Application of NMR Relaxation to determine Hansen Solubility Parameter (HSP) of Nanoparticles

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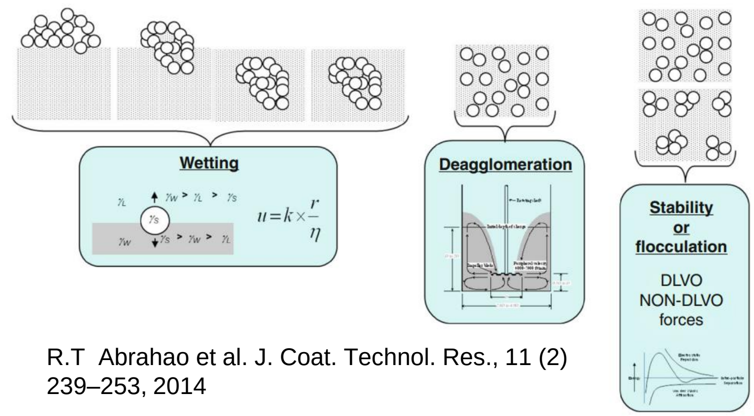
Particle Dispersions important in the development of many commodity products

- Coatings, inks, pharmaceuticals and cosmetics etc., increasingly employ micro- or nano-particles carefully formulated in a variety of carrier fluids

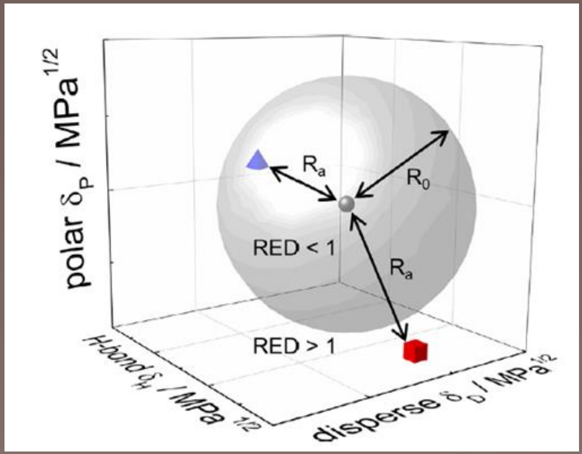


R.T Abrahao et al. J. Coat. Technol. Res., 11 (2) 239–253, 2014

- Dispersion a powder into a liquid phase is a critical process step in formulating and manufacturing
- A predictive method for selecting appropriate solvent or solvent mixture in wetting and dispersion of powders has practical and economic benefits
- **Hansen Solubility Parameter** (HSP) method suggested as a useful approach to predict solvent quality for wetting of powders

Hansen Solubility Parameter (HSP)

HSP originally developed to describe the interaction (solubility) of polymers in different liquids → uses paradigm that "like dissolves like"*



Semi-empirical approach

- Uses measures of interactions: dispersion, D, polar/dipolar, P and hydrogen bonding, H
- provides coordinates of solute in a 3-D interaction space
- Solubility of polymer evaluated in a range of liquids selected across "Hansen space"
- Probe solvents ranked as *good* or *poor* depending on efficiency to dissolve the polymer
- Sphere defining boundary between *good* and *poor* solvent coordinates constructed

Relative Energy Difference

$$RED = \frac{R_a}{R_0}$$

An RED <1 is "good" and an RED >1 is "poor"

* C. Hansen, Hansen Solubility Parameters: A User's Handbook, 2nd Ed., CRC Pres (2007)

HSP applied to dispersion of particles

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- Hansen → sedimentation time used as suitable metric
  - Settling slowest in good solvent; subjective; very time-consuming for nanoparticles; no standard procedure

- Analytical centrifugation (AC) – major advance
  - Significantly faster; provides quantification of particle agglomeration
  - Rank order of solvents → apply HSPiP* software to determine **H**ansen **S**olubility **P**arameter)**
  - SOP developed*** → quantitatively determine HSP of the material

If HSP for a material is known then any combination of solvents - *even "poor" ones* – giving an RED <1 will be suitable for dispersing the material!

