-Bradley term in CHARMM and (ii) the use of arithmetic combination rules for $r_{0,ij}$ and geometric combination rules for ε_{ij} in CHARMM versus geometric combination rules for both $r_{0,ij}$ and ε_{ij} in CVFF. Adsorption energies according to CHARMM-METAL are significantly more reliable compared to CVFF-METAL due to more recent parameter refinements. Adsorption energies by CVFF-METAL, after corrections for three major systematic deviations, essentially represent an estimate of maximum uncertainty. The three major groups of deviations are explained in the following.

(1) For aromatic residues, the magnitude of adsorption on the metal surface is essentially determined by the well depth ε_0 of the aromatic carbon atoms in the 12-6 Lennard-Jones potential. This parameter is only about half in CHARMM22 compared to CVFF. As a simple test, the computation of the cohesive (vaporization) energy of liquid benzene reveals that CHARMM22 parameters, when inserted in CVFF, reproduce the experimentally measured vaporization energy[S1] with +7% deviation while CVFF leads to an overestimate of +84% (Table S1). Therefore, CHARMM22 results are suitable for the aromatic molecules His, Phe, Trp, Tyr, and PPh_3. The systematically lower (negative) adsorption energies using CVFF (Figure S1) are physically not justified and should be disregarded. The vaporization energy of benzene in Table S1 was obtained as the difference in average energy during NVT molecular dynamics in the gaseous and in the liquid state during 1 ns simulation time at equilibrium density (close to experiment), augmented by the volume work of $1RT$ per mole.

Table S1. Vaporization energy of liquid benzene in experiment and in NVT molecular dynamics simulation (kcal/mol). Values generated by the CHARMM force field are acceptable while values generated by the CVFF force field are strongly overestimated and should be disregarded.

Experiment[b]	CHARMM[a]	CVFF
8.03	8.60 ± 0.19	14.79 ± 0.16

[a] Lennard-Jones parameters of CHARMM22 replace the original parameters of CVFF for carbon atoms of benzene. [b] Ref. S1.

(2) For the amino acids Met and Cys, the non-covalent adsorption energy is strongly influenced by the well depth ε_0 of the sulfur atom in the 12-6 Lennard-Jones (LJ) potential. A higher well depth of sulfur in the model reflects a higher polarizability compared to oxygen[52] which is well represented in CHARMM (S: r_0 = 4.0 Å, ε_0 = 0.45 kcal/mol, O: r_0 = 3.4 Å, ε_0 = 0.24 kcal/mol) and rather opposite in CVFF (S: r_0 = 3.78 Å, ε_0 = 0.043 kcal/mol, O: r_0 = 3.21 Å, ε_0 = 0.228 kcal/mol). The significant underestimate of the LJ well depth of the sulfur atom in CVFF-METAL explains the higher value in non-covalent adsorption energy of Met and Cys. Similarly, differences in the LJ well depth (polarizability) of guanidinium nitrogen and lysine nitrogen between CHARMM and CVFF contribute to differences in adsorption energy for the amino acids Arg and Lys. It can be safely assumed that the CHARMM-METAL force field yields better results than CVFF-METAL due to considerably better validation.

(3) For the alkyl chains in the aliphatic surfactants CTAB and HDAC, CHARMM22[32] provides no explicit parameters. We employed homologous structural

elements in Leu and Lys side groups as a substitute (CHARMM_1) as well as polyethylene parameters as defined in CHARMM32[S2,S3] (CHARMM_2). Computed adsorption energies for CTAB are similar in both versions while the adsorption energy of HDAC is slightly higher in version 2 (Figure S2). We also tested two settings of CVFF.[33] The default setting (CVFF_1) involves the default atomic charges of +0.1e for H, −0.2e for C in CH_2 groups, and −0.3e for C in CH_3 groups which appear somewhat too high, and we applied a second setting (CVFF_2) with half these atomic charges and no changes in any other parameters (including van-der-Waals parameters). These two versions result in similar adsorption energies of both CTAB and HDAC (Figure S2). Overall, adsorption energies using CHARMM and CVFF converge better for HDAC while adsorption energies for CTAB are lower using CHARMM compared to CVFF. This is partly associated with a higher well depth ε_0 of carbon atoms in CH_3 groups (0.078 kcal/mol) compared to CH_2 groups (0.056 kcal/mol) in CHARMM while the ε_0 values for C atoms of CH_3 and of CH_2 groups are both lower in CVFF (0.039 kcal/mol). When the CHARMM parameters for the CH_3 group were replaced by CVFF parameters in CHARMM/NAMD simulations, the difference in CTAB adsorption energies between CHARMM and CVFF was reduced by 60%, resulting in the adsorption energy of −25 kcal/mol (Table S2). The experimentally measured polarizability of CH_3 groups versus CH_2 groups is 21% higher[S4] (less than the ~40% increase suggested by CHARMM parameters including the extra hydrogen atom) so that the best estimate for the adsorption energy of a single CTAB molecule on the Au {111} surface in aqueous solution may be –26 ±1 kcal/mol (Figure S2). For HDAC, we assume a best estimate of the adsorption energy between the two CHARMM versions of −24 ±1 kcal/mol.

