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Understanding Importance of Water Sorption Isotherm Shape, Hysteresis, and Models on Pharmaceutical Materials

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Overview

1. Vapor Sorption Techniques

- Molecules as Probes
- Sorption Mechanisms
- Moisture Methods

2. Isotherms

- Shape and Hysteresis
- Isotherm Modeling
- Hydrate Formation

3. Moisture-Induced Phase Changes

- Glassy-Rubbery Transitions
- Amorphous Content
- Raman Spectroscopy

Characterization of Solids

1. Energy as a Probe

- Spectroscopy
- Light, x-rays, lasers, etc.
- Analytical and structural information

2. Heat as a Probe

- Calorimetry
- Thermodynamic information

3. Molecule as a Probe

- Sorption techniques
- Thermodynamic, chemical, and structural Information

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Characterization of Solids

Energy as a Probe

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Energy

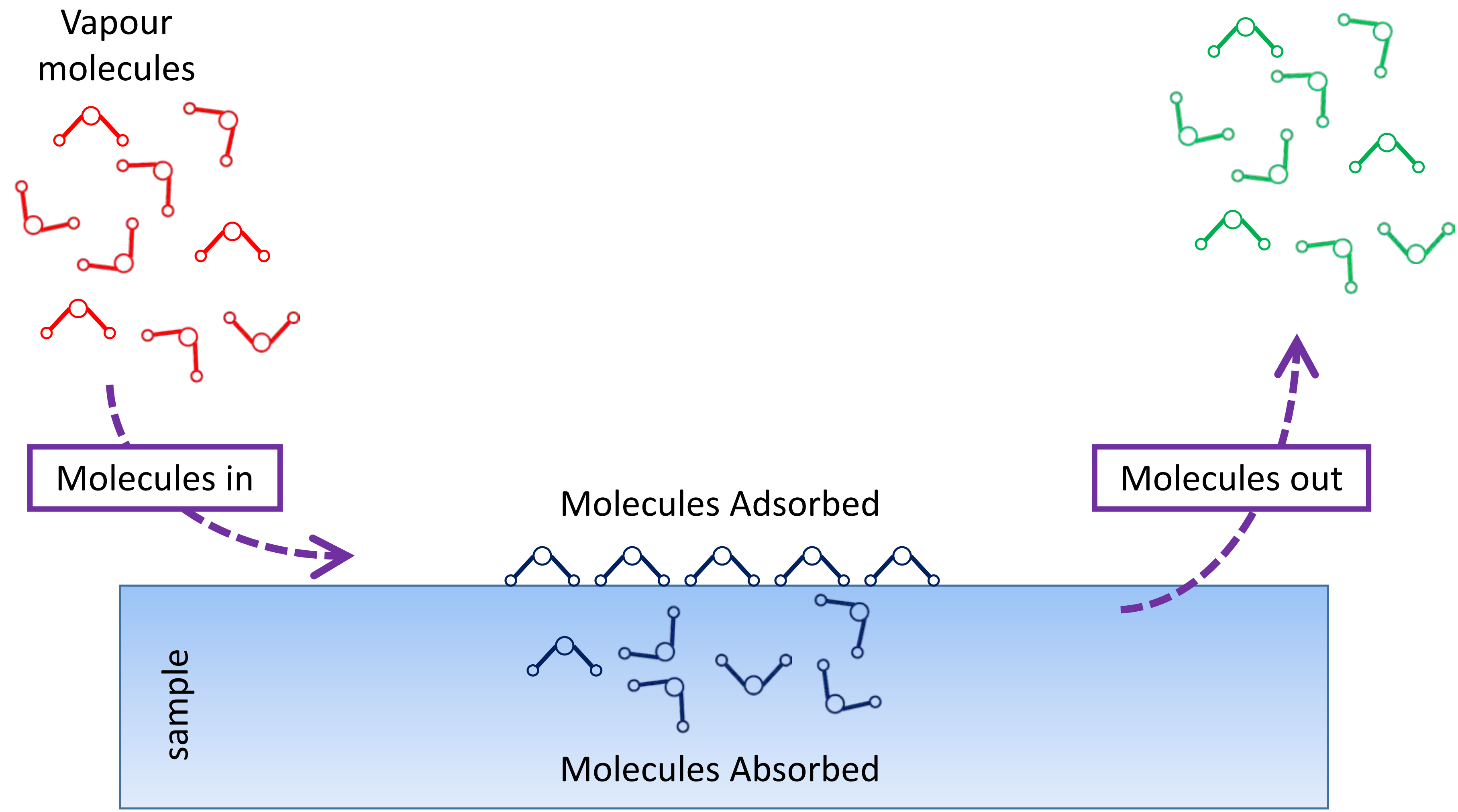
Molecules as a Probe

-Sorption techniques

-Thermodynamic, chemical, and structural Information

Matter

Molecules as a Probe



Molecules as a Probe

Where can Vapour Sorption occur?

- On the surface?
- In pores – micro/meso?
- Between the particles (condensation?)
- Sorbed into the bulk?
- Chemically reacted (hydrate formation)?

What can vapour sorption tell me?

- The stability of materials at different vapour concentrations.
- Vapour-solid interactions important for wide range of industries:
  - food, pharmaceutical, proteins, fuel cells, packaging, high energy materials (explosives), personal care
- Accurately determining water sorption isotherms is critical for proper development and storage of these materials

Quantifying Moisture Content

1. Karl Fischer Titration
2. Loss On Drying
3. Water Activity Meters
4. Near IR
5. Humidity Chambers/Desiccator Jars
6. Dynamic Vapor Sorption Methods

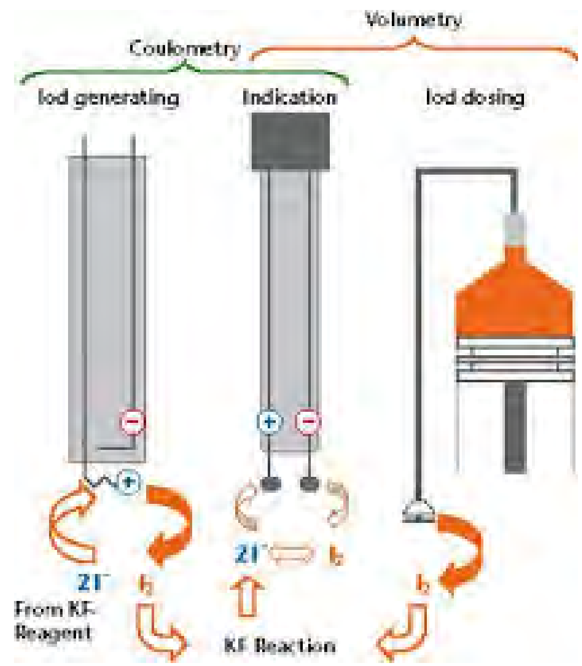
Karl Fischer Titration

$CH_3\,OH + SO_2 + RN \rightarrow [RNH]SO_3CH_3$

$H_2O + I_2 + [RNH]SO_3CH_3 + 2\ RN \rightarrow [RNH]SO_4\ CH_3 + 2\ [RNH]I$

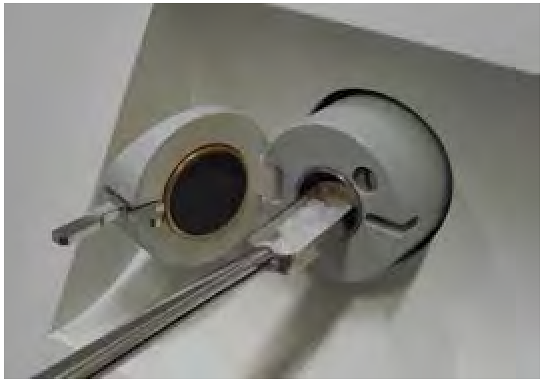
(RN = Base)