* https://www.hansen-solubility.com

** Help and guidance by **Prof. Steven Abbott** regarding use of HSPiP software is acknowledged and appreciated

******* S. Süβ, T. Sobisch, W. Peukert, D. Lerche, D. Segets, *Determination of Hansen Parameters for Particles: A standardized routine based on analytical centrifugation,* Advanced Powder Technology, **29** (2018) 1550-1561

Comparison of the two Techniques: AC vs NMR

Limitations of sedimentation/centrifugation technique

- Based on Stoke's law
  - Assumes laminar flow; no turbulence; Reynolds Number ≤0.2
  - Spherical particles
  - Narrow particle size distribution
  - Particle solids concentration <1 volume %
  - Need to correct for density and viscosity of dispersion fluid

  → Relative Sedimentation Time (RST)

NMR relaxation

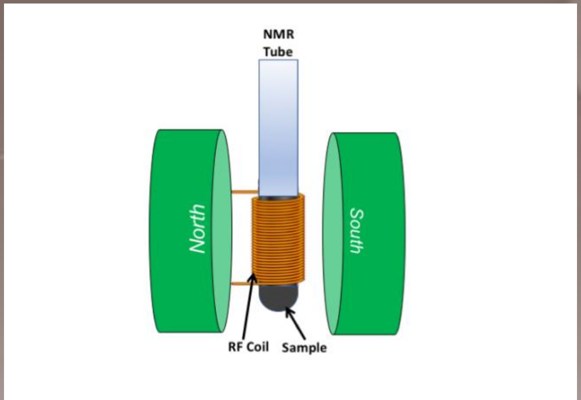
- Fast, direct and simple quiescent measurement
- Size and shape of particle immaterial
- Any industrially relevant solids concentration
- No corrections

Objective and Experimental Task

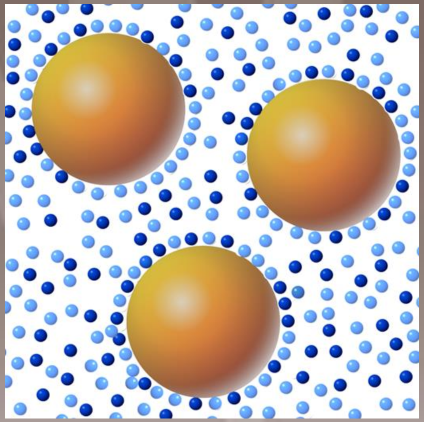
Hypothesis

Can NMR Relaxation time be used to rank order of particle-solvent interactions and so determine the HSP of particles?

- Test of Hypothesis
  → measure NMR relaxation time of various hydrophilic and hydrophobic powders dispersed in a range of polar and non-polar solvents in Hansen Space → determine corresponding score for the dispersed material



Magnet and RF Coil Assembly



liquid molecule that was free

liquid molecule that was bound

Both have a characteristic relaxation time, T, and relaxation rate, R (= 1/T)

Free Liquid: Long Relaxation Time (sec)

Bound Liquid: Short Relaxation Time (msec)

Observe a single relaxation that is a weighted average

$$R_{av} = R_f (1- \Phi) + R_b \Phi$$

Φ : proportion of bound liquid
R_b : relaxation rate of bound liquid
R_f : relaxation rate of free liquid

Current study a “proof-of-concept”

Materials

Zinc Oxide, ZnO

Property	Coating	Nature *	Zeta potential** (mV)	Mean Particle Size (nm)
Hydrophilic	None	Cationic	+39	ca 120
Hydrophilic	SiO_2	Anionic	-55	ca 160
Hydrophobic	Silane	Non-wetting	N/A	ca 140

Alumina, Al_2O_3

Property	Coating	Nature*	Zeta Potential (mV)	Mean Particle Size (nm)
Hydrophilic	None	Cationic	+45	ca 300
Hydrophobic	Silane	Non-wetting	N/A	ca 300

** In water; ** In 10mM KCl (aq)

Solvents*

Zinc Oxide, ZnO

Selected from**:

Acetone, Acetonitrile, Benzyl Alcohol, Benzyl Benzoate, Butanol, Caprolactone, Chloroform, Decyl Alcohol, Dichloromethane, Dimethylformamide, Dimethyl Sulfoxide, Dodecane, Ethanol, Ethyl Acetate, Ethyl Lactate, Ethyl Oleate, Heptane, Hexane, Isopropanol, Methanol, Methyl Cellosolve, Methyl Ethyl Ketone, Methylene Chloride, N-Methyl Pyrrolidone, Propylene Carbonate, Tetrahyrdrofuran, Toluene

Alumina, Al_2O_3

Selected from above plus:

Cyclohexane, Cyclopentanone, Diacetone Alcohol, Dioxane, Heptane, N-Methyl Formamide

* NMR relaxation time sensitive to water and oxygen content

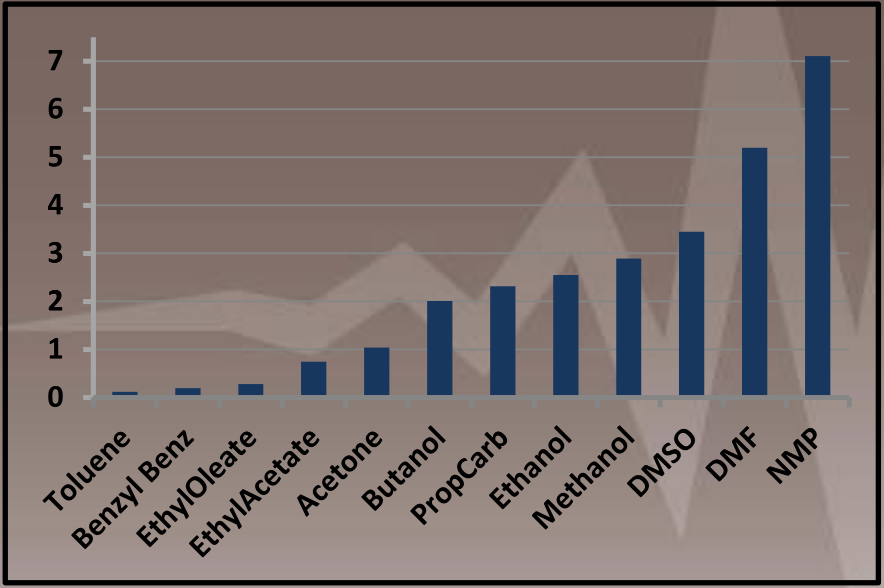
** Hansen recommends a minimum of 12 solvents

Experimental Results: NMR

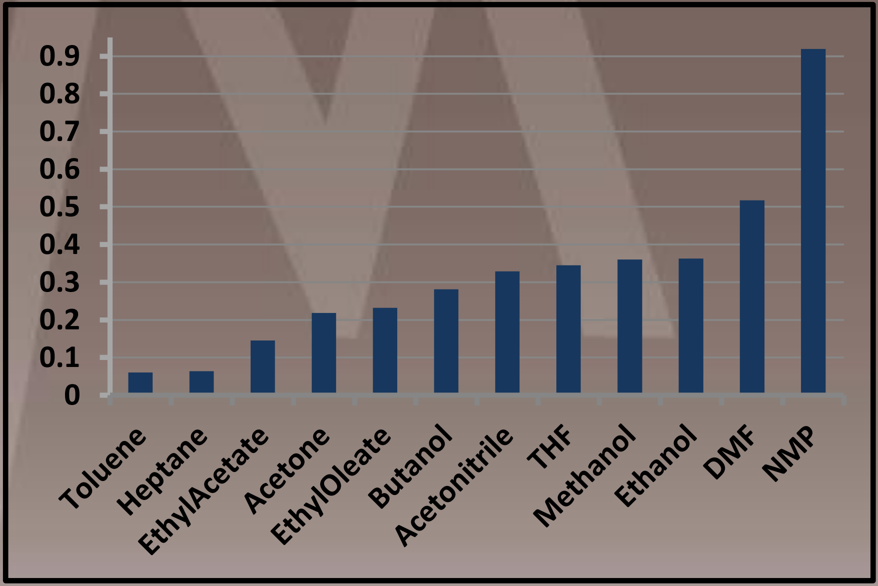
Relative Relaxation Rate, R_{sp}, for two Zinc Oxide powders are significantly different depending on solvent-surface interaction

