Characterisation of Complex Organic Materials – New Insights using Molecular Sorption Probes

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Complex Organic Materials

- Many of the real world materials developed and manufactured by industry for society are complex in terms of the chemical, morphological, structural, compositional and physically properties. Today we will consider solids or semi-solid materials

- Classes of complex materials include:
  - Agrichemicals
  - Pharmaceuticals
  - Biopharmaceuticals
  - Foods
  - Freeze and spray dried products
  - Personal care products
  - Biomaterials
  - Advanced composites
  - Adsorbents
  - Building materials

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Moisture and Complex Organic Materials

What can be the effects of too little or too much water in a complex organic material?

- **Potato crisps loose their crispiness**

  Water decreases T_g of amorphous glass solids → rubbery

- **Crystalline pharmaceutical hydrates become dehydrated solids**

  Thermodynamic stability is compromised by low %RH's

- **Proteins can loose their biological activity**

  Proteins denature at low %RH's

- **Freeze dried powders transform into liquids**

  Amorphous solids and deliquesce forming solutions

- **Free flowing powders turn into rigid/solid cakes**

  Amorphous solids can crystallise at high moisture contents

- **Dry powders aerosols do not disperse**

  Particles adhere to each other or packaging

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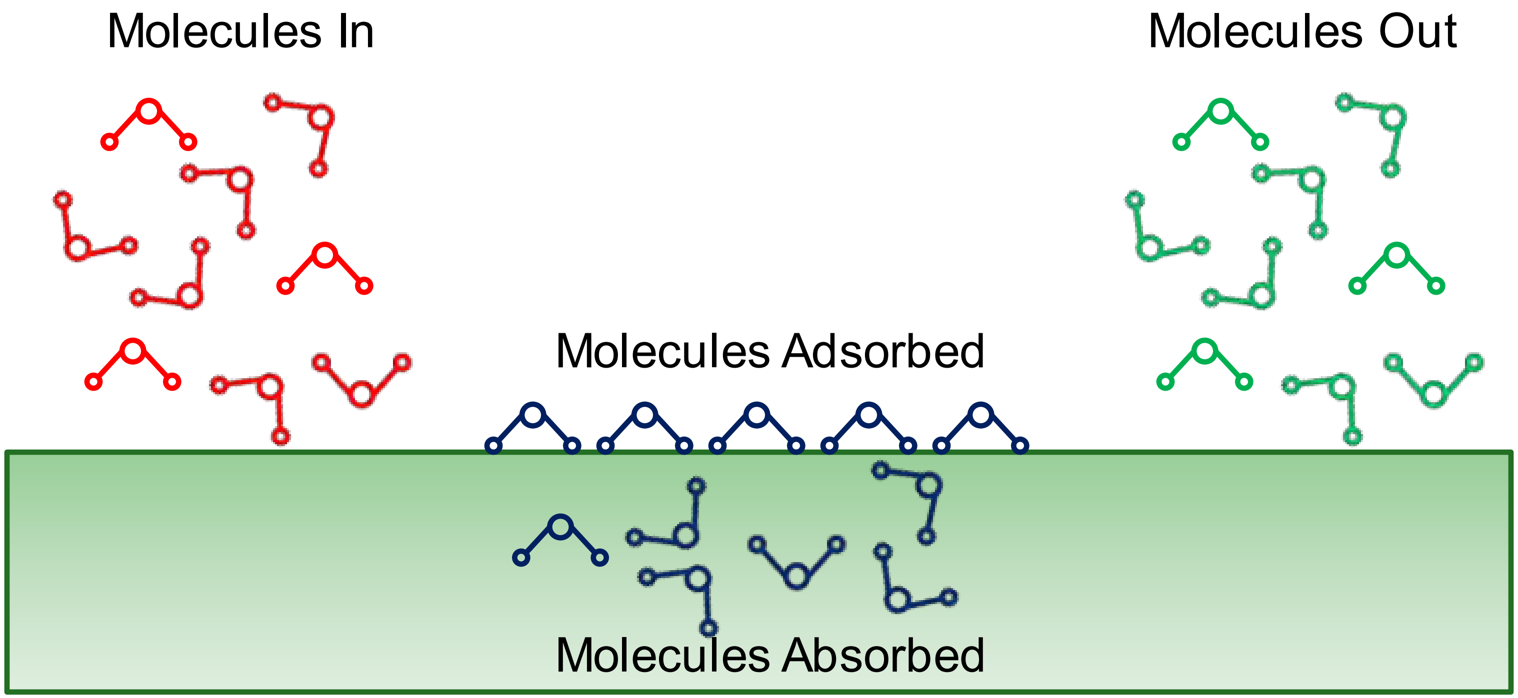
Characterization of Solids

- EM Radiation as a Probe
  - Spectroscopy eg Raman, IR
  - X-Ray Diffraction,NMR
    - Analytical and structural information
- Thermal Energy as a Probe
  - Calorimetry eg DCS, TGA
    - Thermodynamic information on solid
- Molecule as a Probe
  - Sorption techniques eg DVS, IGC
    - Thermodynamic and chemical information on vapour-solid interaction

Molecules as a Probe of Solids



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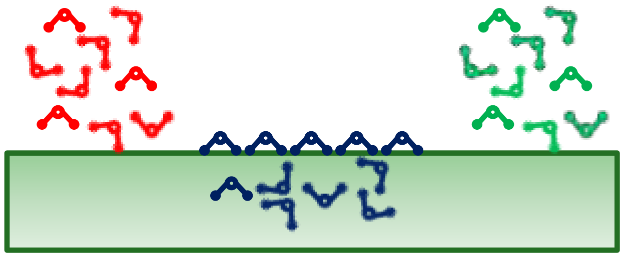
Molecules as a Probe



- **Chemical Interactions**

  IGC, DVS, Wetting, Chemisorption analyzers

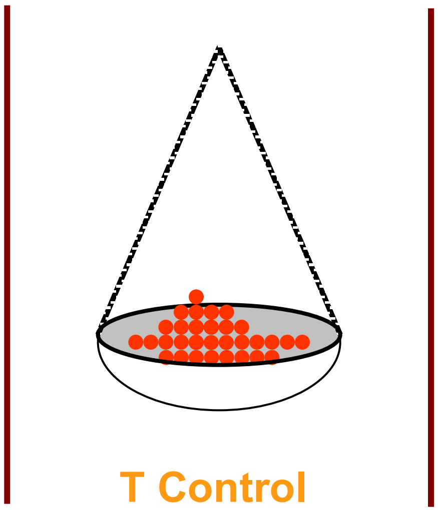
- **Physical Structure (surface area, pore size, density etc.)**

  DVS, IGC, Volumetric sorption (i.e. BET analyzers), Chemisorption, Pycnometer

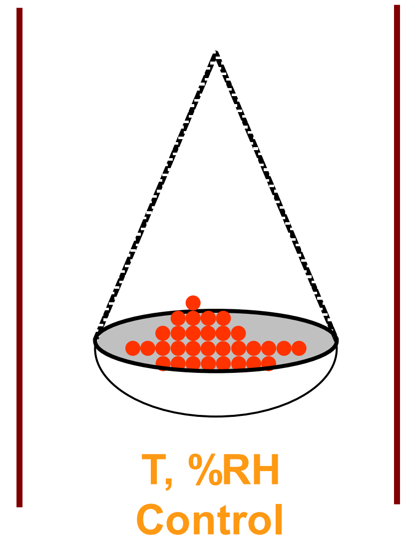
- **Thermodynamic Information**

  IGC, DVS, Thermal Analysis Methods

How do we study these moisture dependent behaviour of solid state materials?



Thermogramimetric Analysis



Dynamic Vapor Sorption

TGA	Method Name	DVS
Gravimetric	Principle	Gravimetric
~5mg	Sample Size	~10mg
Temperature	Primary Variable	% RH
Usually Ramp	Operational Mode	Step and Ramp
Thermal Perturbation	Core Data	Moisture Partitioning
1-4 Hours	Run Time	24 Hours
-200C to 400C	Measurement Range	0 to 100% RH

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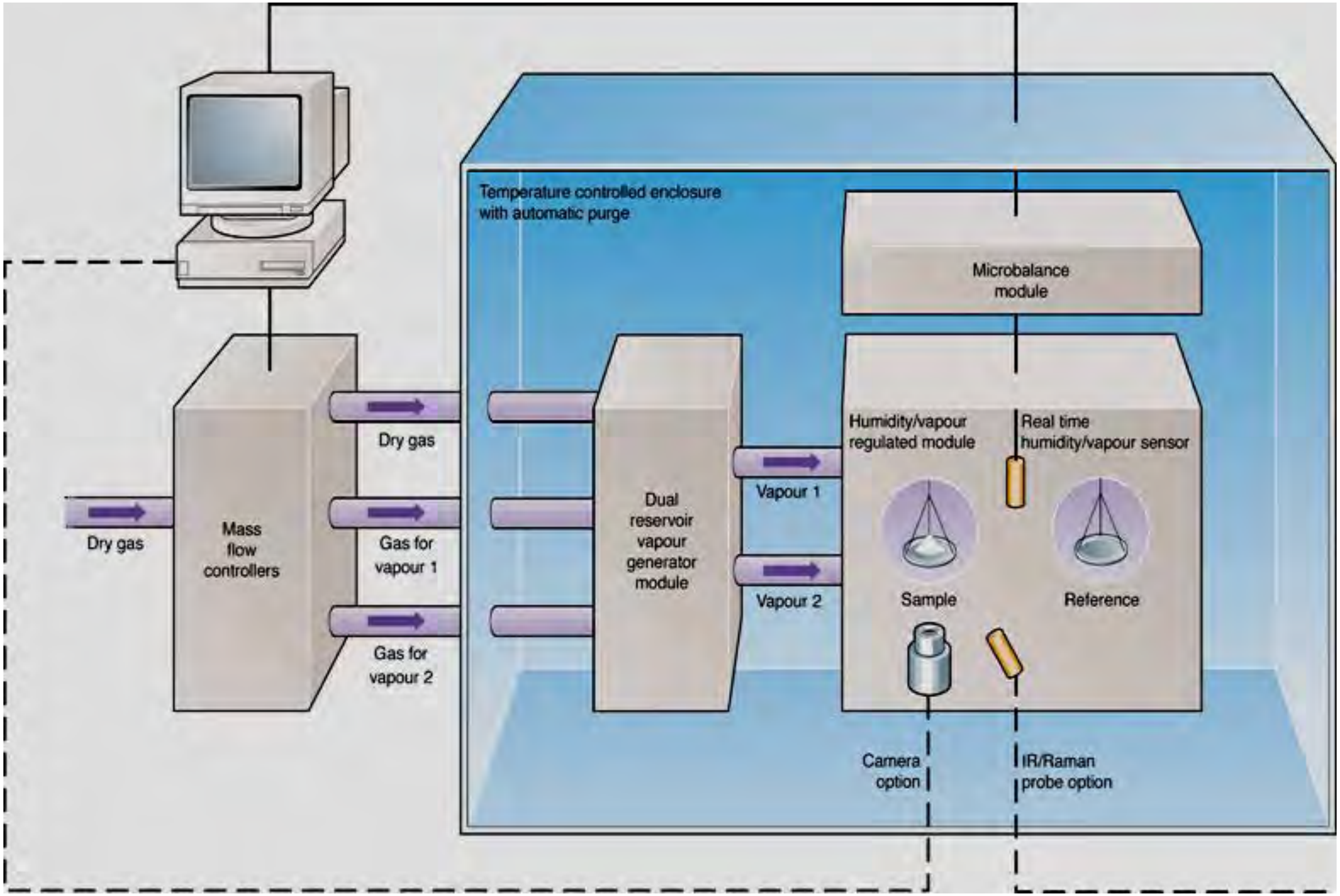
Dynamic Vapour Sorption



