Identifying Safer Solvents Using Hansen Solubility Parameters

A resource pack containing this PPT will be available after the webinar

Professor Steven Abbott

Steven Abbott TCNF Ltd

A Training Webinar for TURI

Note: The webinar is an outline as the main content is based on live use of the HSPiP software and apps

My thanks

- To the very capable TURI team for setting up this webinar

Applying solubility thinking to TUR

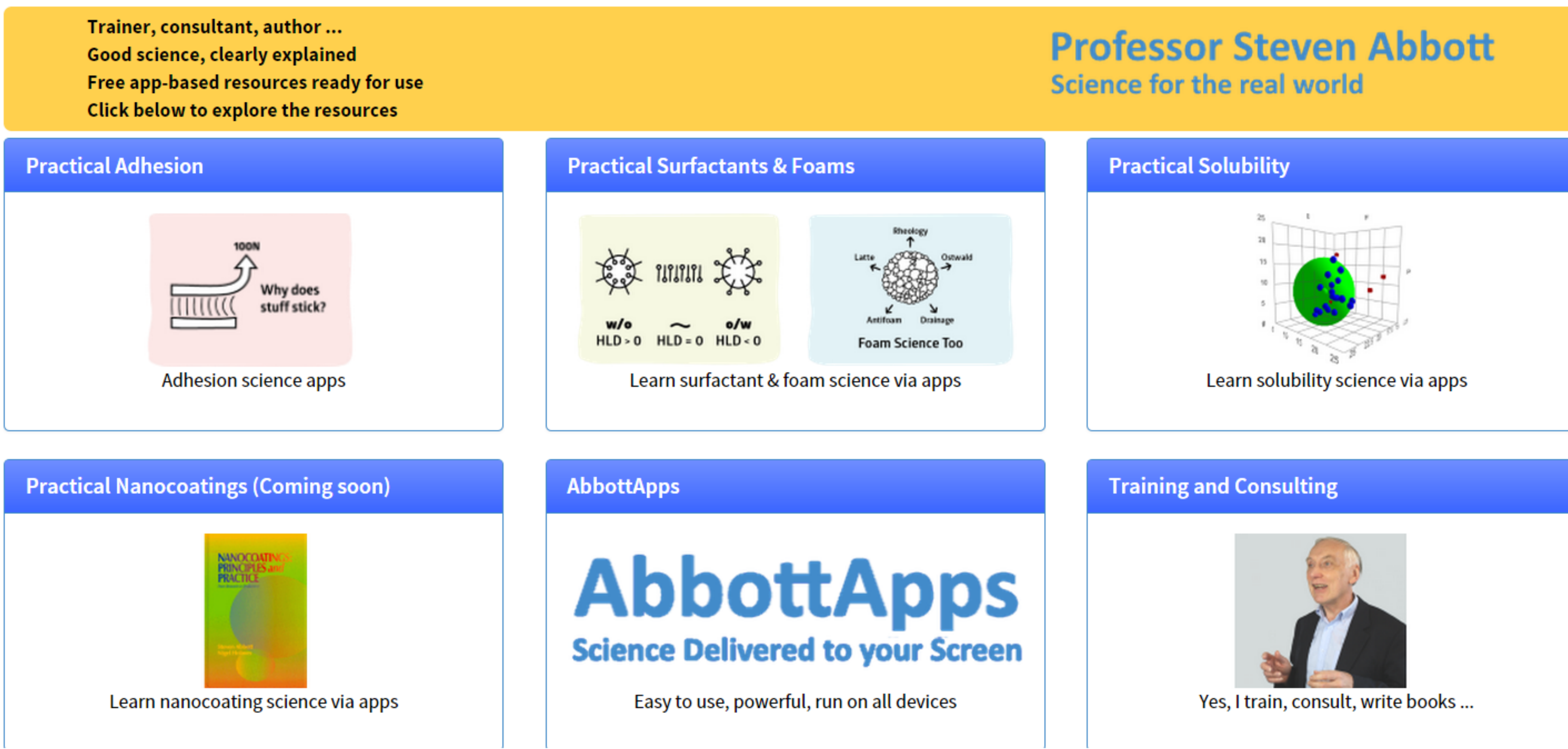
- We will see that a simple but powerful solubility approach allows us to optimise our replacement strategy for
  - Solvents
  - Polymers
  - Plasticisers
  - Fillers
  - etc.
- As a bonus, the same approach can be used for your general formulation development

Who am I?

- A UK-based chemist – who did his Oxford PhD at Harvard
- An industrialist concerned with real-world issues
- A Visiting Professor who likes to bring the best possible science to industrial processes
- Someone who programs powerful technical software and apps
  - Co-author of HSPiP being used today
- An independent consultant

www.stevenabbott.co.uk

- Lots of AbbottApps resources, including Practical Solubility. All free and run on all platforms – PC, Mac, tablets, phones



Solubility?

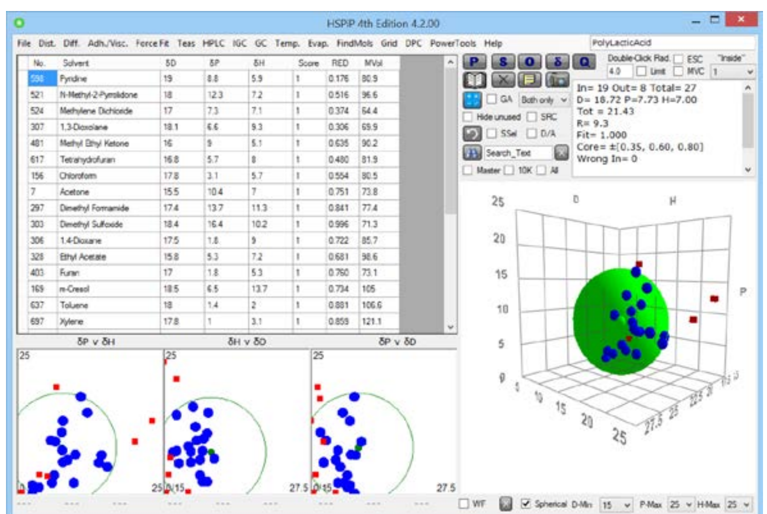
- Even if they are green and safe:
  - A solvent can’t clean or dissolve without the right solubility behaviour
  - A plasticiser is useless (it will bloom over time) if it is insoluble in the polymer
  - A protective polymer is useless if the chemical can readily dissolve and diffuse through it
  - A particle or filler won’t deliver its promise if it is not compatible with (soluble in) the system

But we know about solubility

- No we don’t!
  - Hydrophobic/Hydrophilic, Polar/Non-polar, LogP are too simplistic
  - UNIFAC is usually too expensive and too specialised
  - COSMO-RS (based on quantum calculations) is wonderful but not usually for our sorts of issues
- With 3 Hansen Solubility Parameters we can do a lot
  - Many HSP are in the public domain and my Practical Solubility site has some useful apps and datasets
  - For serious use, HSPiP (Hansen Solubility Parameters in Practice) is the platform of choice – and is used by TURI