- This reaction consumes water and iodine in a 1:1 ratio.
- Coulometric
  - Electrical current measured
  - Good for low moisture contents (<1%)
- Volumetric
  - amount of reagent to convert water
  - Sample dissolved into solvent
  - Moisture contents above 1%



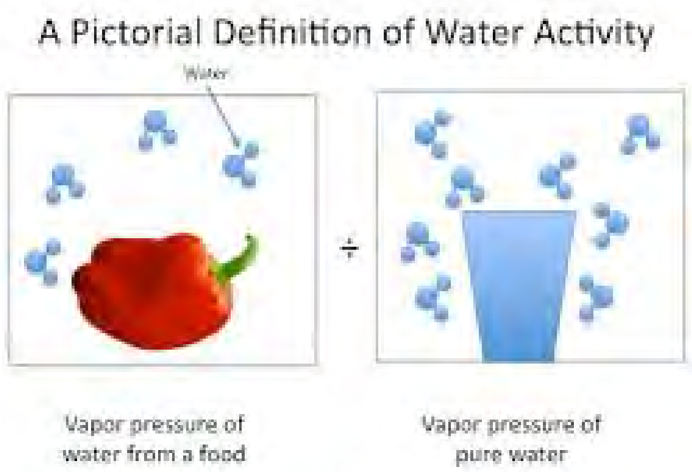
Loss on Drying

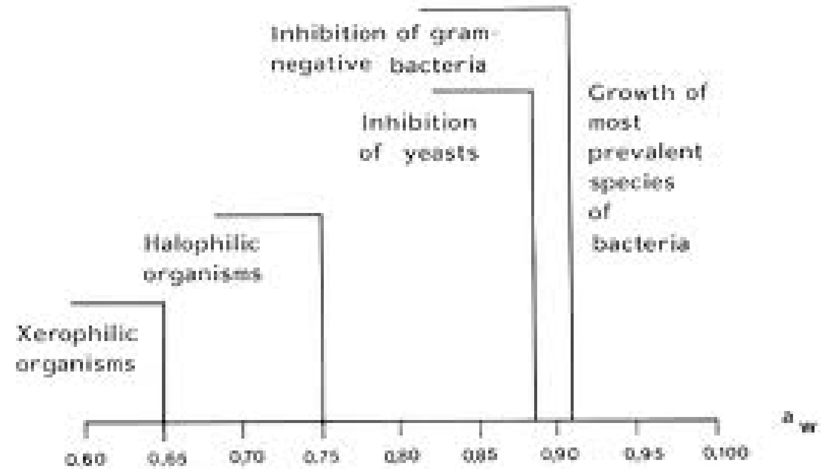
- Sample is weighed, then heated to remove moisture, then weighed again
- Also called moisture balance method
- 0 to 100% moisture content range (~0.2% sensitivity)
- Drying can be done under vacuum or over desiccant
- US and European Pharmacopeia methods
- Could use TGA instrumentation



Water Activity Meters

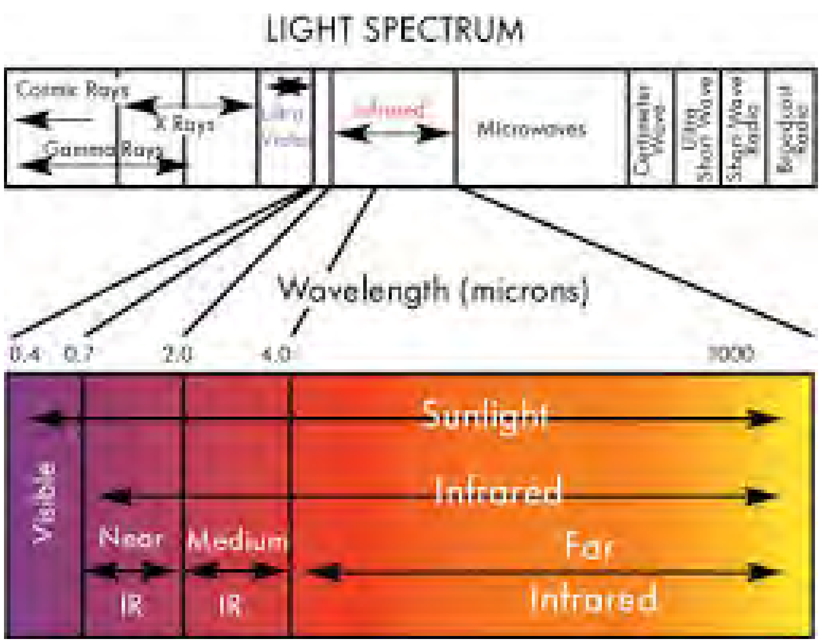
- Sample is placed into a chamber with a dew point analyzer
- Moisture will condense on chilled mirror at defined temperature related to dew point
- Moisture content in air surrounding sample is determined
- Determines ‘free’ water, not ‘bound’ water
- Automated instrumentation
- Often related to microbial growth and product shelf-life
- Commonly measured value in food industry

