

# Prediction of Solubilities and Partition Coefficients in Polymers Using COSMO-RS

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**S** Supporting Information

**ABSTRACT:** Recent results concerning the prediction of thermodynamic properties of solutes in polymers are presented. In particular, the computation of vapor–liquid and gas–liquid equilibria (i.e., liquid and gas solubilities) in different polymers and partition coefficients between the polymer and a solvent phase are addressed. Calculations have been carried out using COSMO-RS theory which combines quantum-chemical calculations with efficient statistical thermodynamics for intermolecular interactions. Predictions for vapor–liquid equilibria and for partition coefficients have been improved by incorporation of polymer-specific entropic contributions due to free volume effects. It is demonstrated that a high predictive accuracy is obtained if the polymer is sufficiently characterized by its composition, density, and crystallinity. The approach is currently limited to gaseous and liquid solutes and to linear, i.e. non-cross-linked polymers without any significant swelling.

## 1. INTRODUCTION

The ability to predict thermodynamic properties in polymers, as for example, the solubility and the partitioning between a polymer and another phase, is of relevance in many areas such as food packaging,<sup>1</sup> adhesive<sup>2</sup> and coating technology,<sup>3</sup> chromatography,<sup>4</sup> membrane separation,<sup>5</sup> and also drug development.<sup>6</sup> Most current computational approaches, and their extensions toward polymers, that may address these issues are strongly parametrized, such as activity coefficient models<sup>7,8</sup> or equations of states (EOS) approaches.<sup>9–13</sup> Once thoroughly fitted to a specific system, EOS methods give very accurate results also for variable pressures and temperatures and are, for example, able to deal with the effect of the glass transition temperature on gas solubilities in polymers.<sup>14,15</sup> However, they are of limited predictivity outside the core region of their parametrization and need to be refitted for novel systems or for mixtures having non-negligible chemical interactions. Other methods such as molecular dynamics or Monte Carlo approaches are somewhat laborious due to costly statistical sampling which is a drawback, for example, for extended screening applications. The conductor-like screening model for realistic solvation,<sup>16</sup> in short COSMO-RS, offers an efficient and also very general alternative route. The basic idea is to compute the chemical potential in solution or, in this case, in a polymer via fast statistical thermodynamics of interacting molecular surface segments which are derived from quantum chemical calculations in a continuum solvation model. The three-dimensional information on the screening charges from the continuum solvation treatment (usually the conductor-like screening model, COSMO<sup>17</sup>) is projected on a histogram of equally binned charge densities, the so-called  $\sigma$ -profile. Using the  $\sigma$ -profile the computation of the chemical potential in the liquid state and hence of all related properties is then only a matter of seconds. Although COSMO-RS also needs some parameters, those are element specific, i.e. no specific interactions are parametrized for each molecule, and thus,

there is no need for any reparametrization for new compounds. Concerning the details of the method we refer to a recent review.<sup>18</sup> Although COSMO-RS was originally developed for liquid phases, it becomes a useful tool for the prediction of thermodynamic properties in polymers under the assumption that polymers can be treated as solutions consisting of monomers or of oligomers with a small number of repeat units. This yields a very accurate enthalpic part of the overall Gibbs free energy. Additionally, as shown in this study, the entropic contribution due to volume effects can be incorporated either by a Flory–Huggins combinatorial term or more accurately, by the free volume approximation of Elbro et al.<sup>19</sup>

COSMO-RS has already been applied to polymer solvents occasionally within the recent years. The following paragraphs briefly list some of this previous work.

Using an early implementation of COSMO-RS Klamt carried out the prediction of the solubilities of a set of gases and small molecules in different polymers which was later published in ref 20. A high correlation with experimental data was found; however, one polymer-specific constant had to be adjusted in order to reach an overall agreement with the experiment.

The effect of the UNIFAC free volume term in combination with COSMO-RS activity coefficients on several polymer–solvent systems has been published by Tukur and co-workers as a conference contribution.<sup>21</sup> They used the combinatorial term of Staverman–Guggenheim *plus* the free volume term of Oishi and Prausnitz on top of the (residual) COSMO-RS term for their calculations for a few polymer solutions. Except for polystyrene/acetone, they found a good agreement between experimental and predicted results.

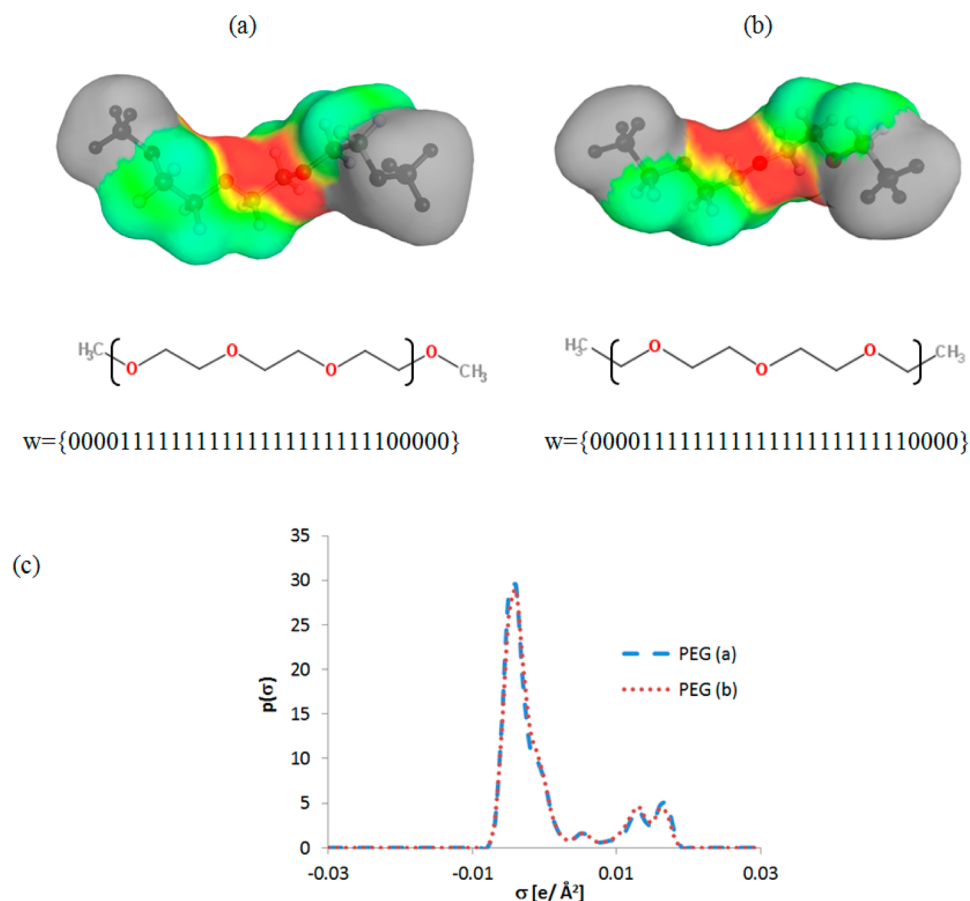
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**Figure 1.** Two alternative COSMO-RS polymer representations of polyethylene glycol (PEG) and the respective weight strings (a), (b), and  $\sigma$ -profiles of those representations (c).