3 Hansen Solubility Parameters

- δD – Dispersion
  - The polarisability of a molecule
  - Alkanes are too boring to be polarisable δD~14
  - Aromatics are more polarisable δD~18
  - Chloro-aromatics even more polarisable .. δD~19
  - … etc



3 HSP

- δP – Polar
  - Alkanes, aromatics are not polar δP~0
  - Acetonitrile is massively polar δP~18
  - The average chemist would have no problem in agreeing with the relative δP rankings of most simple molecules

3 HSP

- δH – Hydrogen bonding
  - Alkanes, aromatics δH~0
  - Methanol > Ethanol δH~20
  - Acetone δH~5
    - It has the ability to be an acceptor in H-bonds
  - Again, the average chemist would have no problem in agreeing with the relative δH rankings of most simple molecules

This slide is for reference purposes to show that HSP are respectable thermodynamics

(+1)

We'll just note that smaller molecules are generally better as solvents

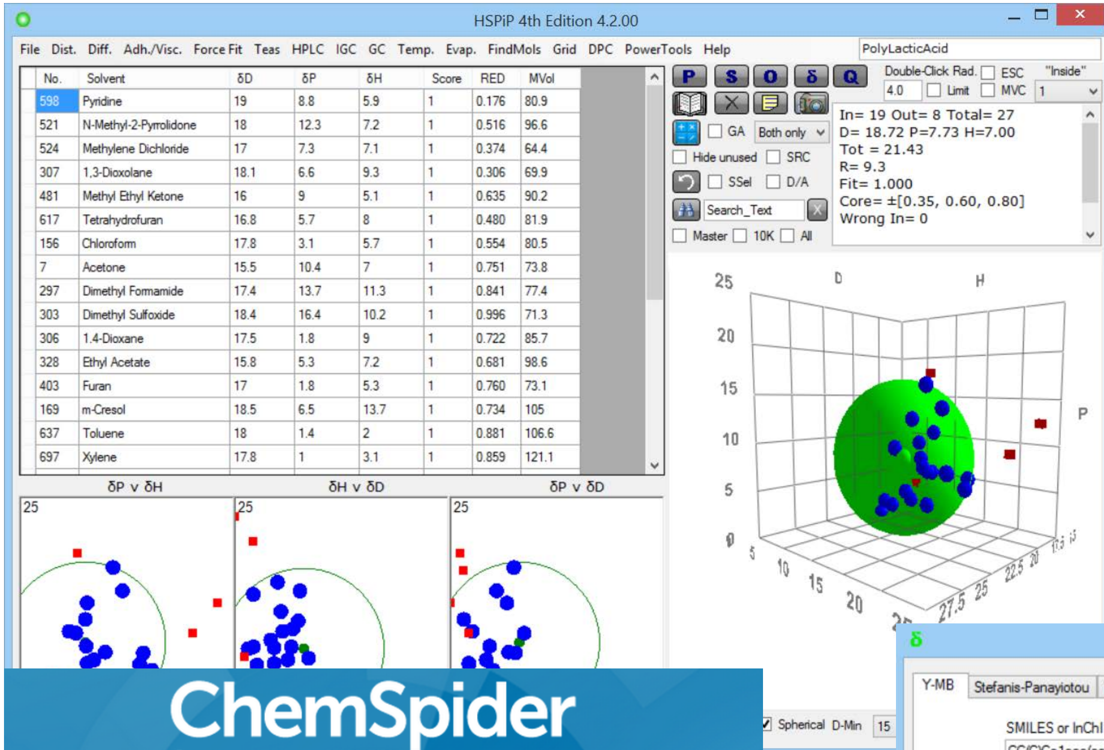
- MVol
  - Molar Volume constrains the numbers
  - HSP come from Cohesive Energy *Density*
  - So bigger means more Cohesive Energy …
  - … but not necessarily more Cohesive Energy Density
- For solubility "Small is Beautiful"
  - thermodynamics (entropy)
  - kinetics (fast diffusion)
- But we'll stick with 3 for the rest of the webinar

Solubility and Compatibility

- "Like dissolves like", "Like is compatible with like"
- Calculate "like" with a simple Distance formula:
  - $D^2 = 4(\delta D_1 - \delta D_2)^2 + (\delta P_1 - \delta P_2)^2 + (\delta H_1 - \delta H_2)^2$
- Just the standard distance in 3D space, with a tweak for δD
- If things are very alike then D is small, if they are not alike, D is large
  - Activity coefficients and/or χ parameters calculated from e^{-D^2}
- The famous HSP formula, working for 40+ years
  - Distance is sometimes shown as Ra