Dynamic Vapour Sorption

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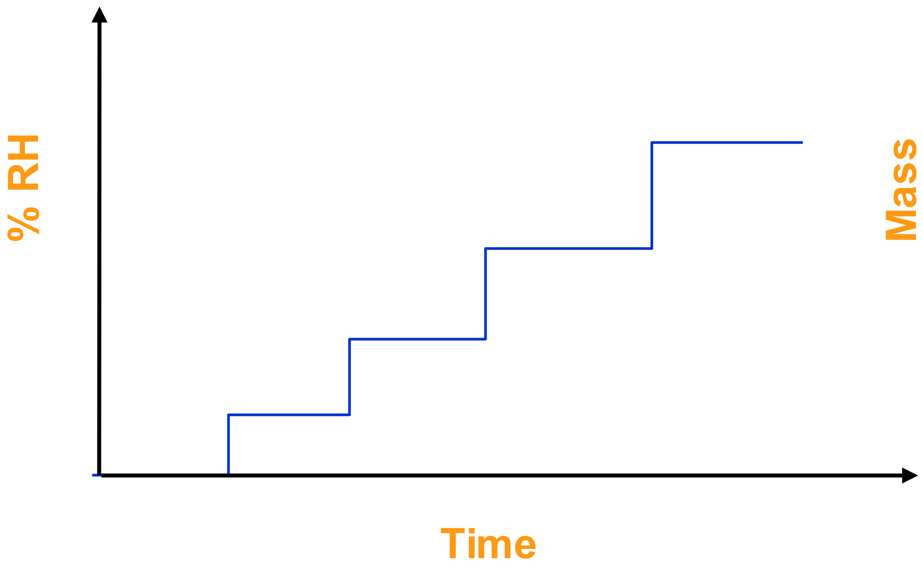
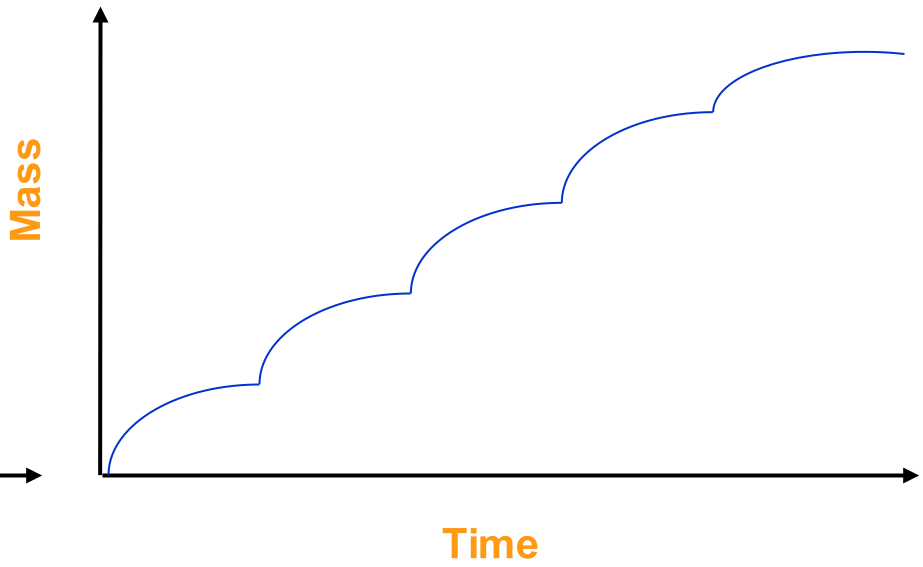
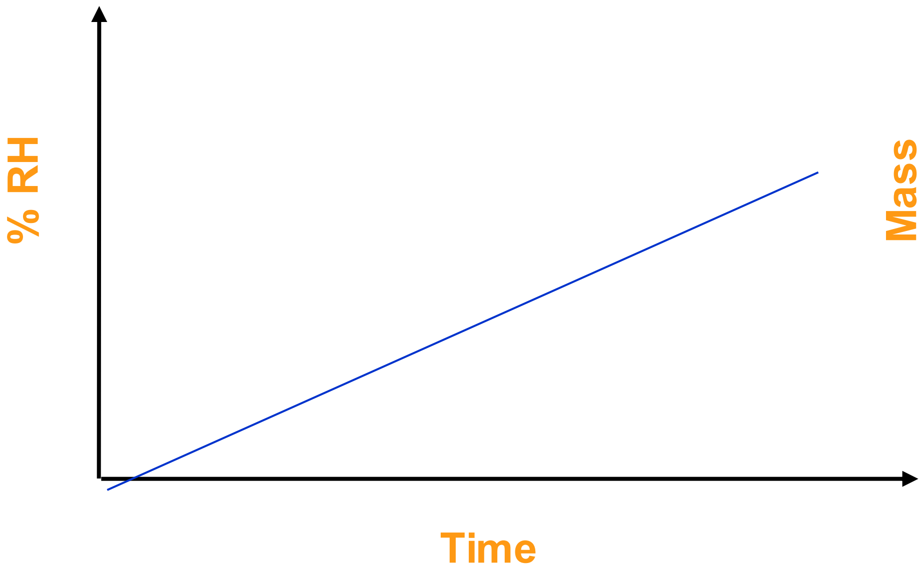
DVS Experimental Methods

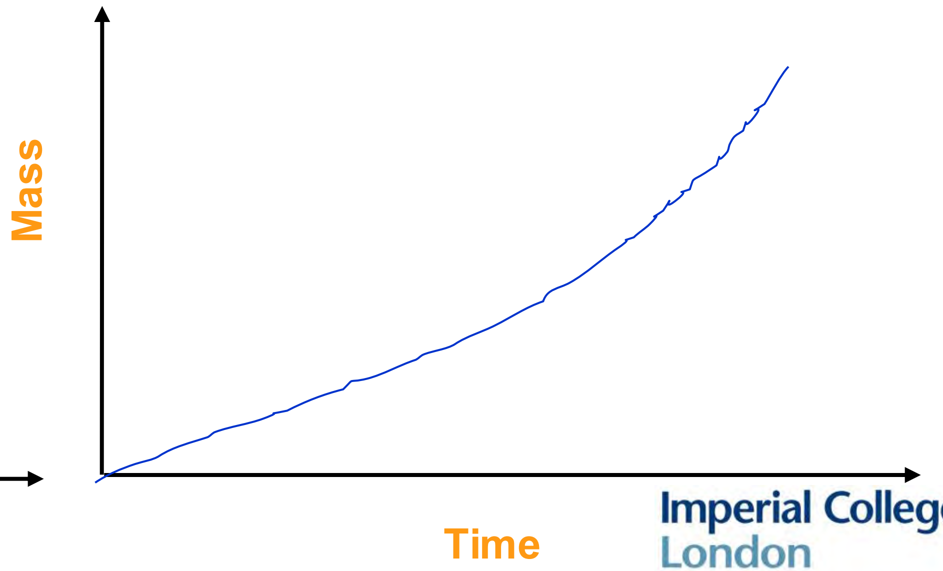
- Traditional approach is a series of steps, each conducted at constant T and %RH with mass monitored as function of time. Output is isotherm.





- Alternate approach is %RH ramp, comparable to a TGA's T ramp experiment





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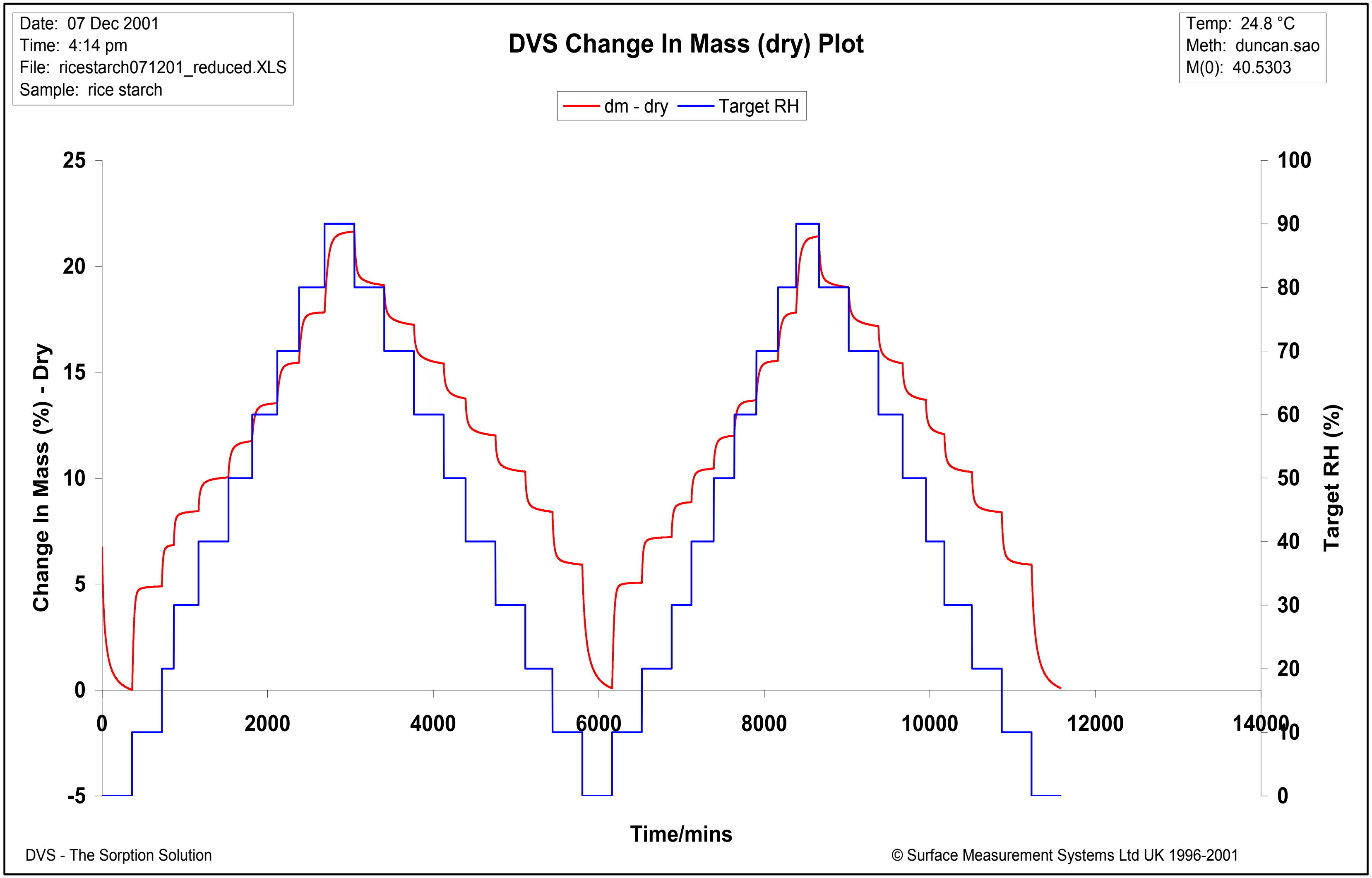
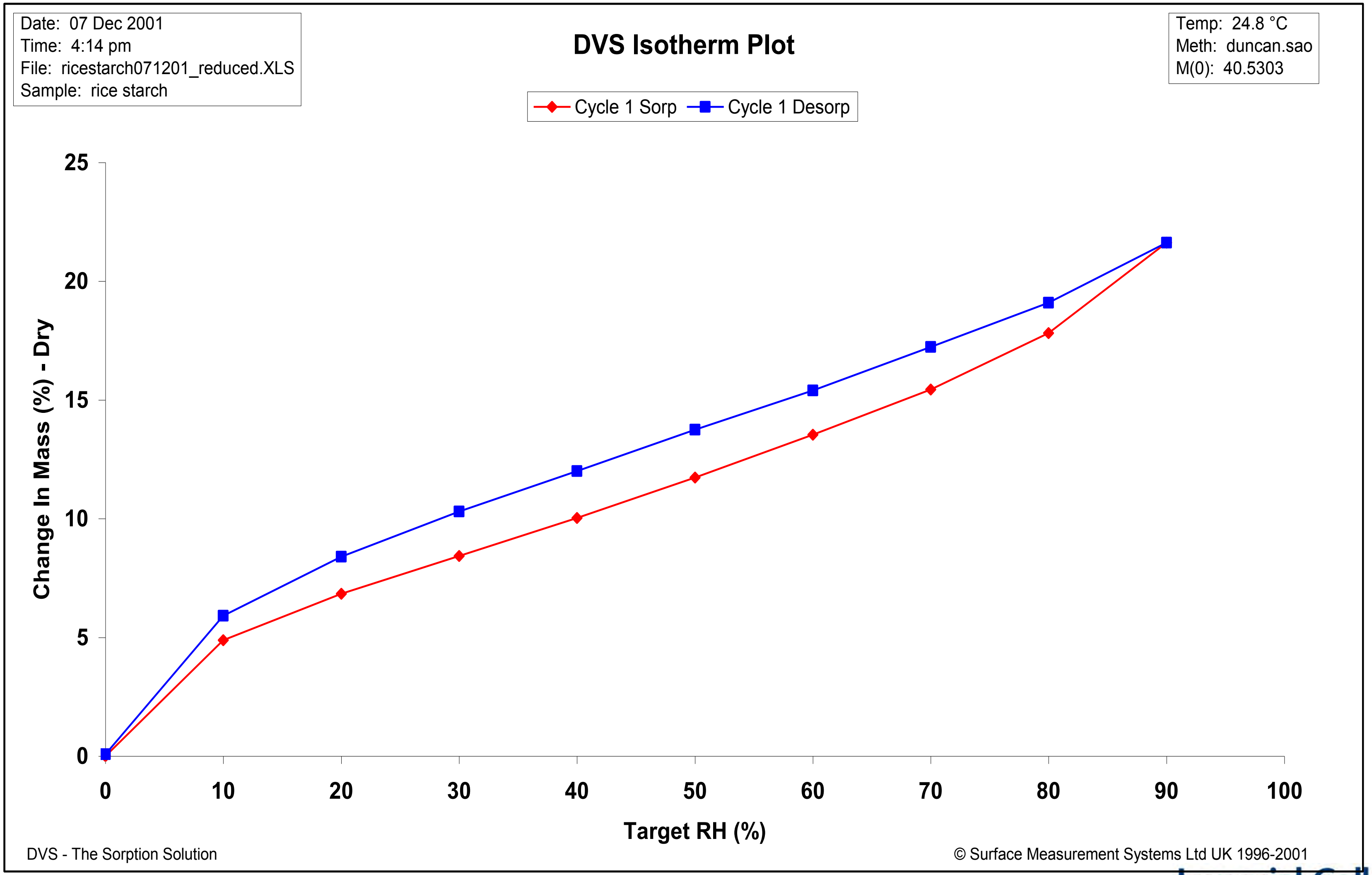
DVS Typical Kinetics Data



