Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting information, specific instructions

The KB-Hydrotrope app at www.stevenabbott.co.uk/practical-solubility/kb-hydrotropes.php serves two functions. First, it provides a significant set of real-world datasets that allow exploration of how different hydrotropes solubilize a variety of solutes. Second, it is a serious computational tool for handling users' datasets. The authors routinely use this tool for analysis of their own solubilization datasets.

For those who wish to explore, all that has to be done is to select the solute/hydrotrope pair from the combobox and look at the various curves of the raw data and their fitting curves along with the G_{ij} curves that explain the solubilization effects as described in the paper.

For those who wish to use the tool for analysis of their own data, the following should provide sufficient detail to make the process practical.

The starting point is the data of solubility versus hydrotrope molar concentration. This can cover as small or as large a range as desired, though accurate fitting requires data across the whole solubilization range. The concentration data should be in mole/liter.

For the hydrotrope, two sets of data are required. The first is density (in g/cc) versus concentration in mole/litre. This is readily obtained with a modern densitometer. The second is osmolality versus molality. Modern vapour pressure osmometers can readily obtain such data; the only difficulty is making sure that the data are in the correct units. If the hydrotrope already exists in the app then these data can be used. Simply copy/paste into your own dataset in the format described below. If you are able to obtain higher-quality data then (a) please use it and (b) please email the improved dataset to the authors so the datasets in the app can be updated.

The larger the concentration range of the hydrotrope data, the more the app can fit G_{ij} data other than G_{u2}. For example, if solubility data goes up to 3 M and either of the hydrotrope datasets goes up only to 2.5 M, the other G_{ij} values are fitted only to 2.5 M.

Now put the data into a simple tab-separated text file (this can conveniently be done from Excel). The data start in row 3 with columns 1 and 2 being the molarity/density, columns 2 and 3 being molality/osmolality and columns 4 and 5 are the molarity of hydrotrope and solute solubility. There is no restriction on the relative number of rows used for each dataset (so density might be 10 data pairs, osmolality might be 8 data pairs and solubility might be 16 data pairs. There is a maximum of 20 data pairs in any row.

The first row of the table contains "Vu", MVol of the solute, "M2", MWt of the hydrotrope, "Ionic" or "Non-ionic" or simply blank. These are data necessary for the calculation. The "Ionic" flag ensures that the osmolality data are interpreted correctly for ionic hydrotropes.

The second row is of no importance but for users' benefit it can contain the column names: c2, ρ g/cc, molal2, Osmol, c2, cu.

The authors' experience is that data to 3 significant figures is good enough. Having seen many solubility datasets from the published literature, it is clear that the limiting factor for good KB fitting is accuracy rather than precision. It is *very* hard to obtain accurate solubility

data. The datasets in the app are “as is” but it seems clear that some intelligent smoothing of the data and removal of rogue points can give more reliable G_{ij} values.

To use the dataset, simply click the select file button in the app (the wording on the button is browser dependent) and find the file on your own computer. The data is *never* shared, it is seen only on your browser.

The data loads immediately and all calculations and graphs appear. A visual check of all the basic graphs allows you check for obvious typos in your dataset. The data can be fixed within the app (just enter a new value in any box) and the results are seen immediately. Because Javascript apps are forbidden from writing data to your computer, any updates you make are *not* saved. Once you have a dataset that makes visual sense, you have to change the values in your original file if you want to use the data at a later time.

There is one output graph that should be checked, other than those fitting the density and osmolality data. This is the plot of $-RT\ln(c_u)$ is fitted to the data. Small errors in the data can be amplified in this curve and excellent fits are not guaranteed. In principle one could choose the fitting function, but for simplicity and universality we have selected a function that does a good general-purpose job. It would not be hard to provide additional fitting function options if users require it.

The ln BindingRatio plot and the line fitting the solubility data are both connected to the “cooperative binding model” briefly described in the paper and not discussed further here.

Assuming the data look OK, the G_{ij} values can be inspected. Moving the mouse over any graph gives a readout of the calculated values. Of especial interest are the relative sizes of G_{u2} the main driver for solubilization and G_{22} which is the tendency of the hydrotrope to cluster and *reduce* the solubilization. We have not seen any example where “water structure” (G_{11}) does anything of interest.

For those who want the data for further analysis, click on the Data Out box, do Ctrl-A to select all and Ctrl-C to copy. The data go on to the Clipboard and can be pasted straight into, say, Excel in a sensible format. Why this convoluted method? Javascript is a secure environment and cannot allow you to save data or to put data onto your Clipboard automatically. The upside is that these apps can be used on corporate networks that will not allow less secure environments such as Java.

If you would like your datasets to become available to other users, please email the text file to Abbott and the file will be added to those already on the server. As stressed in the paper, KB provides understanding but not (yet) prediction. The more open datasets available to theoreticians, the higher the chance of a predictive capability emerging.

The Javascript code is readily found (right click on the app, choose View Page Source, find the link to kb-hydrotrope.js, click on it and it will appear as plain text in your browser). This can be saved or copied/pasted and users are encouraged to critique the code, re-purpose it or use it in any way, within the broad limits of the Creative Commons BY Attribution license. The authors are scientists, not professional coders so the code is not “professional” quality, but it is commented and should be reasonably transparent.