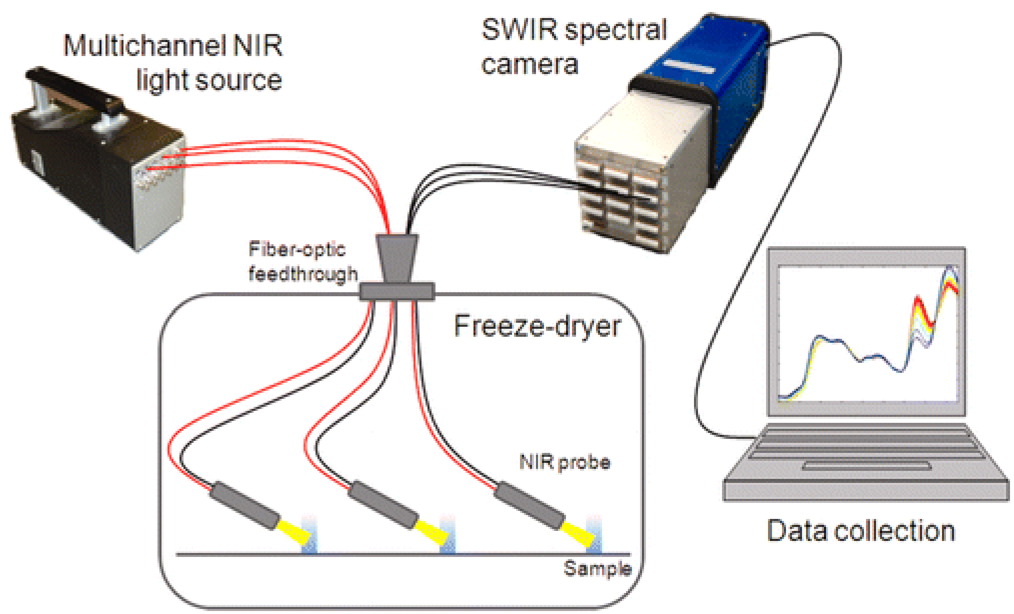




Near-IR

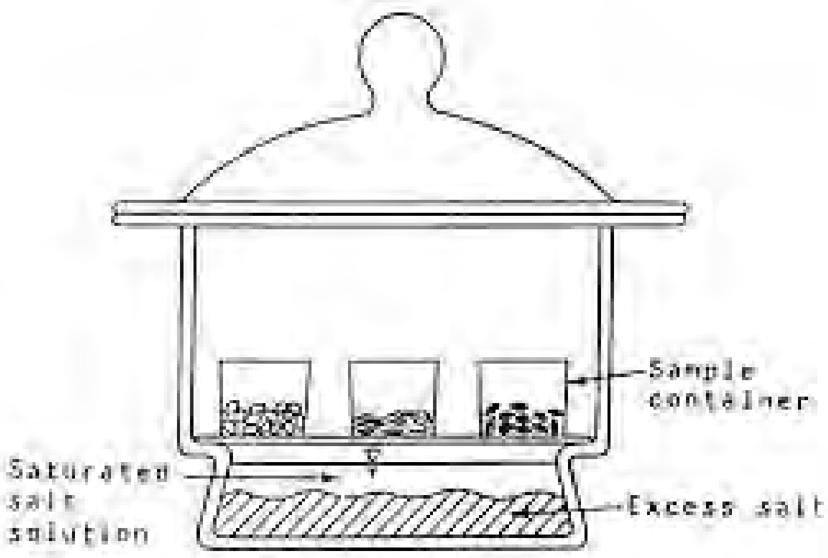
- Utilize principle that water absorbs certain wave-lengths of light
- first overtone of OH stretching around 6800–7100cm^{-1} (1470–1408 nm)
- Combination band of OH stretching and bending at around 5100–5300cm^{-1} (1960–11887 nm)





Desiccator Jars

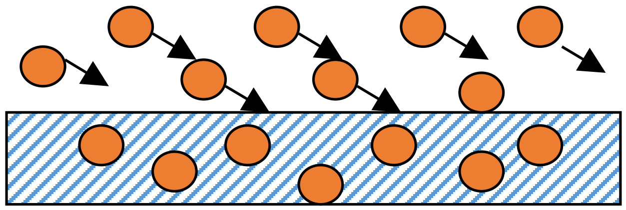
- Jar Method (Static gravimetric method)
- Different jars/chambers at different %RH levels using saturated salt solutions
- Manual technique

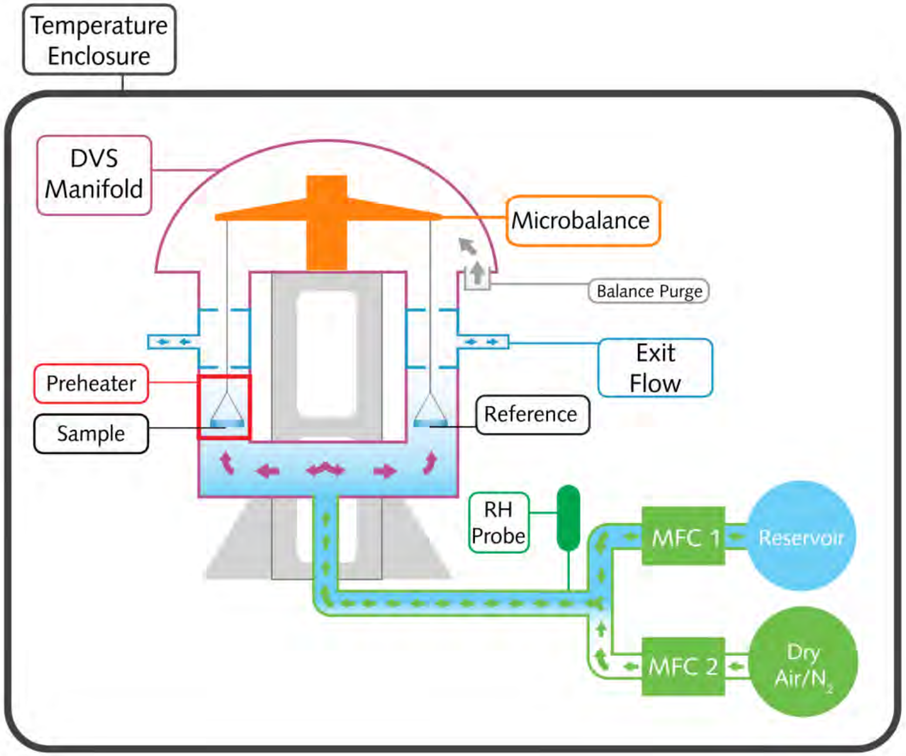


Saturated Salt Solution	Equilibrium Relative Humidity at 20 °C
Lithium Chloride [LiCl]	11.0 %
Potassium Acetate [CH_3COOK]	23.0%
Magnesium Chloride [$MgCl_2$]	33.0%
Potassium Carbonate [K_2CO_3]	43.2%
Sodium Bromide [NaBr]	56.5%
Sodium Chloride [NaCl]	75.4%
Potassium Chloride [KCl]	85.0%
Barium Chloride [BaCl]	90.0%

Dynamic Vapor Sorption Methods

- Automated method
- Sensitive microbalance
- Flow of humidified carrier gas
- Constant weight measurement
- Temperature control