Moisture sorption behavior of rice starch at 25 °C- 2 cycle experiment

Water Sorption Isotherm



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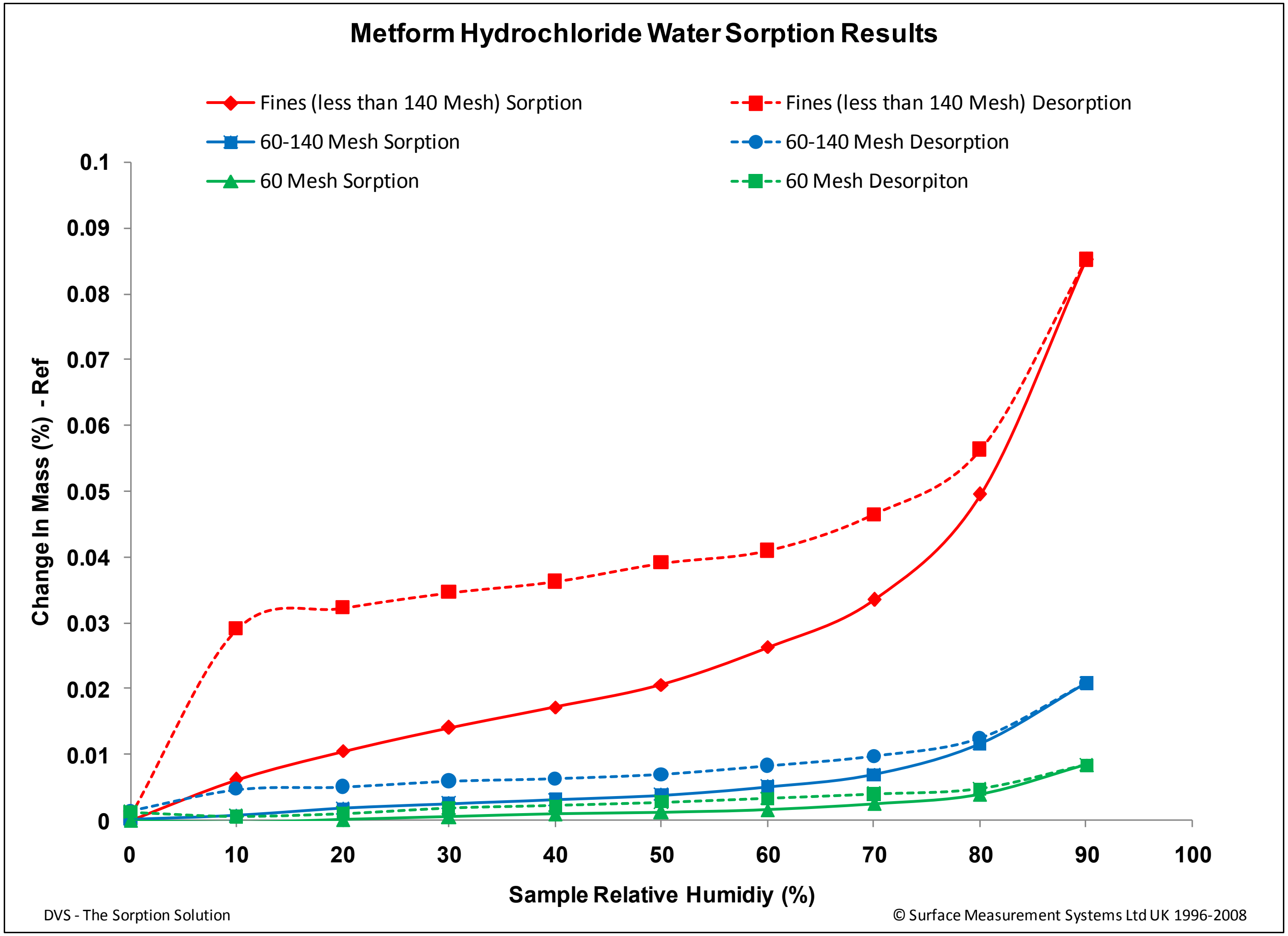
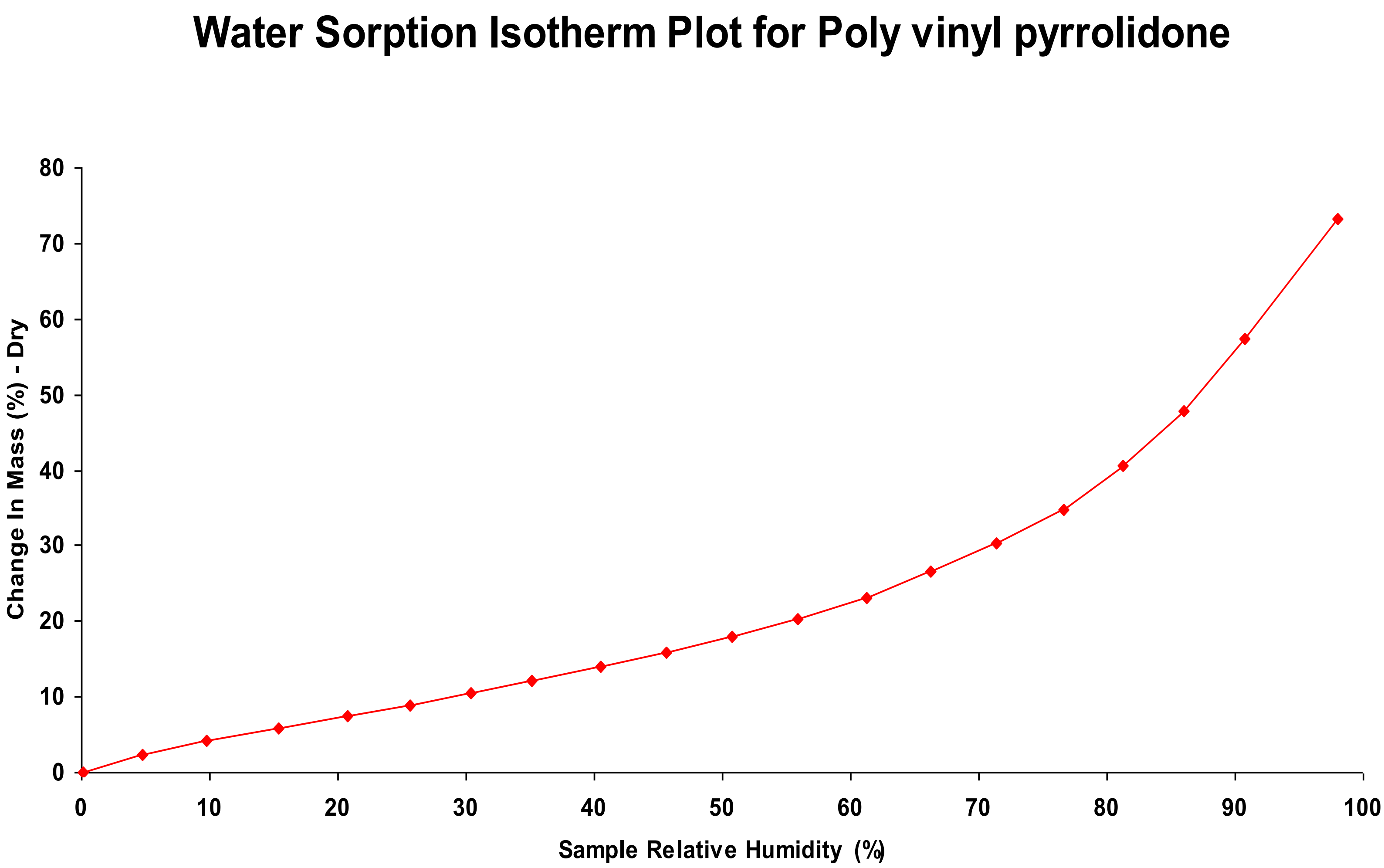
Water Sorption Isotherm for Hydrophobic Powder



- ~150 mg of material
- Higher uptake on smaller particles → Higher surface area

Water Sorption Isotherm for Hydrophillic Polymer



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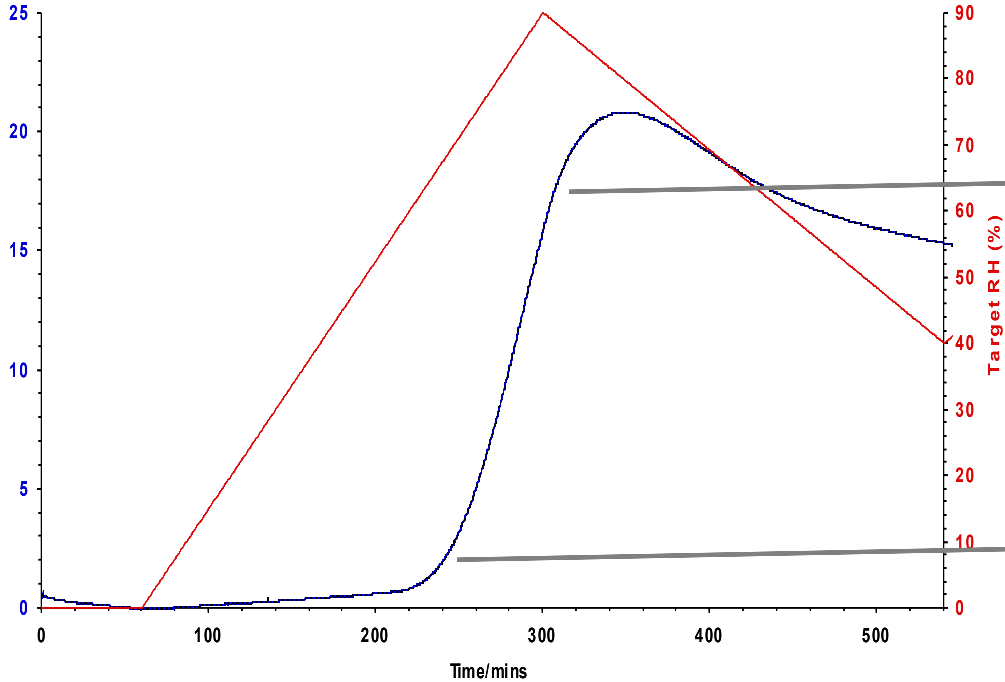
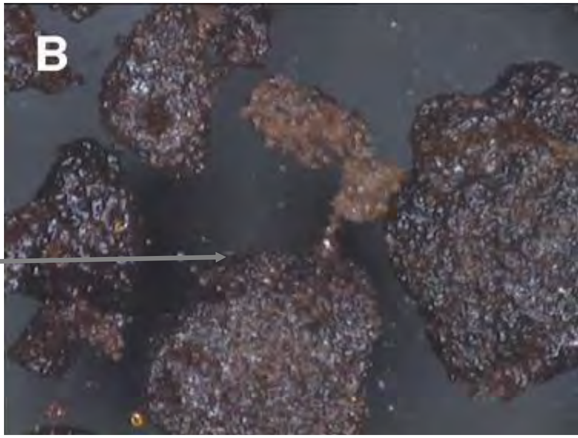
DVS-Microscope Accessory