Kahlen et al. have studied the solubility of cellulose in different ionic liquids using COSMO-RS. They tried different combinatorial contributions for this system such as the one of Flory–Huggins, Staverman–Guggenheim, and corresponding free volume-based contributions but did not find any improvement of their results.<sup>22</sup>

In an extensive study the sorption of organic chemicals into polymeric sorbents, i.e. polymer–air and polymer–water partition coefficients for a set of 25 different polymer systems, was computed lately by Goss.<sup>23</sup> Omitting the combinatorial term COSMO-RS results were regressed against experimental data and a mean squared correlation coefficient of  $R^2 = 0.84$  was obtained on all data sets, while the average regression slope of 0.88 showed slight deviation from unity.

Furthermore, in a cooperation between the GKSS Forschungszentrum Geesthacht and COSMOlogic the absorption in polymer membranes was studied by experiments and accompanying COSMO-RS calculations. The membranes under scrutiny were complex copolymers and partially grafted. Discrepancies between the predicted and experimental polymer solubilities and absorption isotherms were attributed to significant swelling of the polymer material.<sup>24</sup>

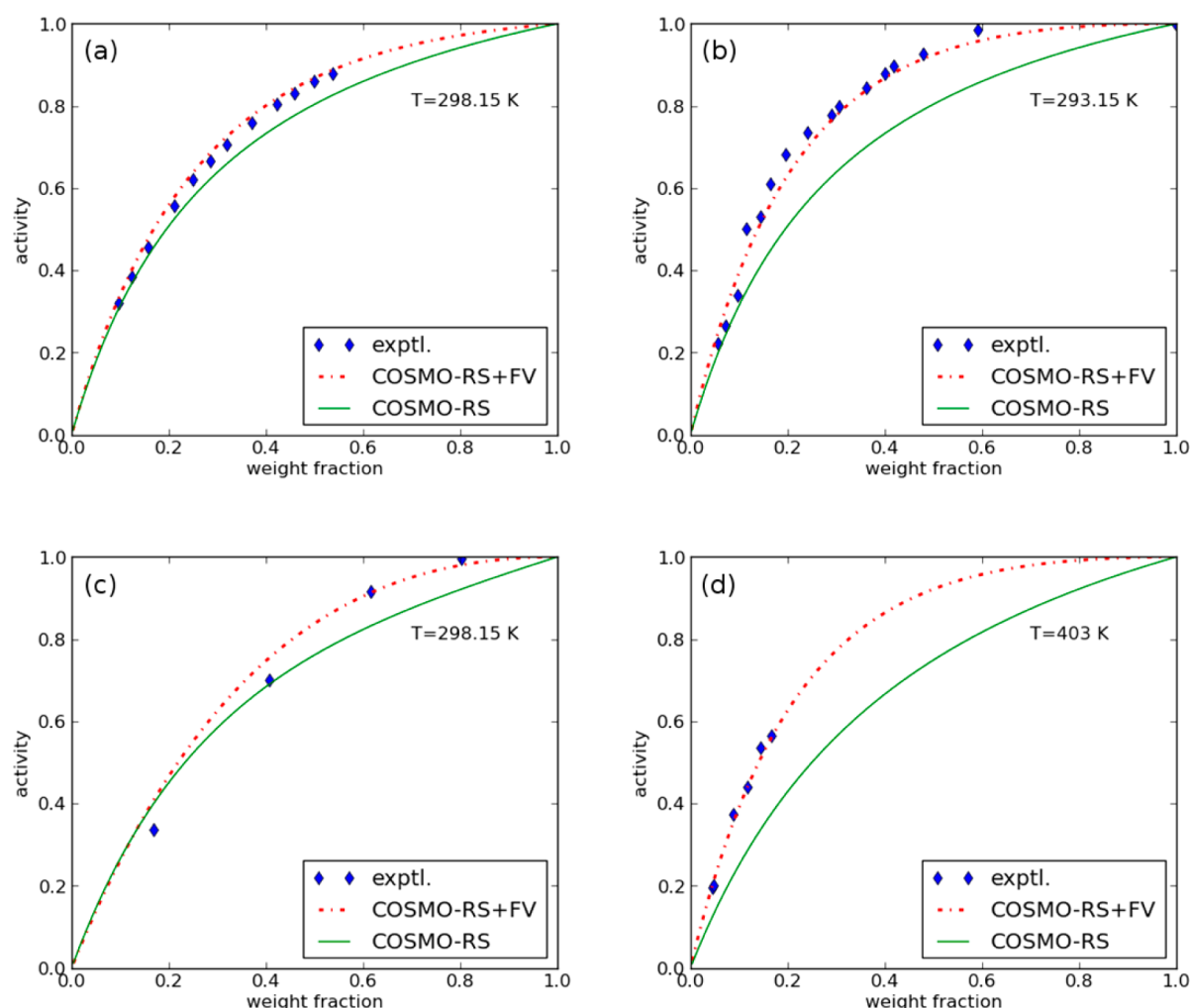
Another study was published evaluating free volume effects for polymer solutions with the COSMO-RS reimplementation, COSMO-SAC, showing an overall improvement when taking into account free volume effects.<sup>25</sup> In a more ample context COSMO and COSMO-RS have also been applied to study kinetics of polymerization reactions.<sup>26–28</sup>

This article is organized as follows: First, computational details concerning the treatment of polymers with COSMO-RS are introduced. Then, some benchmark results on several diverse polymers from a popular vapor–liquid equilibrium data set<sup>29</sup> are presented. This is followed by a study of gas solubilities in several polymers using another extensive data compilation.<sup>30</sup> Finally, computations of the partition coefficients between polymer and solvent phases are evaluated.