$$R_{sp} = [R_{susp}/R_{solv}] - 1$$

Silica coated



Silane coated



More efficient wetting → larger R_{sp} value

Takeda Approach

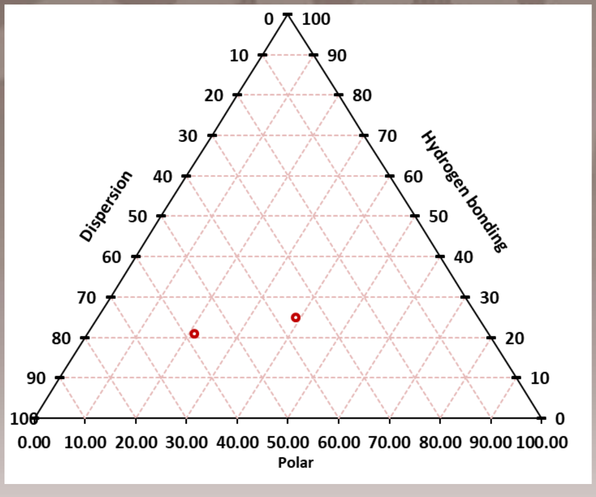
Rank order Relative Relaxation Rate (R_{sp}) data into score: **1** for strong affinity (high R_{sp}); **2** for weaker affinity, (lower R_{sp})

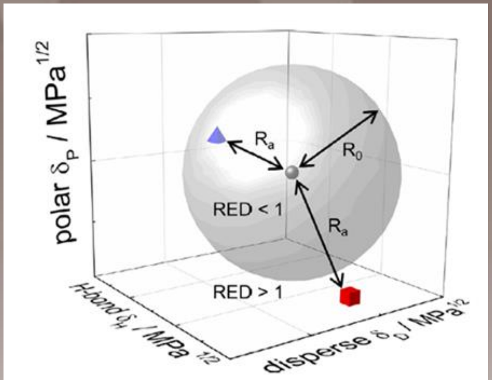
Create Hansen sphere using HSPiP software using first 1- 3 rank ordered solvents as “1” and all others as 2

Increase number of solvents ranked as “1” until goodness of fit has maximized.
This occurs when adding a next solvent as “1” causes the fit to break down (“no fit”)
A value of the radius of the Hansen Sphere is defined (R_o)

The center of the best fit sphere defines the effective Hansen Solubility Parameter (HSP) of the material under investigation

To better visualize a difference in HSP parameters of different materials a TEAS plot is constructed