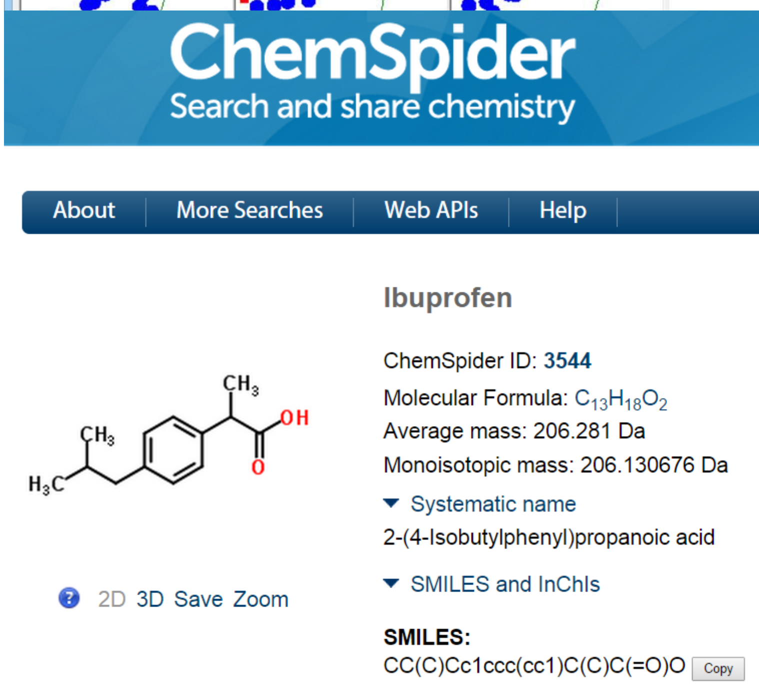
HSP values

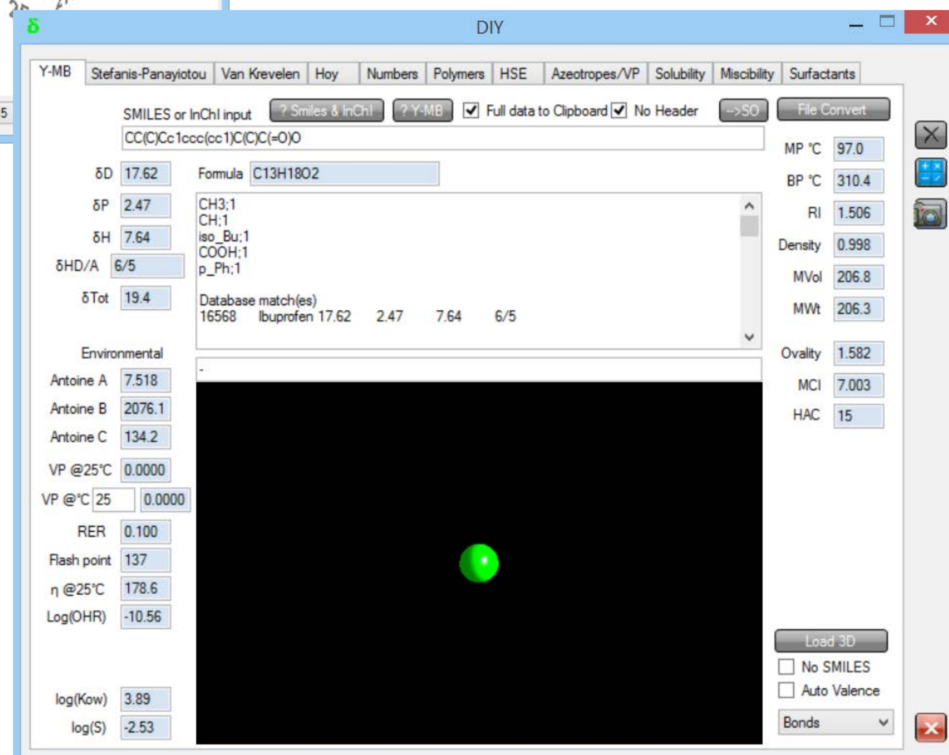
- Thermodynamic relationships:
  - Originally derived for solvents from enthalpy of vapourisation, Refractive index, Dipole moment
- OK for solvents but not for solids and polymers
  - So measure them via a “20 solvent test”
    - Let’s measure the HSP of Poly lactic acid
  - Estimate automatically from SMILES or MolFile
    - Let’s estimate the HSP of ibuprofen
- HSPiP contains tables of solvents, polymers, GRAS, flavours & fragrances, EAFUS…



The HSP Sphere for PLA in 27 solvents

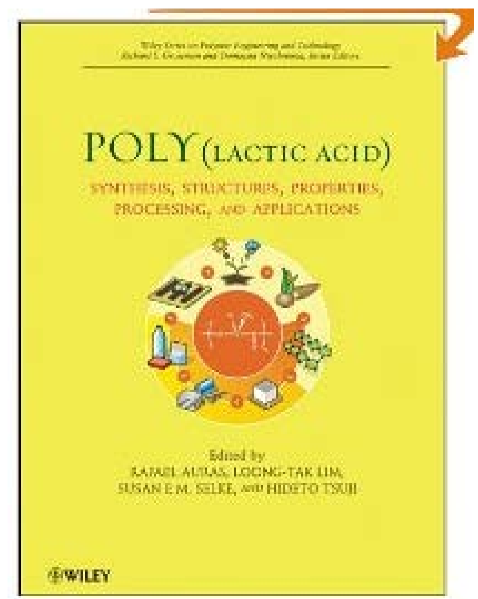
Get the SMILES of ibuprofen from e.g. ChemSpider and calculate automatically





Predicting PLA

- Poly Lactic Acid
  - an important “green” polymer
  - lots of wasted work trying to find plasticisers, fillers, nanoclay barrier properties, controlled release
  - the basics sorted out purely with HSP
    - read my predictions for yourself
    - e.g. don’t package cinnamon buns in PLA



Replacing solvents

- If you know the HSP of your solvent then the best solvent will have a similar HSP
  - Except that “best” also includes cost, odour, vapour pressure, VOC …
- Highly unlikely that any *single* solvent will give you what you need
  - You would probably know it already as it’s easy enough to test a bunch of single solvents

The best single solvent for cleaning?

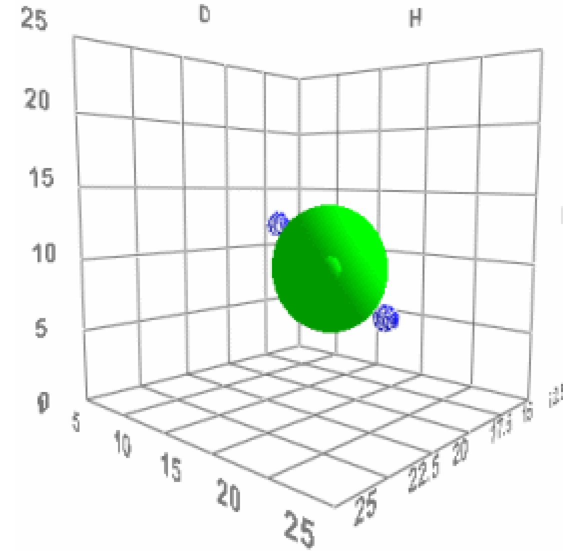
- The John Durkee book is based solidly on HSP principles
  - The tradeoffs between greenness, low VOC and ability to clean (small HSP Distance) discussed in depth

Cleaning with Solvents: Science and Technology, 1st Edition

Author :	J Durkee
Release Date:	30 Jan 2014
Imprint:	William Andrew
eBook ISBN :	9781455731619
Print Book ISBN :	9781455731312
Pages:	780

In this practical handbook, John Durkee guides readers through the technologies and materials of the solvent-based cleaning of surfaces, explaining how to implement successful cleaning procedures and exploring regulatory frameworks, economic factors and environmental concerns.

Smart solvent blends



- Take two *non*-solvents for a polymer
- Mix them 50:50
- What do you get?
- If you do it according to the numbers you can get a good solvent
- The birth of “rational solvent blends”
  - optimise for solubility along with cost, compliance, controlled solubility during evaporation
- Of course you don’t have to use *bad* solvents, this example is to make a point

A green example

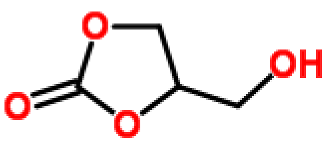
- FAME (Fatty Acid Methyl Esters) are too boring to be much use, but are “green” [16.4, 2.6, 4.5]
- Glycerol carbonate comes from bio-glycerol, CO_2 (in principle) and is bio-degradable – but is much too polar to be highly useful [17.9, 25.5, 17.4]
- A 60:40 mix is an impressive match for a great (but unusable) solvent like Dimethyl Acetamide