## 2. COMPUTATIONAL DETAILS

The following results have been generated with a recent COSMOtherm release and the respective COSMO-RS parametrizations BP\_TZVP\_C30\_1401.ctd.<sup>31</sup> The screening charge densities for COSMOtherm calculations were generated by the TURBOMOLE package,<sup>32</sup> using the BP86 density functional<sup>33,34</sup> with a TZVP basis set.<sup>35</sup> Low-energy conformations taking into account the liquid state for polymers and solutes were generated by the COSMOconf workflow.<sup>36</sup> For polymers only the lowest-energy conformation was used; for all other solutes different conformational states in solutions were taken into account via Boltzmann weighting. Contributions due to combinatorial terms and polymer crystallinity have been computed subsequently on top of the COSMOtherm results.

There are several ways to represent a polymer with the program package COSMOtherm.<sup>31</sup> Only for a low degree of polymerization it is computationally feasible to use the complete molecule, which may be necessary, if end-groups are of importance as for small poly(ethylene glycol) (PEG) entities. Usually, only one or several repeat units are taken into



**Figure 2.** Activities for some polymer solutions as predicted by COSMO-RS and comparison with experiment. COSMO-RS results without combinatorial (solid line) and with a free volume-based term are given (dashed line) for the systems (a) benzene in PS ( $M_n = 800$  g/mol), (b) benzene in PS ( $M_n = 500,000$  g/mol), (c)  $\text{CHCl}_3$  in PS ( $M_n = 90,000$  g/mol), (d) *m*-xylene in PS ( $M_n = 53,700$  g/mol).

account, capped by a suitable end group, which is then deactivated using a so-called “weight string”. The weight string consists of binary digits which allows for selectively switching on/off certain atoms within a cosmo file (see example in Figure 1).

This figure shows two alternative representations for the PEG polymer, which have nearly identical  $\sigma$ -profiles, and thus shows that there is some arbitrariness in the definition of the repeat units. However, care should be taken if polar bonds are capped (Figure 1a), in such cases it may be necessary to use more than just a simple methyl as end group.

Internally, the molecular weight and the COSMO volumes are adopted according to the specified weights by COSMO-therm. Usually it is sufficient to use trimers, i.e. three repeat units capped with a suitable functional group.

Copolymers can be obtained either by explicit construction of one single COSMO file containing both repeat units in their respective proportion, or by using a mixture of several separate homopolymers. The latter approach is somewhat more flexible as it allows for varying the composition of the copolymer.

Within COSMO-RS, the combinatorial (nonideal entropic) contribution to the chemical potential has been developed for molecules of small and moderate size. Therefore, it is usually

recommended to be switched off as it is not well suited for macromolecules.

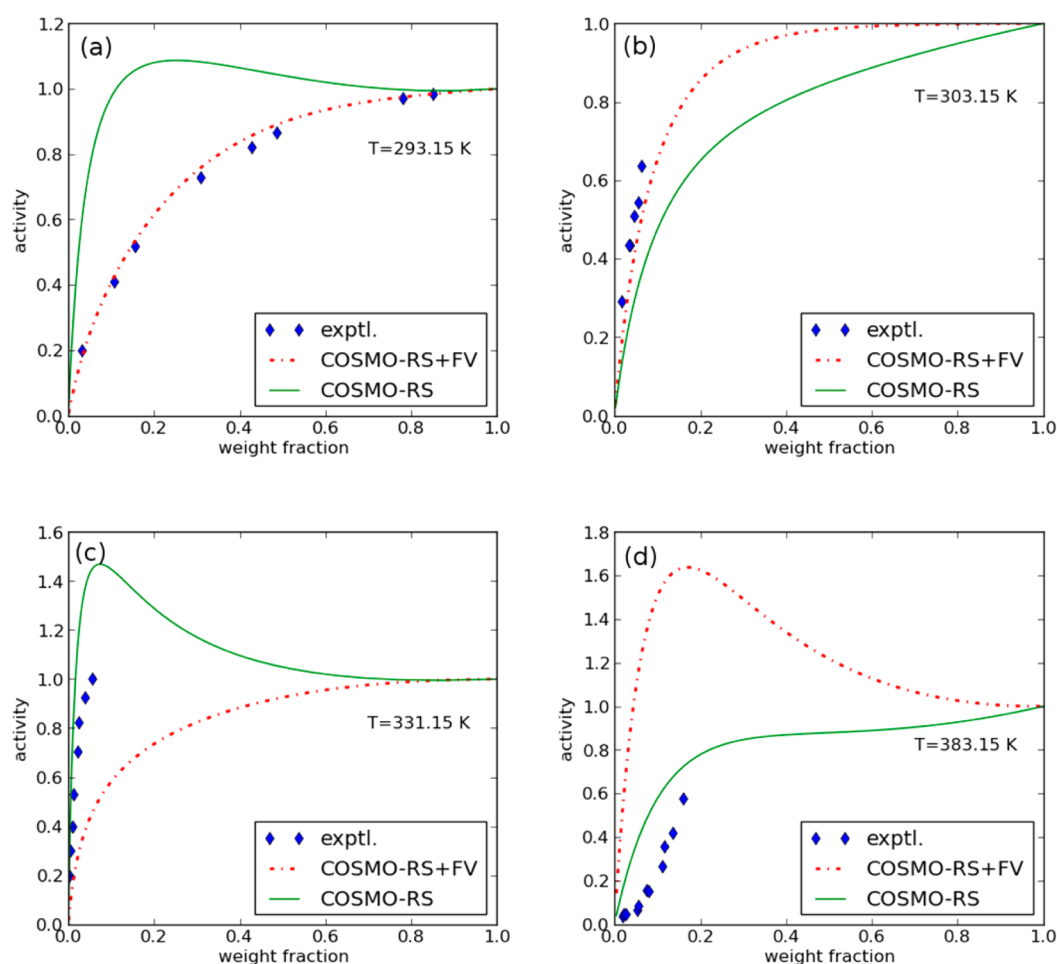
It is well-known that free volume effects play an important role for polymer solutions.<sup>37</sup> Small molecules usually have a higher amount of free volume than polymers, which is significantly reduced upon mixing. There exist several possible definitions of the free volume. Here, the free volume  $V_f$  is defined as the difference between the molar volume  $v_i$  and the molar hard core volume  $v_i^*$  according to Bondi.<sup>38</sup> Elbro and co-workers proposed a simple modification of the excess free energy,<sup>19</sup> which closely resembles the Flory–Huggins combinatorial contribution:

$$G^{\text{comb, fv}} = RT \sum x_i \ln \left( \frac{\varphi_i^{\text{fv}}}{x_i} \right) \quad (1)$$