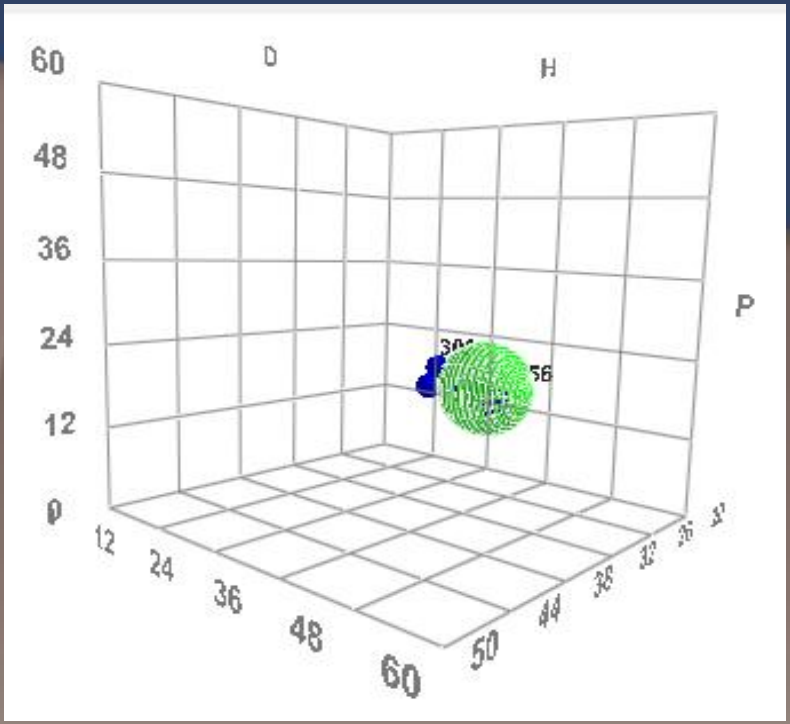




Experimental Results: HSP Silica-coated ZnO

Solvent	R_{sp} Value	Takeda Affinity
NMP	7.104	1
DMF	5.20	1
DMSO	3.451	1
MeOH	2.89	1
EtOH	2.542	2
Acetonitrile	2.405	2
Propylene Carbonate	2.311	2
THF	2.22	2
BuOH	2.013	2
Caprolactone	1.426	2
Acetone	1.038	2
Ethyl Acetate	0.742	2

Hansen Sphere



Estimated HSP for Silica-coated ZnO
D = 16.58; P = 14.82; H = 22.11

Results Summary

Zinc Oxide, ZnO

Property	Coating	D	P	H
Hydrophilic	None	15.95 (35%)	12.18 (27%)	17.64 (39%)
Hydrophilic	SiO_2	16.58 (31%)	14.82 (27%)	22.11 (42%)
Hydrophobic	Silane	18.51 (45%)	8.97 (22%)	14.05 (34%)

Alumina, Al_2O_3

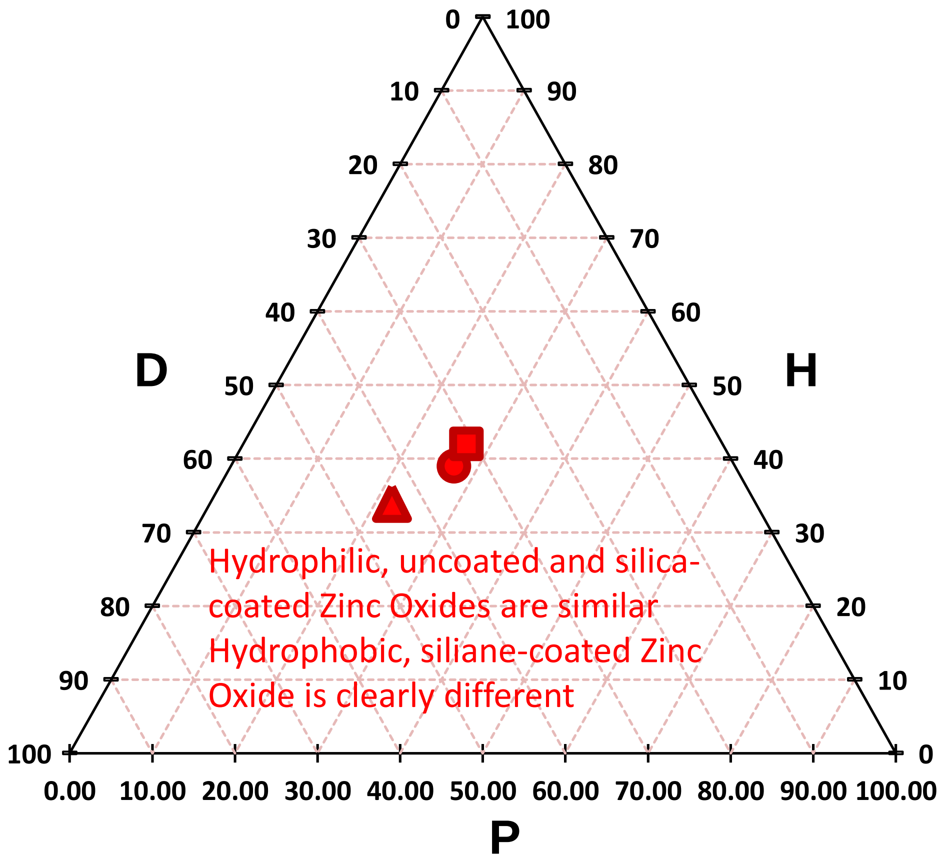
Property	Coating	D	P	H
Hydrophilic	None	18.03 (36%)	12.52 (25%)	19.50 (39%)
Hydrophobic	Silane	17.97 (58%)	6.40 (21%)	6.59 (21%)