Water Sorption on Coffee @ 25 C



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DVS-Microscope Accessory

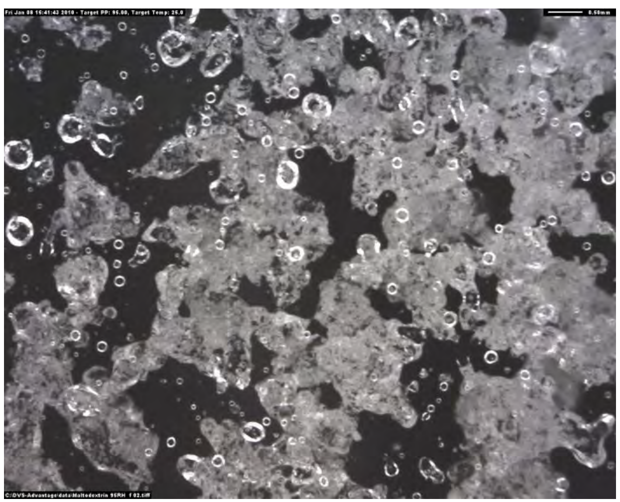
Sucrose Crystals – 0% RH

Sucrose Crystals – 95% RH, 60 minutes

DVS-Microscope Accessory

Maltodextrin – 0% RH

Maltodextrin – 95% RH, 0 minutes



Maltodextrin – 95% RH, 30 minutes

Maltodextrin – 95% RH, 50 minutes

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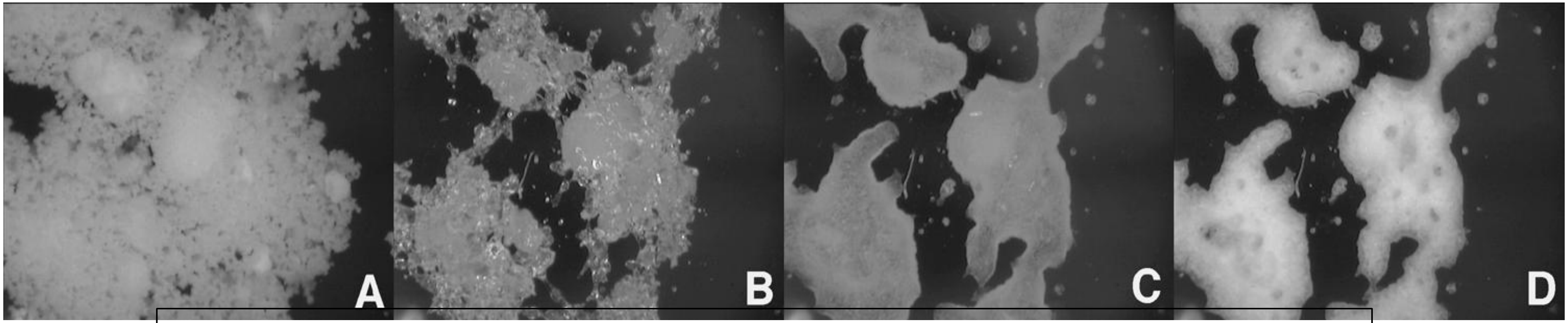
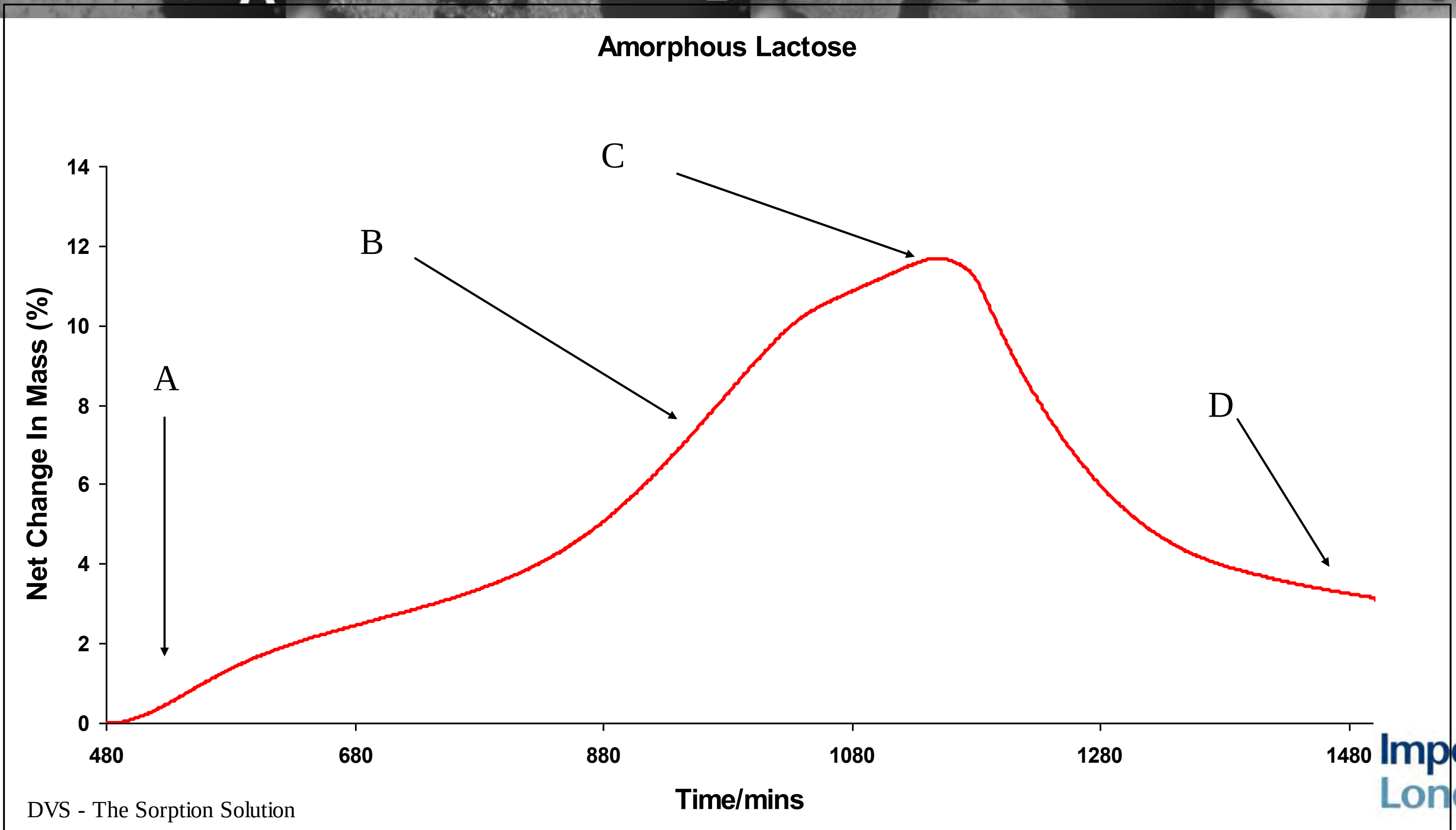
Ramp Results for Spray Dried Lactose (25 °C, 6% RH/hour)





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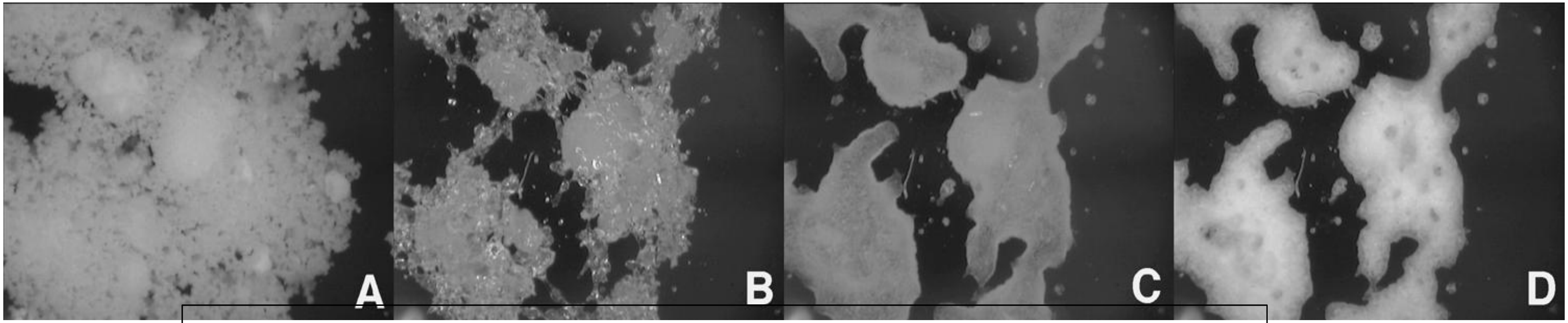

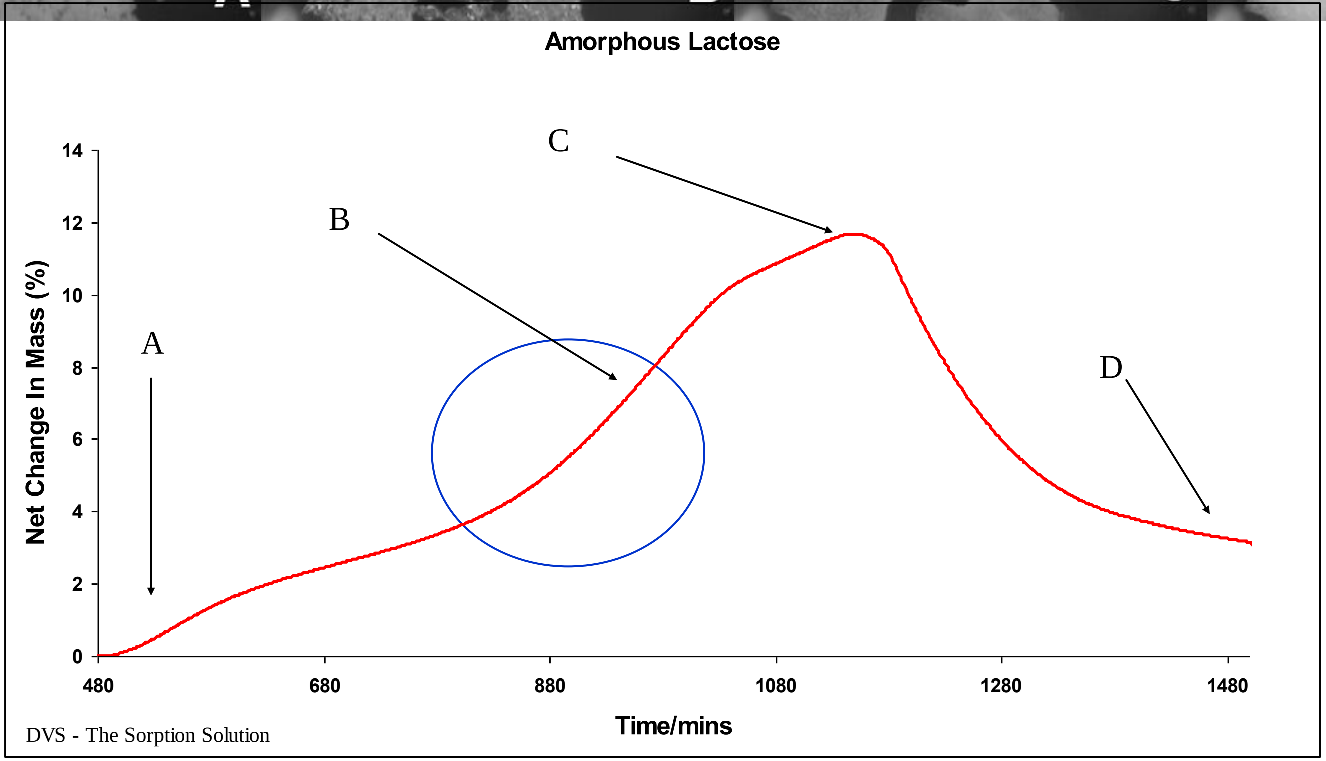

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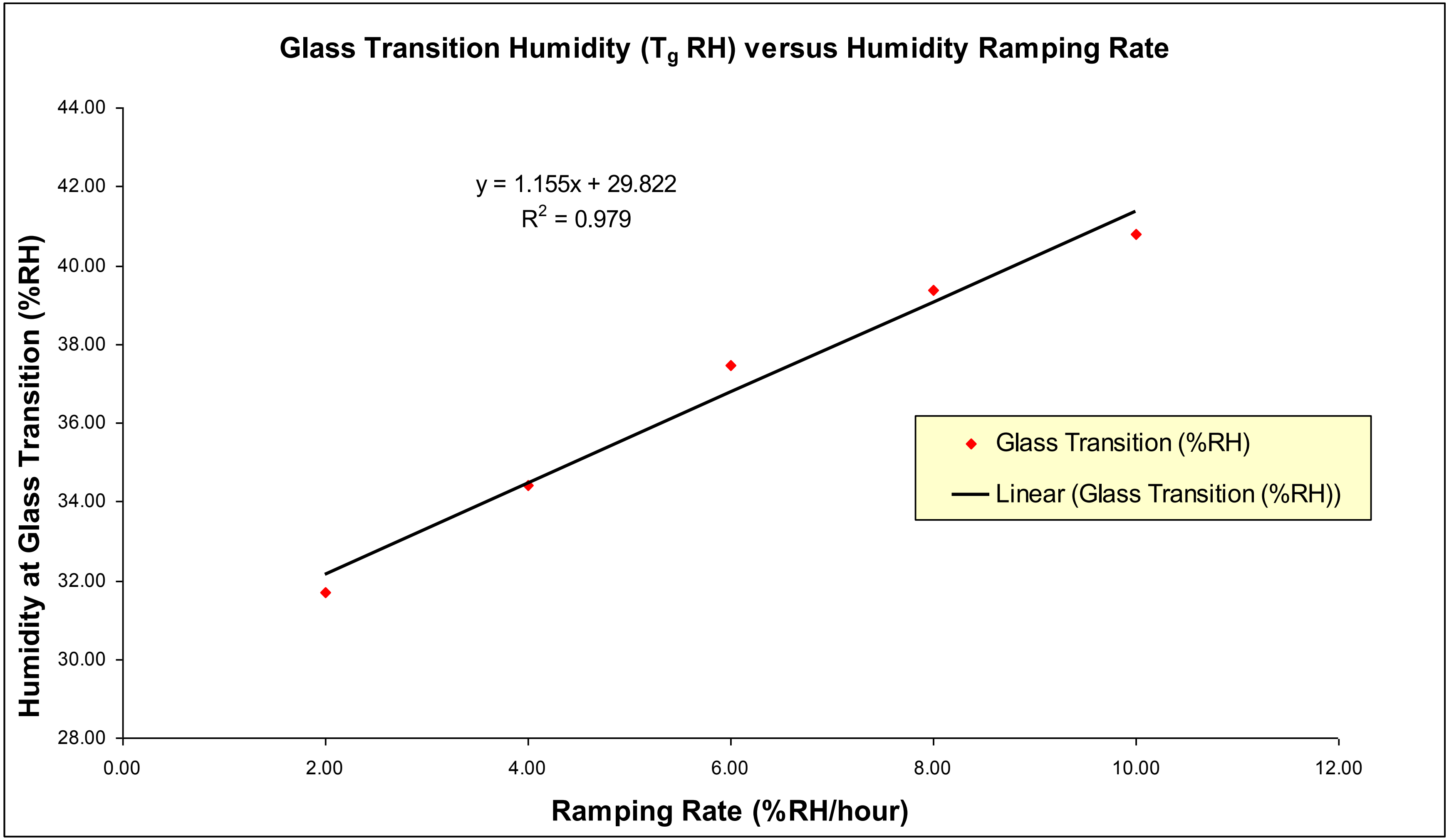
T, RH_{g}: RH versus Ramping Rate



Critical T,RH_g = 30% +/- 1% RH at 25 °C

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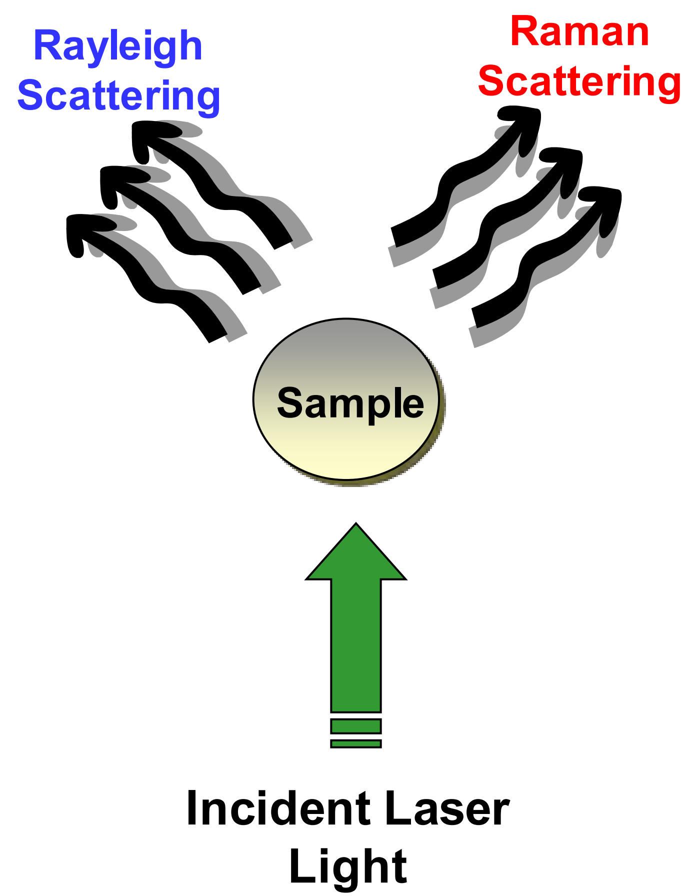
DVS-Raman Accessory

1. Raman spectroscopy is the measurement & detection of the wavelength and intensity of inelastically scattered light from molecules. When electromagnetic radiation passes through matter, most of the radiation continues in its original direction but a small fraction is scattered.