$\varphi_i^{\text{fv}}$  is the free volume fraction of compound  $i$  with mole fraction  $x_i$ .

$$\varphi_i^{\text{fv}} = \frac{x_i(v_i - v_i^*)}{\sum_j x_j(v_j - v_j^*)} \quad (2)$$

The hard core volume may be obtained from Bondi van der Waals volumes or from COSMO volumes (the element specific



**Figure 3.** Activities for some polymer solutions as predicted by COSMO-RS and comparison with experiment. COSMO-RS results without combinatorial (solid line) and with a free volume-based term are given (dashed line) for the systems (a) H<sub>2</sub>O in polyethylene glycol ( $M_n = 200$  g/mol), (b) propanol in poly(vinyl acetate) ( $M_n = 83,400$  g/mol), (c) H<sub>2</sub>O in poly(vinyl acetate) ( $M_n = 83,400$  g/mol), (d) 2-methylheptane in poly(vinyl acetate) ( $M_n = 83,400$  g/mol).

radii used in DFT/COSMO calculation are somewhat larger than the Bondi radii with  $r_{\text{COSMO}} \approx 1.17r_{\text{Bondi}}$ ). This finally leads to the following additional contribution to the activity coefficient:

$$\ln \gamma_i^{\text{fv}} = \ln \left( \frac{\varphi_i^{\text{fv}}}{x_i} \right) + 1 - \frac{\varphi_i^{\text{fv}}}{x_i} \quad (3)$$

With  $x_i$  being the mole fraction with respect to the polymer chain. Thus, care should be taken to use the right definition of the mole fraction, which may be either referring to one mole of the repeat unit or, if the number-average molecular weight of the polymer is available, to one mole of the whole polymer chain. As the molecular weight of the polymer is often either not known or not well-defined, one often works with weight fraction-based quantities for polymer solutions. The weight fraction based activity coefficient  $\Omega$  can be obtained from the mole fraction-based activity coefficient  $\gamma$  according to

$$\Omega_i = \frac{a_i}{w_i} \approx \gamma_i \frac{M_{\text{polymer}}}{M_i} \text{ with } w_i \approx \frac{x_i M_i}{M_{\text{polymer}}} \quad (4)$$

Technically, it is necessary to have the density for each solute and the polymer available, either experimentally or from a QSPR estimation. Interestingly, it was found that the Elbro

term with Bondi van der Waals volumes scaled by a factor of 1.2 resulted in improved results as compared to the original volumes.<sup>39</sup> Furthermore, in the same study the Elbro free volume correction has been reported to be superior to other free volume approaches, as the one of Oishi and Prausnitz<sup>40</sup> for example. Pappa and co-workers compared the Elbro free volume correction with the combinatorial term of Zhong and Masuoka and concluded that the first is being superior.<sup>41</sup> All in all, there seems to be a consensus that among the possible entropic correction the Elbro free volume term is the most favorable one.<sup>25,39,41</sup> In this study the approach of Elbro was used in a modification using COSMO instead of Bondi volumes.

### 3. PREDICTION OF VAPOR–LIQUID EQUILIBRIA

The vapor–liquid equilibrium data used for an extensive evaluation has been taken from the *Polymer Solution Data Collection*.<sup>29</sup> Here, activities of the solutes have been obtained mostly by partial vapor pressure measurements of the mixture as compared to the pure substance vapor pressure with small corrections made due to the nonideal character of the vapor. The data under consideration has been partitioned into systems being above and below their glass transition temperature  $T_g$  and is compiled in Table S1 and S2 in the Supporting Information (SI), respectively.



In 40 out of the 46 investigated systems an improvement of the predicted activities is obtained by taking into account the free volume contribution from Elbro and co-workers. (Figure 2 and Table S1 and Table S2 in the SI). Using a Flory–Huggins-like combinatorial term also leads to improved results that are, however, somewhat inferior to the Elbro correction. The overall root mean squared error or deviation (RMSE) in activities for predictions above the glass transition amounts to an RMSE = 0.15, as compared to the pure COSMO-RS results with an RMSE = 0.21. Somewhat surprisingly, the predictions on systems being below their glass transition (Table S2 in the SI) are of comparable accuracy. One possible explanation for this finding could be the fact that this data set deals mostly with good solvents that are able to soften the glassy polymer structure substantially. For example, in the system benzene in PS at 293 K ( $T_g \approx 373$  K), one sees a considerable kink in the activity curve at a weight fraction of about 0.15 (Figure 2b). At this weight fraction, the solvent benzene most probably induces the PS to undergo a phase transition. In other cases the onset of the experimental data starts at a somewhat higher weight fraction where the softening of the polymer has probably already taken place, and one is not able to carve out an effect due to the glass transition (Figure 2c).

Another interesting finding is that the predictions are quite accurate also at elevated temperatures, although the experimental room temperature density is used. The main reason for this is that the core effect due to free volume entropic changes comes from free volume *differences* between solute and polymer.<sup>19</sup> Because both solute and polymer densities (and free volumes) will scale with temperature, using the density from ambient conditions also at higher temperatures does not introduce large errors at the moderate temperature regime under consideration here (see Figure S1 in the SI for the example *m*-xylene in PS at 293 and 403 K).

Furthermore, it is instructive to examine a few examples where the pure COSMO-RS- and the free volume-augmented computations deviate significantly from the experiment. The two most extreme cases appear for poly(vinyl acetate) (PVAC) with water and with 2-methylheptane respectively, see Figure 3c,d. It seems that the solubility of water in PVAC is completely overestimated for the COSMO-RS + FV calculations, whereas the opposite is true for the solubility of 2-methylheptane in PVAC. The pure COSMO-RS computations both underestimate the solubilities. A possible explanation for a solubility overestimation for water in PVAC could be the chosen experimental setup.<sup>42</sup> The polymer sample was leached in water several weeks at elevated temperature and then dried prior to the solubility experiment. An incomplete drying process could have caused a limited uptake of additional water in PVAC and thus would result in measuring a decreased solubility. Currently, we do not have a better explanation at hand for this particular discrepancy. The case of 2-methylheptane remains particularly puzzling, as other solutes are well described within PVAC, and also alkanes seem to behave well in other polymers (Table S1 in the SI). Moreover, experimentally determined activities of alkanes in ethyl acetate<sup>43</sup> as a similar reference system for PVAC are all somewhat higher than those computed by the standard COSMOtherm. This raises some doubts on the reliability of the experimental data of the 2-methylheptane/PVAC system. The authors of the original work, who used the data also for model building, stated on this particular system, that they were not able to use it for a

meaningful fit of data.<sup>44</sup> A summary over all calculations is presented in Table S1 in the SI.