Clear differences in HSP between material surface coatings

Any combination of solvents producing the same average values for D, P and H will be an efficient wetting fluid

TEAS Plots: Comparing Hydrophilic ZnO and Al_2O_3 *vs* their hydrophobic derivatives

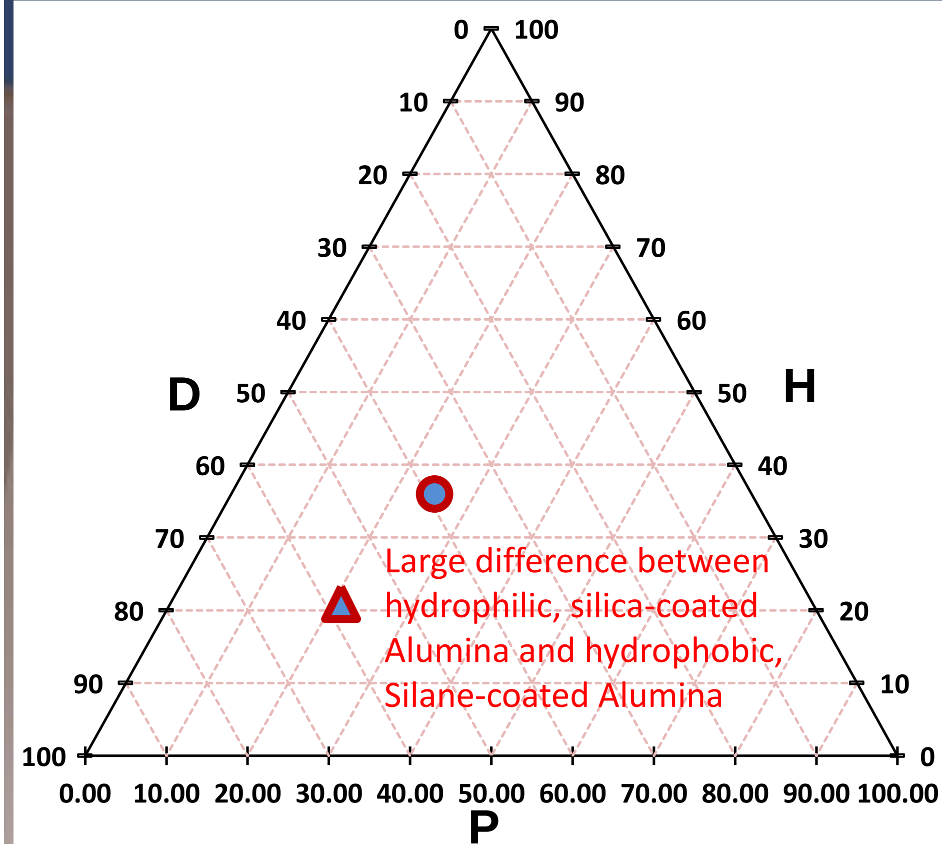
Zinc Oxide



