COSMO-RS Manual

Amsterdam Modeling Suite 2024.1

www.scm.com

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CONTENTS

CHAPTER

ONE

GENERAL

1.1 Introduction

The ADF COSMO-RS (COnductor like Screening MOdel for Realistic Solvents) program is a program that can be used for calculating thermodynamic properties of (mixed) fluids. The COSMO-RS method was developed by Klamt and coworkers[1][2][3]. On the basis of the framework of COSMO-RS, Lin and Sandler[6] suggested a variation, the COSMO-SAC (where SAC denotes segment activity coefficient) model. There are different implementations of COSMO-RS and COSMO-SAC or derivatives, and different parametrizations. The implementation of COSMO-RS in ADF is described in Ref.[4], which is based on the COSMO-RS method developed by Klamt et al.[?]. The implementation of COSMO-SAC 2013-ADF in ADF is based on the COSMO-SAC model developed by Xiong et al.[7]. The implementation of COSMO-SAC 2016-ADF in ADF is based on the COSMO-SAC model developed by Hsieh et al.[5], but the parameters in COSMO-SAC 2016-ADF were optimized by Chen et al., like in[8], for use with ADF. The implementation of COSMO-SAC DHB-ADF in ADF is based on the COSMO-SAC-DHB model developed by Chen et al.[9], but the parameters were reoptimized by Chen et al. for use with ADF.

An alternative to COSMO-SAC or COSMO-RS based methods is the UNIFAC (UNIQUAC Functional-group Activity Coefficients) method, which was developed by Fredenslund, Jones, and Prausnitz, see[10]. The empirical UNIFAC method is a group contribution based method to predict activity coefficients and other thermodynamic properties, in which the group specific parameters and are parametrized against a large data base. The implementation in ADF uses to so called original UNIFAC parameters.

Our COSMO-RS capabilities are summarized on the product page (https://www.scm.com/product/cosmo-rs).

With COSMO-RS it is possible to use a thermodynamically consistent combinatorial contribution to the chemical potential as is used in Ref.[?], and a temperature dependent hydrogen bond interaction, also described in Ref.[?]. The parameters in

[1] A. Klamt, *Conductor-like Screening Model for Real Solvents: A New Approach to the Quantitative Calculation of Solvation Phenomena.* J. Phys. Chem. 99, 2224 (1995) (https://doi.org/10.1021/j100007a062)

[2] A. Klamt, V. Jonas, T. Bürger and J.C. Lohrenz, *Refinement and Parametrization of COSMO-RS.* J. Phys. Chem. A 102, 5074 (1998) (https://doi.org/10.1021/jp980017s)

[3] A. Klamt, *COSMO-RS From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design, Elsevier.* Amsterdam (2005), ISBN 0-444-51994-7.

[6] S.T. Lin and S.I. Sandler, *A Priori Phase Equilibrium Prediction from a Segment Contribution Solvation Model*, Ind. Eng. Chem. Res. 41, 899 (2002) (https://doi.org/10.1021/ie001047w)

[4] C.C. Pye, T. Ziegler, E. van Lenthe, J.N. Louwen, *An implementation of the conductor-like screening model of solvation within the Amsterdam density functional package. Part II. COSMO for real solvents.* Can. J. Chem. 87, 790 (2009) (https://doi.org/10.1139/V09-008)

[7] R. Xiong, S.I. Sandler, R.I. Burnett, *An improvement to COSMO-SAC for predicting thermodynamic properties*, Ind. Eng. Chem. Res. 53, 8265 (2014) (https://doi.org/10.1021/ie404410v)

[5] C.M. Hsieh, S.I. Sandler, S.T. Lin, *Improvements of COSMO-SAC for vapor-liquid and liquid-liquid equilibrium predictions*, Fluid Phase Equilib. 297, 90 (2010) (https://doi.org/10.1016/j.fluid.2010.06.011)

[8] W.L. Chen, C.M. Hsieh, L. Yang, C.C. Hsu, S.T. Lin, *A Critical Evaluation on the Performance of COSMO-SAC Models for Vapor-Liquid and Liquid-Liquid Equilibrium Predictions Based on Different Quantum Chemical Calculations*, Ind. Eng. Chem. Res. 55, 9312 (2016) (https://doi.org/10.1021/acs.iecr.6b02345)

[9] W.L. Chen, S.T. Lin, *Explicit consideration of spatial hydrogen bonding direction for activity coefficient prediction based on implicit solvation calculations*, Phys.Chem.Chem.Phys. 19, 20367 (2017) (https://doi.org/10.1039/c7cp02317k)

[10] A. Fredenslund, R.L. Jones, and J.M. Prausnitz, *Group-contribution estimation of activity coefficients in nonideal liquid mixtures*, AIChE Journal 21, 1086 (1975) (https://doi.org/10.1002/aic.690210607)

the paper[?] were reparametrized for ADF, see Ref.[?] for details.

The parameters in COSMO-SAC 2013-ADF, COSMO-SAC 2016-ADF, and COSMO-SAC DHB-ADF were optimized for use with ADF COSMO result files. Other COSMO-SAC parameter sets exists that were optimized for different QM packages.

The ADF COSMO-RS (and COSMO-SAC) command line program is called *crs*. The main authors of this program are Cory Pye (Saint Mary's University, Halifax NS Canada) and Jaap Louwen (Albemarle Corporation). COSMO-SAC 2013-ADF was implemented in collaboration with R. Xiong and R.I. Burnett (Sandler group, University of Delaware, Newark, USA). Previous COSMO-SAC methods were implemented by Erin McGarrity (TU Delft, the Netherlands). The COSMO-RS GUI *AMScrs* contains an input builder for COSMO-RS and can visualize results, see the COSMO-RS GUI tutorials and the COSMO-RS GUI reference manual.

COSMO-RS (and COSMO-SAC) use the intermediate results from quantum mechanical (QM) calculations on individual molecules to predict thermodynamic properties of mixtures of these molecules, for example, solubility. There are a fair number of reports of accurate prediction by COSMO-RS of thermodynamic properties in general in the literature. Many of these have been written by Klamt and co-workers, see Ref.[?] and references therein. Instead of a relatively expensive QM calculation one can use a fast Quantitative Structure-Property Relationship (QSPR) method to estimate the so called COSMO sigma-profile of a molecule that is needed in COSMO-RS (and COSMO-SAC) calculations.

There are also empirical methods like UNIFAC that can predict thermodynamic properties (including the activity coefficients). These methods contain group specific parameters and are parametrized against a large data base. They will often do better than COSMO-RS or COSMO-SAC methods (especially, of course, if the system of interest was part of the data base used for parameter estimation). An advantage of these methods is that they require no QM calculations to be done in order to provide an estimate of thermodynamics properties. However, these methods cannot handle every type of molecule. In particular when unusual combinations of functional groups occur (such as in drug molecules), no parametrization is available. COSMO-RS and COSMO-SAC methods, on the other hand, only feature general parameters not specific to chemical groups or functionalities. All that is required is that a quantum mechanical calculation can be done on the molecule. Therefore, COSMO-RS or COSMO-SAC can be a valuable tool for the prediction of chemical engineering thermodynamical properties, like, for example, partial vapor pressures, solubilities, and partition coefficients. An additional advantage of COSMO-RS and COSMO-SAC over empirical methods is that the molecules dissolved may in fact be transition states of a chemical reaction. This follows from the fact that all that is required is that one can do a QM calculation on the solute and QM on a transition state has become standard in the last two decades. This affords a unique opportunity to predict the thermodynamics of a reaction including, for instance, the balance between kinetically and thermodynamically favored reaction pathways as a function of the solvent used.

1.2 What's new in COSMO-RS 2024.1

- A new Database module in pyCRS designed for the management of coskf files
- A new CRSManager module in pyCRS facilitates a streamlined scripting process for the creation and execution of CRSJob in conjunction with the Database module

1.3 What's new in COSMO-RS 2023.1

- *pyCRS* (page 81) is a new python module that provides an interface to the pure compound property prediction and sigma profile prediction tools
- SG1: a new *sigma profile prediction* (page 22) method that relies on a database of pre-computed molecular subgraphs
- A new, temperature-dependent pure compound liquid viscosity model
- A synthetic accessibility estimation method – see the *Property prediction documentation* (page 63) for more details.
- Improved convergence criteria that make multispecies calculations more stable

1.4 What's new in COSMO-RS 2022.1

- Pitzer-Debye-Hückel long-range electrostatic correction

1.5 What's new in COSMO-RS 2021.1

- Improved handling of compounds with multi-species components

1.6 What's new in COSMO-RS 2020.1

- Support for compounds with multi-species components
  - conformers
  - dimers, trimers, …
  - dissociation
  - association

CHAPTER

TWO

COSMO-RS, COSMO-SAC, UNIFAC

2.1 COSMO-RS theory

Below some of the COSMO-RS theory is explained, but a more complete description can be found in Refs.[1] and[2].

Although in principle all of chemistry can be predicted by appropriate solutions of the Schrödinger Equation, in practice due to the extreme mathematical complexity of doing so only the smallest systems can be computed at an accuracy rivaling that of the most accurate experiments. However, with suitable approximations, for isolated molecules of up to a few hundred atoms these days quite reasonable results can be obtained. Of course, this means that direct computation of thermodynamic properties is out of reach. Thermodynamic properties can only be computed as an average over a large number of configurations of a large number of molecules. To address this, people have typically resorted to so-called Molecular Dynamics (MD) or Monte Carlo (MC) methods where configurations are generated either by numerically simulating the atomic motions over discrete time steps or by random generation, in either case using empirical molecular models parametrized against quantum mechanical calculations and experimental data to compute energies. However, even these approaches often fall short in generating sufficiently large ensembles, and there is little chance of that situation improving dramatically in the near future.

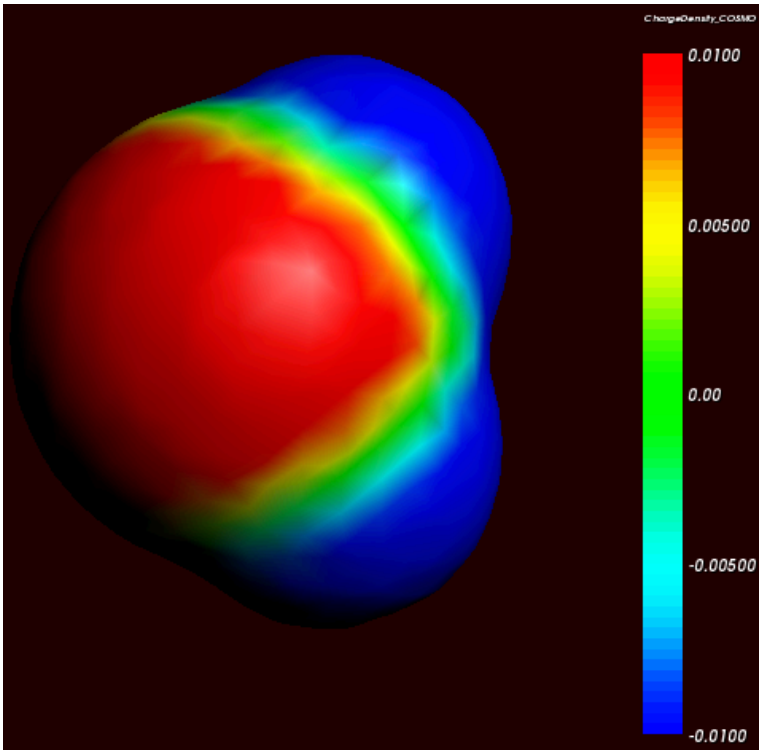
Around 1995, Andreas Klamt, then working for Bayer, hit upon an approach that made it possible to compute the details of molecules quantum mechanically and subsequently use these details in an approximate statistical mechanics procedure[3]. This approach is called COSMO-RS (COnductor like Screening MOdel for Realistic Solvents) and has proven to be quite powerful. It may currently be the best link between the world of chemical quantum mechanics and engineering thermodynamics.

Thermodynamic reference states can be chosen arbitrarily. They do not even have to be physically realizable, as long as it is consistently used. We are at liberty to choose as reference state a molecule embedded in a perfect conductor, that is a material with an infinitely large dielectric constant ('the perfectly screened state'). Suppose a molecule A resides in a molecule shaped cavity. Everywhere outside of this cavity is conductor material. Although it would be hard to realize this in practice, it is relatively easy to do quantum mechanical calculations on this hypothetical state. Since the molecule will in general have a charge distribution and therefore possess an electric field, it will polarize the embedding medium. That will result in another electric field, given by a charge distribution on the surface of the molecule shaped cavity. This charge distribution is generated by the quantum mechanical calculations, for example with ADF if one uses COSMO. From now on the surface of the molecule shaped cavity will be called molecular surface, and the volume of the molecule shaped cavity will be called molecular volume.

[1] A. Klamt, V. Jonas, T. Bürger and J.C. Lohrenz, *Refinement and Parametrization of COSMO-RS.* J. Phys. Chem. A 102, 5074 (1998) (https://doi.org/10.1021/jp980017s)

[2] A. Klamt, *COSMO-RS From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design, Elsevier.* Amsterdam (2005), ISBN 0-444-51994-7.

[3] A. Klamt, *Conductor-like Screening Model for Real Solvents: A New Approach to the Quantitative Calculation of Solvation Phenomena.* J. Phys. Chem. 99, 2224 (1995) (https://doi.org/10.1021/j100007a062)



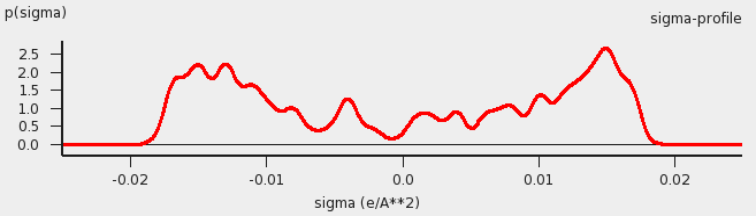
Cosmo charge density on the COSMO surface of water (picture made with AMSview).

Although the actual charge distribution on the molecular surface will be highly detailed, let us for the moment consider the molecular surface as consisting of segments with a constant charge density (i.e. the detailed charge distribution averaged over segments). Now instead of the single molecule A consider, as an arbitrary example, a fluid consisting of three types of molecules: A, B and C. In a fluid not too close too the critical temperature, the molecular surfaces present in the fluid will all be in close contact. That means that the segments of constant density introduced above are in close contact.

We now compare our molecule A in the fluid with our chosen reference state. Any segment of the molecular surface with a charge density of σ_i will be aligned with a segment with charge density σ_j of another molecule. If the two charge densities happen to be opposite (i.e. $\sigma_i + \sigma_j = 0$) the charges required for achieving the perfectly screened state will vanish. However, this will not happen too often and in general an excess charge density is left of $\sigma_i + \sigma_j$ between the two segments. From electrostatic theory it follows that this introduces an energy penalty proportional to the segment size and $(\sigma_i + \sigma_j)^2$. In principle this gives a way to compute the chemical potential of component A, by going over all possible conformations of a large number of molecules A, B and C (in their proper molar fractions) and do computations on the statistical ensemble. However, in practice that would be similar to doing Molecular Dynamics calculations using empirical structure models and about as computationally prohibitive. Instead, an approximation can be made that is not easily justified a priori and must be judged by the results of subsequent simulations. This assumption is that all segments in the fluid are able to make contact independent of one another. In a way it can be said, that the segments are cut loose from the original (rigid) molecular surfaces.

As one would guess, the approximation of independent segments makes the mathematics of computing ensemble properties quite tractable. In fact, computing the chemical potential of component A (or B or C) in the mixture by means of the COSMO-RS and related methods takes in the order of seconds on a normal PC (given the results of quantum mechanical calculations that may have taken days, of course). Note that the molecular surface around the molecule is divided rather arbitrarily in segments and that the assumption was that the segment of one molecule will overlap perfectly with that of another. How can this be true? The answer is that one can split up the molecular surface into segments in an infinite number of ways. However, the molecules in a fluid are always in contact with another. At any given time, molecule A will be in contact with a number of other molecules and share patches of, for example, 7 square Angstroms of its surface with each of the surrounding molecules. At that particular time, the segments will be those patches. A split second later, of course, there will be a different set of segments. That is not a problem. One needs to do statistical mechanics with

charged segments for which one needs to know how many 7 square Angstrom segments a particular molecule brings into the fluid and the probability of any segment having an average charge density σ (for all values of σ). Both can be computed from the results of the quantum mechanical calculation on the molecule in the perfect conductor. Just to get a flavor, in the figure below the so-called σ-profile of water is given. These are the statistical distributions of possible segments over charge densities multiplied by the surface area of the molecular volume. The σ-profile relates to the detailed charge distribution on the molecular surface.



σ-profile of water (picture made with the CRS-GUI), smoothed curve, Delley COSMO surface construction

In principle vapor pressures of pure liquids can be computed directly with COSMO-RS. COSMO-RS calculations yield the chemical potential of a component in a liquid with respect to the perfectly screened reference state. It is easy to compute the energy difference between the reference state and the gas phase by doing an additional quantum mechanical calculation (of the isolated molecule). However, often experimental vapor pressures for the pure liquid are known. Using such experimental data for pure liquids can help in predicting the correct partial vapor pressures in a mixture.

2.1.1 COSMO-RS combinatorial term

In Ref.[?] a thermodynamically inconsistent combinatorial contribution μ_i^{comb} to the chemical potential was used:

$$\mu_i^{comb} = -\lambda RTln(q_{av}/\text{Å}^2)$$
$$q_{av} = \sum_i x_i q_i$$

In this equation q_i is the surface area of the molecular volume of compound i, x_i is the molar fraction of compound i in the solution, and λ is a COSMO-RS parameter.

The importance of using a thermodynamically consistent combinatorial contribution is discussed in Ref.[?]. In the ADF COSMO-RS program it is possible to use a thermodynamically consistent combinatorial contribution of the form (Equation C.4 of Ref.[?], with $\lambda_0 = \lambda_1 = \lambda_2 = \lambda$):

$$\mu_i^{comb} = \lambda RT(1 - r_i/r_{av} + ln(r_i/r_{av}) + 1 - q_i/q_{av} - ln(q_{av}/\text{Å}^2))$$
$$r_{av} = \sum_i x_i r_i$$

In this equation r_i is the molecular volume of compound i. In the ADF COSMO-RS program this combinatorial term is used by default, see also Ref.[4].

[4] C.C. Pye, T. Ziegler, E. van Lenthe, J.N. Louwen, *An implementation of the conductor-like screening model of solvation within the Amsterdam density functional package. Part II. COSMO for real solvents.* Can. J. Chem. 87, 790 (2009) (https://doi.org/10.1139/V09-008)

2.1.2 Fast approximation for COSMO-RS calculations

In the 1998 COSMO-RS model each segment of the molecular surface has a charge density of σ_v , but also a second charge density $\sigma_v^{\perp}$, which is a descriptor for the correlation between the charge density on the segment with its surrounding. In the original ADF COSMO-RS implementation this was treated as a 2-dimensional problem, in the fast approximation this is effectively reduced to 1-dimension. Starting from COSMO-RS 2010 this fast approximation is now the default. This approximation reduces the computation time, especially in cases of more than 1 compound.

2.1.3 Temperature dependent hydrogen bond interaction

In Ref.[?] a temperature dependent hydrogen bond interaction is suggested, which is used by default in the ADF COSMO-RS program. The temperature dependence (Equation 6.2 of Ref.[?]) is of the form:

$$term(T) = Tln[1 + exp(20kJ/mol/RT)/200]$$
$$f_{hb}(T) = term(T)/term(298.15K)$$

Note that here the correct formula is used with a plus sign before 20 kJ/mol (there is a sign error in Equation 6.2 of Ref.[?], see online 'List of Errata in the COSMO-RS book' by Andreas Klamt), such that this factor goes to zero for large T. In this equation R is the gas constant and T the temperature (in Kelvin). In the ADF COSMO-RS program the hydrogen bond interaction of Ref.[?] is multiplied by this factor f_{hb} (T) to make the hydrogen bond interaction temperature dependent.

2.2 COSMO-SAC 2013-ADF, 2016-ADF, DHB-ADF

On the basis of the framework of COSMO-RS, Lin and Sandler[1] suggested a variation, the COSMO-SAC (where SAC denotes segment activity coefficient) model by invoking a necessary thermodynamic consistency criterion. Although there are differences, COSMO-RS and COSMO-SAC share some similarities. Later improvements of COSMO-SAC appeared, like in Refs.[2][3][4].

The COSMO-SAC 2013-ADF method used in ADF is the one developed by Xiong et al., which is described in detail in Ref.[?]. The COSMO-SAC 2013-ADF parameters in Ref.[?] were optimized for use with ADF COSMO result files. COSMO-SAC 2013-ADF is an improved COSMO-SAC method compatible to ADF and different than previous COSMO-SAC methods. The main difference compared to previous COSMO-SAC methods is that the COSMO-SAC 2013 model includes a dispersion contribution in the mixture interaction.

In Ref.[5] COSMO-SAC model parameters were optimized by Chen et al. for different quantum mechanical calculations. The authors of Ref.[?] also reoptimized the revised COSMO-SAC model[?] parameters for quantum mechanical calculations with ADF, which will be called here the COSMO-SAC 2016-ADF method.

In Ref.[6] a COSMO-SAC model was proposed that uses a directional hydrogen bond approach, denoted as the COSMO-SAC(DHB) model. The parameters were reoptimized by Chen et al. for use with ADF, which will be called here the COSMO-SAC DHB-ADF method.

[1] S.T. Lin and S.I. Sandler, *A Priori Phase Equilibrium Prediction from a Segment Contribution Solvation Model*, Ind. Eng. Chem. Res. 41, 899 (2002) (https://doi.org/10.1021/ie001047w)

[2] S. Wang, S.I. Sandler, C.C. Chen, *Refinement of COSMO-SAC and the Applications*, Ind. Eng. Chem. Res. 46, 7275 (2007) (https://doi.org/10.1021/ie070465z)

[3] C.M. Hsieh, S.I. Sandler, S.T. Lin, *Improvements of COSMO-SAC for vapor-liquid and liquid-liquid equilibrium predictions*, Fluid Phase Equilib. 297, 90 (2010) (https://doi.org/10.1016/j.fluid.2010.06.011)

[4] R. Xiong, S.I. Sandler, R.I. Burnett, *An improvement to COSMO-SAC for predicting thermodynamic properties*, Ind. Eng. Chem. Res. 53, 8265 (2014) (https://doi.org/10.1021/ie404410v)

[5] W.L. Chen, C.M. Hsieh, L. Yang, C.C. Hsu, S.T. Lin, *A Critical Evaluation on the Performance of COSMO-SAC Models for Vapor-Liquid and Liquid-Liquid Equilibrium Predictions Based on Different Quantum Chemical Calculations*, Ind. Eng. Chem. Res. 55, 9312 (2016) (https://doi.org/10.1021/acs.iecr.6b02345)

[6] W.L. Chen, S.T. Lin, *Explicit consideration of spatial hydrogen bonding direction for activity coefficient prediction based on implicit solvation calculations*, Phys.Chem.Chem.Phys. 19, 20367 (2017) (https://doi.org/10.1039/c7cp02317k)

The ADF COSMO-RS program can calculate activity coefficients using the COSMO-SAC 2013-ADF model or the COSMO-SAC 2016-ADF model. Like in the COSMO-RS method, pure compound vapor pressures can be given as input, for example, if experimental values are available. In case of the COSMO-SAC 2013-ADF model, if these values are not specified then the pure compound vapor pressure will be calculated according to the COSMO-SAC 2013-ADF model. However, in case of COSMO-SAC 2016-ADF, if these values are not specified then the pure compound vapor pressures will be approximated using a method similar as in the COSMO-RS method. It is also possible to use some earlier COSMO-SAC methods[??], but note that the parameters in those papers were not optimized for use with ADF COSMO result files.

The COSMO-SAC 2013 model includes a dispersion contribution in the mixture interaction. This dispersion contribution is a complicated expression which also depends on the liquid molar volume of the pure compounds and on the molar volume of the mixture. The molar volume of the mixture is calculated from the pure compound liquid molar volumes assuming ideal mixing. In the input for the ADF COSMO-RS program one include for each compound the experimental pure compound liquid density (kg/L), from which the program can calculated the pure compound liquid molar volumes. If this density is not given the pure compound liquid molar volume will be calculated from its COSMO volume. Note that in the calculations with the COSMO-SAC 2013-ADF model in Ref.[?] often experimental pure compound liquid molar volumes were used.

2.3 UNIFAC theory

Below some of the UNIFAC method is explained, but a more complete description can be found in Ref.[1].

The UNIFAC method is an activity coefficient model derived from the UNIQUAC model. Both UNIFAC and UNIQUAC are thermodynamic models based on local composition theory, which holds that the local environment of a molecule in solution can be used to calculate the probabilities of molecular configurations in the bulk solution. While UNIQUAC requires parameters for every compound in solution and interaction parameters for every pair of compounds, UNIFAC estimates these parameters as functions of the number of occurrences of various molecular substructures, or groups, in a molecule. This means that UNIFAC can be applied to estimate activity coefficients for arbitrary systems, so long as every group is defined and an interaction parameter exists for every pair of groups in the composition.

The UNIFAC method calculates the activity coefficient as a function of two contributions: (1) the residual contribution, meant to account for the interactions of groups in the mixture; and (2) the combinatorial contribution, meant to account for entropic effects due to differences in molecular shape. Using these two components, the activity coefficient for each compound *i* is calculated as follows:

$$\ln \gamma_i = \ln \gamma_i^R + \ln \gamma_i^C$$

where $\ln \gamma_i^R$ corresponds to the residual contribution to the activity coefficient and $\ln \gamma_i^C$ to the combinatorial contribution.

2.3.1 Residual term

In the UNIFAC method, we first define n_i^k to be the number of times group *k* occurs in molecule *i*. Using this with the mole fraction x_i of each compound *i*, we calculate the group mole fraction, X_k, or the amount of groups of type *k* as a fraction of the total groups:

$$X_k = \frac{\sum\limits_i x_i n_i^k}{\sum\limits_i \sum\limits_j x_i n_i^j}$$

We use the X_k values to then determine the relative surface area each group represents in the mixture. This is done by taking an average of the X_k values weighted with the surface area contributions, Q_k, of each group *k*. We define the

[1] A. Fredenslund, R.L. Jones, and J.M. Prausnitz, *Group-contribution estimation of activity coefficients in nonideal liquid mixtures*, AIChE Journal 21, 1086 (1975) (https://doi.org/10.1002/aic.690210607)

result as the area fraction of group *k*:

$$\Theta_k = \frac{X_k Q_k}{\sum_m x_m Q_m}$$

the surface area and volume of a molecule is estimated as a linear function of the number and types of groups that are present. Each group *k* occurs a n_i^k times in molecule *i*.

Additionally, between every pair of groups, *k* and *m* an interaction energy is defined as a_{km}. This energy is given in Kelvin and is used to calculate the group interaction paramter Ψ_{km}:

$$\Psi_{km} = \exp\left(\frac{-a_{km}}{T}\right)$$

where *T* is the temperature of the system in Kelvin. Note that $\Psi_{km} \neq \Psi_{mk}$.

These parameters are then used to calculate the residual contribution to the activity coefficient for each group *k*:

$$\ln \Gamma_k = Q_k \left(1 - \ln \sum_m \Theta_m \Psi_{mk} - \sum_m \frac{\Theta_m \Psi_{km}}{\sum_n \Theta_n \Psi_{nm}}\right)$$

Additionally, one must also calculate $\ln \Gamma_k^{(i)}$, which follows the same procedure as above for each compound assuming it exists in a pure form, i.e., $x_i = 1$. Then, the residual contribution to the activity coefficient is calculated as follows:

$$\ln \gamma_i^R = \sum_k n_i^k \left(\ln \Gamma_k - \ln \Gamma_k^{(i)}\right)$$

2.3.2 Combinatorial term

To estimate the combinatorial contribution to the activity coefficient, first the surface area, q_i, and volume, r_i, of molecule *i* are estimated as follows:

$$q_i = \sum_i Q_k n_i^k \qquad r_i = \sum_i R_k n_i^k$$

where Q_k is the surface area contribution of group *k* and R_k is the volume contribution. Using these parameters we can define the relative surface area and relative volume (also called fractional surface area and fractional volume) corresponding to molecule *i* in solution. This is simply an average of the surface areas/volumes of each compound weighted by the mole fraction of that compound in solution:

$$\theta_i = \frac{x_i q_i}{\sum_j x_j q_j} \qquad \phi_i = \frac{x_i r_i}{\sum_j x_j r_j}$$

Additionally, we calculate the parameter L_i:

$$L_i = \frac{z}{2}(r_i - q_i) - (r_i - 1)$$

where z is the coordination number and is usually taken to be equal to 10. All of these parameters are then used to calculate the combinatorial contribution to the activity coefficient:

$$\ln \gamma_i^C = \ln \frac{\phi_i}{x_i} + \frac{z}{2} q_i \ln \frac{\theta_i}{\phi_i} + L_i - \frac{\phi_i}{x_i} \sum_j x_j L_j$$

2.4 Calculation of properties

The COSMO-RS method allows to calculate the (pseudo-)chemical potential of a compound in the liquid phase, as well as in the gas phase, see the the COSMO-RS theory that was discussed before and Ref.[1]. In the ADF COSMO-RS implementation the following equations were used to calculate properties using these chemical potentials.

$$\begin{aligned}
\sum_i x_i &= \sum_i y_i^{vapor} = \sum_i w_i = 1 \\
w_i &= x_i M_i^{pure}/M^{ave} \\
M^{ave} &= \sum_i x_i M_i^{pure} \\
p_i^{pure} &= exp\{(\mu_i^{pure} - \mu_i^{gas})/RT\} \\
p_i^{vapor} &= x_i exp\{(\mu_i^{solv} - \mu_i^{gas})/RT\} \\
p^{vapor} &= \sum_i p_i^{vapor} \\
y_i^{vapor} &= p_i^{vapor}/p^{vapor} \\
\gamma_i &= exp\{(\mu_i^{solv} - \mu_i^{pure})/RT\} \\
a_i &= \gamma_i x_i \\
G^E &= H^E - TS^E = \sum_i x_i(\mu_i^{solv} - \mu_i^{pure}) \\
H^E &= -RT^2 \partial\{G^E/RT\}/\partial T \\
G^{mix} &= G^E + RT\sum_i x_i \ln(x_i) \\
\Delta_{vap}H &= RT^2/p^{vapor}\partial\{p^{vapor}\}/\partial T \\
k_H &= 1/V_{solvent} exp\{(\mu_i^{gas} - \mu_i^{solv})/RT\} \\
k_H^{cc} &= 1/(k_H V_{solvent}) = \gamma_i p_i^{pure} \\
x_i^{SOL} &= 1/\gamma_i (T > T_m) \\
x_i^{SOL} &= 1/\gamma_i exp\{\Delta H_{fus}(1/T_m - 1/T)/R - \Delta C_p(ln(T_m/T) - T_m/T + 1)/R\} (T < T_m) \\
\Delta G_{solv}^{liq-solv} &= \mu_i^{solv} - \mu_i^{pure} \\
\Delta G_{solv}^{gas-solv} &= \mu_i^{solv} - \mu_i^{gas} + RTln(V_{solvent}/V_{gas}) \\
log_{10}P_{solv1/solv2} &= 1/ln(10)(\mu_i^{solv2} - \mu_i^{solv1})/RT + log_{10}(V_{solv1}/V_{solv2}) \\
1/LFL_{mix} &= \sum_i (y_i^{vapor}/LFL_i)
\end{aligned}$$

The above equations are not always exact, some assume perfect gas behavior, for example.

The molar fraction x_i of each compound i of the solvent should add up to 1.

With the COSMO-RS method it is possible to predict vapor pressures. In the COSMO-RS model the free energy difference between the chemical potential in the gas phase (perfect gas with a reference state of 1 bar) and the chemical potential of the liquid phase has been defined in such a way that the equation: $p_i = exp(\mu_i^{pure} - \mu_i^{gas})/RT$, will give the pressure in units of bar. It is also possible to use experimental vapor pressures of pure compounds as input data for the calculation. This may increase the accuracy of the calculated vapor pressures in a mixture, for example.

In the COSMO-RS method the volume of 1 molecule in the liquid phase is approximated with the volume of the molecule shaped cavity, that is used in the COSMO calculations. In this way it is possible to calculate the volume of 1 mole of

[1] A. Klamt, V. Jonas, T. Bürger and J.C. Lohrenz, *Refinement and Parametrization of COSMO-RS.* J. Phys. Chem. A 102, 5074 (1998) (https://doi.org/10.1021/jp980017s)

solvent molecules in the liquid phase. However, for properties that depend on such volumes, one can also use (related) experimental data as input data for the calculation.

The calculation of the boiling temperature of a solvent is performed with an iterative method. The temperature is varied until the calculated vapor pressure is within a certain threshold of the desired pressure.

Also the calculation of solubility of compound i is performed with an iterative method, since the activity coefficient γ_i depends on the molar fraction of this compound. The COSMO-RS method does not predict ΔH_{fus}, ΔC_p , or T_m . These can be given as input data for the calculation of solubility calculations of solid compounds.

Starting from ADF2012 the Gibbs-Helmholtz equation is used to calculate the excess enthalpy of a mixture. Previously it was estimated using the misfit and hydrogen bonding energy of the mixture and its pure compounds.

Quantity	Meaning
R	Gas constant
T	Temperature
x_i	The molar fraction of compound i in a liquid solution
y_i vapor	The molar fraction of compound i in the gas phase
w_i	The mass fraction of compound i in a liquid solution
M_i pure	The molar mass of the pure compound i
M^{ave}	The average molar mass of the mixture
γ_i	Activity coefficient of compound i in a liquid solution
a_i	Activity of compound i in a liquid solution
p_i^{pure}	The vapor pressure of the pure compound i
p_i^{vapor}	The partial vapor pressure of compound i
p^{vapor}	The total vapor pressure
μ_{i} gas	The pseudochemical potential of the pure compound i in the gas phase
μ_{i} pure	The pseudochemical potential of the pure compound i in the liquid phase
μ_{i} solv	The pseudochemical potential of compound i in a liquid solution
G^E	The excess Gibbs free energy
H^E	The excess enthalpy, Gibbs-Helmholtz equation
G^{mix}	The Gibbs energy of mixing
$\Delta_{vap}H$	The enthalpy of vaporization, Clausius-Clapeyron equation
$E_i^{HB\ pure}$	The hydrogen bond energy of the pure compound i in the liquid phase, see Ref.[?]
E_i^{HB}	The partial hydrogen bond energy of compound i in a liquid solution
$E_i^{misfit\ pure}$	The misfit energy of the pure compound i in the liquid phase, see Ref.[?]
E_i^{misfit}	The partial misfit energy of compound i in a liquid solution
$\Delta G_{solv}^{liq-solv}$	The solvation Gibbs free energy from the pure compound liquid phase
	to the solvated phase
$\Delta G_{solv}^{gas-solv}$	The solvation Gibbs free energy from the pure compound gas phase
	to the solvated phase, with a reference state of 1 mol/L in both phases
k_H	Henry's law constant: ratio between the liquid phase concentration of a compound
	and its partial vapor pressure in the gas phase
k_H^{cc}	dimensionless Henry's law constant: ratio between the liquid phase concentration
	of a compound and its gas phase concentration
$k_{H\ inv}^{px}$	Henry's law constant, representing the volatility instead of the solubility,
	ratio between the partial vapor pressure of a compound in the gas phas
	and the molar fraction in the liquid phase"
$V_{solvent}$	Volume of 1 mole of solvent molecules in the liquid phase
V_{gas}	Volume of 1 mole of molecules in the gas phase (at 1 atm, perfect gas)
x_i^{SOL}	Solubility of compound i in a solvent (molar fraction)
ΔH_{fus}	The enthalpy of fusion of compound i

continues on next page

Table 2.1 – continued from previous page

Quantity	Meaning
ΔC_p	The Δ heat capacity of fusion of compound i
T_m	The melting temperature of compound i
$log_{10}P_{solv1/solv2}$	The logarithm of the partition coefficient P, which is the ratio of the concentrations
	of a compound in two immiscible solvents, solvent 1 and solvent 2
LFL_i	The flash point (lower flammable limit, LFL) of compound i
LFL_{mix}	The flash point (lower flammable limit, LFL) of a mixture, Le Chatelier's mixing rule

See also the COSMO-RS GUI tutorial for the calculation of the following properties:

- solvent vapor pressure [1, 2]
- boiling point of a solvent [1]
- partition coefficients (log P) [1, 2], Octanol-Water partition coefficients (log P_{OW}) [1]
- activity coefficients [1, 2], solvation free energies [1], Henry's law constants [1], pK_a values [1]
- solubility [1, 2]
- vapor-liquid diagram binary mixture (VLE/LLE) [1, 2]

Ionic liquids in COSMO-RS 2020

The activity coefficient of a compound i solvated in an ionic liquid is an important thermodynamic property. In COSMO-RS 2020 one can treat the ionic liquid as one compound, which means that the value of the activity coefficient is calculated in the standard way most applications report them. In particular, in COSMO-RS 2020 one can treat the ionic liquid as one compound, which only has the dissociated form.

- ionic liquids tutorial

Ionic liquids in COSMO-RS <=2019

The activity coefficient of a compound i solvated in an ionic liquid is an important thermodynamic property. The cation and anion, which have been treated separately, will be used in equal amounts to ensure an electroneutral mixture in the COSMO-RS calculation.

In other applications cation-anion pair have been treated as one molecule, however, below we will treat the cation and anion as two separate molecules, which is needed in older versions of COSMO-RS <=2019. This has consequences for the value of the activity coefficient.

For example, for a 1:1 IL (i.e., $[A]^+$ $[B]^-$), the activity coefficient at a finite concentration of solute i in the binary mixture (IL + solute) can be calculated by

$$\gamma_i^{bin} = (\gamma_i^{tern} x_i^{tern})/x_i^{bin} = \gamma_i^{tern}/(1+x_{IL}^{bin})$$

where the superscript "tern" represents the hypothetical ternary system comprising cation, anion and solute i, with

$$x_{cation}^{tern} = x_{anion}^{tern}$$

$$x_{cation}^{tern} + x_{anion}^{tern} + x_i^{tern} = 1$$

and the superscript "bin" represents the binary mixture comprising solute and IL, with

$$x_{IL}^{bin} + x_i^{bin} = 1$$

Accordingly, the activity coefficient of a solute i in the binary mixture (IL + solute) at infinite dilution is simplified as

$$\gamma_i^{\,bin} = 0.5\ \gamma_i^{\,tern} \quad \text{(at infinite dilution)}$$

Thus in this case we should scale the activity coefficient at infinite dilution $\gamma_i^{\,tern}$, which is directly obtained from the COSMO-RS calculation, with a factor of 0.5.

Similarly, for a ternary system comprising component i, component j and an ionic liquid, the activity coefficient at finite concentration of component i can be calculated by

$$\gamma_i^{\,tern} = \gamma_i^{\,quart} /(1+x_{IL}^{\,tern})$$

where the superscript “quart” represents the hypothetical quaternary system comprised of cation, anion, solute i and solute j, with:

$$x_{cation}^{\,quart} = x_{anion}^{\,quart}$$

$$x_{cation}^{\,quart} + x_{anion}^{\,quart} + x_i^{\,quart} + x_j^{\,quart} = 1$$

and the superscript “tern” represents the ternary mixture comprising solute i, j, and IL, with

$$x_{IL}^{\,tern} + x_i^{\,tern} + x_j^{\,tern} = 1$$

CHAPTER

THREE

COSMO RESULT FILES

COSMO-RS needs as input for the calculation so called COSMO result files for each compound, which are results of quantum mechanical calculation using COSMO. In ADF such a COSMO result file is called an adf.rkf file (previously ADF<=2019 known as TAPE21 or as a .t21 file) or a COSKF file (.coskf). With Fast Sigma such a COSMO result file is a COMPKF file (.compkf). With MOPAC such a COSMO result file is a .cos file, which can be converted to a COSKF file. In other programs such a file can be a .cosmo file. ADF has databases of .coskf files, the COSMO-RS compound database *ADFCRS-2018* (page 20) (including ionic liquids) and the COSMO-RS polymer database *ADFCRS-2019* (page 22). At http://www.design.che.vt.edu/VT-Databases.html a database of .cosmo files can be found, which were made with a different program. Note that the optimal COSMO-RS parameters may depend on the program chosen.

3.1 ADF COSMO calculation

3.1.1 ADF COSMO settings

Here it is described briefly how to make COSMO result files consistent with the way they were made for the ADF parametrization of COSMO-RS to ensure full parameter applicability. First a gas phase geometry optimization should be performed with ADF, with a small core TZP basis set, the Becke-Perdew functional (BP86), the relativistic scalar ZORA method (which is the default in ADF2020), and good numerical integration quality:

```
AMS_JOBNAME=GASPHASE "$AMSBIN/ams" << eor
Task GeometryOptimization
System
   Atoms
      ...
   End
End
Engine ADF
   Basis
      Type TZP
      Core Small
      PerAtomType Symbol=I File=ZORA/TZ2P/I.4p
   End
   XC
      GGA Becke Perdew
   End
   BeckeGrid
      Quality Good
   End
   Relativity
      Level Scalar
      Formalism ZORA
```

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```
   End
EndEngine
eor
```

For heavier elements than krypton (Z>36), like iodine, a small core TZ2P basis set is required. The resulting adf.rkf (previously ADF<=2019 TAPE21 file or .t21 file) of the molecule is used as a restart file in the COSMO calculation, and the system is loaded using the resulting ams.rkf. The ADF COSMO calculation is performed with the following settings:

```
AMS_JOBNAME=COSMO "$AMSBIN/ams" << eor
Task SinglePoint
LoadSystem
   File GASPHASE/ams.rkf
End
EngineRestart GASPHASE/adf.rkf
Engine ADF
   Basis
      Type TZP
      Core Small
      PerAtomType Symbol=I File=ZORA/TZ2P/I.4p
   End
   XC
      GGA Becke Perdew
   End
   BeckeGrid
      Quality Good
   End
   Relativity
      Level Scalar
      Formalism ZORA
   End
   Symmetry NOSYM
   SOLVATION
      Surf Delley
      Solvent name=CRS emp=0.0 cav0=0.0 cav1=0.0
      Charged method=CONJ corr
      C-Mat EXACT
      SCF VAR ALL
      RADII
         H  1.30
         C  2.00
         N  1.83
         O  1.72
         F  1.72
         Si 2.48
         P  2.13
         S  2.16
         Cl 2.05
         Br 2.16
         I  2.32
      SubEnd
   END
EndEngine
eor
```

In this COSMO calculation the Delley type of cavity construction is chosen (See Ref.[1] for details on the Delley surface

[1] B. Delley, *The conductor-like screening model for polymers and surfaces.* Molecular Simulation 32, 117 (2006) (https://doi.org/10.1080/08927020600589684)

construction). The name of the solvent is CRS, which sets the dielectric constant to infinite and sets the radius of the probing sphere to determine the solvent excluded part of the surface to 1.3 Angstrom.

In case of a cation or an anion, in both the gas phase calculations as well as in the COSMO calculation one should include the charge with the subkey CHARGE of the key SYSTEM in the AMS part of the input.

In the Radii subblock key the Klamt atomic cavity radii are chosen. The parameters emp, cav0, and cav1 are zero. The corr option to the CHARGED subkey constrains the computed solvent surface charges to add up to the negative of the molecular charge. Specifying exact for the C-MAT subkey causes ADF to compute straightforwardly the Coulomb potential due to the charge q in each point of the molecular numerical integration grid and integrate against the electronic charge density. This is, in principle, exact but may have inaccuracies when the numerical integration points are very close to the positions of a charge q. To remedy this, starting from ADF2010 the electrostatic potential is damped in case of (very) close lying numerical integration points and COSMO surface points. The numerical stability of the results compare to those of ADF2009 was increased as a result of this. Specifying exact for the C-MAT subkey also requires that the ADF calculation uses SYMMETRY NOSYM.

The resulting adf.rkf (previously ADF<=2019 TAPE21 file or .t21 file) of the COSMO calculation is a COSMO result file.

In a COSMO-RS calculation only the 'COSMO' part of this file is needed. One can make a kf file compound.coskf, which only consists of the section 'COSMO' if one does:

```
$AMSBIN/cpkf adf.rkf compound.coskf "COSMO"
```

The file compound.coskf should not exist before this command is given. Note that such a .coskf file is not a complete adf.rkf anymore. For example, only the COSMO surface can be viewed with AMSview. It is useful mostly for COSMO-RS calculations.

Links COSMO-RS GUI tutorial: COSMO result files [1]

3.1.2 Atomic cation or anion

In case of an atomic calculation one should of course not perform a geometry optimization. In case of a cation or an anion, in both the gas phase calculations as well as in the COSMO calculation one should include the charge with the key CHARGE. Only for atomic calculations one should include the argument `method=atom` to the subkey Charged of the key SOLVATION:

```
SOLVATION
  Surf Delley
  Solvent name=CRS cav0=0.0 cav1=0.0
  Charged method=atom corr
  C-Mat EXACT
  SCF VAR ALL
END
```

3.1.3 Accuracy

Several parameters in the COSMO calculation can influence the accuracy of the result of the quantum mechanical calculation. Some of these parameters will be discussed. Note that if one chooses different parameters in the COSMO calculation one may also have to reparametrize the ADF COSMO-RS parameters. A list of some of the ADF COSMO parameters.

- XC functional
- basis set
- fit set

- atomic cavity radii and radius of the probing sphere
- cavity construction
- geometry

The atomic cavity radii and the radius of the probing sphere are the same as in Ref.[2], which describes the COSMO-RS method developed by Klamt et al., which is implemented in ADF. The Becke Perdew functional is relatively good for weakly bound systems, but may not be so good in other cases. The basis set TZP is a compromise basis set. For heavier elements than krypton (Z>36), like iodine, a TZ2P basis set is required, including the relativistic scalar ZORA method. Since the relativistic method hardly cost extra time compared to a non-relativistic method, the scalar relativistic scalar ZORA method is recommended to be used also for light elements. The Delley type of cavity construction in ADF can give a large number of COSMO points. The XC functional, basis set, and cavity construction chosen in the ADF COSMO calculation have a similar accuracy as those that were used in Ref.[?]. Note that they are not exactly the same as were used in Ref.[?], since in that paper a different quantum mechanical program was used.

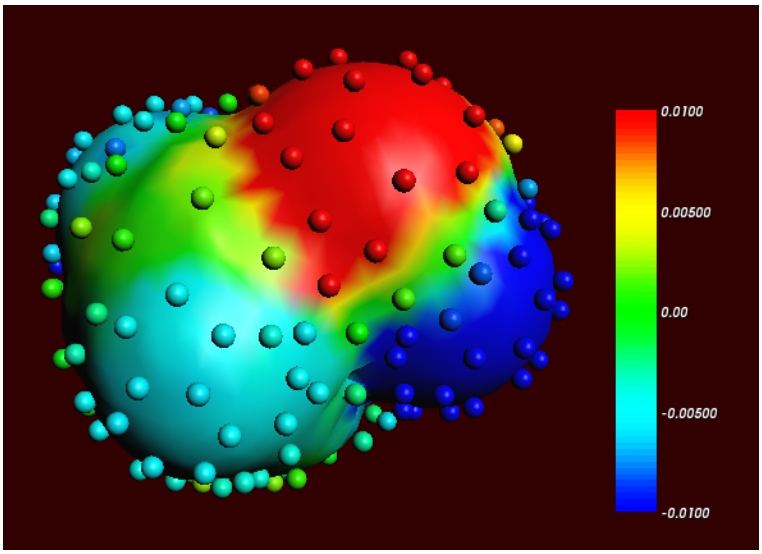
In the parametrization for ADF the same geometry was used for the gas phase and the COSMO calculation, which is different than in Ref.[?]. It depends on the actual solvent if reoptimizing the molecule in the COSMO calculation may give better results. Note that the dielectric medium used in the COSMO model has an infinite dielectric constant in the COSMO-RS model. Thus a geometry optimization of the molecule in the COSMO calculation might be more appropriate for a molecule dissolved in water than for a molecule dissolved in n-hexane.

The fit set in ADF is not always able to describe the Coulomb potential accurately at each of the COSMO surface points. In regular ADF calculations this problem is not apparent since the numerical errors in the integrals computed in the vicinity of the COSMO surface have little impact. However, in COSMO calculations this may have some effect. This is why the option C-Mat exact was selected above, instead of the default C-Mat pot option. Another possibility is to add more fit functions, for example, using 'FitQuality Good' for the key ZlmFit in the input for the adf calculation.

3.1.4 Cavity construction

The Esurf type of cavity construction in ADF with default settings does not give a large number of COSMO points. Therefore it is recommended to use the so called Delley type of cavity construction (Ref.[?]), which allows one to construct a surface which has many more points. The Esurf type of cavity construction also allows many more points if one sets the option NFDiv of the subkey DIV of the key SOLVENT to a larger value than the default value of 1. This will not be discussed here further. In ADF2010 the numerical stability of the Delley surface has been improved, by merging close lying COSMO surface points, and removing COSMO surface points with a small surface area. A figure of a COSMO surface with the Esurf type of cavity construction with default settings is given below. In this figure the small spheres represent the COSMO surface points that are used for the construction of the COSMO surface. The red part represents positive COSMO charge density, the blue part negative COSMO charge density (the coloring scheme is chosen to match the one by Klamt):

[2] A. Klamt, V. Jonas, T. Bürger and J.C. Lohrenz, *Refinement and Parametrization of COSMO-RS.* J. Phys. Chem. A 102, 5074 (1998) (https://doi.org/10.1021/jp980017s)

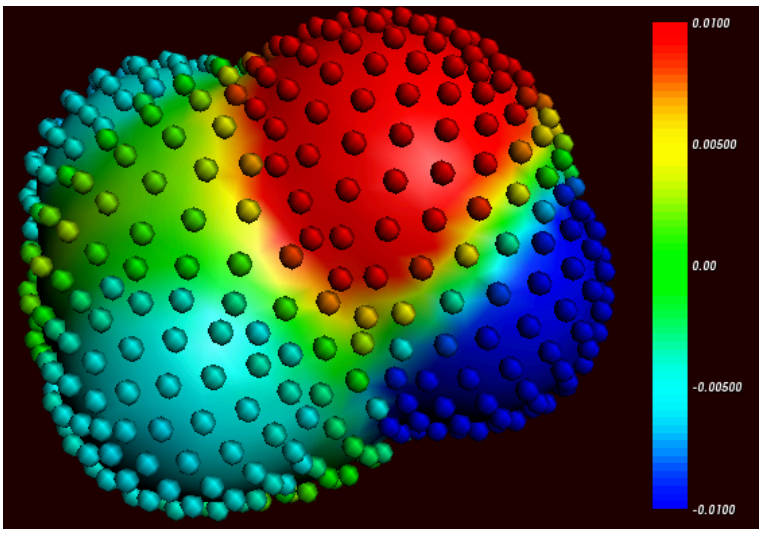


Cosmo charge density on the COSMO surface of methanol, Esurf surface (picture made with AMSview).

One can construct a surface which has many more points using a so called Delley surface. For the subkey SURF of the key SOLVENT one can choose delley. The subkey DIV of the key SOLVENT has extra options leb1 (default value 23), leb2 (default value 29), and rleb (default value 1.5 Angstrom). If the cavity radius of an atom is lower than rleb use leb1, otherwise use leb2. These values can be changed: using a higher value for leb1 and leb2 gives more surface points (maximal value leb1, leb2 is 29). A value of 23 means 194 surface points in case of a single atom, and 29 means 302 surface points in case of a single atom Typically one could use leb1 for the surface point of H, and leb2 for the surface points of other elements.

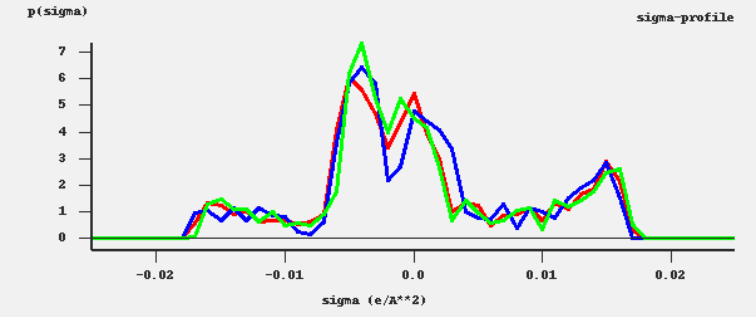
The next figure is made with the following (default for the Delley surface) settings:

```
SOLVATION
    SURF Delley
    DIV leb1=23 leb2=29 rleb=1.5
END
```



Cosmo charge density on the COSMO surface of methanol, Delley surface (picture made with AMSview).

The different ways of constructing the cavity has some consequences for the σ-profile of methanol, see the figure below:



σ-profiles of methanol (picture made with the CRS-GUI). In this picture the blue line is the σ-profile with the Esurf type of construction, the red line is that with the Delley type of construction with many surface points. For comparison, the green line is the σ-profile of methanol if a large QZ4P basis set is used, again with the Delley type of construction with many surface points.

3.2 ADFCRS-2018 Database

The COSMO-RS Database ADFCRS-2018 contains 2560 compounds. This database combines the COSMO-RS database ADFCRS-2010, the ionic liquid database ADFCRS-IL-2014, and some extra compounds.

Follow the COSMO-RS GUI Tutorial on the COSMO-RS compound database for more information on how to download and install the zipped COSMO-RS Database ADFCRS-2018 https://downloads.scm.com/Downloads/crs/ADFCRS-2018.zip, and how to use it.

The database contains CAS Registry Numbers. CAS Registry Number is a Registered Trademark of the American Chemical Society.

Note: Update on ADFCRS-2018-4 Some compounds have been updated with the correct CAS number and SMILES. Upon updating the SMILES, the coskf file has been rerun.

Table 3.1: Update on ADFCRS-2018-4

File Name	Corrected SMILES/CAS number
2-Mercaptobenzothiazole.coskf	S=C1SC=2C=CC=CC2N1
2-Hydroxypyridine.coskf	O=C1C=CC=CN1
2-Hydroxynicotinic_acid.coskf	O=C(O)C1=CC=CNC1=O
2-Hydroxy-6-methylnicotinic_acid.coskf	O=C(O)C1=CC=C(NC1=O)C
Chloropyrifos.coskf	S=P(OC1=NC(Cl)=C(Cl)C=C1Cl)(OCC)OCC
Phosphorus_pentasulfide.coskf	P12(=S)SP3(=S)SP(=S)(S1)SP(=S)(S2)S3
tert-Dodecyl_mercaptan.coskf	CC(C)C(C)(C)C(C)(C)C(C)(C)S
Hypophosphorous_acid.coskf	O=[PH2]O
Perfluoro-n-hexadecane.coskf	FC(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F
Dehydroabietylamine.coskf	CC(C)C1=CC2=C(C=C1)[C@]3(CCC[C@@]([C@@H]3CC2)(C)CN)C
4-Methyl-1H-imidazole.coskf	CC1=CN=CN1
Cellobiose.coskf	C([C@@H]1[C@H]([C@@H]([C@H]([C@@H](O1)O[C@@H]2[C@H](OC([C@@H]([C@H]2O)O)O)C
Triolein.coskf	O=C(OCC(OC(=O)CCCCCCCC=CCCCCCCCC)COC(=O)CCCCCCCC=CCCCCCCCC)CCCCCCCC=
Perfluoro-n-dodecane.coskf	FC(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)F
1,2-ethane_diphosphonic_acid.coskf	O=P(O)(O)CCP(=O)(O)O
Trilinolein.coskf	C(OC(CCCCCCC/C=CC/C=CCCCCC)=O)(COC(CCCCCCC/C=CC/C=CCCCCC)=O)COC(CCCCCCC/
Tetramantane.coskf	C123C4C5C67C(C1C8C(C4CC(C2)C8)C6)C9C(C3)C5CC(C7)C9
2-Ethyl-1-hexanol.coskf	OCC(CC)CCCC
4-Bromobenzoic_acid.coskf	586-76-5

3.2.1 ADFCRS-2010

The COSMO-RS Database ADFCRS-2010 contains 1892 compounds, mostly solvents and small molecules. This database consists of ADF COSMO result (.coskf) files, which are results of ADF quantum mechanical calculations using COSMO, with settings suitable for use in our COSMO-RS module. The geometries have been optimized with ADF. This database makes the COSMO-RS functionality much easier and faster (the time-consuming DFT step is already done ..) to use.

The starting point for this database was a database of structures made by Prof. Sandler's group at the University of Delaware. The work of the Sandler group is based in part on earlier work by the group of Prof. Liu at Virginia Technical University, reported in these papers:

Mullins, E.; Oldland, R.; Liu, Y.A.; Wang, S.; Sandler, S.I.; Chen, C.-C.; Zwolak, M.; Seavey, K.C. *Sigma-Profile Database for Using COSMO-Based Thermodynamic Methods.* Ind. Eng. Chem. Res. 2006, 45 (12), 4389-4415. (https://doi.org/10.1021/ie060370h)

Mullins, E.; Liu, Y.A.; Ghaderi, A.; Fast, S.D. *Sigma Profile Database for Predicting Solid Solubility in Pure and Mixed Sol-*

vent Mixtures for Organic Pharmacological Compounds with COSMO-Based Thermodynamic Methods. Ind. Eng. Chem. Res. 2008, 47 (5), 1707-1725. (https://doi.org/10.1021/ie0711022)

Phillips, K.L.; Sandler, S.I.; Greene, R.W.; Di Toro, D.M. *Quantum Mechanical Predictions of the Henry's Law Constants and Their Temperature Dependence for the 209 Polychlorinated Biphenyl Congeners.* Environ. Sci. Technol. 2008, 42 (22), 8412-8418. (https://doi.org/10.1021/es800876w)

All structures in the database ADFCRS-2010 differ from those in the papers above, as they are the result of ADF geometry optimizations.

3.2.2 ADFCRS-IL-2014

Ionic liquids (ILs), usually consisting of a large organic cation and a small inorganic polyatomic anion, have attracted considerable attention in recent years due to their unique thermophysical properties. The low vapor pressure and high conductivity of these molten salts combined with highly tunable properties, have resulted in highly diverse applications across many different fields in chemistry, materials science (battery electrolytes), chemical engineering (gas sorption and purification), and many more.

The COSMO-RS ionic liquid database ADFCRS-IL-2014 contains 80 cations and 56 anions. This ADFCRS-IL-2014 database consists of ADF COSMO result (.coskf) files, from standard ADF quantum mechanical calculations, as described in COSMO-RS GUI Tutorial: COSMO result files.

SCM gratefully acknowledges Prof. Zhigang Lei's research group (State Key Laboratory of Chemical Resource Engineering, Beijing University of Chemical Technology, China) for providing the ionic liquid database as well as the corresponding tutorial.

The work of Zhigang Lei group based on the COSMO-RS model using the ADF software is listed as follows:

Z. Lei, C. Dai, J. Zhu, B. Chen, *Extractive distillation with ionic liquids: A review*, AIChE Journal 60, 3312 (2014) (https://doi.org/10.1002/aic.14537)

Z. Lei, C. Dai, B. Chen, *Gas solubility in ionic liquids*, Chemical Reviews 14, 1289 (2014) (https://doi.org/10.1021/cr300497a)

Z. Lei, J. Han, Q. Li, and B. Chen, *Process Intensification on the Supercritical Carbon Dioxide Extraction of Low-Concentration Ethanol from Aqueous Solutions*, Industrial Engineering Chemistry research 51, 2730 (2012) (https://doi.org/10.1021/ie2021027)

Z. Lei, J. Han, B. Zhang, Q. Li, J. Zhu, and B. Chen, *Solubility of* CO_2 *in Binary Mixtures of Room-Temperature Ionic Liquids at High Pressures*, Journal of Chemical Engineering data 57, 2153 (2012) (https://doi.org/10.1021/je300016q)

Z. Lei, C. Dai, X. Liu, L. Xiao, and B. Chen, *Extension of the UNIFAC Model for Ionic Liquids*, Industrial Engineering Chemistry research 51, 12135 (2012) (https://doi.org/10.1021/ie301159v)

Z. Lei, C. Dai, Q. Yang, J. Zhu, and B. Chen, *UNIFAC model for ionic liquid*-CO (H_2) *systems: An experimental and modeling study on gas solubility*, AIChE Journal (2014), DOI: 10.1002/aic.14606 (https://doi.org/10.1002/aic.14606)

3.3 ADFCRS-POLYMERS-2019 Database

The COSMO-RS database ADFCRS-POLYMERS-2019 contains data for more than 200 polymers. The zipped COSMO-RS database ADFCRS-POLYMERS-2019 can be downloaded from https://downloads.scm.com/Downloads/crs/ADFCRS-POLYMERS-2019.zip. The database needs to be unzipped.

3.4 FastSigma: a QSPR method to estimate COSMO sigma-profiles

3.4.1 Introduction

The traditional workflow for performing a COSMO-RS/-SAC calculation first involves a very expensive DFT geometry optimization and single point calculation in the COSMO phase to generate σ-profiles and other necessary parameters for COSMO-RS/-SAC. Once these parameters are known, the COSMO-RS/-SAC calculation can be performed extremely efficiently, often in only a matter of milliseconds. This imbalance of computational expense means there is a significant opportunity in circumventing the expensive DFT steps.

The `FastSigma` program reads a molecule in several possible formats (SMILES, .mol, .sdf) and estimates all of the properties required for a COSMO-RS/-SAC calculation: the HB-/Non-HB-/OT-/OH- σ-profiles, COSMO surface area, and COSMO volume as well as bond energies that can be important for vapor phase or multispecies calculations. This code incorporates two distinct methods that are able to estimate these important COSMO-RS/-SAC properties. The first uses QSPR techniques similar to those applied in our Property Prediction program which shares the same accepted atom types. The second uses a database of σ-profiles and a custom molecular graph hashing algorithm to build σ-profiles for query molecules using a set of the σ-profiles from molecules in the database containing similar substructures.

Both of these techniques are extremely efficient and are capable of providing estimates for these essential COSMO-RS/-SAC properties in milliseconds. This allows for quick thermodynamic calculations to be done for a new molecule of interest as well as drastically expedites searches through screening databases of molecular candidates as compared to the traditional, full-fledged COSMO-RS/-SAC workflow.

Important: To use the `SG1` method, users will have to first download the **Subgraph Sigma Profile Estimation (SG1) Database** (molsg_sg1db) using the AMS Package Manager.

Note: *pyCRS* (page 81) can be used for python scripting with FastSigma. Several python examples are given in the pyCRS documentation.

3.4.2 Input options

A list of the input options and examples of their usage is given below.

Flag	Purpose	Example
-h [–help]	Produces help message	$AMSBIN/fast_sigma –help
-s [–smiles]	Input molecule as SMILES sting	$AMSBIN/fast_sigma –smiles <SMILES> …
-m [–mol]	Input molecule as .mol file	$AMSBIN/fast_sigma –mol <mol file> …
–sdf	Input molecule as an .sdf file	$AMSBIN/fast_sigma –sdf <file.sdf> …
–model	Choose from 2 possible techniques	$AMSBIN/fast_sigma –model FS1 …
-d [–display]	Display problem results	$AMSBIN/fast_sigma -d …
-o [–output]	Write output to file	$AMSBIN/fast_sigma –o <output.compkf> …
–method	Chose a COSMO-RS/-SAC method	$AMSBIN/fast_sigma –method COSMO-RS …

--model FS1 The FS1 model is a QSPR model. It currently has two supported methods: **COSMO-RS** and **COSMOSAC2016**. One of these method names must be entered after the –method flag. The default method is COSMO-RS.

--model SG1 The SG1 model is based on substructure hashing and database searching. It currently has two supported methods: **COSMO-RS** and **COSMOSAC2013**.

Note: This model can take a few seconds to load the required database. If the user would like to use this method to estimate multiple compounds, it is recommended to use pyCRS. With pyCRS, the database will only be loaded during the first calculation and then stay in memory.

-o <output.compkf> The fast sigma program writes the output results to a file in .compkf format. The chosen output filename should generally end with .compkf. This suffix helps other parts of the code (COSMO-RS/-SAC/-UNIFAC/Solvent Optimization) recognize the format and use the file accordingly. If no filename is supplied the program writes to a file called CRSKF.compkf.

-s <SMILES_string or .mol file> Though COSMO-RS/-SAC can make estimates for many types of molecular species, the fast sigma program currently only supports organic, neutral, closed shell molecules.

3.4.3 GUI Input

The simplest way to use the Fast Sigma program is through the COSMO-RS GUI. There are two ways to do this:

- SMILES string: **Compounds → List of Compounds → Add Compound using FastSigma → SMILES** and select Add.
- .xyz file: **Compounds → List of Compounds → Add Compound using FastSigma → .xyz**, and select Add.

A .compkf file will be saved that can be used as input in COSMO-RS calculations.

3.4.4 Examples

This example calculates COSMO-RS (the default) parameters for phenol:

```
$AMSBIN/fast_sigma --smiles "c1ccccc1(O)" -d
```

```
       sigma value       Total profile          HB profile
            -0.025               0.000               0.000
            -0.024               0.000               0.000
            -0.023               0.000               0.000
            -0.022               0.002               0.002
            -0.021               0.054               0.054
            -0.020               0.263               0.263
            -0.019               0.523               0.523
            -0.018               0.684               0.684
            -0.017               0.828               0.828
            -0.016               0.801               0.801
            -0.015               0.732               0.716
            -0.014               0.642               0.597
            -0.013               0.653               0.519
            -0.012               0.678               0.487
            -0.011               0.607               0.423
            -0.010               0.567               0.382
            -0.009               0.646               0.245
```

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```
            -0.008                4.183                0.023
            -0.007                7.405                0.000
            -0.006                7.912                0.000
            -0.005                6.701                0.000
            -0.004                5.544                0.000
            -0.003                4.658                0.000
            -0.002                3.899                0.000
            -0.001                4.097                0.000
             0.000                6.109                0.000
             0.001                7.854                0.000
             0.002                8.640                0.000
             0.003                9.726                0.000
             0.004               11.175                0.000
             0.005               12.524                0.000
             0.006                8.673                0.000
             0.007                2.255                0.000
             0.008                1.174                0.161
             0.009                1.279                1.159
             0.010                1.442                1.442
             0.011                1.759                1.751
             0.012                1.795                1.788
             0.013                0.838                0.829
             0.014                0.095                0.093
             0.015                0.054                0.054
             0.016                0.030                0.030
             0.017                0.000                0.000
             0.018                0.000                0.000
             0.019                0.000                0.000
             0.020                0.000                0.000
             0.021                0.000                0.000
             0.022                0.000                0.000
             0.023                0.000                0.000
             0.024                0.000                0.000
             0.025                0.000                0.000
       Molecular Mass =         94.0418648120 g/mol
           COSMO Area =        127.5012207186 Angstrom**2
         COSMO Volume =        122.0791950835 Angstrom**3
Gas Phase Bond Energy =         -2.9875007647 Hartree
          Bond Energy =         -2.9968155744 Hartree
           Dispersion =         -4.5319123638 kcal/mol
           Deltaediel =          0.0000000000 Hartree
                Nring =          6
     Chemical Formula =          C6H6O
               SMILES =          c1ccccc1(O)
```

Additionally, we calculate the COSMOSAC2016 parameters for Ibuprofen as a mol file:

```
$AMSBIN/fast_sigma --mol Ibuprofen.mol --method COSMOSAC2016 -d
```

```
       sigma value       Total profile          OH profile          OT profile
            -0.025               0.000               0.000               0.000
            -0.024               0.000               0.000               0.000
            -0.023               0.000               0.000               0.000
            -0.022               0.000               0.000               0.000
            -0.021               0.009               0.009               0.000
            -0.020               0.062               0.061               0.000
```

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```
          -0.019              0.395              0.385              0.000
          -0.018              0.914              0.881              0.000
          -0.017              0.925              0.879              0.000
          -0.016              0.840              0.781              0.000
          -0.015              0.652              0.590              0.000
          -0.014              0.697              0.606              0.000
          -0.013              0.604              0.499              0.000
          -0.012              0.561              0.398              0.000
          -0.011              0.725              0.418              0.000
          -0.010              0.833              0.350              0.000
          -0.009              1.282              0.230              0.000
          -0.008              2.141              0.158              0.000
          -0.007              5.133              0.085              0.000
          -0.006             10.428              0.048              0.000
          -0.005             14.386              0.000              0.000
          -0.004             23.816              0.000              0.000
          -0.003             26.081              0.000              0.000
          -0.002             23.295              0.000              0.000
          -0.001             21.443              0.000              0.000
           0.000             22.124              0.000              0.000
           0.001             20.652              0.000              0.000
           0.002             24.315              0.036              0.000
           0.003             15.722              0.086              0.035
           0.004             11.878              0.171              0.092
           0.005             13.670              0.288              0.197
           0.006             10.405              0.381              0.307
           0.007              5.479              0.561              0.413
           0.008              3.525              0.713              0.613
           0.009              3.358              0.823              1.055
           0.010              3.879              0.639              1.840
           0.011              4.503              0.180              3.025
           0.012              2.708              0.083              2.006
           0.013              0.930              0.020              0.745
           0.014              0.061              0.000              0.104
           0.015              0.000              0.000              0.000
           0.016              0.000              0.000              0.000
           0.017              0.000              0.000              0.000
           0.018              0.000              0.000              0.000
           0.019              0.000              0.000              0.000
           0.020              0.000              0.000              0.000
           0.021              0.000              0.000              0.000
           0.022              0.000              0.000              0.000
           0.023              0.000              0.000              0.000
           0.024              0.000              0.000              0.000
           0.025              0.000              0.000              0.000
      Molecular Mass =      206.1306798160 g/mol
          COSMO Area =      278.4276940312 Angstrom**2
        COSMO Volume =      279.3341044098 Angstrom**3
Gas Phase Bond Energy =       -7.1463537624 Hartree
         Bond Energy =       -7.1619486814 Hartree
          Dispersion =       -9.7153055452 kcal/mol
          Deltaediel =        0.0007518662 Hartree
               Nring =        6
    Chemical Formula =        C13H18O2
              SMILES =        CC(C)Cc1ccc(C(C)C(=O)O)cc1
```

We can also use the `SG1` model for phenol.

```
$AMSBIN/fast_sigma --smiles "c1ccccc1(O)" --model SG1 -d
```

```
       sigma value       Total profile          HB profile
            -0.025               0.000               0.000
            -0.024               0.000               0.000
            -0.023               0.000               0.000
            -0.022               0.003               0.003
            -0.021               0.067               0.067
            -0.020               0.434               0.434
            -0.019               0.878               0.878
            -0.018               0.995               0.995
            -0.017               0.996               0.996
            -0.016               0.942               0.940
            -0.015               0.771               0.766
            -0.014               0.684               0.635
            -0.013               0.610               0.549
            -0.012               0.693               0.486
            -0.011               0.671               0.397
            -0.010               0.755               0.350
            -0.009               1.344               0.255
            -0.008               4.312               0.026
            -0.007               7.751               0.000
            -0.006               7.855               0.000
            -0.005               6.819               0.000
            -0.004               6.226               0.000
            -0.003               5.612               0.000
            -0.002               4.654               0.000
            -0.001               4.679               0.000
             0.000               4.969               0.000
             0.001               5.814               0.000
             0.002               7.672               0.000
             0.003              10.711               0.000
             0.004              12.231               0.000
             0.005              12.061               0.000
             0.006               8.394               0.000
             0.007               3.355               0.000
             0.008               1.677               0.153
             0.009               1.434               1.226
             0.010               1.566               1.566
             0.011               1.972               1.972
             0.012               2.133               2.133
             0.013               0.966               0.966
             0.014               0.062               0.062
             0.015               0.000               0.000
             0.016               0.000               0.000
             0.017               0.000               0.000
             0.018               0.000               0.000
             0.019               0.000               0.000
             0.020               0.000               0.000
             0.021               0.000               0.000
             0.022               0.000               0.000
             0.023               0.000               0.000
             0.024               0.000               0.000
             0.025               0.000               0.000
      Molecular Mass =        94.0418648120 g/mol
          COSMO Area =       133.1606910587 Angstrom**2
        COSMO Volume =       122.0268006780 Angstrom**3
```

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```
Gas Phase Bond Energy =        -2.9830476046 Hartree
          Bond Energy =        -2.9928087890 Hartree
           Dispersion =         0.0000000000 kcal/mol
           Deltaediel =         0.0000000000 Hartree
                Nring =         6
     Chemical Formula =         C6H6O
               SMILES =         c1ccccc1(O)
```

The warning message will be displayed if a molecule contains atoms or substructures that are not listed in the accepted atom types table. For example, in the compound C1=CC=[Ge]C=C1, the atom 'Ge' is not available in the QSPR method. As a result, the property prediction tool will yield incorrect sigma profile.

```
$AMSBIN/fast_sigma --smiles "C1=CC=[Ge]C=C1" -d
```

```
 WARNING: there are atoms and/or substructures in the molecule which cannot be␣
↪estimated.
 This will affect the accuracy of the results.

 Atoms which cannot be estimated:
 Ge

      sigma value       Total profile          HB profile
           -0.025               0.000               0.000
           -0.024               0.000               0.000
           -0.023               0.000               0.000
           -0.022               0.000               0.000
           -0.021               0.000               0.000
           -0.020               0.000               0.000
           -0.019               0.000               0.000
           -0.018               0.000               0.000
           -0.017               0.000               0.000
           -0.016               0.000               0.000
           -0.015               0.000               0.000
           -0.014               0.000               0.000
           -0.013               0.000               0.000
           -0.012               0.000               0.000
           -0.011               0.000               0.000
           -0.010               0.000               0.000
           -0.009               0.000               0.000
           -0.008               0.896               0.000
           -0.007               2.280               0.000
           -0.006               5.170               0.000
           -0.005               9.078               0.000
           -0.004               9.044               0.000
           -0.003               4.854               0.000
           -0.002               4.211               0.000
           -0.001               4.505               0.000
           -0.000               4.415               0.000
            0.001               4.824               0.000
            0.002               4.750               0.000
            0.003               5.745               0.000
            0.004               3.006               0.000
            0.005               4.904               0.000
            0.006               5.411               0.000
            0.007               4.222               0.000
            0.008               2.623               0.000
```

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```
             0.009               0.000               0.000
             0.010               0.000               0.000
             0.011               0.000               0.000
             0.012               0.000               0.000
             0.013               0.000               0.000
             0.014               0.000               0.000
             0.015               0.000               0.000
             0.016               0.000               0.000
             0.017               0.000               0.000
             0.018               0.000               0.000
             0.019               0.000               0.000
             0.020               0.000               0.000
             0.021               0.000               0.000
             0.022               0.000               0.000
             0.023               0.000               0.000
             0.024               0.000               0.000
             0.025               0.000               0.000
       Molecular Mass =       138.9603029600 g/mol
           COSMO Area =        79.9378826526 Angstrom**2
         COSMO Volume =        88.0443110798 Angstrom**3
Gas Phase Bond Energy =        -2.2538026599 Hartree
          Bond Energy =        -2.2571102789 Hartree
           Dispersion =        -2.9625031363 kcal/mol
           Deltaediel =         0.0000000000 Hartree
                Nring =         6
     Chemical Formula =         C5H5Ge
               SMILES =         C1=CC=[Ge]C=C1
```

3.5 MOPAC COSMO calculation

Here it is described briefly how to make MOPAC COSMO result files.

The simplest way is to use AMSinput. Draw the molecule using AMSinput, and save the .ams file. Select **Right Panel → MOPAC → Solvation method → COSMO-CRS**. Select 362 for NSPA. Press Run to run the MOPAC calculation. A .coskf file will be saved that can be used as input in COSMO-RS calculations.

In AMS2019 AMSinput uses the MOPAC engine, which is part of the AMS driver. Note that this is different than in AMS2018 and before. In the Atoms block key in the AMS driver part of the input one puts the coordinates of the molecule. The main input keys for the AMS driver and the MOPAC engine are:

```
$AMSBIN/ams << eor
Task GeometryOptimization
System
    Atoms
       ....
    End
End

Engine MOPAC
    Solvation
        Enabled Yes
        NSPA 362
        Solvent
            Name CRS
```

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```
        End
    End
EndEngine

eor
```

The use of the solvent CRS makes the MOPAC engine to create a .cos file, which is converted to a .coskf file by $AMSBIN/cosmo2kf

```
cosmo2kf file.cos file.coskf
```

Note that this is automatically done if one uses AMSinput.

Compared to the default ADF COSMO-RS values a few *COSMO-RS parameters* (page 31) were reoptimized for MOPAC PM6 COSMO result files to improve the calculation of a number of partition coefficients, when compared to experimental values. Note that MOPAC is a semi-empirical quantum chemistry program, whereas ADF is based on density functional theory (DFT). Thus the MOPAC COSMO result files will not be of the same quality as the ADF COSMO result files.

CHAPTER

FOUR

THE COSMO-RS PROGRAM

The ADF COSMO-RS command line program *crs* is described here, including all input options.

4.1 Running the COSMO-RS program

Running the COSMO-RS program involves the following steps:

- Construct an ASCII input file, say in.
- Run the program by typing (under UNIX): $AMSBIN/crs < in > out
- Move / copy relevant result files (in particular CRSKF) to the directory where you want to save them, and give them appropriate names.
- Inspect the standard output file out to verify that all has gone well.

Note that in the one can also put the call to $AMSBIN/crs inside a script, which could be named, for example, 'example.run'. Such shell script 'example.run' needs be executable, if it isn't you will need to make it executable, e.g. `chmod u+x example.run`. The 'example.run' file needs to be executed as a shell script, not as input to $AMSBIN/crs.

4.2 COSMO-RS and COSMO-SAC parameters

The COSMO-RS model has general parameters and element specific parameters. ADF's COSMO-SAC 2013-ADF model has general parameters, but also uses some of the COSMO-RS parameters, such as the element specific parameters. There are also technical and accuracy parameters, such as convergence criteria. This section explains how to set these parameters, and shows the default values for these parameters. By default the COSMO-RS method is chosen.

4.2.1 COSMO-RS general parameters

```
CRSPARAMETERS
  {RAV          rav}
  {APRIME       aprime}
  {FCORR        fcorr}
  {CHB          chb}
  {SIGMAHBOND   sigmahbond}
  {AEFF         aeff}
  {LAMBDA       lambda}
  {OMEGA        omega}
  {ETA          eta}
  {CHORTF       chortf}
```

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```
  {combi1998 | combi2005}
  {hb_all    | hb_hnof}
  {hb_temp   | hb_notemp}
  {fast      | nofast}
End
```

The ADF default values are optimized parameters for ADF calculations. The Klamt values can be found in Ref.[1]. See also Ref.[?] for the meaning of the parameters.

symbol	ADF Default	ADF combi1998	Klamt	MOPAC PM6
	Ref.[2]	Ref.[?]	Ref.[?]	
rav (r_{av})	0.400	0.415	0.5	0.400
aprime (a')	1510.0	1515.0	1288.0	1550.0
fcorr (f_{corr})	2.802	2.812	2.4	2.802
chb (c_{hb})	8850.0	8850.0	7400.0	8400.0
sigmahbond (σ_{hb})	0.00854	0.00849	0.0082	0.00978
aeff (a_{eff})	6.94	7.62	7.1	5.96
lambda (λ)	0.130	0.129	0.14	0.135
omega (ω)	-0.212	-0.217	-0.21	-0.212
eta (η)	-9.65	-9.91	-9.15	-9.65
chortf ($c^{\perp}$)	0.816	0.816	0.816	0.816
combi1998 | combi2005	combi2005	combi1998	combi1998	combi2005
hb_all | hb_hnof	hb_hnof	hb_hnof	hb_hnof	hb_hnof
hb_temp | hb_notemp	hb_temp	hb_notemp	hb_notemp	hb_temp
fast | nofast	fast	fast	fast	fast

chortf See Ref.[?] for the definitions: $\sigma_v^{\perp} = \sigma_v^0 - c^{\perp}\sigma_v$

combi1998 | combi2005 If the subkey combi1998 is included a thermodynamically inconsistent combinatorial contribution to the chemical potential μ_i^{comb} of Ref.[?] is used. If the subkey combi2005 is included (default) a thermodynamically consistent combinatorial contribution of Ref.[3] is used. See *the section on the combinatorial term* (page 7) and Ref.[?].

hb_all | hb_hnof If the subkey hb_all is included hydrogen bond interaction can be included between segments that belong to H atoms and all other segments. If the subkey hb_hbnof is included (default) hydrogen bond interaction can be included only between segments that belong to H atoms that are bonded to N, O, or, F, and segments that belong to N, O, or F atoms.

hb_temp | hb_notemp If the subkey hb_notemp is included the hydrogen bond interaction is not temperature dependent, as in Ref.[?]. If the subkey hb_temp is included (default) the hydrogen bond interaction is temperature dependent, as in Ref.[?]. See *the section on the temperature dependent hydrogen bond interaction* (page 8) and Ref.[?].

fast | nofast If the subkey fast is included the fast approximation is used. This fast approximation is the default. Use nofast for the original approach. See *the section on the fast approximation for COSMO-RS calculations* (page 7).

Links COSMO-RS GUI tutorial: set COSMO-RS parameters [1]

[1] A. Klamt, V. Jonas, T. Bürger and J.C. Lohrenz, *Refinement and Parametrization of COSMO-RS.* J. Phys. Chem. A 102, 5074 (1998) (https://doi.org/10.1021/jp980017s)

[2] C.C. Pye, T. Ziegler, E. van Lenthe, J.N. Louwen, *An implementation of the conductor-like screening model of solvation within the Amsterdam density functional package. Part II. COSMO for real solvents.* Can. J. Chem. 87, 790 (2009) (https://doi.org/10.1139/V09-008)

[3] A. Klamt, *COSMO-RS From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design, Elsevier.* Amsterdam (2005), ISBN 0-444-51994-7.

4.2.2 COSMO-RS element specific parameters

```
DISPERSION
  {H  dispH}
  {C  dispC}
  {N  dispN}
  {...}
End
```

The following table gives the element specific dispersion constants. The ADF default values are optimized parameters for ADF calculations. The Klamt values can again be found in Ref.[?]. The constants for F, Si, P, S, Br, and I in the ADF defaults were only fitted to a small number of experimental values or taken from Ref.[?].

element	ADF Default	ADF combi1998	Klamt
			Ref.[?]
H	-0.0340	-0.0346	-0.041
C	-0.0356	-0.0356	-0.037
N	-0.0224	-0.0225	-0.027
O	-0.0333	-0.0322	-0.042
Cl	-0.0485	-0.0487	-0.052
F	-0.026		
Si	-0.04		
P	-0.045		
S	-0.052		
Br	-0.055		
I	-0.062		

Note that not for all elements in the periodic system COSMO-RS parameters were fitted.

Links COSMO-RS GUI tutorial: set COSMO-RS parameters [1]

4.2.3 COSMO-SAC general parameters

The ADF COSMO-RS program can calculate activity coefficients using the COSMO-SAC 2013-ADF model, based on Ref.[4]. Like in the COSMO-RS method, pure compound vapor pressures can be given as input, for example, if experimental values are available. If these values are not specified then the pure compound vapor pressure will be calculated according to the COSMO-SAC 2013-ADF model. This part of the COSMO-SAC 2013-ADF has been implemented in ADF2016. The COSMO-SAC 2013-ADF parameters in Ref.[?] are optimized parameters for use with ADF COSMO result files. The authors of Ref.[6] reoptimized the revised COSMO-SAC model[5] parameters for use with ADF COSMO result files, which is called here the COSMO-SAC 2016-ADF method. Note that the earlier COSMO-SAC papers[7?] do not include parameters that were optimized for use with ADF COSMO result files. The key COSMOSAC2013 needs to be included if one wants to do a COSMO-SAC 2013-ADF calculation. The key COSMOSACDHB needs to be included if one wants to do a COSMO-SAC DHB-ADF calculation. For other COSMO-SAC methods one needs to include the key COSMOSAC.

[4] R. Xiong, S.I. Sandler, R.I. Burnett, *An improvement to COSMO-SAC for predicting thermodynamic properties*, Ind. Eng. Chem. Res. 53, 8265 (2014) (https://doi.org/10.1021/ie404410v)

[6] W.L. Chen, C.M. Hsieh, L. Yang, C.C. Hsu, S.T. Lin, *A Critical Evaluation on the Performance of COSMO-SAC Models for Vapor-Liquid and Liquid-Liquid Equilibrium Predictions Based on Different Quantum Chemical Calculations*, Ind. Eng. Chem. Res. 55, 9312 (2016) (https://doi.org/10.1021/acs.iecr.6b02345)

[5] C.M. Hsieh, S.I. Sandler, S.T. Lin, *Improvements of COSMO-SAC for vapor-liquid and liquid-liquid equilibrium predictions*, Fluid Phase Equilib. 297, 90 (2010) (https://doi.org/10.1016/j.fluid.2010.06.011)

[7] S. Wang, S.I. Sandler, C.C. Chen, *Refinement of COSMO-SAC and the Applications*, Ind. Eng. Chem. Res. 46, 7275 (2007) (https://doi.org/10.1021/ie070465z)

```
COSMOSAC2013 | COSMOSAC | COSMOSACDHB
SACPARAMETERS
  {AEFF         aeff}
  {FDECAY       fdecay}
  {SIGMA0       sigma0}
  {RN           rn}
  {QN           qn}
  {AES          aes}
  {BES          bes}
  {COHOH        cohoh}
  {COTOT        cotot}
  {COHOT        cohot}
  {RAV          rav}
  {QS           qs}
  {rhbcut       rhbcut}
  {hb_temp    | hb_notemp}
End
```

symbol	2013-ADF Xiong	2016-ADF Chen	DHB-ADF Chen	2010 Hsieh	2007 Wang
	Ref.[?]	Ref.[?]	Ref.[8]	Ref.[?]	Ref.[?]
aeff (a_{eff})	6.4813	5.8447	5.8447	7.25	7.25
fdecay (f_{decay})		3.57	3.57	3.57	3.57
sigma0 (σ_0)	0.01233	0.007	0.0063	0.007	0.007
rn (r)		66.69	66.69	66.69	66.69
qn (q)	79.352	79.53	79.53	79.53	79.53
aes (A_{ES})	7877.13	5920.84	5920.84	6525.69	8451.77
bes (B_{ES})	0.0	$1.3950\ 10^8$	$1.3950\ 10^8$	$1.4859\ 10^8$	0.0
cohoh ($c_{OH\text{-}OH}$)	5786.72	3551.10	33306.83	4013.78	3484.42
cotot ($c_{OT\text{-}OT}$)	2739.58	1077.26	33306.83	932.31	3484.42
cohot ($c_{OH\text{-}OT}$)	4707.75	3099.31	33306.83	3016.43	3484.42
rav (r_{av})	0.51				
qs (q_s)	0.57				
rhbcut			1.4432		
hb_temp | hb_notemp	hb_notemp	hb_notemp	hb_notemp	hb_notemp	hb_notemp

See also Refs.[??] for the meaning of the parameters a_{eff} , f_{decay} , σ_0 , r, q, A_{ES} , B_{ES} , $c_{OH\text{-}OH}$, $c_{OT\text{-}OT}$, $c_{OH\text{-}OT}$, r_{av} , q_s . The parameter names in[?] have been translated into parameter names used in Ref.[?], by calculating A_{ES} from 0.3 f_{pol} $a_{eff}^{3/2}$ /(2ϵ_0), using B_{ES} = 0, and using $c_{OH\text{-}OH}$ = $c_{OT\text{-}OT}$ = $c_{OH\text{-}OT}$ = c_{hb} . The parameters f_{decay} and r are not used in COSMO-SAC 2013-ADF[?]. The parameters r_{av} and q_s are only used in COSMO-SAC 2013-ADF. The element specific COSMO-SAC 2013-ADF epsilon constants can be set with the block key *EPSILON* (page 35). These element specific epsilon constants can not be used in ADF's implementation of earlier COSMO-SAC methods. The parameter rhbcut is only used in COSMO-SAC DHB-ADF[?]. Note that the parameters for COSMO-SAC DHB-ADF were reoptimized by Chen et al., and are different than in Ref.[?].

hb_temp | hb_notemp If the subkey hb_notemp is included (default) the hydrogen bond interaction is not temperature dependent, as in Refs.[???]. If the subkey hb_temp is included the temperature dependence of the hydrogen bond interaction f_{hb} (T) is the same as is described in *the section on the temperature dependent hydrogen bond interaction* (page 8).

Except for COSMO-SAC 2013-ADF, some COSMO-RS specific parameters are used in the next COSMO-SAC methods:

[8] W.L. Chen, S.T. Lin, *Explicit consideration of spatial hydrogen bonding direction for activity coefficient prediction based on implicit solvation calculations*, Phys.Chem.Chem.Phys. 19, 20367 (2017) (https://doi.org/10.1039/c7cp02317k)

```
COSMOSAC
SACPARAMETERS
  ...
  {OMEGA        omega}
  {ETA          eta}
End
```

symbol	2013-ADF Xiong	2016-ADF Chen, DHB-ADF Chen, 2010 Hsieh, 2007 Wang
omega (ω)		-0.212
eta (η)		-9.00

In ADF2016 these parameters are not used in the COSMO-SAC 2013-ADF method, only in the ADF implementation of the other COSMO-SAC methods. The parameters ω, η and the element specific COSMO-RS dispersion constants are taken from the COSMO-RS model. The element specific COSMO-RS dispersion constants can be set with the block key DISPERSION. ω, η, and the element specific COSMO-RS dispersion constants are used in a COSMO-RS like method for the calculation of pure compound vapor pressures.

4.2.4 COSMO-SAC element specific parameters

```
COSMOSAC2013
EPSILON
  {H  epsH}
  {C  epsC}
  {N  epsN}
  {...}
End
```

The following table gives the element specific epsilon constants in case of COSMO-SAC 2013-ADF, see Ref.[?]. Like in the COSMO-RS method, pure compound vapor pressures can be given as input, for example, if experimental values are available. In these values ar not given, in ADF2016 the pure compound vapor pressure will be approximated using the the COSMO-SAC 2013-ADF method, which depend on these element specific epsilon constants. These constants will also have an effect on the calculated activity coefficients in case of a mixture. Note that these only have an effect in the ADF's COSMO-SAC 2013-ADF implementation.

element	2013-ADF Xiong
	Ref.[7]
H	338.13
C.sp3	29160.92
C.sp2	30951.83
C.sp	20685.98
N.sp3	23488.54
N.sp2	22663.34
N.sp	6390.40
O.sp3-H	8527.06
O.sp3	8484.38
O.sp2	6736.85
O.sp2-N	12145.28
Cl	8435.13
F	82512.21
P	56067.81
S	45065.19
Br	62947.83
I	105910.88

Note that not for all elements in the periodic system COSMO-SAC 2013-ADF parameters were fitted.

If one leaves the EPSILON block keyword empty the contribution of the mixture dispersion to the activity coefficient will be zero.

```
EPSILON
End
```

Links COSMO-RS GUI tutorial: Expert option: set COSMO-SAC 2013-ADF parameters [1]

4.2.5 Technical and accuracy parameters

```
TECHNICAL
  {RSCONV rsconv}
  {SACCONV sacconv}
  {MAXITER maxiter}
  {BPCONV bpconv}
  {BPMAXITER bpmaxiter}
  {SOLCONV solconv}
  {SOLMAXITER solmaxiter}
  {SOLXILARGE solxilarge}
  {EHDELTAT ehdeltaT}
End
```

symbol	Default values
rsconv	10^{-7} kcal/mol
sacconv	10^{-7}
maxiter	10000
bpconv	10^{-6} bar
bpmaxiter	40
solconv	10^{-5} molar fraction
solmaxiter	40
solxilarge	0.99 molar fraction
ehdeltaT	1.0 Kelvin

rsconv Convergence criterion in kcal/mol in chemical potential calculation, not used in COSMO-SAC 2013-ADF. Default value 1e-7 kcal/mol.

sacconv Convergence criterion in activity coefficient calculation, only used in COSMO-SAC 2013-ADF. Default value 1e-7.

maxiter Maximum number of cycles in chemical potential or activity coefficients calculation. Default value 10000.

bpconv Convergence criterion (bar) for isobar or solvent boiling point calculation. Default value 1e-6 bar.

bpmaxiter Maximum number of cycles in isobar or solvent boiling point calculation. Default value 40.

solconv Convergence criterion (molar fraction) used in solubility calculations. Default value 1e-5 molar fraction.

solmaxiter Maximum number of cycles in solubility calculation. Default value 40.

solxilarge Threshold for (im-)miscibility (molar fraction) in solubility calculations. Above this value the mixture is considered to be fully miscible. Default value 0.99.

ehdeltaT ΔT (Kelvin) used in the calculation of the excess enthalpy using the Gibbs-Helmholtz equation and in the calculation of the enthalpy of vaporization using the Clausius-Clapeyron equation using a numerical derivative with respect to T. Default value 1.0 Kelvin.

Links COSMO-RS GUI tutorial: set COSMO-RS or COSMO-SAC 2013-ADF parameters [1]

4.3 Compounds

For each compound one has to add the keyword COMPOUND

```
COMPOUND filename
{cosmofile}
{drophbond}
{NRING nring}
{FRAC1 frac1}
{FRAC2 frac2}
{PVAP pvap}
{TVAP tvap}
{Antoine A B C}
{MELTINGPOINT meltingpoint}
{HFUSION hfusion}
{CPFUSION cpfusion}
{FLASHPOINT flashpoint}
{DENSITY density}
{SCALEAREA scalearea}
End
```

filename The filename (can be a full path, otherwise relative path is assumed) should be a COSMO result file. How to make an ADF COSMO result file can be found *here* (page 14).

cosmofile If the subkey cosmofile is included the file should be an ASCII COSMO file (.cosmo). If not specified (default) the file should be a kf file, either an ADF COSMO result file adf.rkf (previously ADF<=2019 TAPE21 file or .t21 file) or a COSKF file (.coskf).

drophbond If the subkey drophbond is included no hydrogen-bond terms will be included for this compound. If not specified (default) the hydrogen-bond terms are included for this compound.

nring The number of ring atoms. This is a COSMO-RS parameter. It should be 6 for benzene, for example. Default value is 0.

frac1 The molar fraction of the compound in the solvent (mass fraction if the key MASSFRACTION is used). This is solvent 1 in case of the calculation of partition coefficients (Log P) or in case of a composition line.

frac2 The molar fraction of solvent 2 (mass fraction if the key MASSFRACTION is used), only used in case of the calculation of partition coefficients (Log P) or in case of a composition line.

pvap, tvap Pure compound vapor pressure pvap (bar) at temperature tvap (Kelvin). Used only if both pvap and tvap are specified, and then will have an effect on the calculated vapor pressures or boiling points. Alternative is to set the Antoine coefficients. If both are not specified the pure compound vapor pressure is approximated using the COSMO-RS method.

A, B, C A, B, and C are the pure compound Antoine coefficients, such that: log P = A - B/(T+C). This Antoine equation is a 3-parameter fit to experimental pure compound vapor pressures P (bar) over a restricted temperature T (Kelvin) range. If the Antoine coefficients are specified this will have an effect on the calculated vapor pressures or boiling points. Alternative is to give input values for the pure compound vapor pressure at a fixed temperature. If both are not specified the pure compound vapor pressure is approximated using the COSMO-RS method.

meltingpoint, hfusion, cpfusion Pure compound melting point meltingpoint (Kelvin), pure compound enthalpy of fusion hfusion (kcal/mol), and pure compound heat capacity of fusion cpfusion (kcal/(mol K)). Only used if both meltingpoint and hfusion are specified (cpfusion optional), and will then have an effect in solubility calculations if the temperature of the solvent is below the melting point.

flashpoint Pure compound flash point flashpoint (Kelvin).

density Pure compound density density (kg/L). Used for calculating the volume of a solvent molecule.

dielectric_const The dielectric constant of the solvent.

scalearea Input scaling of COSMO surface area for a given compound. Default value 1.0 means the COSMO surface area is not scaled. Changing this value is an expert option, for example, to fit to experiment.

Links COSMO-RS GUI tutorial: set pure compound parameters [1]

4.4 Temperature

```
TEMPERATURE temperature {temperature_high ntemp}
```

temperature Temperature (Kelvin) at which temperature the COSMO-RS calculation should take place. Default room temperature 298.15. The first temperature in case of a range of temperatures.

temperature_high The last temperature (Kelvin) in case of a range of temperatures. Only used in case of solvent vapor pressure calculations or solubility calculations.

ntemp The number of temperatures in case of a range of temperatures.

4.5 Pressure

```
PRESSURE pressure {pressure_high npress}
```

pressure Pressure (bar) at which pressure the COSMO-RS calculation should take place. Default 1.01325 bar (1 atm). The first pressure in case of a range of pressures.

pressure_high The last pressure (bar) in case of a range of pressures. Only used in case of solvent boiling point calculations.

npress The number of pressures in case of a range of pressures.

4.6 Molar fractions and mass fraction

By default the ADF COSMO-RS program assumes molar fractions as input. This can be changed into mass fractions if one includes:

```
MASSFRACTION
```

4.7 Properties

4.7.1 Vapor pressure

The vapor pressure of a mixture can be calculated with:

```
PROPERTY vaporpressure
End
```

In case of a mixture the mole fraction of each compound of the solvent should be given with the subkey FRAC1 of the key COMPOUND for each compound. In case of a mixture also activity coefficients, and excess energies are calculated.

To calculate pure compound vapor pressures for more than one compound use:

```
PROPERTY purevaporpressure
End
```

It is possible to calculate the vapor pressure for a temperature range, see key TEMPERATURE.

The input pure compound vapor pressure will be used in the calculation of the vapor pressure of this compound if it is supplied with the key COMPOUND for this compound. If it is not specified then it will be approximated using the COSMO-RS method.

Links COSMO-RS GUI tutorial: solvent vapor pressure [1, 2]

4.7.2 Boiling point

The boiling point of a mixture can be calculated with the block key:

```
PROPERTY boilingpoint
End
```

In case of a mixture the mole fraction of each compound of the solvent should be given with the subkey FRAC1 of the key COMPOUND for each compound. In case of a mixture also activity coefficients, and excess energies are calculated.

To calculate pure compound boiling points for more than one compound use:

```
PROPERTY pureboilingpoint
End
```

It is possible to calculate the boiling temperature for a pressure range, see key PRESSURE.

The input pure compound vapor pressure will be used in the calculation of the vapor pressure of this compound in the mixture if it is supplied with the key COMPOUND for this compound. If it is not specified then it will be approximated using the COSMO-RS method.

The COSMO-RS calculation of the boiling temperature of a solvent is performed with an iterative method. The temperature is varied until the calculated vapor pressure is within a certain threshold of the desired pressure.

Links COSMO-RS GUI tutorial: boiling point of a solvent [1]

4.7.3 Solvent flash point

The flash point (lower flammable limit) of a compound is the lowest temperature at which the vapor of the compound forms an ignitable mixture in air. The COSMO-RS module can calculate the flash point of a mixture. The COSMO-RS module, however, does not calculate or predict the flash point of pure compounds. The COSMO-RS method is used to calculate the partial vapor pressures of each compound in the mixture, and it uses Le Chatelier's mixing rule to calculate the flash point of this mixture in the gas phase. Input pure compound flash points should be provided by the user, with the subkey FLASHPOINT flashpoint of the key COMPOUND.

```
PROPERTY flashpoint
End
```

The mole fraction of each compound of the solvent should be given with the subkey FRAC1 of the key COMPOUND for each compound.

4.7.4 Partition coefficients (LogP)

The partition coefficient of a compound in a mixture of two immiscible solvents, can be calculated with:

```
PROPERTY logp
{VOLUMEQUOTIENT volumequotient}
End
```

volumequotient If the subkey VOLUMEQUOTIENT is included the volumequotient will be used for quotient of the molar volumes of solvent 1 and solvent 2 instead of calculated values.

The mole fraction of each compound of the solvent 1 and solvent 2 should be given with the subkey FRAC1 and subkey FRAC2 of the key COMPOUND for each compound, respectively. In case of partly miscible liquids, like, for example, the Octanol-rich phase of Octanol and Water, both components have nonzero mole fractions. The compounds that are

included without a given mole fraction are considered to be infinite diluted solutes. The partition coefficients are calculated for all compounds.

One can use some compounds that are present in $AMSHOME/atomicdata/ADFCRS (Water, 1-Octanol, Benzene, Ethoxyethane, Hexane), or one can use compounds from the ADFCRS-2010 database. For example, for Octanol/Water partition coefficients one can use:

```
Property logp
  VolumeQuotient 4.93
End
Compound "$AMSHOME/atomicdata/ADFCRS/1-Octanol.coskf"
  frac1 0.725
End
Compound "$AMSHOME/atomicdata/ADFCRS/Water.coskf"
  frac1 0.275
  frac2 1.0
End
```

Links COSMO-RS GUI tutorial: partition coefficients (log P) [1, 2], Octanol-Water partition coefficients (log P_{OW}) [1]

4.7.5 Activity coefficients solvent and solute

The mole fraction of each compound of the solvent should be given with the subkey FRAC1 of the key COMPOUND for each compound. The compounds that are included without a given mole fraction are considered to be infinite diluted solutes. The activity coefficients are calculated for all compounds.