A green example

Solvent	δD	δP	δH	MVol	Other Names	RER	Weight	Vol%		Distance	AA
FAME	16.4	2.6	4.5	280.9	Fatty Acid Methyl Ester	0.2	100	60.0	☑	10.60	9.6
Glycerol Carbonate	17.9	25.5	17.4	83.2		0	100	40.0	☑	15.90	-8.244
Methyl iso-Butyl Carbinol	15.4	3.3	12.3	127.2	MIBCOL	27	100		☐	8.92	7.56
Methyl Iso-Butyl Ketone...	15.3	6.1	4.1	125.8	4-Methyl-pentan-2-one	162	100		☐	8.68	6.686
Methyl iso-Amyl Ketone	16	5.7	4.1	141.3	MIAK	50	100		☐	8.57	7.259
Methyl Cyclohexane	16	0	1	128.2		300	100		☐	14.81	7.001
Methyl Ethyl Ketone (M...	16	9	5.1	90.2	2-Butanone	380	100		☐	5.90	7.063
Methyl Oleate	16.2	3.8	4.5	340.7		0	100		☐	9.66	7.516
Methylene Chloride	17	7.3	7.1	64.4	Dichloromethane	1450	100		☐	5.24	7.08
N,N-Dimethyl Acetamide	16.8	11.5	10.2	93	DMA	13.8	100		☐	0.00	7.3
N,N-Dimethyl Formamid...	17.4	13.7	11.3	77.4	DMF	10	100		☐	2.74	7.241
Methyl Cellosolve	16	8.2	15	79.3	2-Methoxy Ethanol	53	100		☐	6.04	8.097
Methyl Propyl Ketone	16	7.6	4.7	107.3		240	100		☐	6.93	7.354

DMA is the target of 16.8, 11.5, 10.2
The 60:40 blend is 17, 11.8, 9.5
The Distance is 0.7 – rather close

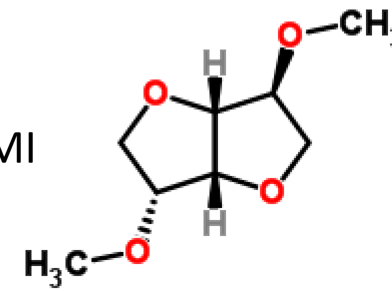
Rational green solvent design



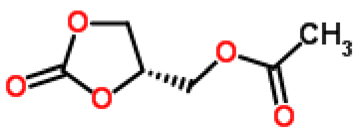
[17.9, 25.5, 17.4]

Glycerol carbonate
δP, δH too high
Only good in mixtures

Dimethyl Isosorbide – DMI
Excellent solvent for skin delivery
But *not* green (2 reasons)



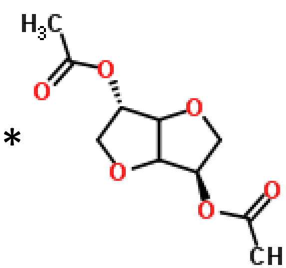
[17.6, 7.1, 7.5]

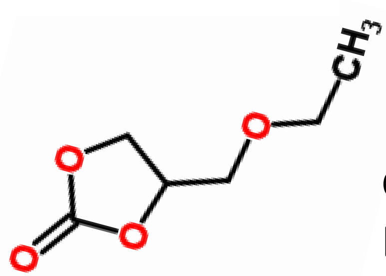


Glycerol carbonate acetate
Excellent potential solvent

[17.1, 14.7, 9.2]

Diacetate of Isosorbide
Should be excellent solvent*
Will be green





Glycerol carbonate ethyl ether
Excellent potential solvent

[16.7, 7.5, 8.9]

[16.8, 18.5, 8.7]

Assumes the carbonates can be made without phosgene!

*Solid at RT – needs ester mixture

Cleaning a nylon residue

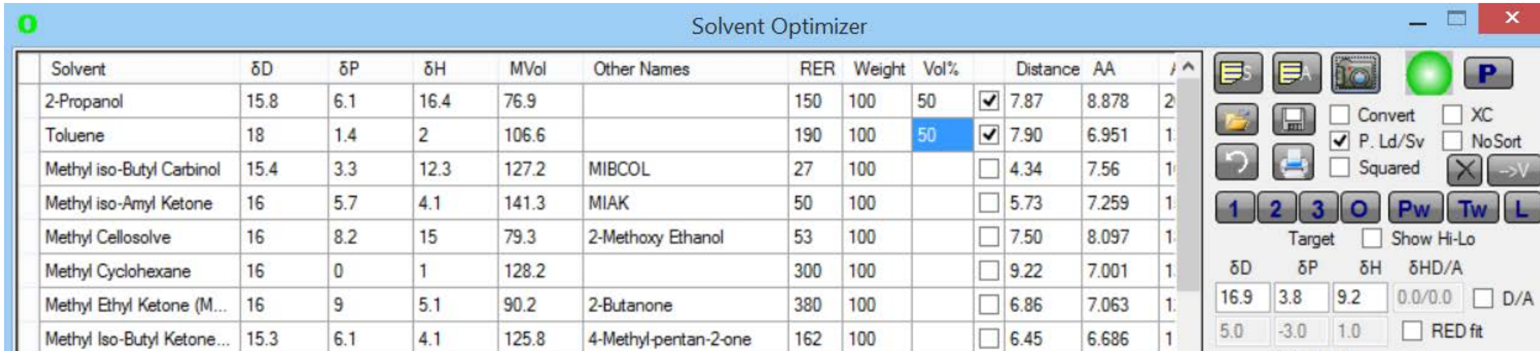
A personal example

- Toluene/IPA an excellent* solvent blend for a specific nylon used on a coating machine
- Operators hated the cleaning job
- I had tested it on the small scale and proved it was fine – but on the large scale it was awful!
- Reformulated using HSPiP: DBE:Dowanol PnB
  - Larger distance, somewhat slower
  - Much less volatile – just leave then wipe off later
    - DBE:Dowanol PM not so good because PM too volatile
  - Great success!

*This was some time ago before toluene tox limits were lowered even further

The original blend.