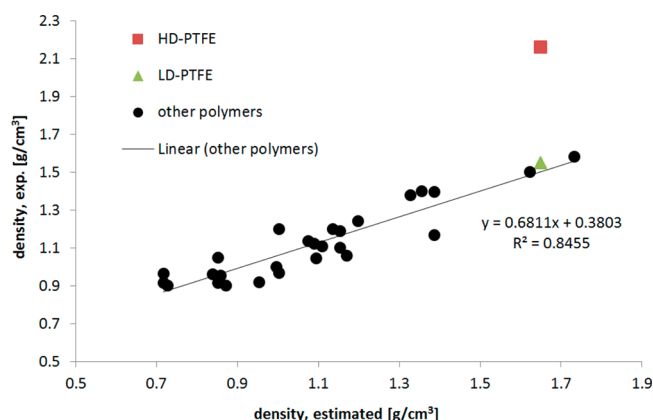
These results indicate that a clear improvement is obtained for polymer solutions by consideration of a polymer-specific entropy change upon mixing. As a drawback a sufficiently accurate density of the polymer has to be specified, as well as the number-average molecular weight  $M_n$ . The free volume term is considerably sensitive to small changes in the density, which in principle allows for example differentiating between low-density and high-density polyethylene, which otherwise is not possible. The  $M_n$  is less influential, as typically molecular weights >10,000 g/mol do not change results based on the Elbro free volume term anymore. Accordingly, in cases with unknown molecular weight  $M_n = 10,000$  g/mol is used as a guess for the subsequent solubility and the partition coefficient calculations. The typical large polymer molecular weights affect the ideal entropic mixture contribution  $RT \ln(x)$ , which becomes almost zero except for very small solute–polymer weight fractions (i.e., where the solute mole fraction  $x$  is significantly different from unity). Thus, using the free volume term typically raises the chemical potential, as overall free volume is lost in the mixture as compared to the pure solutes, and the  $RT \ln(x)$  term becomes less negative. Only water seems to be an exception; based on COSMO volumes it has a small free volume of only 14.5% which lies below the polymer average of 17.1% (Table S1 in the SI). Thus, in many cases additional free volume is gained when mixed with a polymer, and the free volume effect lowers the activity of water in most polymers.

Although these results demonstrate that it is possible to compute the chemical potential of small solutes in nonglassy polymers quite reliably, attempts to model liquid–liquid equilibria (LLE) for polymer–solvent systems have not been particularly successful so far. First of all, this is due to the fact that the temperature dependency of the density and hence of the free volume is not taken into account. Second, the computation of the LLE phase diagram affords an accurate estimate of the overall free energy and thus of the chemical potential of the polymer in the solvent, which probably is not yet accurate enough for this purpose.

#### 4. POLYMER DENSITY ESTIMATION

As experimentally determined densities of polymers are often not available, it may be advantageous to use estimated values. Figure 4 plots the densities of polymers as obtained by the default COSMOtherm QSPR<sup>31</sup> against experimental data. Using a simple linear regression to adapt these estimations for polymer solvents (and keeping the default QSPR for the solutes) and subsequent computations of activities on the data set from the previous section leads to an overall RMSE = 0.14 with respect to the activities as compared to an RMSE = 0.12 using experimental densities.<sup>45</sup>

It has not yet been tried to improve this relation, which has been used in this form for the sake of simplicity, with some additional descriptors and more data points. Concerning the outlier in Figure 4, PTFE, its density seems to vary strongly; values from 2.2 g/cm<sup>3</sup> (high density PTFE) to 1.55 g/cm<sup>3</sup> (low density) are reported in the literature.<sup>45</sup> Alternatively, other density models for polymers could also have been employed like the group contribution GCVOL method and the Tait equation.<sup>41</sup> However, as the free volume contribution is very sensitive to small changes in the density, it is certainly desirable



**Figure 4.** Polymer densities as predicted by the COSMOtherm QSPR model against experimental data. An outlier is polytetrafluoroethylene (PTFE), which according to ref 45, however, has a broad range of experimental densities, between its low-density (LD-PTFE) and high-density variants (HD-PTFE).

to use experimental data which will be most often available or easily obtainable.

## 5. PREDICTION OF SOLUBILITY COEFFICIENTS OF GASES AND SMALL MOLECULES (GAS–LIQUID EQUILIBRIA)

For this study experimental gas solubilities have been taken from the compilation of Pauly.<sup>30</sup> As an extension to an earlier work from one of us,<sup>20</sup> the aim of this study was to re-examine the data set with an actual implementation of COSMO-RS and also to include free volume effects, in order to get rid of the polymer-specific constant that had been necessary before.

The gas solubility  $S$  in polymers is often given in the following or related units:

$$\text{Units of } S: \frac{\text{cm}^3 \{\text{STP}\}}{\text{cm}^3 \text{ Pa}} \quad (5)$$

i.e. the dissolved volume of gas at standard temperature and pressure (STP: 273.15 K and  $1.013 \times 10^5$  Pa) in  $\text{cm}^3$  in volume of polymer in  $\text{cm}^3$ . Please note that unfortunately there is a typo in the introductory part of the Pauly data collection concerning the units of permeability which directly translates into wrong units for the solubility ( $\text{cm}^2$  instead of  $\text{cm}^3$  in the numerator of  $S$ ). The solubility  $S$  as defined according to eq 5 equals the inverse of the Henry's law constant. Within COSMOtherm the Henry's law constant is computed in a reference state corresponding to mole fractions of gas per mole of fractions of solvent. Therefore, it has to be converted to the right reference state first, before it can be used to obtain  $S$  by simple inversion:

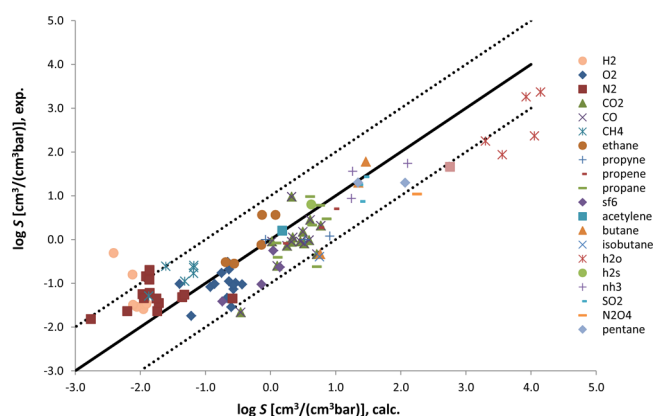
$$S \left[ \frac{\text{cm}^3}{\text{cm}^3 \text{ bar}} \right] = \frac{1}{H[\text{bar}]} \frac{\rho_{\text{solvent}}[\text{g}/\text{cm}^3]}{\text{MW}_{\text{solvent}}[\text{g}/\text{mol}]} \times V_{\text{IG}}[\text{l}/\text{mol}] \times 1000 \quad (6)$$

Here,  $\rho_{\text{solvent}}$  is the density of the polymer,  $\text{MW}_{\text{solvent}}$  is the molecular weight of the polymer solvent,  $V_{\text{IG}}$  is the molar volume of the ideal gas, and  $H$  is the Henry constant in the COSMO-RS reference state. The Henry law constant  $H$  for compound  $i$  in solvent  $S$  is computed by COSMOtherm as

$$H_S^i = \exp(\mu_S^i - \mu_{\text{IG}}^i/RT) = \gamma_S^i p_{\text{vap}}^{i,\text{IG}} \quad (7)$$

whereas  $\mu_S^i$  and  $\mu_{\text{IG}}^i$  are the pseudochemical potential<sup>46</sup> of compound  $i$  in solvent  $S$  and in the gas phase, assuming ideal gas behavior, respectively. Furthermore,  $\gamma_S^i$  and  $p_{\text{vap}}^{i,\text{IG}}$  are the activity coefficient of solute  $i$  in solvent  $S$  and the pure compound vapor pressure of  $i$  assuming ideal gas behavior. In the following, the experimental vapor pressures have been used, in combination with the COSMOtherm computed activity coefficients. To estimate vapor pressures for small gases with critical temperatures below 298 K, an extrapolation via Wagner coefficients has been done. If those coefficients were not available, for example, for cases where the critical temperature was below room temperature, an extrapolation on the basis of COSMOtherm has been carried out using an experimental starting point for the vapor pressure. Such an extrapolation beyond the critical temperature is a common approximation for the determination of Henry's law constants<sup>47</sup> and, as long as the gas will behave almost ideally at the (vapor) pressures under consideration, is expected to give reasonable results. Please note that most of the experimental gas solubilities of the Pauly data set have been measured indirectly, i.e. by measuring the permeability  $P$  and the diffusivity  $D$ , according to  $S = P/D$ , which is possibly less reliable than a direct measurement of  $S$ .<sup>48</sup>

The results of the gas solubility predictions are summarized for 15 different polymers in Figure 5 and Table 1. This table



**Figure 5.** Predicted versus experimental gas solubilities in different polymers. Results for HDPE, LDPE, and PTFE have been corrected assuming a crystalline fraction  $\alpha$  (see Table 2). COSMO-RS results have been modified by using the free volume combinatorial contribution. A perfect prediction (full line) and a  $\pm 1$  log unit corridor (dashed line) are plotted additionally.

shows three different COSMO-RS runs, using no combinatorial contribution at all, the Elbro free volume and the Flory–Huggins term. The combinatorial contribution does not have a significant influence on the outcome, an overall squared correlation coefficient  $R^2$  of about 0.8 and a RMSE of  $\log_{10}(S)$  of about 0.6 is obtained for any of the approaches chosen. However, for the polymers HDPE, LDPE, and PTFE there was initially a systematic shift in the predicted solubilities. This shift can be explained by the fact that these polymers are semicrystalline, i.e. containing a significant crystalline fraction, and assuming that sorption takes place only in the amorphous and not in the crystalline region. The crystalline fraction  $\alpha$  of a polymer can be estimated by its actual density, if the density of the crystalline and the amorphous region are known, according to

**Table 1.** Computed Gas Solubilities Using No Combinatorial Contribution (CRS,no comb.), Using a Free Volume Term (CRS +FV) and the Flory–Huggins term (CRS+FH) and Their Comparison with Experiment ( $T = 298\text{ K}$ )<sup>30a</sup>

polymer	<i>n</i>	CRS, no comb.		CRS+FV		CRS+FH	
		RMSE	<i>R</i> <sup>2</sup>	RMSE	<i>R</i> <sup>2</sup>	RMSE	<i>R</i> <sup>2</sup>
ethylcellulose <sup>b</sup>	11	0.69	0.86	0.63	0.90	0.64	0.90
HDPE	10	0.67	0.59	0.68	0.59	0.68	0.60
nitrocellulose	8	0.62	0.80	0.51	0.93	0.50	0.94
PEMA <sup>b</sup>	6	0.39	0.93	0.79	0.93	0.79	0.92
polyisopren	10	0.51	0.79	0.53	0.78	0.57	0.77
PTFE <sup>b</sup>	10	1.02	0.53	1.03	0.53	1.02	0.51
PVC <sup>b</sup>	7	0.69	0.76	0.90	0.78	0.89	0.78
LDPE	11	0.65	0.68	0.66	0.68	0.68	0.67
polychloropren	6	0.56	0.79	0.43	0.92	0.40	0.93
PDMS	4	0.90	0.51	0.90	0.51	0.90	0.51
PODP <sup>b</sup>	2	1.07	1.00	0.87	1.00	0.78	1.00
polybutadiene	4	0.52	0.91	0.51	0.91	0.49	0.91
polydimethylbutadiene	4	0.51	0.93	0.50	0.93	0.45	0.93
polyvinylbenzoate <sup>b</sup>	4	0.40	0.92	0.39	0.93	0.34	0.95
PET (40% cryst.)	4	0.39	0.82	0.37	0.84	0.29	0.91
PET (amorphous)	4	0.31	0.86	0.29	0.87	0.20	0.94
average		0.62	0.79	0.62	0.81	0.60	0.82

<sup>a</sup>Results for HDPE, LDPE, and PTFE have been corrected assuming a crystalline fraction  $\alpha$  (see Table 2). The number of gas solutes is given by *n*. RMSE and *R*<sup>2</sup> are given with respect to the logarithmic solubility  $\log_{10}(S)$ , with *S* given in [ $\text{cm}^3/\text{cm}^3\text{ bar}$ ]. <sup>b</sup>Polymers having a glass transition above room temperature.