Uncoated ● Silica coated ■

Silane coated ▲

Alumina



Uncoated ● Silane coated ▲

TEAS Plots: Comparing ZnO and Al_2O_3 and their hydrophobic derivatives

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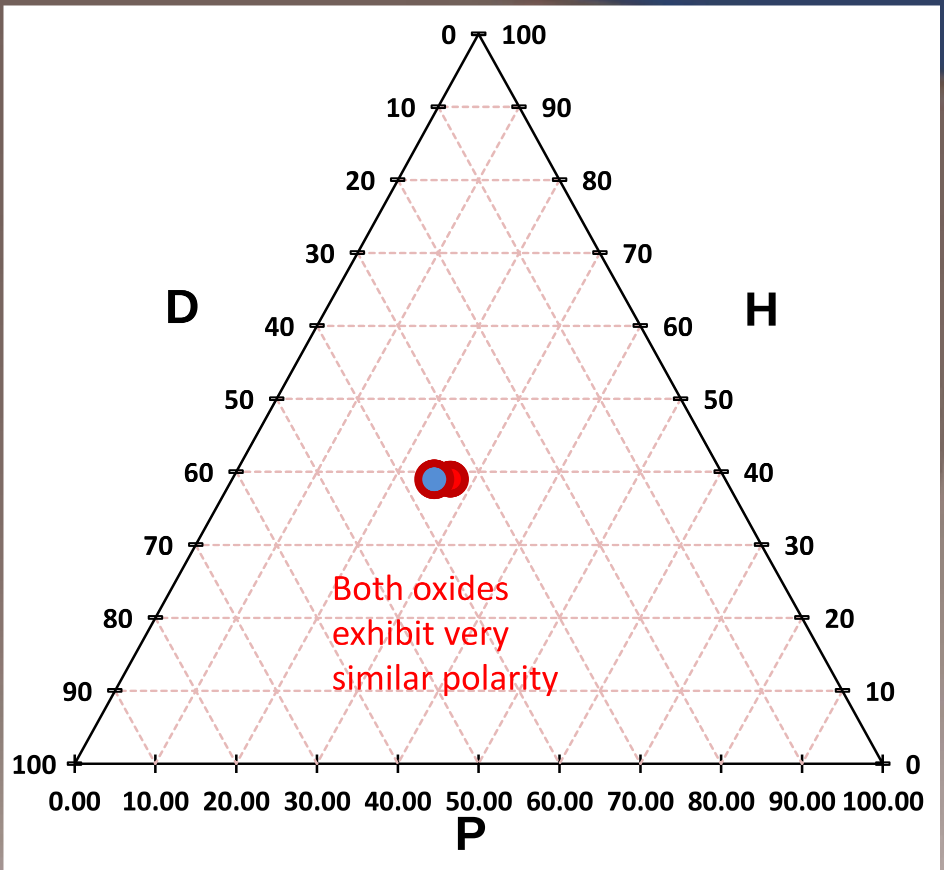
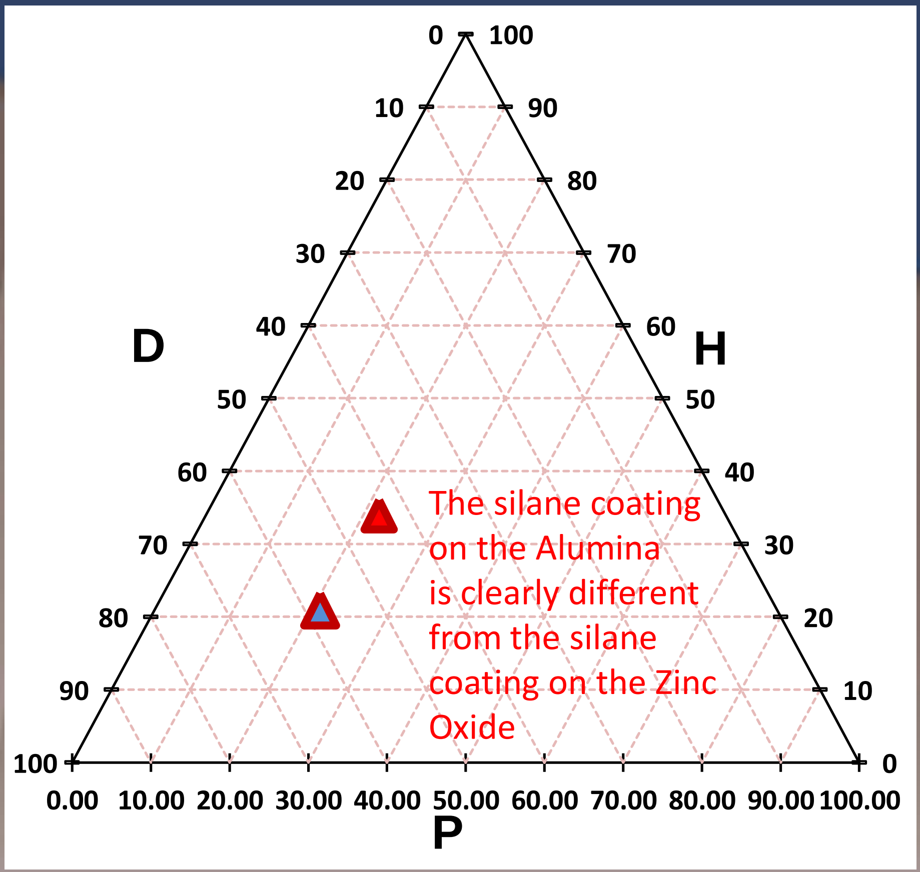
ZnO/Al_2O_3 Uncoated