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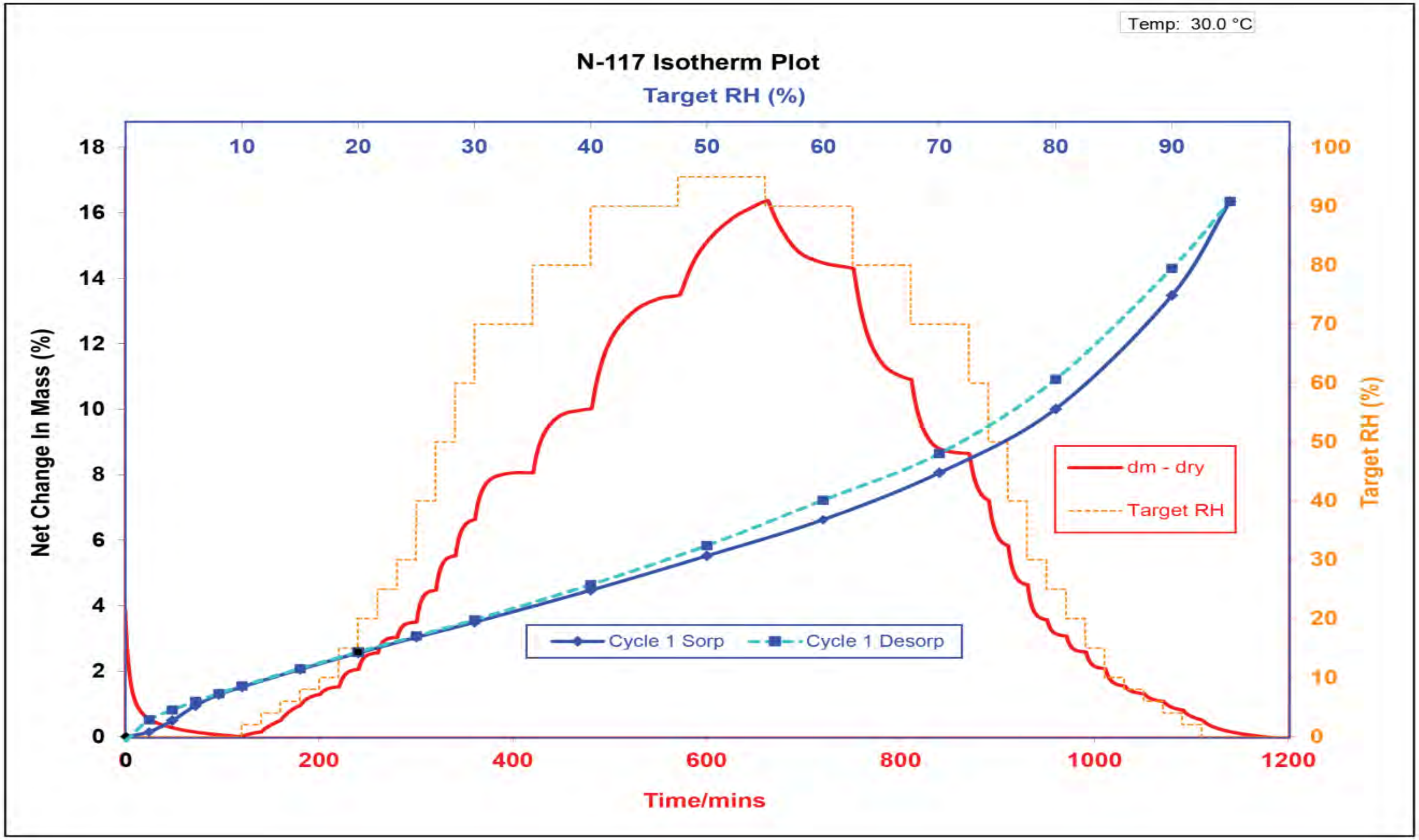
Typical Water Sorption Data



Moisture sorption/desorption **kinetics** (bottom and left axis) and **isotherms** (top and left axis) for proton exchange membrane (N-117) at 30°C.

Typical Water Sorption Isotherm

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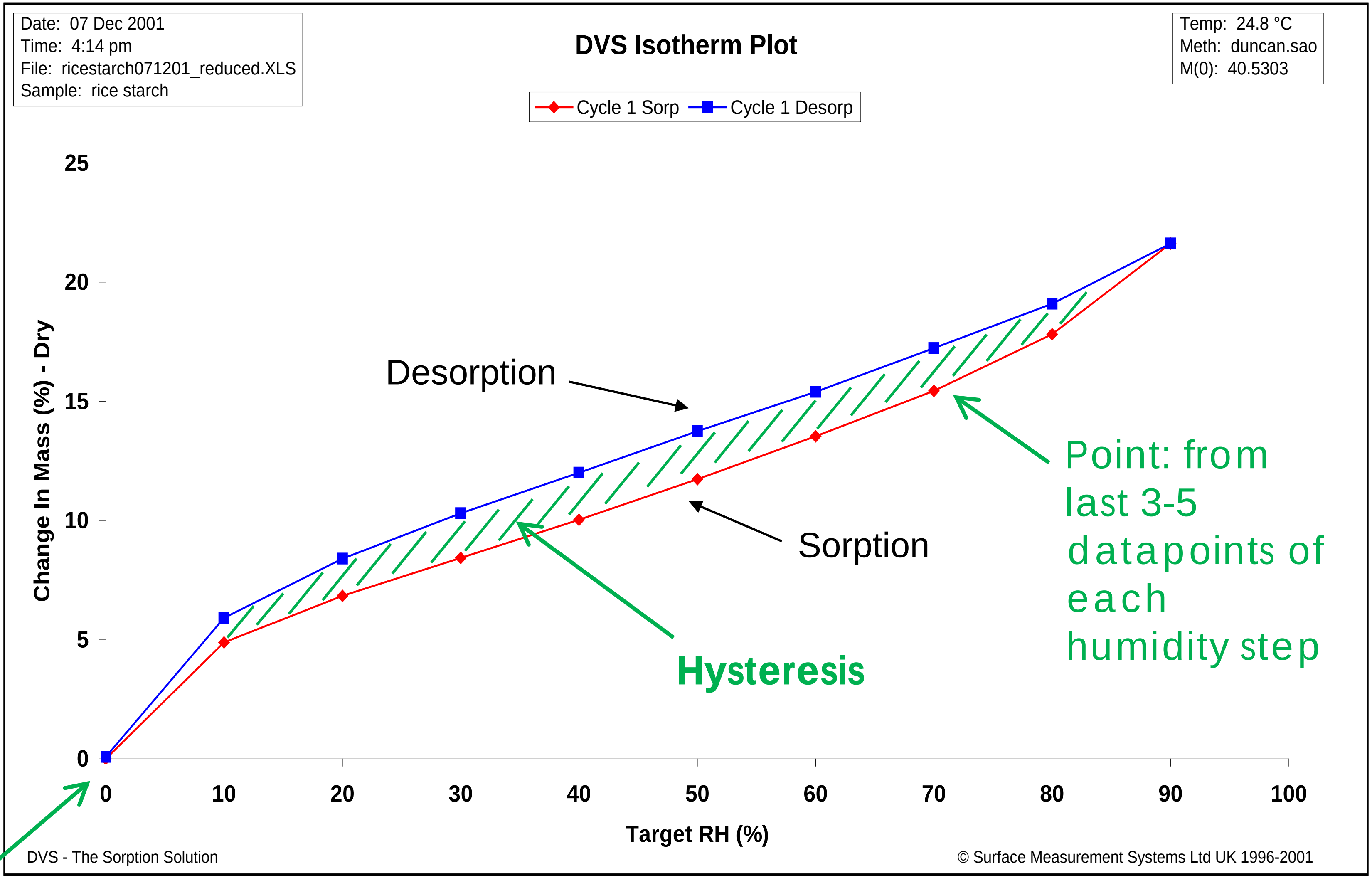
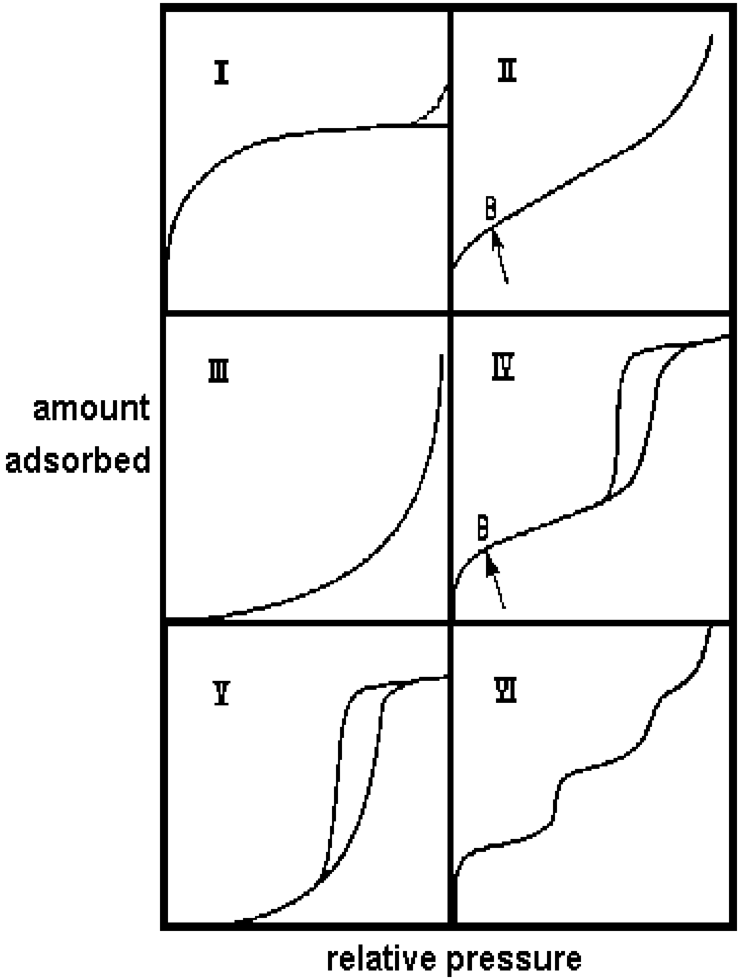
DVS- Rice Starch Isotherms