$$\alpha = \frac{\rho_{\text{cryst.}}(\rho - \rho_{\text{amorph.}})}{\rho(\rho_{\text{cryst.}} - \rho_{\text{amorph.}})} \quad (8)$$

Table 2 shows the experimental crystalline fraction and  $\alpha$  as obtained by the systematic shifts obtained from the COSMO-

**Table 2.** Crystalline Fractions  $\alpha$  As Computed from the Gas Solubility *S* for the Semicrystalline Polymers LDPE, HDPE, and PTFE<sup>a</sup>

polymer	$\rho[\text{g}/\text{cm}^3]$	$\rho$ , cryst.	$\rho$ , amorph.	$\alpha$ , exp	$\alpha$ , predicted
LDPE	0.91	1.00	0.85	0.47	0.63
HDPE	0.96	1.00	0.85	0.79	0.91
PTFE	2.20	2.35	2.00	0.61	0.73

<sup>a</sup>Experimental values for  $\alpha$  have been obtained using the known density, and the densities of the amorphous and the crystalline states according to eq 8.

RS results. Predicted and experimental crystalline fractions agree reasonably with the predicted fractions being somewhat overestimated.

Concerning PET, separate experimental data for the amorphous and the semicrystalline polymer were given. Figure 5 shows that there are some outliers at either end of the solubility spectrum due to  $\text{H}_2$  and to  $\text{H}_2\text{O}$ . The strong outliers for  $\text{H}_2$  in PTFE and LDPE, which have been corrected for semicrystallinity, could be due to the fact that hydrogen as opposite to the other larger solutes is partially soluble also in the crystalline regions of those polymers. A possible explanation for the overestimation of the solubility of water is the fact that the constraints resulting from the polymer structure are suppressing the local structure formation required for the efficient solvation of a water molecule with its four strong interaction sites. Indeed, the polymers for which the solubility of water is overestimated have glass transitions above room temperature (PEMA, PVC, PODP, ethylcellulose), except for nitrocellulose, where the overestimation is smallest, and which

has a glass transition below room temperature.<sup>45</sup> Interestingly, apart from this issue, no significant difference in predictive accuracy is found within this data set irrespective of whether the pure polymer systems are above or below their respective glass transition. This may be explained by the comparatively high liquid solubility of most compounds within the polymers of this study. This may also be the reason why taking into account the free volume effect does not influence the gas solubility results significantly. The high liquid solubility within the polymers of this study results in a free volume fraction  $\phi_i^{\text{fv}}$  close to one. Furthermore, the computed  $\log_{10}(S)$  values have a significant contribution originating from the compound vapor pressure (eq 7), mitigating any modifications made to  $\ln(\gamma)$  and hence the liquid phase.

## 6. PREDICTION OF PARTITION COEFFICIENTS

Partition coefficients  $\log_{10}(P)$  between a polymer phase and another phase may be computed according to

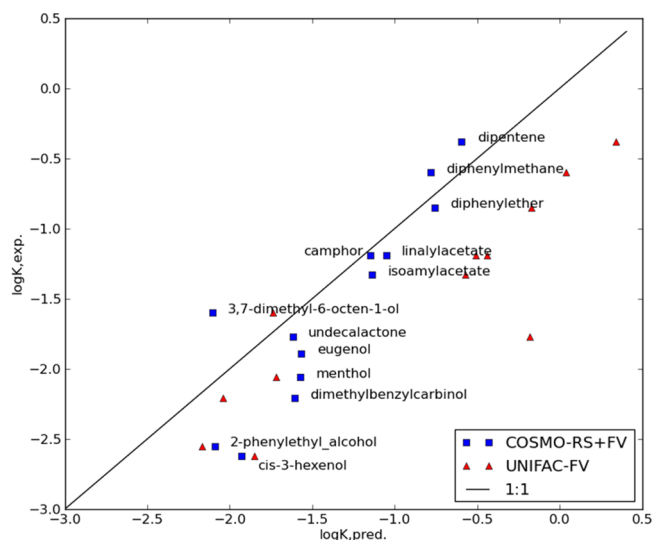
$$\log_{10}(P_{\text{poly},X}^i) = (\mu_X^i - \mu_{\text{poly}}^i / RT \ln(10)) + \log_{10}(V_{\text{m,poly}}/V_{\text{m},X}) + \log_{10}(1.0 - \alpha) \quad (9)$$

where  $\mu_X^i$  and  $\mu_{\text{poly}}^i$  are the pseudochemical potentials<sup>46</sup> of solute *i* in solvent *X* and in the polymer,  $V_{\text{m}}$  is the molar volume, and  $\alpha$  is the crystalline fraction in case the polymer is semicrystalline.

The first experimental data set under consideration concerning partition coefficients for the system polyethylene–ethanol at room temperature has been taken from ref 49. This source contains also partition coefficients computed by UNIFAC plus a free volume correction (UNIFAC-FV).

Experimental and computed results are being compared in Figure 6. Taking into account the Elbro free volume term and  $\alpha = 0.63$  for LDPE as determined from the gas solubility calculations, the COSMO-RS prediction yield RMSE = 0.34





**Figure 6.** Experimental versus predicted partition coefficients between PE and ethanol for some fragrances as computed by COSMO-RS. Experimental data and UNIFAC-FV data have been taken from ref 49.

and  $R^2 = 0.80$ , compared to UNIFAC-FV with  $RMSE = 0.77$  and  $R^2 = 0.66$  (Figure 6), see also ref 49.

Another data set containing polymer–water partition coefficients has been extracted from the work of Gasslander et al.<sup>50</sup> They have investigated the partition of molecules covering a broad range of polarity for the polymers polyethylene, polypropylene and polyethylene-*co*-butyl acrylate (17 wt % butyl acrylate). Unfortunately, neither a density nor crystalline fraction of those polymers are specified in the paper. Thus, the crystalline fraction  $\alpha$  had to be treated as a fitting constant ( $\alpha_{fit}$  in Table 3), which basically lowers the computed  $\log P$  values by a constant shift, see eq 9. The polymer–water partition coefficients in ref 50 have been determined indirectly via linear regression from liquid chromatographic retention times using acetonitrile, ethanol and isopropyl alcohol. Accordingly, no dissociation correction for acidic molecules in the water phase had to be taken into account.

