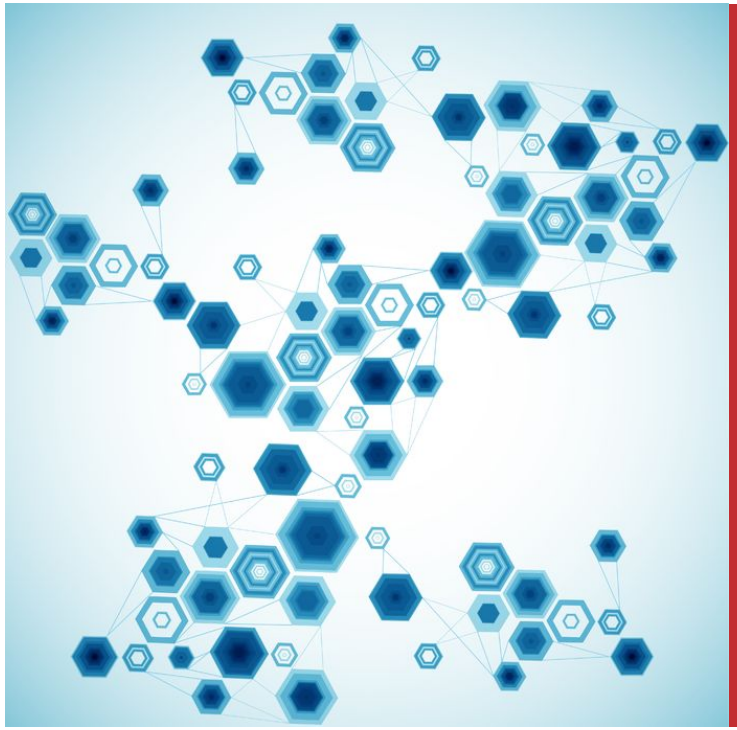


Recent advances in Inverse Gas Chromatography - IGC - measurements of HSP

RALF DUEMPELMANN,
ERIC BRENDLE and STEVEN ABBOTT

inolytix

Adscientis
Smart Inverse Chromatography

Content

- Introduction
- Inverse Chromatography
  - Some principles
- How to determine HSP using IGC?
  - Principle
  - Key Assumptions
- What happens if key assumptions are not respected?
- Example of application
  - Sesame oil
  - Pharmaceutical excipients
  - Ionic Liquids
- Conclusions and Outlook

Who are we?

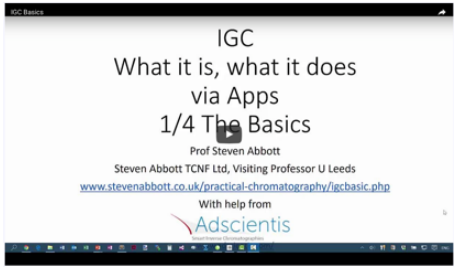
Eric Brendle (France)

Adscientis
Smart Inverse Chromatography

- 15 years IGC service for industry
- founder of Adscientis

Steven Abbott (UK)

- enthusiastic expert and advisor
- creator of apps and videos



Ralf Duempelmann (CH)

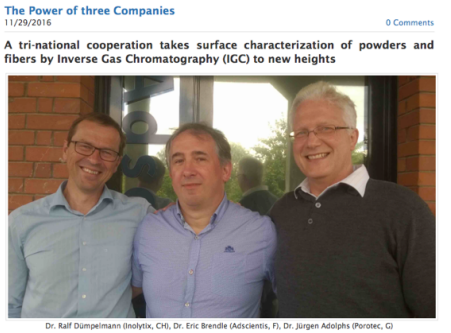
- 20 years R&D work in industry
- founder of Inolytix for better insights

Collaborations (D)