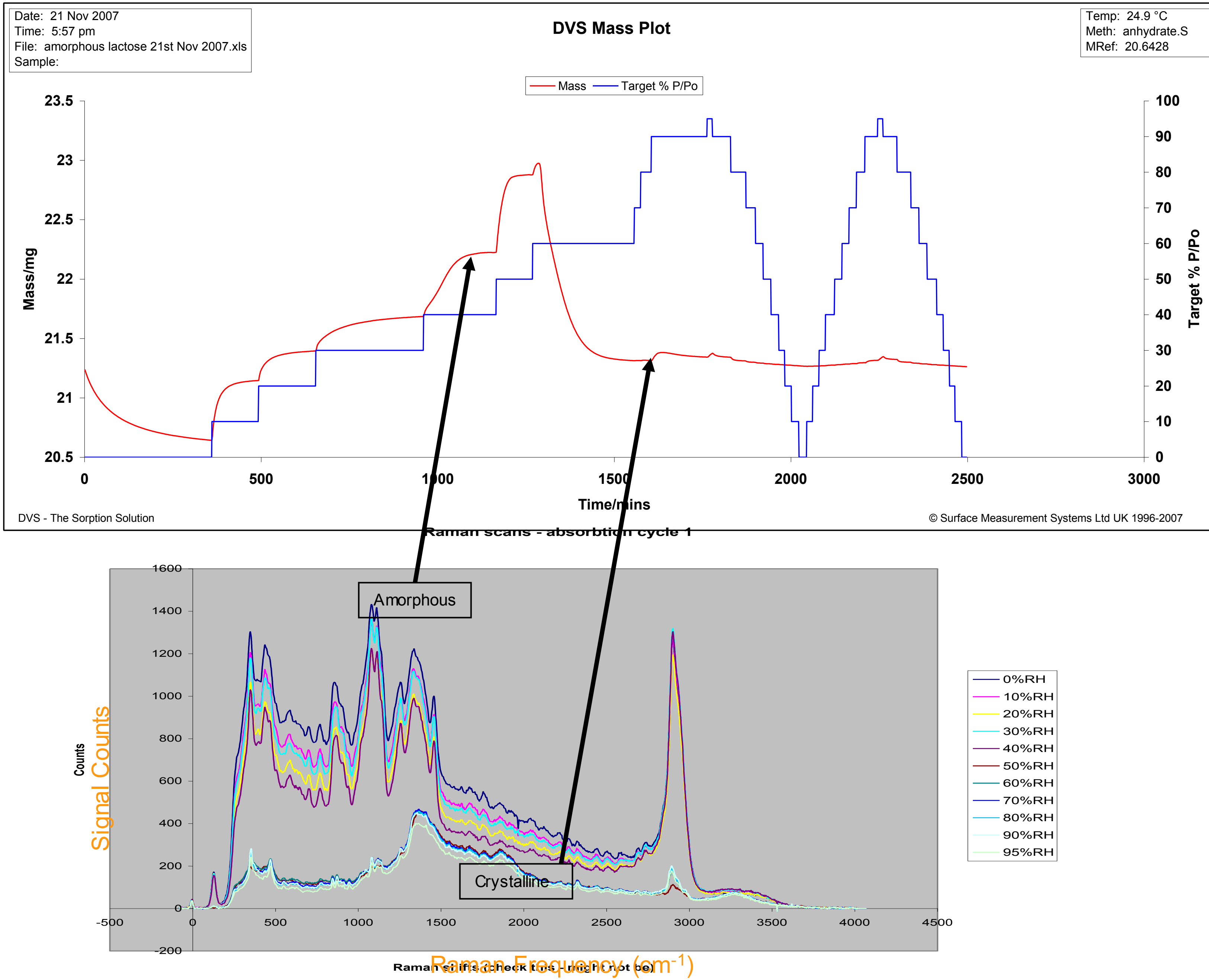
2. **Rayleigh scattering**: Light that is scattered at the same wavelength as the incoming light.

3. **Raman scattering**: Light that is scattered due to vibrations in molecules or optical phonons in solids.

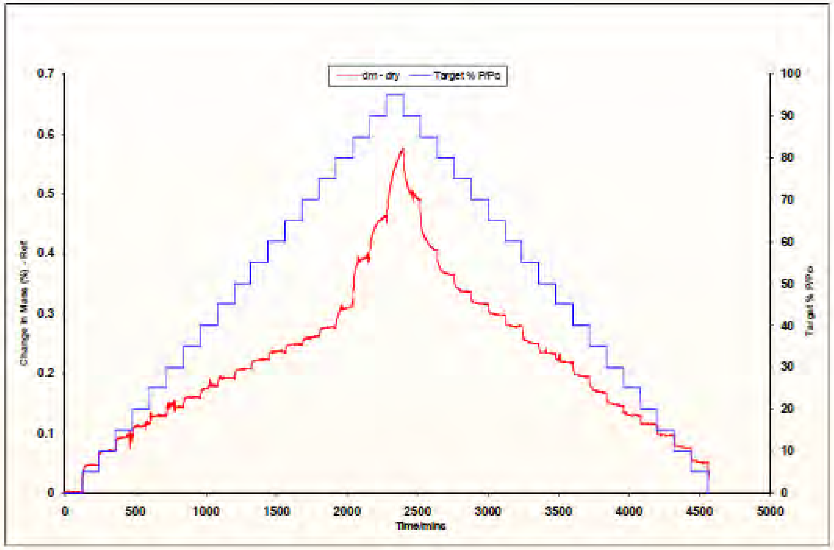
4. The majority of scattered light is elastic and only one in 10^6 optical photons are scattered at frequencies different to the incident light – This is the weaker Raman scattered light.



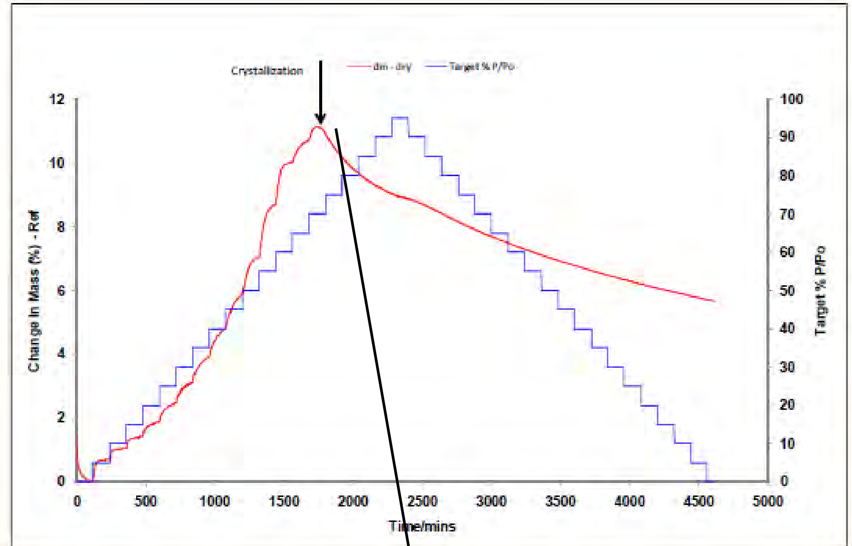
Step Data for Spray Dried Lactose



Amorphous versus Crystalline Salbutamol Sulphate

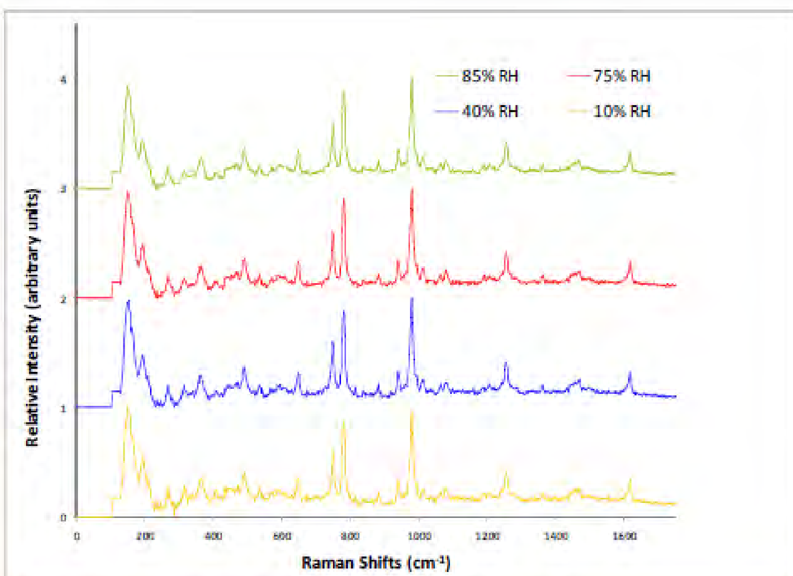


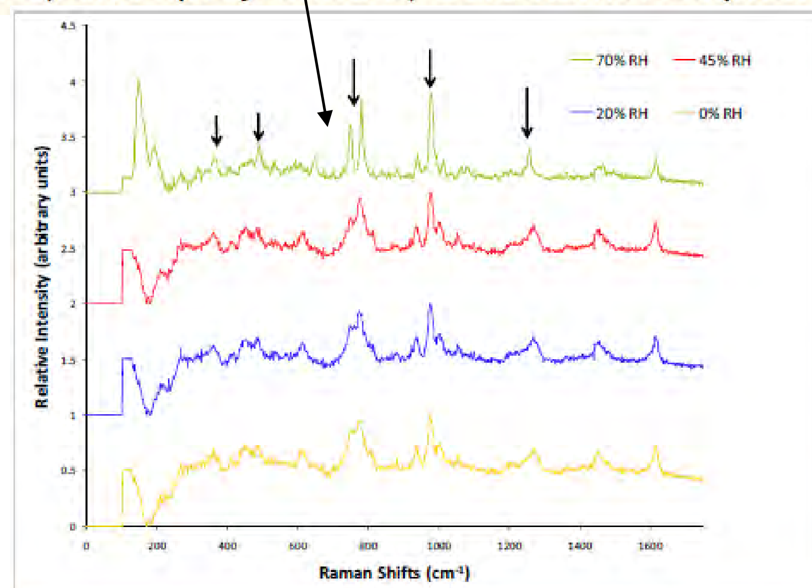
a)



b)

Figure 5. DVS water sorption at 25 °C on re-crystallized a) and spray-dried b) Salbutamol Sulphate