Back to 0 → reversible

Isotherm Types (BDDT)



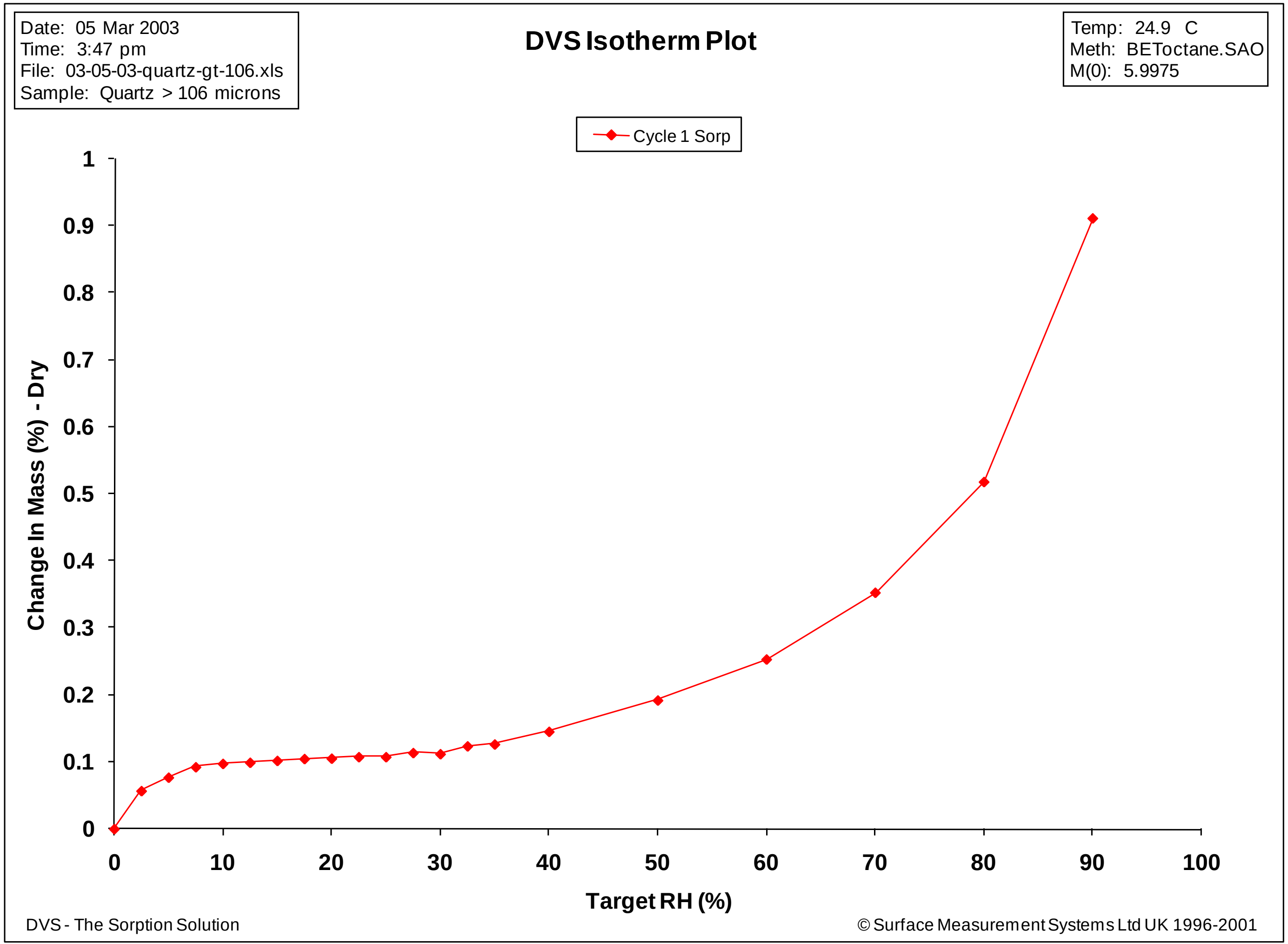
- Type I: Lanmuir isotherm; chemisorption
- Type II: Monolayer formation, BET equation
- Type III: Strong sorbate-sorbate interactions; water often has this behavior
- Type IV: Monolayer formation, BET equation, capillary condensation at high pressures
- Type V: Strong sorbate-sorbate interacitons; capillary condensation at high pressures
- Type VI: only at liquid Kr temperatures

