CYCLE DE CONFÉRENCES DE CHIMIE

Avec le concours de : Université Clermont Auvergne
INP Clermont Auvergne

Jeudi 17 octobre à 16 h

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Solubility prediction from molecular simulation

The solubility of a chemical component is its (thermodynamic) concentration limit in a given chemical medium beyond which it separates into a distinct phase. For a solid this is the concentration of the solid in solution in a solvent at equilibrium with the solid phase. Formally, this is the amount of solid *s* accommodated in solution at the point when the chemical potential of the solid and that of the solid in solution are identical at a defined temperature *T* and pressure *p*, $\mu_{solid}(T,p) = \mu_{solution}(T,p,s)$ (Figure 1).

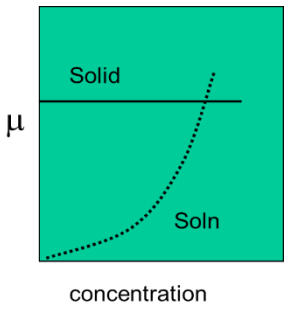

Figure 1. Chemical potential of a solute in the solid state and that of the solute in solution as function of solute concentration. The solubility is the solute concentration at the intersection point.

Solubility is a fundamental property which is at the heart of phase behaviour, from crystallisation of pure phases to the formation and stability of complex sub-cellular structures. It has a significant and a pervasive role as well as impact across a diverse spectrum of disciplines and areas, which include weathering of of terrestrial environment, formation and dynamics of ecological environments such as soil, delivery of micronutrients, translocation of pollutants, erosion of built environments, chemical toxicity, formulation of foods, and development of chemical and pharmaceutical products. The ability to predict solubility is important to devising relevant interventions. In particular areas e.g. pharmaceutical development, such a capability would be a 'game-changer'.

Despite the interest and significance, accurate prediction of solubility is still an outstanding problem. Whilst there are many computational models for predicting the solubility, none are truly based on first principles. These models invariably employ correlation, being optimised using a training set of experimental data. Such models cannot predict solubility at non-standard temperatures, in different solvents, or at other pHs. The uncertainty in the predicted solubility for such models is generally about ±1.0 log unit, which can degrade significantly when presented with structures and chemical moieties that did not appear in the training set. It is notable that despite the consideration of hundreds of distinct molecular descriptors and the use of a variety of algorithms including neural networks and support vector machines, the accuracy has not improved and the limitations remain. Clearly, there is a need to develop a first principles approach that has wider applicability (different solvents, temperature and pH) and has the potential to be more accurate.

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A potentially powerful and a first-principles approach is to predict solubility from molecular simulations, where the input parameters are intermolecular interactions. I will review how molecular simulations can be employed to predict solubility and will identify the challenges that exist. I will then present a novel and an efficient molecular simulation approach developed by us based on density of state calculations, and present results for the prediction of the aqueous solubility of NaCl and Urea[1,2]

1. S Boothroyd, A Kerridge, A Broo, D Buttar, J Anwar* (2018) Solubility prediction from first principles: a density of states approach, Physical Chemistry Chemical Physics 20 (32), 20981-20987

2. S Boothroyd, J Anwar* (2019) Solubility prediction for a soluble organic molecule via chemical potentials from density of states, Journal of Chemical Physics 151 (18), 184113