POROTEC
VERTRIEB VON WISSENSCHAFTLICHEN GERÄTEN GMBH

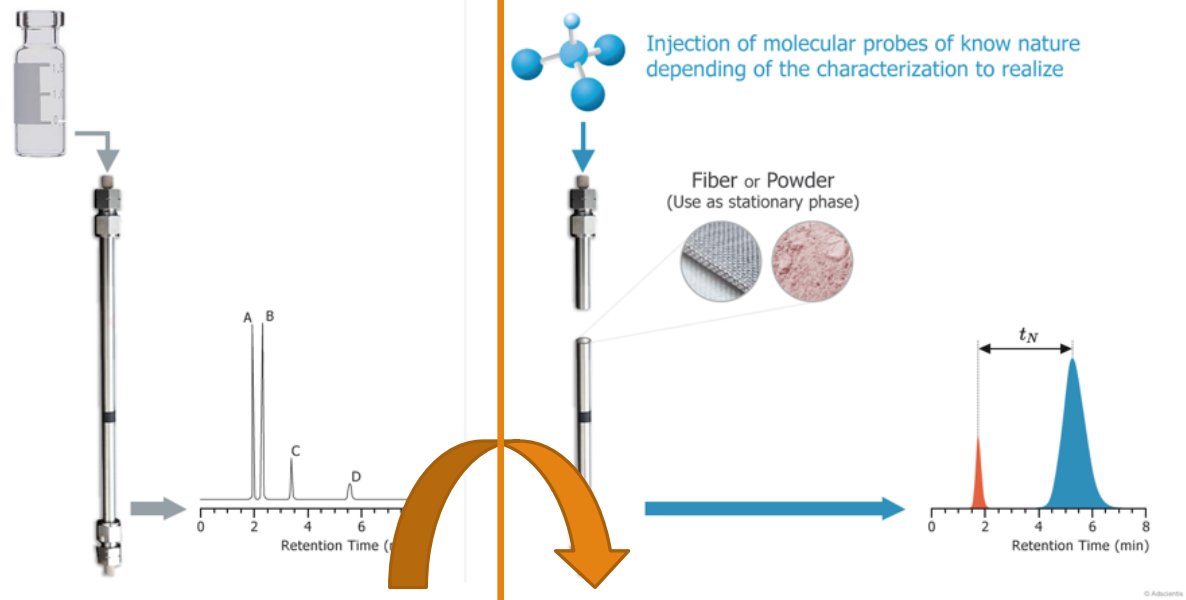
together

- new, fully automated and most-versatile IGC instrument

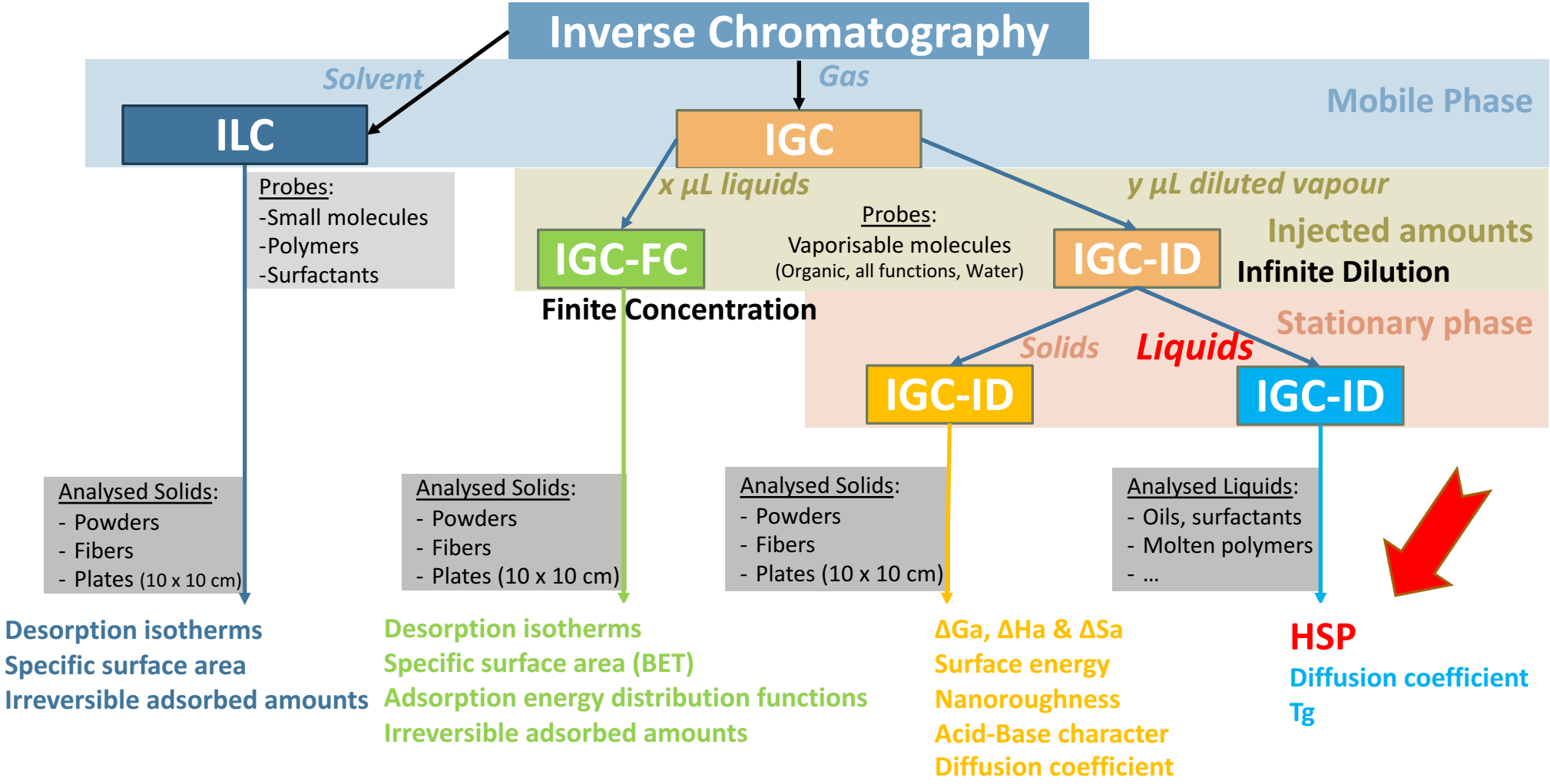


The Inverse Chromatography

Goal: Physicochemical measurements of surface properties or HSP

	analytical chromatography	inverse chromatography
		
Mobile phase	**unknown mixture**	**known gas probe**
Stationary phase	**solid packing**	**unknown "solid" properties**

Various “Inverse Chromatography” techniques



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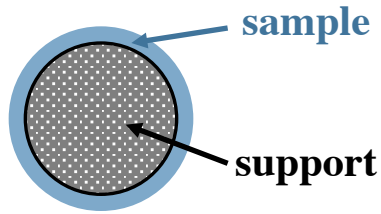
Preparation of IGC on liquids for HSP

Sample (HSP) is deposited on a solid support

Support is often Chromosorb P AW-DMDCS

- Acid washed and treated with dimethyldichlorosilane
- Assumed inert surface (!!)



Target surface coverage: 15-20% in weight

- Several impregnation methods exists

Impregnated support filled into column

- 1/8” or 1/4” stainless steel tubing

Column installed in IGC instrument (can be GC ...)