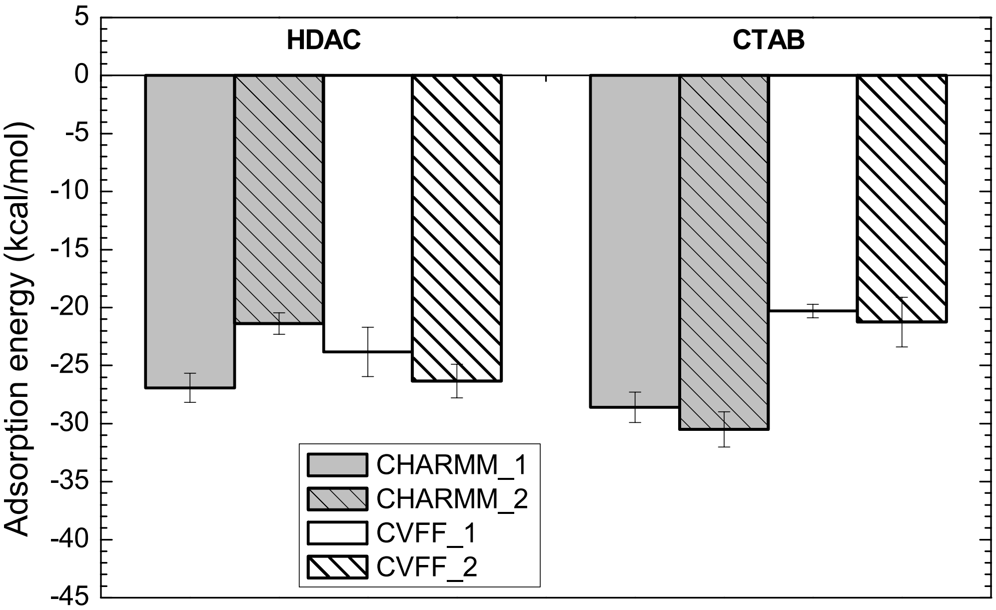

Figure S2. Comparison of adsorption energies of CTAB and HDAC using different settings in CHARMM and CVFF (see text).

Table S2. Comparison of adsorption energy (kcal/mol) of CTAB using CHARMM_2, CVFF_2 and adjusted well depth for CH_3 carbon atoms (M-CHARMM).

	CHARMM_2	CVFF_2	M-CHARMM[a]
CTAB	-30.51 ± 1.52	-21.25 ± 2.15	-24.74 ± 1.28

[a] Lennard-Jones parameters for carbon atoms in CH_3 groups in CHARMM_2 ($\varepsilon = 0.078$ kcal/mol and $\frac{R_{\min}}{2} = 2.04$ Å) were replaced by CVFF_2 parameters ($\varepsilon = 0.039$ kcal/mol and $\frac{R_{\min}}{2} = 2.175$ Å) in CHARMM/NAMD simulations.

We also note that the Lennard-Jones parameters for fcc metals are compatible with other force fields, including AMBER, OPLS-AA, PCFF, and COMPASS.[22]

References

S1 Timmermans, J. *Physico-Chemical Constants of Pure Organic Compounds*; Elsevier: New York, 1950, p. 149.

S2 Vorobyov, I.; Anisimov, V. M.; Greene, S.; Venable, R. M.; Moser, A.; Pastor, R. W.; MacKerell, A. D., Jr. *J. Chem. Theory Comput.* **2007**, *3*, 1120-1133.

S3 Lee, H.; Venable, R. M.; MacKerell, A. D., Jr.; Pastor, R. W. *Biophysical J.* **2008**, *95*, 1590-1599.

S4 Heinz, H.; Suter, U. W.; Leontidis, E. *J. Am. Chem. Soc.* **2001**, *123*, 11229-11236.