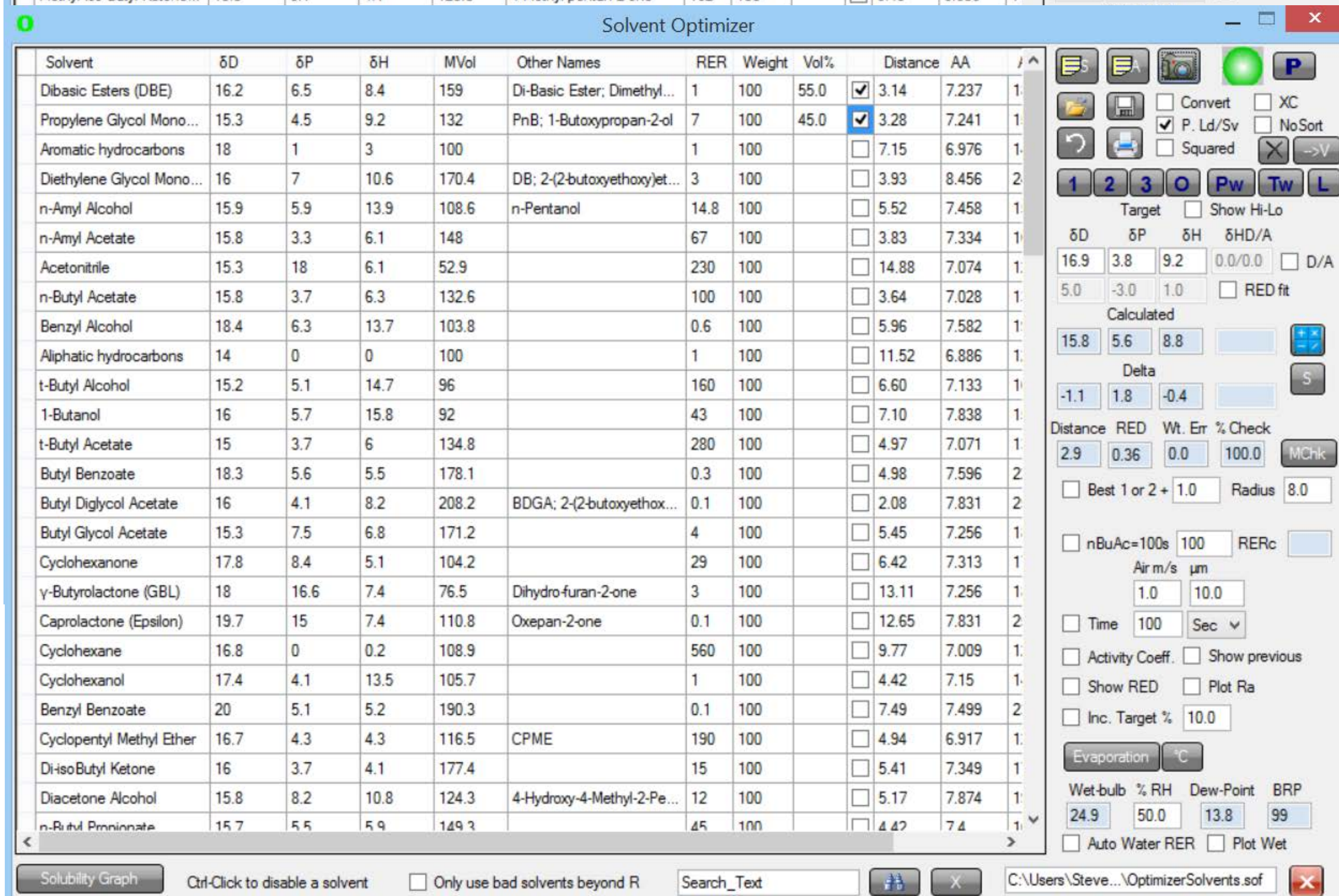
RER ~160



Solvent	δD	δP	δH	MVol	Other Names	RER	Weight	Vol%		Distance	AA	
2-Propanol	15.8	6.1	16.4	76.9		150	100	50	✓	7.87	8.878	2
Toluene	18	1.4	2	106.6		190	100	50	✓	7.90	6.951	1
Methyl iso-Butyl Carbinol	15.4	3.3	12.3	127.2	MIBCOL	27	100			4.34	7.56	1
Methyl iso-Amyl Ketone	16	5.7	4.1	141.3	MIAK	50	100			5.73	7.259	1
Methyl Cellosolve	16	8.2	15	79.3	2-Methoxy Ethanol	53	100			7.50	8.097	1
Methyl Cyclohexane	16	0	1	128.2		300	100			9.22	7.001	1
Methyl Ethyl Ketone (M...	16	9	5.1	90.2	2-Butanone	380	100			6.86	7.063	1
Methyl Iso-Butyl Ketone...	15.3	6.1	4.1	125.8	4-Methyl-pentan-2-one	162	100			6.45	6.686	1

The revised blend.

RER ~ 5



Solvent	δD	δP	δH	MVol	Other Names	RER	Weight	Vol%		Distance	AA	
Dibasic Esters (DBE)	16.2	6.5	8.4	159	Di-Basic Ester; Dimethyl...	1	100	55.0	✓	3.14	7.237	1
Propylene Glycol Mono...	15.3	4.5	9.2	132	PnB; 1-Butoxypropan-2-ol	7	100	45.0	✓	3.28	7.241	1
Aromatic hydrocarbons	18	1	3	100		1	100			7.15	6.976	1
Diethylene Glycol Mono...	16	7	10.6	170.4	DB; 2-(2-butoxyethoxy)et...	3	100			3.93	8.456	2
n-Amyl Alcohol	15.9	5.9	13.9	108.6	n-Pentanol	14.8	100			5.52	7.458	1
n-Amyl Acetate	15.8	3.3	6.1	148		67	100			3.83	7.334	1
Acetonitrile	15.3	18	6.1	52.9		230	100			14.88	7.074	1
n-Butyl Acetate	15.8	3.7	6.3	132.6		100	100			3.64	7.028	1
Benzyl Alcohol	18.4	6.3	13.7	103.8		0.6	100			5.96	7.582	1
Aliphatic hydrocarbons	14	0	0	100		1	100			11.52	6.886	1
t-Butyl Alcohol	15.2	5.1	14.7	96		160	100			6.60	7.133	1
1-Butanol	16	5.7	15.8	92		43	100			7.10	7.838	1
t-Butyl Acetate	15	3.7	6	134.8		280	100			4.97	7.071	1
Butyl Benzoate	18.3	5.6	5.5	178.1		0.3	100			4.98	7.596	2
Butyl Diglycol Acetate	16	4.1	8.2	208.2	BDGA; 2-(2-butoxyethox...	0.1	100			2.08	7.831	2
Butyl Glycol Acetate	15.3	7.5	6.8	171.2		4	100			5.45	7.256	1
Cyclohexanone	17.8	8.4	5.1	104.2		29	100			6.42	7.313	1
γ-Butyrolactone (GBL)	18	16.6	7.4	76.5	Dihydro-furan-2-one	3	100			13.11	7.256	1
Caprolactone (Epsilon)	19.7	15	7.4	110.8	Oxepan-2-one	0.1	100			12.65	7.831	2
Cyclohexane	16.8	0	0.2	108.9		560	100			9.77	7.009	1
Cyclohexanol	17.4	4.1	13.5	105.7		1	100			4.42	7.15	1
Benzyl Benzoate	20	5.1	5.2	190.3		0.1	100			7.49	7.499	2
Cyclopentyl Methyl Ether	16.7	4.3	4.3	116.5	CPME	190	100			4.94	6.917	1
Di-isoButyl Ketone	16	3.7	4.1	177.4		15	100			5.41	7.349	1
Diacetone Alcohol	15.8	8.2	10.8	124.3	4-Hydroxy-4-Methyl-2-Pe...	12	100			5.17	7.874	1
n-Butyl Propionate	15.7	5.5	5.9	149.3		45	100			4.42	7.4	1

Replacing IPA

- An email request after the first webinar requested a non-flammable replacement for IPA
- I suggested a mix of PG (propylene glycol) and DBE (Dibasic Ester)
- It won’t be as great a solvent and will be very slow
  - And also slow to evaporate which is inconvenient but necessary for non-flammable!
- TUR *always* results in compromises. But a non-volatile compromise might turn out to have unexpected advantages in the long term
  - TUR might require changes in habits

Replacing DCM (1)

- Dichloromethane is useful but must be replaced. Previous webinar Q&D demanded answers!
- Two HSP approaches
  - Use Solvent Optimizer to find all Pairwise blends and think through the possible matches
    - Spreadsheet sent to TURI to examine options

Solvent 1	Solvent 2	Vol% 1	Vol% 2	Distance
Butyl Diglycol Acetate	Propylene Carbonate	76	24	0.196
Cyclohexanone	Dipropylene Glycol Methyl Ethe	66	34	0.2
Propylene Glycol Monomet	Cyclohexanone	40	60	0.201
1,4-Dioxane (High P)	Isophorone	72	28	0.234
Butyl Glycol Acetate	Dimethyl Isosorbide	27	73	0.234
1,3-Dioxolane	Methyl Propyl Ketone	50	50	0.245

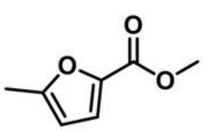
Replacing DCM (2)

Disclaimer: I am simply reporting what happened over 10 days from the previous webinar. I cannot comment on whether these "408s" will be safer or useful in practice.