Ethanol vapor induced polymorph conversion δ → β mannitol

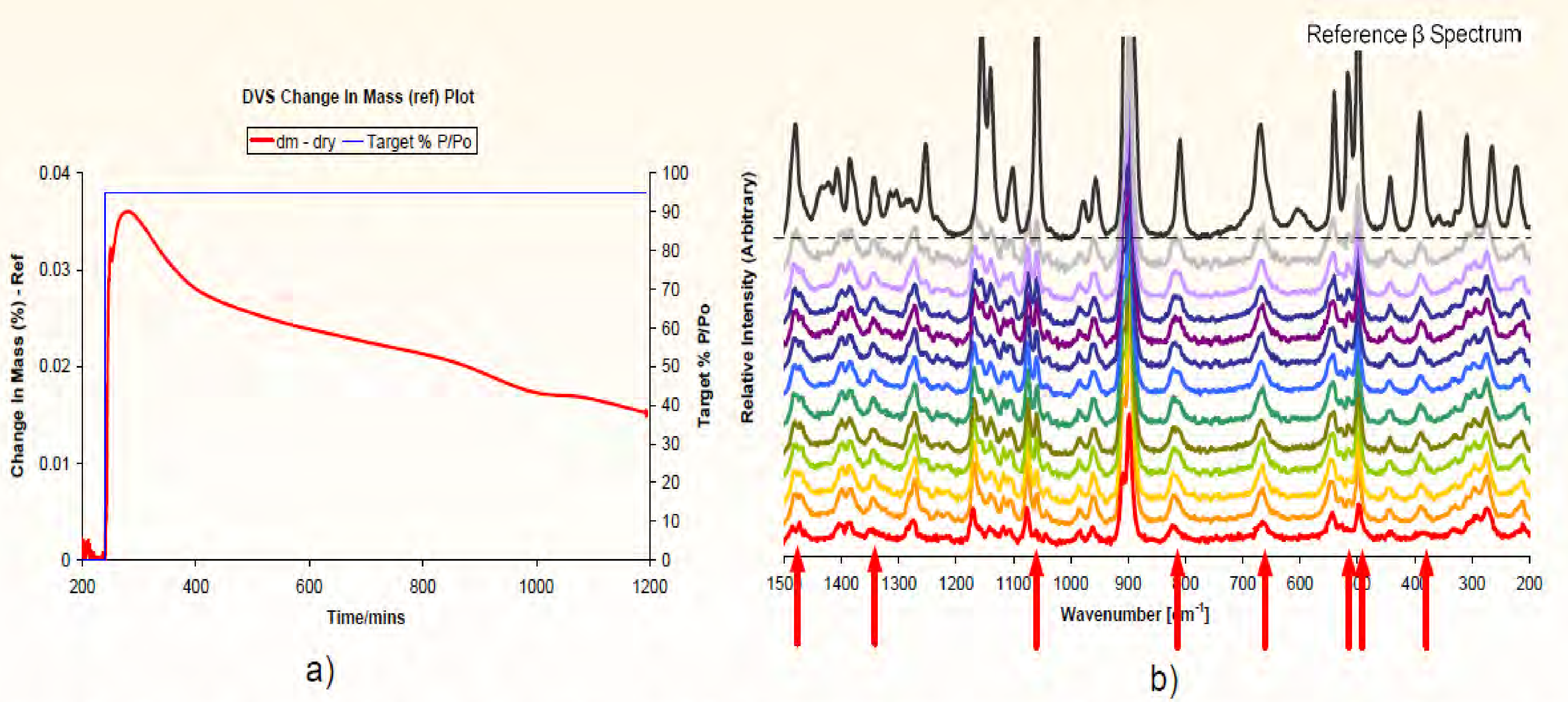
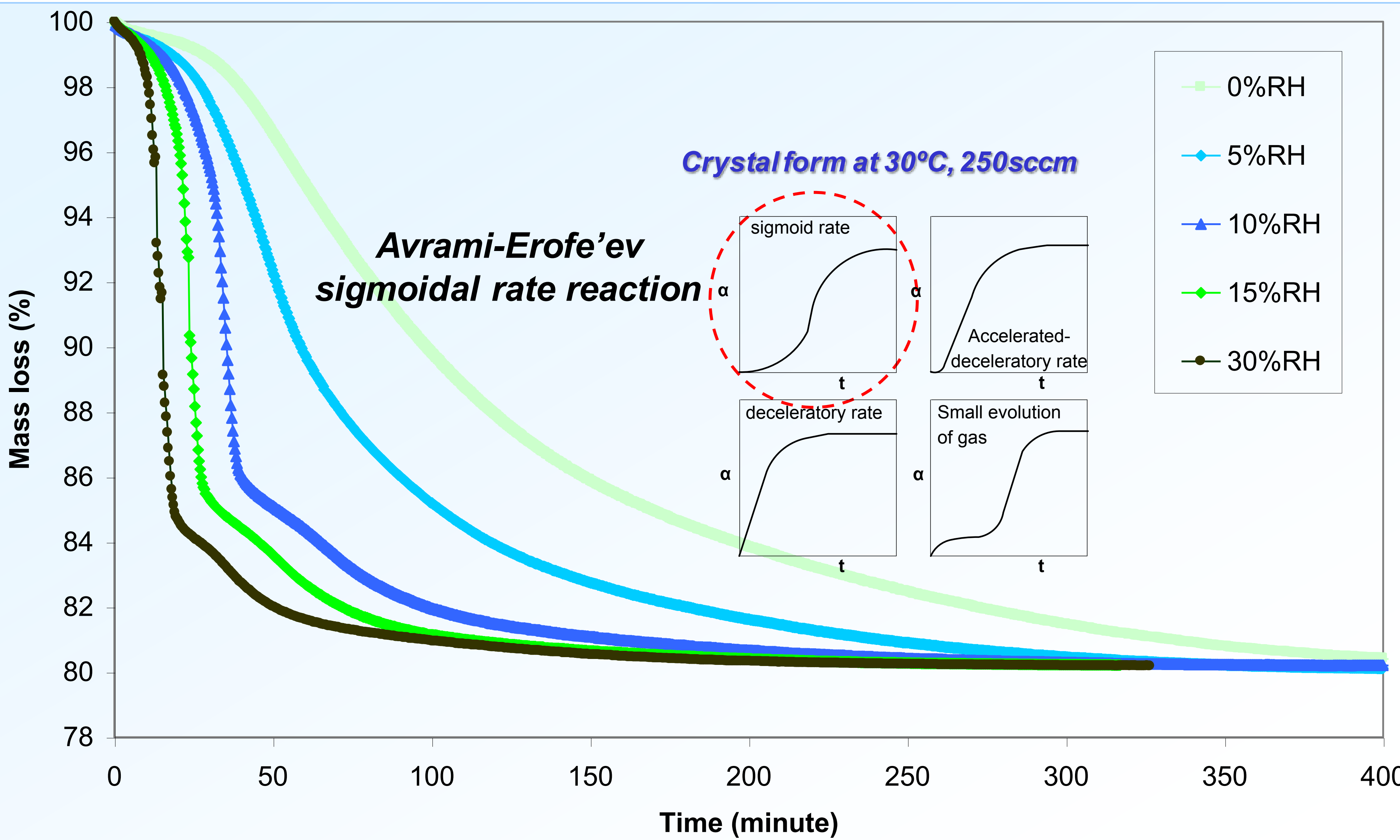


Figure 4. DVS a) ethanol at 95%P/P_0 at 45°C and b) Raman spectra taken at 2-hour intervals for δ D-mannitol.

Carbamazepine Acetone Solvate: Desolvation Kinetics at 30C



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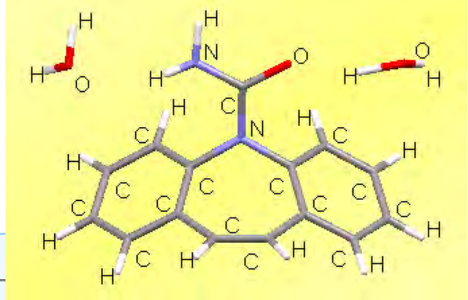
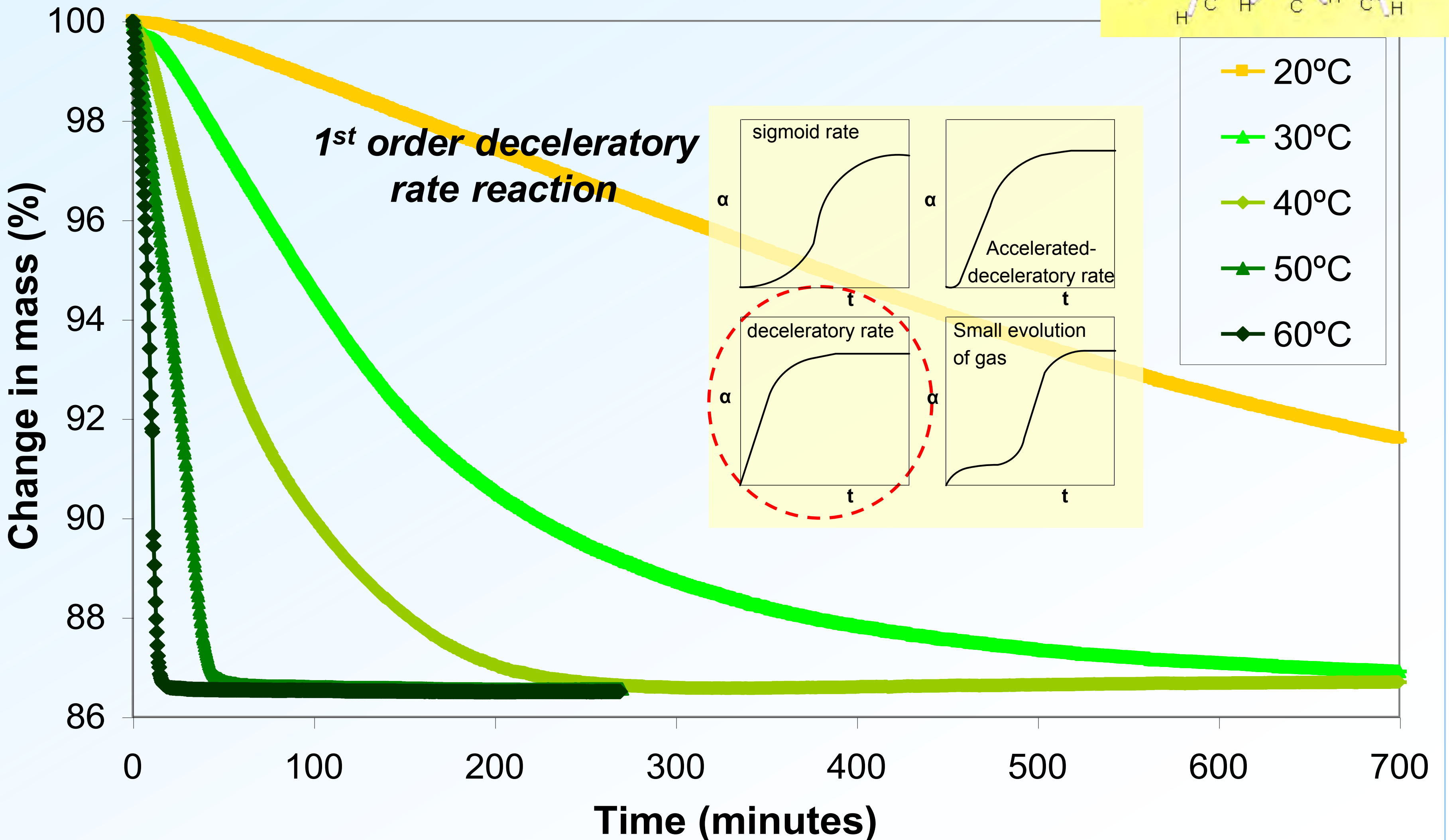
Carbamazepine Dehydration Rates





The Future **for** DVS

- Multi-component gas-vapour mixtures
  - BET of a hydrate
  - Competitive adsorption

- More Fibre optic spectroscopy- IR, NIR

- Smaller samples, faster analysis eg a few hours

- Advanced modelling of isotherms for understanding sorption parameters from polymer solution theory eg χ

- True high throughput sampling

Conclusion

•Water Sorption in organic materials can be a complex phenomena

•DVS data describes physical, morphological and chemical state of the materials, including recrystallisation and amorphous collapse events

•Raman spectroscopy and video images support the comprehensive understanding of DVS sorption data

•DVS information not often attainable using any other approach

Thank You

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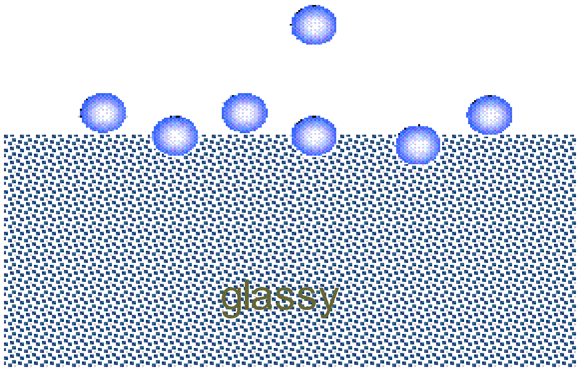
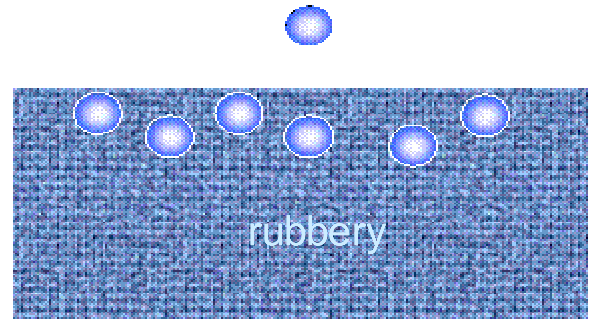
Verentas Model of Solute-Polymer Dissolution