```
PROPERTY activitycoef
{DENSITYSOLVENT densitysolvent}
End
```

densitysolvent If the subkey DENSITYSOLVENT is included the densitysolvent will be used for the density of the solvent (kg/L) instead of calculated values. Relevant for the calculation of the Henry's law constant.

The input pure compound vapor pressure will be used in the calculation of the partial vapor pressure of this compound in the mixture if it is supplied with the key COMPOUND for this compound. If it is not specified then it will be approximated using the COSMO-RS method. Relevant for the calculation of the Henry's law constant.

The Henry's law constants are calculated in 2 units. The Henry's law constant k_H is the ratio between the liquid phase concentration of a compound and its partial vapor pressure in the gas phase. The dimensionless Henry's law constant $k_H{}^{cc}$ is the ratio between the liquid phase concentration of a compound and its gas phase concentration.

Also calculated is $\Delta G_{solv}^{liq-solv}$, which is the solvation Gibbs free energy from the pure compound liquid phase to the solvated phase, and $\Delta G_{solv}^{gas-solv}$, which is the solvation Gibbs free energy from the pure compound gas phase to the solvated phase, with a reference state of 1 mol/L in both phases. In addition a Gibbs free energy is calculated which is the free energy of the solvated compound with respect to the gas phase energy of the spin restricted spherical averaged neutral atoms, the compound consist of. Note that zero-point vibrational energies are not taken into account in the calculation of this free energy. This energy could be used in the calculation of pK_a values.

Links COSMO-RS GUI tutorial: activity coefficients [1, 2], solvation free energies [1], Henry's law constants [1], pK_a values [1]

4.7.6 Solubility

The solubility of solutes in 1 mixture can be calculated with:

```
PROPERTY solubility
End
```

The mole fraction of each compound of the solvent should be given with the subkey FRAC1 of the key COMPOUND for each compound, and should add up to 1.0. The solutes should have zero molar fraction in the solvent. The solubility of 1 solute in pure solvents can be calculated with

```
PROPERTY puresolubility
End
```

The mole fraction of each pure solvent should be 1.0, and should be set the subkey FRAC1 of the key COMPOUND for each compound. The solute should have zero molar fraction in the solvent. It is possible to calculate the solubility of a solute at a temperature range, see key TEMPERATURE.

For solubility calculations of a solid compound one should add the pure compound melting point T_m , pure compound enthalpy of fusion ΔH_{fus} , and optionally the pure compound heat capacity of fusion ΔC_p using the subkeys meltingpoint, hfusion, and cpfusion, respectively, of the key COMPOUND for this compound. The COSMO-RS method does not predict these ΔH_{fus}, ΔC_p, or T_m .

The assumption made in the solubility calculation may be invalid in case of a solubility of a liquid in a solvent, especially if the solubility of the solvent in the liquid is high. For binary systems one may check this by calculating the miscibility gap in the binary mixture of the two liquids. It is possible to calculate the solubility of a gas in a solvent, if one adds the subkey isobar and adds the partial vapor pressure partialvaporpressure (bar) of the gas as argument for the key PRESSURE:

```
PROPERTY solubility
  isobar
End

PRESSURE partialvaporpressure
```

The solubility of a gas in a solvent can also be calculated using Henry's law, which is valid for ideal dilute solutions, see see the key PROPERTY activitycoef. The COSMO-RS calculation of the solubility of a compound is performed with an iterative method, since the activity coefficient of the compound depends on the molar fraction of this compound.

Links COSMO-RS GUI tutorial: solubility [1, 2]

4.7.7 Binary mixture (VLE/LLE)

The COSMO-RS module can automatically calculate properties of a binary mixture, by calculating these properties for a number of different compositions.

Exactly two compounds should be given in the input file.

```
PROPERTY binmixcoef
{Nfrac nfrac}
{isotherm | isobar | flashpoint}
End
```

nfrac Number of different mixtures for which the binary mixture is calculated will be nfrac+5. Default value for nfrac is 10, which means 15 different mixtures.

isotherm | isobar |flashpoint If the subkey isotherm is included (default) the binary mixture will be calculated at a fixed temperature. If the subkey isobar is included the binary mixture will be calculated at a fixed vapor pressure. If the subkey flashpoint is included the flash point of the binary mixture will be calculated.

The input pure compound vapor pressure will be used in the calculation of the partial vapor pressure of this compound in the mixture if it is supplied with the key COMPOUND for this compound. If it is not specified then it will be approximated using the COSMO-RS method.

In case of a miscibility gap (LLE) data of the 2 immiscible liquid phases will be calculated. Also information about possible azeotropes will be calculated. With the COSMO-RS GUI, activity coefficients, (partial) vapor pressures, and excess energies can be viewed.

Links COSMO-RS GUI tutorial: vapor-liquid diagram binary mixture (VLE/LLE) [1, 2]

4.7.8 Ternary mixture (VLE/LLE)

The COSMO-RS module can automatically calculate properties of a ternary mixture, by calculating these properties for a number of different compositions. Exactly three compounds should be given in the input file.

```
PROPERTY ternarymix
  {Nfrac nfrac}
  {isotherm | isobar |flashpoint}
End
```

nfrac Number of different mixtures for which the ternary mixture is calculated will be (nfrac+1)*(nfrac+2)/2. Default value for nfrac is 10, which means 55 different mixtures.

isotherm | isobar | flashpoint If the subkey isotherm is included (default) the ternary mixture will be calculated at a fixed temperature. If the subkey isobar is included the ternary mixture will be calculated at a fixed vapor pressure. If the subkey flashpoint is included the flash point of the ternary mixture will be calculated.

The input pure compound vapor pressure will be used in the calculation of the partial vapor pressure of this compound in the mixture if it is supplied with the key COMPOUND for this compound. If it is not specified then it will be approximated using the COSMO-RS method.

In case of a miscibility gap liquid-liquid equilibrium (LLE) data such as tie lines and an approximate phase diagram, are calculated. With the COSMO-RS GUI, activity coefficients, (partial) vapor pressures, and excess energies can be viewed as a colormap in a 2-dimensional plot with 2 of the liquid compositions on the axes.

Links COSMO-RS GUI tutorial: ternary mixtures (VLE/LLE) [1]

4.7.9 Solvents s1 - s2 Composition Line

The COSMO-RS module can linear interpolate between the compositions of solvent 1 and solvent 2, which both could be mixtures, and calculate properties, like activity coefficients, and excess energies. This property calculation does not calculate a possible miscibility gap. The mole fraction of each compound of the solvent 1 and solvent 2 should be given with the subkey FRAC1 and subkey FRAC2 of the key COMPOUND for each compound, respectively.

```
PROPERTY compositionline
  {Nfrac nfrac}
  {isotherm | isobar | flashpoint}
End
```

nfrac Number of different mixtures of the 2 solvents is calculated will be (nfrac+1). Default value for nfrac is 10, which means 11 different mixtures.

isotherm | isobar | flashpoint If the subkey isotherm is included (default) a fixed temperature will be used. If the subkey isobar is included a fixed vapor pressure will be used. If the subkey flashpoint is included the flashpoint will be calculated.

Links COSMO-RS GUI tutorial: A composition line between solvents s1 and s2 [1]

4.8 Analysis

4.8.1 Sigma profile

The sigma profile of a mixture can be calculated with:

```
PROPERTY sigmaprofile
{Nprofile nprofile}
{SigmaMax sigmamax}
End
```

In case of a mixture the mole fraction of each compound in the mixture should be given with the subkey FRAC1 of the key COMPOUND for this compound.

The sigma profile pure compounds can be calculated with:

```
PROPERTY puresigmaprofile
{Nprofile nprofile}
{SigmaMax sigmamax}
End
```

nprofile Number of data points for which to calculate the sigma profile. default value 50.

sigmamax The sigma profile is calculated between -sigmamax and sigmamax. Default value 0.025.

The hydrogen bonding part (HB) of the sigma profile(s) will also be calculated. In case of a COSMO-SAC 2013-ADF calculation also the OH component of hydrogen bonding (HB-OH) is calculated, and the other type component of hydrogen bonding (HB-OT) is calculated.

Links COSMO-RS GUI tutorial: sigma profile [1]

4.8.2 Sigma potential

The sigma potential of a mixture can be calculated with:

```
PROPERTY sigmapotential
{Nprofile nprofile}
{SigmaMax sigmamax}
End
```

In case of a mixture the mole fraction of each compound in the mixture should be given with the subkey FRAC1 of the key COMPOUND for this compound.

The sigma profile pure compounds can be calculated with:

```
PROPERTY puresigmapotential
{Nprofile nprofile}
{SigmaMax sigmamax}
End
```

nprofile Number of data points for which to calculate the sigma potential. default value 50.

sigmamax The sigma potential is calculated between -sigmamax and sigmamax. Default value 0.025.

Links COSMO-RS GUI tutorial: sigma potential [1]

4.9 Other inputs

4.9.1 Pitzer-Debye-Hückel long-range electrostatic correction

```
PDH_CORRECTION Yes/No
```

PDH_CORRECTION

Type Bool

Default value No

Description Logical to use Pitzer Debye-Hueckel electrostatic correction

4.9.2 Elbro Combinatorial term for polymers

```
USEPOLYCOMBIFORPOLYMER Yes/No
```

USEPOLYCOMBIFORPOLYMER

Type Bool

Default value Yes

Description Logical to use polymer-specific combinatorial term

CHAPTER

FIVE

POLYMERS WITH COSMO-RS(-SAC)

Many types of polymers can be described with COSMO-RS theory. However, the typical procedure for calculating σ-profiles (a geometry optimization with ADF, a single point COSMO calculation, processing the surface points to make a σ-profile) is far too expensive for generating the σ-profiles of polymers. Instead, the σ-profile of a polymer can be represented as the σ-profile of a monomer scaled to the size of the polymer. This means that given a σ-profile of an "average monomer," we can generate a σ-profile for the polymer by multiplying the monomer σ-profile by a factor equal to the number of repeat units in the polymer. This procedure, though not without some shortcomings, makes the treatment of polymers with COSMO-RS computationally tractable.

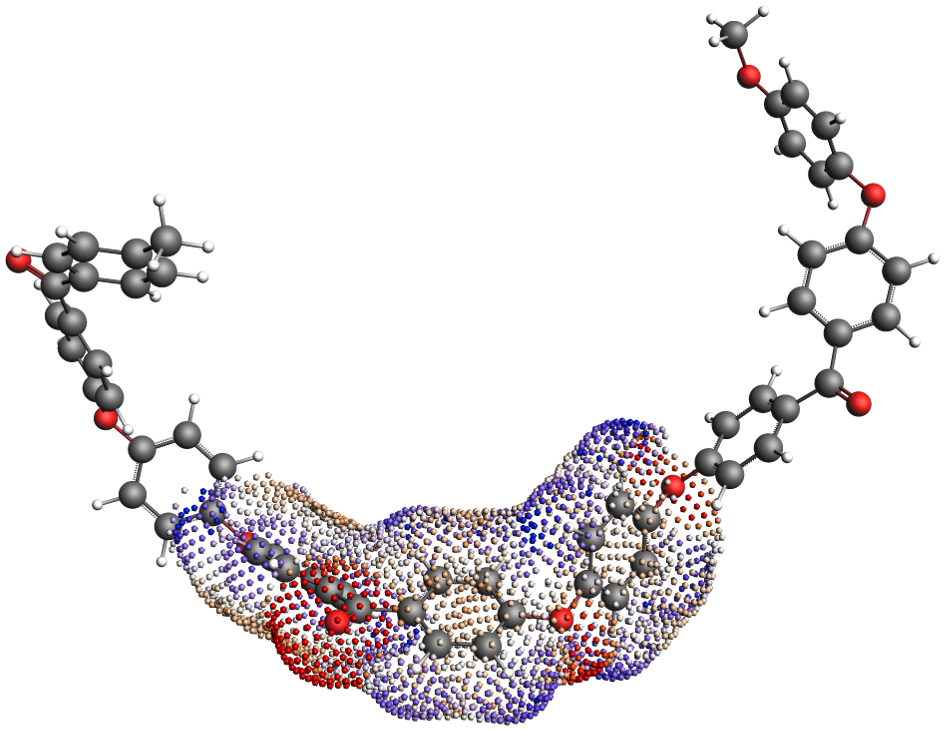

Fig. 5.1: COSMO surface of the Polyether ether ketone (PEEK) monomer within a trimer. The "average monomer" σ-profile is calculated from the central monomer unit of the trimer.

There are many possible approaches to generating the σ-profile for an "average monomer." The approach used to generate the monomers in the 2019 ADFCRS-Polymer Database is the following:

(1) Construct a trimer from 3 units of the monomer

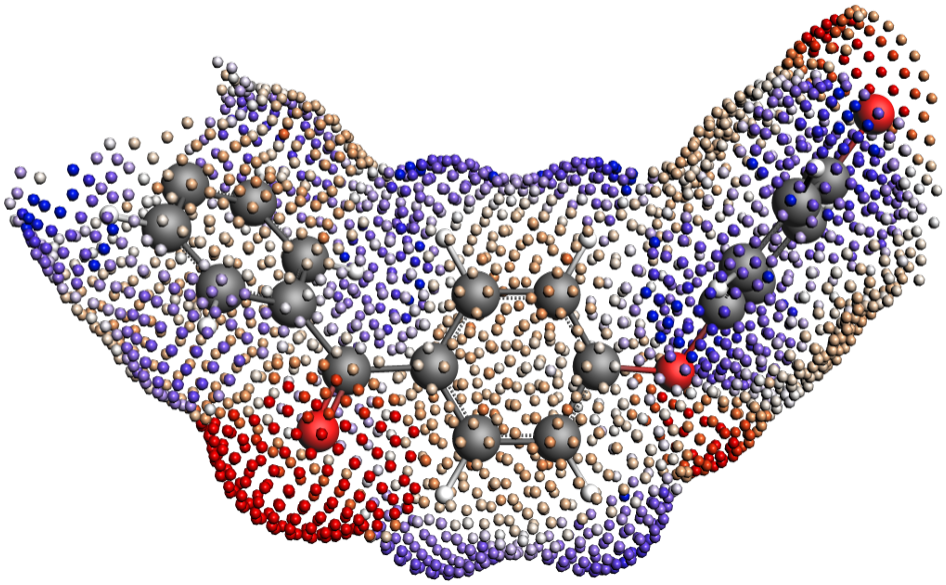

Fig. 5.2: COSMO surface of the isolated Polyether ether ketone (PEEK) monomer.

(2) Cap the ends of the outer two monomers with methyl groups
(3) Optimize the geometry of the trimer with ADF
(4) Do a single point COSMO calculation
(5) Generate the σ-profile for *only the central unit* of the trimer

This method provides the σ-profile of a monomer surrounded by two copies of itself on either side. Though perhaps longer polymer chains could be considered in the determination of the "average monomer," the trimer representation was found to be sufficiently accurate for calculating various thermodynamic properties while not being exorbitantly expensive in the ADF step. In cases where this monomer representation fails to capture the behavior of the polymer, the following alternative procedures are possible:

- Generating a structure from a longer polymer chain and taking the "average monomer" σ-profile as an average of the σ-profiles of all of the interior monomers
- Sampling the conformational space of the polymer and using different structures for different problems (e.g., a polymer with a possible intramolecular H-bond may exhibit this internal H-bonding in a neutral solvent but not in a more polar one)

5.1 Additional properties/units for polymer systems

5.1.1 Average molecular weight

As mentioned above, polymers in COSMO-RS are calculated using a scaled version of a monomer's σ-profile. However, because polymers come in many different lengths, we must be able to adjust the length of the polymer and accordingly adjust the scaling of the monomer σ-profile. This is done with an average molecular weight parameter, which represents

the Number Average Molecular Weight M^N, defined as the following:

$$M^N = \frac{\sum_j n_j w_j}{\sum_j n_j}$$

where *j* is in index over all different molecules (different-length polymers are different molecules) in solution, w_j is the weight of each molecule, and n_j is the number of molecules of type *j* in solution. Because this parameter is adjustable, the same monomer σ-profile can be used for calculations with polymers of different lengths. Note that a default value of 10000 g/mol is used if no input is given.

5.1.2 Mole fractions of the monomers and polymers

Because a typical polymer consists of many polymer chains of different lengths, the mole fraction of the polymer is well-defined. In the COSMO-RS program, there are two mole fractions defined:

x(monomer)

x(monomer) is simply the mole fraction of a monomer in the solution, treating all polymeric species as a number of monomers equal to the length of the polymer chain. For non-polymeric components, x(monomer) is the mole fraction in relation to a solution of monomers.

x(polymer)

x(polymer) defines a mol of each polymer chain using the average molecular weight parameter to determine the average chain length. Specifically, we can define a term R_i as the number of repeat units in the average polymer of species *i*. For non-polymeric components, $R_i = 1$. R_i is shown below:

$$R_i = \frac{M_i^N}{M(monomer)_i}$$

where $M(monomer)_i$ refers to the molar mass of the monomer. Using this R_i, we can define $x(polymer)_i$:

$$x(polymer)_i = \frac{x(monomer)_i / R_i}{\sum_j x(monomer)_j / R_j}$$

where now *j* is an index over all distinct components. All polymers of the same type are assumed to be of length R_i.

5.1.3 Weight- and volume-fraction activity coefficients

As a further consequence of the ill-defined mole fraction for polymer solutions, activity coefficients are often reported in the literature in terms of weight- or volume-fraction. These are also reported for calculations in the COSMO-RS program in which at least one species is a polymer. They are defined from the activity of each species:

$$a_i = \gamma_i x(polymer)_i$$

where γ_i is the activity coefficient in relation to the polymer mole fractions. Note: this is the default value for γ_i in polymer calculations. The weight-fraction activity coefficient (Ω_i) can then be calculated as:

$$\Omega_i = \frac{a_i}{w_i}$$

where w_i is the weight fraction of component *i*. Finally, the volume fraction activity coefficient (γ_i^ϕ) can be defined as follows:

$$\gamma_i^\phi = \frac{a_i}{\phi_i}$$

where ϕ_i is the volume fraction of component *i*.

5.1.4 Flory-Huggins parameter

The Flory-Huggins model is used extensively for binary polymer/solvent and polymer/polymer mixtures. In the Flory-Huggins model, the χ parameter is the single system-specific parameter and is intended to quantify the enthalpic interactions between system components. Users of the Flory-Huggins model can deduce important system behavior (phase stability, solubility, etc.) from the value of the χ parameter.

The χ parameter was originally intended to be composition-and temperature- independent, although it is now known to vary significantly across compositions and temperatures for many systems. Fortunately, system changes related to composition and temperature are captured in the COSMO-RS program and are reflected in the calculation of the Flory-Huggins χ parameter. This is due to the calculation of the χ parameter from the free energy of mixing of two species:

$$\frac{G_{mix}}{RTV} = \frac{\phi_1}{v_1} ln(\phi_1) + \frac{\phi_2}{v_2} ln(\phi_2) + \frac{\phi_1 \phi_2 \chi_{12}}{v_r}$$

where G_{mix} is the free energy of mixing, *R* is the gas constant, *T* is the absolute temperature, *V* is the system volume, ϕ_i is the volume fraction of component *i*, v_i is the molar volume of species *i*, and v_r is a reference volume. Note that the difference in v_1 and v_2 can be significant in the case of a polymer/solvent mixture. Since G_{mix} does vary with composition and temperature, the χ parameter will also exhibit this variance.

Important: Reference volumes (v_r) used in calculating the Flory-Huggins parameter

- polymer/solvent systems: v_r is equal to the molar volume of the solvent
- polymer/polymer systems: v_r is set to a value of $0.6022140857\ L/mol$, which corresponds to a site size of $1\ nm^3$

The COSMO-RS program can calculate thermodynamic properties for multi-component systems, including polymer-containing systems. However, the Flory-Huggins χ parameter is traditionally defined for binary mixtures (although some extensions to multi-component mixtures exist). In the case of multi-component mixtures containing polymers, we calculate a χ parameter for each species. This is summarized in the following:

Note: Calculating the Flory-Huggins parameter for systems with more than 2 components

For systems with more than 2 components, a χ parameter is defined for each component. This χ_i parameter is calculated as the χ parameter for a species *i* as if all the other species in solution were combined into one component. This means that for a ternary mixture of solvent/polymer A/polymer B, the χ parameter of the solvent would correspond to the χ parameter of the system defined by the solvent and the *co-polymer* of A and B. Similarly, the χ parameter of polymer A would correspond to the χ parameter of the binary system of polymer A and the meta-solvent of a combination of polymer B and the solvent.

5.2 Modified combinatorial term

The entropy of polymer solutions cannot be calculated in the same way as the entropy of small molecule solutions. For this reason, the normal combinatorial term in COSMO-RS is replaced with a polymer-specific combinatorial term. Specifically, the combinatorial term used is that of Elbro (1990)[1], which has previously been applied successfully in the context of COSMO-RS[2]. The Elbro combinatorial requires the free volume fraction (ϕ_i^{fv}) of each component:

$$\phi_i^{fv} = \frac{x_i(v_i - v_i^*)}{\sum_j x_j(v_j - v_j^*)}$$

[1] H.S. Elbro, A. Fredenslund, and P. Rasmussen, *A new simple equation for the prediction of solvent activities in polymer solutions*, Macromolecules 23, 4707 (1990) (https://doi.org/10.1039/c7cp02317k)

[2] C. Loschen and A. Klamt, *Prediction of solubilities and partition coefficients in polymers using COSMO-RS*, Industrial & Engineering Chemistry Research 53, 11478 (2014) (https://doi.org/10.1021/ie501669z)

where x_i is the (polymer) mole fraction of compound *i*, v_i is the molar volume of compound *i*, v_i^* is the molar hard-core volume of compound *i*, and *j* is also an index over the compounds. Using the values of ϕ_i^{fv} for each component, the combinatorial contribution to the activity coefficient can be defined as follows:

$$ln(\gamma_i^{fv}) = ln\left(\frac{\phi_i^{fv}}{x_i}\right) + 1 - \frac{\phi_i^{fv}}{x_i}$$

Finally, this combinatorial term is used to calculate the final activity coefficient:

$$ln(\gamma_i) = ln(\gamma_i^{crs}) + ln(\gamma_i^{fv})$$

where γ_i^{crs} is the activity coefficient calculated with COSMO-RS without any combinatorial corrections.

5.3 General application guidelines/warnings

At present, the quality of the predictions of the COSMO-RS program is *unreliable* or *untested* for the following types of systems:

- **Cross-linked polymers.** The structures of cross-linked polymers are not perfectly compatible with the assumptions in the COSMO-RS model for polymers. These types of systems are not recommended to be used with COSMO-RS.
- **Polymers with significant swelling behavior.** Polymer swelling is not easily captured with COSMO-RS. It is likely that some of the error due to swelling can be offset by using correct molar volume values for the polymers in different solvents/at different temperatures.

5.4 Downloading the ADFCRS-POLYMER-2019 database

See the *section on the ADFCRS-POLYMER-2019 database* (page 22) on how to download this database.

5.5 Tutorial on polymer calculations

There is a tutorial on COSMO-RS calculations with polymers that demonstrates basic the basic functionality of the COSMO-RS GUI with polymers. This will cover calculations using the polymer database as well as *inputting your own polymer structures.*

CHAPTER

SIX

PITZER-DEBYE-HÜCKEL LONG-RANGE ELECTROSTATIC CORRECTION

Systems with charged species often demonstrate behavior that is not easily captured with standard thermodynamic models meant for neutral molecules. A major reason for this that the chemical potential requires an additional contribution due to the electrostatic potential. The electrostatic potential decays with r^{-1}, where r is the distance between two charges. This inverse dependence on r makes the electrostatic potential a long-range term, especially as compared to other intermolecular energetic contributions, which are typically only relevant at short distances. One successful model for adding necessary electrostatic corrections for systems with charged species is the Pitzer-Debye-Hückel (PDH)[1] model. In the COSMO-RS package, we use a modification of the PDH term that allows for mixed solvents.

6.1 Mixing rules and required property inputs for the PDH term

In the original publication, the PDH model is used only for pure solvents. To generalize to mixed solvent systems, we have included mixing rules to estimate required parameters for the PDH model. These are discussed below in addition to required parameters.

6.1.1 Molecular weight

No additional input is needed for this property as this is directly determined by the atomic composition of a molecule. The average molecular weight for the entire system, M, is given as a function of all the individual molecular weights m_i :

$$M = \frac{\sum_i n_i m_i}{\sum_i n_i}$$

where n_i is the number of moles of species i.

6.1.2 Density

The density of each compound is also required for the calculation of the PDH term. For ionic species, one may simply use the density of the combined salt. The average density for the entire system, D, is given as a function of all the individual densities d_i :

$$D = \frac{\sum_i n_i}{\sum_i \frac{n_i}{d_i}}$$

[1] Pitzer, Kenneth S., and John M. Simonson. *Thermodynamics of multicomponent, miscible, ionic systems: theory and equations.* The Journal of Physical Chemistry 90 (1986): 3005-3009. (https://doi.org/10.1021/j100404a042)

6.1.3 Dielectric constant

Additionally, the dielectric constant of each compound is required for the PDH term. These terms do not need to be experimentally accurate numbers, but should be approximate. The dielectric constant of a combined salt can be used for the individual ionic species. The average dielectric constant for the entire system, $\mathcal{E}$, is given as a function of all the individual dielectric constants ϵ_i :

$$\mathcal{E} = \frac{\sum_i n_i \frac{m_i \epsilon_i}{d_i}}{\sum_i n_i \frac{m_i}{d_i}}$$

6.2 Derivation of the PDH term for general mixtures

In[?] , the Debye-Hückel model is adapted to account for higher concentrations of ions (the Debye-Hückel model works well for low concentrations). The authors choose from a variety of possible models, ultimately deciding on one that is deemed most accurate empirically. The expression for the PDH excess energy (long range electrostatic correction) is given below.

$$\frac{G^{PDH}}{RT} = -4 \left(\frac{1000}{M} \right)^{1/2} \frac{N A_x I_x}{\rho} \ln(1 + \rho I_x^{1/2})$$

where I_x is the ionic strength of the system, which is a function of the charge z_i of each species:

$$I_x = \frac{1}{2} \frac{\sum_i n_i z_i^2}{\sum_i n_i}$$

and A_x is the Debye-Hückel parameter, defined as:

$$A_x = \frac{1}{3} \frac{(2\pi N_A D e^6)^{1/2}}{(4\pi\epsilon_0 \mathcal{E} k T)^{3/2}}$$

where e is the charge of the electron, N_A is Avogadro's number, k is the Boltzmann constant, and ϵ_0 is the permittivity of free space.

Finally, ρ is the closest approach parameter. The specifics of this parameter are still under development, and for now the following simple formula from[?] is used.

$$\rho = 2150 \left(\frac{D}{\mathcal{E} T} \right)^{1/2}$$

Finally, we can calculate the PDH contribution to the activity coefficient as follows:

$$\begin{aligned}
\ln(\gamma_i^{PDH}) =& \frac{\delta}{\delta n_i} \left(\frac{G^{PDH}}{RT} \right)_{T,P} \\
=& -4 \left(\frac{1000}{M} \right)^{1/2} \frac{A_x I_x}{\rho} \Bigg[\ln(1 + \rho I_x^{1/2}) \left(\frac{M - m_i}{2M} + \frac{z_i^2}{2I} \right. \\
&+ \frac{1}{2} \left(1 - \frac{D}{d_i} \right) + \frac{3N}{2} \frac{m_i}{d_i \sum_j n_j \frac{m_j}{d_j}} \left(1 - \frac{\epsilon_i}{\mathcal{E}} \right) - \frac{N}{\rho} \frac{\delta \rho}{\delta n_i} \Bigg) \\
&+ \frac{1}{1 + \rho I_x^{1/2}} \left(\frac{\rho I_x^{1/2}}{2N} \left(\frac{z_i^2}{2I} - 1 \right) + I_x^{1/2} \frac{\delta \rho}{\delta n_i} \right) \Bigg]
\end{aligned}$$

Note that in the above, the analytical form of the term $\frac{\delta \rho}{\delta n_i}$ is not used to simplify the expression.

6.3 Tutorial on using the PDH correction

There is a tutorial on using the PDH correction that demonstrates the use of this correction with the GUI.

References

CHAPTER

SEVEN

THE UNIFAC PROGRAM

Using the UNIFAC program from the command line is documented in the following:

7.1 Compound Input

7.1.1 Basic Input

In the UNIFAC program, compounds are expected to be input as SMILES strings, and their ratios are expected as mole fractions. A summary of basic compound input is given below:

Flag	Purpose	Example
-h	Produces help message	$AMSBIN/unifac –help
-smiles	Input molecule as SMILES sting	$AMSBIN/unifac -smiles <SMILES1> <SMILES2> …
-frac	Input the mole fractions	$AMSBIN/unifac -frac <mol fraction 1> <mol fraction 2> …
-solute	Specify a molecule as a solute	$AMSBIN/unifac -smiles CCC -solute -smiles …
-o	Write output to file	$AMSBIN/unifac -o <output file> …

Note that the -smiles and -frac flags are only specified one time and all information (SMILES strings and mole fractions) comes after these flags. It is assumed that the order of the mole fractions after the -frac corresponds to the order of the SMILES strings after the -smiles flag. A simple example demonstrating an activity coefficient calculation for a mixture of three compounds is given below:

```
$AMSBIN/unifac -smiles CCCCCC CCCO CCCCBr -solute -frac 0.2 0.3 0.5 -t ACTIVITYCOEF
```

The -solute flag is used to specify which compounds should be treated as solutes for the PURESOLUBILITY template. See the PURESOLUBILITY section for more information.

7.1.2 Physical Property Input

A number of problem templates require physical property information to be input. Physical property information should be input directly after a compound's SMILES representation. A list of the physical property flags and examples of usage are given below:

Flag	Purpose	Example
-pvap	Vapor pressure (bar)	$AMSBIN/unifac -smiles <SMILES> -pvap 0.43 …
-tvap	Temperature (K) corresponding to pvap	$AMSBIN/unifac -smiles <SMILES> -tvap 320.1 …
-antoine	Antoine coefficients for compound	$AMSBIN/unifac -smiles <SMILES> -antoine 7.23 1504.2 246.87 …
-hfusion	Enthalpy of fusion in kJ/mol	$AMSBIN/unifac -smiles <SMILES> -hfusion 6.4
-meltingpoint	Melting point of compound (K)	$AMSBIN/unifac -smiles <SMILES> -meltingpoint 421.12

Below is an example (with synthetic antoine parameters) demonstrating the command line input for a binary mixture calculation (BINMIXCOEF) using vapor pressure estimated from the antoine parameters.

```
$AMSBIN/unifac -smiles "CCCCOCC" -antoine 5 1500 30 \
"CCCCCC" -antoine 6 1234 10 -t BINMIXCOEF
```

Additionally, we present an example for calculating the solubility of DDT in ethanol. Since DDT is a solid at room temperature, this requires us to input Enthalpy of Fusion and Melting Point data.

```
$AMSBIN/unifac -smiles \
"C1=CC(=CC=C1C(C2=CC=C(C=C2)Cl)C(Cl)(Cl)Cl)Cl" -hfusion 26.28 -meltingpoint 383 \
"CCO" -frac 0.0 1.0 -t SOLUBILITY
```

7.2 Program Input

7.2.1 List of possible input flags

The UNIFAC program accepts a few additional flags to specify system conditions, choose a template for the calculation, or set the number of points taken over a provided range (e.g., a temperature range). A summary of these input options is provided below. In the following section, examples are given for each flag.

Flag	Meaning
-t	One of a number of template strings to indicate the problem type
-temperature	One/two values (K) to specify the system temperature/temperature range
-steps	the number of steps taken if a range is specified or for a BINMIXCOEF or TERNARYMIX calculation
-preset	an integer to indicate which solvent system is chosen for logP calculations

7.2.2 Examples of general program flags

In this section, we provide a brief example of each of the above flags.

-t

The -t flag has been shown in previous examples and will be described in more detail in the following section. The -t flag must be followed by one of the following template names:

```
LOGP
ACTIVITYCOEF
PURESOLUBILITY
SOLUBILITY
VAPORPRESSURE
PUREVAPORPRESSURE
BINMIXCOEF
TERNARYMIX
```

A brief example of this for the ACTIVITYCOEF template is given below:

```
$AMSBIN/unifac -smiles "CCCCO" "CCCOCCC" -frac 0.5 0.5 -t SOLUBILITY
```

-temperature

In this example, we take the previous DDT solubility calculation and perform the calculation at a temperature of 310 K. This is shown below:

```
$AMSBIN/unifac -smiles \
"C1=CC(=CC=C1C(C2=CC=C(C=C2)Cl)C(Cl)(Cl)Cl)Cl" -hfusion 26.28 -meltingpoint 383 \
"CCO" -frac 0.0 1.0 -temperature 310 -t SOLUBILITY
```

If we want to calculate the solubility over a temperature range (say, 310-350 K), we need to specify the temperature flag twice and also include a number of steps to take between the two temperatures with the -steps flag. This looks like the following:

```
$AMSBIN/unifac -smiles \
"C1=CC(=CC=C1C(C2=CC=C(C=C2)Cl)C(Cl)(Cl)Cl)Cl" -hfusion 26.28 -meltingpoint 383 \
"CCO" -frac 0.0 1.0 -temperature 310 -temperature 350 -steps 10 -t SOLUBILITY
```

-steps

The -steps flag specifies a number of steps to take between a temperature range or the number of steps to take along each mole fraction axis for a BINMIXCOEF or a TERNARYMIX calculation. For an input value of N for the -steps flag, the BINMIXCOEF and TERNARYMIX templates consider the following number of distinct mole fraction combinations:

Template	Number of distinct systems considered
BINMIXCOEF	N+5
TERNARYMIX	(N+1)(N+2)/2

If we wanted to calculate the thermodynamic properties of a binary mixture with a very small step size, we could input a N value of 1000 to take 1005 samples of the mole fraction space:

```
$AMSBIN/unifac -smiles \
"CCCCOCC" -antoine 5 1500 30 \
"CCCCCC" -antoine 6 1234 10 \
-t BINMIXCOEF -steps 1000
```

-preset

The preset flag is used for a logP calculation. A preset of 2 (default) indicates that that we do a logP calculation on the traditional Octanol/Water system. This looks like the following:

```
$AMSBIN/unifac -smiles "CCCCOCC" -t LOGP -preset 2
```

More information on the preset flag options for the LOGP template will be given in the templates section.

7.3 Templates

The -t flag indicates which of several problem types, or templates, should be used. Different templates expect different input options and produce different results. A summary of the different templates is given below.

7.3.1 ACTIVITYCOEF

Number of compounds required	>= 2
Mole fraction values (-frac) required	Yes
-solute flag used	No
-antoine or pvap/tvap required	No
-hfusion/-meltingpoint required	No

The activity coefficient template calculates activity coefficients from a set of mole fraction values. In the following example, we calculate the activity coefficients of the water/propanol system over a temperature range of 230-298.15 K.

```
$AMSBIN/unifac -smiles "O" "CCCO" -frac 0.2 0.8 \
-t ACTIVITYCOEF -temperature 230 -temperature 298.15 -steps 20
```

7.3.2 LOGP

Number of compounds required	>= 1
Mole fraction values (-frac) required	No
-solute flag used	No
-antoine or pvap/tvap required	No
-hfusion/-meltingpoint required	No

The logP template calculate the partition coefficient (P) of input structures between a variety of common liquid/liquid systems. The specific set of liquids can be chosen with the -preset flag. A summary of the -preset options is given below:

-preset value	Liquid phases
2	Octanol/Water
3	Benzene/Water
4	Diethyl ether/Water
5	Hexane/Water

In the following example, we calculate the logP of Sertraline in the Octanol/Water system.

```
$AMSBIN/unifac -smiles "CNC1CCC(C2=CC=CC=C12)C3=CC(=C(C=C3)Cl)Cl" -t LOGP -preset 2
```

7.3.3 PURESOLUBILITY

Number of compounds required	>= 2
Mole fraction values (-frac) required	No
-solute flag used	Yes
-antoine or pvap/tvap required	No
-hfusion/-meltingpoint required	if solute is a solid

The pure solubility template calculates the solubility of a solute (designated by the -solute flag) in a variety of pure solutes. More specifically, the solute's solubility is calculated in every one of the other input molecules.

In the following example we calculate the solubility of Undecanedioic acid (a solid at 298.15 K) in n-Hexane, Benzene, Water, and Ethanol.

```
$AMSBIN/unifac -smiles \
"C(CCCCC(=O)O)CCCCC(=O)O" -hfusion 39.65 -meltingpoint 385 -solute \
"CCCCCC" "c1ccccc1" "O" "CCO" -t PURESOLUBILITY
```

7.3.4 SOLUBILITY

Number of compounds required	>= 2
Mole fraction values (-frac) required	Yes
-solute flag used	No
-antoine or pvap/tvap required	No
-hfusion/-meltingpoint required	if solute is a solid

The solubility template calculates the solubility of every input molecule in the system defined by the remaining molecules. For example, assume we input a system with molecules A, B, and C with mole fractions 0.2, 0.6, and 0.2. The solubility of molecule A is then calculated in a mixture of B/C where the mole fraction ratio is fixed to 3/1 (from the 0.6/0.2 in the input). The solubility of A may very well be 0.6, but this would mean the remaining mole fractions would be 0.3/0.1 (B/C). The same calculation is then also done for B and C.

In the following example we calculate the solubilities of Benzene, n-Hexane, 1-Hexanol, and Acetic acid. Note that the mole fraction of Benzene is set to 0.0. This means that Benzene's solubility will still be calculated, but it will not be part of the solvent system when the other molecules' solubilities are being calculated.

```
$AMSBIN/unifac \
-smiles "c1ccccc1" "CCCCCC" "CCCCCCO" "CC(=O)O" \
-frac 0.0 0.2 0.3 0.5 -t SOLUBILITY
```

7.3.5 PUREVAPORPRESSURE

Number of compounds required	>= 1
Mole fraction values (-frac) required	No
-solute flag used	No
-antoine or pvap/tvap required	Yes
-hfusion/-meltingpoint required	No

The pure vapor pressure template simply calculates the vapor pressure of a pure component. Because this requires the antoine parameters as input, this template simply evaluates the antoine equation, possibly over a temperature range.

The following example calculates the pure vapor pressure (again using synthetic antoine coefficients) for two molecules over a temperature range:

```
$AMSBIN/unifac \
-smiles "c1ccccc1" -antoine 4 1245 123 \
"CCCCC" -antoine 5 1241 242 \
-t PUREVAPORPRESSURE -temperature 320 -temperature 350 -steps 10
```

7.3.6 VAPORPRESSURE

Number of compounds required	>= 1
Mole fraction values (-frac) required	Yes
-solute flag used	No
-antoine or pvap/tvap required	Yes
-hfusion/-meltingpoint required	No

The vapor pressure template calculates the vapor pressure of a mixture (or a pure component if only one compound is entered). This again requires the antoine parameters for each compound as input.

We repeat the previous example, now calculating the vapor pressure of the 0.2/0.8 mole fraction mixture.

```
$AMSBIN/unifac \
-smiles "c1ccccc1" -antoine 4 1245 123 \
"CCCCC" -antoine 5 1241 242 \
-frac 0.2 0.8 \
-t VAPORPRESSURE -temperature 320 -temperature 350 -steps 10
```

7.3.7 BINMIXCOEF

Number of compounds required	2
Mole fraction values (-frac) required	No
-solute flag used	No
-antoine or pvap/tvap required	Yes
-hfusion/-meltingpoint required	No

The binary mixture template takes exactly 2 compounds as input. Unlike other templates where thermodynamic properties are calculated over a range of temperatures, the binary mixture template calculates properties over a range of mole fractions. In other words, it takes a number of samples of the mole fraction space. If no antoine coefficients are given, then no gas phase thermodynamic properties are reported.

In this example we calculate binary mixture properties for the Water/Ethanol system (again with synthetic antoine parameters).

```
$AMSBIN/unifac -smiles "O" -antoine 4 1245 123 "CCO" \
-antoine 5 1241 242 -t BINMIXCOEF -steps 10
```

7.3.8 TERNARYMIX

Number of compounds required	3
Mole fraction values (-frac) required	No
-solute flag used	No
-antoine or pvap/tvap required	Yes
-hfusion/-meltingpoint required	No

The ternary mixture template takes exactly 3 molecules as input and performs similar calculations to those done in the binary mixture template. Note that tie lines are not calculated like they are in the COSMO-RS/-SAC programs.

In this example we add a Acetone to our previous two compounds and change the temperature to 330 K.

```
$AMSBIN/unifac -smiles "O" -antoine 4 1245 123
"CCO" -antoine 5 1241 242 \
"CC(=O)C" -antoine 6 2414 221 \
-t TERNARYMIX -steps 20 -temperature 330
```

CHAPTER

EIGHT

PURE COMPOUND PROPERTY PREDICTION

8.1 Introduction

The Property Prediction program in ADF provides quick, accurate estimates for many important pure component physical properties. At its core, the Property Prediction program maps various QSPR descriptors of an input molecule onto a single numerical value, the property estimate. Many of these property models rely on easy-to-evaluate QSPR descriptors and numerically straightforward computations, meaning that an estimate can be provided for every property in << 1s per molecule. The general expression for the models used in the Property Prediction program is as follows:

$$f(P) = C + g\left(\sum_i c_i n_i\right) + h\left(\sum_i d_i n_i, T\right)$$

where *f* is a function that transforms the property value space, *g* is a function that maps QSPR descriptors onto a numerical value, and *h* is a function which also captures temperature-dependence of certain properties by including temperature, *T*, as an input. Additionally, *C* is a constant, n_i refers to QSPR values of QSPR descriptor *i*, and c_i and d_i are fitted coefficients corresponding to each QSPR descriptor *i*.

The accuracy of the property estimates depends on the nature/complexity of the input molecular structure. For many common organic structures, the property estimates should be reasonably accurate. However, as is always the case with QSPR models, the Property Prediction program will likely lose accuracy for molecules outside its training domain, i.e., for molecules that are very "dissimilar" to compounds which occur in the training set. In general, the program can be used for molecules with the following atom types:

Accepted atom types	Example functional groups which can be used with atom type
H	Alkanes, Alkenes, Alkynes, Aldehydes, Amides, Amines, Aromatics, Carboxylic Acids, Hydroxides, Sulfides, Thiols
C	Acid chlorides, Alkanes, Alkenes, Alkynes, Aldehydes, Amides, Aromatics, Carboxylic Acids, Esters, Ethers, Ketones, C-X (halogens)
N	Amides, Amines, Aromatics, Cyanides, Imines, Nitro groups
O	Acid chlorides, Aldehydes, Amides, Aromatics, Carboxylic Acids, Esters, Ethers, Ketones, Nitro groups
F	-CF, -CF2, -CF3
S	Sulfides, Thiols
Cl	Acid chlorides, -CCl, -CCl2, -CCl3
Br	-CBr
I	-CI

A brief description of molecule types for which this method will not work well is given in the General warnings section. Common molecules for which this method will fail are: (1) those that contain only one non-hydrogen atom, e.g., Methane or Water; (2) those that contain atoms not listed in the table above.

8.2 Available properties

The Property Prediction program can predict the values of various pure component physical properties. These properties can be of interest themselves or can be used in conjunction with other COSMO-RS property calculations (e.g., to calculate the solubility of a solid in a liquid, we must know the enthalpy of fusion and melting point of the solid – both of these properties can be estimated with the Property Prediction program). The available properties and their units are listed below:

Property Name	Units	Additional Information	Typical error
Boiling point	K	at 1 atm	15 K
Critical Pressure	bar		1.5 bar
Critical Temperature	K		30 K
Critical Volume	L/mol		0.02 L/mol
Dielectric Constant			3
Ideal Gas Entropy	J/(mol K)	at 298.15 K and 1 bar	20 J/(mol K)
Flash point	K		15 K
Gibbs Energy Ideal Gas	kJ/mol	at 298.15 K and 1 bar	25 kJ/mol
Enthalpy of Combustion	kJ/mol	at 298.15 K	50 kJ/mol
Std. Enthalpy of Formation	kJ/mol	at 298.15 K and 1 bar	30 kJ/mol
Enthalpy of Fusion	kJ/mol	at Normal Melting Point	4 kJ/mol
Enthalpy of Form. Ideal Gas	kJ/mol	at 298.15 K and 1 bar	25 kJ/mol
Enthalpy of Sublimation	kJ/mol		5 kJ/mol
Melting point	K	at 1 atm	35 K
Liquid Molar volume	L/mol	at 298.15 K	0.005 L/mol
(Liquid Density)	kg/L	at 298.15 K	uses Liquid Molar Volume
Liquid Vapor Pressure	bar		10-30%
Liquid Viscosity (μ)	Pa-s		20-50%
Parachor			7
Solubility Parameter	(cal/cm^3)^1/2	at 298.15 K	0.7
Synthetic accessibility[1]	scored from 1 (easy) to 10 (hard)		
Triple point temperature	K		35 K
Van der Waals Area	$Å^2$		6 $Å^2$
Van der Waals Volume	$Å^3$		3 $Å^3$

[1] P. Ertl and A. Schuffenhauer. *Estimation of synthetic accessibility score of drug-like molecules based on molecular complexity and fragment contributions* Journal of cheminformatics 1 (2009): 1-11. (https://doi.org/10.1186/1758-2946-1-8)

8.3 Running the Property Prediction program

The Property Prediction program can be run from the command line. The following general flags are used by the program:

Flag	Purpose	Example
`-h [--help]`	Produces help message	`$AMSBIN/prop_prediction --help`
`-s [--smiles]`	Input molecule as SMILES sting	`$AMSBIN/prop_prediction --smiles <SMILES> ...`
`-m [--mol]`	Input molecule as .mol file	`$AMSBIN/prop_prediction --mol <mol file> ...`
`--sdf`	Input molecule as an .sdf file	`$AMSBIN/prop_prediction --sdf <file.sdf> ...`
`--temperature`	Set temperature/range (K)	`$AMSBIN/prop_prediction --temperature 298.15 ...`
`-n`	number of steps for temperature range	`$AMSBIN/prop_prediction --n 20 ...`
`-d [--display]`	Display calculated properties	`$AMSBIN/prop_prediction --d ...`
`-o [--output]`	Write output to file	`$AMSBIN/prop_prediction --o <output file> ...`

Note, if no output flag is supplied, then the results are written to a file called CRSKF by default. Additionally, the user may enter as many compounds as desired on the command line in either of the two available input formats.

The program can be run in 2 ways:

- Estimating all available properties for every molecule
- Estimating specific properties for every molecule

To estimate all properties for every input compound, simply execute the program with all molecules specified on the command line. Don't forget that the -d flag is required to display the results in the terminal. An example of this is below.

