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SUPPORTING INFORMATION

COSMO*plex*: Self-consistent simulation of self-organizing inhomogeneous systems based on COSMO-RS

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The AUTOBOX tool for the generation of COSMOplex input

One of the main challenges associated with the self-consistent generation of micelles, membranes, interfaces, microemulsions etc., was the generation of a physically meaningful and general initial guess. It appeared during the tests that many initial guesses could result in different, but self-consistent solutions, much like depending on the initial geometry provided by the user, different self-consistent optimized geometries can be obtained from the same quantum-chemical geometry optimization procedure. There are many local optima for probabilities of atoms to be in each layer and we are interested in those that represent the physical reality that we are targeting.

In this context, the effort towards physically reasonable initial guesses was oriented such that most of the initial guess scheme could be valid for any self-organizing system (SOS).

Because the goal of the initial guess was to provide a simulation box for COSMO*plex*, it was called AUTOBOX.

Definition of microphases

All self-organizing systems, e.g., membranes, micelles, microemulsions, interfaces, are formed by a series of two or more microphases in the AUTOBOX scheme. For example, micelles consist of a surfactant-rich microphase and a bulk liquid microphase, normally water. The composition of the individual microphases can be estimated in different ways, which are directly implemented in the AUTOBOX scheme: all compounds of the whole system can be distributed to the microphases in an empirical way, either simply based on their molecular polarities (e.g., a microemulsion would consist of a nonpolar phase, a polar phase and an intermediate surfactant-rich phase in between), or by particular liquid-liquid equilibrium (LLE) calculations for all phase boundaries, or making use of the liquid extraction functionality in COSMO*therm*. All calculations in this manuscript are performed by the latter, if not stated otherwise. The individual microphase compositions can also defined by the user, in addition to the total system composition.

The individual microphases can be composed of pre-oriented molecules, called SOS core herein. For example, surfactant-rich microphases with a clear orientation especially of the surfactant molecules with respect to their alkyl tails and polar head groups. Polarity moment vectors, representing the extent and direction of the internal polarity gradient of a molecule, are calculated, and the polarity moment vector is set to be parallel to the z direction of the SOS core for each molecule. For inverse systems (e.g., inverse micelles) each molecule is placed antiparallel (in -z direction) to the polarity moment vector, instead. All molecules are placed according to the similarity of their polarities with the adjacent microphases. In the case of a polar solvent and a less polar SOS core, the least polar molecule has its polarity center furthest and the most polar molecule (e. g. water) has its polarity center closest to the limit of the SOS core. From the position of the polarity center of each molecule and its orientation so that its polarity moment vector is parallel to the z direction, all z coordinates of all atoms of all molecules are known and placed,

As far as bulk liquid phases are concerned, the molecules are placed in a uniform way without pre-orientations taking place.

Once all compounds are placed in all microphases, the atom probabilities are smoothed by a Gaussian function around their initial positions in the whole system. After a last normalization, step, a full initial probability matrix for each atom in each layer is obtained.

After generation of the microphases, the system is sliced into virtual layers. For softer microphase transitions (e.g., membranes, micelles), a layer size – or “resolution” – of 2 Å is selected per default; for tight interfaces, a layer size of 1 Å in z-direction.

Micelles and membranes

Micelles and membrane occur when amphiphilic molecules are immersed in very polar or very nonpolar solvents. They are constructed by two microphases, a surfactant-rich SOS core phase and a bulk solvent phase of either spherical, cylindrical or lamellar geometry. For polar solvents, in micelles or membranes, the most nonpolar parts of molecules are oriented towards the interior of the SOS core, while the most

polar parts of molecules are oriented so that they maximize contacts with solvent molecules [1]. For nonpolar solvents, this occurs the other way around. Experimentally [2] and from molecular dynamics simulations [3], some mixing is observed between the surrounding solvent and micelles/membranes. Therefore, it is of interest to start the simulation with a sufficient number of initially homogeneous bulk solvent layers on the top of the plex.
Geometrical constraints limit the radii of hydrophobic cores of micelles, and they have been theoretically estimated to measure roughly 80% of the extended alkyl chain length [4], which is understandable since chains are not necessarily extended. Generalizing this reasoning to the whole molecule and allowing treatment of mixtures, a simple and reproducible assumption could be that the initial inhomogeneity zone, which contains the SOS core, has the maximal length of the surfactant molecule in the system, i.e. the compound with the largest polarity moment. An even better approximation would be only a fraction of this maximal length, like 80%, but in the initial publication [4], for alkyl chains, this proportion has been found to vary depending on alkyl chain length, and therefore any general tuning of this parameter would be bound to a good estimation of the general molecular flexibility. So, for the examples used to test and develop the method, we used the maximum diameter of the longest surfactant conformer. This length defines the radius of the SOS core system in a spherical or cylindrical case and, thus, the volume of the SOS core. Per default, the same radius is used for the second bulk solvent phase.