- Sample conditioning (dry He stream, removes the volatile substance

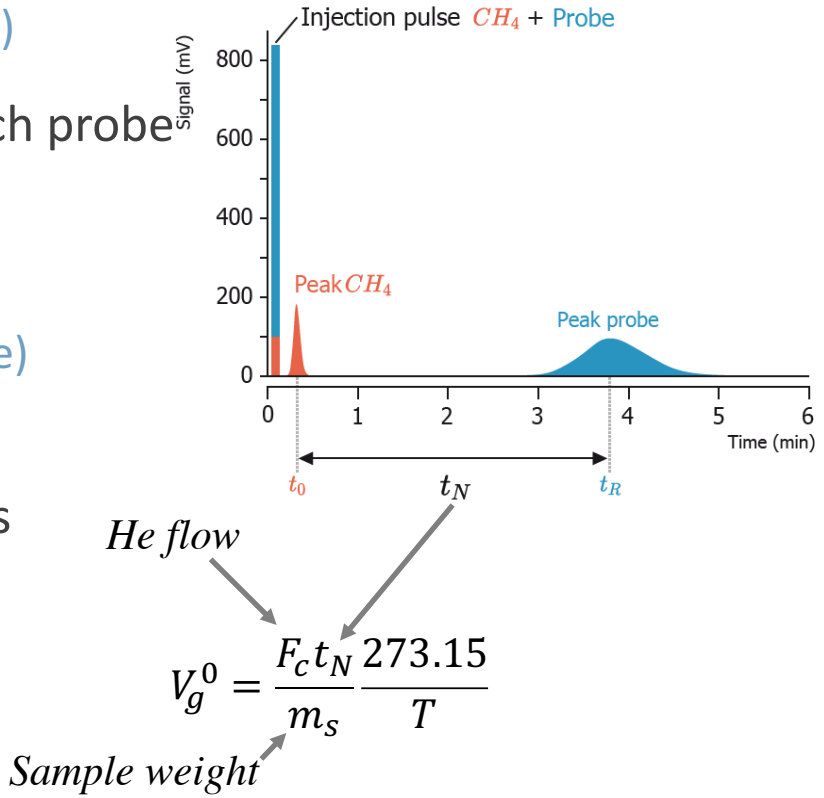
Ready for the IGC measurements

Sample characteristics:

- **liquids:** oils, mixtures, any not volatile samples
- **Polymers**: above T_g
- **Support amounts:** 200 < Support < 1000 mg
- **Sample amounts:** 30 < Sample < 200 mg
- **Measurement T° range:** 20 < $T°_{analysis}$ < 200°C (or more)

Operation and calculation of liquids for HSP

- Injection of probe molecules (test solvents)
  - Infinite dilution condition
  - Methane for t_0 determination
- Several molecular probes are injected (between 20 and 22 solvents)
  - Covering a broad HSP parameter domain (S. Abbott)
- Measurement of t_N, the net retention time of each probe
  - t_N is the time spent into the liquid samples
- Computation of the corresponding V_g :
  - Specific retention volume (normalized to 1 g sample)
  - Inert gas (He) volume required to elute the probe
- Use of HSPiP software to compute the HSP values
  - Direct import of the V_g values



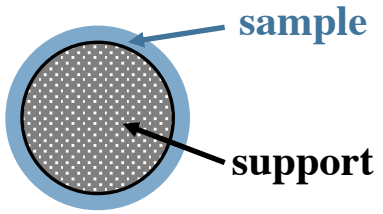
Key assumptions

- Injections at infinite dilution (IGC-ID)
  - No overloading, i.e. no solvent-solvent interactions to the retention time
- No significant sample (=liquid) amount modification
  - Evaporation / bad FID signal
  - Degradation / non reproducible

Easy to check

- Uniform and perfect support surface coverage by the liquid sample
  - No contribution of the support surface to the retention time
  - No interaction between the solvents (= gas probe) and the support

Less obvious to check…



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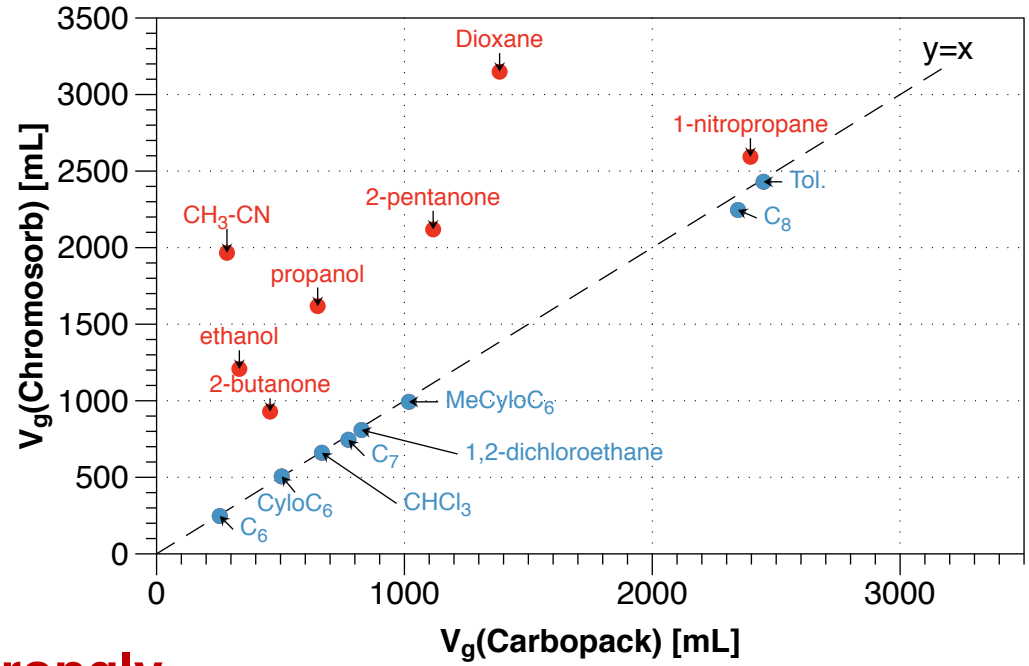
Characteristics of chromatographic supports

- Determined at 25°C using IGC-ID
- Chromosorb P AW DMCS
  - Silica (diatomaceous earth) treated with dimethylchlorosilane treated and acid washed
  - **Low disperse surface energy (24.1 mJ/m^2)**
  - High polar adsorption sites remain
  - Sometimes difficult to wet
- Carbopack C80
  - Graphitized carbon
  - **High disperse surface energy (133.4 mJ/m^2)**
  - Poorly polar
  - Highly nanorough (size exclusion)