Adsorption Isotherm Models

Isotherm	Year of report	Number of model parameters	Original Paper
Freundlich	1906	2	Freundlich, H.M.F. J. Phys. Chem. 1906, 57, 385-471
Langmuir	1918	1	Langmuir, I. J Am. Chem. Soc. 1918, 40, 1361-1402
BET	1938	2	Brunauer, S.; Emmett, P.H.; Teller, E. J. Am. Chem. Soc. 1938, 60, 309-319
Oswin	1946	2	Oswin, C.R. J. Soc. Chem. Ind. 1946, 65, 419-42
Hailwood–Horrobin	1946	3	Hailwood, A.J.; Horrobin, S. Trans. Faraday Soc. 1946, 42B, 84-92
Smith	1947	2	Smith, S.E. J. Am. Chem. Soc. 1947, 69, 646-651
Henderson	1952	2	Henderson, S.M. Agric. Eng. 1952, 33, 29–3
GAB	1966	3	Guggenheim, E.A. Application of Statistical Mechanics. Clarendon Press: Oxford, 1966, Vol.1, Ch. 11, pp 186-207
Caurie	1970	3	Caurie, M. J. Food. Techn. 1970, 5, 301-307
D'Arcy–Watt	1976	≥ 3	Watt, I.C.; D'Arcy, R.L. J. Polym. Sci. Symp. 1976, 55, 144-166
Peleg	1993	4	Peleg, M. J. Food Proc. Eng. 1993, 16, 21-37

Quartz-Surface Adsorption

- Isotherm shape (Type II) and low uptake indicate surface dominated sorption



Effect of Sorbate Polarity

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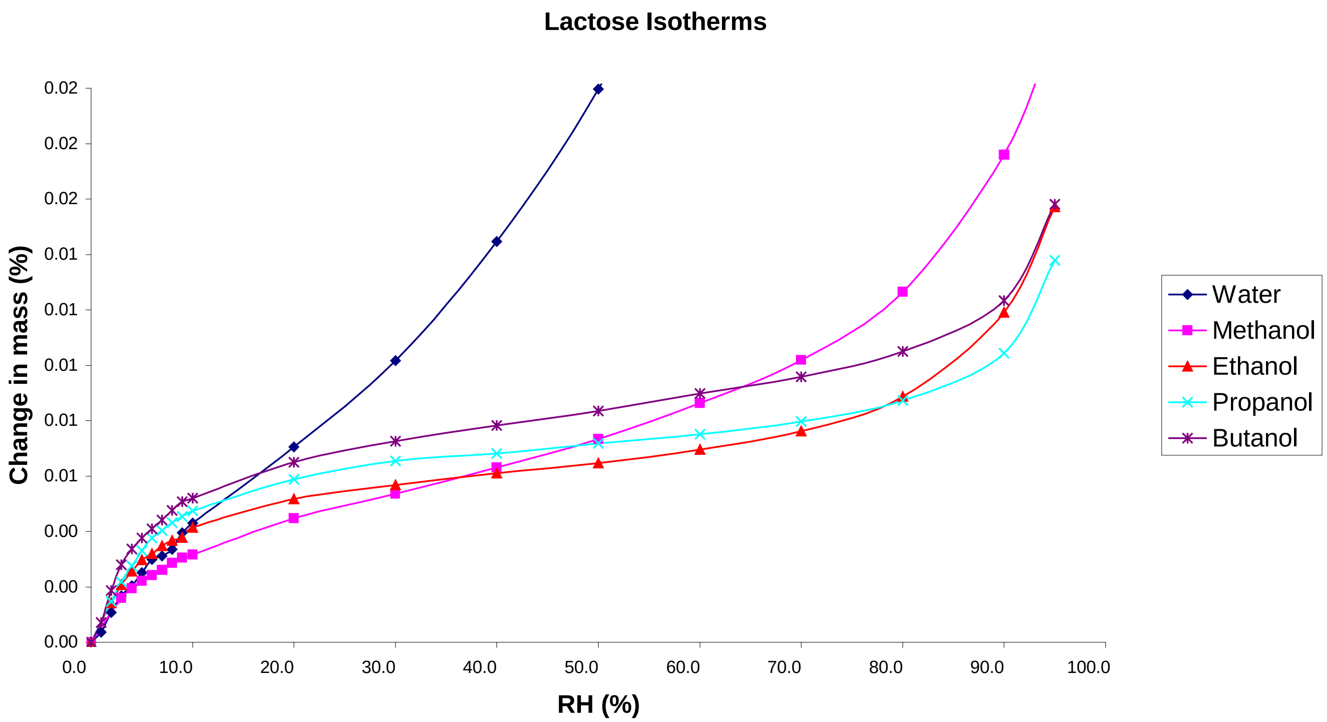
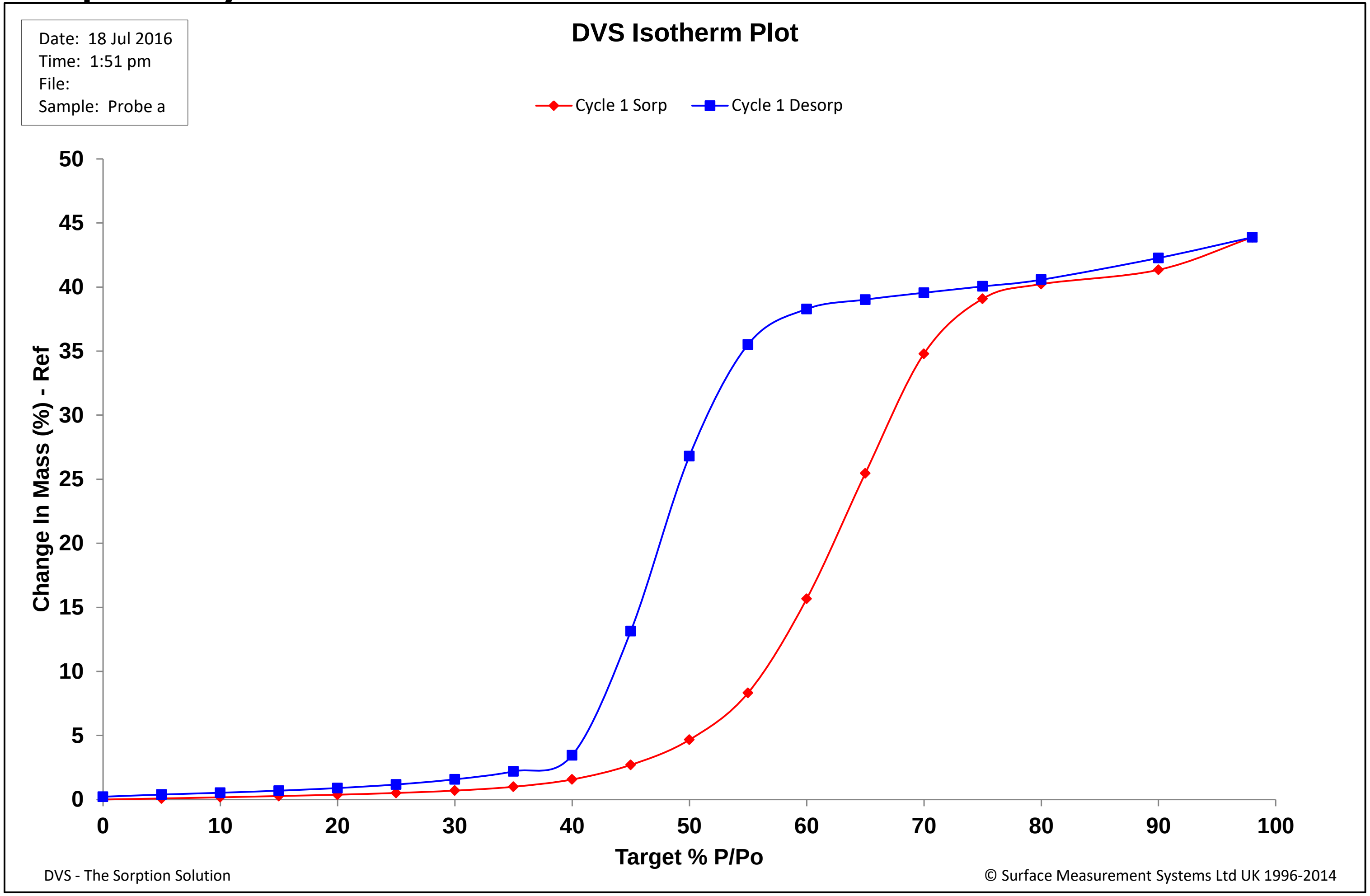
- Isotherm changes from Type II to Type III