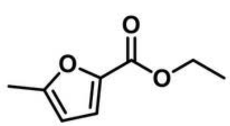
- By chance a potential source for a substituted methyl furoate came to my attention
- Many furoates are food safe and using HSPiP's automatic estimation, these furoates seem a good match for DCM 17,7.3,7.1
  - TURI is now involved
  - Preliminary testing confirms DCM-like solubility
  - But, of course, slower and much less volatile!

Solvent	δD	δP	δH
Methyl 5-Methyl Furoate	17.41	8.06	5.64
Ethyl 5-Methyl Furoate	17.06	7.55	5.08
Isopropyl 5-Methyl Furoate	16.73	6.7	4.23
Butyl 5-Methyl Furoate	16.85	6.46	4.61

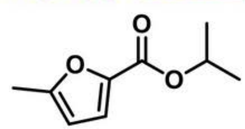
Methyl 408



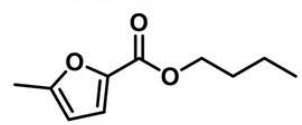
Ethyl 408



Isopropyl 408



Butyl 408

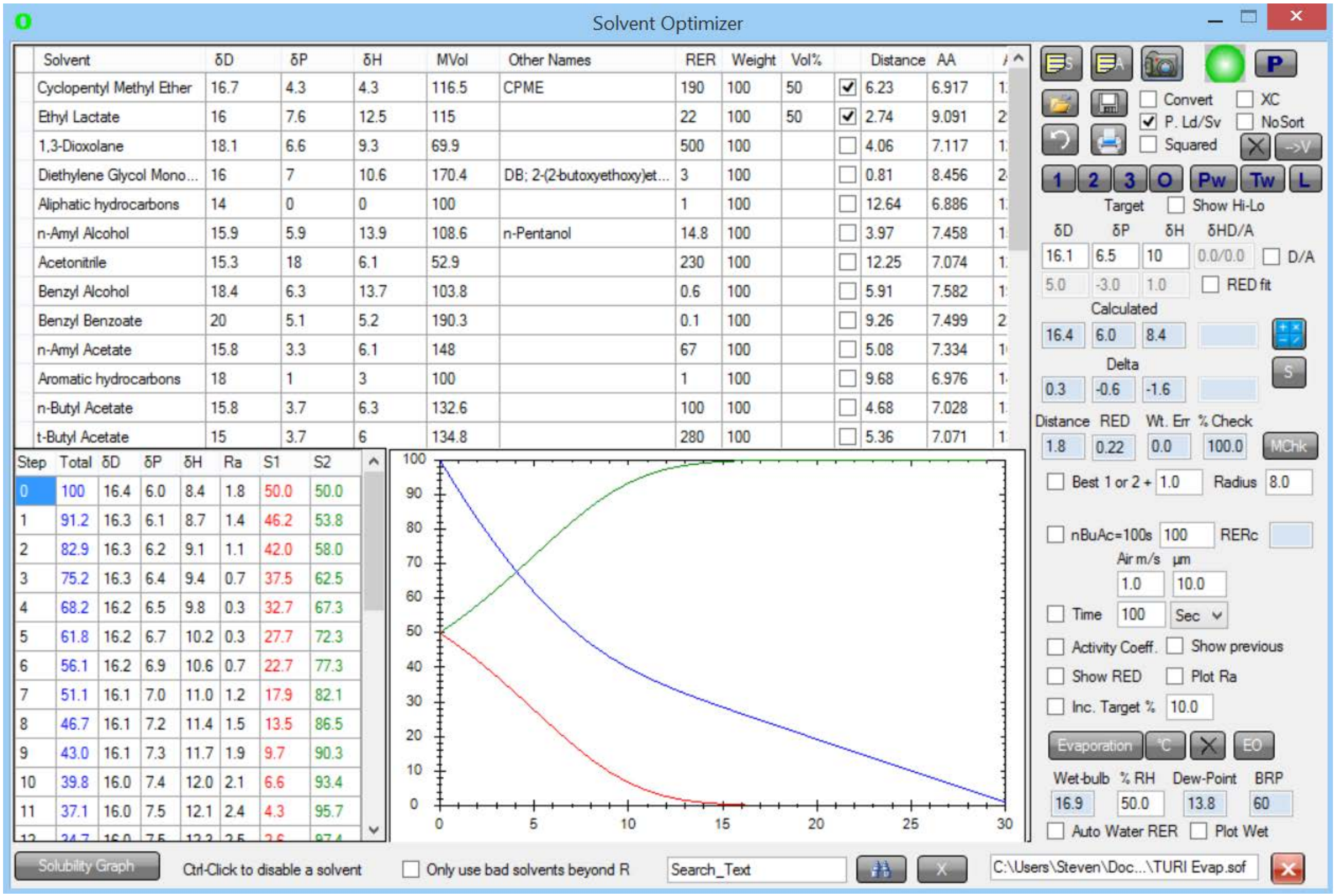


http://xftechnologies.com/technology/products/

Smart evaporation in solvent blends

- Solvent blends allow smart tricks
- HSPiP has the RER of the solvents (or Antoine Constants for VP at higher T)
- So we can have the best solvent evaporate faster
  - To make the solute crash out quickly
- Or we can have the worse solvent evaporate faster
  - To keep things in solution for as long as possible