	Chromosorb	Carbopack
Surface energy (γ_s^d)	**24,1 ± 1,0 mJ/m^2**	**133,4 ± 3,9 mJ/m^2**
Specific interactions	**ΔG_a^{SP} [kJ/mol]**	**ΔG_a^{SP} [kJ/mol]**
1,2-dichloroethane	15,3 ± 0,1	4,9 ± 0,2
Acetonitrile	17,3 ± 0,2	5,1 ± 0,5
Chloroform	15,4 ± 0,1	6,0 ± 0,2
1-nitropropane	14,7 ± 0,1	-2,3 ± 0,4
Ethanol	16,7 ± 0,2	3,8 ± 0,5
Propanol	16,4 ± 0,1	1,5 ± 0,3
Dioxane 1,4	11,5 ± 0,2	-4,9 ± 0,5
Et-Acetate	8,5 ± 0,1	-2,0 ± 0,4
butanone	10,7 ± 0,1	0,6 ± 0,3
2-pentanone	10,0 ± 0,2	-0,2 ± 0,4
Toluene	10,2 ± 0,1	6,2 ± 0,4

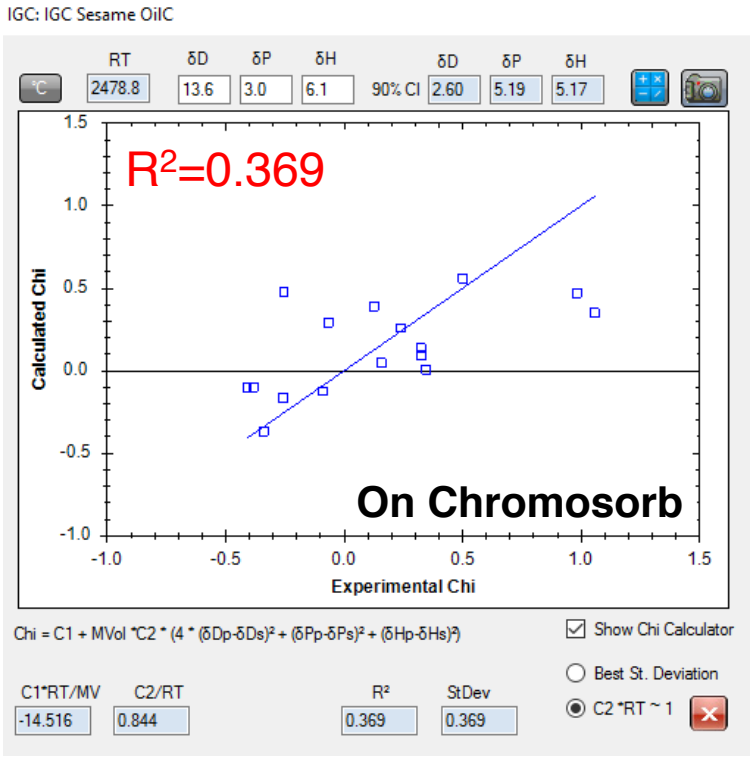
Influence of the support on the measured V_g

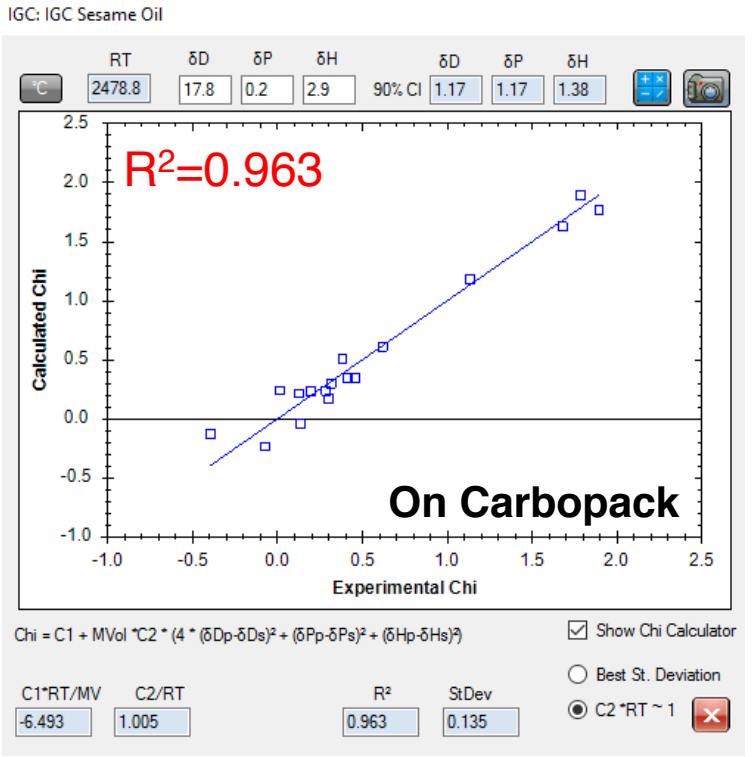
- Comparison of the V_g measured for **sesame oil** deposited on carbopack and chromosorb
- Measurements at 25°C, all things equal otherwise
- If no influence of the support: V_g(chromosorb)=V_g(carbopack)
- True for:
  - Apolar solvents and Toluene
  - $CHCl_3$ and 1,2-dichloroethane (because Chromosorb is DMCS treated?)
- False for all the other polar probes