```
$AMSBIN/prop_prediction --smiles CCCCCCO -o example.crskf -temperature 298.15 -
↪temperature 398.15 -n 20 -d
```

```
Boiling point at standard pressure :
CCCCCCO              435.777  K
Critical pressure :
CCCCCCO              34.3493  bar
Critical temperature :
CCCCCCO              576.466  K
Critical volume  :
CCCCCCO             0.404124  L/mol
Liquid density :
CCCCCCO              0.79182  kg/L
Dielectric constant :
CCCCCCO              10.9512
Absolute entropy of an ideal gas at 298.15 K and 1 bar :
CCCCCCO              439.885  J/(mol K)
Flash point :
CCCCCCO              342.271  K
Gibbs energy of formation for an ideal gas at 298.15 K and 1 bar :
```

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```
CCCCCCO             -131.869  kJ/mol
Net enthalpy of combustion at 298.15 K  :
CCCCCCO             -3678.12  kJ/mol
Standard state enthalpy of formation at 298.15 K and 1 bar :
CCCCCCO             -384.388  kJ/mol
Enthalpy of fusion at normal melting point :
CCCCCCO              18.5054  kJ/mol
Enthalpy of formation for an ideal gas 298.15 K :
CCCCCCO             -316.821  kJ/mol
Enthalpy of sublimation :
CCCCCCO              80.9799  kJ/mol
Melting point at 1 atm :
CCCCCCO              231.141  K
Liquid molar volume :
CCCCCCO             0.128949  L/mol
Parachor :
CCCCCCO              289.059
Solubility parameter :
CCCCCCO              10.1294  (cal/cm^3)^0.5
Triple point temperature :
CCCCCCO              230.404  K
Van der Waals area :
CCCCCCO              171.059  Å^2
Van der Waals volume :
CCCCCCO              120.519  Å^3
Liquid viscosity :
Molecule: CCCCCCO
   Temperature (K)     Liquid viscosity (Pa-s)
    298.15                 0.004465
    303.15                 0.003865
    308.15                 0.003364
    313.15                 0.002942
    318.15                 0.002584
    323.15                 0.002281
    328.15                 0.002021
    333.15                 0.001798
    338.15                 0.001606
    343.15                 0.001439
    348.15                 0.001294
    353.15                 0.001168
    358.15                 0.001057
    363.15                 0.000959
    368.15                 0.000873
    373.15                 0.000797
    378.15                 0.000729
    383.15                 0.000669
    388.15                 0.000615
    393.15                 0.000567
    398.15                 0.000523
Liquid vapor pressure :
Molecule: CCCCCCO
   Temperature (K)     Vapor pressure (bar)
    298.15                 0.001229
    303.15                 0.001809
    308.15                 0.002623
    313.15                 0.003750
    318.15                 0.005289
```

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```
    323.15                  0.007362
    328.15                  0.010123
    333.15                  0.013757
    338.15                  0.018487
    343.15                  0.024582
    348.15                  0.032357
    353.15                  0.042182
    358.15                  0.054484
    363.15                  0.069757
    368.15                  0.088563
    373.15                  0.111537
    378.15                  0.139394
    383.15                  0.172929
    388.15                  0.213022
    393.15                  0.260644
    398.15                  0.316852
```

For most applications, it is not necessary to calculate all of the available physical properties (although doing so is practically just as fast). In these cases, additional property flags need to be specified on the command line to restrict the program to calculating only certain physical properties. For example, if we were doing solid/liquid solubility calculations on Ibuprofen and Paracetamol, we would require the Enthalpy of Fusion and the Melting Point of both compounds. To calculate only these two properties, we simply have to add the two property flags "-hfusion" and "-meltingpoint" to the command line. Using the .mol file for Ibuprofen and the SMILES string for Paracetamol, we execute the following:

```
$AMSBIN/prop_prediction -d -m Ibuprofen.mol -s 'CC(=O)NC1=CC=C(C=C1)O' -hfusion -
↪meltingpoint
```

```
Enthalpy of fusion at normal melting point :
CC(=O)NC1=CC=C(C=C1)O       33.0298  kJ/mol
Ibuprofen.mol               24.0336  kJ/mol

Melting point at 1 atm :
CC(=O)NC1=CC=C(C=C1)O       469.282  K
Ibuprofen.mol               331.887  K
```

8.4 Index of property keys

The available properties and their corresponding property flags are listed below:

Property Name	Property Flag
Boiling point	`--boilingpoint`
Critical Pressure	`--criticalpressure`
Critical Temperature	`--criticaltemp`
Critical Volume	`--criticalvol`
Dielectric Constant	`--dielectricconstant`
Ideal Gas Entropy	`--entropygas`
Flash point	`--flashpoint`
Gibbs Energy Ideal Gas	`--gidealgas`
Enthalpy of Combustion	`--hcombust`
Std. Enthalpy of Formation	`--hformstd`
Enthalpy of Fusion	`--hfusion`
Enthalpy of Form. Ideal Gas	`--hidealgas`
Enthalpy of Sublimation	`--hsublimation`
Melting point	`--meltingpoint`
Liquid Molar volume	`--molarvol`
(Liquid Density)	`--molarvol`
Liquid Vapor Pressure	`--vaporpressure`
Liquid Viscosity	`--liquidviscosity`
Parachor	`--parachor`
Solubility Parameter	`--solubilityparam`
Synthetic accessibility	`--synacc`
Triple point temperature	`--tpt`
Van der Waals Area	`--vdwarea`
Van der Waals Volume	`--vdwvol`

8.5 General warnings

This method will **fail** for the following types of molecules:

- Those that contain *only one non-hydrogen atom* (e.g., Methane or Water). However, experimental data is ample for these small molecules. The vapor pressure model is the exception in that it *can* represent such small structures.
- Those that contain atoms or substructures that are not listed in the *Accepted atom types table* (page 65) above.
- Polymers and Ionic Liquids

This method will **lose accuracy** for some properties in the following domains:

- Molecules with *many different types of functional groups*
- Molecules that are *extremely light* (< 3 non-Hydrogen atoms) or *heavy* (> 30 non-Hydrogen atoms)

8.6 Equations for temperature-dependent properties

8.6.1 VPM1: liquid vapor pressure

$$\ln(P) = A/T + B\ln(T) + CT + D$$

Symbol	Meaning
P	vapor pressure
T	absolute temperature
A,B,C,D	estimated constants

8.6.2 empirical-VIS1: Liquid Viscosity

$$\ln(\mu) = A + B/T + C\ln(T) + (D/T)\exp(E/T)$$

Symbol	Meaning
μ	liquid viscosity
T	absolute temperature
A,B,C,D,E	estimated constants

8.7 References

CHAPTER

NINE

SOLVENT OPTIMIZATION

9.1 Introduction

The choice of solvent or solvent system can have a dramatic impact on the solubility of solutes, the performance of the solvent system for liquid-liquid extraction, or reaction rates/selectivities for many chemical reactions. The solvent is also one of the most accessible variables in formulation/reaction/extraction design as many of the other species in these problems (active ingredients, co-solvents, reactants, catalysts, extracts, raffinates, etc.) are often fixed or tightly constrained. However, the solvent selection problem is combinatorially complex and non-trivial. As an example of this complexity, consider the problem of choosing up to 4 solvents for a process from a set of 100 possible solvents. The number of combinations alone is over 4 million, a number that makes laboratory- or pilot-scale testing for every system untenable. An additional complication is that the identities of the solvents alone do not determine a solvent system: we must also know the mole fractions. Of course, there are an infinite number of possible mole fraction values for a solvent system (a value of $x_1 = 0.3$, $x_2 = 0.7$ is just as valid as $x_1 = 0.29999$, $x_2 = 0.70001$), meaning a high-throughput approach would still require multiple mole fraction values for each solvent system to effectively sample the mole fraction space.

Luckily, the complexity of this problem can be addressed with modern mathematical optimization approaches. Following the approach of[1], we re-structure the COSMO-RS/-SAC parameters and equations and incorporate them into a Mixed Integer Nonlinear Programming (MINLP) formulation. Using this generic formulation, we can apply a number of optimization solvers and solution techniques to the problem of determining an optimal solvent system. We note that the optimization methods currently in use only guarantee local solutions, but the formulation should be robust enough to provide high-quality solutions for many types of problems. In fact, for most of our example problems, our optimization approach was able to find the globally optimal solution (as determined by an exhaustive enumeration of the solvent space and dense sampling of the mole fractions space). There are additionally some features in the program (e.g., the -multistart flag) which help to provide a diversity of starting conditions so the solvers can find high-quality solutions.

9.2 Problem types

At present, the program has two problem templates:

- The **SOLUBILITY** template: this selects a solvent system and mole fractions in order to maximize or minimize the mole fraction solubility of a solid solute in the liquid mixture. Note that currently only solid/liquid equilibria calculations are supported.
- The **LLEXTRACTION** template: this selects a two-phase solvent system and mole fractions in order to maximize (or minimize) the distribution ratio (D) of two solutes between the two liquid phases. The distribution ratio for these problems is defined in terms of mole fractions rather than concentrations. The formula for this is given in an equation below. Note that LLEXTRACTION problems will fail if all possible solvents are miscible.

[1] N.D. Austin, N.V. Sahinidis, D.W. Trahan, *COSMO-based computer-aided molecular/mixture design: A focus on reaction solvents*, AIChE Journal 64, 104 (2018) (https://doi.org/10.1002/aic.15871)

Because liquid densities are not always known, we calculate the distribution ratio (D) in terms of mole fractions. The liquid-liquid phase equilibrium condition provides an equivalent expression for D. More precisely, this means that D can be calculated as follows:

$$D = max\left(\frac{\gamma_1^I}{\gamma_1^{II}}\frac{\gamma_2^{II}}{\gamma_2^I}, \frac{\gamma_2^I}{\gamma_2^{II}}\frac{\gamma_1^{II}}{\gamma_1^I}\right)$$

where γ_i^j represents the activity coefficient of solute *i* in phase *j*. Here, we assume that the two solutes to be separated are indexed with $i \in \{1, 2\}$. The max operator, though not used in the optimization problem itself, allows us to express the correct value of D in the equation above. In other words, the max operator removes the dependence of the D value on arbitrary indexing of solutes and phases.

Note: For LLEXTRACTION problems, the mole fractions of the solutes are fixed to 0 unless they are also specified as solvents. This means that the distribution coefficient is calculated using the infinite dilution activity coefficients.

A brief summary of what to expect for solvent optimization problems using the two templates is given below:

	SOLUBILITY	LLEXTRACTION
Minimum number of solvents	1	2
Preferred number of solvents	>1	>4
Typical solution times	<2s	1-30s
Recommended multistarts	<5 if any	5-10
Warmstart recommended	No	Problem-dependent

The warmstart and multistart options will be explained in a later section.

9.3 Running the Solvent Optimization program

The Solvent Optimization program can be run from the command line. The following general flags are used by the program:

Flag	Purpose	Example
-h [–help]	Produces help message	$AMSBIN/solvent_opt –help
-s [–smiles]	Input molecule as SMILES sting	$AMSBIN/solvent_opt –smiles <SMILES> …
-m [–mol]	Input molecule as .mol file	$AMSBIN/solvent_opt –mol <mol file> …
-c [–coskf]	Input molecule as .coskf file	$AMSBIN/solvent_opt –coskf <.coskf file> …
-d [–display]	Display problem results	$AMSBIN/solvent_opt –d …
-o [–output]	Write output to file	$AMSBIN/solvent_opt –o <output file> …

Additionally, physical properties required for the calculation can be input on the command line. Presently, only two physical properties (Enthalpy of Fusion and Melting Point) are required for certain calculations. These flags must follow a molecule input and be followed by the property value. Some examples are given below:

Flag	Property	Example
-hfusion	H of Fusion (kJ/mol)	$AMSBIN/solvent_opt -c Ibuprofen.coskf -hfusion 26.6 …
-meltingpoint	Melting point (K)	$AMSBIN/solvent_opt -c Ibuprofen.coskf -meltingpoint 349.2 …

Optimization problem specifications and method options can be input with the following flags:

Flag	Meaning	Example
-method	Choice of method (COSMO-RS COSMOSAC2016)	… -method COSMO-RS …
-max	maximize the Solubility/Extraction ratio	
-min	minimize the Solubility/Extraction ratio	
-solute	specify which molecules are solutes	… -s CCCO -solute …
-t [–template]	choose a problem template	… -t LLEXTRACTION …
-temperature	input 1 or 2 temperatures (K)	… -temperature 298.15 …

Note that, like the -hfusion and -meltingpoint flags, the -solute flag comes *after* a compound identifier (SMILES string/filename).

Finally, there are two more optimization problem flags which can be altered for problems that do not converge. The first is the -multistart flag. This flag takes an integer N as input and instructs the algorithm to begin from N randomly-generated starting points. This can be useful for difficult problems because not only will the algorithm begin from more starting points, but it will also adjust internal parameters every time a problem fails. The -warmstart flag instructs the main algorithm to attempt to make the convert the initial starting point to a high-quality, feasible starting point which can then be given to the optimization algorithm. This option can be helpful for many problems, especially those with small numbers of solvents or LLEXTRACTION problems where the solvents are extremely immiscible (e.g., Water and n-Hexane). A summary of these options is presented below:

Flag	Meaning	Example
-multistart	Start from a number of random starting points	… -multistart 5 …
-warmstart	Use the warmstart strategy	$AMSBIN/solvent_opt –warmstart …

9.4 Examples

In this section, we provide a few example problems to demonstrate a few of the features available in the Solvent Optimization program. We first do a sample problem with the SOLUBILITY template, and then we provide an example of the usage of the LLEXTRACTION template.

9.4.1 Solubility

For a first example, we determine a mixture of solvents to maximize the solubility of Paracetamol. For the purposes of illustrating features, we assume that we do not have an available .coskf file for Paracetamol and must use its SMILES string. We can use a few common solvents from the ADFCRS-2018 database:

```
$AMSBIN/solvent_opt -t SOLUBILITY -d -max \
  -s "CC(=O)NC1=CC=C(C=C1)O" -solute -meltingpoint 443.1 \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Acetic_acid.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Hexane.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Toluene.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Butanoic_acid.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Ethanol.coskf
```

```
================================================
       Estimating missing property values
================================================

                                      Estimated values
-------------------------------------------------------------------------------------------
 Molecule                                    Missing Property    Estimated Value
-------------------------------------------------------------------------------------------
 CC(=O)NC1=CC=C(C=C1)O                       Hfusion             7.89433
-------------------------------------------------------------------------------------------


================================================
     Beginning solvent optimization problem
================================================

*********************************************
                Iteration 1
*********************************************

Initial guess x1:   0.0235183
Initial guess x2:   0.0758477
Initial guess x3:   0.220089
Initial guess x4:   0.283974
Initial guess x5:   0.314382
Initial guess x6:   0.082189
------> Solver Status: CONVERGED
Objective value: 0.159729
-------------------------------------------------------------------------------------------
                                  Variable values
-------------------------------------------------------------------------------------------
              x1:   0.159729       CC(=O)NC1=CC=C(C=C1)O
              x2:   0              Acetic_acid.coskf
              x3:   0              Hexane.coskf
              x4:   0              Toluene.coskf
              x5:   0              Butanoic_acid.coskf
              x6:   0.840271       Ethanol.coskf
```

The problem correctly selects Ethanol as the solvent in which Paracetamol is most soluble. Single solvent solutions are common in SOLUBILITY problems as often no mixed solvent system outperforms single solvents. Notice that in this example any required property values for solid/liquid equilibria that are missing are estimated based on the input SMILES string. Because the -meltingpoint flag provided a value for the Melting Point, only the Enthalpy of Fusion is estimated.

9.4.2 Liquid-liquid extraction

Our next example focuses on a classic liquid-liquid extraction problem: separating Acetic acid and Water. In this example, we assume that we want to replace a standard solvent for this extraction (n-Hexane) with something more environmentally-friendly. Consulting GSK's Solvent Selection Guide[2], we restrict our problem to the solvents with the fewest issues: Water, 1-Butanol, 2-Butanol, t-Butyl acetate, Isopropyl acetate, Propyl acetate, and Dimethyl carbonate.

```
$AMSBIN/solvent_opt -d -t LLEXTRACTION -max \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Acetic_acid.coskf -solute \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Water.coskf -solute \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Water.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/1-Butanol.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/2-Butanol.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/tert-Butyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Isopropyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Propyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Dimethyl_carbonate.coskf
```

Notice that water is repeated because it is both a solute and a solvent in the solvent space. The output produced is the following:

```
Removing duplicate entry: /home/austin/amshome/atomicdata/ADFCRS-2018/Water.coskf
================================================
     Beginning solvent optimization problem
================================================

*******************************************
                Iteration 1
*******************************************
                     Phase I        Phase II
Initial guess x1:   0.0818796      0.241048
Initial guess x2:   0.162378       0.185238
Initial guess x3:   0.198892       0.0429676
Initial guess x4:   0.114387       0.152842
Initial guess x5:   0.0267187      0.0437898
Initial guess x6:   0.232349       0.042073
Initial guess x7:   0.112232       0.182333
Initial guess x8:   0.071164       0.109708
------> Solver Status: CONVERGED
Objective value: 232.779
-------------------------------------------------------------------------------
                                Variable values
-------------------------------------------------------------------------------
              x1:   0              0                   Acetic_acid.coskf
              x2:   0.994592       0.0358616           Water.coskf
              x3:   0              0                   1-Butanol.coskf
              x4:   0              0                   2-Butanol.coskf
              x5:   0.000100098    0.186012            tert-Butyl_acetate.coskf
              x6:   0              0                   Isopropyl_acetate.coskf
              x7:   0              0                   Propyl_acetate.coskf
              x8:   0.00530747     0.778127            Dimethyl_carbonate.coskf
-------------------------------------------------------------------------------
                               Extraction values
-------------------------------------------------------------------------------
 Distribution
 coefficient (D)         log10(D)
```

(continues on next page)

[2] GSK Solvent Selection Guide. Accessed 1/9/18. http://www.rsc.org/suppdata/gc/c0/c0gc00918k/c0gc00918k.pdf

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```
 ---------------------------------
 232.779                   2.36694

Solute 1 ID:        Acetic_acid.coskf
Solute 2 ID:        Water.coskf

                   -------------------------
                       Partition ratio           Partition
                    Phase I        Phase II      coefficient (P)     log10(P)
                   ------------------------------------------------------------
Solute 1:          1              8.39321       0.119144            -0.923928
Solute 2:          27.7342        1             27.7342             1.44302
```

In this problem, we obtain a mostly aqueous phase and a dimethyl carbonate/tert-butyl acetate phase as the solution. This solvent system provides a distribution coefficient (D) of 232.779. This is a good value for a separation, but it is still worse than the distribution coefficient of the water/hexane solvent system (D = 1372.14) by roughly a factor of 6.

We then increase our solvent search space to include the solvents deemed to have "some issues" by GSK and are also present in our database: Ethanol, 1-Propanol, 2-Propanol, Methanol, Ethyl acetate, Methyl acetate, Methyl isobutyl ketone, Acetone, p-xylene, Toluene, Isooctane, Cyclohexane, Heptane, and DMSO.

```
$AMSBIN/solvent_opt -d -t LLEXTRACTION -max \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Acetic_acid.coskf -solute \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Water.coskf -solute \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Water.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/1-Butanol.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/2-Butanol.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/tert-Butyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Isopropyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Propyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Dimethyl_carbonate.coskf
  -c $AMSHOME/atomicdata/ADFCRS-2018/Ethanol.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/1-Propanol.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/2-Propanol.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Methanol.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Ethyl_acetate.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Methyl_acetate.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Methyl_isobutyl_ketone.coskf \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Acetone.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/p-Xylene.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Toluene.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/2,2,4-Trimethylpentane.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Cyclohexane.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Heptane.coskf  \
  -c $AMSHOME/atomicdata/ADFCRS-2018/Dimethyl_sulfoxide.coskf
```

This produces the following:

```
...
------------------------------------------------------------------------------
                                Variable values
------------------------------------------------------------------------------
              ...
              x2:   0.999972       7.50215e-05         Water.coskf
              ...
              x15:  5.58242e-06    0.00252496          Methyl_isobutyl_ketone.coskf
              ...
```

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```
              x20:  2.27012e-05    0.9974              Cyclohexane.coskf
              ...
-------------------------------------------------------------------------------
                                Extraction values
-------------------------------------------------------------------------------
 Distribution
 coefficient (D)          log10(D)
 ---------------------------------
 1892.42                   3.27702

Solute 1 ID:        Acetic_acid.coskf
Solute 2 ID:        Water.coskf

                   -------------------------
                        Partition ratio           Partition
                    Phase I        Phase II       coefficient (P)     log10(P)
                   ------------------------------------------------------------
Solute 1:           7.04343        1              7.04343             0.847784
Solute 2:           13329.1        1              13329.1             4.1248
```

As shown, this solvent system has a D value of 1892.42, better than that of the hexane/water system. Removing cyclohexane from the possible solvents, we still obtain a solution with a D value of 1891.09. Successively removing the best non-aqueous solvents from the solvent list, we obtain solutions with D values of: 1864.41, 1645.38, 1597.42, and finally 232.779 again. The number of good solutions for this problem lends credence to the idea of using such a solvent selection algorithm in general extraction design.

Additionally, there is a tutorial on solvent optimization which demonstrates running the program from the COSMO-RS GUI.

9.5 Guidelines for difficult problems

The Solvent Optimization program should produce high-quality solutions for many problems. However, there may be examples where the algorithm struggles to produce solutions at all. Below we list troubleshooting guidelines to help solve problematic solvent optimizations:

(1) For LLEXTRACTION problems, ensure that there are at least 2 immiscible solvents

Because the LLEXTRACTION template requires that both the liquid-liquid phase equilibria condition is met and that there are two distinct liquid phases, the Solvent Optimization program will fail if all of the available solvents are miscible in all mole fractions (no phase separation is possible).

(2) Re-execute the program several times

The Solvent Optimization program is not entirely deterministic. In particular, starting points are selected at random for every iteration. These starting points affect the convergence of the problem and in some cases can have a large impact on the optimization. This means that if one execution of the Solvent Optimization program fails to produce a solution, then it is possible that a subsequent execution could succeed. If the program continues to fail after multiple attempts at re-execution, consider using the *multistart* or *warmstart* flags.

(3) Use the -multistart flag

This flag executes the program multiple times from multiple starting points. If problems fail, the program uses information from these problems and updates internal optimization parameters to aid in the convergence of successive problems. Because each iteration takes a relatively short amount of time, the multistart flag can be used with high numbers of different starting points. It is useful to first try a smaller number of multistarts (5-15). If this produces no solution, try

using the -warmstart flag in addition to the multistarts. If the problems continue to fail, use gradually higher numbers of multistarts (20,40,60,80,100+).

(4) Use the -warmstart flag

If this flag is present, the program attempts to find a good starting point for LLEXTRACTION problems rather than simply using the randomly-generated starting point. This can be useful with or without the -multistart flag and is very problem-dependent. In our experience, LLEXTRACTION problems sometimes have difficulty converging if there are a small number of solvents and/or if the solution contains two highly-immiscible liquids (e.g., Hexane/Water). We reiterate that this is very problem-dependent.

9.6 Differences from standard implementations

The COSMO-RS method of the Solvent Optimization program is nearly identical to the ADF combi2005 implementation (the default COSMO-RS method). The single difference is that there is no *f_corr* parameter in the Solvent Optimization implementation. This parameter is used for the perpendicular component of the sigma values and has only a small effect on the results. Removing it from the Solvent Optimization program was done to improve solution times and robustness. Though the calculated values will be similar, results from the Solvent Optimization program can easily be input to ADFCRS and checked against the full ADF combi2005 method if desired.

The COSMOSAC2016 implementation in Solvent Optimization is identical to the 2016-ADF Chen implementation in ADFCRS.

To reproduce the results from the Solvent Optimization program to within tolerance, parameters must be changed in the GUI or from the command line. The following parameter changes are required:

Method	Required parameter changes
COSMO-RS	set *f_corr* to 0
COSMOSAC2016	none

In the current version of the program, the COSMO-RS/-SAC parameters *cannot* be changed/customized.

CHAPTER

TEN

PYTHON SCRIPTING WITH COSMO-RS

10.1 pyCRS: a python wrapper for thermodynamic calculation

10.1.1 General Information

Attention: Windows and Mac users may find it helpful to first read the *Getting Started* guides for scripting: scripting with Windows | scripting with MacOS

It is recommended to use the version of python that is shipped with AMS. This version ensures that all the necessary libraries (e.g., PLAMS) are properly imported and are mutually compatible. The best way to do this is to run the `amspython` program. That can be executed from the command line as follows:

```
$AMSBIN/amspython <your_program.py>
```

Furthermore, interactive usage of the amsipython program can be beneficial. To do so, execute the following command in your terminal:

```
$AMSBIN/amsipython      # in terminal
```

```
run <your_program.py>   # in interactive python
```

where `<your_program.py>` should of course be replaced by the name of your program.

10.1.2 Overview

The `pyCRS` Python library offers a convenient wrapper for various thermodynamic calculations, providing the following utilities:

Modules	API	Description
Database (page 82)	*API* (page 89)	Provides an interface to a SQL database for managing COSKF files with conformers.
CRSManager (page 84)	*API* (page 97)	It's a python wrapper based on PLAMS library for facilitating the COSMO-RS calculation. It is designed to be used in conjunction with Database.
PropPred	*API*	Predicts physical properties based on QSPR descriptors derived from SMILES. (page 101)
FastSigma	*API*	Predicts sigma profiles based on QSPR descriptors derived from SMILES. (page 102)

Future releases will incorporate more functionality.

In addition to introducing the Database and CRSManager in the following section, the *examples section* (page 111) contains various template scripts and helpful examples. Exploring the example section is one of the simplest ways to get started with the module.

Database

Introduction

The sql database contains the following tables.

Table name	Description
Compound	contains unique compounds along with their COSKF file based on either CAS number or any preferred identifier
Conformer	contains multiple conformers along with their COSKF file
PhysicalProperty	contains the physical properties input by user
PropPred	contains the estimated physical properties using QSPR methods based on SMILES

These tables can be visualized using open-source tools like DB Browser (https://sqlitebrowser.org) or accessed directly through methods within the COSKFDatabase class.

Attention: This module currently does not support charged species, polymers, or multiple-species with dissociation and association. While it's feasible to add these compounds to the database, it's worth noting that the SMILES generated from the coordinates using OpenBabel might be inaccurate. Additionally, the PropPred tool should not be utilized for charged species and polymers.

Note: Currently, the `.coskf` files themselves are stored as raw `.coskf` files in a directory called `SCM_PYCRS_COSKF_DB`, which will be created in the parent directory of the `path` variable. This database will

not be overwritten or deleted by this `COSKFDatabase` class. This directory exists for the convenience of the user, but it is best to access all files via the API below as the exact format of the database may evolve over time.

Basic Usage

In this brief example, we'll demonstrate how to interact with the database. This includes adding a compound, searching for a compound, specifying experimental physical properties, and utilizing PropPred to estimate physical properties.

There are a few important points to note when using the add_compound method:
1. If the `coskf_path` parameter is not provided by the user, the method will attempt to locate the ADFCRS-2018 database path if it's available. Please ensure to install the ADFCRS-2018 database via amspackages (SCM->Packages) before running the below script.
2. If the `cas` parameter is not provided by the user, the method will attempt to use the value stored in the 'Compound Data' section within the .coskf file if it's available.
3. If the `name` parameter is not provided by the user, the method will prioritize using the IUPAC name, CAS number, identifier, or the name of the .coskf file. The IUPAC name will be attempted to be retrieved from the 'Compound Data' section within the .coskf file.

```
from pyCRS.Database import COSKFDatabase
import os

#Please ensure to install the

db = COSKFDatabase("my_coskf_db.db")
db.add_compound("Water.coskf", name="Water", cas="7732-18-5")
db.add_compound("Methanol.coskf")
db.add_compound("Ethanol.coskf")
db.add_compound("Benzene.coskf")
db.add_compound("Ibuprofen.coskf")

rows = db.get_compounds(["7732-18-5","Ibuprofen"])
for r in rows:
    print(r)

db.add_physical_property("Ibuprofen","meltingpoint",347.6)
db.add_physical_property("Ibuprofen","hfusion",27.94,unit="kJ/mol")
db.estimate_physical_property("Ibuprofen")

EXP = db.get_physical_properties("Ibuprofen")[0]
QSPR = db.get_physical_properties("Ibuprofen",source="PropPred")[0]

print("experimental value = ", EXP.hfusion, " estimated value = ",QSPR.hfusion)
```

The output produced is the following:

```
CompoundRow(compound_id=1, conformer_id=1, name='water', cas='7732-18-5',␣
↪identifier=None, smiles='O', resolved_smiles='O', coskf='Water_1.coskf', Egas=-323.
↪935, Ecosmo=-330.386, nring=0)
CompoundRow(compound_id=4, conformer_id=4, name='ibuprofen', cas='15687-27-1',␣
↪identifier=None, smiles='CC(Cc1ccc(cc1)[C@@H](C(=O)O)C)C', resolved_smiles=
↪'CC(Cc1ccc(cc1)[C@@H](C(=O)O)C)C', coskf='Ibuprofen_1.coskf', Egas=-4486.784,␣
↪Ecosmo=-4494.859, nring=6)
```

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```
experimental value =  6.678  estimated value =  5.744
```

Adding multiple conformers

When adding multiple conformers (i.e. multiple COSKF files) of a compound to the database using `add_compound` method, three confirmation steps are attempted:

1. Initially, the set of conformers in the database is retrieved by matching the CAS numner or identifier. If it's not found the compound will be added to the database as a new compound.

2. Subsequently, it attempts to generate the canonical SMILES from its coordinates to confirm that the compound matches the one in the database. If this resolution fails, one can bypass this check by setting *ignore_smiles_check=True*.

3. Lastly, it conducts duplicate recognition using UniqueConformersCrest in AMSConformer tool to ensure that it's not a duplicate in the database. If this recognition fails, one can skip this step by setting *ignore_duplicates=True*.

By default, the conformer with the lowest gas phase bond energy is stored in the COMPOUND TABLE. However, a specific conformer can be chosen using its conformer ID through the `update_compound_by_conformer_id` method.

For detailed information on these methods, please refer to the *Database API documentation* (page 89).

CRSManager

Introduction

The module provides a user-friendly approach for configuring standard crsJob setups via Python scripting.

For instance, here is an example how we set up the solid solubility calculation using CRSManager once the database has been set up in advance. This approach provides a more convenient method for conducting high-throughput calculations without the need for specific handling, such as *solubility screening* (page 132).

Python code using pyCRS

```
from pyCRS.CRSManager import CRSSystem
System = CRSSystem()
mixture = {}
mixture["Water"] = 1.0
mixture["Ibuprofen"] = 0
System.add_Mixture( mixture,
                    database="my_coskf_db.db",
                    temperature=298.15,
                    problem_type="solubility",
                    solute="solid")
print(System.get_input(0))
```

Alternatively, the same calculation can be set up through PLAMS, as demonstrated below. This approach requires users to input correct settings but provides greater flexibility in managing complex workflows. For example, the *advanced scripting example section* (page 128) demonstrates various tasks, such as eutectic and ionic liquid calculations, and more.

Python code using PLAMS

```
from scm.plams import Settings, init, finish, CRSJob
import os

########  Note: Please ensure to install the ADFCRS-2018 database via amspackages␣
↪(SCM->Packages) before running the below script  ########

coskf_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"] , "ADFCRS-2018")

settings = Settings()
settings.input.property._h = "SOLUBILITY"
settings.input.method = "COSMORS"

num_compounds = 2
compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = os.path.join(coskf_path, "Water.coskf" )
compounds[0].frac1 = 1.0
compounds[1]._h = os.path.join(coskf_path, "Ibuprofen.coskf" )
compounds[1].frac1 = 0.0
compounds[1].nring = 6
compounds[1].hfusion = 27.94/4.184
compounds[1].meltingpoint = 347.6

settings.input.temperature = 298.15

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
print(my_job.get_input())
```

Attention: This module currently does not support charged species, polymers, or multiple-species with dissociation and association.

Basic Usage

In this example, we'll create a database containing ethanol and benzene from the ADFCRS-2018 database. Then, we'll instantiate a CRSSystem and generate several CRSMixture instances using the add_Mixture method. After executing the calculation with the runCRSJob method, the corresponding CRSResults instances will be generated and stored in the outputs attribute. Finally, we can retrieve the .crskf file and the activity coefficient using methods provided by CRSResults.

```
from scm.plams import Settings, init, finish, CRSJob, config
from pyCRS.CRSManager import CRSSystem
from pyCRS.Database import COSKFDatabase
import numpy as np
import os, sys

init()
config.log.stdout = 0  # suppress plams output default=3
```

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```
#create a database containing ethanol and benzene. please ensure install the ADFCRS-
↪2018 database first via amspackages (SCM -> Packages)
db = COSKFDatabase("my_coskf_db.db")
db.add_compound("Ethanol.coskf")
db.add_compound("Benzene.coskf",cas="71-43-2")

#create a CRSSystem instance
System = CRSSystem()

#generate several CRSMixture instance
for i, x in enumerate(np.linspace(0, 1, 11)):
    mixture = {}
    mixture["ethanol"] = x
    mixture["71-43-2"] = 1-x
    System.add_Mixture(mixture,database="my_coskf_db.db",temperature=298.15,problem_
↪type="ACTIVITYCOEF",method="COSMORS")

#print out the first calculation setting in the CRSSystem class
#print(System.get_input(0))

#execution calculation for all CRSMixture
System.runCRSJob()

gamma_ethanol = []
gamma_benzene = []
#retrieve result using methods provided by CRSResults
for out in System.outputs:
    crskf = out.kfpath()
    res = out.get_results()
    gamma_ethanol.append(res["gamma"][0][0])
    gamma_benzene.append(res["gamma"][1][0])

print(f"the last crskf file = {os.path.basename(crskf)}")
print(f"activity coefficient of ethanol = {gamma_ethanol}")
print(f"activity coefficient of benzene = {gamma_benzene}")


finish()
```

This generates the following output:

```
the last crskf file = crsJob_10.crskf
activity coefficient of ethanol = [41.59625151549539, 3.539543443573337, 2.
↪234237060852824, 1.712495443157569, 1.4321494593043322, 1.2612087014707123, 1.
↪1507589807729406, 1.0784886266786704, 1.0329501218595156, 1.0079137778145097, 1.0]
activity coefficient of benzene = [1.0, 1.0632078891234995, 1.1497425466225775, 1.
↪2547602114699132, 1.3804970769948137, 1.5309168719748845, 1.7115353244885652, 1.
↪9297200775482874, 2.1952374886461046, 2.521062652267439, 2.9247536001030006]
```

Additional Keywords

Additional keywords can be used in conjunction with certain problem types:

Keywords name	Description
vp_corr	When set to True, it attempts to use the vapor pressure of pure compounds to adjust the gas phase chemical potential, potentially increasing vapor pressures in a mixture. The default value is False.
density_corr	When set to True, it attempts to utilize the volume of a pure compound derived from its density instead of the cavity volume used in the COSMO calculation. The default value is False.
solute	This parameter allows you to specify 'solid', 'gas', or 'liquid,' applicable to SOLUBILITY and PURESOLUBILITY problem types. The default value is 'solid'.
iso	This parameter offers the choice between 'isotherm', 'isobar' or 'flashpoint', applicable to BINMIXCOEF, TERNARYMIX, and COMPOSITIONLINE. The default value is 'isotherm'.
additional_sett	This parameter provides the PLAMS approach to set up various parameters such as the VolumeQuotient in LOP, DensitySolvent in SOLUBILITY, Nfrac in BINMIXCOEF/TERNARYMIX/COMPOSITIONLINE, Nprofile/SigmaMax in SIGMAPROFILE/SIGMAPOTENTIAL.

For certain problem types, necessary physical properties are retrieved from the PhysicalProperty TABLE and PropPred TABLE in the database. The value from the PhysicalProperty TABLE is prioritized; if unavailable, the system attempts to use the value from the PropPred TABLE instead. Failure to obtain either value may result in calculation failure.

For instance, you can find the following examples.

```
# Solid solubility calculation
db.add_physical_property("Benzene","hfusion",2.37,unit="kcal/mol")
db.add_physical_property("Benzene","meltingpoint",278.7)
mixture = {}
mixture["Water"]   = 1
mixture["Benzene"] = 0
System.add_Mixture( mixture,
                    database="my_coskf_db.db",
                    temperature="273.15 373.15 10",
                    problem_type="SOLUBILITY",
                    solute="solid")

# Binary isobar VLE using the vapor pressure from PropPred
mixture = {}
mixture["methanol"] = 0.5
mixture["ethanol"] = 0.5
db.estimate_physical_property(["methanol","ethanol"])
additional_sett = Settings()
additional_sett.input.property.Nfrac = 10
System.add_Mixture( mixture,
                    database="my_coskf_db.db",
                    pressure=1.01325,
                    problem_type="BINMIXCOEF",
                    iso="isobar",
                    additional_sett=additional_sett,
                    vp_corr=True)

# Partition Coefficient for benzene/water
mixture = {}
mixture["benzene"] = [1, 0]  #[mole fraction in phase1, mole fraction in phase2]
```

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```
mixture["water"]   = [0, 1]  #[mole fraction in phase1, mole fraction in phase2]
mixture["ethanol"] = [0, 0]  #[0, 0] for solute
additional_sett = Settings()
additional_sett.input.property.VolumeQuotient = 4.93
System.add_Mixture( mixture,
                    database="my_coskf_db.db",
                    problem_type="LOGP",
                    additional_sett=additional_sett)

# Sigma profile
mixture = {}
mixture["benzene"] = 1
additional_sett = Settings()
additional_sett.input.property.Nprofile = 100
additional_sett.input.property.SigmaMax = 0.05
System.add_Mixture( mixture,
                    database = "my_coskf_db.db",
                    problem_type="PURESIGMAPROFILE",
                    method="COSMORS",
                    additional_sett=additional_sett)
```

The available problem types is listed below.

`problem_type` value	Problem type
ACTIVITYCOEF	Activity Coefficient
BINMIXCOEF	Binary mixture LLE/VLE
TERNARYMIX	Ternary mixture LLE/VLE
COMPOSITIONLINE	Solvent composition line interpolation
SOLUBILITY	Solubility calculation in a mixed solvent
PURESOLUBILITY	Solubility calculation in a pure solvent
LOGP	Partition coefficient calculation
VAPORPRESSURE	Vapor pressure calculation for a mixed solvent
PUREVAPORPRES-SURE	Vapor pressure calculation for a pure solvent
BOILINGPOINT	Boiling point calculation for a mixture
PUREBOILINGPOINT	Boiling point calculation for a pure solvent(s)
FLASHPOINT	Flashpoint calculation for a mixture
SIGMAPROFILE	Sigma profile calculation for a mixture
PURESIGMAPROFILE	Sigma profile calculation for a pure component(s)
SIGMAPOTENTIAL	Sigma potential calculation for a mixture
PURESIGMAPOTEN-TIAL	Sigma potential calculation for a pure component(s)

For detailed information on these methods, please refer to the *CRSManager API documentation* (page 97).

10.1.3 API

Database

The submodule contain several class for providing an interface to a sql database for managing COSKF files and physical properties.

class pyCRS.Database.**COSKFDatabase**(*path*)

A class provide an interface to a sql database containing the following tables.

Table name	Description
Compound	contains unique compounds along with their COSKF file based on either CAS number or any prefered identifier
Conformer	contains mutiple conformers along with their COSKF file
PhysicalProperty	contains the physical properties input by user
PropPred	contains the estimated physical properties using QSPR methods based on SMILES

Parameters **path** (str) – a path to the database file. If this file does not exist, it will be created.

add_compound(*coskf_file*, *name=None*, *cas=None*, *identifier=None*, *coskf_path=None*, *smiles=None*, *nring=None*, *ignore_smiles_check=False*, *ignore_duplicates=False*)

Adds a new .coskf file to the database.

Parameters **coskf_file** (str) – a path to the .coskf file, or alternatively, the file name of the .coskf file if the coskf_path is provided.

Keyword Arguments

- **name** (str) – The entry's name, such as the compound name. If not provided, it will prioritize using the IUPAC name, CAS number, identifier, or the name of the .coskf file if such value is provided through the add_compound() method or stored in the 'Compound Data' section in the .coskf file.
- **cas** (str) – The CAS number of the molecule. If not provided, it will attempt to use the CAS within the .coskf file if available.
- **identifier** (str) – The chemical identifier of the molecule.
- **coskf_path** (str) – The directory path to the coskf file. If not provided, it will attempt to locate the path of ADFCRS-2018 database.
- **smiles** (str) – The SMILES string of the molecule. If not provided, it will attempt to use the SMILES within the .coskf file if available
- **nring** (int) – The numbr of ring atoms. If not provided, it will attempt to use the Nring within the .coskf file if available
- **ignore_smiles_check** (bool) – If set to True, skip generating the SMILES from compound's coordinates to confirm its identity against the database. Default is False.
- **ignore_duplicates** (bool) – If set to True, skip duplicate recognition using UniqueConformersCrest in AMSConformer tool. Default is False.

Note: Ensure every compound has a unique representation, either by CAS number or a preferred identifier. During the add_compound process, both the CAS number and identifier are checked for uniqueness in the database. If multiple compounds share the same CAS number and identifier, an ERROR will be raised. For instance, the below operation is not allowed since both compound shared the same identifier='CRS0001'

```
db.add_compound("Benzene.coskf",cas="71-43-2",identifier="CRS0001")
db.add_compound("Ethanol.coskf",cas="64-17-5",identifier="CRS0001")
```

add_physical_property (*identifier*, *attribute*, *value*, *unit=None*)
Add a value of a physical property to the PhysicalProperty TABLE in the database by compound's identifier

Parameters

- **identifier** (str) – the string representing either CAS, identifier or name of a compound
- **attribute** (str) – the name of the physical property (eg. meltingpoint or hfusion)
- **value** (float) – the value of the physical property

Keyword Arguments **unit** (str) – (optional) the unit of the input value. The default unit is K and kcal/mol. The accepted unit now has K, C, kcal/mol, kJ/mol, cal/g, J/g

Example

db.add_physical_property('Benzene','meltingpoint',278.7) db.add_physical_property('Benzene','hfusion',9.91,unit='kJ/mol')

del_row (*dbrow: pyCRS.Database.CompoundRow.CompoundRow*)
Remove a compound from the database and delete the corresponding .coskf file.

Parameters **dbrow** (*CompoundRow* (page 93)) – the row to remove from the database

del_row_by_conformer_id (*conformer_id*)
Remove the conformer from the database.

Parameters **conformer_id** (int) – A integer of intergers representing the conformer in the CONFORMER TABLE.

Example

db.del_row_by_conformer_id(1)

del_rows (*dbrows*)
Remove multiple compounds from the database and delete the corresponding .coskf files.

Parameters **dbrows** (list) – the rows to remove from the database, represented as a list of CompoundRow objects

Example

db.del_rows(db.get_compounds('benzene'))

estimate_physical_property(*identifier=None*, *compound_id=None*)
Estimate the physical properties using the property prediction tool and add the values to the PropPred TABLE in the database

Keyword Arguments

- **identifier** (str or list) – a string or a list of string representing either CAS, identifier or name of a compound
- **compound_id** (int or list) – an integer or a list representing the compound ID(s).

Note: The QSPR descriptor used in the property prediction tool is determined from the SMILES string. It first attempts to use the SMILES string provided by user via the *add_compound* method or *modify_attribute_by_compound_id* method. If unavailable, it will used the SMILES generating by OpenBabel using the compound's coordinates in the COSKF file. Please note that the resolved SMILES may be incorrect for some molecules, for instance when bond orders cannot be automatically determined and species with charges.

Example :

```
db.estimate_physical_property("Benzene")
```

get_all_compounds()
Collect all compounds in the database

Returns The full list of CompoundRow instances in the database

Return type list of CompoundRow

get_all_conformers()
Collects all conformers in the database

Returns The full list of ConformerRow instances in the database.

Return type List of ConformerRow

get_all_physical_properties(*source='PhysicalProperty'*)
Collect all physical properties in the database

Keyword Arguments **source** (str) – The string should be either 'PhysicalProperty' or 'PropPred'. Defaults to 'PhysicalProperty', returning properties from the PhysicalProperty TABLE. If set to 'PropPred', it will return the estimated properties in PropPred TABLE.

Returns The full list of PhysicalPropertyRow instances or PropPredRow instances in the database

get_attribute_by_compound_id(*attributes*, *compound_id*)
Retrieve the list of values for compounds with specified compound_id(s)

Parameters

- **attributes** (str or list) – A string or a list of strings used for searching for in the COMPOUND TABLE.
- **compound_id** (int or list) – A integer or a list of intergers used to search for compounds in the COMPOUND TABLE.

Returns A list of tuples containing the values of the specified attributes for the compounds.

Return type list of attributes

get_compounds (*values*)
Retrieves compounds from the COMPOUND TABLE in the database by matching CAS number, chemical identifier, or name.

Parameters **values** (str or list) – A string or a list of strings used for searching, representing CAS numbers, chemical identifiers, or names.

Returns A list of CompoundRow instances that match the search criteria

Return type list of CompoundRow

get_compounds_id (*values*)
Retrieves compound id from the COMPOUND TABLE in the database by matching CAS number, chemical identifier, or name.

Parameters **values** (str or list) – A string or a list of strings used for searching, representing CAS numbers, chemical identifiers, or names.

Returns A list of compound IDs that match the search criteria.

Return type list of int

get_conformers (*values*)
Retrieves conformers from the CONFORMER TABLE in the database by matching CAS number, chemical identifier, or name.

Parameters **values** (str or list) – A string or a list of strings used for searching, representing CAS numbers, chemical identifiers, or names.

Returns A list of ConformerRow instances that match the search criteria.

Return type list of ConformerRow

get_physical_properties (*identifier=None*, *compound_id=None*, *source='PhysicalProperty'*)
Collect physical properties in the database by matching CAS number, chemical identifier, name or compound id.

Keyword Arguments

- **identifier** (str or list) – a string or a list of string representing either CAS, identifier or name of a compound
- **compound_id** (int or list) – An integer or a list of integers representing the compound ID(s) in the database.
- **source** (str) – The string should be either 'PhysicalProperty' or 'PropPred'. Defaults to 'PhysicalProperty', returning properties from the PhysicalProperty TABLE. The set to 'PropPred', it will return the estimated properties in PropPred TABLE.

Returns The list of PhysicalPropertyRow instances or PropPredRow instances in the database

Return type list of PhysicalPropertyRow or *PropPredRow* (page 96)

modify_attribute_by_compound_id (*attribute*, *value*, *compound_id*)
Modify the attribute value for an entry associated with the compound id.

Parameters

- **attribute** (str) – the attribute to be modified. It can be one of the following: 'name', 'cas', 'identifier', 'smiles', 'nring'.
- **value** (str) – the new value of the specified attribute for the compound ID(s).
- **compound_id** (int) – an integer representing the compound ID.

Example :

```
db.modify_attribute_by_compound_id("identifier","InChI=1S/C6H6/c1-2-4-6-5-3-1/
↪h1-6H", 0)
```

update_compound_by_conformer_id(*compound_id*, *conformer_id*)
Update the data for a compound ID row in the COMPOUND TABLE using the data from a conformer ID row in the CONFORMER TABLE.

Parameters

- **compound_id** (int) – A integer representing compound id corresponding to a specific row in the COMPOUND TABLE of the database
- **conformer_id** (int) – A integer representing conformer id corresponding to a specific row in the CONFORMER TABLE of the database

update_compound_by_lowestE(*compound_id=None*)
Update the data for a compound ID row in the COMPOUND TABLE using the data from a conformer ID row with the lowest energy having the same compound ID in the CONFORMER TABLE.

Keyword Arguments

- **compound_id** (int or list) – An integer or a list of integers representing the compound id(s) that represent specific rows in the COMPOUND TABLE of the database.
- **the compound_id is not specified, the method will be applied to the whole database.** (*If*) –

visualize_conformers(*compound_id*)
Visualize a set of conformers in the order of the conformers id

Parameters **compound_id** (int or list) – an integer or a list representing the compound ID(s).

class pyCRS.Database.**CompoundRow**(*compound_id: int*, *conformer_id: int*, *name: str*, *cas: str*, *identifier: str*, *smiles: str*, *resolved_smiles: str*, *coskf: str*, *Egas: float*, *Ecosmo: float*, *nring: int*)
A data class to represent the contents of a row in a COMPOUND TABLE in COSKFDatabase

compound_id
A unique identifer for a specific row in the COMPOUND TABLE of the database

Type int

conformer_id
A unique identifer for a specific row in the CONFORMER TABLE of the database

Type int

name
The name associated with the row in the COMPOUND TABLE

Type str

cas
The CAS number associated with the row, i.e., the compound

Type str

identifier
The chemical identifier associated with the row, i.e., the compound

Type str

smiles
The SMILES string provided by user

Type str

resolved_smiles
The derived SMILES string obtained using OpenBabel from the coordinates in the COSKF file.

Type str

coskf
The filename of the .coskf file stored in the local SCM_PYCRS_COSKF_DB directory

Type str

Egas
The gas phase bond energy rounded to 3 decimal places in kcal/mol

Type float

Ecosmo
The bond energy in a perfect conductor rounded to 3 decimal places in kcal/mol

Type float

nring
The number of ring atoms

Type int

db_path
The path to the .coskf file directory

Type str

get_full_coskf_path()
Returns the full path of the corresponding .coskf file

read_coskf()
Opens the .coskf file corresponding to the database entry and returns a scm.plams.KFFile instance

class pyCRS.Database.**ConformerRow**(*conformer_id: int*, *compound_id: int*, *name: str*, *cas: str*, *identifier: str*, *smiles: str*, *resolved_smiles: str*, *coskf: str*, *Egas: float*, *Ecosmo: float*, *nring: int*)
A data class to represent the contents of a row in a CONFORMER TABLE in COSKFDatabase

conformer_id
A unique identifer for a specific row in the CONFORMER TABLE of the database

Type int

compound_id
A unique identifer for a specific row in the COMPOUND TABLE of the database

Type int

name
The name associated with the row in the CONFORMER TABLE

Type str

cas
The CAS number associated with the row, i.e., the compound

Type str

identifier
The chemical identifier associated with the row, i.e., the compound

Type str

smiles
The SMILES string provided by user

Type str

resolved_smiles
The derived SMILES string obtained using OpenBabel from the coordinates in the COSKF file

Type str

coskf
The filename of the .coskf file stored in the local SCM_PYCRS_COSKF_DB directory

Type str

Egas
The gas phase bond energy rounded to 3 decimal places in kcal/mol

Type float

Ecosmo
The bond energy in a perfect conductor rounded to 3 decimal places in kcal/mol

Type float

nring
The number of ring atoms

Type int

db_path
The path to the .coskf file directory

Type str

get_full_coskf_path()
Returns the full path of the corresponding .coskf file

read_coskf()
Opens the .coskf file corresponding to the database entry and returns a scm.plams.KFFile instance

class pyCRS.Database.**PhysicalPropertyRow**(*compound_id: int*, *meltingpoint: float*, *hfusion: float*, *cpfusion: float*, *boilingpoint: float*, *density: float*, *flashpoint: float*, *dielectricconstant: float*, *vp_equation: str*, *vp_params: str*, *Mn: float*)
A data class to represent the contents of a row in a PhysicalProperty TABLE in COSKFDatabase

compound_id
A unique identifer for a specific row in the COMPOUND TABLE of the database

Type int

meltingpoint
melting temperature (K)

Type float

hfusion
enthalpy of husion (kcal/mol)

Type float

cpfusion
heat capacity of fusion (kcal/mol-K) calculated as the difference between the heat capacity in the liquid state and the heat capacity in the solid state.

Type float

boilingpoint
boiling pointK (K)

Type float

density
liquid density (kg/L)

Type float

flashpoint
flash point (K)

Type float

dielectricconstant
dielectric constant

Type flash

vp_equation

Type str

vp_params

Type str or list

Mn
polymer average molecular weight (g/mol)

Type float

class pyCRS.Database.**PropPredRow**(*compound_id: int*, *adopt_smiles: str*, *meltingpoint: float*, *hfusion: float*, *boilingpoint: float*, *density: float*, *flashpoint: float*, *dielectricconstant: float*, *vp_equation: str*, *vp_params: str*)
A data class to represent the contents of a row in a PropPred TABLE in COSKFDatabase

compound_id
A unique identifer for a specific row in the COMPOUND TABLE of the database

Type int

adopt_smiles
The SMILES used for QSPR method

Type str

meltingpoint
melting temperature (K)

Type float

hfusion
enthalpy of husion (kcal/mol)

Type float

boilingpoint
boiling pointK (K)

Type `float`

density
liquid density (kg/L)

Type `float`

flashpoint
flash point (K)

Type `float`

dielectricconstant
dielectric constant

Type `flash`

vp_equation

Type `str`

vp_params

Type `str or list`

CRSManager

This submodule facilitate the creation, execution, and output processes for mutiple `crsJob` and is intended to be used in conjunction with the pyCRS.database module.

class `pyCRS.CRSManager.`**CRSSystem**
This class is designed to manage multiple instances of the `CRSMixture` class, facilitating the creation, execution, and output processes.

A `CRSSsytem` instance can create mutiple `CRSMixute` instance associated with its `mixture` attribute by `add_compound` method. The resulting mutiple `CRSResults` will be stored in its `outputs` attribute. This functionality requires the concurrent use of the pyCRS.database module.

num_mix
The numbers of mixture

Type `int`

mixture
A list of `CRSMixture` class

Type `list of |CRSMixture|`

outputs
A list of *CRSResults* class corresponding to the each `CRSMixture` in the `mixture`

Type `list of |CRSResults|`

add_Mixture(*mixture: dict*, *temperature=298.15*, *problem_type='activitycoef'*, *database='my_coskf_db.db'*, *method='COSMORS'*, *pressure=1.01325*, *jobname=None*, *conformer=False*, *massfraction=False*, *density_corr=False*, *vp_corr=False*, *solute='solid'*, *iso='isotherm'*, *additional_sett=None*, *multi_species=None*)
Add a new `CRSMixture` to the mixture attribute in `CRSSystem` class

Parameters **mixture** (`dictionary`) – A dictionary representing the composition of the mixture, where keys are Identifiers and values are mole fractions or mass fractions.