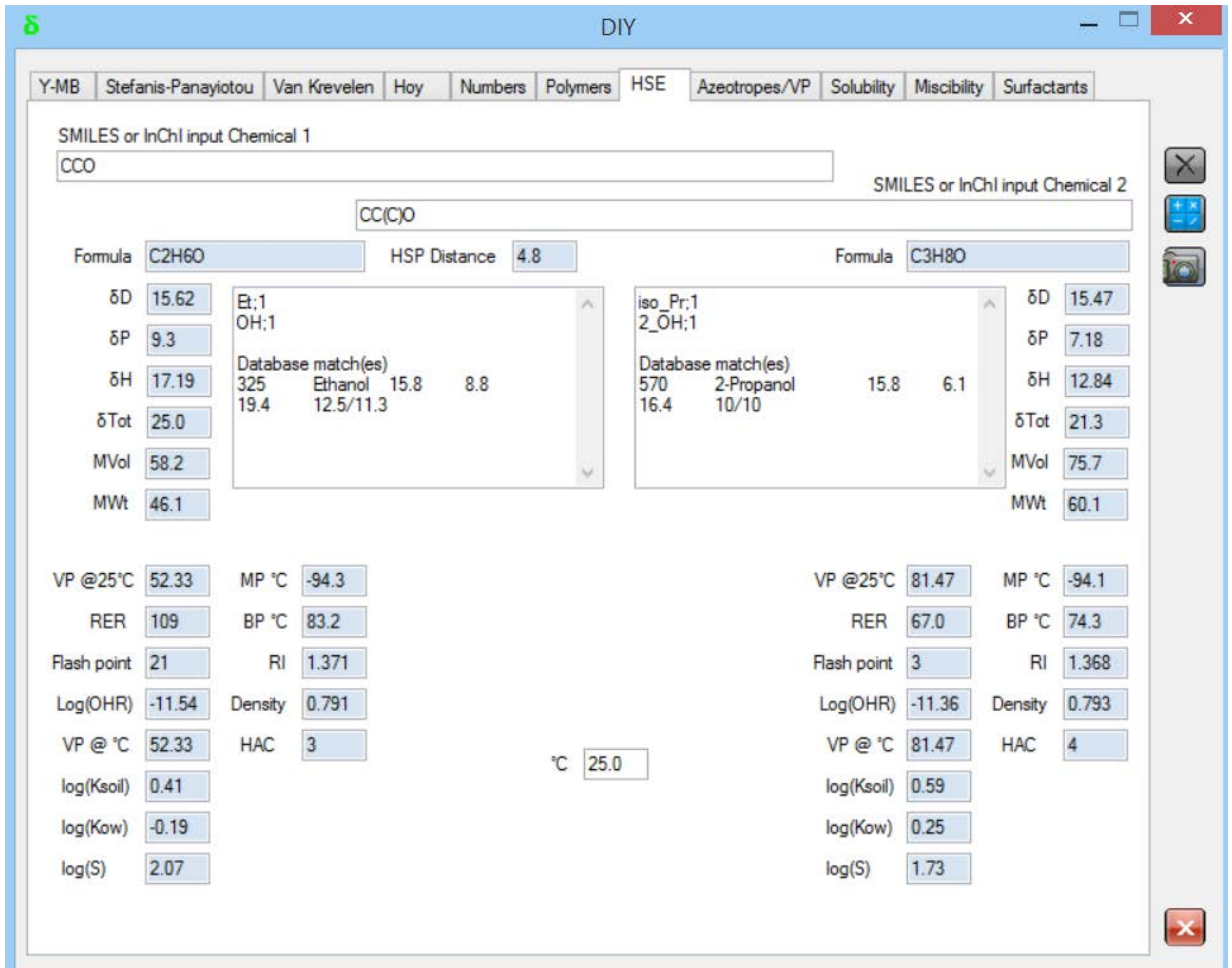
A blend of CPME and ethyl lactate is a good match for the target
CPME is a worse solvent but is more volatile (RER=190 versus 22)
So the Ra (HSP Distance) stays OK through the whole process



Read across

Compare two molecules using their SMILES. Can then "read across" in safety terms with whatever parameters are relevant to you

Using EtOH and 2-PrOH as an example where you know what to look for!



EAFUS, GRAS, TURI

- HSPiP has lots of data tables, e.g. EAFUS
  - Everything Added to Food in the United States

No.	Solvent	δD	δP	δH	Score	RED	MVol	CAS
694	Acetal	15	3.4	4	-	-	143.9	105-57-7
695	Acetaldehyde	14.7	12.5	7.9	-	-	56.5	75-07-0
696	Acetaldehyde Di-Cis-3-He...	16.1	3.4	4.5	-	-	260.8	63449-64-9
698	Acetaldehyde Di-Isobutyla...	15.0	3.4	5.1	-	-	210.8	5669-09-0
697	Acetaldehyde Diisoamyl A...	15.2	3.2	5.0	-	-	243.1	13002-09-0
699	Acetaldehyde Ethyl Cis-3-...	15.8	3.9	4.4	-	-	200.9	28069-74-1
700	Acetaldehyde Ethyl Isobut...	15.1	3.9	4.8	-	-	175.9	6986-51-2
10	(+/-)-Acetaldehyde Ethyl I...	15.2	4.2	4.8	-	-	158.1	25334-93-4
701	Acetaldehyde Phenethyl ...	17.3	4.1	4.9	-	-	219.5	7493-57-4
702	Acetaldehyde, Butyl Phen...	17.2	4.5	4.7	-	-	236.5	64577-91-9
703	Acetamide	17.3	18.7	19.3	-	-	59	60-35-5
704	Acetanisole	18.9	11.2	7	-	-	137.8	100-06-1
705	Acetic Acid	14.5	8	13.5	-	-	57.6	64-19-7
706	Acetic Anhydride	16	11.7	10.2	-	-	95	108-24-7
707	Acetoin	16.2	12.1	18.2	-	-	88.3	513-86-0
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]			[illegible]	[illegible]

- e.g. GRAS but is only ~80 chemicals
- We can have TURI lists
  - Started with 800+ of the MA Reportables