Surface polarity of Chromosorb strongly influences the obtained V_g values

Influence on the determined HSP values





HSP: δ_D=13.6 ; δ_P=3.0 ; δ_H=6.1

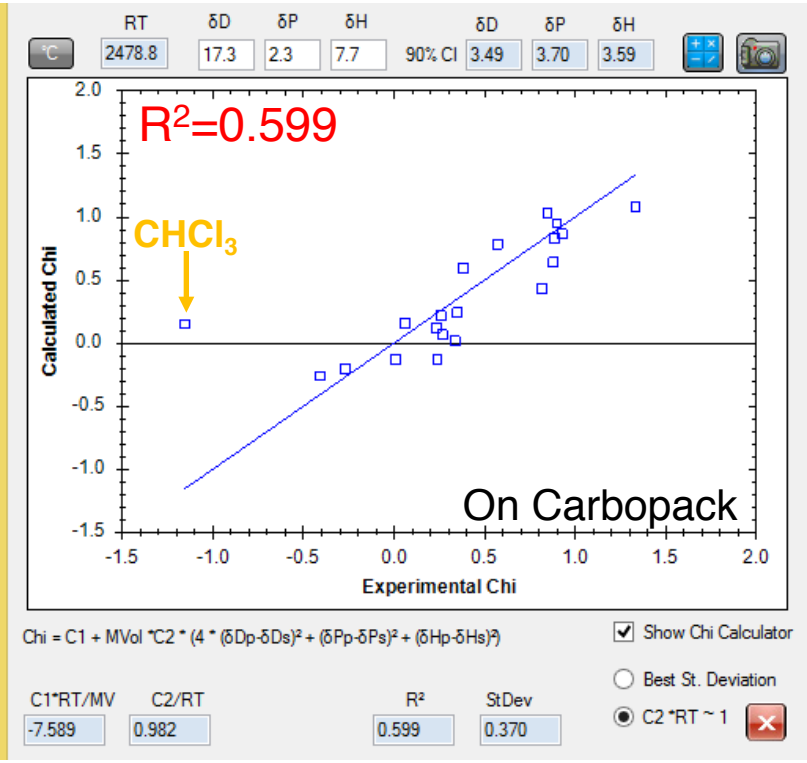
HSP: δ_D=17.8 ; δ_P=0.2 ; δ_H=2.9

- Major differences
- Good coefficient of determination (R^2) with Carbopack, very poor with Chromosorb

Over 70 HSPs of excipients measured

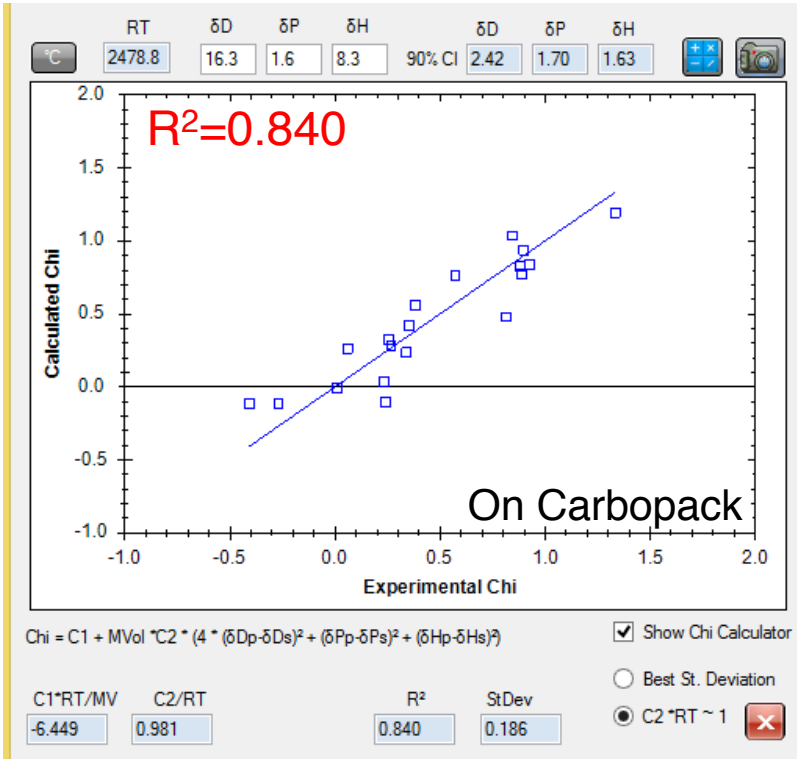
- Mostly good fittings with $R^2 > 0.8$
- Developed in collaboration with S. Abbott
  - Improvement of the molecular probe list
  - HSPiP computations
- Impregnation on Carbopack (range 15-18% in weight)
- Measurements at 25°C
- Injection of 20 selected molecular probes (test solvents)
  - heptane, octane, nonane, decane, cyclohexane and methylcyclohexane
  - tetrachloromethane, chloroform,1,2-dichloroethane
  - acetonitrile, nitropropane, toluene
  - ether, THF, dioxane
  - ethanol, propanol
  - ethyl acetate, 2-butanone, 2-pentanone
- Computation of HSP parameters using HSPiP Software

Example: HSP on pharmaceutical excipients X



HSP: δ_D=17.3 ; δ_P=2.3 ; δ_H=7.7

w/o $CHCl_3$

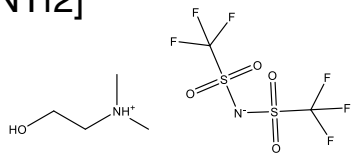


HSP: δ_D=16.3 ; δ_P=1.6 ; δ_H=8.3

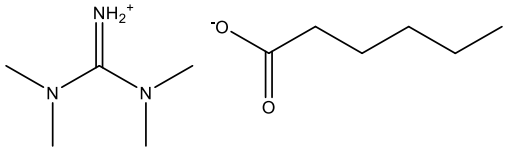
- Observation: chloroform is sometimes out of range…

Advanced: HSP determination on ionic liquids

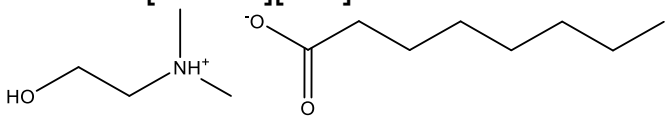
N,N-Dimethylethanolammonium bis(trifluoromethane)sulfonylimide
[DMEA][NTf2]



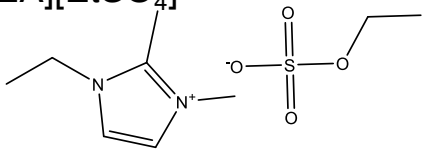
Tetramethylguanidinium hexanoate
[TMG][Hex]