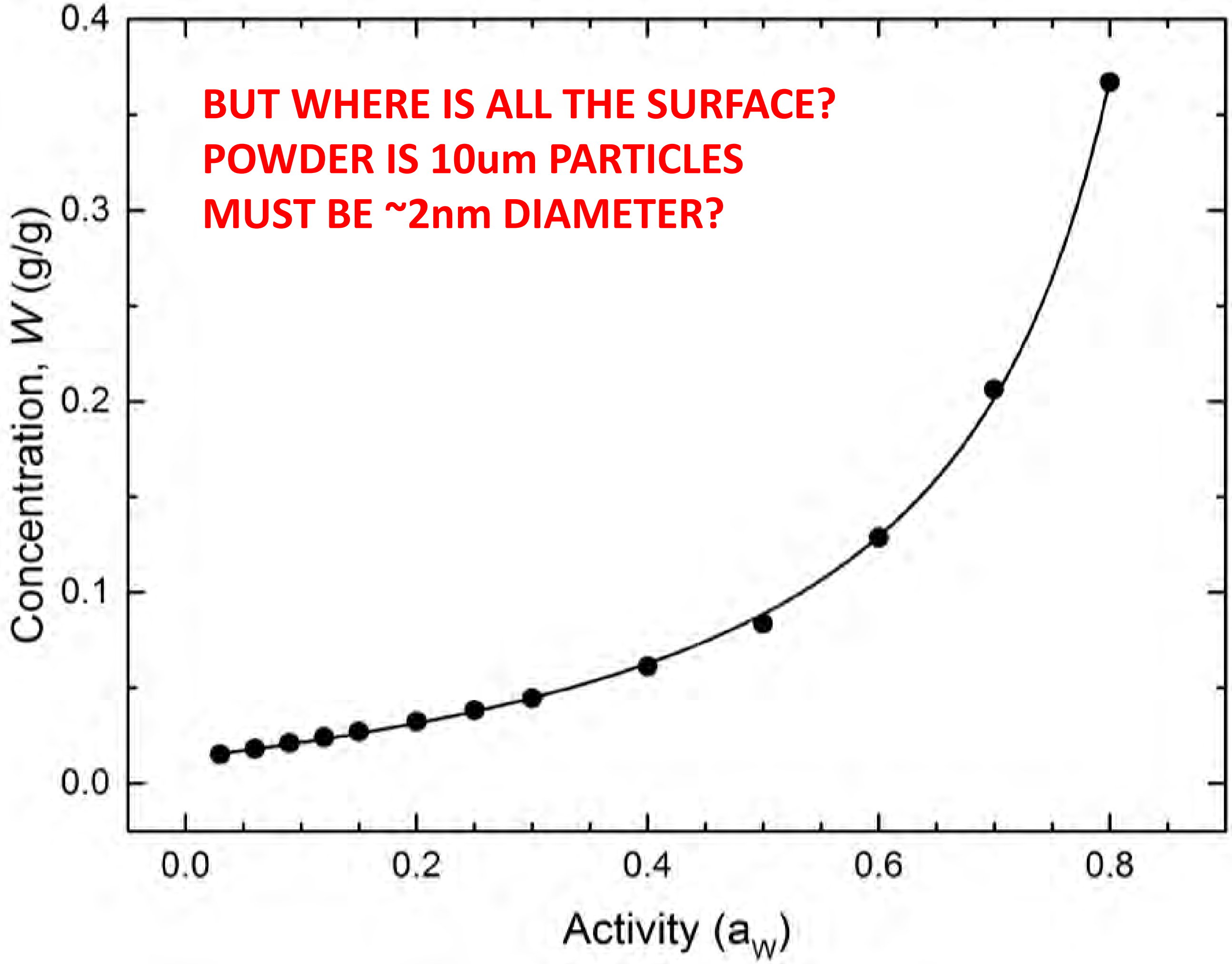
Amorphous Carbon

- Hysteresis gap suggests mesoporosity (2 to 50 nm)
- Capillary Condensation



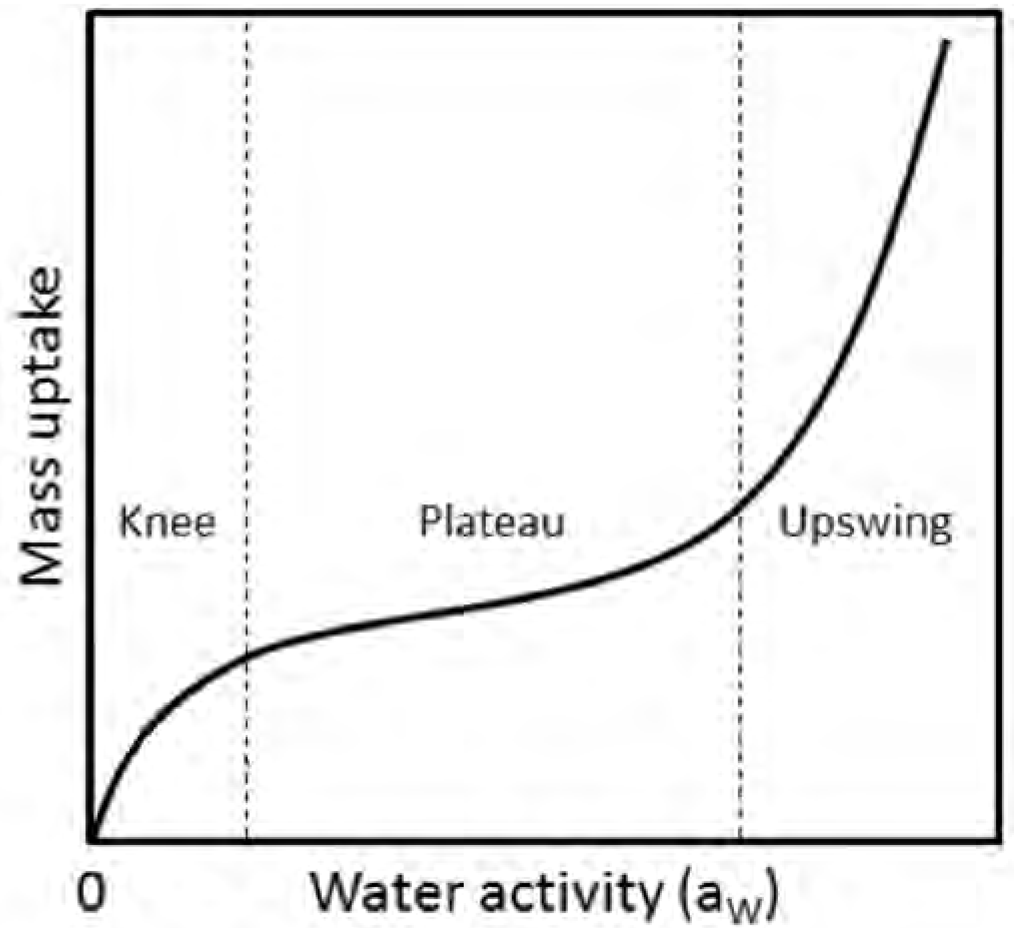
Surface vs Bulk Sorption

Water Sorption Isotherm for amorphous porcine lipase : fitted to D'Arcy–Watt adsorption model



Water Sorption Isotherms- Model Amorphous Proteins

The water sorption isotherm of an amorphous protein such as BSA has three features (knee, plateau, upswing) and coincidentally resembles the shape of a BET type II physical adsorption isotherm



Water Sorption Isotherms- Model Amorphous Proteins

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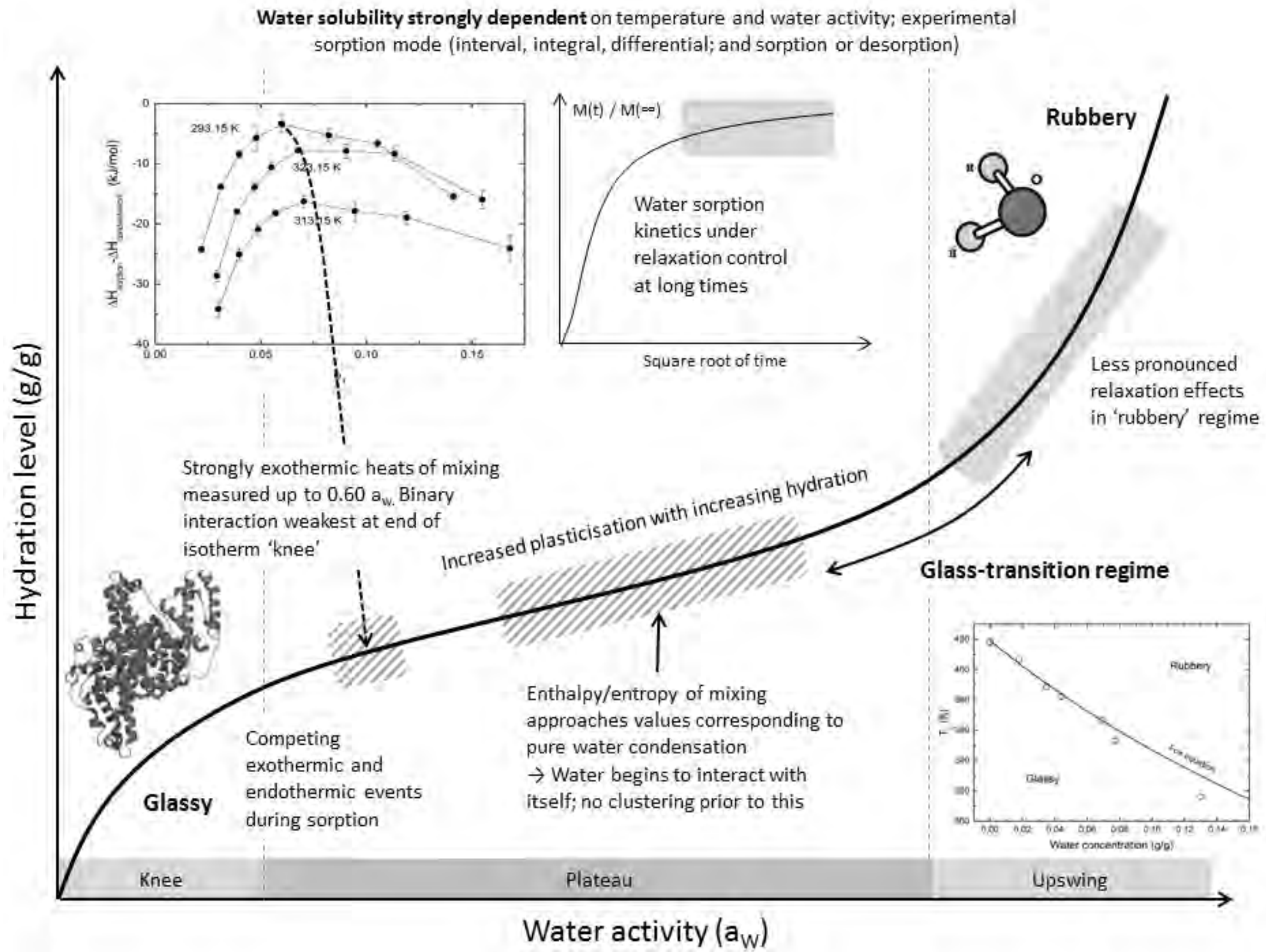
Amorphous proteins interact in a truly complex way with water that cannot be captured by adsorption models or simple solution approaches as the system is not even in equilibrium



Polymer-Solvent Isotherm Models

Model	Year of report	Type	Original Paper