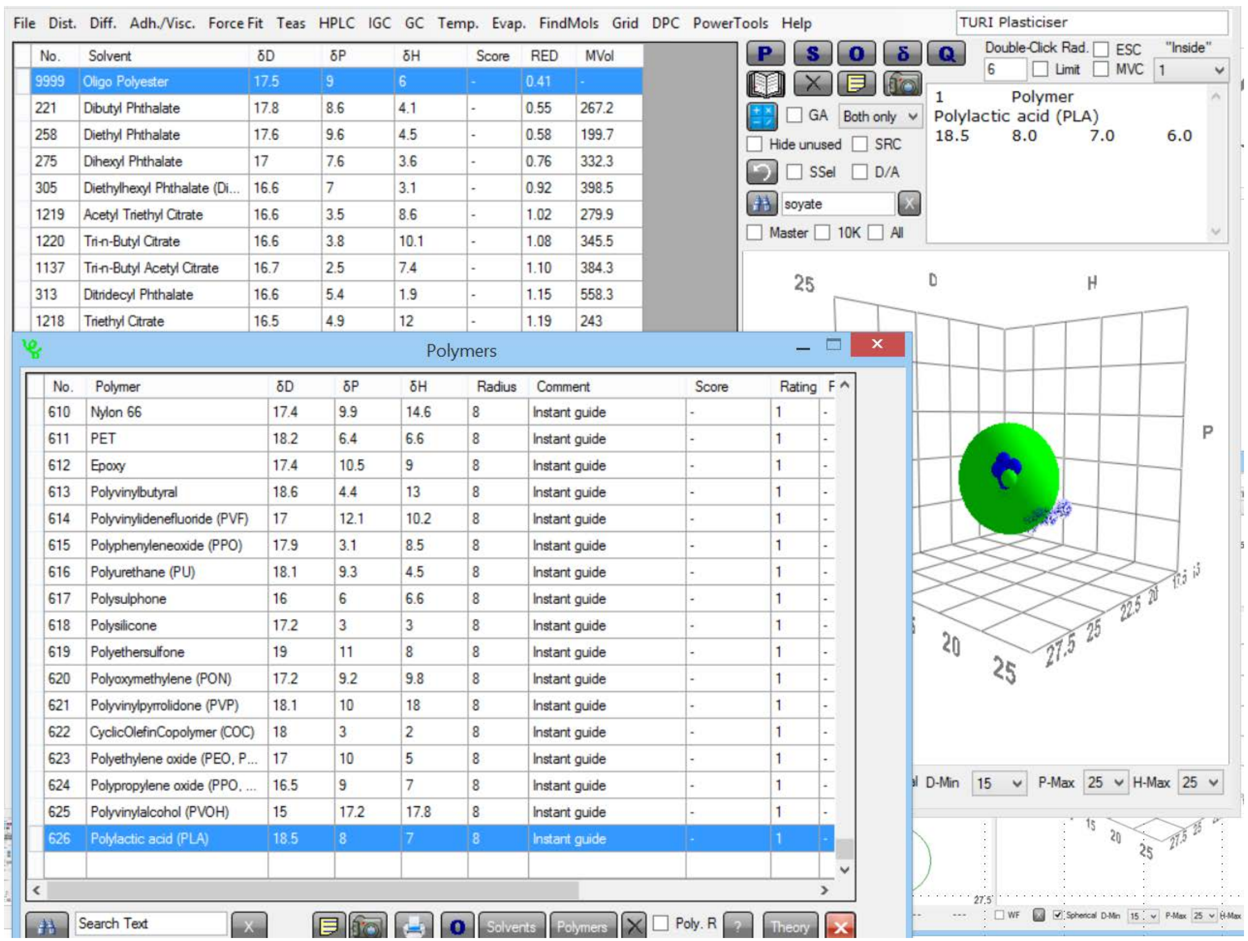
Rational green plasticisers

- Company X had 5 “green” synthons
- These could be combined in many ways to give 1000’s of possible plasticiser molecules for some common polymers
- Too many to synthesise and test
- So calculated HSP, MPt, VP, etc. of each molecule
  - Took 5min from a list of SMILES
- Rejected all with low MPt or high VP
- For each polymer could identify lowest HSP distance
  - Could then synthesise, test … and patent!

In miniature

- The best plasticiser for PLA?

Table of plasticisers created (mostly) automatically from HSPiP plus one extra.
The phthalates are great but can’t be used. The citrates are green but are useless
A polyester is ideal



HSP and particles

- Illustrated with CNT
- Shake with test solvents and score from "Happy" (on the left) to "Unhappy" on the right
- Can calculate HSP of CNT …
- … then predict optimized practical blends
  - e.g. CNT are easily dispersed in PLA

Works for nanoclays too. Working with U.Mass Lowell!

CNT "happiness" – photos courtesy Dr S Detriche, U. Namur

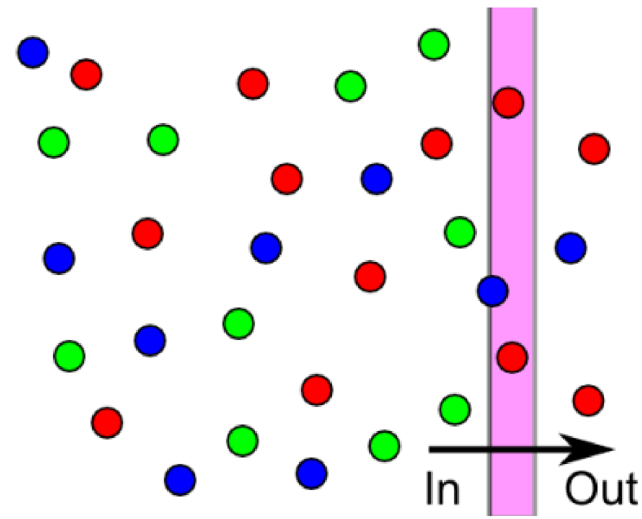
Diffusion for safety, environment & practical packaging

- Diffusion across a polymer barrier (gloves, environmental membrane, protection suit, packaging of food or chemicals) controlled by
  - Polymer (it is what it is)
  - Chemical shape/size (it is what it is)
  - Concentration gradient
    - So a high solubility in the top 1nm means a large concentration gradient which means faster diffusion
    - So can predict glove safety, chemical protection, flavour scalping, shipping containers, consumer packaging via HSP

A flavour scalping example

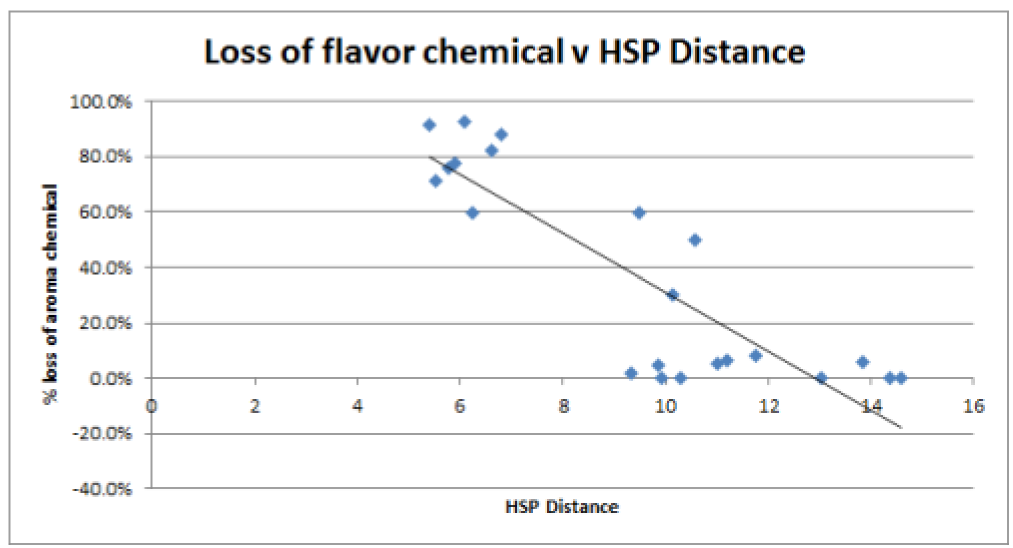
A new juice concept was great, but lost many of its flavour molecules after a few weeks.

The “red” molecules are more soluble (lower HSP Distance) than the “green” ones so you lose more of the red flavour through the packaging



Real data of 20 different flavour molecules in the juice.

All the ones with small HSP Distances were disappearing through the walls



Your formulations too

- HSPiP does a great job with safety-specific questions
- But it is also used for many other reasons all around the world
  - Large corporations, Small companies, Single consultants
  - Polymers, Drug delivery, Environmental, Cosmetics formulations, Organophotovoltaics, Paints, Coatings, …

What now?

- There’s a resource pack containing this PPT, an HSP Excel workbook, a list of links, including to short HSPiP videos on YouTube
- I am actively working with TURI to offer help, guidance, support on HSPiP for your community
  - After the last webinar I’ve helped with 2 TURs!
- I’m happy to answer your questions by email, telecon or weblink
- And now to your webinar questions …