Zinc Oxide ● Alumina ●

ZnO/Al_2O_3 Silane coated

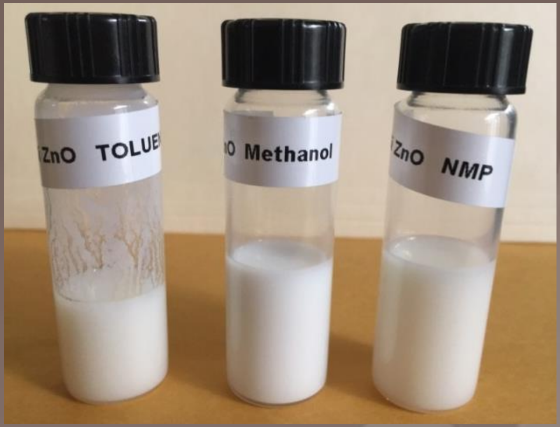


Zinc Oxide ▲ Alumina ▲

NMR Results: Wetting and Dispersibility

Silica-coated Zinc Oxide dispersed in three different solvents

(a) After initial sonication



Poor wetting of the glass vial by the Toluene suspension; **Methanol and NMP suspensions both look good**

Relaxation rates differ significantly:
NMP (7.10) > MeOH (2.89) > Toluene (0.12)
Toluene is very poor wetting agent for the zinc oxide powder.; NMP is most efficient

(b) After 4 hours

Toluene suspension: separated and flocculated.
Methanol suspension: noticeable sediment
NMP suspension: virtually no sediment
MeOH able to wet the powder but is a less efficient dispersant

Conclusion

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- NMR relaxation is a useful complimentary technique for selecting suitable solvents for wetting and dispersion of powders
  - measurements can:
    discriminate between surface chemical coatings
    distinguish between suspensions that visually look, initially, to be similar
    provide time-saving information in formulation.

- Proof-of-concept study suggest that NMR relaxation measurements may provide relatively fast and simple way to determine the HSP of solid materials

Future Work

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Test the predictive ability of NMR relaxation

Expand study to other industrially useful materials
Carbon black, graphene, metals, etc

Explore applicability to poorly water-soluble drugs

Determine usefulness for surfactants/dispersants in water

Thank you!

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For more information, to send samples or to arrange a demonstration at your facility, or to speak to a technical applications specialist, please contact:

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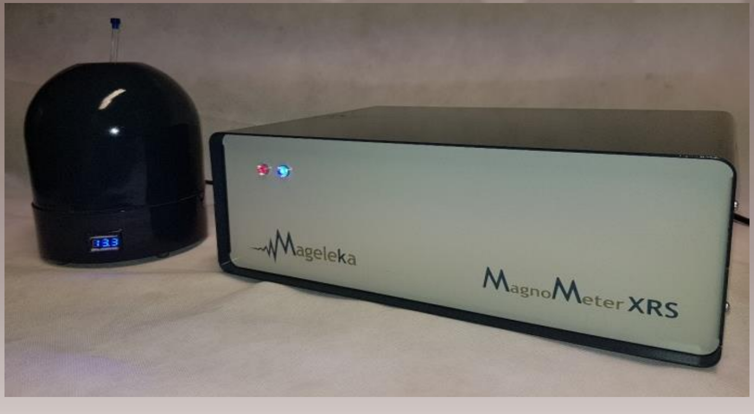

Low field NMR
new technique for suspension and emulsion analysis

- Inexpensive, simple benchtop device
- Easy operation
- Industrial R&D, QC/QA and process laboratories