Interestingly, as summarized in Table 3, the regression slope of the predictions versus the experimental data is for all three polymers significantly below unity. This is partially due to the experimental data points belonging to the rather nonpolar compounds, octadecyl 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-propanoate and bis(2-ethylhexyl)phthalate, having very high  $\log K$  values, which are possibly out of range of what is reliably measurable. However, even excluding the two most extreme data points (see Table 3) the regression slope remains still

somewhat low. Experimental and predicted values for the three systems are shown in Table S5 in the SI.

In this context it has been reported, that polymer–solvent partitioning coefficients as measured by *gas–liquid* chromatography retention data are found to be consistently lower than those measured gravimetrically, by a factor of about 0.6.<sup>3</sup> However, to the best of our knowledge, no such effect has been reported yet for liquid chromatography data. For the system PE–water, exhibiting the lowest slope, the data point belonging to 4-hydroxybenzoic acid has strong leverage. However, its position seems to be at least surprising if not questionable if this solute’s predicted and experimental  $\log K$  values for example in EBA having a similar polarity are considered.

All in all, the experimental trend is predicted quite reliably, reflected by a squared correlation coefficient for all polymers of about 0.9, see also Figure 7. Furthermore, the results of Table 3 clearly show that more consistent results are obtained if the free volume combinatorial term is included. The crystalline fraction, which has been treated as a fitting constant, corresponds roughly to what can be expected from experience. The regression slope is somewhat higher with the free volume term, though still not unity, leading to a better coincidence with the experimental data and consequently a lower root mean squared error (RMSE).

## 7. CONCLUSION

In summary, it is feasible to make quantitative predictions using COSMO-RS theory for vapor/gas–liquid data and partition coefficients on systems containing polymers. In many cases consideration of free volume effects seems to improve the results as compared to the omission of the combinatorial term. However, this requires some additional information to be taken into account, i.e. the density of polymer and solute, the molecular weight and the crystallinity of the polymer. For the examined data it was sufficient to estimate the free volume simply based on the computed COSMO volumes and experimental densities. Sometimes, the study of polymer systems is hampered by the fact that experimental conditions are not specified with sufficient accuracy. Then, those missing parameters have to be fitted using the remaining experimental information.

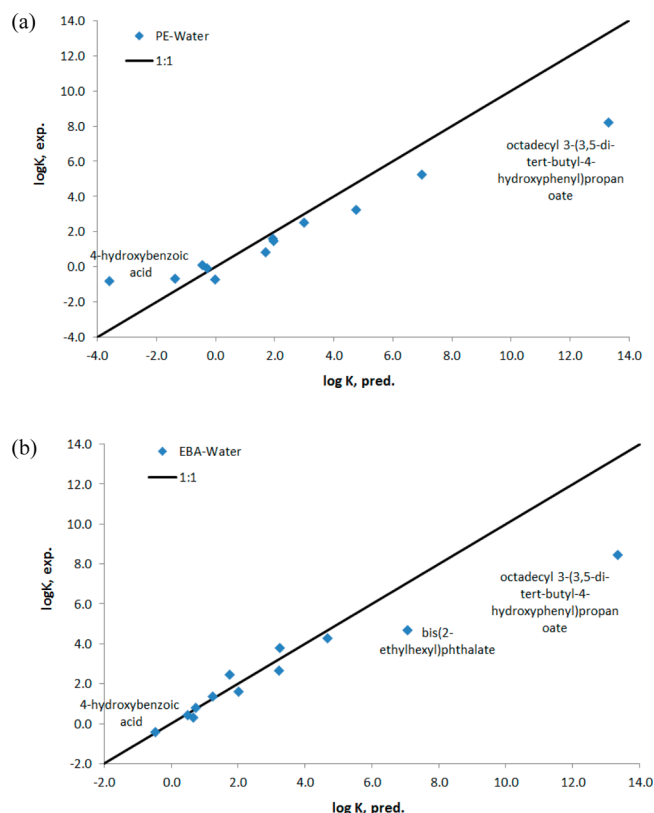
Most of the investigated polymer systems were of a rather simple chemical structure. Furthermore, cross-linking and polymer swelling effects were not examined so far. It remains to be shown whether such effects, which will play an important role in many practical applications, can be incorporated into COSMO-RS calculations.

**Table 3.** Results for the Prediction of Partition Coefficients for the Data Set in Ref 50<sup>a</sup>

system	level	$\alpha_{fit}$	$R^2$	RMSE	slope	$n$
PE	CRS	0.97(0.998)	0.87(0.97)	1.83(3.25)	0.42(0.45)	10(12)
PP	CRS	0.99(0.999)	0.90(0.92)	1.09(3.47)	0.57(0.38)	8(10)
EBA	CRS	0.96(0.998)	0.92(0.95)	1.11(2.99)	0.58(0.44)	10(12)
PE	CRS+FV	0.67(0.91)	0.86(0.96)	1.13(1.76)	0.55(0.60)	10(12)
PP	CRS+FV	0.79(0.97)	0.91(0.92)	0.55(2.02)	0.79(0.516)	8(10)
EBA	CRS+FV	0.52(0.89)	0.95(0.95)	0.38(1.53)	0.89(0.62)	10(12)

<sup>a</sup>RMSE and  $R^2$  have been determined with respect to the  $\log_{10}(P)_{polymer,water}$  for COSMO-RS without combinatorial term (CRS) and COSMO-RS using a free volume entropic term (CRS+FV). The slope of the linear regression and the number of data points  $n$  are also given.  $\alpha_{fit}$  designates the fitted crystalline fraction. In parentheses results including the two potential outliers bis(2-ethylhexyl)phthalate and octadecyl 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propanoate are given.





**Figure 7.** Experimental versus predicted partition coefficients between PE-water (a) and EBA-water (b). Experimental data has been taken from ref 50. Predictions have been obtained using the free-volume combinatorial term and a (fitted) crystalline fraction of  $\alpha = 0.67$  (PE) and  $\alpha = 0.52$  (EBA).

The solubility prediction for larger, e.g. drug-like, solutes is not yet addressed here. Unfortunately, since very long equilibration times in polymers are involved, reliable experimental solubility data for such systems are quite scarce.

Finally, with the herein presented revised solute chemical potentials at hand, the chemical reactivity in polymers such as degradation or polymerization reactions may be addressed with improved accuracy.

## ■ ASSOCIATED CONTENT

### ● Supporting Information

Predicted vapor–liquid equilibrium, gas–liquid equilibrium and partition coefficient data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare the following competing financial interest(s): Andreas Klamt is CEO and Christoph Loschen is an employee of COSMOlogic. COSMOlogic commercially distributes the COSMOtherm software used in this paper.

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