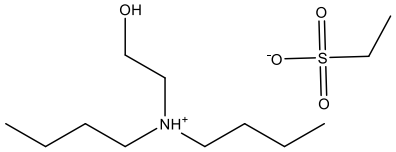
N,N-Dimethylethanolammonium octanoate
[DMEA][Oct]



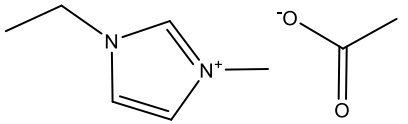
N,N-dimethylethanolammonium ethane sulfonate
[DMEA][$EtSO_4$]



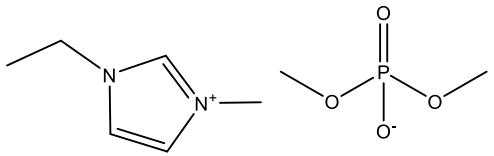
N-Butyldiethanolammonium trifluoromethanesulfonate
[$Bu(CH_2(CH_2OH)_2NH][F_3CSO_3]$



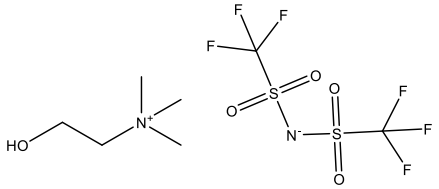
1-Ethyl-3-methylimidazolium acetate
[EM(m)Oac]



1,2-dimethylimidazoliumdimethylphosphate
[EmIm][Me_2PO_4]



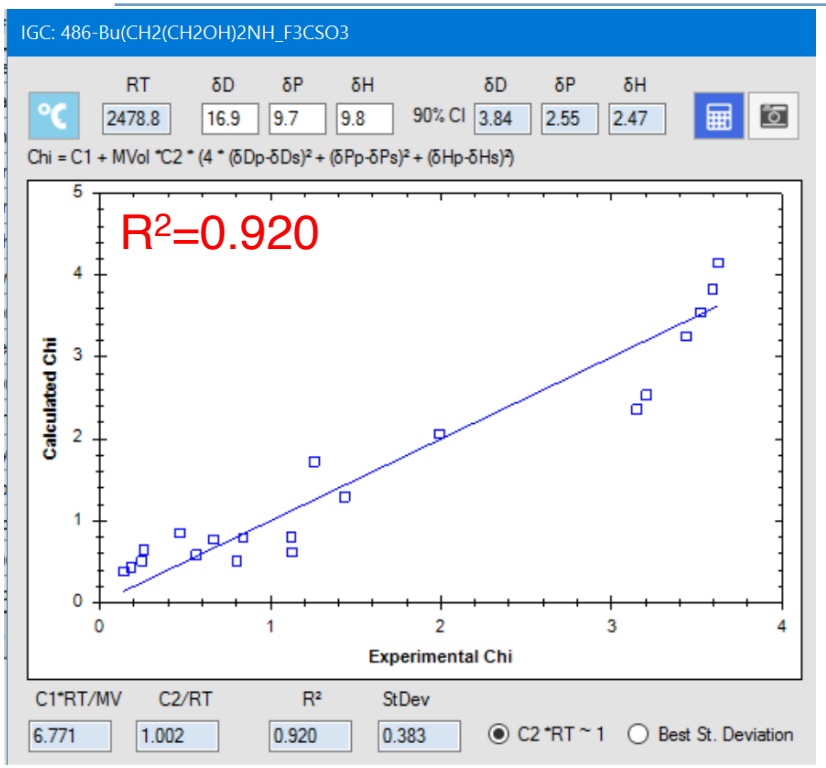
Choline bis(trifluoromethanesulfonyl)imide
[$Me_3NCH_2CH_2OH)(N(SO_2CF_3)_2$]



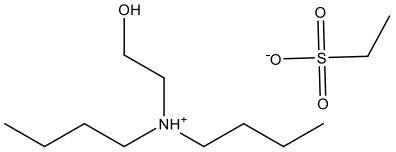
HSP determination on ionic liquids

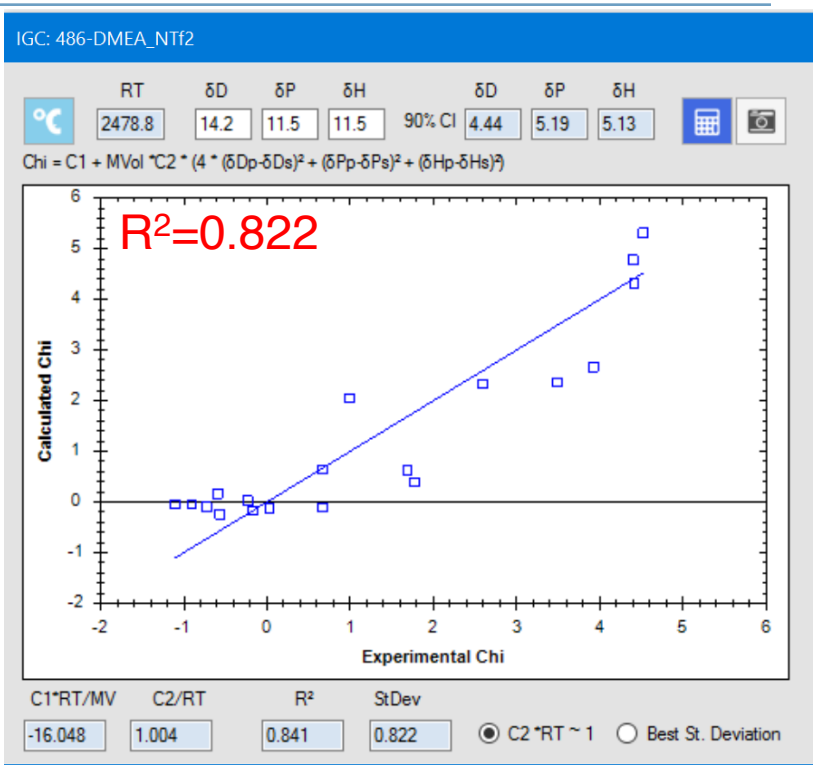
- Impregnation on Carbopack (range 15-18% in weight)
- Measurements at 25°C (He carrier gas)
- Injection of 20 selected molecular probes (test solvents):
  - heptane, octane, nonane, decane, cyclohexane and methylcyclohexane
  - tetrachloromethane, chloroform,1,2-dichloroethane
  - acetonitrile, nitropropane
  - ether, THF, dioxane
  - ethanol, propanol
  - ethyl acetate
  - 2-butanone, 2-pentanone
  - toluene
- Computation of HSP parameters using HSPiP Software

HSP determination on ionic liquids – good!