Keyword Arguments

- **temperature** (float) – The temperature in Kelvin. Default is 298.15K.
- **problem_type** (str) – The type of problem for the calculation. Default is 'activitycoef'.
- **database** (str) – The fullpath of a COSKFDatabase. Default is 'my_coskf_db.db'.
- **method** (str) – A str indicating the version of COSMORS or COSMOSAC to be used. Default is 'COSMORS'.
- **pressure** (float) – The pressure in bar. Default is 1.01325bar
- **jobname** (str) – The name of the job and the directory within plam_workdir. Defaults to "crsJob_0", "crsJob_1", etc.
- **conformer** (bool) – A boolean indicating if multiple conformers are used in COSMO-RS. Default is False.
- **massfraction** (bool) – A boolean indicating if the input fraction is a mass fraction. Default is False.
- **density_corr** (bool) – A boolean indicating whether to correct the volume of the compound using the density of the pure compound. Default is False, indicating the COSMO volume will be used instead.
- **vp_corr** (bool) – A boolean indicating whether to correct the gas phase chemical potentail using the vapor pressure. Default is False.
- **solute** (str) – A str indicating the solute state to be 'solid', 'gas' or 'liquid', applicable to problem type SOLUBILITY and PURESOLUBILITY. Default is 'solid'.
- **iso** (str) – A str indicating the calculation condition to be 'isotherm', 'isobar' or 'flashpoint', applicable to problem types BINMIXCOEF, TERNARYMIX and COMPOSITIONLINE. Default is 'isotherm'
- **additional_sett** (|Settings|) – A *Settings* object that allows for additional customized settings.
- **multi_species** (dictionary) – A dictionary representing multi-species settings, where keys are Identifiers and values are *Settings* objects

---

Note: The identifiers for a compound can be the name, the CAS number, or the chemical identifier stored in the pyCRS.database. When searching in the database, the input string will be converted to lowercase, except when it starts with 'InChI'.

The available problem types is listed below.

problem_type value	Problem type
ACTIVITYCOEF	Activity Coefficient
BINMIXCOEF	Binary mixture LLE/VLE
TERNARYMIX	Ternary mixture LLE/VLE
COMPOSITION-LINE	Solvent composition line interpolation
SOLUBILITY	Solubility calculation in a mixed solvent
PURESOLUBILITY	Solubility calculation in a pure solvent
LOGP	Partition coefficient calculation
VAPORPRESSURE	Vapor pressure calculation for a mixed solvent
PUREVAPORPRES-SURE	Vapor pressure calculation for a pure solvent
BOILINGPOINT	Boiling point calculation for a mixture
PUREBOILING-POINT	Boiling point calculation for a pure solvent(s)
FLASHPOINT	Flashpoint calculation for a mixture
SIGMAPROFILE	Sigma profile calculation for a mixture
PURESIGMAPRO-FILE	Sigma profile calculation for a pure component(s)
SIGMAPOTENTIAL	Sigma potential calculation for a mixture
PURESIGMAPO-TENTIAL	Sigma potential calculation for a pure component(s)

get_activity_coefficients(*idx=None*)
Return the activity coefficient of all `CRSMixture` or the ith `CRSMixture`.

Keyword Arguments **idx** (`interger`) – Index of the specific `CRSMixture` to be returned

runCRSJob()
Run all `CRSJob``_ in each ``CRSMixture`

class pyCRS.CRSManager.**CRSMixture**(***kwargs*)
This class is used to generate the *CRSJob* class

CRSJob
The *CRSJob* class.

Type `|CRSJob|`

mixture
A dictionary representing the composition of the mixture, where keys are Identifiers and values are mole fractions or mass fractions.

Type `dictionary`

temperature
The temperature in Kelvin. Default is 298.15K.

Type `float`

problem_type
The type of problem for the calculation. Default is 'activitycoef'.

Type `str`

database
The fullpath of a COSKFDatabase. Default is 'my_coskf_db.db'.

Type str

method
A str indicating the version of COSMORS or COSMOSAC to be used. Default is 'COSMORS'.

Type str

pressure
The pressure in bar. Default is 1.01325bar

Type float

jobname
The name of the job and the directory within plam_workdir. Defaults to "crsJob_0", "crsJob_1", etc.

Type str

conformer
A boolean indicating if multiple conformers are used in COSMO-RS. Default is False.

Type bool

massfraction
A boolean indicating if the input fraction is a mass fraction. Default is False.

Type bool

density_corr
A boolean indicating whether to correct the volume of the compound using the density of the pure compound. Default is False, indicating the COSMO volume will be used instead.

Type bool

vp_corr
A boolean indicating whether to correct the gas phase chemical potentail using the vapor pressure. Default is False.

Type bool

solute
A str indicating the solute state to be 'solid', 'gas' or 'liquid', applicable to problem type SOLUBILITY and PURESOLUBILITY. Default is 'solid'.

Type str

iso
A str indicating the calculation condition to be 'isotherm', 'isobar' or 'flashpoint', applicable to problem types BINMIXCOEF, TERNARYMIX and COMPOSITIONLINE. Default is 'isotherm'

Type str

additional_sett
A *Settings* object that allows for additional customized settings.

Type |Settings|

multi_species
A dictionary representing multi-species settings, where keys are Identifiers and values are *Settings* objects

Type dictionary

Reference

Settings exmples with COSMO-RS (page 106)

Settings API
CRSJob API
CRSResults API

PropPred

An interface to the PropPred program for the prediction of physical properties.

`pyCRS.PropPred.`**`units`**
a dictionary which maps property names to strings representing the units

Type `dict`

`pyCRS.PropPred.`**`available_properties`**
a list of the property names available in PropPrediction

Type `list`

`PropPred.`**`estimate`**(*molecule: pyCRS_internal.Molecule*, *properties: Union[str, List[str]] = 'all'*, *temperatures: List[float] = [298.1499938964844]*, *show_errors: bool = False*) → None
Estimates one or more properties with PropPrediction. The results are written to the pyCRS.Molecule object provided to the function.

Parameters

- **`molecule`** (*pyCRS.Molecule* (page 104)) – A pyCRS.Molecule object
- **`properties`** (`str or list(str)`) – a string naming a property for calculating a single property value or a list of strings naming all the desired properties to calculate
- **`temperatures`** (`list(float)`) – a list of temperature values with which to calculate the temperature-dependent properties
- **`show_errors`** (`bool`) – indicate whether errors should be shown in std out

Example

```
import pyCRS
mol = pyCRS.Input.read_smiles("c1ccccc1(OCC)")
# estimate all properties by default
pyCRS.PropPred.estimate(mol, temperatures=[290,295,300,305])

for prop, value in mol.properties.items():
    unit = pyCRS.PropPred.units[prop]
    print(f'{prop:<20s}: {value:.3f} {unit}')

for prop, value in mol.properties_tdep.items():
    print(f'{prop:<20s}:')
    unit = pyCRS.PropPred.units[prop]
    propunit = f'{prop} ({unit})'
    print("T (K)".rjust(30)+f'{propunit:>30s}')
    for t,v in value:
        print(f'{t:>30.3f}{v:>30.8g}')
```

```
boilingpoint         : 432.028 K
criticalpressure     : 34.205 bar
criticaltemp         : 569.012 K
```

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```
criticalvol          : 0.376 L/mol
density              : 0.958 kg/L (298.15 K)
dielectricconstant   : -3.824
entropygas           : 366.424 J/(mol K)
flashpoint           : 319.734 K
gidealgas            : 29.448 kJ/mol
hcombust             : -4173.723 kJ/mol
hformstd             : -165.241 kJ/mol
hfusion              : 10.622 kJ/mol
hidealgas            : -115.682 kJ/mol
hsublimation         : 66.720 kJ/mol
meltingpoint         : 202.182 K
molarvol             : 0.127 L/mol
parachor             : 305.809
solubilityparam      : 9.356 √(cal/cm^3)
synacc               : 1.042
tpt                  : 201.439 K
vdwarea              : 161.566 Å²
vdwvol               : 122.256 Å³
liquidviscosity      :
                          T (K)        liquidviscosity (Pa-s)
                       290.000                  0.0014622948
                       295.000                  0.0013171559
                       300.000                  0.0011921719
                       305.000                  0.0010839762
vaporpressure        :
                          T (K)           vaporpressure (bar)
                       290.000                  0.0010699197
                       295.000                  0.0015221786
                       300.000                  0.0021369822
                       305.000                  0.0029624981
```

FastSigma

This submodule provides an interface to the FastSigma program.

pyCRS.FastSigma.**estimate**(*molecule: pyCRS_internal.Molecule*, *method: str = 'COSMO-RS'*, *model: str = 'FS1'*, *display: bool = False*) → None

Uses the FastSigma program to estimate a sigma profile. The results are written to the pyCRS.Molecule object provided to the function.

Parameters

- **molecule** (*pyCRS.Molecule* (page 104)) – the molecule to estimate
- **method** (str) – the COSMO-RS/-SAC method to use. Available options are (COSMO-RS,COSMOSAC2013,COSMOSAC2016). Not every method is available for every model.
- **model** (str) – the estimation technique for the sigma profile. Available options are (FS1, SG1). FS1 is a QSPR approach and SG1 uses a database of sigma profiles and matches the query molecule's substructures against substructures in that database.
- **display** (bool) – whether to display the results to standard out

Example

```
import pyCRS
mol = pyCRS.Input.read_smiles("c1ccccc1(OCC)")
pyCRS.FastSigma.estimate(mol, method='COSMO-RS', model='SG1', display=True)
```

```
       sigma value       Total profile          HB profile
            ...               ...                 ...
            -0.002             10.689              0.000
            -0.001              9.453              0.000
             0.000              9.216              0.000
             0.001             10.264              0.000
             0.002             12.356              0.000
             0.003             12.007              0.000
             0.004             13.050              0.000
             0.005             11.818              0.000
             0.006              7.250              0.000
             0.007              2.643              0.000
             0.008              1.218              0.101
             0.009              1.131              0.890
             0.010              1.248              1.185
             0.011              1.209              1.181
             0.012              1.251              1.239
             0.013              1.233              1.228
             0.014              0.422              0.420
             0.015              0.025              0.024
            ...                ...                 ...
       Molecular Mass =       122.0731649400 g/mol
           COSMO Area =       174.8609437511 Angstrom**2
         COSMO Volume =       165.2344104876 Angstrom**3
Gas Phase Bond Energy =        -4.1647328138 Hartree
          Bond Energy =        -4.1720958091 Hartree
            ...                ...
```

Input

This submodule provides functions used to initialize a pyCRS.Molecule.

`Input.`**`read_smiles`**(*smiles: str*) → pyCRS_internal.Molecule

Parameters **`smiles`** (`string`) – the SMILES string to be used

Example

```
import pyCRS
mol = pyCRS.Input.read_smiles("c1ccccc1(OCC)")
mol = pyCRS.Input.read_smiles("c1cccccdfg1(OCC)")
print ("Check if the molecule is valid:", mol.is_valid)
```

`Input.`**`read_sdf`**(*filename: str*) → pyCRS_internal.Molecule

Parameters **`filename`** (`string`) – the .sdf file containing the input molecule

Example

```
import pyCRS
mol = pyCRS.Input.read_sdf("molecule.sdf")
```

Output

This submodule provides functions to write output in kf format.

pyCRS.Output.**write_kf**(*molecule: pyCRS_internal.Molecule*, *filename: str*) → None
writes a molecule to a kf file with the name <filename>. The saved file can then be used directly with AMS COSMO-RS/-SAC.

Parameters

- **molecule** (*pyCRS.Molecule* (page 104)) – the molecule to write to kf
- **filename** (str) – the filename for the output file. If the filename does not end with .compkf, then this extension is appended

Example

```
import pyCRS
mol = pyCRS.Input.read_smiles("c1ccccc1(OCC)")
pyCRS.FastSigma.estimate(mol)
pyCRS.Output.write_kf(mol,"example.compkf")
```

Molecule

class pyCRS.**Molecule**
This class stores inforation about a molecule and serves as the main interface for accessing estimated properties.

Attributes

area	The COSMO surface area of the molecule
bond_energy	The Bond Energy (in Hartrees) for the molecule in the COSMO conductor phase.
dispersion	The dispersion energy
formula	The molecular formula
gas_phase_bond_energy	The Bond Energy (in Hartrees) for the molecule in the gas phase
is_valid	A bool that indicates whether the molecule is valid or if there were errors in processing it (e.g., invalid SMILESS)
method	The method (COSMO-RS, COSMO-SAC, etc.) for which the estimate is made.
molar_mass	The molar mass in g/mol
nring	The nring parameter used in COSMO-RS

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Table 10.1 – continued from previous page

parameters	A dictionary of parameters that can be used for certain models (e.g., vapor pressure model parameters)
properties	A dictionary of property values for temperature-independent properties
properties_tdep	A dictionary of (temperature,property) pairs for temperature-dependent properties
smiles	The SMILES string of a molecule, if available
volume	The COSMO volume of the molecule

Methods

get_sigma_profile (*self: pyCRS_internal.Molecule*) → Dict[str, List[float]]

Returns a dictionary of sigma profiles values. For COSMO-RS, the dictionary has two entries (Total Profile and H-Bonding Profile). For COSMO-SAC, the dictionary has Total Profile, OH Profile, and OT Profile entries.

Example

```
import pyCRS
mol = pyCRS.Input.read_smiles("CCCCCN")
pyCRS.FastSigma.estimate(mol, method='COSMO-RS', model = 'FS1', display=False)
for k,v in mol.get_sigma_profile().items():
    print(k, v)
```

```
H-Bonding Profile [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.051576871269907, 0.
↪093772696234738, ... , 0.36159288378918, 0.14796979638662, 0.0]
Total Profile [0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.051576871269907, 0.
↪094440478268766, ... , 0.36159288378918, 0.147976661591423, 0.0]
```

get_tdep_values (*self: pyCRS_internal.Molecule*, *arg0: str*) → Tuple[List[float], List[float]]

Returns a tuple of (temperatures, values) for a temperature-dependent property given as an argument to the function.

Example

```
import pyCRS
mol = pyCRS.Input.read_smiles("OCCCCCC")
pyCRS.PropPred.estimate(mol, 'vaporpressure', temperatures=list(range(270,330,
↪10)))
unit = pyCRS.PropPred.units['vaporpressure']
print( "Temperature (K)".rjust(15)+f'Vapor pressure ({unit})'.rjust(25) )
for temp, val in zip(*mol.get_tdep_values('vaporpressure')):
    print(f'{temp:>15.3f}{val:>25.3f}')
```

```
Temperature (K)     Vapor pressure (bar)
        270.000                    0.000
        280.000                    0.000
        290.000                    0.001
        300.000                    0.001
        310.000                    0.003
        320.000                    0.006
```

has_missing_atoms (*self: pyCRS_internal.Molecule*, *arg0: str*) → bool

missing_atoms (*self: pyCRS_internal.Molecule*, *arg0: str*) → List[str]
A list of atom symbols which could not be mapped to a descriptor

10.2 Python scripting for COSMO-RS with PLAMS

10.2.1 General Information

Attention: Windows and Mac users may find it helpful to first read the *Getting Started* guides for scripting: scripting with Windows | scripting with MacOS

Python and the PLAMS library can be used for scripting with COSMO-RS. Due to the speed of COSMO-RS calculations, these jobs can be run interactively from the python interpreter. Larger numbers of jobs or high-throughput calculations can also easily be automated with python scripting. All results are returned as a python object, meaning the properties calculated with COSMO-RS can immediately be post-processed or used directly in other python functions.

Note: COSMO-RS calculations require a `.coskf` or `.compkf` file for every compound in the system. `.coskf` and `.compkf` files only need to be calculated once and then are stored in a database and can be used for any future calculation containing the corresponding compound. Generating these files requires calculating the COSMO surface with ADF (a relatively more expensive DFT calculation). Setting up these calculations is not directly supported with this version of PLAMS but can be done using scripting with amsprep.

10.2.2 Executing the code from the command line

It is recommended to use the version of python that is shipped with AMS. This version ensures that all the necessary libraries (e.g., PLAMS) are properly imported and are mutually compatible. The best way to do this is to run the `amspython` program. That can be executed from the command line as follows:

```
$AMSBIN/amspython <your_program.py>
```

where `<your_program.py>` should of course be replaced by the name of your program.

10.2.3 Specifying a problem type

To run COSMO-RS, the user must first provide a problem type for the calculation. This can be done by first creating a `Settings` object and then specifying the `.input.property._h` attribute. For example, to set up an activity coefficient calculation, we do the following:

```
from scm.plams import Settings, init, finish, CRSJob

settings = Settings()
settings.input.property._h = 'ACTIVITYCOEF'
```

For other problem types, the `.input.property._h` attribute must be set to other values. The other options for this value are summarized below:

`._h` value	Problem type
ACTIVITYCOEF	Activity Coefficient
BINMIXCOEF	Binary mixture LLE/VLE
TERNARYMIX	Ternary mixture LLE/VLE
COMPOSITIONLINE	Solvent composition line interpolation
SOLUBILITY	Solubility calculation in a mixed solvent
PURESOLUBILITY	Solubility calculation in a pure solvent
LOGP	Partition coefficient calculation
VAPORPRESSURE	Vapor pressure calculation for a mixed solvent
PUREVAPORPRES-SURE	Vapor pressure calculation for a pure solvent
BOILINGPOINT	Boiling point calculation for a mixture
PUREBOILINGPOINT	Boiling point calculation for a pure solvent(s)
FLASHPOINT	Flashpoint calculation for a mixture
SIGMAPROFILE	Sigma profile calculation for a mixture
PURESIGMAPROFILE	Sigma profile calculation for a pure component(s)
SIGMAPOTENTIAL	Sigma potential calculation for a mixture
PURESIGMAPOTEN-TIAL	Sigma potential calculation for a pure component(s)

10.2.4 Inputting Compounds

In PLAMS, each compound is also input as a `Settings` object. Additional information about the compounds required for the calculation (e.g., mole fraction) can be specified as an attribute of the compound's `Settings` object. An example for a calculation with two compounds is given below.

```
# set the number of compounds
num_compounds = 2

compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = "Water.coskf"
compounds[1]._h = "1-Hexanol.coskf"
```

10.2.5 Specifying mole fractions, temperatures, and pressures

Mole fractions are attributes of the compound `Settings` object. There are two types of mole fractions used in COSMO-RS. `frac1` is for standard specification of mole fractions in most problem types. `frac2` is used when the problem type requires two distinct liquid phases (COMPOSITIONLINE or LOGP). Additionally, the temperature can be specified using the `input.temperature` attribute of the `Settings` object. An example of this is shown below:

```
#set compound mole fractions
compounds[0].frac1 = 0.3
compounds[1].frac1 = 0.7

#set temperature (range)
#to specify a range, use 3 numbers: (1) the lowest temperature,
#(2) the highest temperature, and (3) the steps taken between these temperatures
settings.input.temperature = "298.15"
```

To specify a temperature range, set the `input.temperature` object equal to a python `str` which contains the lower temperature, upper temperature, and number of steps taken between the temperatures. These values should simply be

separated by spaces. For example, to specify that a calculation should go over the temperature range 298.15K to 398.15K with 10 temperature steps, do the following:

```
settings.input.temperature = "298.15 398.15 10"
```

Pressure works in much the same way. To input the system pressure (in bar), do the following:

```
settings.input.pressure = "1.5"
```

10.2.6 Running jobs

To run a job with COSMO-RS, first assign the `input.compound` attribute to the list of compound `Settings` objects used previously. Then, simply create the job using `CRSJob(settings=<your previously defined Settings object>)`. Once a job is created, you can run it with the `.run()` function. An example of this is given below:

```
# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# run the job
init()
out = my_job.run()
finish()
```

10.2.7 Reading the results of a job

Once a job has finished running, we can access the results directly in python. First, we can check to see which properties are available. We can do this using the `get_prop_names()` function on the output. For example, adding the line:

```
# check for the available properties
print( "Available properties:", out.get_prop_names() )
```

gives us the available properties as a python `set` for our calculation type ("ACTIVITYCOEF" in this case). The result of the print statement is the following:

```
Available properties: {'henrycnodim', 'property', 'deltag', 'henryc', 'nitems', 'gamma
↪',
'ncomp', 'filename', 'temperature', 'frac1', 'G solute', 'mu gas', 'molmass', 'E gas',
'mu', 'usepolyunits', 'mu pure', 'method'}
```

We can also convert all of the calculation results to a python `dict` using the `get_results()` function. For example, to collect all of the results and then print the activity coefficient values ("gamma"), we write the following code:

```
# convert all the results into a python dict
res = out.get_results()
print( "Activity coef values:\n", res["gamma"] )
```

This results in the following program output:

```
Activity coef values:
 [[ 3.71486   ]
 [ 1.04484607]]
```

Here the two activity coefficient values are returned as elements in a `numpy.ndarray`. Properties with multiple values are always stored as a numpy array.

Note: For properties with multiple values, the dictionary values are stored as a `numpy.ndarray`. If applicable to the calculation, the rows of the array represent different compounds and the columns represent different steps of the calculation (e.g., different temperatures/pressures or different mole fractions for a binary/ternary mixture calculation).

Putting all the previous code together, we have the following working example for calculating activity coefficients for 2 components:

```
from scm.plams import Settings, init, finish, CRSJob
import os

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")


# initialize settings object
settings = Settings()
settings.input.property._h = "ACTIVITYCOEF"

# set the number of compounds
num_compounds = 2

compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = os.path.join(database_path, "Water.coskf")
compounds[1]._h = os.path.join(database_path, "1-Hexanol.coskf")

# set compound mole fractions
compounds[0].frac1 = 0.3
compounds[1].frac1 = 0.7

# set temperature (range)
# to specify a range, use 3 numbers: (1) the lowest temperature,
# (2) the highest temperature, and (3) the steps taken between these temperatures
settings.input.temperature = "298.15"

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# run the job
init()
out = my_job.run()
finish()

# check for the available properties
print("Available properties:", out.get_prop_names())

# convert all the results into a python dict
res = out.get_results()
print("Activity coef values:\n", res["gamma"])
```

10.2.8 Plotting results

2D graphs can also be generated to visualize the results with the `plot` function. The `plot` function takes as a first argument any (or multiple) of the following:

- a `numpy.ndarray` object. This can be passed to the function as a dictionary value after calling the `get_results()` function.
- the name of a property. This property is read from the results and plotted. For a list of available properties, use the `get_prop_names()` function.

Additionally, the `plot` function takes the following keyword arguments:

- `x_axis`. This can be the name of a property or a `numpy.ndarray` object. This represents the independent variable in the plot. This value must be one dimensional, meaning it cannot be indexed over both compounds and temperatures.
- `x_label`. This can be used to label the x axis in the plot.
- `y_label`. This can be used to label the y axis in the plot.
- `plot_fig`. This is set to True/False to indicate whether a plotted figure should be displayed. The default is True.

The results of `plot` are returned as a `matplotlib.pyplot` object and can be further modified.

To demonstrate the use of plot, we do an example in which we calculate the solubility of methane gas in 1-Octanol and Ethanol across the temperature range from 298.15K to 398.15K. We also include the vapor pressure of methane using the VPM1 model. The code is shown below:

```
from scm.plams import Settings, init, finish, CRSJob
import os

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")


# initialize settings object
settings = Settings()
settings.input.property._h = "PURESOLUBILITY"

# this indicates we're calculating gas solubility
settings.input.property.isobar = ""

# set the number of compounds
num_compounds = 3

compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = os.path.join(database_path, "Methane.coskf")
compounds[1]._h = os.path.join(database_path, "1-Octanol.coskf")
compounds[2]._h = os.path.join(database_path, "Ethanol.coskf")

# set compound mole fractions
# for pure solubility the solvent gets a mole fraction of 1
# and the solute does not have the frac1 attribute
compounds[1].frac1 = 1
compounds[2].frac1 = 1
```

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```
# specify the vapor pressure equation for methane
compounds[0].vp_equation = "VPM1"
compounds[0].vp_params = "-1039.67755001 -0.183945615995 0.00061368649128 10.
↪1113503603315 0.0"

# set temperature (range)
# to specify a range, use 3 numbers: (1) the lowest temperature,
# (2) the highest temperature, and (3) the steps taken between these temperatures
settings.input.temperature = "298.15 398.15 10"

# 1 atm = 1.01325 bar
settings.input.pressure = "1.01325"

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# run the job
init()
out = my_job.run()
finish()

# convert all the results into a python dict
res = out.get_results()

# plot the solubilities in g/L solution
# the [1:] indicates that we're not plotting the values for methane (these are␣
↪automatically set to 0)
plt = out.plot(
    res["solubility g_per_L_solution"][1:],
    x_axis="temperature",
    x_label="Temperature",
    y_label="solubility g/L solution",
)
# plt.savefig("./PLAMS_gas_solubility.png")
```

This code generates the following plot:

10.3 Examples for pyCRS/PLAMS

10.3.1 pyCRS : Basic usage for Database and CRSManager

Adding compound to a pyCRS database

First, we'll add ethanol and water to the database and search for a list of compounds. When adding a compound, along with the COSKF file, it is necessary to provide a compound name and an unique chemical identifier. If only the COSKF file is provided, the method will attempt to utilize the IUPAC as the compound name and the CAS number as the chemical identifier, extracted from the Compound Data section within the COSKF file. In case such data is unavailable in the COSKF file, the user can specify the name parameter to define the compound name and either cas or identifier as the chemical identifier.

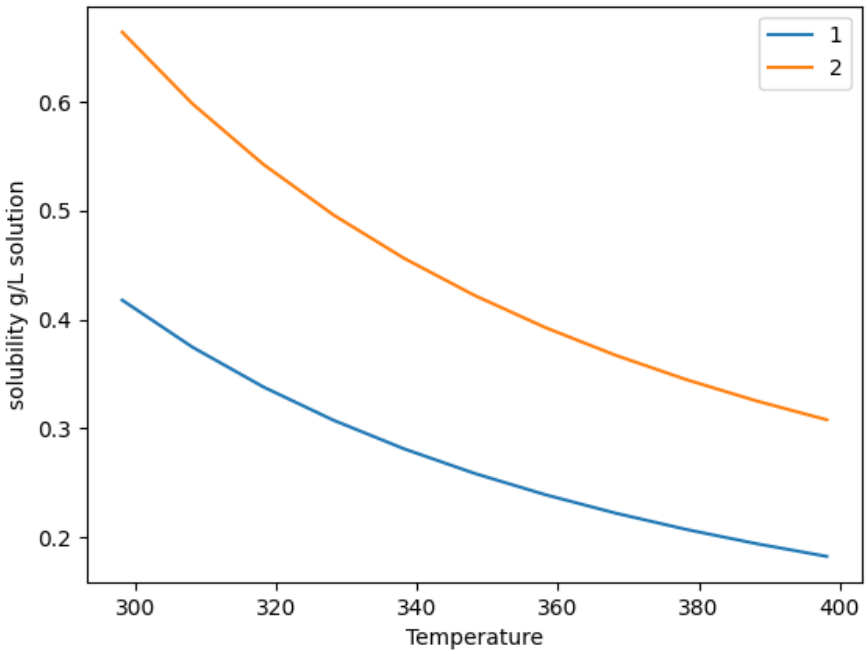

Fig. 10.1: The output of the `plot` function for a gas solubility calculation.

```
from pyCRS.Database import COSKFDatabase
from pyCRS.CRSManager import CRSSystem
import os

########  Note: Please ensure to install the ADFCRS-2018 database via amspackages␣
↪(SCM->Packages) before running the below script  ########


db = COSKFDatabase("my_coskf_db.db")
db.add_compound("1-Hexanol.coskf", cas="111-27-3")
db.add_compound("Water.coskf", identifier="InChI=1S/H2O/h1H2")

rows = db.get_compounds(["111-27-3", "Water"])
for r in rows:
    print(r)
```

The output produced is the following

```
Succesfully add new COMPOUND :compound_id=1  conformer_id=1  name=1-hexanol
Succesfully add new COMPOUND :compound_id=2  conformer_id=2  name=water
CompoundRow(compound_id=1, conformer_id=1, name='1-hexanol', cas='111-27-3',␣
↪identifier=None, smiles='CCCCCCO', resolved_smiles='CCCCCCO', coskf='1-Hexanol.coskf
↪', Egas=-2562.015, Ecosmo=-2567.296, nring=0)
CompoundRow(compound_id=2, conformer_id=2, name='water', cas='7732-18-5', identifier=
↪'InChI=1S/H2O/h1H2', smiles='O', resolved_smiles='O', coskf='Water.coskf', Egas=-
↪323.935, Ecosmo=-330.386, nring=0)
```

Activity coefficient calculation

```
from scm.plams import Settings, init, finish, CRSJob
from pyCRS.Database import COSKFDatabase
from pyCRS.CRSManager import CRSSystem

db = COSKFDatabase("my_coskf_db.db")
System = CRSSystem()

mixture = {}
mixture["7732-18-5"] = 0.3
mixture["111-27-3"] = 0.7

System.add_Mixture(mixture, database="my_coskf_db.db", temperature=298.15, problem_
↪type="activitycoef")

init()
System.runCRSJob()
finish()

for out in System.outputs:
    print(f"Property = {out.section}")
    res = out.get_results()
    for name, x, gamma in zip(res["name"], res["frac1"], res["gamma"]):
        print(name, x, gamma)
```

The output produced is the following

```
Property = ACTIVITYCOEF
water [0.3] [3.71486029]
1-hexanol [0.7] [1.04484603]
```

Solid Solubility calculation

Next, we can add the melting point and heat of fusion if experimental data is available or estimate these values using PropPred and then perform the solid solubility calculation.

```
from scm.plams import Settings, init, finish, CRSJob
from pyCRS.Database import COSKFDatabase
from pyCRS.CRSManager import CRSSystem
import os

########  Note: Please ensure to install the ADFCRS-2018 database via amspackages␣
↪(SCM->Packages) before running the below script  ########

db = COSKFDatabase("my_coskf_db.db")

db.add_compound("Ibuprofen.coskf")
db.add_compound("Water.coskf")
db.add_physical_property("Ibuprofen", "hfusion", 27.94, unit="kJ/mol")
db.add_physical_property("Ibuprofen", "meltingpoint", 347.6)
db.estimate_physical_property("Ibuprofen")

EXP = db.get_physical_properties("Ibuprofen")[0]
QSPR = db.get_physical_properties("Ibuprofen", source="PropPred")[0]
```

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```
print("experimental value = ", EXP.hfusion, " estimated value = ", QSPR.hfusion)

mixture = {}
mixture["Water"] = 1.0
mixture["Ibuprofen"] = 0

init()

System = CRSSystem()
System.add_Mixture(mixture, database="my_coskf_db.db", temperature=293.15, problem_
↪type="solubility", solute="solid")

System.runCRSJob()

for out in System.outputs:
    print(f"Property = {out.section}")
    res = out.get_results()
    print(f"{res['name'][1]} in {res['name'][0]} (g/L)= {res['solubility g_per_L_
↪solvent'][1][0]}")

finish()
```

The output produced is the following

```
experimental value =  6.678  estimated value =  5.744
Property = SOLUBILITY
ibuprofen in water (g/L)= 0.022067656192544072
```

Establishment of a pyCRS database from the ADFCRS-2018 database

The script facilitates the automatic creation of a sql database utilizing the COSKF file from the *ADFCRS-2018 database* (page 20).

```
from scm.plams import KFFile
from pyCRS.Database import COSKFDatabase
import glob, os, sys

########  Note: Please ensure to install the ADFCRS-2018 database via amspackages␣
↪(SCM->Packages) before running the below script  ########

db = COSKFDatabase("ADFCRS-2018.db")

files = glob.glob(os.path.join(db.ADFCRS2018_path, "*.coskf"))

for f in files:

    coskf = os.path.basename(f)

    if "IL_" != coskf[0:3]:
        db.add_compound(coskf)
```

10.3.2 pyCRS : Conformer usage for Database and CRSManager

Generating multiple conformers for a compound

Different conformers of a molecule can have significantly different sigma profiles, which can lead to big differences in predicted properties with COSMO-RS. For this reason, it's important for COSMO-RS calculations to use geometries corresponding to the lowest-energy conformer or a set of low-energy conformers when it's possible several conformers may exist in significant amounts. The script shows how to use the adfcosmorsconformers recipe based on the ConformerTools functionality in AMS to generate a set of low-energy conformers, refine the geometries with a semi-empirical method and finally perform the ADF and COSMO calculations necessary to produce `.coskf` files.

```
from scm.plams import Settings, init, finish, from_smiles
from scm.plams.recipes.adfcosmorsconformers import ADFCOSMORSConfJob,␣
↪ADFCOSMORSConfFilter
from scm.conformers import ConformersJob

init()

mol = from_smiles("CC(=O)O")

conf_sett = Settings()
conf_sett.input.AMS.Generator.RDKit
conf_sett.input.AMS.Generator.RDKit.InitialNConformers = 50
conf_job = ConformersJob(name="conformers_uff", molecule=mol, settings=conf_sett)

dftb_sett = Settings()
dftb_sett.input.AMS.Task = "Optimize"
dftb_sett.input.DFTB

# ADFCOSMORSConfFilter(max number of conformers, max energy range)
fil1 = ADFCOSMORSConfFilter(20, 22)  # applied to UFF
fil2 = ADFCOSMORSConfFilter(10, 12)  # applied to DFTB
fil3 = ADFCOSMORSConfFilter(5, 7)  # applied to ADF gas phase

mol_info = {"CAS":"64-19-7", "IUPAC":"Acetic acid", "SMILES":"CC(=O)O"}

job = ADFCOSMORSConfJob(
    mol,
    conf_gen=conf_job,
    first_filter=fil1,
    additional=[(dftb_sett, fil2)],
    final_filter=fil3,
    coskf_name="acetic_acid",
    coskf_dir="coskf_acetic_acid",
    mol_info=mol_info,
)
job.run()

finish()
```

Adding conformers to the database

This script shows how to add mutiple conformers into the database. Please generate the conformers for acetic acid using above script or download the files from the below link before running the below script.

Download relevant coskf file

```
from pyCRS.Database import COSKFDatabase
from pyCRS.CRSManager import CRSSystem
import os, glob

##################  Note: Ensure to download the coskf_acetic_acid or generating␣
↪conformers for acetic acid before running the script  ##################

conformer_path = os.path.join(os.getcwd(), "coskf_acetic_acid")

db = COSKFDatabase("my_coskf_db.db")

db.add_compound("acetic_acid_0.coskf",coskf_path=conformer_path)
db.add_compound("acetic_acid_1.coskf",coskf_path=conformer_path)

print("Displaying all conformers for acetic acid")
for row in db.get_conformers("Acetic acid"):
    print(row)

print("Displaying the conformer with lowest energy structure for acetic acid")
for row in db.get_compounds("Acetic acid"):
    print(row)
```

The output produced is the following

```
Displaying all conformers for acetic acid
ConformerRow(conformer_id=1, compound_id=1, name='acetic acid', cas='64-19-7',␣
↪identifier=None, smiles='CC(=O)O', resolved_smiles='CC(=O)O', coskf='acetic_acid_0.
↪coskf', Egas=-1061.593, Ecosmo=-1068.344, nring=0)
ConformerRow(conformer_id=2, compound_id=1, name='acetic acid', cas='64-19-7',␣
↪identifier=None, smiles='CC(=O)O', resolved_smiles='CC(=O)O', coskf='acetic_acid_1.
↪coskf', Egas=-1056.631, Ecosmo=-1066.71, nring=0)
Displaying the conformer with lowest energy structure for acetic acid
CompoundRow(compound_id=1, conformer_id=1, name='acetic acid', cas='64-19-7',␣
↪identifier=None, smiles='CC(=O)O', resolved_smiles='CC(=O)O', coskf='acetic_acid_0.
↪coskf', Egas=-1061.593, Ecosmo=-1068.344, nring=0)
```

Activity coefficient calculation considering conformers

This calculation models acetic acid as a mixture of conformers and plots activity coefficients and the conformer distribution over the mole fraction range. Please generate the conformers for acetic acid using above script or download the files from the below link before running the below script.

Download relevant coskf file

```
from scm.plams import Settings, init, finish, CRSJob
from pyCRS.Database import COSKFDatabase
from pyCRS.CRSManager import CRSSystem
import matplotlib.pyplot as plt
import numpy as np
import os, glob
```

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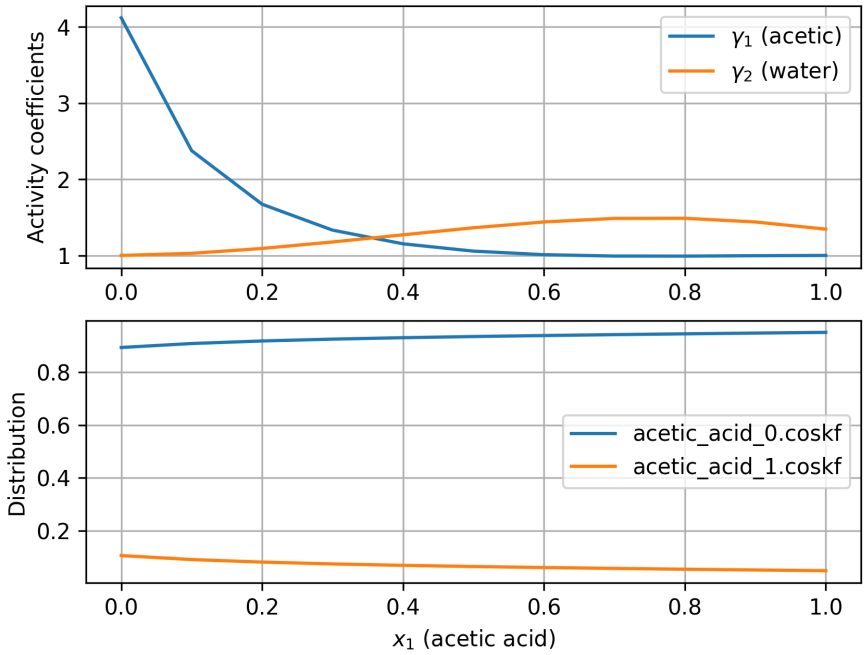
```
######## Note: Please ensure to install the ADFCRS-2018 database via amspackages␣
↪(SCM->Packages) before running the below script ########

db = COSKFDatabase("my_coskf_db.db")

db.add_compound("Water.coskf")

System = CRSSystem()

mixture = {}
x_range = np.linspace(0, 1, 11)
for x in x_range:
    mixture["Acetic acid"] = x
    mixture["Water"] = 1 - x
    System.add_Mixture(
        mixture, database="my_coskf_db.db", temperature=298.15, problem_type=
↪"activitycoef", conformer=True
    )

init()
System.runCRSJob()
finish()

gamma_water = []
gamma_acid = []
comp_acetic = {}
for out in System.outputs:
    res = out.get_results()
    gamma_acid.append(res["gamma"][0])
    gamma_water.append(res["gamma"][1])
    if comp_acetic == {}:
        comp_acetic = out.get_multispecies_dist()[0]
    else:
        tmp_comp_acetic = out.get_multispecies_dist()[0]
        for key in comp_acetic:
            comp_acetic[key].extend(tmp_comp_acetic[key])

fig, axs = plt.subplots(2)
axs[0].plot(x_range, gamma_acid, label="$\gamma_1$ (acetic)")
axs[0].plot(x_range, gamma_water, label="$\gamma_2$ (water)")

for struct, val in comp_acetic.items():
    axs[1].plot(x_range, val, label=os.path.basename(struct))

plt.setp(axs[0], ylabel="Activity coefficients")
plt.setp(axs[1], ylabel="Distribution")
for i in range(2):
    axs[i].legend()
    axs[i].grid()

plt.xlabel("$x_1$ (acetic acid)")
# plt.savefig('./pyCRS_activitycoef_conformer',dpi=300)
plt.show()
```

This code produces the following figure which plots activity coefficients and the distribution of two conformers.



10.3.3 pyCRS : Basic usage for PropPred and FastSigma

Basic usage

This basic example provides a minimal script input a molecule (paracetamol) as a smiles string, calculate a single property, and then estimate the default (COSMO-RS) sigma profile.

```
import pyCRS

mol = pyCRS.Input.read_smiles("CC(=O)Nc1ccc(O)cc1")  # paracetamol

print("available properties:", pyCRS.PropPred.available_properties)

pyCRS.PropPred.estimate(mol, "hfusion")
print("hfusion value:", mol.properties["hfusion"], pyCRS.PropPred.units["hfusion"])

pyCRS.FastSigma.estimate(mol, method="COSMO-RS", display=False)

sigma_profiles = mol.get_sigma_profile()
print("Total sigma profile:")
print(sigma_profiles["Total Profile"])
print("H-Bonding:")
print(sigma_profiles["H-Bonding Profile"])
```

The output produced is the following:

```
available properties: ['acentricfactor', 'autoignitiontemp', 'boilingpoint',
↪'critcompress', 'criticalpressure', 'criticaltemp', 'criticalvol', 'density',
↪'dielectricconstant', 'dipolemoment', 'entropygas', 'entropystd', 'flashpoint',
↪'gformstd', 'gidealgas', 'hcombust', 'hformstd', 'hfusion', 'hidealgas',
↪'hsublimation', 'liquidviscosity', 'lowflamlimper', 'meltingpoint', 'molecmass',
↪'parachor', 'radgyration', 'refractiveindex', 'solubilityparam', 'synacc', 'tpp',
↪'tpt', 'upflamlimper', 'vaporpressure', 'vdwarea', 'vdwvol']
```

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```
hfusion value: 28.084352493286133 kJ/mol
Total sigma profile:
[0.0, 0.0, 0.0, 0.002353191375733, 0.050697326660157, 0.24713134765625, 0.
↪5523872375488279, 0.840805053710938, 1.301651000976562, 1.316818237304688, 1.
↪408416748046875, 1.173583984375, 1.027912139892578, 1.160888671875, 0.
↪979301452636719, 0.8482666015625, 0.5888519287109371, 5.276319718325397, 11.
↪539728505193898, 13.300330108724362, 12.906459205297642, 10.834775504652777, 8.
↪539289410607651, 7.653812772468701, 7.964459592741903, 6.8641550757498555, 9.
↪304299127480718, 7.66864582217209, 11.452185796196918, 12.639082653211547, 13.
↪748599090727417, 11.745518829550344, 3.4796992518586065, 3.1053283341103315, 2.
↪864667892456055, 3.6309814453125, 4.3218994140625, 3.9415283203125, 2.786376953125,␣
↪0.968017578125, 0.48760986328125, 0.319122314453125, 0.047515869140625, 0.0, 0.0, 0.
↪0, 0.0, 0.0, 0.0, 0.0, 0.0]
H-Bonding:
[0.0, 0.0, 0.0, 0.002353191375733, 0.050697326660157, 0.246719360351562, 0.
↪552310943603516, 0.840805053710938, 1.301651000976562, 1.313278198242188, 1.
↪3948974609375, 1.173583984375, 1.027912139892578, 1.15216064453125, 0.
↪979301452636719, 0.8482666015625, 0.5888519287109371, 0.065513610839843, 0.0, 0.0,␣
↪0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.0, 0.277877807617188,␣
↪2.451416015625, 3.6309814453125, 4.3218994140625, 3.9354248046875, 2.78125, 0.
↪968017578125, 0.48760986328125, 0.319122314453125, 0.047515869140625, 0.0, 0.0, 0.0,
↪ 0.0, 0.0, 0.0, 0.0, 0.0]
```

Temperature-dependent properties

This example calculates the vapor pressure and produces a plot of vapor pressure against temperature.

```
import pyCRS
import matplotlib.pyplot as plt

mol = pyCRS.Input.read_smiles("CCCCCCO")

prop_name = "vaporpressure"
pyCRS.PropPred.estimate(mol, temperatures=[290, 295, 300, 305, 310, 315])
print("Results:", mol.properties_tdep[prop_name])

x, y = mol.get_tdep_values(prop_name)
unit = pyCRS.PropPred.units[prop_name]
plt.plot(x, y, "-o")
plt.ylabel(f"vapor pressure ({unit})")
plt.xlabel("Temperature (K)")
# plt.savefig('./pyCRS_PropPred_Tdep.png')
plt.show()
```

The output shows the format of the results: (temperature, vapor pressure) pairs

```
Results: [(290.0, 0.0006316340979498092), (295.0, 0.0009549864170162676), (300.0, 0.
↪0014201952225525484), (305.0, 0.002079200184963613), (310.0, 0.0029991100667307634),
↪ (315.0, 0.004265490872465904)]
```

Finally, the plot produced is the following:

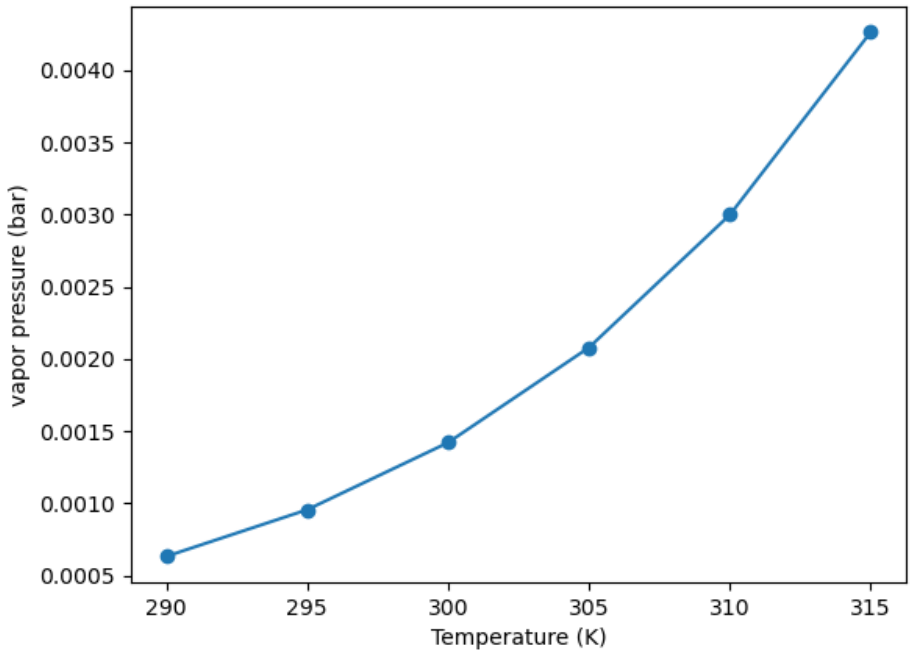

Fig. 10.2: The estimated vapor pressure versus temperature for 1-Hexanol

Estimating multiple properties

Estimating multiple properties is as simple as supplying a list of property names to the `PropPred` interface. All properties are estimated by default if no property argument is supplied. In this example, we first estimate a few properties, and then estimate all properties.

```
import pyCRS


def print_props(mol):
    for prop, value in mol.properties.items():
        unit = pyCRS.PropPred.units[prop]
        print(f"{prop:<20s}: {value:.3f} {unit}")

    for prop, value in mol.properties_tdep.items():
        print(f"{prop:<20s}:")
        unit = pyCRS.PropPred.units[prop]
        propunit = f"{prop} ({unit})"
        print("T (K)".rjust(30) + f"{propunit:>30s}")

        for t, v in value:
            print(f"{t:>30.3f}{v:>30.8g}")


mol = pyCRS.Input.read_smiles("CCCCCCO")

props = ["meltingpoint", "boilingpoint", "density", "flashpoint", "vaporpressure"]
pyCRS.PropPred.estimate(mol, props, temperatures=[298.15, 308.15, 318.15, 328.15])
```

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```
print("Results (temp-independent) :", mol.properties)
print("Results (temp-dependent)   :", mol.properties_tdep)

# we can also estimate all properties by supplying the property name 'all' or simply␣
↪omitting this argument
pyCRS.PropPred.estimate(mol, temperatures=[298.15, 308.15, 318.15, 328.15])
print_props(mol)
```

The output produced is the following:

```
Results (temp-independent) : {'boilingpoint': 435.7771752780941, 'density': 0.
↪7918196941677842, 'flashpoint': 342.2705857793571, 'meltingpoint': 231.
↪1412353515625, 'molarvol': 0.1289491355419159}
Results (temp-dependent)   : {'vaporpressure': [(298.1499938964844, 0.
↪00122854727137622), (308.1499938964844, 0.0026233569814824815), (318.1499938964844,␣
↪0.005288582928457778), (328.1499938964844, 0.010122673317257832)]}
boilingpoint        : 435.777 K
criticalpressure    : 34.349 bar
criticaltemp        : 878.101 K
criticalvol         : 0.404 L/mol
density             : 0.792 kg/L (298.15 K)
dielectricconstant  : 10.951
entropygas          : 439.885 J/(mol K)
flashpoint          : 342.271 K
gidealgas           : -131.869 kJ/mol
hcombust            : -3678.121 kJ/mol
hformstd            : -384.388 kJ/mol
hfusion             : 18.505 kJ/mol
hidealgas           : -316.821 kJ/mol
hsublimation        : 80.980 kJ/mol
meltingpoint        : 231.141 K
molarvol            : 0.129 L/mol
parachor            : 289.059
solubilityparam     : 10.129 √(cal/cm^3)
synacc              : 6.747
tpt                 : 230.404 K
vdwarea             : 171.059 Å²
vdwvol              : 120.519 Å³
liquidviscosity     :
                        T (K)        liquidviscosity (Pa-s)
                      298.150                   0.0044653385
                      308.150                    0.003363708
                      318.150                   0.0025843814
                      328.150                   0.0020210327
vaporpressure       :
                        T (K)           vaporpressure (bar)
                      298.150                   0.0012285473
                      308.150                    0.002623357
                      318.150                   0.0052885829
                      328.150                    0.010122673
```

Calculating sigma profiles with all models

This example demonstrates how to calculate COSMO-RS sigma profiles with both available models (SG1 and FS1). We'll use 4-Methylphenol for this example. The variable `ref_sp` in the script is the σ-profile calculated in the AMS COSMO-RS.

```
import pyCRS
import matplotlib.pyplot as plt

chdens = [-0.025 + 0.001 * x for x in range(51)]
ref_sp = [
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
    0.17050209,
    0.73517288,
    0.98383886,
    0.86397332,
    1.15571158,
    0.67051286,
    0.79380670,
    0.71422825,
    0.68854784,
    0.72126747,
    0.72414167,
    0.83293801,
    2.33617486,
    5.42197092,
    8.58230745,
    9.84294559,
    8.81993395,
    8.80932110,
    6.79578176,
    6.57764296,
    6.07802490,
    9.19651976,
    11.04721719,
    12.80255519,
    11.17672544,
    12.28788009,
    10.72121222,
    2.77829981,
    1.11136819,
    1.58235813,
    1.13444125,
    1.81316980,
    2.44468560,
    2.02558727,
    0.01243933,
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
```

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```
    0.00000000,
    0.00000000,
    0.00000000,
    0.00000000,
]

mol = pyCRS.Input.read_smiles("Cc1ccc(O)cc1")

pyCRS.FastSigma.estimate(mol, method="COSMO-RS", model="FS1")
sp_fs1 = mol.get_sigma_profile()["Total Profile"]

pyCRS.FastSigma.estimate(mol, method="COSMO-RS", model="SG1")
sp_sg1 = mol.get_sigma_profile()["Total Profile"]

plt.plot(chdens, ref_sp, "--", label="Reference $\sigma$-profile")
plt.plot(chdens, sp_fs1, label="FS1 $\sigma$-profile")
plt.plot(chdens, sp_sg1, label="SG1 $\sigma$-profile")
plt.ylabel("Area ($\AA^2$)")
plt.xlabel("$\sigma$")
plt.grid()
plt.legend()
# plt.savefig('./pyCRS_PropPred_SigmaProfile.png')
plt.show()
```

Finally, the plot produced shows the various σ-profiles produced.