Bragg–Williams	1934	Lattice*	Bragg, W.L.; Williams, E.J. Proc. Roy. Soc. 1934, A145, 699
Flory–Huggins	1942	Lattice*	Flory, P.J. J. Chem. Phys. 1942, 10, 51-61
FOV	1964	Cell	Flory, P.J.; Orwoll, R.A.; Vrij. A. J. Am. Chem. Soc. 1964, 86, 3507-3514
Sanchez–Lacombe	1978	Lattice-fluid	Sanchez, I.C.; Lacombe, R.H. Macromolecules 1978, 11, 1145-1156
Simha–Somcynsky	1980	Hole model	Jain, R.K.; Simha, R. Macromolecules 1980, 13, 1501-1508
SAFT	1990	Tangent-sphere	Chapman, W.G.; Gubbins, K.E.; Jackson, G.; Radosz, M. Ind. & Eng. Chem. Res. 1990, 29, 1709-1721
Vrentas–Vrentas	1991	Glassy sorption, based on lattice*	Vrentas, J.S.; Vrentas, C.M. Macromolecules 1991, 24(9), 2404-2412
PHSC	1994	Tangent-sphere	Song, Y.; Lambert, S.M.; Prausnitz, J.M. Chem. Eng. Sci. 1994, 49, 2765.
NE-LF	1996	Lattice-fluid	Doghieri, F.; Sarti, G.C. Macromolecules 1996, 29, 7885-7896

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Reversible Hydrate