Vrentas' model

$$\left[p_1 / p_1^{\,0} \right] = \phi_1 \exp\left(\phi_2 + \chi \phi_2^{\,2} + F\right)$$

$$\left[p_1 / p_1^{\,0} \right] = \phi_1 \exp\left(\phi_2 + \chi \phi_2^{\,2}\right)$$

$$F = \left\{ M_1 w_2^{\,2} \left(c_{pg} - c_p\right) \left(dT_{gm} / dw_1 \right) \left(\left(T / T_g \right) - 1 \right) \right\} / RT$$

$$F = 0$$

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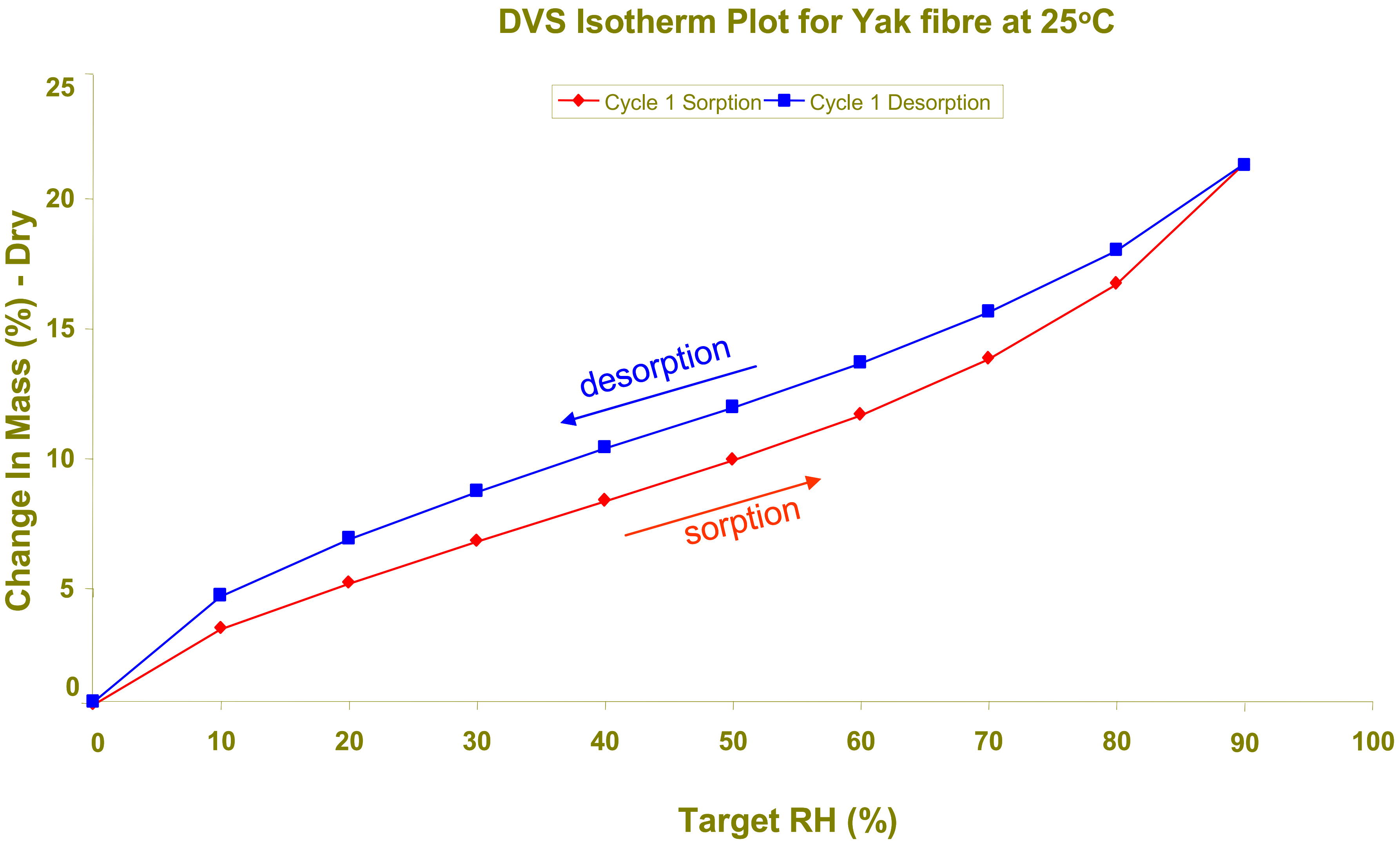
Does the BET model work for Water Sorption in Amorphous Solids?

- Define “Work”
- Can we fit data to model- YES
- But so to do many other models eg Young and Nelson
- Does the model provide a physical insight into the sorption process? NO
- Does that mean the BET model has no use, certainly not.
- Do better models exist……

Water Sorption Keratin Fibres 25C



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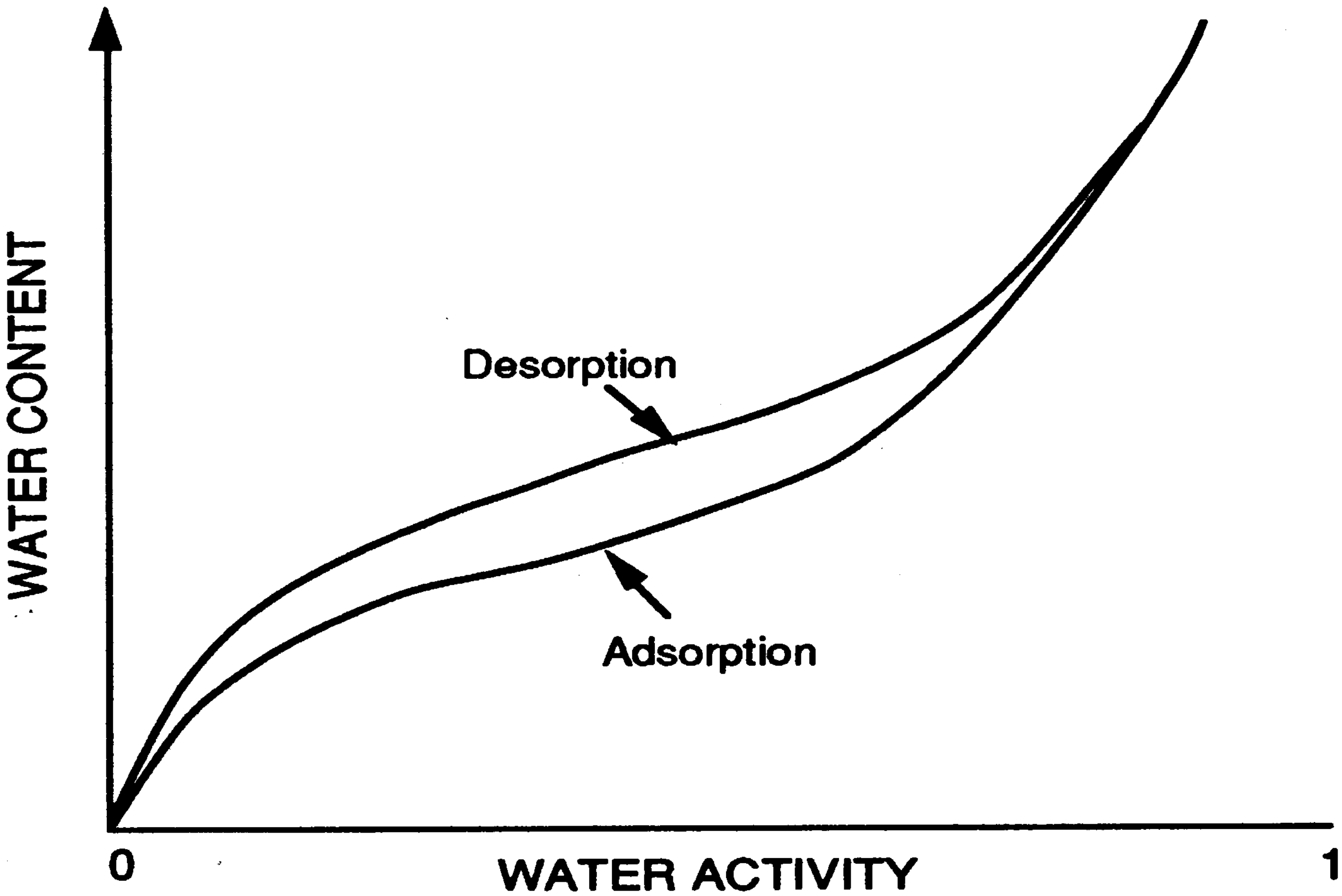
The Water Sorption Isotherm



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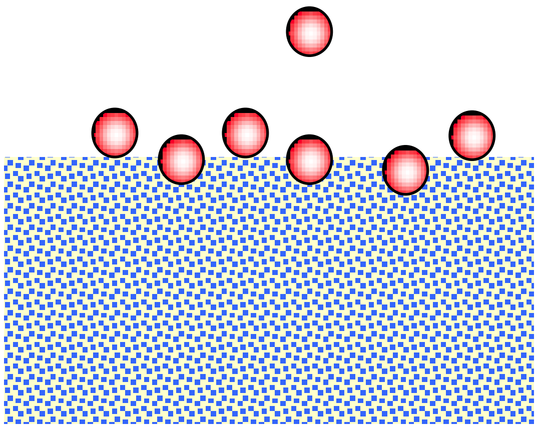
Glass Transition Temperatures and Adsorption/Sorption

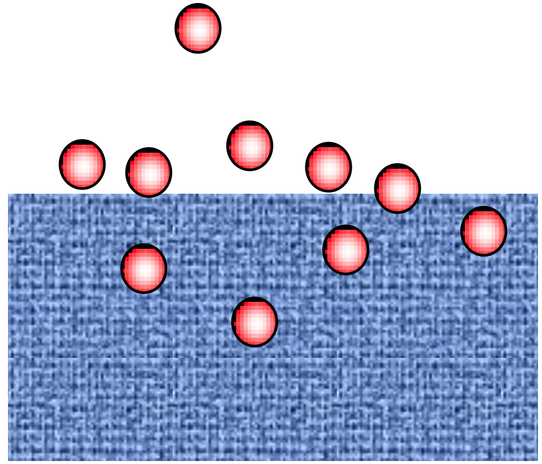


Amorphous-Glassy Solid

T <Tg

Surface and local bulk adsorption

Fast kinetics, low uptake levels

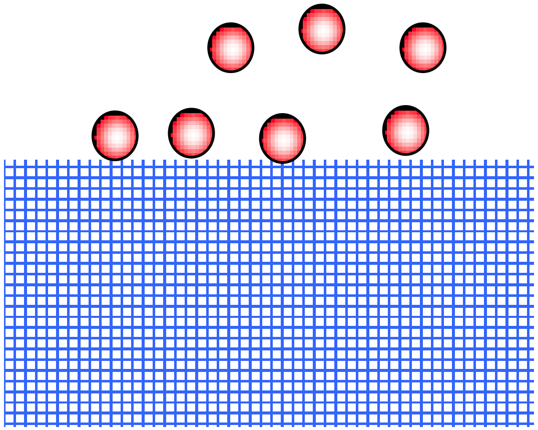


Amorphous-Rubbery Solid

T >Tg

Deep bulk sorption

Slower kinetics, medium to high uptake levels



Crystalline

No Tg

Surface adsorption

Very fast kinetics, very low uptake levels

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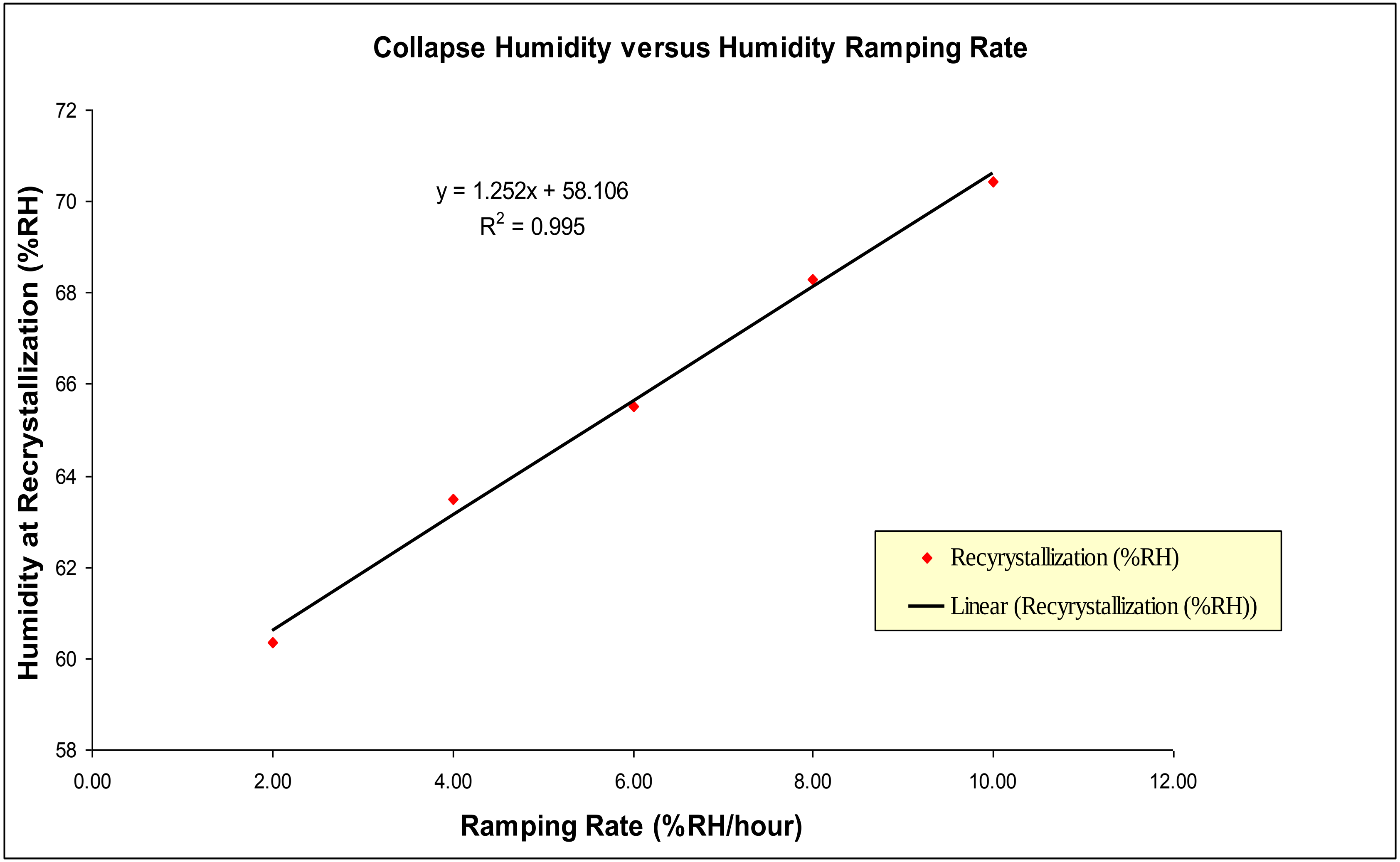
Collapse RH versus Ramping Rate



- **Critical Collapse RH = 58% RH at 25 °C**

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Sorption behaviour is Complex

- Solute uptake levels of 0.02% to 60%
- Isotherm shapes can vary widely
- Sorption kinetics : a few minutes to a few days
- Solutes- water to hydrocarbons
- Substrates
  - Inorganic or organic
  - Glassy
  - Crystalline
  - Porous
  - Reactive
  - Combinations of all of the above

- No one theory can account for all of these !!
- What about the BET model!