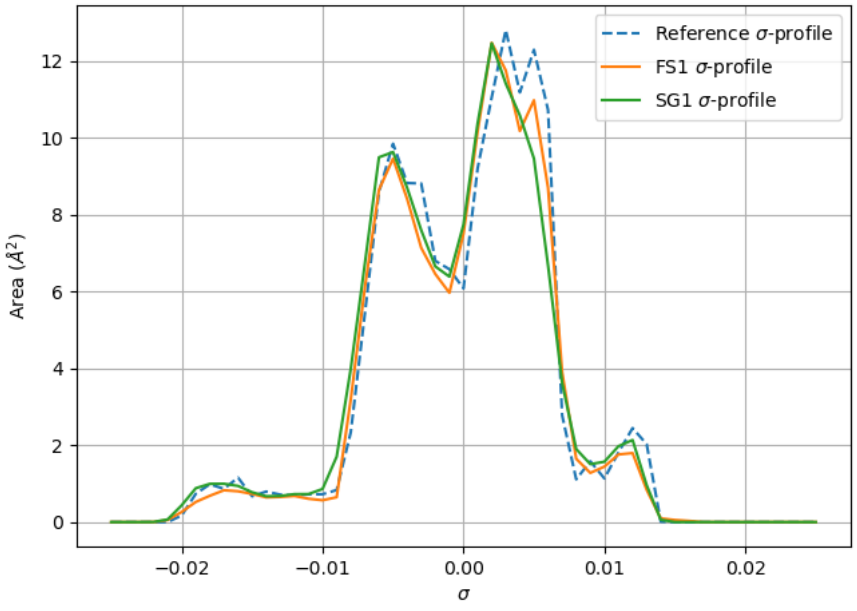

Fig. 10.3: The sigma profile of 4-Methylphenol

10.3.4 Examples using PLAMS

Partition coefficient

In this example, we calculate the logP of Ibuprofen. We use the standard octanol/water system. The code is as follows:

```
from scm.plams import Settings, init, finish, CRSJob
import os

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")


# initialize settings object
settings = Settings()
settings.input.property._h = "LOGP"

# set the number of compounds
num_compounds = 3

compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = os.path.join(database_path, "1-Octanol.coskf")
compounds[1]._h = os.path.join(database_path, "Water.coskf")
compounds[2]._h = os.path.join(database_path, "Ibuprofen.coskf")

# phase1 (octanol phase)
compounds[0].frac1 = 0.725
compounds[1].frac1 = 0.275

# phase2 (water phase)
compounds[0].frac2 = 0
compounds[1].frac2 = 1

# set temperature (range)
# to specify a range, use 3 numbers: (1) the lowest temperature,
# (2) the highest temperature, and (3) the steps taken between these temperatures
settings.input.temperature = "298.15"

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# run the job
init()
out = my_job.run()
finish()

# convert all the results into a python dict
res = out.get_results()

# print the logP of Ibuprofen
print("logP of Ibuprofen:", res["logp"][2])
```

This generates the following output:

```
logP of Ibuprofen: [ 4.67381309]
```

Binary mixture

In this example, we calculate a binary mixture of water and 2-Hexanone and plot the vapor pressures as a function of composition. We also show how to change the method and calculate the binary mixture with the COSMO-SAC2013-Xiong model.

```
from scm.plams import Settings, init, finish, CRSJob
import os

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

# initialize settings object
settings = Settings()
settings.input.property._h = "BINMIXCOEF"

# let's also change to the COSMOSAC2013 method
settings.input.method = "COSMOSAC2013"

# set the number of compounds
num_compounds = 2

compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = os.path.join(database_path, "Water.coskf")
compounds[1]._h = os.path.join(database_path, "2-Hexanone.coskf")

# use the vapor pressures from the VPM1 model
compounds[0].vp_equation = "VPM1"
compounds[0].vp_params = "-6093.40215895 -3.09584608667 0.000498622924643 34.
↪47450247140318 0.0"
compounds[1].vp_equation = "VPM1"
compounds[1].vp_params = "-6474.348470271438 -6.057589837807771 0.003390587477679571␣
↪51.07134238467479 0.0"

# set temperature (range)
# to specify a range, use 3 numbers: (1) the lowest temperature,
# (2) the highest temperature, and (3) the steps taken between these temperatures
settings.input.temperature = "298.15"

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# run the job
init()
out = my_job.run()
finish()

# convert all the results into a python dict
res = out.get_results()
```

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```
# plot all the pressures as a function of mole fraction of water
out.plot(
    "vapor pressure",
    "pressure",
    x_axis=res["molar fraction"][0],
    x_label="mole fraction water",
    y_label="Pressure (bar)",
)
```

The code generates the following plot:

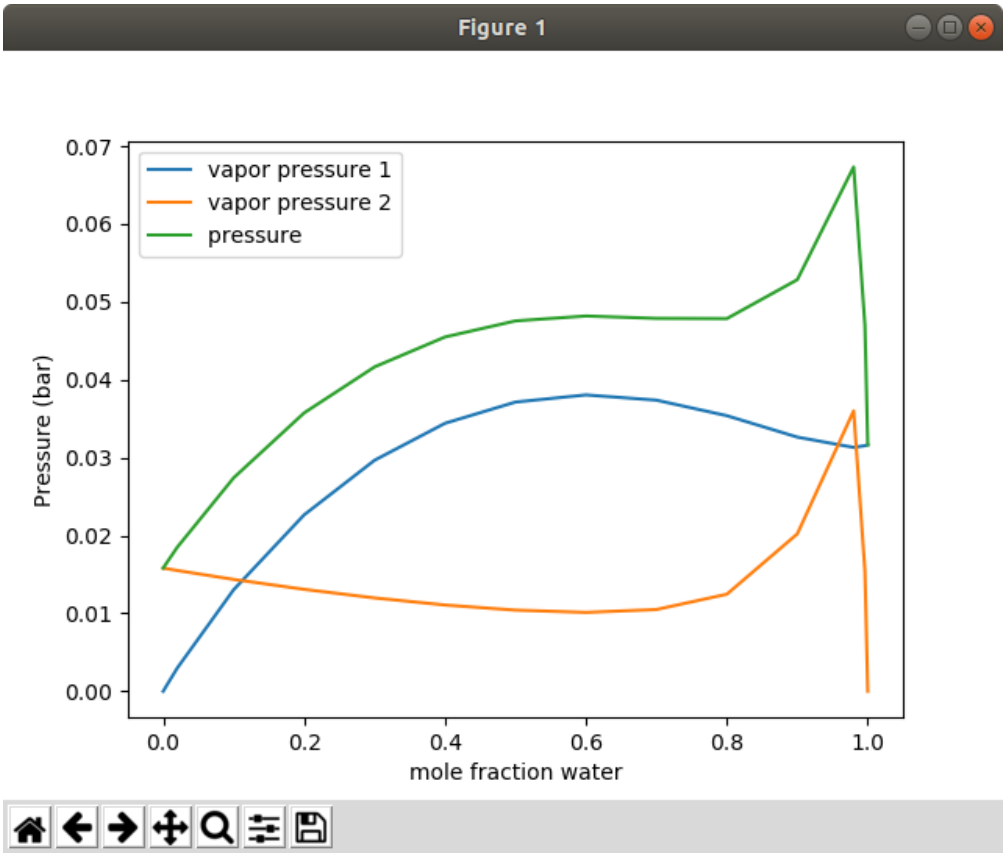

Fig. 10.4: A plot showing the total and partial vapor pressures for the water/2-Hexanone system.

Water and 2-Hexanone do not mix so well, thus there will be a miscibility gap, which is not taken into account in the graph. COSMO-SAC calculates the miscibility gap for the water/2-Hexanone system for molar fraction of water between around 0.29 and around 0.998. Within the miscibility gap the results shown in the graph use the unphysical condition that the two liquids are forced to mix.

Solid solubility

In this example, we calculate the solubility of ibuprofen in water at 298.15K. When considering a compound in its solid state, it's essential to account for the energy change of a compound from the subcooled liquid state to the ordered solid state. The energy change can be estimated using its heat of fusion and melting point. The heat capacity of fusion, while beneficial, is often not readily available.

```
from scm.plams import Settings, init, finish, CRSJob
import os

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

settings = Settings()
settings.input.property._h = "SOLUBILITY"
settings.input.method = "COSMORS"

num_compounds = 2
compounds = [Settings() for i in range(num_compounds)]
compounds[0]._h = os.path.join(database_path, "Water.coskf")
compounds[0].frac1 = 1.0
compounds[1]._h = os.path.join(database_path, "Ibuprofen.coskf")
compounds[1].frac1 = 0.0
compounds[1].nring = 6
compounds[1].hfusion = 27.94 / 4.184  # kcal/mol
compounds[1].meltingpoint = 347.6  # K
# compounds[1].cpfusion =           #kcal/mol-K

settings.input.temperature = 298.15

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# print out the input file
# print(my_job.get_input())

# run the job
init()
out = my_job.run()
finish()

# convert all the results into a python dict
res = out.get_results()

# print the solubility of Ibuprofen in water
print("Solubility of Ibuprofen in water [g/L]:", res["solubility g_per_L_solvent"][1])
```

This generates the following output:

```
Solubility of Ibuprofen in water [g/L]: [0.02799089]
```

10.3.5 Advanced scripting examples with PLAMS/pyCRS

COSMO-RS is capable of calculating a wide variety of important thermodynamic properties, but not all of those properties are easily available from the GUI. In this section, several scripts are provided that calculate more complex properties and demonstrate additional useful workflows. These scripts can be used as they are or used as a template to develop additional or more specific functionality.

Note: To ensure compatibility among the necessary python modules, it is recommended to use SCM's python distribution, `amspython`. Executing the scripts in this section from the command line can be done simply as follows: `amspython <script_name.py>`. Those users with more python experience or who prefer to use their own version of python are welcome to use alternatives to `amspython`.

Table of Contents:

Changing the default parameters or re-parameterizing the COSMO-RS/-SAC methods

There are many situations for which changing the default COSMO-RS/-SAC parameters may be useful. Most commonly, users may wish to try a certain parameterization that is not available from the program. Alternatively, some users may have a customized or proprietary dataset which they would like to use to re-fit the main model parameters. All of these tasks are straightforward via python scripting.

The following scripts will demonstrate how to alter parameters for COSMO-RS and COSMO-SAC.

Python code (COSMO-RS parameters)

```
import os
from scm.plams import Settings, init, finish, CRSJob, config

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")


init()
# suppress plams output
config.log.stdout = 0

# our system of interest
files = ["Acetone.coskf", "Water.coskf"]
fracs = [0.3, 0.7]

# initialize settings object
settings = Settings()
settings.input.property._h = "ACTIVITYCOEF"
settings.input.temperature = 298.15
```

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```
compounds = [Settings() for i in range(len(files))]
for i, (name, frac) in enumerate(zip(files, fracs)):
    compounds[i]._h = os.path.join(database_path, name)
    compounds[i].frac1 = frac

settings.input.compound = compounds

# Here, we will change the method parameters specific to COSMO-RS
# Main CRS parameters
settings.input.CRSParameters.rav = 0.400
settings.input.CRSParameters.aprime = 1510.0
settings.input.CRSParameters.fcorr = 2.802
settings.input.CRSParameters.chb = 8850.0
settings.input.CRSParameters.sigmahbond = 0.00854
settings.input.CRSParameters.aeff = 6.94
settings.input.CRSParameters.Lambda = 0.130
settings.input.CRSParameters.omega = -0.212
settings.input.CRSParameters.eta = -9.65
settings.input.CRSParameters.chortf = 0.816
settings.input.CRSParameters.HB_HNOF = ""  # hb for only H,N,O,F
# settings.input.CRSParameters.HB_ALL     = "" # hb for all elements
settings.input.CRSParameters.HB_TEMP = ""  # temperature-dependent H-bond
# settings.input.CRSParameters.HB_NOTEMP  = "" # non-temperature-dependent H-bond
settings.input.CRSParameters.COMBI2005 = ""  # default combinatorial term
# settings.input.CRSParameters.COMBI1998  = ""

# Dispersion parameters
settings.input.Dispersion.H = -0.0340
settings.input.Dispersion.C = -0.0356
settings.input.Dispersion.N = -0.0224
settings.input.Dispersion.O = -0.0333
settings.input.Dispersion.F = -0.026
settings.input.Dispersion.Si = -0.04
settings.input.Dispersion.P = -0.045
settings.input.Dispersion.S = -0.052
settings.input.Dispersion.Cl = -0.0485
settings.input.Dispersion.Br = -0.055
settings.input.Dispersion.I = -0.062

# Technical and accuracy parameters
settings.input.Technical.rsconv = 1e-7
settings.input.Technical.maxiter = 10000
settings.input.Technical.bpconv = 1e-6
settings.input.Technical.bpmaxiter = 40
settings.input.Technical.solconv = 1e-5
settings.input.Technical.solmaxiter = 40
settings.input.Technical.solxilarge = 0.99
settings.input.Technical.ehdeltaT = 1.0

# We will vary the chb parameter (default value 8850.0)
# and observe the effect on activity coefficients

print("Resulting Activity Coefficients:")
print("chb value".ljust(15), "activity coefficients".ljust(20))
hbvals = [8700.0 + 50 * i for i in range(7)]
for hbval in hbvals:
```

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```
    settings.input.CRSParameters.chb = hbval
    # create a job that can be run by COSMO-RS
    my_job = CRSJob(settings=settings)
    # run the job
    out = my_job.run()
    # convert all the results into a python dict
    res = out.get_results()

    print(str(hbval).ljust(15), str(res["gamma"].flatten()).ljust(20))

finish()
```

Python code (COSMO-SAC parameters)

```
import os
from scm.plams import Settings, init, finish, CRSJob, config

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

init()
# suppress plams output
config.log.stdout = 0

# our system of interest
files = ["Acetone.coskf", "Water.coskf"]
fracs = [0.3, 0.7]

# initialize settings object
settings = Settings()
settings.input.property._h = "ACTIVITYCOEF"
settings.input.temperature = 298.15

compounds = [Settings() for i in range(len(files))]
for i, (name, frac) in enumerate(zip(files, fracs)):
    compounds[i]._h = os.path.join(database_path, name)
    compounds[i].frac1 = frac

settings.input.compound = compounds

# Here, we will change the method parameters specific to COSMO-SAC
# First, change the method to COSMOSAC2013
settings.input.method = "COSMOSAC2013"

# Main SAC parameters
settings.input.SACParameters.aeff = 6.4813
settings.input.SACParameters.fdecay = 0.0
settings.input.SACParameters.sigma0 = 0.01233
settings.input.SACParameters.rn = 0.0
settings.input.SACParameters.qn = 79.532
```

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```
settings.input.SACParameters.aes = 7877.13
settings.input.SACParameters.bes = 0.0
settings.input.SACParameters.cohoh = 5786.72
settings.input.SACParameters.cotot = 2739.58
settings.input.SACParameters.cohot = 4707.75
settings.input.SACParameters.rav = 0.51
settings.input.SACParameters.qs = 0.57
settings.input.SACParameters.rhbcut = 0.0
settings.input.SACParameters.omega = 0.0
settings.input.SACParameters.eta = 0.0
settings.input.SACParameters.HB_NOTEMP = ""  # non-temperature-dependent H-bonding
↪(default)
# settings.input.SACParameters.HB_TEMP = "" # temperature-dependent H-bonding

# Epsilon Constants
settings.input.Epsilon.H = 338.13
settings.input.Epsilon["C.sp3"] = 29160.92
settings.input.Epsilon["C.sp2"] = 30951.83
settings.input.Epsilon["C.sp"] = 20685.98
settings.input.Epsilon["N.sp3"] = 23488.54
settings.input.Epsilon["N.sp2"] = 22663.38
settings.input.Epsilon["N.sp"] = 6390.40
settings.input.Epsilon["O.sp3-H"] = 8527.06
settings.input.Epsilon["O.sp3"] = 8484.38
settings.input.Epsilon["O.sp2"] = 6736.85
settings.input.Epsilon["O.sp2-N"] = 12145.28
settings.input.Epsilon.F = 8435.13
settings.input.Epsilon.P = 82512.21
settings.input.Epsilon.S = 56067.81
settings.input.Epsilon.Cl = 45065.19
settings.input.Epsilon.Br = 62947.83
settings.input.Epsilon.I = 105910.88

# Technical and accuracy parameters
settings.input.Technical.sacconv = 1e-7
settings.input.Technical.maxiter = 10000
settings.input.Technical.bpconv = 1e-6
settings.input.Technical.bpmaxiter = 40
settings.input.Technical.solconv = 1e-5
settings.input.Technical.solmaxiter = 40
settings.input.Technical.solxilarge = 0.99
settings.input.Technical.ehdeltaT = 1.0

# We will vary the cohot parameter (default value 4707.75)
# and observe the effect on activity coefficients
print("Resulting Activity Coefficients:")
print("cohot value".ljust(15), "activity coefficients".ljust(20))
cohot_vals = [4707.75 + 50 * i for i in range(-3, 4)]
for cohot in cohot_vals:

    settings.input.SACParameters.cohot = cohot
    # create a job that can be run by COSMO-RS
    my_job = CRSJob(settings=settings)
    # run the job
    out = my_job.run()
    # convert all the results into a python dict
    res = out.get_results()
```

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```
    print(str(cohot).ljust(15), str(res["gamma"].flatten()).ljust(20))

finish()
```

Solubility screening for solid solute

`Download relevant coskf file`

In this example, we explore the solubility of avobenzone in several solvents and compare the predicted solubility with experimental data[1]. When conducting solid solubility calculations, it's crucial to provide the melting point and melting enthalpy of the solid solute. If experimental melting properties are not available, it's possible to estimate these values using the pure properties prediction tool, which is based on the group contribution method. Alternatively, the ranking of solubility can also be compared using the infinite dilution activity coefficient.

In the first script example, it utilizes the *pyCRS.Database* (page 82) and *pyCRS.CRSManager* (page 84) modules to systematically set up solubility calculations and infinite dilution activity coefficients calculation. These modules significantly simplify the process, providing users with a direct and efficient method to perform high-throughput screening tasks.

Python code using pyCRS

```
from scm.plams import Settings, init, finish, CRSJob, config, JobRunner, KFFile
from pyCRS.Database import COSKFDatabase
from pyCRS.CRSManager import CRSSystem
import os, glob, multiprocessing
import matplotlib.pyplot as plt
import numpy as np

init()

####### Step 1 : add compounds to a pyCRS.databse. Ensure coskf_solubility is␣
↪downloaded #######

#######  Note: Ensure to download the coskf_solubility before running the script  ####
↪##########

db = COSKFDatabase("my_coskf_db.db")

coskf_path = os.path.join(os.getcwd(), "coskf_solubility")

if not os.path.exists(coskf_path):
    raise OSError(f"The provided path does not exist. Exiting.")

files = glob.glob(os.path.join(coskf_path, "*.coskf"))
for f in files:

    coskf = os.path.basename(f)

    if coskf == "avobenzone.coskf":
        db.add_compound(
            coskf,
```

(continues on next page)

[1] Benazzouz, Adrien, et al. "Hansen approach versus COSMO-RS for predicting the solubility of an organic UV filter in cosmetic solvents." Colloids and Surfaces A: Physicochemical and Engineering Aspects 458 (2014): 101-109.

(continued from previous page)

```
            name="avobenzone",
            cas="70356-09-1",
            coskf_path=coskf_path,
        )
        db.add_physical_property("avobenzone", "meltingpoint", 347.6)
        db.add_physical_property("avobenzone", "hfusion", 5.565, unit="kcal/mol")
        db.estimate_physical_property("avobenzone")

    else:
        db.add_compound(coskf,coskf_path=coskf_path)


# Experimental solubility data in %w/w
exp_data = {
    "Glycerol": 0.1,
    "1,2-Propylene glycol": 0.2,
    "Hexadecane": 1,
    "Ethanol": 2,
    "Di-n-octyl ether": 5,
    "beta-Pinene": 7.7,
    "Isopropyl myristate": 10,
    "Propylene carbonate": 10.7,
    "Di-2-ethylhexyl-adipate": 12,
    "Dimethyl-isosorbide": 38.2,
    "Dimethoxymethane": 73,
}

####### Step2 : Iterately set up calculation for solubility and activitycoef #######

## Set up for parallel run ##
if True:
    config.default_jobrunner = JobRunner(
        parallel=True, maxjobs=8
    )  # Set jobrunner to be parallel and specify the numbers of jobs run␣
↪simutaneously (eg. multiprocessing.cpu_count())
    config.default_jobmanager.settings.hashing = None  # Disable rerun prevention
    config.job.runscript.nproc = 1  # Number of cores for each job
    config.log.stdout = 1  # suppress plams output default=3

System = CRSSystem()
System2 = CRSSystem()

for solvent in exp_data.keys():
    mixture = {}
    mixture[solvent] = 1.0
    mixture["avobenzone"] = 0.0

    System.add_Mixture(
        mixture,
        database="my_coskf_db.db",
        temperature=298.15,
        problem_type="solubility",
        solute="solid",
        jobname="solubility",
    )
    System2.add_Mixture(
        mixture, database="my_coskf_db.db", temperature=298.15, problem_type=
↪"activitycoef", jobname="IDAC"
```

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```
    )


System.runCRSJob()
System2.runCRSJob()

####### Step3 : Output processing to retrive results for plotting #######

solubility = []
lnIDAC = []
for out, out2 in zip(System.outputs, System2.outputs):
    res = out.get_results()
    res2 = out2.get_results()

    solubility.append(res["solubility massfrac"][1][0] * 100)
    lnIDAC.append(np.log(res2["gamma"][1][0]))


plt.rcParams["figure.figsize"] = (9, 4)
fig, axs = plt.subplots(1, 2)
axs[0].plot(solubility, exp_data.values(), "o", color="Red", markerfacecolor="none")
axs[0].plot([-5, 80], [-5, 80], color="gray")
axs[0].set_xlim([-5, 80])
axs[0].set_ylim([-5, 80])
axs[0].set_xlabel("predicted solubility(%w/w)")
axs[0].set_ylabel("experimental solubility(%w/w)")

axs[1].plot(lnIDAC, exp_data.values(), "o", color="Blue", markerfacecolor="none")
axs[1].set_xlabel("ln(infinite dilution activitycoef) ")
axs[1].set_ylabel("experimental solubility(%w/w)")
plt.tight_layout()
# plt.savefig('./pyCRS_solubility_screening.png',dpi=300)
plt.show()

finish()
```

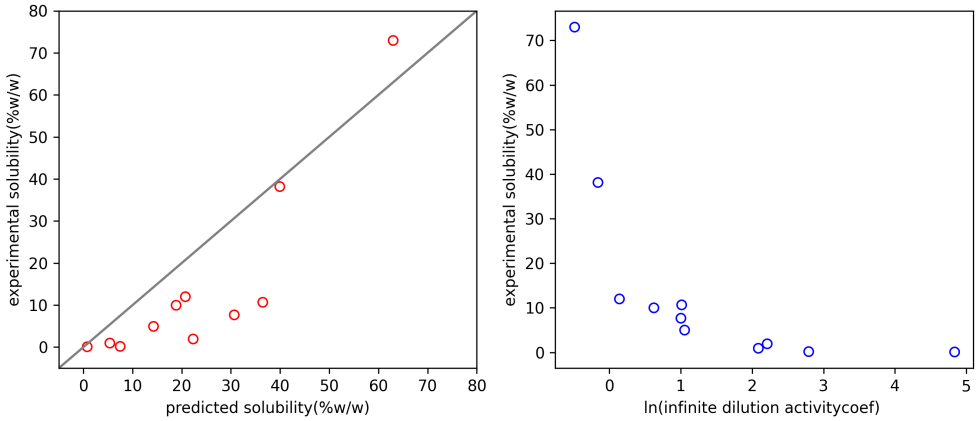

Fig. 10.5: The comparison of experimental solubility with (1) predicted solubility and (2) infinite dilution activity coefficient.

In the second script example, the solubility screening is configured using the *set_CRSJob_solubility* function within the script. While this approach require appropriately setting up the *PLAMS input setting* (page 106) within the function, it

provide greater flexibility for configuring unconventional calculations, such as *ionic liquids screening* (page 140).

Python code using PLAMS

```
import os, time
import multiprocessing
import numpy as np
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config, JobRunner

init()

#######  Note: Ensure to download the coskf_solubility before running the script  ####
↪###


def set_CRSJob_solubility(index, ncomp, coskf, database_path, cal_type, method,␣
↪temperature, comp_input={}):

    s = Settings()  # initialize a settings object
    s.input.property._h = cal_type  # specify problem type
    s.input.method = method  # specify method
    s.input.temperature = temperature  # specify temperature

    compounds = [Settings() for i in range(ncomp)]  # initialization of compounds
    for i in range(ncomp):
        compounds[i]._h = os.path.join(database_path, coskf[i])  # specify absolute␣
↪directory of coskf file
        for column, value in comp_input.items():  # specify compound's information␣
↪through comp_input, for example
            if value[i] != None:  # column: frac1, meltingpoint, hfusion
                compounds[i][column] = value[i]
    s.input.compound = compounds

    my_job = CRSJob(settings=s)  # create jobs
    my_job.name = cal_type + "_" + str(index)  # specify job name

    return my_job


Parallel_run = True
Plot_option = True

if Parallel_run:
    config.default_jobrunner = JobRunner(
        parallel=True, maxjobs=8
    )  # Set jobrunner to be parallel and specify the numbers of jobs run␣
↪simutaneously (eg. multiprocessing.cpu_count())
    config.default_jobmanager.settings.hashing = None  # Disable rerun prevention
    config.job.runscript.nproc = 1  # Number of cores for each job
    config.log.stdout = 1  # suppress plams output default=3

###----INPUT YOUR DATA HERE----###

database_path = os.path.join(os.getcwd(), "coskf_solubility")
cal_type = "solubility"
```

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```
method = "COSMORS"
ncomp = 2
solvents = [
    "Glycerol.coskf",
    "1,2-Propylene_glycol.coskf",
    "Hexadecane.coskf",
    "Ethanol.coskf",
    "Di-n-octyl_ether.coskf",
    "beta-Pinene.coskf",
    "Isopropyl_myristate.coskf",
    "Propylene_carbonate.coskf",
    "Di-2-ethylhexyl-adipate.coskf",
    "Dimethyl-isosorbide.coskf",
    "Dimethoxymethane.coskf",
]
solute = "avobenzone.coskf"

temperature = 298.15  # K

# store input data along with the necessary thermal property in comp_input dictionary
comp_input = {}
comp_input["name"] = ["solvent", "solute"]
comp_input["frac1"] = [1, 0]  # mole fraction
comp_input["meltingpoint"] = [None, 355]  # melting point(K)
comp_input["hfusion"] = [None, 5.565]  # heat of fusion(Kcal/mol)

# Experimental solubility data in %w/w
exp_sol = [0.1, 0.2, 1, 2, 5, 7.7, 10, 10.7, 12, 38.2, 73]

###----INPUT END----###

index = 0
outputs = []
for solv in solvents:
    coskf = [solv, solute]
    job = set_CRSJob_solubility(index, ncomp, coskf, database_path, cal_type, method,␣
↪temperature, comp_input)
    index = index + 1
    outputs.append(job.run())

print(job.get_input())


# In a parallel run, the get_results function will wait for the completion of the␣
↪corresponding jobs.
results = []
for out in outputs:
    results.append(out.get_results())

if Plot_option:
    if cal_type == "solubility":

        cal_sol = [res["solubility massfrac"][1][0] * 100 for res in results]
        cal_lnact = [np.log(res["gamma"][1][0]) for res in results]

        plt.figure(figsize=(5, 4))
        plt.plot(cal_sol, exp_sol, "o", color="Red", markerfacecolor="none",␣
↪label=method)
```

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```
        plt.plot([-5, 80], [-5, 80], color="gray")
        plt.xlim([-5, 80])
        plt.ylim([-5, 80])
        plt.xlabel("predicted solubility(%w/w)")
        plt.ylabel("experimental solubility(%w/w)")

        plt.tight_layout()
        # plt.savefig('./PLAMS_solubility_screening.png',dpi=300)
        plt.show()

finish()
```

References

Screening for cocrystals

In this section, we provide an example application that can be used as a template for many high-throughput screening scripts. Cocrystals are crystals formed from two or more compounds in a defined stoichiometry. There are many uses for cocrystals, especially for pharmaceutical applications where one compound is an active pharmaceutical ingredient (API). This example problem screens multiple compounds for their potential as components of a (1:2) cocrystal with Itraconazole. This problem uses the excess enthalpy for a hypothetical supercooled liquid phase as a proxy for cocrystallization affinity. The rankings of the solvents are in good agreement with model and experimental results for this problem given in[1] .

Download relevant coskf file: coskf_Hex.zip

Python code

```
import os, time
import multiprocessing
import numpy as np
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config, JobRunner


def set_CRSJob_Hex_conf(index, ncomp, coskf, database_path, cal_type, method,␣
↪temperature, comp_input={}, comp_type=[]):

    s = Settings()  # initialize a settings object
    s.input.property._h = cal_type  # specify problem type
    s.input.method = method  # specify method
    s.input.temperature = temperature  # specify temperature

    compounds = [Settings() for i in range(ncomp)]  # initialization of compounds
    for i in range(ncomp):
        if len(comp_type) > i:
            if "conf" in comp_type[i]:
                form = [Settings() for i in range(len(coskf[i]))]  # initialize␣
↪compound in multiple form
                for j in range(len(coskf[i])):
                    form[j]._h = os.path.join(
```

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[1] Abramov, Yuriy A., Christoph Loschen, and Andreas Klamt. "Rational coformer or solvent selection for pharmaceutical cocrystallization or desolvation." Journal of pharmaceutical sciences 101.10 (2012): 3687-3697. (https://doi.org/10.1002/jps.23227)

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```
                        database_path, coskf[i][j]
                    )  # specify conformer's coskf file for each form
                compounds[i].form = form
            else:
                compounds[i]._h = os.path.join(database_path, coskf[i])  # specify␣
↪absolute directory of coskf file
        else:
            compounds[i]._h = os.path.join(database_path, coskf[i])  # specify␣
↪absolute directory of coskf file

        for column, value in comp_input.items():  # specify compound's information␣
↪through comp_input, for example
            if value[i] != None:  # column: frac1, meltingpoint, hfusion
                compounds[i][column] = value[i]

    s.input.compound = compounds

    my_job = CRSJob(settings=s)  # create jobs
    my_job.name = cal_type + "_" + str(index)  # specify job name

    return my_job


init()

Parallel_run = True
Plot_option = True

if Parallel_run:
    config.default_jobrunner = JobRunner(
        parallel=True, maxjobs=8
    )  # Set jobrunner to be parallel and specify the numbers of jobs run␣
↪simutaneously (eg. multiprocessing.cpu_count())
    config.default_jobmanager.settings.hashing = None  # Disable rerun prevention
    config.job.runscript.nproc = 1  # Number of cores for each job
    config.log.stdout = 1  # suppress plams output default=3

###----INPUT YOUR DATA HERE----###

database_path = os.path.join(os.getcwd(), "coskf_Hex")
cal_type = "VAPORPRESSURE"
method = "COSMORS"
ncomp = 2
solute = "itz_c1.coskf"

# a list of different conformers for the screening each line contains 3 conformers of␣
↪the same molecule
solvents = [
    ["tartaric_acid_c1.coskf", "tartaric_acid_c2.coskf", "tartaric_acid_c3.coskf"],
    ["fumaric_acid_c1.coskf", "fumaric_acid_c2.coskf", "fumaric_acid_c3.coskf"],
    ["succinic_acid_c1.coskf", "succinic_acid_c2.coskf", "succinic_acid_c3.coskf"],
    ["malic_acid_c1.coskf", "malic_acid_c2.coskf", "malic_acid_c3.coskf"],
    ["glutaric_acid_c1.coskf", "glutaric_acid_c2.coskf", "glutaric_acid_c3.coskf"],
    ["malonic_acid_c1.coskf", "malonic_acid_c2.coskf", "malonic_acid_c3.coskf"],
    ["adipic_acid_c1.coskf", "adipic_acid_c2.coskf", "adipic_acid_c3.coskf"],
    ["maleic_acid_c1.coskf", "maleic_acid_c2.coskf", "maleic_acid_c3.coskf"],
]
```

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```
temperature = 298.15  # K

# store input data along with the necessary thermal property in comp_input dictionary
comp_input = {}
comp_input["frac1"] = [0.33333, 0.66667]  # the stoichiometric ratio of the co-
↪crystal (solvent:solute)

# enter 'conf' for compound with multiple conformers; '' for compound with single␣
↪structure
comp_type = ["conf", ""]

###----INPUT END----###

outputs = []
solv_name = []
for index, solv in enumerate(solvents):
    solv_name.append(solv[0].replace("_c1.coskf", ""))
    coskf = [solv, solute]
    comp_input["name"] = [solv[0].replace("_c1.coskf", ""), solute.replace("_c1.coskf
↪", "")]

    job = set_CRSJob_Hex_conf(index, ncomp, coskf, database_path, cal_type, method,␣
↪temperature, comp_input, comp_type)
    outputs.append(job.run())

finish()

# In a parallel run, the get_results function will wait for the completion of the␣
↪corresponding jobs.
results = []
excess_h = []
print("")
print("Solvent".ljust(14), "Population of solvent's conformers")
for out, name in zip(outputs, solv_name):
    res = out.get_results()
    results.append(res)
    excess_h.append(res["excess H"])

    compositions = out.get_multispecies_dist()[0]
    print(name.ljust(15), end="")
    for conf, frac in compositions.items():
        print(f"{frac[0]:.5f}", end=" ")
    print("")

print("")
print("Solvent".ljust(15), "Excess enthalpy (kcal/mol)")
for (
    name,
    Hex,
) in zip(solv_name, excess_h):
    print(name.ljust(15), round(Hex, 5))


if Plot_option:
    plt_index = [i for i in range(len(excess_h))]
    plt.xlabel("Excess enthalpy (kcal/mol)")
```

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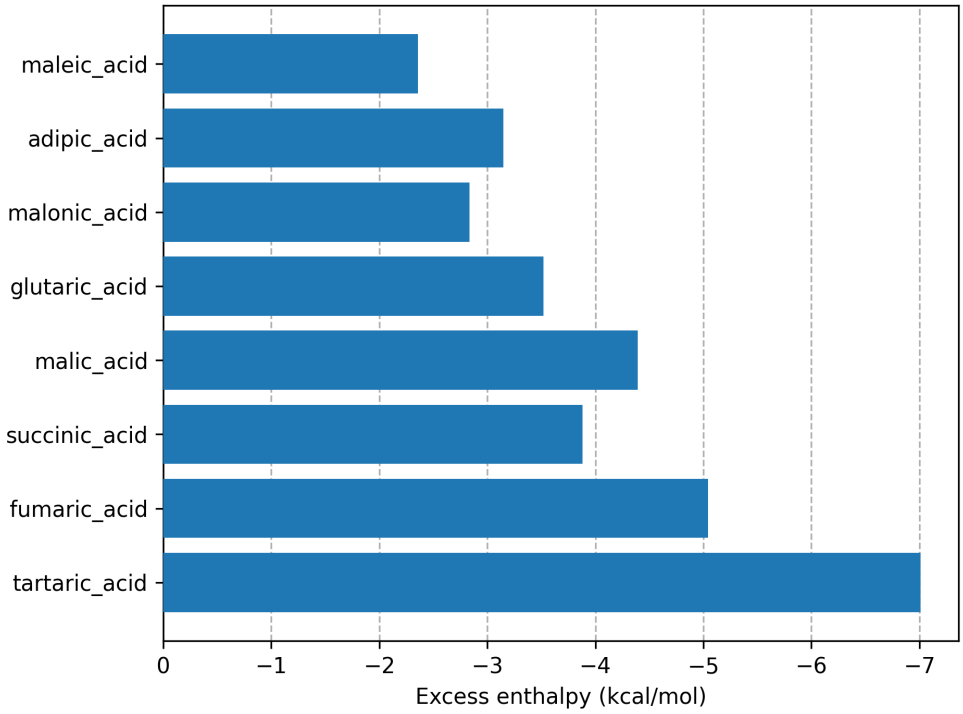
```
    plt.barh(plt_index, excess_h, zorder=3)
    plt.yticks(plt_index, solv_name)
    plt.grid(axis="x", ls="--", zorder=0)
    plt.gca().invert_xaxis()
    plt.tight_layout()
    # plt.savefig('./Cocrystal_screening.png',dpi=300)
    plt.show()
```

This figure (produced by the code) shows the excess enthalpy values of all solvents in a supercooled liquid mixture with Itraconazole. The lowest 4 excess enthalpy values correspond to 4 solvent for which a stable co-crystal with Itraconazole is known[?] .



References

Automated screening of ionic liquids

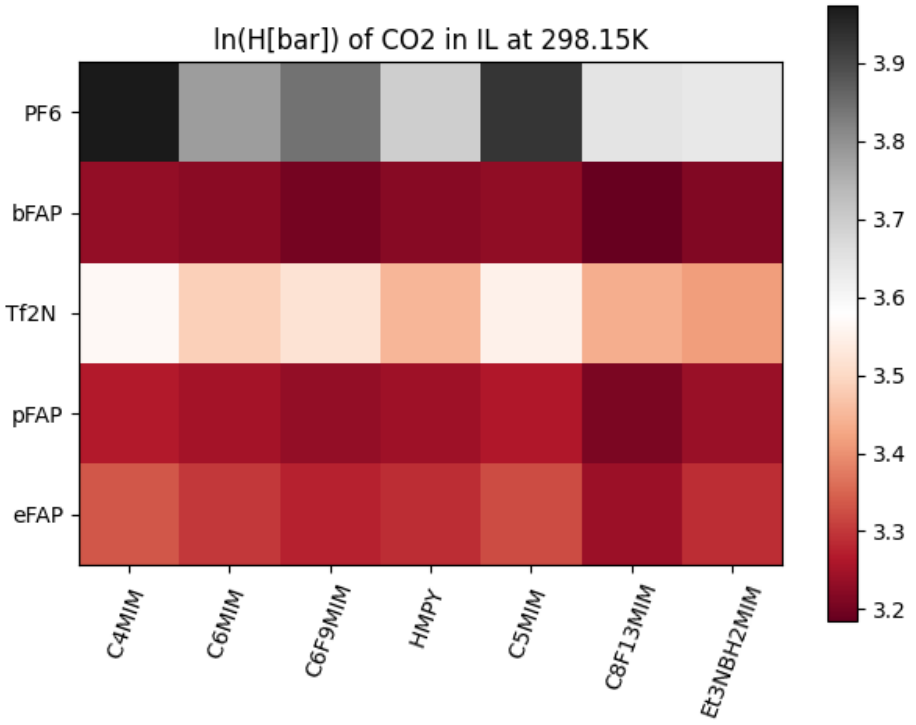
`Download python script and relevant file`

In this example, we provide a template for the high-throughput screening with ionic liquid. The script will automates the screening of the infinite dilution activity coefficient (IDAC) of a solute among all combinations of available ionic liquids in the directory. The *set_CRSJob_IL* in this script adopt the same structure as *set_CRSJob_Hex_conf* in previous example but have an additional input variable, *comp_stoichiometric*, to specify the stoichiometric number of cation and anion. The stoichiometric number will be determined from their charge, and it is crucial to ensure that the **IL_list.csv** file contains the minimum required information for each ion, such as abbreviation, charge and coskf file name. Furthermore, if the vapor pressure of the solute (Pvap) is provided, you can calculate the Henry's constant and solute solubility at 1 bar under

the assumption of ideal gas by setting cal_Henry=True.

$$H(bar) = IDAC * Pvap$$
$$x(1bar) = 1bar/H(bar)$$

This figure (produced by the code) illustrates the screening outcomes for carbon dioxide involving 7 cations and 5 anions which have proven to be useful tool for searching good candidates[1] .



Python code

```
import os, sys, time, glob
import multiprocessing
import numpy as np
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config, JobRunner
import pandas as pd
from math import gcd

#######  Note: Ensure to download the coskf_IL before running the script  #######

"""
The Python script automates the screening of the infinite dilution activity␣
↪coefficient (IDAC)
of a solute among all combinations of available ionic liquids in the corresponding␣
↪directory.
```

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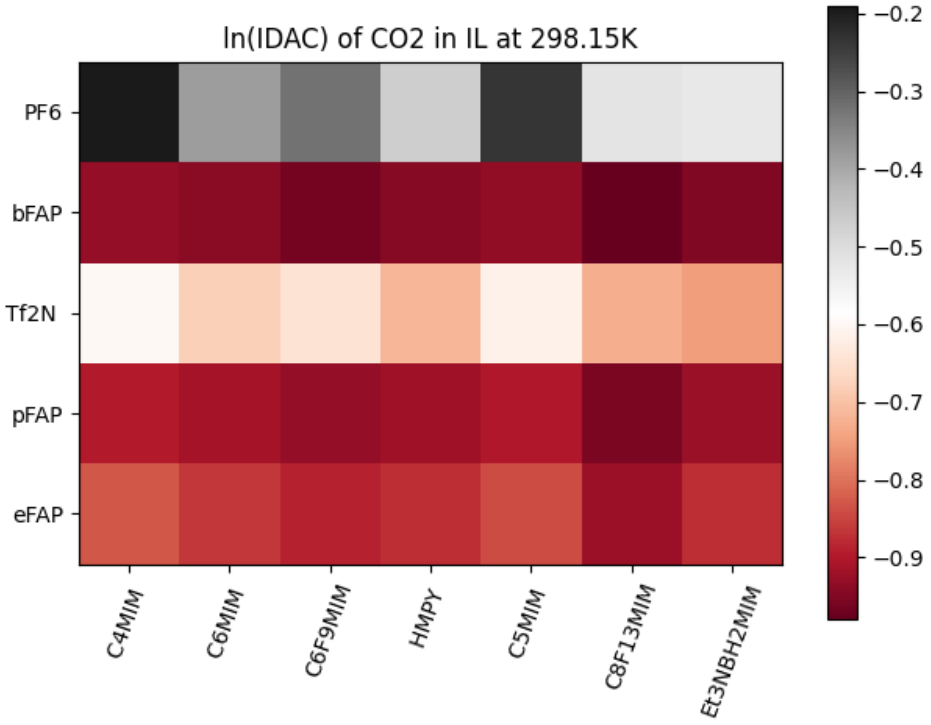
[1] Zhang, Xiaochun, Zhiping Liu, and Wenchuan Wang. "Screening of ionic liquids to capture CO2 by COSMO-RS and experiments." AIChE journal 56.10 (2008): 5617-5628.



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```
To run the script, ensure that the coskf file of ions and solute is stored in the␣
↪database_path
and the coskf file of ions follows a specific naming convention, such as IL_*cation_*.
↪coskf or IL_*anion_*.coskf.
For example, you should have files like IL_cation_1-butyl-3-methyl-imidazolium.coskf,
IL_anion_hexafluorophosphate.coskf and Carbon_dioxide.coskf in ./coskf-IL/

Additionally, you need to provide the ion's information in the IL_list.csv file as␣
↪input including:
    name, [abbreviation], type, charge, coskf, smiles(optional)
    1-butyl-3-methyl-imidazolium, [C4MIM ; C4C1im ; BMIM], cation, 1.0, IL_cation_1-
↪butyl-3-methyl-imidazolium.coskf, CCCCn1cc[n+](C)c1
The IL_list.csv file contain the information of 80 cations and 56 anions in the␣
↪ADFCRS-IL-2014 database.

Furthermore, if the vapor pressure of the solute (Pvap) is provided, you can␣
↪calculate the Henry's constant and
solute solubility at 1 bar under the assumption of ideal gas by setting cal_
↪Henry=True.
    H(bar) = IDAC*Pvap
    x(1bar)= 1bar/H

The parallel calculation can be enabled by setting the Parallel_run=True and␣
↪maxjobs=numners_of_processes.

The calculated result will be saved in a pandas dataframe (df) and a csv file (result_
↪csv='IL_screening.csv').

The visualization of the result using a contour plot can be enable by setting Plot_
↪option=True.
```

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```
Please ensure that you have installed the Pandas library. It's recommended to install␣
↪it through AMSpackages.
    "${AMSBIN}/amspackages" install pandas
"""

init()


def set_CRSJob_IL(
    index,
    ncomp,
    coskf,
    database_path,
    cal_type,
    method,
    temperature,
    comp_input={},
    comp_type=[],
    comp_stoichiometric=[],
):

    s = Settings()  # initialize a settings object
    s.input.property._h = cal_type  # specify problem type
    s.input.method = method  # specify method
    s.input.temperature = temperature  # specify temperature

    compounds = [Settings() for i in range(ncomp)]  # initialization of compounds
    for i in range(ncomp):
        if len(comp_type) > i:
            if "conf" in comp_type[i]:
                form = [Settings() for i in range(len(coskf[i]))]  # initialize␣
↪compound in multiple form
                for j in range(len(coskf[i])):
                    form[j]._h = os.path.join(
                        database_path, coskf[i][j]
                    )  # specify conformer's coskf file for each form
                compounds[i].form = form
            elif "IL" in comp_type[i]:
                form = [Settings() for j in range(1)]  # initialize IL in one form:␣
↪dissociated IL
                species = [Settings() for j in range(2)]  # initialize dissociated IL␣
↪in two species: cation and anion
                for j in range(2):
                    struct = [Settings() for k in range(1)]  # initialize cation and␣
↪anion in one structure
                    struct[0]._h = os.path.join(database_path, coskf[i][j])
                    struct[0].count = comp_stoichiometric[i][j]  # specify the␣
↪Stoichiometric number of cation and anion
                    species[j] = struct
                form[0].species = species
                compounds[i].form = form
            else:
                compounds[i]._h = os.path.join(database_path, coskf[i])  # specify␣
↪absolute directory of coskf file
        else:
            compounds[i]._h = os.path.join(database_path, coskf[i])  # specify␣
↪absolute directory of coskf file
```

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```
        for column, value in comp_input.items():  # specify compound's information␣
↪through comp_input, for example
            if value[i] != None:  # column: frac1, meltingpoint, hfusion
                compounds[i][column] = value[i]

    s.input.compound = compounds

    my_job = CRSJob(settings=s)  # create jobs
    my_job.name = cal_type + "_" + str(index)  # specify job name

    return my_job


Parallel_run = True  # If True -> parallel calculation
cal_Henry = True  # If True -> calculation of Henry's constant using IDAC*Pvap
Plot_option = True  # If True -> visualization of the results with a contour plot

if Parallel_run:
    config.default_jobrunner = JobRunner(
        parallel=True, maxjobs=8
    )  # Set jobrunner to be parallel and specify the numbers of jobs run␣
↪simutaneously (eg. multiprocessing.cpu_count())
    config.default_jobmanager.settings.hashing = None  # Disable rerun prevention
    config.job.runscript.nproc = 1  # Number of cores for each job
    config.log.stdout = 1  # suppress plams output default=3

###----INPUT YOUR DATA HERE----###

database_path = os.path.join(os.getcwd(), "coskf_IL")
cal_type = "activitycoef"
method = "COSMORS"
ncomp = 2
solute = "Carbon_dioxide.coskf"
solute_abb = "CO2"
temperature = 298.15

# Retrive all coskf file for cation and anion in database_path. Note the file must be␣
↪named as: IL_*cation_*.coskf and IL_*anion*.coskf
cations_coskf = [os.path.basename(x) for x in glob.glob(os.path.join(database_path,
↪"IL_*cation_*.coskf"))]
anions_coskf = [os.path.basename(x) for x in glob.glob(os.path.join(database_path,
↪"IL_*anion_*.coskf"))]

# store input data along with the necessary thermal property in comp_input dictionary
comp_input = {}
comp_input["frac1"] = [1.0, 0.0]

# enter 'IL' for ionic liquid; 'conf' for compound with multiple conformers; '' for␣
↪compound with single structure
comp_type = ["IL", ""]

# Read ion's information from IL_list.csv where contain name, [abbreviation], type,␣
↪charge, coskf, smiles(optional)
df_IL = pd.read_csv("IL_list.csv")

# Write the screening result
```

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```
result_csv = "result_IL_screening.csv"

###----INPUT END----###

index = 0
outputs = []
df = pd.DataFrame()
for cation in cations_coskf:
    for anion in anions_coskf:

        cur_df = df_IL.loc[df_IL["coskf"] == cation]
        cation_abb = cur_df["abbreviation"].values[0].split(";")[0].rstrip()  #␣
↪abbreviation
        cation_charge = int(cur_df["charge"].values[0])  # charge

        cur_df = df_IL.loc[df_IL["coskf"] == anion]
        anion_abb = cur_df["abbreviation"].values[0].split(";")[0].rstrip()  #␣
↪abbreviation
        anion_charge = int(cur_df["charge"].values[0])  # charge

        # find the Least Common Multiple of cation charge and anion charge
        IL_lcm = cation_charge * anion_charge / gcd(cation_charge, anion_charge)
        cation_v = -IL_lcm / cation_charge  # stoichiometric number of cation
        anion_v = IL_lcm / anion_charge  # stoichiometric number of anion

        IL_abb = [cation_abb, anion_abb]  # abbreviation
        IL_coskf = [cation, anion]
        IL_v = [cation_v, anion_v]  # stoichiometric number

        coskf = [IL_coskf, solute]
        comp_stoichiometric = [IL_v, 1.0]  # stoichiometric number used for multi-
↪species

        comp_input["name"] = [cation_abb + "_" + anion_abb, solute_abb]

        df.loc[index, "cation"] = cation_abb
        df.loc[index, "anion"] = anion_abb
        df.loc[index, "solute"] = solute.replace(".coskf", "")
        df.loc[index, "charge_c"] = int(cation_charge)
        df.loc[index, "charge_a"] = int(anion_charge)

        job = set_CRSJob_IL(
            index,
            ncomp,
            coskf,
            database_path,
            cal_type,
            method,
            temperature,
            comp_input,
            comp_type,
            comp_stoichiometric,
        )
        outputs.append(job.run())

        index = index + 1
```

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```
# In a parallel run, the get_results function will wait for the completion of the␣
↪corresponding jobs.
results = []
for index, out in enumerate(outputs):
    res = out.get_results()
    results.append(res)
    df.loc[index, "IDAC"] = res["gamma"][-1][0]

if cal_Henry:
    if solute == "Carbon_dioxide.coskf":
        Pvap = np.power(10, 6.35537 - 2067.0 / (temperature + 156.462))
        # antonie equation(unit in bar), parameters are fitted by SCM in temperature␣
↪range 260-305K
    else:
        Pvap = np.nan
        print("The vapor pressure of the solute is not defined")
    if not np.isnan(Pvap):
        df["H(bar)"] = df["IDAC"] * Pvap
        df["x(1bar)"] = 1 / (df["IDAC"] * Pvap)

df.to_csv(result_csv, index=None)


if Plot_option:
    # contour visulization
    nx = len(cations_coskf)
    ny = len(anions_coskf)

    # Extract the 1st abbreviation of the ions. For instance, [C4MIM ; C4C1im ; BMIM]␣
↪-> C4MIM
    cation_name = [df_IL.loc[df_IL["coskf"] == x]["abbreviation"].values[0].split(";
↪")[0] for x in cations_coskf]
    anion_name = [df_IL.loc[df_IL["coskf"] == x]["abbreviation"].values[0].split(";
↪")[0] for x in anions_coskf]

    x = [i for i in range(nx)]
    y = [i for i in range(ny)]

    if cal_Henry and not np.isnan(Pvap):
        cal_data = df["H(bar)"].values
        sub_title = "ln(H[bar]) of " + solute_abb + " in IL at " + str(temperature) +
↪"K"
        fig_title = "IL_screening_lnH.png"
    else:
        cal_data = df["IDAC"].values
        sub_title = "ln(IDAC) of " + solute_abb.replace("_", " ") + " in IL at " +␣
↪str(temperature) + "K"
        fig_title = "IL_screening_lnIDAC.png"

    plt_data = np.zeros((ny, nx))
    for i in range(ny):
        for j in range(nx):
            plt_data[i][j] = np.log(cal_data[j * ny + i])

    fig, ax = plt.subplots()
```

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```
    plt.imshow(plt_data, cmap="RdGy", interpolation="nearest")
    if len(x) > 10:
        x = [0 + 5 * n for n in range((len(x) // 5) + 1)]
        plt.xticks(x, x, rotation=70)
    else:
        plt.xticks(x, cation_name, rotation=70)
    if len(y) > 10:
        y = [0 + 5 * n for n in range((len(y) // 5) + 1)]
        plt.yticks(y, y)
    else:
        plt.yticks(y, anion_name)
    plt.colorbar()
    plt.title(sub_title)
    plt.tight_layout()
    # plt.savefig(fig_title)
    plt.show()

finish()
```

References

Calculating and estimating sigma profiles

Sigma profiles are one of the fundamental pieces of a COSMO-RS/-SAC calculation. They are also widely used as an important empirical descriptor for a molecule's behavior in a solution as well as for a molecule's properties in a number of applications. In the standard COSMO-RS/-SAC workflow, sigma profiles are generated after a sequence of DFT calculations which – for large molecular systems – can take considerable time to complete. For computationally expensive systems or high-throughput screening applications, it is sometimes advantageous to approximate sigma profiles using tools like `fast_sigma` from AMS.

