

COSMOmic for micelles and biomembranes

... validated applications

- partition coefficients
- probability distributions
- free energy profile
- neutral and ionic solutes
- spherical micelles
- lamellar micelles like phospholipid biomembranes (DMPC and DPPC)

... further potential applications

- permeability coefficients of solutes through membranes
- determination of Flory-Huggins like parameters that can serve as input for meso-scale applications like DPD

COSMOlogic Products

- COSMOtherm: Software for Life Science and general Fluid Phase Thermodynamics
- COSMObase: Database of 3500 DFT/ COSMO files for common solvents and compounds
- TURBOMOLE: Fast Quantum Chemical Program (Prof. R. Ahlrichs, Univ. of Karlsruhe, Redistribution and Support by COSMOlogic)
- COSMOfrag: Software for rapid screening and HTS applications with COSMOtherm, including various options for structure and conformational analysis and tautomer generation
- COSMOsim: Similarity Screening based on σ -Profiles

COSMOlogic Services

- Consulting in Computational Chemistry and Fluid Phase Thermodynamics
- Contract Calculations in the Context of COSMOtherm
- Contract Research, Development, and Programming in Computational Chemistry related Areas

Cover picture: DMPC bilayer phospholipid membrane

COSMOlogic GmbH & Co. KG

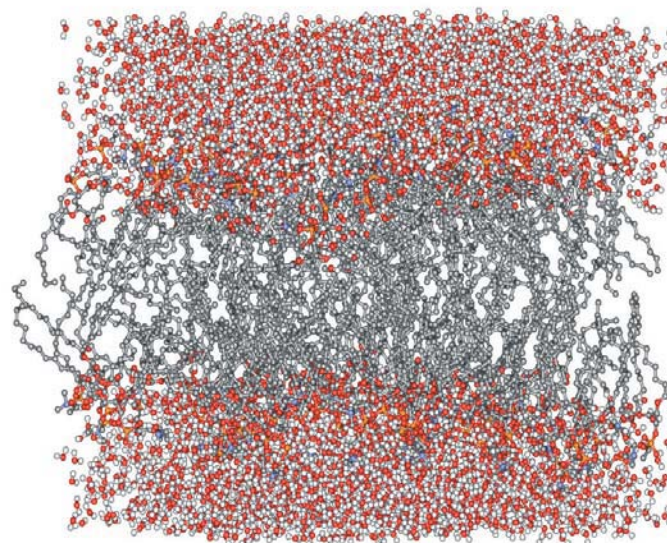
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COSMOmic

Treating solutes in micelles and biomembranes



COSMO-RS for surfactants, micelles
and biomembranes

COSMOmic models surfactant micelles or biomembranes as inhomogeneous, layered liquids, allowing the calculation of membrane partition coefficients of solutes in a micelle or a membrane of spherical, cylindrical or lamellar type.

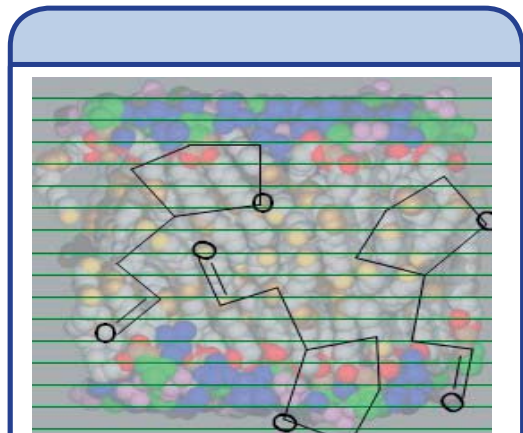
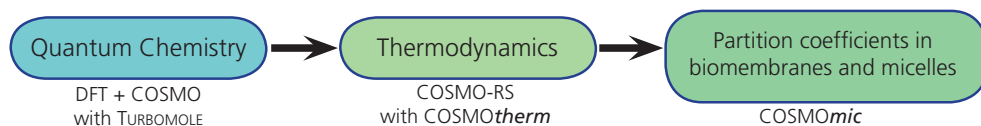


Fig. 1. Membrane described by liquid layers, various solute orientations and positions [3]

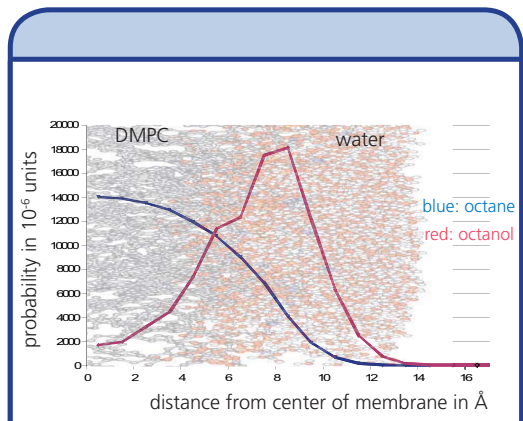


Fig. 2. Probability distribution of octanol and octane in DMPC bilayer membrane

Methodology

COSMOmic is based on the COSMO-RS theory that derives the thermophysical behavior of liquids from quantum mechanical DFT calculations.