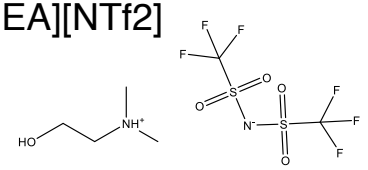


N-Butyldiethanolammonium trifluoromethanesulfonate
$[Bu(CH_2(CH_2OH)_2NH][F_3CSO_3]$



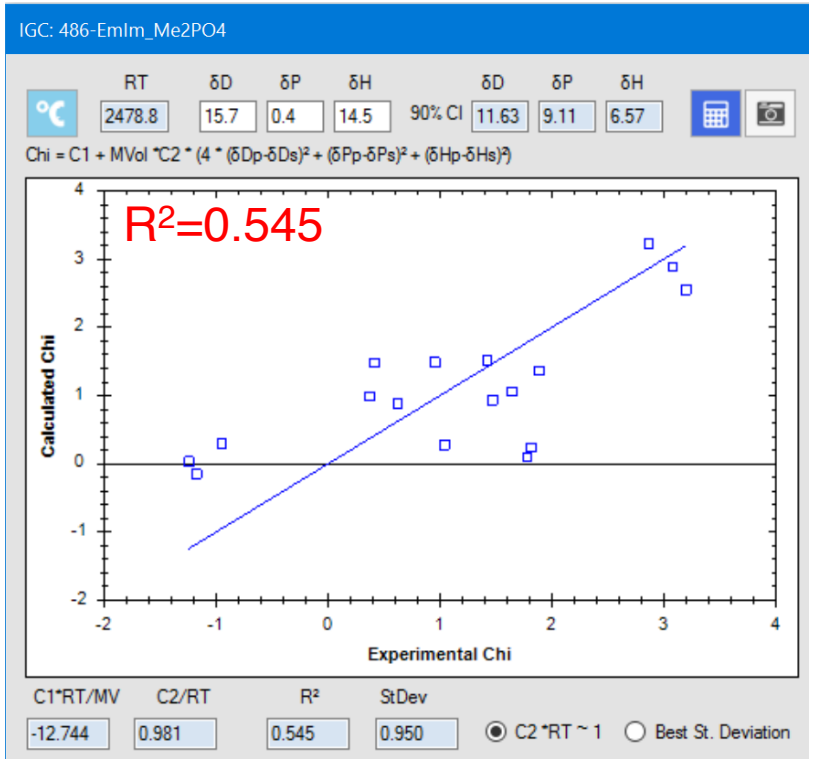


N,N-Dimethylethanolammonium bis(trifluoromethane)sulfonylimide
[DMEA][NTf2]

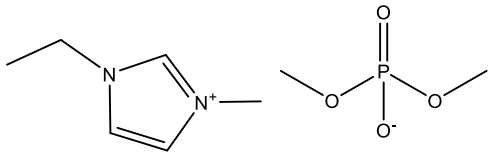


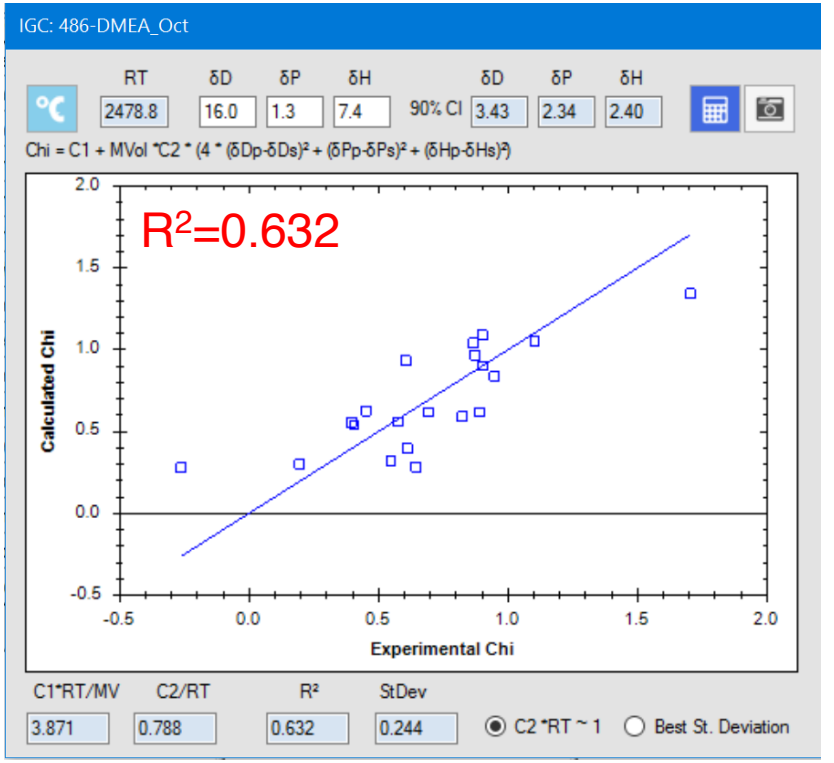
- Sometimes relative good fittings are obtained

HSP determination on ionic liquids – bad?