In the following python script, we generate sigma profiles for n-Hexanoic acid using the two approaches discussed above. The function `calc_sigma_profile` will generate sigma profiles from `.coskf` files, and the function `fast_sigma` will generate sigma profiles from SMILES strings using the `fast_sigma` tool.

Python code

```
import os
import numpy as np
import matplotlib.pyplot as plt

from scm.utils.runsubprocess import RunSubprocess
from scm.plams import Settings, init, finish, CRSJob, config, KFFile
import subprocess

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

init()
```

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```
# suppress plams output
config.log.stdout = 0


class SigmaProfile:
    def __init__(self, chdens, profiles, profile_names):
        if len(profiles) != len(profile_names):
            print("Error: profiles_names and profiles of different sizes")
        self.chdens = chdens.flatten() if isinstance(chdens, np.ndarray) else chdens
        self.profiles = {
            name: prof.flatten() if isinstance(prof, np.ndarray) else prof
            for name, prof in zip(profile_names, profiles)
        }

    def __str__(self):
        line = "-" * (15 * (1 + len(self.profiles)))
        ret = (
            line
            + "\n"
            + "".join(["Charge Dens.".ljust(15)] + [name.ljust(15) for name in self.
↪profiles])
            + "\n"
            + line
            + "\n"
        )
        for i in range(len(self.chdens)):
            ret += "{0:.5g}".format(self.chdens[i]).ljust(15) + "".join(
                ["{0:.5g}".format(v[i]).ljust(15) for k, v in self.profiles.items()]
            )
            ret += "\n"
        return ret


def fast_sigma(smiles):

    results_file = "tmp_results18954.compkf"
    subprocess_string = " --smiles '" + smiles + "'"

    if not os.path.isfile(os.path.join(os.path.expandvars("$AMSBIN"), "fast_sigma")):
        raise OSError("ERROR: cannot find fast_sigma ... has amsbashrc been executed?
↪")

    fs = os.path.join(os.path.expandvars("$AMSBIN"), "fast_sigma")
    scm_sp = RunSubprocess(fs + subprocess_string + " -o " + results_file)

    if os.path.isfile(results_file):
        crskf = KFFile(results_file)
        res = crskf.read_section("PURESIGMAPROFILE")
        sp = SigmaProfile(
            chdens=res["chdval"],
            profiles=[res["profil"], res["hbprofil"]],
            profile_names=["total_profile", "HB_profile"],
        )
        os.remove(results_file)
        return sp, scm_sp
    else:
        return None, scm_sp
```

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```
def calc_sigma_profile(coskf_file, cosmosac=False):

    # initialize settings object
    settings = Settings()
    settings.input.property._h = "SIGMAPROFILE"

    # set the number of compounds
    compounds = [Settings()]
    compounds[0]._h = os.path.join(database_path, coskf_file)
    compounds[0].frac1 = 1

    # to change to the COSMOSAC2013 method
    if cosmosac:
        settings.input.method = "COSMOSAC2013"

    # specify the compounds as the compounds to be used in the calculation
    settings.input.compound = compounds
    # create a job that can be run by COSMO-RS
    my_job = CRSJob(settings=settings)

    out = my_job.run()
    res = out.get_results()

    if cosmosac:
        prof_len = len(res["hbprofil"]) // 3
        sp = SigmaProfile(
            chdens=res["chdval"],
            profiles=[res["profil"]] + [res["hbprofil"][i * prof_len : (i + 1) * prof_
↪len] for i in range(3)],
            profile_names=["total_profile", "HB", "HB-OH", "HB-OT"],
        )
    else:
        sp = SigmaProfile(
            chdens=res["chdval"],
            profiles=[res["profil"], res["hbprofil"]],
            profile_names=["total_profile", "HB_profile"],
        )
    return sp


# regular way to generate a sigma profile from a .coskf file
filename = "n-Hexanoic_acid.coskf"
sp = calc_sigma_profile(filename, cosmosac=False)

# way using the fast_sigma estimation method
fs_sp, err = fast_sigma("CCCCCC(=O)O")
if fs_sp is None or len(err[1]) > 0:
    print("fast_sigma generated the following output:\n" + err[1])

plt.xlabel("σ value (e/A^2)")
plt.ylabel("p(σ)")

plt.plot(sp.chdens, sp.profiles["total_profile"], label="Calculated sigma profile")
if fs_sp is not None:
    plt.plot(fs_sp.chdens, fs_sp.profiles["total_profile"], label="Estimated sigma␣
↪profile")
```

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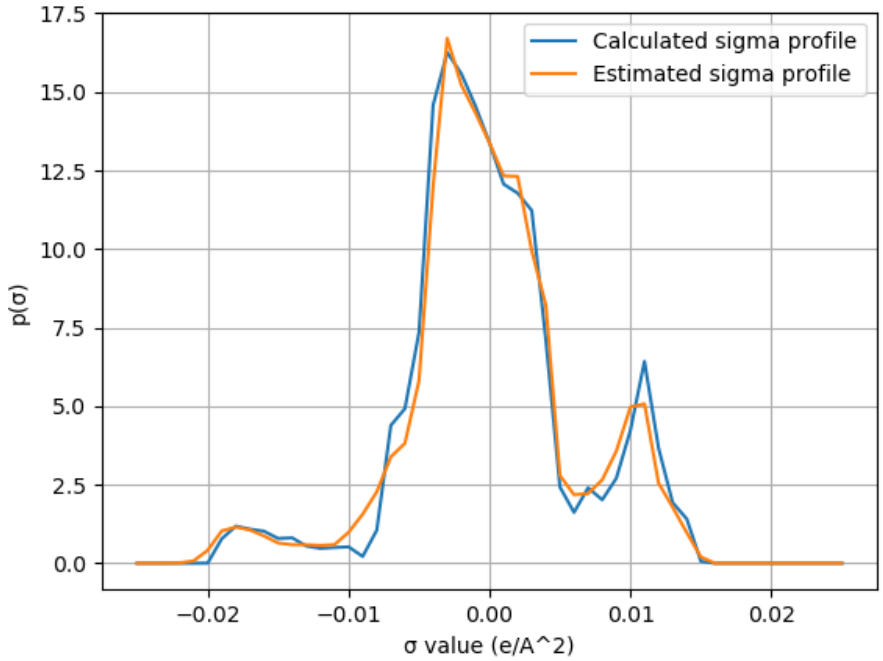
```
plt.legend(loc="upper right")
plt.grid()
# plt.savefig(f"./Sigma_profile.png")
plt.show()

finish()
```

This code produces the following output:



Sigma Moments

Sigma moments are useful chemical descriptors derived from the sigma profile. They are analogous to moments of a statistical distribution and can be thought of as a way to reduce the high-dimensional information present in a sigma profile to a smaller number of descriptors that characterize that sigma profile. Sigma moments are known to be valuable descriptors in QSPR and are thought to represent the solvent space well[1].

The following script will calculate the first several sigma moments as well as a H-bond acceptor and H-bond donor moment for a few common molecules.

[1] A. Klamt, *COSMO-RS From Quantum Chemistry to Fluid Phase Thermodynamics and Drug Design, Elsevier.* Amsterdam (2005), ISBN 0-444-51994-7.

Python code

```
import os
import numpy as np
from scm.plams import Settings, init, finish, CRSJob, config

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")


init()

# suppress plams output
config.log.stdout = 0


class SigmaMoments:

    def __init__(self, filenames, hb_cutoff=0.00854):
        self.filenames = filenames
        self.hb_cutoff = hb_cutoff

    def calculate_moments(self) -> dict:
        self.moments = {}
        self.calc_profiles_and_chdens()
        self.calc_standard_moments()
        self.calc_hb_moments()
        return self.moments

    def calc_profiles_and_chdens(self):

        # initialize settings object
        settings = Settings()
        settings.input.property._h = "PURESIGMAPROFILE"
        # set the cutoff value for h-bonding
        settings.parameters.sigmahbond = self.hb_cutoff
        compounds = [Settings() for i in range(len(self.filenames))]
        for i, filename in enumerate(filenames):
            compounds[i]._h = os.path.join(database_path, filename)

        settings.input.compound = compounds
        # create a job that can be run by COSMO-RS
        my_job = CRSJob(settings=settings)
        # run the job
        out = my_job.run()
        # convert all the results into a python dict
        res = out.get_results()
        # retain profiles and charge density values
        self.tot_profiles = res["profil"]
        self.hb_profiles = res["hbprofil"]
        self.chdens = res["chdval"]

    def calc_standard_moments(self, max_power=3):
```

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```
        for i in range(max_power + 1):
            tmp_moms = []
            for prof in self.tot_profiles:
                tmp_moms.append(np.sum(prof * np.power(self.chdens, i)))
            self.moments["MOM_" + str(i)] = tmp_moms

    def calc_hb_moments(self):
        self.moments["MOM_hb_acc"] = []
        self.moments["MOM_hb_don"] = []
        zeros = np.zeros(len(self.chdens))
        for prof in self.hb_profiles:
            self.moments["MOM_hb_acc"].append(np.sum(prof * np.maximum(zeros, self.
↪chdens - self.hb_cutoff)))
            self.moments["MOM_hb_don"].append(np.sum(prof * np.maximum(zeros, -self.
↪chdens - self.hb_cutoff)))


# the files we want to use to calculate sigma moments
filenames = ["Water.coskf", "Hexane.coskf", "Ethanol.coskf", "Acetone.coskf"]

sm = SigmaMoments(filenames)
moms = sm.calculate_moments()
max_mom_len = max([len(m) for m in moms])

print()
print((" " * 5).join(["Moment".ljust(max_mom_len)] + filenames))
lens = [len(fn) for fn in filenames]
for mom_name in moms:
    print(
        (" " * 5).join(
            [mom_name.ljust(max_mom_len)] + [("{0:.5g}".format(m)).rjust(l) for m, l␣
↪in zip(moms[mom_name], lens)]
        )
    )

finish()
```

The output produced is the following

```
Moment          Water.coskf     Hexane.coskf     Ethanol.coskf     Acetone.coskf
MOM_0                43.011           160.38            90.019            103.28
MOM_1            0.00026666         0.002145        0.00089555         0.0011418
MOM_2             0.0062556         0.001061         0.0046302          0.004566
MOM_3           -3.8253e-07       1.1557e-07        1.5947e-05         2.883e-05
MOM_hb_acc         0.078179                0           0.06562          0.068401
MOM_hb_don         0.078272                0          0.034516                 0
```

References

Eutectic systems

A eutectic point of a chemical mixture defines the minimum melting composition of that system over the composition range. In other words, the eutectic point will have a lower melting point than the pure components making up the mixture as well any other possible mixture. In this example, we calculate the eutectic point of a binary mixture of ethanol and water as the intersection of the solid-liquid equilibrium curves of two systems: (1) Solid ethanol dissolved in water and (2) Solid water dissolved in ethanol. This script will output the mole fraction of ethanol at the eutectic point as well as the temperature. For comparison, Takaizumi and Wakabayashi[1] provide an experimental eutectic point with a mole fraction value of 0.86 for ethanol and a melting temperature of -124.3 °C.

Python code

```
import os
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

init()
# suppress plams output
config.log.stdout = 0


# the ethanol water system
# experimental numbers for this eutectic are 0.86 mole fraction ethanol at a␣
↪temperature of -124.3 degrees C
files = ["Ethanol.coskf", "Water.coskf"]
tm = [158.5, 273.15]  # K
hfus = [1.2, 1.43]  # kcal/mol
initial_t_range = [100, 300]  # K -- the temperature range over which the eutectic␣
↪search is done
steps = 20  # number of steps to take within the temperature range

# another eutectic system
# files = ["L-Menthol.coskf","Camphor.coskf"]
# tm    = [316.2,451.5] #K
# hfus  = [2.84,1.63] #kcal/mol
# initial_t_range = [100,460] #K
# steps           = 20

# if we know the eutectic temperature is bounded to within a range of <= estimate_
↪precision, we simply use a linear interpolation between two x,T pairs
estimate_precision = 1.0  # K
```

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[1] Takaizumi, K., and T. Wakabayashi. "The freezing process in methanol-, ethanol-, and propanol-water systems as revealed by differential scanning calorimetry." Journal of solution chemistry 26.10 (1997): 927-939.

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```
class Eutectic:

    def __init__(self, files, tm, hfus, steps=10):
        self.files = files
        self.tm = tm
        self.hfus = hfus
        self.steps = steps

        if not (len(self.files) == len(self.tm) == len(self.hfus)):
            print("Error.  Inputs must be the same length.")

    def calc_xt_curves(self, t_range):

        # initialize settings object
        settings = Settings()
        settings.input.property._h = "SOLUBILITY"
        # optionally, change to the COSMOSAC2013 method
        settings.input.method = "COSMOSAC2013"

        # make compounds
        compounds = [Settings() for i in range(len(files))]
        for i, file in enumerate(self.files):
            compounds[i]._h = os.path.join(database_path, file)
            compounds[i].meltingpoint = self.tm[i]
            compounds[i].hfusion = self.hfus[i]

        comp1_fracs = []
        for i, frac1 in enumerate([0.0, 1.0]):
            compounds[0].frac1 = frac1
            compounds[1].frac1 = 1.0 - frac1

            settings.input.temperature = " ".join([str(t) for t in t_range] +␣
↪[str(self.steps)])

            # add the compounds to the settings object
            settings.input.compound = compounds
            # create a job that can be run by COSMO-RS
            my_job = CRSJob(settings=settings)
            # run the job
            out = my_job.run()
            # convert all the results into a python dict
            res = out.get_results()

            if i == 0:
                comp1_fracs.append(res["molar fraction"][0])
            else:
                comp1_fracs.append(1.0 - res["molar fraction"][1])

        return comp1_fracs

    def calc_eutectic(self, t_range, history=[[], [], []]):

        comp1_fracs = self.calc_xt_curves(t_range)

        # the temperatures used in the calculation
        temps = [t_range[0] + (t_range[1] - t_range[0]) / self.steps * i for i in␣
↪range(self.steps + 1)]
```

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```
        history[0].extend(comp1_fracs[0])
        history[1].extend(comp1_fracs[1])
        history[2].extend(temps)
        # the difference between compound 1's mole fraction in the two calculations
        # when these mole fractions are the same, we've found the eutectic
        diffs = comp1_fracs[0] - comp1_fracs[1]
        # find where the sign changes (intersection of SLE lines)
        for i in range(self.steps):
            if diffs[i] * diffs[i + 1] < 0:

                if temps[i + 1] - temps[i] < estimate_precision:
                    # use linear combination of t's
                    tot = abs(diffs[i]) + abs(diffs[i + 1])
                    w1 = tot - abs(diffs[i])  # same as abs(diffs[i+1])
                    w2 = tot - abs(diffs[i + 1])
                    return (
                        (
                            (w1 * comp1_fracs[0][i] + w2 * comp1_fracs[1][i + 1]) /␣
↪tot,
                            (w1 * temps[i] + w2 * temps[i + 1]) / tot,
                        )
                    ), history
                else:
                    return self.calc_eutectic([temps[i], temps[i + 1]], history)

        return None, None


eutectic_calc = Eutectic(files, tm, hfus, steps=steps)
eutectic, history = eutectic_calc.calc_eutectic(initial_t_range)

if not eutectic:
    print("No eutectic point found in the temperature range")
else:
    print("Found eutectic point:")
    print("x_1".rjust(10), "T (K)".rjust(10), "T (C)".rjust(10))
    x, t = eutectic
    print(str(x.round(5)).rjust(10), str(t.round(5)).rjust(10), str((-273.15 + t).
↪round(5)).rjust(10))

    # plot the solubility curves and eutectic point
    h_s1 = sorted(list(zip(history[0], history[2])), key=lambda x: x[0])
    h_s2 = sorted(list(zip(history[1], history[2])), key=lambda x: x[0])

    h_s1 = [x for x in h_s1 if x[0] >= eutectic[0] and x[1] >= eutectic[1]]
    h_s2 = [x for x in h_s2 if x[0] <= eutectic[0] and x[1] >= eutectic[1]]

    # adjust the melting point back to the correct value for high or low solubility
    for i in range(len(h_s1)):
        if h_s1[i][0] > 0.9999:
            h_s1[i] = (h_s1[i][0], tm[0])
    for i in range(len(h_s2)):
        if h_s2[i][0] < 0.0001:
            h_s2[i] = (h_s2[i][0], tm[1])

    plt.plot([x[0] for x in h_s1], [x[1] for x in h_s1], label="x_1 (solvent compound␣
↪1)")
```

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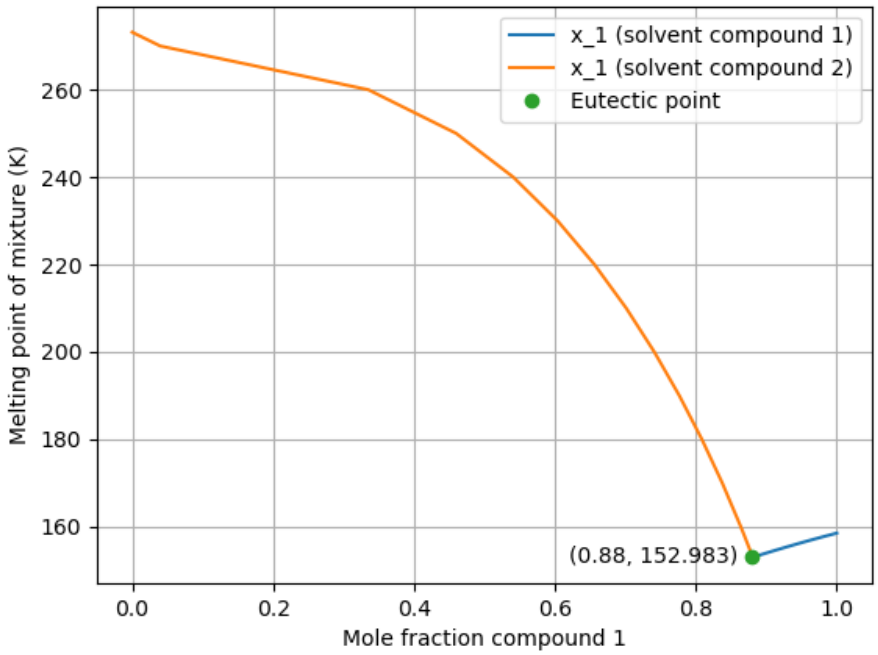
```
    plt.plot([x[0] for x in h_s2], [x[1] for x in h_s2], label="x_1 (solvent compound␣
↪2)")
    plt.plot(eutectic[0], eutectic[1], "o", label="Eutectic point")
    if eutectic[0] < 0.5:
        plt.annotate("  " + str(tuple([xt.round(3) for xt in eutectic])), eutectic,␣
↪va="center", ha="left")
    else:
        plt.annotate(str(tuple([xt.round(3) for xt in eutectic])) + "  ", eutectic,␣
↪va="center", ha="right")

    plt.xlabel("Mole fraction compound 1")
    plt.ylabel("Melting point of mixture (K)")
    plt.legend(loc="upper right")
    plt.grid()
    plt.show()

finish()
```

This figure (produced by the code) shows the two solubility curves calculated by the program.




```
Found eutectic point:
       x_1       T (K)       T (C)
   0.88028  152.98252 -120.16748
```

References

Binodal and Spinodal Curves

Binodal and spinodal curves are useful for understanding phase stability. The binodal curve (or coexistence curve) defines the temperatures and compositions at which phase separation is thermodynamically favorable. The spinodal curve is located within the binodal curve and indicates the limit of local phase stability. Compositions between the spinodal and binodal curves – while not thermodynamically stable – are robust against small fluctuations (i.e., the free energy surface is locally convex for points in this region).

Python code (Binary mixture)

```
import os
import numpy as np
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config

########  Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory  ########

database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

init()
# suppress plams output
config.log.stdout = 0


files = ["Nitrobenzene.coskf", "Hexane.coskf"]
nring = [6, 0]
# problem paramters
temp_range = [203.15, 243.15]  # K -- the temperature range over which the curves are␣
↪calculated
steps = 40  # number of steps to take within the temperature range


def binmix_at_T(files, temp):

    # initialize settings object
    settings = Settings()
    settings.input.property._h = "BINMIXCOEF"

    settings.input.property.nfrac = 100

    # make compounds
    compounds = [Settings() for i in range(len(files))]
    for i, (file, nr) in enumerate(zip(files, nring)):
        compounds[i]._h = os.path.join(database_path, file)
        compounds[i].nring = nr

    settings.input.temperature = temp

    # optionally, change to the COSMOSAC2013 method
    settings.input.method = "COSMOSAC2013"
```

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```
    # we'll also tighten the convergence threshold for better numerical accuracy
    settings.input.Technical.sacconv = 1e-10

    # add the compounds to the settings object
    settings.input.compound = compounds
    # create a job that can be run by COSMO-RS
    my_job = CRSJob(settings=settings)
    # run the job
    out = my_job.run()
    # convert all the results into a python dict
    res = out.get_results()

    return res


def calc_binodal_at_T(res):

    # this is the miscibility gap, so we can use the result calculated by the program
    if res["showmiscgap"]:
        return res["xlle"][:2]
    else:
        return None


def calc_spinodal_at_T(res):

    # here, we'll look for points with d^2(G_mix)/dx^2 = 0
    # we'll calculate a numerical second derivative for every point
    spinodal = []
    gmix = res["Gibbs energy of mixing"]
    frac1 = res["molar fraction"][0]
    second_deriv = np.zeros(len(gmix))

    # initial values for endpoints (assuming convexity close to pure compounds)
    second_deriv[0] = 0.0001
    second_deriv[-1] = 0.0001

    for i in range(1, len(gmix) - 1):
        delta1 = frac1[i] - frac1[i - 1]
        delta2 = frac1[i + 1] - frac1[i]
        d1 = (gmix[i] - gmix[i - 1]) / delta1
        d2 = (gmix[i + 1] - gmix[i]) / delta2
        second_deriv[i] = 2 * (d2 - d1) / (delta1 + delta2)

    for i in range(len(second_deriv) - 1):
        if second_deriv[i] * second_deriv[i + 1] < 0:
            dist1 = abs(second_deriv[i])
            dist2 = abs(second_deriv[i + 1])
            tot = dist1 + dist2
            zero = (dist2 * frac1[i] + dist1 * frac1[i + 1]) / tot
            spinodal.append(zero)

    return spinodal if spinodal else None


temps = [temp_range[0] + (temp_range[1] - temp_range[0]) / steps * i for i in␣
↪range(steps + 1)]
```

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```
bin_left_points = []
bin_right_points = []
spin_left_points = []
spin_right_points = []
print("Temperature".ljust(15), "Binodal points".ljust(25), "Spinodal points")
for temp in temps:
    res = binmix_at_T(files, temp)
    binodal = calc_binodal_at_T(res)
    spinodal = calc_spinodal_at_T(res)

    bin_str = "(" + ",".join(["{0:<10.5g}".format(x) for x in binodal]) + ")" if␣
↪binodal is not None else "--"
    spin_str = "(" + ",".join(["{0:<10.5g}".format(x) for x in spinodal]) + ")" if␣
↪spinodal is not None else "--"
    print("{0:.5g}".format(temp).ljust(15), bin_str.ljust(25), spin_str)

    if binodal is not None:
        bin_left_points.append((binodal[0], temp))
        bin_right_points.append((binodal[1], temp))
    if spinodal is not None:
        spin_left_points.append((spinodal[0], temp))
        spin_right_points.append((spinodal[-1], temp))

bin_points = bin_left_points + list(reversed(bin_right_points))
spin_points = spin_left_points + list(reversed(spin_right_points))

plt.plot([x[0] for x in bin_points], [y[1] for y in bin_points], label="Binodal curve
↪")
plt.plot([x[0] for x in spin_points], [y[1] for y in spin_points], label="Spinodal␣
↪curve")
plt.xlabel("Mole fraction compound 1")
plt.ylabel("Temperature (K)")
plt.legend(loc="upper right")
plt.grid()
# plt.savefig('./Binodalspinodal_binary.png',dpi=300)
plt.show()

finish()
```

This code produces the following output:

Python code (Ternary mixture)

Note: This example uses the python package `ternary`, but this is *only required for plotting*. This external python package can be installed from the internet in amspython using pip as follows: `amspython -m pip install python-ternary`. Users may choose to remove the plotting features of the code and not install `ternary`.

```
import os
import numpy as np
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config

######## Note: Ensure to configure the database path to either the installed ADFCRS-
↪2018 directory or your own specified directory ########
```

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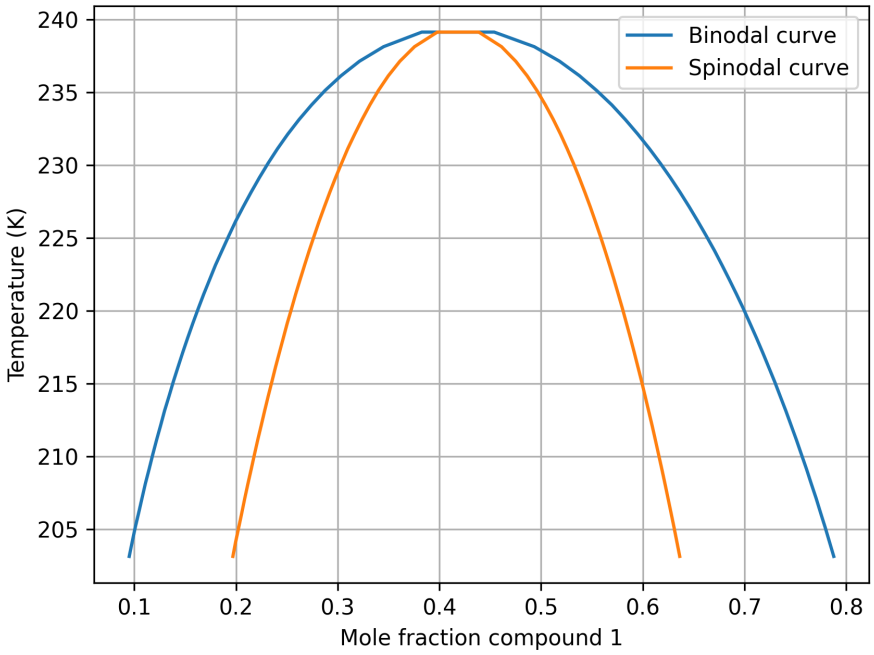

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```
database_path = os.path.join(os.environ["SCM_PKG_ADFCRSDIR"], "ADFCRS-2018")
if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")

init()
# suppress plams output
config.log.stdout = 0


files = ["Nitrobenzene.coskf", "Hexane.coskf"]
nring = [6, 0]
# problem paramters
temp_range = [203.15, 243.15]  # K -- the temperature range over which the curves are␣
↪calculated
steps = 40  # number of steps to take within the temperature range


def binmix_at_T(files, temp):

    # initialize settings object
    settings = Settings()
    settings.input.property._h = "BINMIXCOEF"

    settings.input.property.nfrac = 100

    # make compounds
    compounds = [Settings() for i in range(len(files))]
    for i, (file, nr) in enumerate(zip(files, nring)):
```

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```
        compounds[i]._h = os.path.join(database_path, file)
        compounds[i].nring = nr

    settings.input.temperature = temp

    # optionally, change to the COSMOSAC2013 method
    settings.input.method = "COSMOSAC2013"
    # we'll also tighten the convergence threshold for better numerical accuracy
    settings.input.Technical.sacconv = 1e-10

    # add the compounds to the settings object
    settings.input.compound = compounds
    # create a job that can be run by COSMO-RS
    my_job = CRSJob(settings=settings)
    # run the job
    out = my_job.run()
    # convert all the results into a python dict
    res = out.get_results()

    return res


def calc_binodal_at_T(res):

    # this is the miscibility gap, so we can use the result calculated by the program
    if res["showmiscgap"]:
        return res["xlle"][:2]
    else:
        return None


def calc_spinodal_at_T(res):

    # here, we'll look for points with d^2(G_mix)/dx^2 = 0
    # we'll calculate a numerical second derivative for every point
    spinodal = []
    gmix = res["Gibbs energy of mixing"]
    frac1 = res["molar fraction"][0]
    second_deriv = np.zeros(len(gmix))

    # initial values for endpoints (assuming convexity close to pure compounds)
    second_deriv[0] = 0.0001
    second_deriv[-1] = 0.0001

    for i in range(1, len(gmix) - 1):
        delta1 = frac1[i] - frac1[i - 1]
        delta2 = frac1[i + 1] - frac1[i]
        d1 = (gmix[i] - gmix[i - 1]) / delta1
        d2 = (gmix[i + 1] - gmix[i]) / delta2
        second_deriv[i] = 2 * (d2 - d1) / (delta1 + delta2)

    for i in range(len(second_deriv) - 1):
        if second_deriv[i] * second_deriv[i + 1] < 0:
            dist1 = abs(second_deriv[i])
            dist2 = abs(second_deriv[i + 1])
            tot = dist1 + dist2
            zero = (dist2 * frac1[i] + dist1 * frac1[i + 1]) / tot
```

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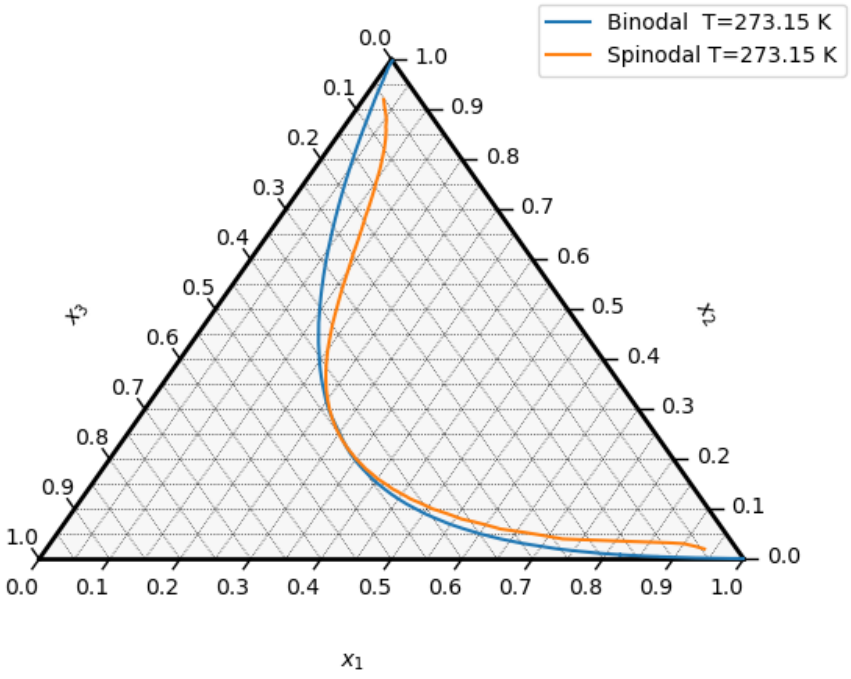
```
            spinodal.append(zero)

    return spinodal if spinodal else None


temps = [temp_range[0] + (temp_range[1] - temp_range[0]) / steps * i for i in␣
↪range(steps + 1)]
bin_left_points = []
bin_right_points = []
spin_left_points = []
spin_right_points = []
print("Temperature".ljust(15), "Binodal points".ljust(25), "Spinodal points")
for temp in temps:
    res = binmix_at_T(files, temp)
    binodal = calc_binodal_at_T(res)
    spinodal = calc_spinodal_at_T(res)

    bin_str = "(" + ",".join(["{0:<10.5g}".format(x) for x in binodal]) + ")" if␣
↪binodal is not None else "--"
    spin_str = "(" + ",".join(["{0:<10.5g}".format(x) for x in spinodal]) + ")" if␣
↪spinodal is not None else "--"
    print("{0:.5g}".format(temp).ljust(15), bin_str.ljust(25), spin_str)

    if binodal is not None:
        bin_left_points.append((binodal[0], temp))
        bin_right_points.append((binodal[1], temp))
    if spinodal is not None:
        spin_left_points.append((spinodal[0], temp))
        spin_right_points.append((spinodal[-1], temp))

bin_points = bin_left_points + list(reversed(bin_right_points))
spin_points = spin_left_points + list(reversed(spin_right_points))

plt.plot([x[0] for x in bin_points], [y[1] for y in bin_points], label="Binodal curve
↪")
plt.plot([x[0] for x in spin_points], [y[1] for y in spin_points], label="Spinodal␣
↪curve")
plt.xlabel("Mole fraction compound 1")
plt.ylabel("Temperature (K)")
plt.legend(loc="upper right")
plt.grid()
plt.show()

finish()
```

This code produces the following output:



Distribution of species in multispecies calculations

COSMO-RS can be used with compounds which can be composed of multiple possible species . For these types of calculations, it is often desirable to know the distribution of the various possible forms/species that constitute a certain compound. In the following script, a binary mixture calculation is performed using benzene and an acetic acid compound which is capable of existing as either of 2 conformers or as a dimer. The distribution of these species is plotted as a function of mole fraction.

`Download relevant coskf file`

Python code (Binary mixture)

```
import os
import matplotlib.pyplot as plt
from scm.plams import Settings, init, finish, CRSJob, config

################## Note: Ensure to download the coskf_acetic_acid before running the␣
↪script ##################
database_path = os.path.abspath("./coskf_acetic_acid")

if not os.path.exists(database_path):
    raise OSError(f"The provided path does not exist. Exiting.")


def adjust_name(s):
    return os.path.basename(s)
```

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```
init()
# suppress plams output
config.log.stdout = 0

# initialize settings object
settings = Settings()
settings.input.property._h = "BINMIXCOEF"
# optionally, change to the COSMOSAC2013 method
# settings.input.method = 'COSMOSAC2013'

# set the number of compounds
num_compounds = 2
compounds = [Settings() for i in range(num_compounds)]

compounds[1].name = "acetic_acid"
form = [Settings() for i in range(3)]

form[0]._h = os.path.join(database_path, "acetic_acid_0.coskf")

form[1]._h = os.path.join(database_path, "acetic_acid_1.coskf")

form[2]._h = os.path.join(database_path, "acetic_dimer.coskf")
form[2].count = 2
form[2].Hcorr = 9.25

compounds[0].form = form

compounds[1]._h = os.path.join(database_path, "Benzene.coskf")
compounds[1].name = "comp1"

settings.input.temperature = 298.15

# specify the compounds as the compounds to be used in the calculation
settings.input.compound = compounds
# create a job that can be run by COSMO-RS
my_job = CRSJob(settings=settings)
# run the job
out = my_job.run()

# convert all the results into a python dict
res = out.get_results()

compositions = out.get_multispecies_dist()

mf1 = res["molar fraction"][0]

plot_comp = 0  # we'll plot the first compound (acetic acid)
for struct, vals in compositions[plot_comp].items():
    plt.plot(mf1, vals, label=adjust_name(struct))

plt.xlabel("Mole fraction compound 1")
plt.ylabel("Species composition of compound")
plt.legend(loc="upper right")
plt.grid()
# plt.savefig("./ms_distribution.png", dpi=300)
plt.show()
```

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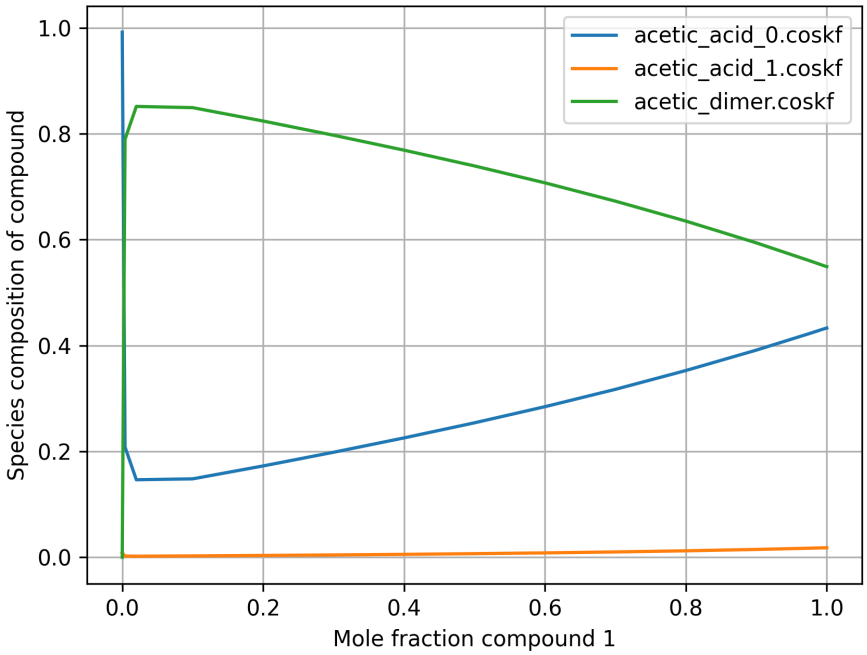
```
finish()
```

This code produces the following output:



Automated pKa calculation

```
Download relevant coskf file
```

Python code

```
import os, math
from scm.plams import Settings, init, finish, CRSJob, config
import matplotlib.pyplot as plt


init()
# suppress plams output
config.log.stdout = 0


class PkaSystem:
    def __init__(
        self,
        comp_protonated: Settings = None,
        comp_deprotonated: Settings = None,
        systype="acid",
```

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```
    ):
        self.comp_protonated = comp_protonated
        self.comp_deprotonated = comp_deprotonated
        self.type = systype.lower()
        self.g_cp = []
        self.g_cd = []
        self.pka = {}
        self.error = self.check_type()

    def check_type(self):
        if not all(isinstance(x, Settings) for x in [self.comp_protonated, self.comp_
↪deprotonated]):
            print("Incorrect input type for compounds in PkaSystem... must be a plams.
↪Settings instance")
            return False
        return True


class PkaCalculator:
    def __init__(
        self,
        systems=None,
        solv_protonated=None,
        solv_deprotonated=None,
        temp_range=[298.15, 298.15],
        steps=0,
        use_correction=True,
    ):

        self.systems = systems
        self.solv_protonated = solv_protonated
        self.solv_deprotonated = solv_deprotonated
        self.temp_range = temp_range
        self.steps = steps
        self.use_correction = use_correction
        self.R_const = 0.001987  # kcal/(mol K)

        self.g_sp = []
        self.g_sd = []

        if self.steps == 0:
            self.temp_vals = [temp_range[0]]
        else:
            self.temp_vals = [
                self.temp_range[0] * (1 - t_idx / self.steps) + self.temp_range[1] *␣
↪(t_idx / self.steps)
                for t_idx in range(self.steps + 1)
            ]

        self.calc_G_values()
        self.calc_pkas()

    def calc_G_values(self):

        for temp in self.temp_vals:
            settings = Settings()
            settings.input.property._h = "ACTIVITYCOEF"
```

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```
            # optionally, change to the COSMOSAC2013 method
            # settings.input.method = 'COSMOSAC2013'
            settings.input.temperature = temp

            compounds = [Settings()] * (2 + 2 * len(systems))
            compounds[0] = self.solv_deprotonated
            compounds[0].frac1 = 1.0
            compounds[1] = self.solv_protonated

            for i, system in enumerate(systems):
                compounds[2 + 2 * i] = system.comp_deprotonated
                compounds[2 + 2 * i + 1] = system.comp_protonated

            settings.input.compound = compounds
            my_job = CRSJob(settings=settings)
            out = my_job.run()
            res = out.get_results()

            g_vals = res["G solute"]
            for i, system in enumerate(systems):
                system.g_cd.append(g_vals[2 + 2 * i])
                system.g_cp.append(g_vals[2 + 2 * i + 1])
            self.g_sd.append(g_vals[0])
            self.g_sp.append(g_vals[1])

    def calc_pkas(self):
        for i, temp in enumerate(self.temp_vals):
            temp_key = round(temp, 3)
            for system in self.systems:
                g_diss = system.g_cd[i] - system.g_cp[i] + self.g_sp[i] - self.g_sd[i]
                if self.use_correction:
                    pka = self.calc_corrected_pka(g_diss, system, temp)
                else:
                    pka = g_diss / (self.R_const * temp * math.log(10)) - 1.74
                system.pka[temp_key] = pka

    def calc_corrected_pka(self, g_diss, system, temp):
        if system.type == "acid":
            return 0.62 * g_diss / (self.R_const * temp * math.log(10)) + 2.1
        else:
            return 0.67 * g_diss / (self.R_const * temp * math.log(10)) - 2.0


if __name__ == "__main__":

    ##################  Note: Ensure to download the coskf_pkas before running the␣
↪script  ##################
    database_path = os.path.abspath("./coskf_pkas")

    if not os.path.exists(database_path):
        raise OSError(f"The provided path does not exist. Exiting.")

    systems = []

    benzoic_acid = Settings({"_h": os.path.join(database_path, "Benzoic_acid.coskf")})
    benzoic_acid_deprotonated = Settings({"_h": os.path.join(database_path,
↪"conjugate_base_Benzoic_acid.coskf")})
```

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```
    systems.append(PkaSystem(comp_protonated=benzoic_acid, comp_deprotonated=benzoic_
↪acid_deprotonated, systype="acid"))

    pyridine = Settings({"_h": os.path.join(database_path, "Pyridine.coskf")})
    pyridineH = Settings({"_h": os.path.join(database_path, "conjugate_acid_Pyridine.
↪coskf")})
    systems.append(PkaSystem(comp_protonated=pyridineH, comp_deprotonated=pyridine,␣
↪systype="base"))

    water = Settings({"_h": os.path.join(database_path, "Water.coskf")})
    h3o = Settings({"_h": os.path.join(database_path, "conjugate_acid_Water.coskf")})

    PkaCalculator(systems, solv_protonated=h3o, solv_deprotonated=water, temp_
↪range=[298.15, 348.15], steps=5)

    for system in systems:
        print(system.pka)

finish()
```

CHAPTER

ELEVEN

COMMAND LINE SCRIPTING WITH COSMO-RS

11.1 AMSprep: construct an ADF COSMO results file

The module amsprep is intended to facilitate scripting. More details on amsprep can be found in the AMSprep section in the Scripting manual. For COSMO-RS the most relevant is the ADFCRS template. The template ADFCRS will perform a gas phase geometry optimization, and next a COSMO calculation at the gas phase optimized geometry.

In the next example the result of the ADF calculation is a file called adfwater.coskf, which is an ADF COSMO result file, that can be used as input for a COSMO-RS calculation, see also the *Example: COSMO-RS Tutorial 1* (page 174).

```
cat << eor > water.xyz
3

H       0.00000000       0.77121000       0.18071000
O       0.00000000      -0.00000000      -0.36142000
H       0.00000000      -0.77121000       0.18071000
eor

"$AMSBIN/amsprep" -t ADFCRS -m water.xyz -j adfwater >job
chmod +x job
./job
```

11.2 CRSprep: generate (multiple) COSMO-RS jobs

The module crsprep is intended to facilitate scripting: it makes it easier to construct proper jobs, from within a script. This module can be used, for example, to run the same type of COSMO-RS job on various compounds, or to change input settings. This module can also be used to put pure compound data on an ADF COSMO result file.

In $AMSHOME/examples/crs one can find examples that follow the COSMO-RS GUI tutorials, which are also described in the section *Scripting Examples* (page 173).

The most convenient way to see the options of crsprep is to run the crsprep command without arguments. You will get output very much alike the following description, but probably more up-to-date.

```
% crsprep -h

CRSprepare (crsprep) saves pure compound data on an ADF COSMO result file
or generates a job script for COSMO-RS calculations,
with user specified changes to input options / method / system.
Required is at least 1 compound and -savecompound or -t template
```

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```
Usage:
   crsprep -savecompound -s compound.coskf
           [-nring nring] [-pvap pvap] [-tvap tvap] [-antoine "A B C"]
           [-meltingpoint meltingpoint] [-hfusion hfusion] [-cpfusion cpfusion]
           [-flashpoint flashpoint] [-density density] [-scalearea scalearea]
   crsprep -t template
           [-s compound.(coskf|compoundlist)] [-c compound.(coskf|compoundlist)]
           [-nring nring] [-pvap pvap] [-tvap tvap] [-antoine "A B C"]
           [-meltingpoint meltingpoint] [-hfusion hfusion] [-cpfusion cpfusion]
           [-flashpoint flashpoint] [-density density] [-scalearea scalearea]
           [-frac1 frac1] [-frac2 frac2]
           [-densitysolvent densitysolvent] [-solphase solphase]
           [-volumequotient volumequotient] [-preset preset]
           [-method method] [-temperature temperature] [-pressure pressure]
           [-iso iso] [-n n] [-inputpurevap inputpurevap]
           [-inputpuredensity inputpuredensity]
           [-sigmax sigmax] [-massfraction] [-file filename] [-j jobname]

SAVE PURE COMPOUND DATA
-savecompound
    use to save pure compound data on an existing ADF COSMO result file

TEMPLATE
-t template
    use for COSMO-RS property calculation
    template should be one of:
        VAPORPRESSURE, PUREVAPORPRESSURE,
        BOILINGPOINT, PUREBOILINGPOINT, FLASHPOINT,
        LOGP, ACTIVITYCOEF, SOLUBILITY, PURESOLUBILITY,
        BINMIXCOEF, TERNARYMIX, COMPOSITIONLINE,
        SIGMAPROFILE, PURESIGMAPROFILE, SIGMAPOTENTIAl, PURESIGMAPOTENTIAL

COMPOUNDS
    at least 1 compound is required
-s file: the special compound(s) to be used, should be a .coskf file,
    or a .compoundlist file. The -s key has to be repeated for each file
-c file: additional compound(s) to be used, should be a .coskf file,
    or a .compoundlist file. The -c key has to be repeated for each file
    the order of the compounds is: first all compound defined with -s,
    then those with -c
    LOGP, ACTIVITYCOEF, SOLUBILITY: use -s for the solvent and -c for the solutes
    PURESOLUBILITY: use -s for the solute and -c for the solvents

PURE COMPOUND DATA
-nring: number of ring atoms
-pvap: pure compound vapor pressure (bar) at tvap
-tvap: at this temperature (Kelvin) pure compound has pressure pvap
-antoine: Antoine coefficients A, B, and C
-meltingpoint: melting point (Kelvin)
-hfusion: enthalpy of fusion (kcal/mol)
-cpfusion: heat capacity of fusion (kcal/(mol K))
-flashpoint: flash point (Kelvin)
-density: liquid density (kg/L)
-scalearea: COSMO surface area scale factor
    these keys can be repeated for each compound,
    first appearance of the key will be for compound 1, second for compound 2, etc.
    note the order of the compounds
```

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```
SOLVENT
-frac1: define solvent
-frac2: define solvent 2 (LogP, composition line)
    the -frac1 and -frac2 key have to be repeated for
    each compound that should have a non-default value
    first appearance of the key will be for compound 1, second for compound 2, etc.
    note the order of the compounds
-densitysolvent: density solvent (kg/L)
-solphase: pure compound phase solute in solubility calculation
-volumequotient: molar volume phase 1/molar volume phase 2 (LogP)
-preset: LogP preset 0, 2, 3, 4, 5
     0: user defined; 2: Octanol/Water; 3: Benzene/Water; 4: Ether/Water;
     5: Hexane/Water

METHOD, SYSTEM
-method: COSMO-RS, COSMOSAC2013, COSMOSAC2016
-temperature: temperature (Kelvin)
    the -temperature key can be used twice to give a range
-pressure: pressure (bar)
    the -pressure key can be used twice to give a range
-iso: isotherm, isobar, flashpoint
-n: number of steps
-inputpurevap: if 1 use input pure compound pvap and tvap or Antoine equation
-inputpuredensity: if 1 use input pure compound liquid density
-sigmax: maximum value sigma (sigma profile, sigma potential)
-massfraction: use mass fractions

INPUT FILE
-file: content of the file will be added at the end of the input for the
    COSMO-RS calculation. The -file key has to be repeated for each file

OUTPUT
-j: produce a fully runnable job (as the .job files from AMSjobs),
    using the specified jobname. The job script produces files like jobname.out,
    jobname.crskf etc. Several job scripts can simply be concatenated,
    the results will be stored in different files using the jobname parameter
    the default is a simple run script

EXAMPLES
crsprep -s benzene.coskf -nring 6 -savecompound
crsprep -t VAPORPRESSURE -temperature 273.15 -temperature 373.15 -s methanol.coskf
```

11.3 AMSreport: generate report

The module amsreport is intended to facilitate scripting. More details on amsreport can be found in the AMSreport section in the Scripting manual. It makes it very easy to get results calculated by COSMO-RS (or other programs in the ADF suite) in your own script. Compared to ADF2014 AMSreport has been extended to get easier results from COSMO-RS result files (.crskf files). It was already possible to report any proper KF variable from the .crskf file. Now a few predefined keys are added. See the $AMSHOME/examples/crs directory for use of amsreport in COSMO-RS calculations. Depending on the kind of calculation one can use:

```
Command line option      Property

TOC                      Table of contents
PROPERTY                 General:Property

METHOD                   Property:Method
NITEMS                   Property:Number of Items
FRAC1                    Property:Solvent: molar fraction
FRAC2                    Property:Solvent 2: molar fraction
SOLVENT-FRACTION         Property:Solvent: solvent fraction
TEMPERATURE              Property:Temperature (in Kelvin)
PRESSURE                 Property:Pressure (in bar)
GIBBS-ENERGY-MIXING      Property:Gibbs free energy of Mixing (in kcal/mol)
GIBBS-ENERGY-SOLVATION   Property:Gibbs free energy of Solvation (in kcal/mol)
GIBBS-ENERGY-SOLUTE      Property:Gibbs free energy solute (in kcal/mol)
EXCESS-G                 Property:Excess Gibbs free energy (in kcal/mol)
EXCESS-H                 Property:Excess Enthalpy (in kcal/mol)
ENTHALPY-VAPORIZATION    Property:Enthalpy of vaporization (in kcal/mol)
LOGP                     Property:LogP
MOLAR-FRACTION           Property:Molar Fraction
ACTIVITY-COEFFICIENT     Property:Activity Coefficient
VAPOR-PRESSURE           Property:Vapor Pressure (in bar)
SOLUBILITY-X             Property:Solubility: molar fraction
SOLUBILITY-M             Property:Solubility: moles per liter (in mol/(L solution))
SOLUBILITY-G             Property:Solubility: gram per liter (in g/(L solution))
SOLUBILITY-MASS-FRACTION Property:Solubility: mass fraction
HENRY                    Property:Henry Constant (in mol/(L atm))
HENRY-NODIM              Property:Henry Constant dimensionless
MISCIBILITY-GAP          Property:Miscibility gap
MISCIBILITY-GAP-T        Property:Miscibility gap temperature (in Kelvin)
MISCIBILITY-GAP-P        Property:Miscibility gap pressure (in bar)
MISCIBILITY-GAP-X        Property:Miscibility gap molar fraction x1 x1'
MISCIBILITY-GAP-A        Property:Miscibility gap activities a1 a2
TIE-LINES-X              Property:Tie Lines molar fraction x1 x2 x3 x1' x2' x3'
TIE-LINES-A              Property:Tie Lines activities a1 a2 a3
CHEMICAL-POTENTIAL       Property:Chemical Potential
CHEMICAL-POTENTIAL-PURE  Property:Chemical Potential Pure Compounds Liquid
CHEMICAL-POTENTIAL-GAS   Property:Chemical Potential Pure Compounds Gas
SIGMA                    Property:Sigma
SIGMA-PROFILE            Property:Sigma Profile
SIGMA-PROFILE-HB         Property:Sigma Profile Hydrogen Bonding part
SIGMA-PROFILE-TOTAL      Property:Total Sigma Profile
SIGMA-PROFILE-HB-TOTAL   Property:Total Sigma Profile Hydrogen Bonding part
SIGMA-POTENTIAL          Property:Sigma Potential
SIGMA-POTENTIAL-TOTAL    Property:Total Sigma Potential

NCOMP                    Compounds:Number of Compounds
COMPOUNDS-FILENAME       Compounds:Filename
COMPOUNDS-NAME           Compounds:Name (from filename)
COMPOUNDS-MOLAR-MASS     Compounds:Molar Mass

Example
"$AMSBIN/amsreport" file.crskf TOC
"$AMSBIN/amsreport" file.crskf ncomp
"$AMSBIN/amsreport" file.crskf ncomp -plain
```

11.4 KF utilities for COSMO-RS

11.4.1 KF browser

With the GUI module kfbrowser one can browse through the raw data on KF files (like the .crskf COSMO-RS result files).