Describing micelles or biomembranes as liquid layers based on COSMO-RS, partition coefficients of solutes are determined very efficiently and **without the need of additional fitting of parameters.**

Results of MD simulations of micelles or membranes are taken as an input to describe the statistics of the atomic distribution of the micelle. Together with COSMO/DFT calculations of the molecules that build up the micelle, as well as for the solutes of interest, this is all that is needed for a **COSMOmic** calculation.

Fig. 1 shows an example of a planar micelle, here a phospholipid biomembrane. Each layer is taken as a liquid, composed from each atom of the molecules in the given slice.

Free energy of solutes in the membrane is calculated for a large number of positions and orientations. This

gives a probability distribution and hence a free energy profile for the solutes in the membrane, as shown in Fig. 2 for octanol and octane in a DMPC phospholipid bilayer in water.

Resulting properties

From this probability distribution, the lipid-water partition coefficient can be derived, as well as the free energy difference between the water phase (outermost layer) and all other layers.

In future versions, it will be possible to derive the permeability coefficients from the calculated energy barriers.

Applications: Biomembranes

A DMPC bilayer (see front cover), taken from an MD simulation, is used to calculate the lipid-water partition coefficient $\log K_{lipw}$ of 100 neutral compounds of different kind (Fig. 3).

With a slope of 0.99 from the regression to experimental data, and $R^2=0.8$, **COSMOmic** gives very good results, without the need to fit parameters to a given training set [2].

Applications: Micelle

The partition coefficients of 12 solutes in an SDS spherical micelle (Fig. 4) have been calculated and compared to experimental data. The correlation factor $R^2=0.94$ shows a very accurate description of the $\log K_{SDS-water}$ for the chosen set of alcohols, alkanes, toluol and ketones (Fig. 4)

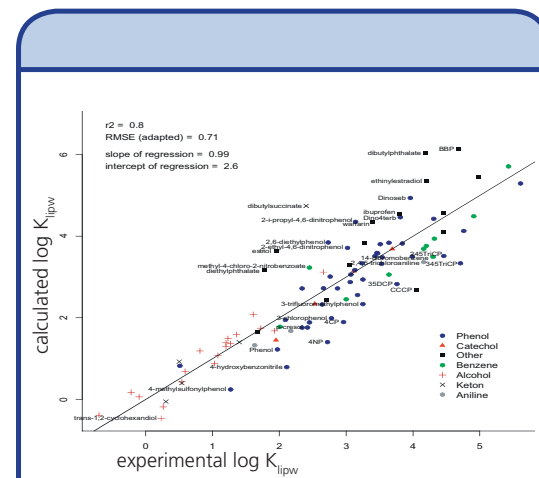


Fig. 3. Calculated $\log K_{lipw}$ vs. experimental $\log K_{lipw}$ [2]

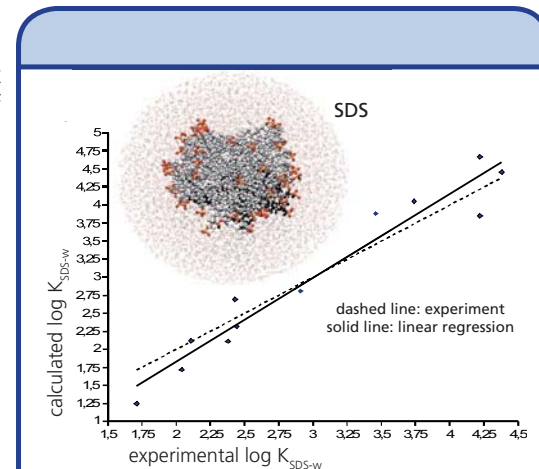


Fig. 4. Calculated $\log K_{SDS-w}$ against experimental $\log K_{SDS-w}$ of 12 solutes in an SDS micelle

References

- 1) A. Klamt, J. Phys. Chem. **99** (1995) 2224
- 2) DMPC $\log K_{lipw}$ values are taken from S. Spycher and B. Escher, EAWAG Dübendorf
- 3) Courtesy of P. Tielemann, University of Calgary
- 4) A. Klamt, *From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design*, Elsevier 2005