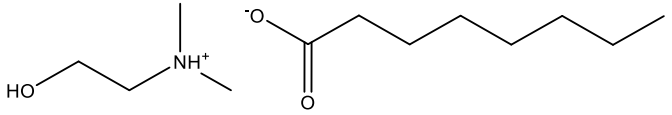


1,2-dimethylimidazoliumdimethylphosphate
[EmIm][Me_2PO_4]





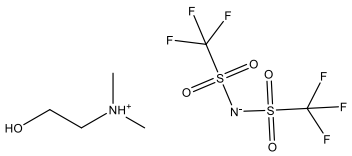
N,N-Dimethylethanolammonium octanoate
[DMEA][Oct]



- Sometimes fittings are bad

Results: HSP on ionic liquids

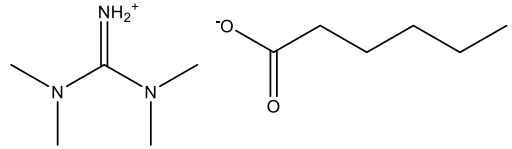
N,N-Dimethylethanolammonium bis(trifluoromethane)sulfonylimide
[DMEA][NTf2]



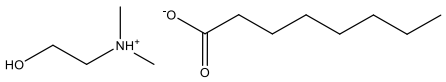
δ_D=14.2
δ_P=11.5
δ_H=11.5 r^2=0.841

Tetramethylguanidinium hexanoate
[TMG][Hex]

δ_D=17.1
δ_P=0.9
δ_H=11.5 r^2=0.532



N,N-Dimethylethanolammonium octanoate
[DMEA][Oct]

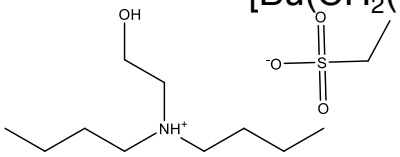


δ_D=16.0
δ_P=1.3
δ_H=7.4 r^2=0.632

N,N-dimethylethanolammonium ethane sulfonate
[DMEA][$EtSO_4$]

δ_D=19.4
δ_P=4.9
δ_H=10.8 r^2=0.801

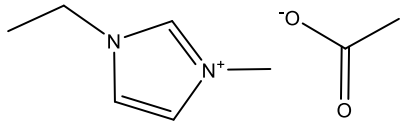
N-Butyldiethanolammonium trifluoromethanesulfonate
[$Bu(CH_2(CH_2OH)_2NH][F_3CSO_3]$



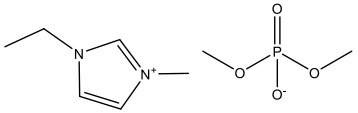
δ_D=16.9
δ_P=9.7
δ_H=9.8 r^2=0.791

1-Ethyl-3-methylimidazolium acetate
[EM(m)Oac]

δ_D=18.2
δ_P=3.8
δ_H=16.8 r^2=0.791



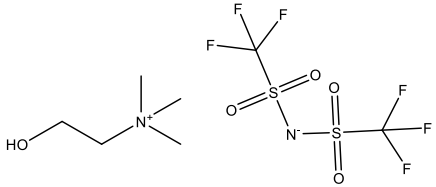
1,2-dimethylimidazoliumdimethylphosphate
[EmIm][Me_2PO_4]



δ_D=15.7
δ_P=0.4
δ_H=14.5 r^2=0.545

Choline bis(trifluoromethanesulfonyl)imide
[$Me_3NCH_2CH_2OH)(N(SO_2CF_3)_2$]

δ_D=16.4
δ_P=12.7
δ_H=8.7 r^2=0.860



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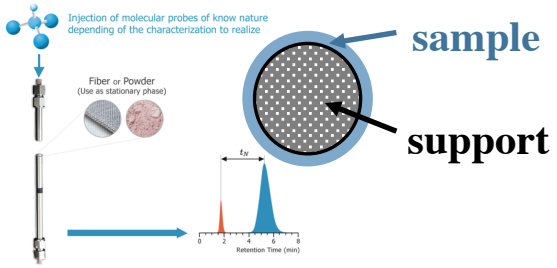
Conclusions

- IGC provides a quick and suitable method for the determination of HSP
  - Low sample amounts required
  - Low solvent amounts needed
  - Possibility to test sample with more than 20 solvents a day



- Key assumptions must be fulfilled
  - Good sample preparation (optimal and homogeneous surface coverage)
  - No influence of the injected solvent amounts (ID conditions must be respected)
  - No influence of the support
- Chromosorb P AW DMCS is not ideal
- Carbopack provides far better results
- Strong experience with excipients and other compounds
  - but still questions for... Ionic Liquids

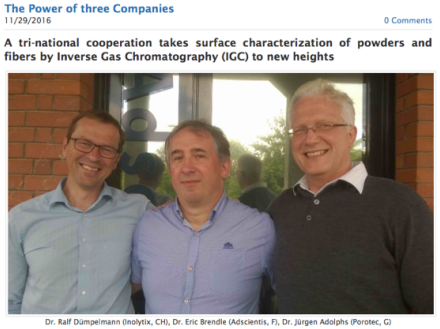
Outlook

- IGC and HSP – Still further understanding and improvement

- Neuronic: a new solution for automated IGC measurements

  neuronIC

  - Simultaneous measurements on two samples (2 analytical channels)
  - Up to 45 test solvents available
  - Coupling with HSPiP


The Power of three Companies
11/29/2016 0 Comments

A tri-national cooperation takes surface characterization of powders and fibers by Inverse Gas Chromatography (IGC) to new heights

Dr. Ralf Dümpelmann (Inolytix, CH), Dr. Eric Brendle (Adscientis, F), Dr. Jürgen Adolphs (Porotec, G)

- Outstanding performance
  - HSP for **two samples (liquids)** with **20 test solvents within one working day** (repeatability tests included)

6. IGC-Symposium 20.06.2017, Cologne

www.inverse-chromatography.com

art'otel in Cologne

THANK YOU FOR YOUR ATTENTION!

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