```
$AMSBIN/kfbrowser file.crskf
```

11.4.2 kf2cosmo and cosmo2kf

The two COSMO-RS command line utility programs *kf2cosmo* and *cosmo2kf* convert COSMO kf files from binary to ASCII and vice versa.

```
kf2cosmo file.coskf file.cosmo
```

kf2cosmo reads from the kf file file.coskf (should exist) the section 'COSMO' and writes to the ASCII file file.cosmo (should not exist). Instead of a .coskf file, the file can also be a TAPE21 file which is a result file from an ADF COSMO calculation.

```
cosmo2kf file.cosmo file.coskf
```

cosmo2kf reads from the ASCII file file.cosmo (should exist) and writes a section 'COSMO' to the kf file file.coskf (should not exist). Note that only a section 'COSMO' is written to the kf file, which means that this file can not be used like an ordinary adf.rkf file (previously ADF<=2019 TAPE21 file or .t21 file).

```
cosmo2kf file.cos file.coskf
```

cosmo2kf can also read a MOPAC COSMO result file file.cos (should exist and should have the file extension .cos) and writes a section 'COSMO' to the kf file file.coskf (should not exist).

11.4.3 pkf, cpkf, dmpkf, udmpkf

```
pkf file.crskf
```

pkf prints a summary of the contents of a kf file

```
cpkf adf.rkf file.coskf COSMO
```

With the ADF kf utility *cpkf* one can copy the section 'COSMO' from an adf.rkf (should exist) to a file.coskf (should not exist). The file file.t21 should be a result of an ADF COSMO calculation. The file file.coskf is much smaller than adf.rkf. This file file.coskf can not be used like an ordinary adf.rkf file, but it contains all necessary information such that it can be used as input for a COSMO-RS calculations.

With the ADF kf utilities *dmpkf* and *udmpkf* one can also convert COSMO kf files from binary to ASCII and vice versa. Note that the ASCII files in this case are not so called .cosmo files.

```
dmpkf file.coskf > ascii_result
udmpkf < ascii_result newfile.coskf
```

11.5 Scripting Examples

11.5.1 Example: COSMO result files

Download COSMO_files.run

```
#! /bin/sh

# This example tries to do the same as in the COSMO-RS GUI Tutorial: COSMO result␣
↪files,
# using scripts.
#
# In the first part of the example you will find how to use amsprep to construct
# an ADF COSMO results file.
# The template ADFCRS will perform a gas phase geometry optimization (for water, in␣
↪this case),
# and next a COSMO calculation at the gas phase optimized geometry.
# The result file adfwater.coskf, which is an ADF COSMO result file, can be used as␣
↪input for
# a COSMO-RS calculation. amsreport is used to extract data from the resulting .coskf␣
↪file.

echo "Results"

rm -f water.xyz
rm -f job.sh
cat << eor > water.xyz
3

H       0.00000000       0.77121000       0.18071000
O       0.00000000      -0.00000000      -0.36142000
H       0.00000000      -0.77121000       0.18071000
eor

"$AMSBIN/amsprep" -t GO -runtype "COSMO-RS Compound" -m water.xyz -j adfwater >job.sh
chmod +x job.sh
./job.sh

echo "ADF"
"$AMSBIN/amsreport" adfwater.results geometry-a
cp adfwater.coskf adffile.coskf
"$AMSBIN/amsreport" adffile.coskf energies

# The template ADFCRS can also be used for generating an "average monomer" COSMO␣
↪result file.
# The calculation could take up quite some time.

echo "POLYMER"
$AMSBIN/amsprep -t GO -runtype "COSMO-RS Compound" -smiles "C{-}C{n+}(c1ccccc1)" -j␣
↪adfpolystyrene >job3.sh
grep -i coskfatoms job3.sh |wc -w


# A MOPAC COSMO result file can also be constructed.
# Note that the syntax for MOPAC is not the same as in ADF2018.
# The template MOPAC-GO will perform a COSMO geometry optimization,
# if -g "mopac.solvation.enabled 1" -g "mopac.solvation.solvent.name CRS" is included.
```

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```
# If -g "mopac.solvation.nspa 362" is included the maximum number of COSMO surface␣
↪points
# is 362, which is more than the default 42.
# The result file mopacwaterresults/mopac.coskf is a MOPAC COSMO result file,
# which can be used as input for a COSMO-RS calculation.

"$AMSBIN/amsprep" -t MOPAC-GO -m water.xyz -g "mopac.solvation.enabled 1" \
                  -g "mopac.solvation.solvent.name CRS" -g "mopac.solvation.nspa 362"␣
↪\
                  -j mopacwater >job2.sh
chmod +x job2.sh
./job2.sh

echo "MOPAC"
"$AMSBIN/amsreport" mopacwater.results geometry-a
"$AMSBIN/amsreport" mopacwater.results/mopac.coskf energies

# Fast Sigma can provide estimates of COSMO-RS sigma profiles in milliseconds.

echo "FAST SIGMA"
"$AMSBIN/fast_sigma" --smiles "CC(Cc1ccc(cc1)[C@@H](C(=O)O)C)C" -o ibuprofen.compkf
"$AMSBIN/amsreport" ibuprofen.compkf formula
"$AMSBIN/amsreport" ibuprofen.compkf energies

echo "Ready"
```

11.5.2 Example: COSMO-RS parameters and analysis

Download Parameters_and_Analysis.run

```
#! /bin/sh

# This example tries to part of the COSMO-RS GUI Tutorial: parameters and analysis␣
↪using scripts.
#
# First some .coskf files are copied to the location where the scripts are running.

cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/benzene.coskf .
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/ethanol.coskf .
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/methanol.coskf .
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/water.coskf .

# Set pure compound parameters
# ----------------------------

# In the first part of the example you will find how to use crsprep to set pure␣
↪compound parameters,
# in this case to set the number of ring atoms for the benzene molecule, which has 6␣
↪ring atoms.
# The file benzene.coskf is changed, such that it contains the value "6" for the␣
↪number of ring compounds.

"$AMSBIN/crsprep" -c benzene.coskf -nring 6 -savecompound

# The sigma profile and the sigma potential
```

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```
# ----------------------------------------
#
# Next for convenience a file tutorial2.compoundlist is made that consists of 4 coskf␣
↪files.


rm -f tutorial2.compoundlist
rm -f job
cat << eor > tutorial2.compoundlist
benzene.coskf
ethanol.coskf
methanol.coskf
water.coskf
eor

# In the second part of the example sigma profiles are calculated for the four␣
↪compounds
# (result file step6.crskf), and next the sigma potentials of the four pure compounds
# (result file step7.crskf).
# With *amsreport* one can get the calculated sigma profile or sigma potential from
# the .crskf file on standard output.


"$AMSBIN/crsprep" -t PURESIGMAPROFILE -c tutorial2.compoundlist -j step6 > job.sh
"$AMSBIN/crsprep" -t PURESIGMAPOTENTIAL -c tutorial2.compoundlist -j step7 >> job.sh
chmod +x job.sh
./job.sh
echo "Results"
"$AMSBIN/amsreport" step6.crskf sigma
"$AMSBIN/amsreport" step6.crskf sigma-profile
"$AMSBIN/amsreport" step6.crskf sigma-profile-hb
"$AMSBIN/amsreport" step7.crskf sigma-potential
echo "Ready"
```

11.5.3 Example: COSMO-RS properties

Download Properties.run

```
#! /bin/sh

# This example tries to do the same as COSMO-RS GUI Tutorial: Properties, using␣
↪scripts.

echo "Results"

# This example starts with copying 4 coskf files to the current directory,
# and modifying the benzene.coskf file such that the number of ring atoms is 6,
# like in the previous example.

rm -f job.sh
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/benzene.coskf .
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/ethanol.coskf .
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/methanol.coskf .
cp $AMSHOME/examples/COSMO-RS/Parameters_and_Analysis/water.coskf .
cp $AMSHOME/examples/COSMO-RS/Properties/2-hexanone.coskf .
```

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```
cp $AMSHOME/examples/COSMO-RS/Properties/acetic_acid.coskf .

"$AMSBIN/crsprep" -c benzene.coskf -nring 6 -savecompound

# Step 2: Vapor pressure
# ----------------------

# In step 2 of the example the vapor pressure of methanol is calculated at the
# default temperature of 298.15 K (result file step2a.crskf),
# and next for a series of temperatures ranging from 273.15 K to 373.15 K
# in 10 steps (result file step2b.crskf).


touch job.sh
chmod +x job.sh
"$AMSBIN/crsprep" -t PUREVAPORPRESSURE -j step2a \
                  -c methanol.coskf > job.sh
"$AMSBIN/crsprep" -t PUREVAPORPRESSURE -temperature 273.15 -temperature 373.15 -j␣
↪step2b \
                  -c methanol.coskf >> job.sh
./job.sh
echo "Step 2a"
"$AMSBIN/amsreport" step2a.crskf temperature
"$AMSBIN/amsreport" step2a.crskf pressure
"$AMSBIN/amsreport" step2a.crskf enthalpy-vaporization
echo "Step 2b"
"$AMSBIN/amsreport" step2b.crskf temperature
"$AMSBIN/amsreport" step2b.crskf pressure
"$AMSBIN/amsreport" step2b.crskf enthalpy-vaporization


# Step 3: Boiling point
# ---------------------

# In step 3 of the example the boiling point of a mixture of methanol and ethanol
# is calculated, for a series of pressures ranging from 0.101325 to 1.01325 bar
# in 10 steps (result file step3.crskf).
# This mixture consist of 50% mole fraction methanol and 50% mole fraction ethanol.

"$AMSBIN/crsprep" -t BOILINGPOINT -pressure 0.101325 -pressure 1.01325 -j step3 \
                  -c methanol.coskf -frac1 0.5 \
                  -c ethanol.coskf -frac1 0.5 > job.sh
./job.sh
echo "Step 3"
"$AMSBIN/amsreport" step3.crskf temperature
"$AMSBIN/amsreport" step3.crskf pressure


# Step 4: Flash point
# -------------------

# In step 4 of the example the flash point of a mixture of ethanol and water
# is calculated (result file step4.crskf).
# This mixture consist of 44.2% mass fraction methanol and 55.8% mass fraction␣
↪ethanol.
# For a flash point calculation the pure compound flash points are needed as input,
# since COSMO-RS does not predict pure compound flash points.
```

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```
# For pure ethanol a flash point of 286 K is saved in the file ethanol.coskf.


"$AMSBIN/crsprep" -c ethanol.coskf -flashpoint 286 -savecompound

"$AMSBIN/crsprep" -t FLASHPOINT -massfraction -j step4 \
                  -c ethanol.coskf -frac1 0.442 \
                  -c water.coskf -frac1 0.558 > job.sh
./job.sh
echo "Step 4 flash point"
$AMSBIN/amsreport step4.crskf temperature

# Step 5: Activity coefficients, Henry coefficients, Solvation free energies
# --------------------------------------------------------------------------

# In step 5 of the example the infinite diluted solutes benzene, methanol,and
# ethanol are calculated in the solvent water (result file step5.crskf).
# Activity coefficients, Henry coefficients and solvation free energies
# will be calculated.
# One one should include -s flag for water, since it is the solvent,
# and considered here to be a special compound.


"$AMSBIN/crsprep" -t ACTIVITYCOEF -j step5 \
                  -s water.coskf \
                  -c benzene.coskf -c ethanol.coskf -c methanol.coskf > job.sh
./job.sh
echo "Step 5 Activity coefficients, Henry's law constants, Solvation energy"
"$AMSBIN/amsreport" step5.crskf Activity-Coefficient
"$AMSBIN/amsreport" step5.crskf Henry
"$AMSBIN/amsreport" step5.crskf Gibbs-energy-solvation

# Step 6: Partition coefficients (log P)
# --------------------------------------

# In step 6 of the example the partition coefficients of infinitely diluted
# solutes in a mixture of two immiscible solvents are calculated.
# In step 6a the default Octanol/Water partition coefficients are calculated
# (default -preset 2) (result file step6a.crskf).
# In step 6b a user defined (-preset 0) Benzene/Water partition coefficients
# are calculated (result file step6b.crskf).
# In this case one should include -s flag for benzene and water, since these
# are the two immiscible solvents, and considered here to be the special compounds.
# The order of the compounds benzene and water is important, because the
# molar volume of phase 1 (benzene) divided by the the molar volume of phase 2
# (water) is given with the flag -volumequotient.


"$AMSBIN/crsprep" -t LOGP -j step6a \
                  -c benzene.coskf -c ethanol.coskf -c methanol.coskf > job.sh
"$AMSBIN/crsprep" -t LOGP -preset 0 -volumequotient 4.93 -j step6b \
                  -s benzene.coskf -s water.coskf \
                  -c ethanol.coskf -c methanol.coskf >> job.sh
./job.sh
echo "Step 6a octanol/water"
"$AMSBIN/amsreport" step6a.crskf logp
echo "Step 6b benzene/water"
```

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```
"$AMSBIN/amsreport" step6b.crskf logp

# Step 7: Solubility
# ------------------

# In step 7 of the example the solubility of a compound is calculated.
# The solute can either be a liquid, solid, or gas.
# First some pure compound properties for benzene are set: the melting point,
# enthalpy of fusion, and the boiling point (file benzene.coskf).


"$AMSBIN/crsprep" -c benzene.coskf -meltingpoint 278.7 -hfusion 2.37 -savecompound
"$AMSBIN/crsprep" -c benzene.coskf -tvap 353.3 -pvap 1.01325 -savecompound

# In step 7a the solubility of benzene in water is calculated for a range of
# temperatures ranging from 273.15 K to 373.15 K in 10 steps (result file step7a.
↪crskf).
# If the template PURESOLUBILITY is used, the special compound is the solute,
# benzene in this case.
# Below 278.7 K, benzene is a solid. This will be taken into account, since the
# melting point and enthalpy of fusion are present on the file benzene.coskf.
# At higher temperatures benzene is assumed to be a liquid.
# Note that tn this calcuation above the normal boiling point of benzene
# the vapor pressure of benzene will be higher than 1.01325 bar.

"$AMSBIN/crsprep" -t PURESOLUBILITY -temperature 273.15 -temperature 373.15 -j step7a␣
↪\
                  -s benzene.coskf \
                  -c water.coskf > job.sh

# In step 7b again the solubility of benzene in water is calculated for a (different)
# range of temperatures (result file step7b.crs) using the template SOLUBILITY.
# If the template SOLUBILITY is used, the special compound is the solvent,
# water in this case.
# For the density of the solvent water 1.0 kg/L is used.
# Below 278.7 K benzene is a solid. This will be taken into account, since the melting
# point and enthalpy of fusion are present on the file benzene.coskf.
# At higher temperatures benzene is assumed to be a liquid.

"$AMSBIN/crsprep" -t SOLUBILITY -temperature 273.15 -temperature 283.15 \
                   -densitysolvent 1.0 -j step7b \
                  -s water.coskf \
                  -c benzene.coskf >> job.sh
# In step 7c again the solubility of benzene in water is calculated for a range
# of temperatures above the boiling point of benzene (result file step7c.crs)
# using the template SOLUBILITY.
# If the template SOLUBILITY is used, the special compound is the solvent,
# water in this case.
# For the density of water 1.0 kg/L is used.
# For the vapor pressure of benzene 1.01325 bar is used.

"$AMSBIN/crsprep" -t SOLUBILITY -temperature 353.3 -temperature 373.15 \
                  -densitysolvent 1.0 -solphase Gas -pressure 1.01325 -j step7c \
                  -s water.coskf \
                  -c benzene.coskf >> job.sh

# The solubility of a gas in a solvent can also be calculated using Henry's law,
```

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```
# which is valid for ideal dilute solutions.
# Henry coefficients can be calculated with the template ACTIVITYCOEF.
# In step 7d of the example the infinite diluted solutes benzene is calculated
# in the solvent water (result file step7d.crskf)
# at a temperature of 363.15 K.
# If the template ACTIVITYCOEF is used, the special compound is the solvent,
# water in this case.
# For the density of water 1.0 kg/L is used.

"$AMSBIN/crsprep" -t ACTIVITYCOEF -temperature 363.15 -densitysolvent 1.0 -j step7d \
                  -s water.coskf \
                  -c benzene.coskf >> job.sh

# Next the job.sh is run which will produce the crskf files,
# and a report is made for all calculations in step 7.

./job.sh
echo "Step 7a"
"$AMSBIN/amsreport" step7a.crskf solubility-x
echo "Step 7b"
"$AMSBIN/amsreport" step7b.crskf solubility-g
echo "Step 7c"
"$AMSBIN/amsreport" step7c.crskf solubility-m
echo "Step 7d"
"$AMSBIN/amsreport" step7d.crskf henry


# Step 8: Binary mixtures VLE/LLE
# -------------------------------

# In step 8 phase diagrams of a mixture of two components are be calculated
# with the template BINMIXCOEF.
# Exactly two compound should be given.
# In step 8a of the example a binary mixture of water and methanol
# is calculated at 298.14 K (result file step8a.crskf).

"$AMSBIN/crsprep" -t BINMIXCOEF -temperature 298.14 -j step8a \
                  -s water.coskf \
                  -s methanol.coskf > job.sh

# In step 8b of the example a binary mixture of water and ethanol is calculated
# at 322.45 K (result file step8b.crskf).
# Pure compound vapor pressures are given with -tvap (temperature in K)
# and -pvap (vapor pressure in bar).
# Preferably both -tvap and -pvap should be included for both compounds.
# If only one -tvap and one -pvap is given, it is assumed to be for the first␣
↪compound.
# Note that these pure compound values are not saved to water.coskf or
# ethanol.coskf in this case.


"$AMSBIN/crsprep" -t BINMIXCOEF -temperature 322.45 -j step8b \
                  -s water.coskf -tvap 322.45 -pvap 0.123416 \
                  -s ethanol.coskf -tvap 322.45 -pvap 0.294896 >> job.sh

# In step 8c of the example a binary mixture of water and benzene
# is calculated at 323.15 K (result file step8c.crskf).
```

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```
# Water and benzene do not mix very well. In this case a
# liquid-liquid equilibrium (LLE) will be calculated.
# The number of mixtures for which the binary mixture is calculated should be not too␣
↪small,
# otherwise the properties of the 2 immiscible liquid phases will not be so accurate.
# In this case for the number of mixtures 100 is chosen.
# The actual number of mixtures is 5 more, thus 105 in this case.

"$AMSBIN/crsprep" -t BINMIXCOEF -temperature 323.15 -n 100 -j step8c \
                  -s water.coskf \
                  -s benzene.coskf >> job.sh

# In step 8d of the example a binary mixture of methanol and ethanol is calculated
# at a constant total vapor pressure (-iso isobar) of 1.01325 bar (result file step8d.
↪crskf).
# Pure compound vapor pressures are given with -tvap (temperature in K)
# and -pvap (vapor pressure in bar).
# Preferably both -tvap and -pvap should be included for both compounds.
# If only one -tvap and one -pvap is given, it is assumed to be for the first␣
↪compound.
# Note that these pure compound values are not saved to methanol.coskf
# or ethanol.coskf in this case.

"$AMSBIN/crsprep" -t BINMIXCOEF -iso isobar -pressure 1.01325 -j step8d \
                  -s methanol.coskf -tvap 338 -pvap 1.01325 \
                  -s ethanol.coskf -tvap 351 -pvap 1.01325 >> job.sh

# Next the job.sh is run which will produce the crskf files,
# and a report is made for all calculations in step 8.

./job.sh
echo "Step 8a"
"$AMSBIN/amsreport" step8a.crskf molar-fraction
"$AMSBIN/amsreport" step8a.crskf excess-g
"$AMSBIN/amsreport" step8a.crskf excess-h
echo "Step 8b"
"$AMSBIN/amsreport" step8b.crskf vapor-pressure
echo "Step 8c"
"$AMSBIN/amsreport" step8c.crskf miscibility-gap
"$AMSBIN/amsreport" step8c.crskf miscibility-gap-x
"$AMSBIN/amsreport" step8c.crskf miscibility-gap-a
echo "Step 8d"
"$AMSBIN/amsreport" step8d.crskf temperature


# Step 9: Ternary mixtures VLE/LLE
# --------------------------------
#
# In step 9 phase diagrams of a mixture of three components are be calculated
# with the template TERNARYMIX.
# Exactly three compound should be given.
# For convenience first some pure compound properties (normal boiling points)
# are saved to the .coskf files.


"$AMSBIN/crsprep" -c water.coskf    -tvap 373.15 -pvap 1.01325 -savecompound
"$AMSBIN/crsprep" -c methanol.coskf -tvap 338    -pvap 1.01325 -savecompound
```

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```
"$AMSBIN/crsprep" -c ethanol.coskf  -tvap 351    -pvap 1.01325 -savecompound
"$AMSBIN/crsprep" -c benzene.coskf  -tvap 353.3  -pvap 1.01325 -savecompound

# In step 9a of the example a ternary mixture of methanol, ethanol, and benzene
# is calculated at 343.15 K (result file step9a.crskf).
# In step 9b of the example a ternary mixture of water, ethanol, and benzene is␣
↪calculated
# at a constant total vapor pressure (-iso isobar) of 1.01325 bar (result file step9b.
↪crskf).
# In step 9b a miscibility gap of the ternary mixture will be calculated.
# In this case, within the miscibility gap there are two immiscible phases of
# the liquid in equilibrium.
# The composition of the two phases, which are in equilibrium,
# can be found at the end points of the tie lines, that are calculated.

"$AMSBIN/crsprep" -t TERNARYMIX -temperature 343.15 -j step9a \
                  -s methanol.coskf -s ethanol.coskf -s benzene.coskf  > job.sh
"$AMSBIN/crsprep" -t TERNARYMIX -iso isobar -pressure 1.01325 -j step9b \
                  -s water.coskf -s ethanol.coskf -s benzene.coskf >> job.sh
./job.sh
echo "Step 9a"
"$AMSBIN/amsreport" step9a.crskf molar-fraction
"$AMSBIN/amsreport" step9a.crskf pressure
"$AMSBIN/amsreport" step9a.crskf miscibility-gap
echo "Step 9b"
"$AMSBIN/amsreport" step9b.crskf miscibility-gap
echo "First 4 tie-lines"
"$AMSBIN/amsreport" step9b.crskf -r "TERNARYMIX%xll#1:24#12.4f##6"
"$AMSBIN/amsreport" step9b.crskf temperature

# Note that for printing all tie-lines that are calculated in step9b one can simply␣
↪use
# "$AMSBIN/amsreport" step9b.crskf tie-lines-x
# instead of the more complicated
# "$AMSBIN/amsreport" step9b.crskf -r "TERNARYMIX%xll#1:24#12.4f##6"
# which also only reports the first 4 tie-lines

# Step 10: A composition line between solvents s1 and s2
# ------------------------------------------------------

# In step 10 a phase diagram of a mixture of two solvents, which both are mixtures,
# is calculated with the template COMPOSITIONLINE.
# In this step one of the tie lines of the ternary mixture of water, ethanol, and␣
↪benzene
# of step 9b will be investigated in more detail.
# Note that here the .coskf files are used in which the normal boiling points were␣
↪saved to (in step 9).
# The mixture will be calculated for a list of molar (or mass) fractions of the␣
↪solvents
# between zero and one, and the compositions of solvent 1 and solvent 2 are linearly␣
↪interpolated.
# In this case solvent 1 consists of 0.3 molar fraction ethanol and 0.7 molar␣
↪fraction benzene, and
# solvent 2 consists of 0.9 molar fraction water and 0.1 molar fraction ethanol.
# In step 10a of the example this mixture is calculated at a constant total vapor␣
↪pressure (-iso isobar)
# of 1.01325 bar (result file step10a.crskf).
```

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```
# In step 10b of the example this mixture is calculated at 341.05 K (result file␣
↪step10b.crskf).
# Why this temperature was chosen can be found in step 10 of COSMO-RS GUI Tutorial:␣
↪Properties.

"$AMSBIN/crsprep" -t COMPOSITIONLINE -iso isobar -pressure 1.01325 -n 100 -j step10a \
                  -s water.coskf   -frac1 0.0 -frac2 0.9 \
                  -s ethanol.coskf -frac1 0.3 -frac2 0.1 \
                  -s benzene.coskf -frac1 0.7 -frac2 0.0 > job.sh
"$AMSBIN/crsprep" -t COMPOSITIONLINE -temperature 341.05 -n 100 -j step10b \
                  -s water.coskf   -frac1 0.0 -frac2 0.9 \
                  -s ethanol.coskf -frac1 0.3 -frac2 0.1 \
                  -s benzene.coskf -frac1 0.7 -frac2 0.0 >> job.sh
./job.sh
echo "Step 10a"
$AMSBIN/amsreport step10a.crskf ncomp
$AMSBIN/amsreport step10a.crskf frac1
$AMSBIN/amsreport step10a.crskf frac2
$AMSBIN/amsreport step10a.crskf solvent-fraction
$AMSBIN/amsreport step10a.crskf molar-fraction
$AMSBIN/amsreport step10a.crskf activity-coefficient

echo "Step 10b"
$AMSBIN/amsreport step10b.crskf Gibbs-energy-mixing

# Step 11: Pure Compound Properties
# ---------------------------------

# In step 11 a QSPR (Quantitative Structure-Property Relationship) method is used
# to estimate some pure compound properties.
# This QSPR method needs a SMILES string as input.

echo "Step 11"
"$AMSBIN"/prop_prediction --smiles "c1ccccc1" --boilingpoint -d

# Step 12: Solvent Optimizations: Optimize Solubility
# ---------------------------------------------------

# In this step a solvent is optimized in order to maximize or minimize
# the mole fraction solubility of a solid solute in the liquid mixture.

echo "Step 12"
"$AMSBIN"/solvent_opt -t SOLUBILITY -method COSMO-RS -temperature 273.15 -max \
                      -c "benzene.coskf" -solute -meltingpoint 278.7 -hfusion 2.37 \
                      -c "ethanol.coskf" -c "methanol.coskf" -c "water.coskf" -d >␣
↪max_solubility
grep benzene.coskf max_solubility
grep " ethanol.coskf" max_solubility
"$AMSBIN"/solvent_opt -t SOLUBILITY -method COSMO-RS -temperature 273.15 -min \
                      -c "benzene.coskf" -solute -meltingpoint 278.7 -hfusion 2.37 \
                      -c "ethanol.coskf" -c "methanol.coskf" -c "water.coskf" -d >␣
↪min_solubility
grep benzene.coskf min_solubility
grep water.coskf min_solubility

# Step 13: Solvent Optimizations: Optimize Liquid-Liquid Extraction
# -----------------------------------------------------------------
```

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```
# In this step a mixture of immiscible solvents is optimized in order to maximize or
↪minimize
# the distribution ratio (D) of two solutes between the two liquid phases.

"$AMSBIN"/solvent_opt -t LLEXTRACTION -method COSMO-RS -multistart 10 -temperature
↪298.15 -max \
                      -c "water.coskf" -solute  -c "acetic_acid.coskf" -solute \
                      -c "benzene.coskf" -c "water.coskf" -c "2-hexanone.coskf" -c
↪"ethanol.coskf" -d > max_lle

echo "Step 13"
"$AMSBIN/amsreport" CRSKF -r "OPT_LLEXTRACTION%obj#8.3f"

echo "Ready"
```

11.5.4 Example: The COSMO-RS compound database

Download Database.run

```
#! /bin/sh

# This example tries to do the same as in the COSMO-RS GUI Tutorial: The COSMO-RS
↪compound database,
# using scripts.
# In many of the next examples fewer compounds are included than in the COSMO-RS GUI
↪Tutorial.


# First some .coskf files are copied to the location where the scripts are running.
# These .coskf files are a sample of the full database.

echo "Results"

cp $AMSHOME/examples/COSMO-RS/Database/*coskf .

rm -f job.sh
touch job.sh
chmod +x job.sh

# 4.2 Octanol-Water partition coefficients (log P_OW)
# ---------------------------------------------------

"$AMSBIN/crsprep" -t LOGP -j t4.2 \
                  -c Methanol.coskf > job.sh
./job.sh
echo "4.2"
"$AMSBIN/amsreport" t4.2.crskf compounds-name
"$AMSBIN/amsreport" t4.2.crskf logp



# 4.3: Henry's law constants
# --------------------------
```

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```
"$AMSBIN/crsprep" -t ACTIVITYCOEF -temperature 293.15 -densitysolvent 0.998 -j t4.3a \
                  -s Water.coskf \
                  -c Acetone.coskf -c Benzene.coskf -c Ethanol.coskf -c Methanol.
↪coskf > job.sh
./job.sh
echo "4.3a"
"$AMSBIN/amsreport" t4.3a.crskf compounds-name
"$AMSBIN/amsreport" t4.3a.crskf henry

"$AMSBIN/crsprep" -s Acetone.coskf  -pvap 0.246 -tvap 293.15 -savecompound
"$AMSBIN/crsprep" -s Benzene.coskf  -pvap 0.100 -tvap 293.15 -savecompound
"$AMSBIN/crsprep" -s Ethanol.coskf  -pvap 0.059 -tvap 293.15 -savecompound
"$AMSBIN/crsprep" -s Methanol.coskf -pvap 0.129 -tvap 293.15 -savecompound
"$AMSBIN/crsprep" -s Water.coskf    -pvap 0.02536 -tvap 293.15 -savecompound

"$AMSBIN/crsprep" -t ACTIVITYCOEF -temperature 293.15 -densitysolvent 0.998 -j t4.3b \
                  -s Water.coskf \
                  -c Benzene.coskf -c Ethanol.coskf -c Methanol.coskf > job.sh
./job.sh
echo "4.3b"
"$AMSBIN/amsreport" t4.3b.crskf henry


# 4.4: Solubility of Vanillin in organic solvents
# -----------------------------------------------

"$AMSBIN/crsprep" -s Vanillin.coskf -meltingpoint 355 -hfusion 5.35 -savecompound
"$AMSBIN/crsprep" -t PURESOLUBILITY -j t4.4 \
                  -s Vanillin.coskf \
                  -c Ethanol.coskf -c Methanol.coskf -c Water.coskf > job.sh
./job.sh
echo "4.4"
"$AMSBIN/amsreport" t4.4.crskf compounds-name
"$AMSBIN/amsreport" t4.4.crskf solubility-x
"$AMSBIN/amsreport" t4.4.crskf solubility-m

# 4.5: Binary mixture of Methanol and Hexane
# ------------------------------------------

"$AMSBIN/crsprep" -s Methanol.coskf -pvap 0.845 -tvap 333.15 -savecompound
"$AMSBIN/crsprep" -s Hexane.coskf   -pvap 0.77  -tvap 333.15 -savecompound
"$AMSBIN/crsprep" -t BINMIXCOEF -temperature 333.15 -n 100 -j t4.5a \
                  -s Methanol.coskf \
                  -s Hexane.coskf > job.sh
./job.sh
echo "4.5a"
"$AMSBIN/amsreport" t4.5a.crskf compounds-name
"$AMSBIN/amsreport" t4.5a.crskf molar-fraction
"$AMSBIN/amsreport" t4.5a.crskf pressure
"$AMSBIN/amsreport" t4.5a.crskf miscibility-gap
"$AMSBIN/amsreport" t4.5a.crskf miscibility-gap-x
"$AMSBIN/amsreport" t4.5a.crskf miscibility-gap-a

"$AMSBIN/crsprep" -s Methanol.coskf -pvap 1.01325 -tvap 337.8 -savecompound
"$AMSBIN/crsprep" -s Hexane.coskf   -pvap 1.01325 -tvap 342   -savecompound
"$AMSBIN/crsprep" -t BINMIXCOEF -pressure 1.01325 -iso isobar -n 100 -j t4.5b \
                  -s Methanol.coskf \
```

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```
                  -s Hexane.coskf > job.sh
./job.sh
echo "4.5b"
"$AMSBIN/amsreport" t4.5b.crskf molar-fraction
"$AMSBIN/amsreport" t4.5b.crskf temperature
"$AMSBIN/amsreport" t4.5b.crskf miscibility-gap
"$AMSBIN/amsreport" t4.5b.crskf miscibility-gap-x
"$AMSBIN/amsreport" t4.5b.crskf miscibility-gap-a

# 4.6: Large infinite dilution activity coefficients in Water
# ------------------------------------------------------------

"$AMSBIN/crsprep" -t ACTIVITYCOEF -temperature 298.15 -j t4.6 \
                  -s Water.coskf \
                  -c Benzene.coskf > job.sh
./job.sh
echo "4.6"
"$AMSBIN/amsreport" t4.6.crskf compounds-name
"$AMSBIN/amsreport" t4.6.crskf activity-coefficient


# 4.7: Parametrization of ADF COSMO-RS: solvation energies,
# vapor pressures, partition coefficients
# ------------------------------------------------------------

cat << eor > small.compoundlist
Hexane.coskf
Methanol.coskf
Ethanol.coskf
Acetone.coskf
Benzene.coskf
Water.coskf
eor

"$AMSBIN/crsprep" -t ACTIVITYCOEF -temperature 298.15 -densitysolvent 0.997 -j t4.7a \
                  -inputpurevap 0 \
                  -s Water.coskf \
                  -c small.compoundlist > job.sh
./job.sh
echo "4.7a"
"$AMSBIN/amsreport" t4.7a.crskf compounds-name
"$AMSBIN/amsreport" t4.7a.crskf gibbs-energy-solvation

"$AMSBIN/crsprep" -t PUREVAPORPRESSURE -temperature 298.15 -j t4.7b \
                  -c small.compoundlist -inputpurevap 0 > job.sh
./job.sh
echo "4.7b"
"$AMSBIN/amsreport" t4.7b.crskf compounds-name
"$AMSBIN/amsreport" t4.7b.crskf vapor-pressure

"$AMSBIN/crsprep" -t LOGP -j t4.7c -c small.compoundlist > job.sh
./job.sh
echo "4.7c Octanol/Water"
"$AMSBIN/amsreport" t4.7c.crskf compounds-name
"$AMSBIN/amsreport" t4.7c.crskf logp

"$AMSBIN/crsprep" -t LOGP -preset 5 -j t4.7d -c small.compoundlist > job.sh
```

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```
./job.sh
echo "4.7d Hexane/Water"
"$AMSBIN/amsreport" t4.7d.crskf logp

"$AMSBIN/crsprep" -t LOGP -preset 3 -j t4.7e -c small.compoundlist > job.sh
./job.sh
echo "4.7e Benzene/Water"
"$AMSBIN/amsreport" t4.7e.crskf logp

"$AMSBIN/crsprep" -t LOGP -preset 4 -j t4.7f -c small.compoundlist > job.sh
./job.sh
echo "4.7f Ether/Water"
"$AMSBIN/amsreport" t4.7f.crskf logp


# 4.8: COSMO-SAC 2013-ADF
# -----------------------

"$AMSBIN/crsprep" -t PURESIGMAPROFILE -method COSMOSAC2013 -c Water.coskf \
                  -c Ethanol.coskf -j t4.8a > job.sh
./job.sh
echo "4.8a"
"$AMSBIN/amsreport" t4.8a.crskf sigma
"$AMSBIN/amsreport" t4.8a.crskf sigma-profile
"$AMSBIN/amsreport" t4.8a.crskf sigma-profile-hb

"$AMSBIN/crsprep" -s Methanol.coskf -density 0.7918  -savecompound
"$AMSBIN/crsprep" -s Ethanol.coskf  -density 0.789  -savecompound
"$AMSBIN/crsprep" -s Acetone.coskf  -density 0.791  -savecompound

"$AMSBIN/crsprep" -t LOGP -method COSMOSAC2013 -j t4.8b \
                  -c Methanol.coskf -c Ethanol.coskf -c Acetone.coskf > job.sh
./job.sh
echo "4.8b Octanol/Water"
"$AMSBIN/amsreport" t4.8b.crskf compounds-name
"$AMSBIN/amsreport" t4.8b.crskf logp

"$AMSBIN/crsprep" -t LOGP -method COSMOSAC2013 -preset 5 -j t4.8c \
                  -c Methanol.coskf -c Ethanol.coskf -c Acetone.coskf > job.sh
./job.sh
echo "4.8c Hexane/Water"
"$AMSBIN/amsreport" t4.8c.crskf logp

"$AMSBIN/crsprep" -t LOGP -method COSMOSAC2013 -preset 3 -j t4.8d \
                  -c Methanol.coskf -c Ethanol.coskf -c Acetone.coskf > job.sh
./job.sh
echo "4.8d Benzene/Water"
"$AMSBIN/amsreport" t4.8d.crskf logp

"$AMSBIN/crsprep" -t LOGP -method COSMOSAC2013 -preset 4 -j t4.8e \
                  -c Methanol.coskf -c Ethanol.coskf -c Acetone.coskf > job.sh
./job.sh
echo "4.8e Ether/Water"
"$AMSBIN/amsreport" t4.8e.crskf logp

"$AMSBIN/crsprep" -s Acetone.coskf -density 0.791 -pvap 3.7     -tvap 373.15 -
↪savecompound
```

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```
"$AMSBIN/crsprep" -s Water.coskf   -density 0.997 -pvap 1.01325 -tvap 373.15 -
↪savecompound

"$AMSBIN/crsprep" -t BINMIXCOEF -method COSMOSAC2013 -temperature 373.15 -n 20 -j t4.
↪8f \
                  -s Acetone.coskf \
                  -s Water.coskf > job.sh
./job.sh
echo "4.8f"
"$AMSBIN/amsreport" t4.8f.crskf molar-fraction
"$AMSBIN/amsreport" t4.8f.crskf vapor-pressure
"$AMSBIN/amsreport" t4.8f.crskf pressure

echo "Ready"
```

11.5.5 Example: pKa values

Download pKa.run

```
#! /bin/sh

# This example tries to do the same as in the COSMO-RS GUI Tutorial: pKa values,
# using scripts
# First some .coskf files are copied to the location where the scripts are running,
# next the jobs are prepared and the reports are made.
# Check the COSMO-RS GUI Tutorial: pKa values to see what to do with the results.

echo "Results"

rm -f job.sh
cp $AMSHOME/examples/COSMO-RS/pKa/*.coskf .
cp $AMSHOME/examples/COSMO-RS/pKa/*compoundlist .

touch job.sh
chmod +x job.sh

echo "Acids"
"$AMSBIN/crsprep" -t ACTIVITYCOEF -j t5.1a \
                  -c tutoral5.1_acid.compoundlist -no_pdh > job.sh
./job.sh
"$AMSBIN/amsreport" t5.1a.crskf compounds-name
"$AMSBIN/amsreport" t5.1a.crskf Activity-Coefficient
"$AMSBIN/amsreport" t5.1a.crskf Gibbs-energy-solvation
"$AMSBIN/amsreport" t5.1a.crskf Gibbs-energy-solute

"$AMSBIN/crsprep" -t ACTIVITYCOEF -j t5.1b \
                  -c tutoral5.1_base.compoundlist -no_pdh > job.sh
./job.sh
"$AMSBIN/amsreport" t5.1b.crskf compounds-name
"$AMSBIN/amsreport" t5.1b.crskf Activity-Coefficient
"$AMSBIN/amsreport" t5.1b.crskf Gibbs-energy-solvation
"$AMSBIN/amsreport" t5.1b.crskf Gibbs-energy-solute

echo "Ready"
```

11.5.6 Example: Polymers

Download Polymers.run

```
#! /bin/sh

# This example tries to do the same as in the COSMO-RS GUI Tutorial: Polymers,
# using scripts.

# First some .coskf files are copied to the location where the scripts are running.
# Some of the .coskf files are a sample of the full polymer database ADFCRS-POLYMERS-
↪2019.
# In the first part of the example crsprep is used to set pure compound parameters.
# Pure compound densities are required for every species in a calculation involving␣
↪any polymers.
# For some pure compounds the VPM1 vapor pressure equation is set including vapor␣
↪pressure coefficients.

echo "Results"

cp $AMSHOME/examples/COSMO-RS/Database/*coskf .
cp $AMSHOME/examples/COSMO-RS/Polymers/*coskf .

"$AMSBIN/crsprep" -c Benzene.coskf -density 0.876 -savecompound
"$AMSBIN/crsprep" -c Water.coskf -density 1.0 -savecompound
"$AMSBIN/crsprep" -c Methanol.coskf -density 0.792 -savecompound \
                  -vp_equation VPM1 -vp_params "-7057.597287 -9.936895562 0.
↪00608530790 77.10002032 0"
"$AMSBIN/crsprep" -c Hexane.coskf -density 0.655 -savecompound \
                  -vp_equation VPM1 -vp_params "-5575.417318 -6.612402250 0.
↪00437376138 53.36969532 0"

rm -f job.sh
touch job.sh
chmod +x job.sh

"$AMSBIN/crsprep" -t ACTIVITYCOEF -j Polymers.1 \
                  -s "Poly(ethylene).coskf" -frac1 0.5 -s Benzene.coskf -frac1 0.5 \
                  -massfraction > job.sh
./job.sh
echo "Polymers.1"
"$AMSBIN/amsreport" Polymers.1.crskf compounds-name Flory-Huggins WF-activity-
↪coefficient

"$AMSBIN/crsprep" -t VAPORPRESSURE -temperature 298.15 -temperature 398.15 -n 10 -j␣
↪Polymers.2 \
                  -s "Poly(dimethylsiloxane).coskf" -frac1 0.5 -s Methanol.coskf -
↪frac1 0.25 \
                  -s Hexane.coskf -frac1 0.25 \
                  -massfraction > job.sh
./job.sh
echo "Polymers.2"
"$AMSBIN/amsreport" Polymers.2.crskf compounds-name temperature pressure

"$AMSBIN/crsprep" -t LOGP -preset 0 -j Polymers.3 \
                  -s "Poly(ethylene).coskf" -s Water.coskf \
                  -c Methanol.coskf > job.sh
./job.sh
```

(continues on next page)

(continued from previous page)

```
echo "Polymers.3"
"$AMSBIN/amsreport" Polymers.3.crskf logp

"$AMSBIN/crsprep" -t PURESOLUBILITY -temperature 398.15 -temperature 498.15 -n 10 -j␣
↪Polymers.4 \
                  -s Hexane.coskf -solphase Gas -pressure 1.01325 \
                  -c "Poly(styrene).coskf" > job.sh
./job.sh
echo "Polymers.4"
"$AMSBIN/amsreport" Polymers.4.crskf solubility-g

"$AMSBIN/crsprep" -t BINMIXCOEF -method COSMOSAC2013 -j Polymers.5 \
                  -s "Poly(ethyl_ethylene).coskf" -s Benzene.coskf \
                  -massfraction > job.sh
./job.sh
echo "Polymers.5"
"$AMSBIN/amsreport" Polymers.5.crskf polymer-fraction Flory-Huggins

echo "Ready"
```

CHAPTER

TWELVE

REQUIRED CITATIONS

When you publish results in the scientific literature that were obtained with programs of the ADF package, you are required to include references to the program package with the appropriate release number, and a few key publications.

12.1 General References

For calculations with the COSMO-RS program, version 2023.1:

1. C.C. Pye, T. Ziegler, E. van Lenthe, J.N. Louwen, *An implementation of the conductor-like screening model of solvation within the Amsterdam density functional package. Part II. COSMO for real solvents*, Can. J. Chem. 87, 790 (2009) (https://doi.org/10.1139/V09-008)

2. AMS 2024.1 COSMO-RS, SCM, Theoretical Chemistry, Vrije Universiteit, Amsterdam, The Netherlands, http://www.scm.com Optionally, you may add the following list of authors and contributors: J.N. Louwen, C.C. Pye, E. van Lenthe, N.D. Austin, E.S. McGarrity, R. Xiong, S.I. Sandler, R.I. Burnett

If you use COSMO-SAC 2013-ADF you must also add

3. R. Xiong, S.I. Sandler, R.I. Burnett, *An improvement to COSMO-SAC for predicting thermodynamic properties*, Ind. Eng. Chem. Res. 53, 8265 (2014) (https://doi.org/10.1021/ie404410v)

12.2 Solvent Optimizations

For solvent optimizations:

N.D. Austin, N.V. Sahinidis, D.W. Trahan, *COSMO-based computer-aided molecular/mixture design: A focus on reaction solvents*, AIChE Journal 64, 104 (2018) (https://doi.org/10.1002/aic.15871)

12.3 External programs and Libraries

Click here for the list of programs and/or libraries used in the ADF package. On some platforms optimized libraries have been used and/or vendor specific MPI implementations.

CHAPTER

THIRTEEN

KEYWORDS

CHAPTER

FOURTEEN

FAQ

14.1 I want to include solvent effects, do I need COSMO-RS?

You do not need COSMO-RS to do ADF calculations with continuum solvation (see COSMO vs COSMO-RS FAQ). If you want to calculate thermodynamic properties like partition coefficients, VLE, solubilities, etc. you do need COSMO-RS. COSMO-RS usually also yields more accurate solvation free energies and pKa values than COSMO.

14.2 Can I use a .cosmo file from COSMOlogic, Dmol3, or Gaussian with ADF COSMO-RS?

In principle, yes, but your are advised to rerun the COSMO calculation with ADF rather than using sigma profiles from Turbomole, Gaussian, DMol3 or another code. Since ADF uses a slightly different procedure (gas phase optimization followed by COSMO calculation with an infinite dielectric constant) as well as different technical settings (scalar relativistic, triple-zeta Slater-type basis set, integration, surface charge generation with a finer grid), our COSMO-RS implementation has been reparametrized specifically for use with sigma profiles generated in that way. Therefore, you are advised to follow the set procedure in ADF, easiest is to use the COSMO-RS preset in the ADF GUI. See for details: C.C. Pye, T. Ziegler, E. van Lenthe, J.N. Louwen, An implementation of the conductor-like screening model of solvation within the Amsterdam density functional package. Part II. COSMO for real solvents, Can. J. Chem.87, 790 (2009) (http://dx.doi.org/10.1139/V09-008). If you do insist on using sigma profiles generated with the other programs with different defaults, you can use the *cosmo2kf* (page 173) utility to convert the plain ascii cosmo files to our binary file format. There are also *scripting tools for COSMO-RS* (page 169) to facilitate screening solvent (combinations) for activities, partition coefficients, VLE, etc.

14.3 For which compounds do you have sigma profiles in the database?

We have text files for the regular compounds (https://www.scm.com/wp-content/uploads/COSMO-RS_compounds_database.txt) and ionic liquids (https://www.scm.com/wp-content/uploads/COSMO-RS_ionic_liquids_database.txt). If you install the databases you can also search on elemental composition.

14.4 I have COSMO-RS download permissions but I can not automatically download the COSMO-RS databases?

Some firewalls prevent the automatic download of the COSMO-RS database. With your SCM User ID and password you can *download the compounds database manually <ADFCRS-2018>* (see also video on how to install it on Windows (https://downloads.scm.com/distr/adfcrs_from_zip.mp4) for AMS2021).

PYTHON MODULE INDEX

p

INDEX

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W