Interfaces

Interfaces occur when two different, often immiscible and equilibrated liquids are put into contact. They are represented by two lamellar microphases by the AUTOBOX algorithm. The zone of contact, where the molecules of one of the phases undergo unfavorable interactions with the molecules of the other phase, is said to be of the order of the "bulk correlation length" [5]. This bulk correlation length is the average distance between one molecule and the point at which we consider the composition of the liquid to be the same as the average composition. Here, we considered that this length is below or equal to the length of the longest conformer of the longest molecule $l_{\max}$, which enables some degree of homogeneity with the scheme used for micelles and membranes. The simulation box is enlarged to arrive at – ideally homogeneous – bulk phase compositions at both outer boundaries: for both microphases, a minimum size of 3 $l_{\max}$ is chosen per default, which turned out to be an acceptable compromise between calculational time and interfacial tension accuracies.

Even though interfacial enrichment is not considered by the manuscript (i.e., IFT of mixtures with surface-active components), the AUTOBOX scheme is flexible enough to define those systems, as well.

Microemulsions

Microemulsions are observed when the interfacial tension between two antagonistic phases becomes zero due to the presence of a middle phase concentrating surface-active compounds (surfactants) [6]. A given emulsion, with known mole or volume fractions of all components, can be simulated as a SOS. Thus, microemulsions are set up by three microphases: a nonpolar bulk solvent phase, a surfactant-rich SOS core and a polar bulk solvent phase.

Similar to micellar systems, the maximum diameter of the longest surfactant conformer $l_{\mathrm{max,surfactant}}$ is used to define the length of the SOS core system. Per default, the same length is used again for both bulk solvent phases. Thus, the total system has a standard size of 3 $l_{\mathrm{max,surfactant}}$. Again, the surfactant is identified by the compound with the largest polarity moment in the system.

Table SI1: Experimental and predicted interfacial tensions for 40 compounds with two levels of COSMO*plex*.

Nr	**Name**	**IFT Experimental[11]**	**IFT COSMO*plex***	**IFT DIRPLEX**
1	n-heptane	50.1	25.1	47.4
2	cyclohexane	50.0	19.9	29.9
3	hexane	49.7	23.6	47.4
4	CS2	48.6	24.6	49.2
5	tetrachloroethylene	45.9	26.2	37.6
6	CCl4	44.3	21.0	40.1
7	1,1,1-trichloroethane	36.6	16.9	29.1
8	ethylbenzene	36.5	19.9	43.3
9	trichlorethylene	36.9	21.4	38.2
10	1,2-dimethylbenzene	36.4	20.5	40.1
11	1,4-dimethylbenzene	35.7	20.7	44.2
12	1,3-dimethylbenzene	35.5	19.7	45.6
13	toluene	35.4	18.6	39.2
14	benzene	33.8	17.7	29.8
15	CHCl3	30.8	15.6	25.9
16	chlorobenzene	30.3	19.6	36.3
17	cis-dichloroethylene	30.0	16.1	26.9
18	1,1,2-trichloroethane	29.6	17.1	25.6
19	CH2Cl2	28.9	11.2	19.4
20	1,2-dichloroethane	28.4	14.4	24.5
21	trans-dichloroethylene	25.5	17.5	35.1
22	nitrobenzene	25.2	15.5	20.6
23	diisopropylether	17.7	8.2	10.7
24	1-butylacetate	14.5	3.5	10.9
25	2-ethyl-1-hexanol	13.3	7.9	14.8
26	acetophenone	13.2	4.8	10.4
27	diethylether	11.0	5.4	8.5
28	4-methyl-2-pentanone	10.4	1.7	7.0

29	nitromethane	9.3	5.8	8.5
30	1-octanol	8.1	6.1	11.5
31	1-heptanol	7.7	3.5	2.0
32	aniline	6.9	7.9	13.3
33	1-hexanol	6.6	5.3	3.6
34	ethylacetate	6.4	0.6	1.3
35	1-pentanol	4.6	6.0	9.8
36	cyclohexanone	3.9	0.0	0.0
37	cyclohexanol	3.7	2.5	7.9
38	2-butanol	2.0	2.7	2.9
39	1-butanol	1.8	2.7	5.4
40	methylacetate	1.6	0.0	0.0

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