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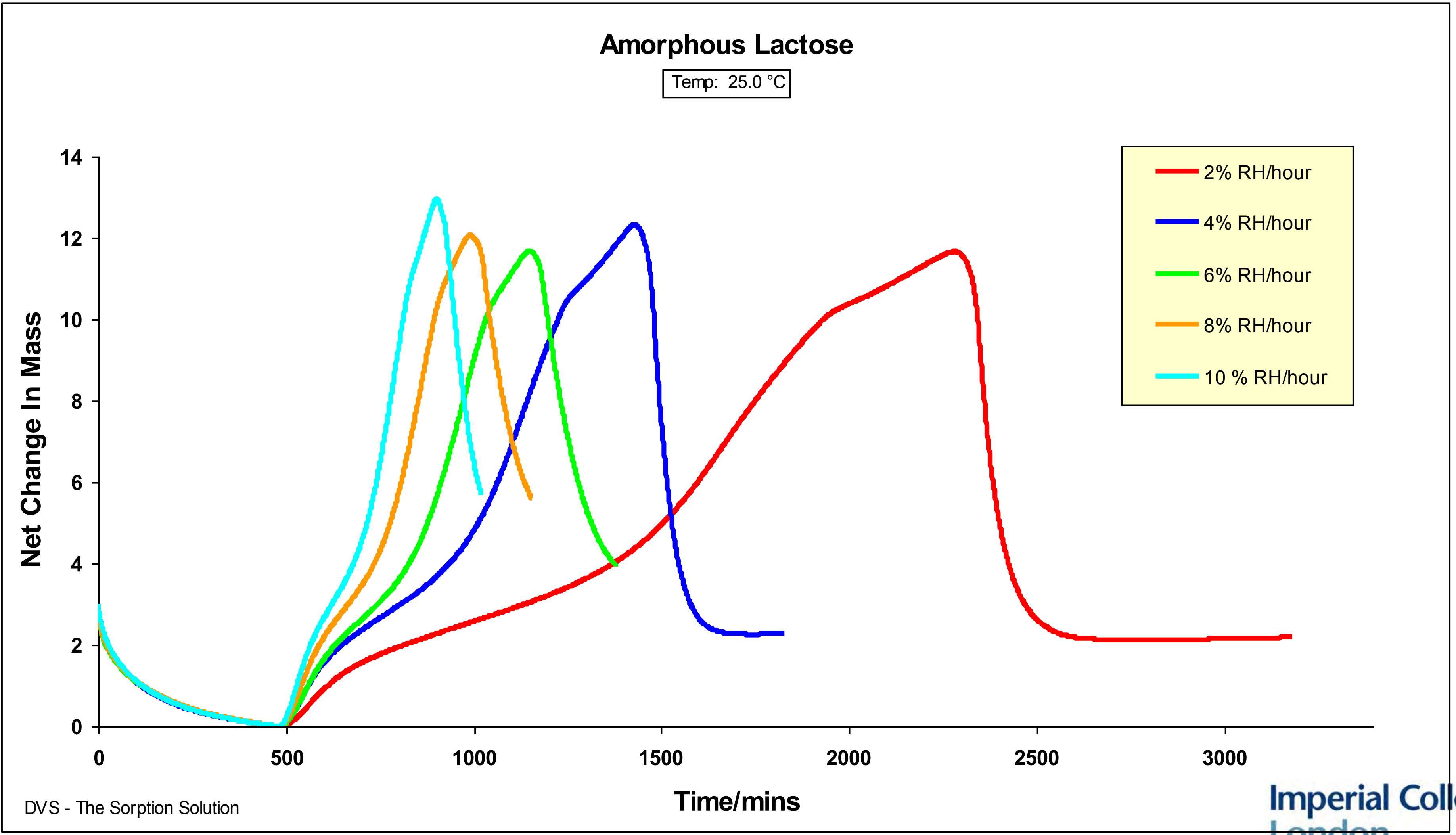
0 to 90% RH for Different Ramping Rates



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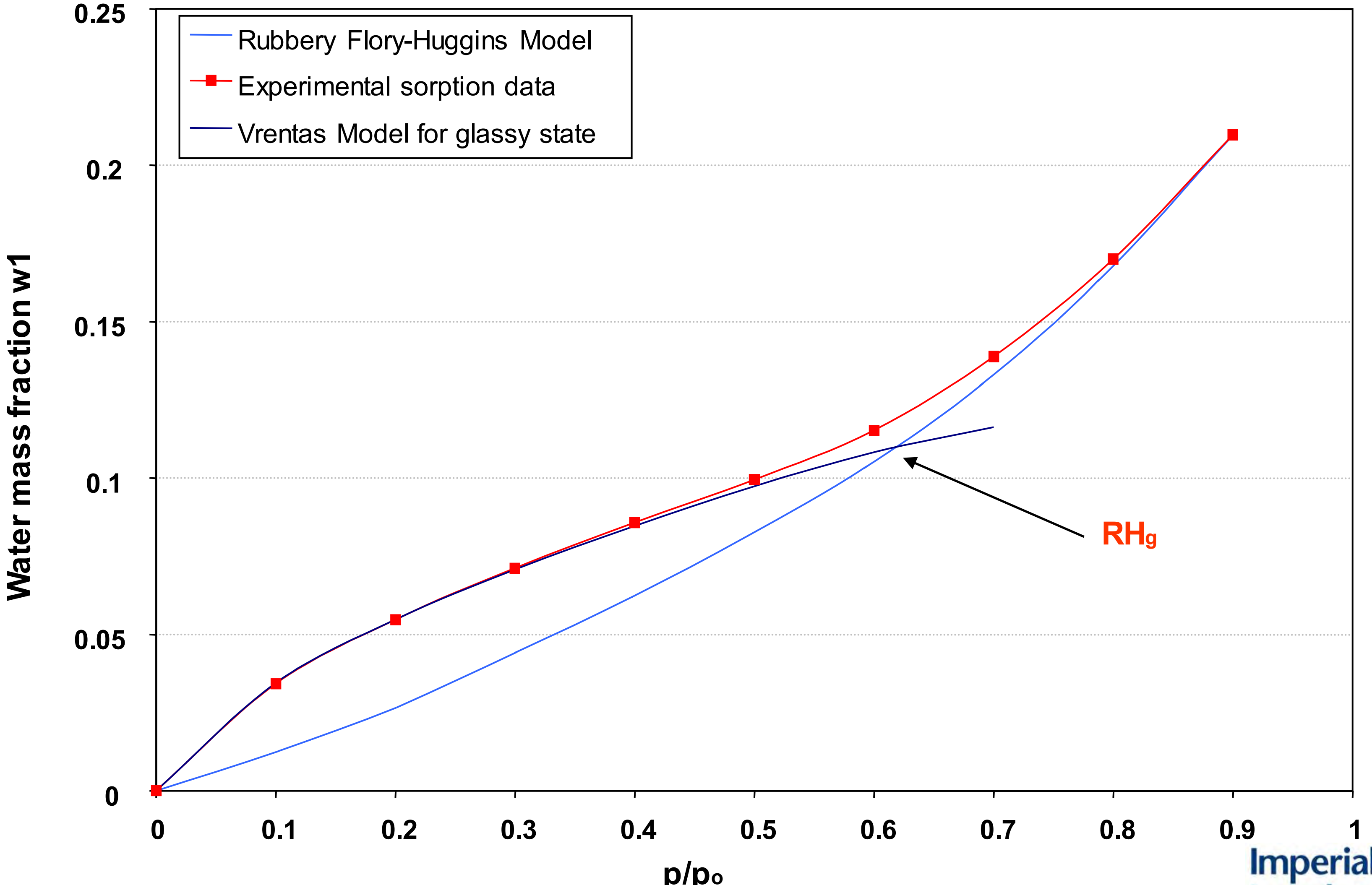
Vrentas' model: Water Sorption in Keratin



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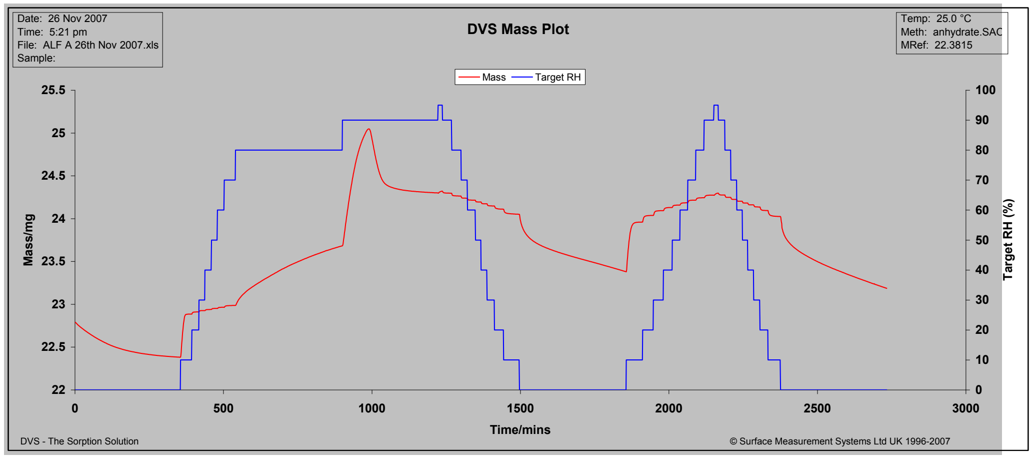
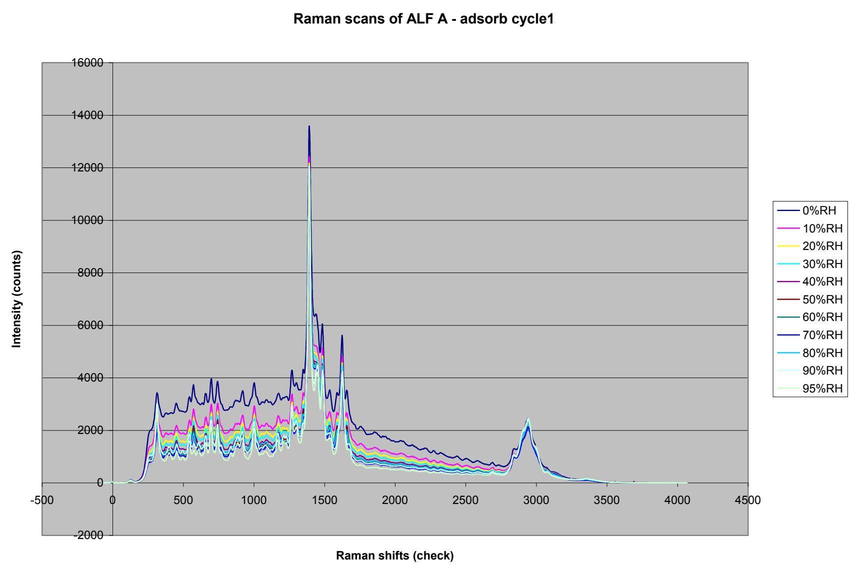
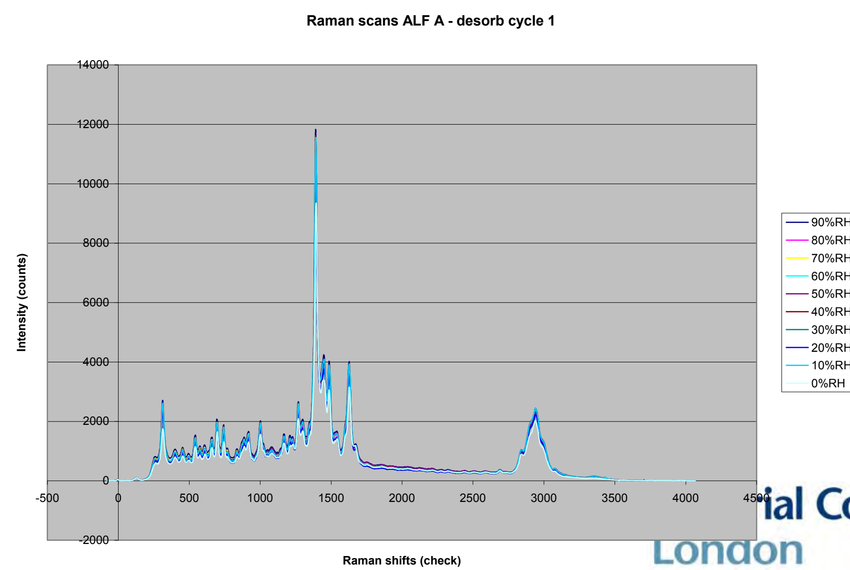
Example: ALF A (Example Anhydrate Drug)



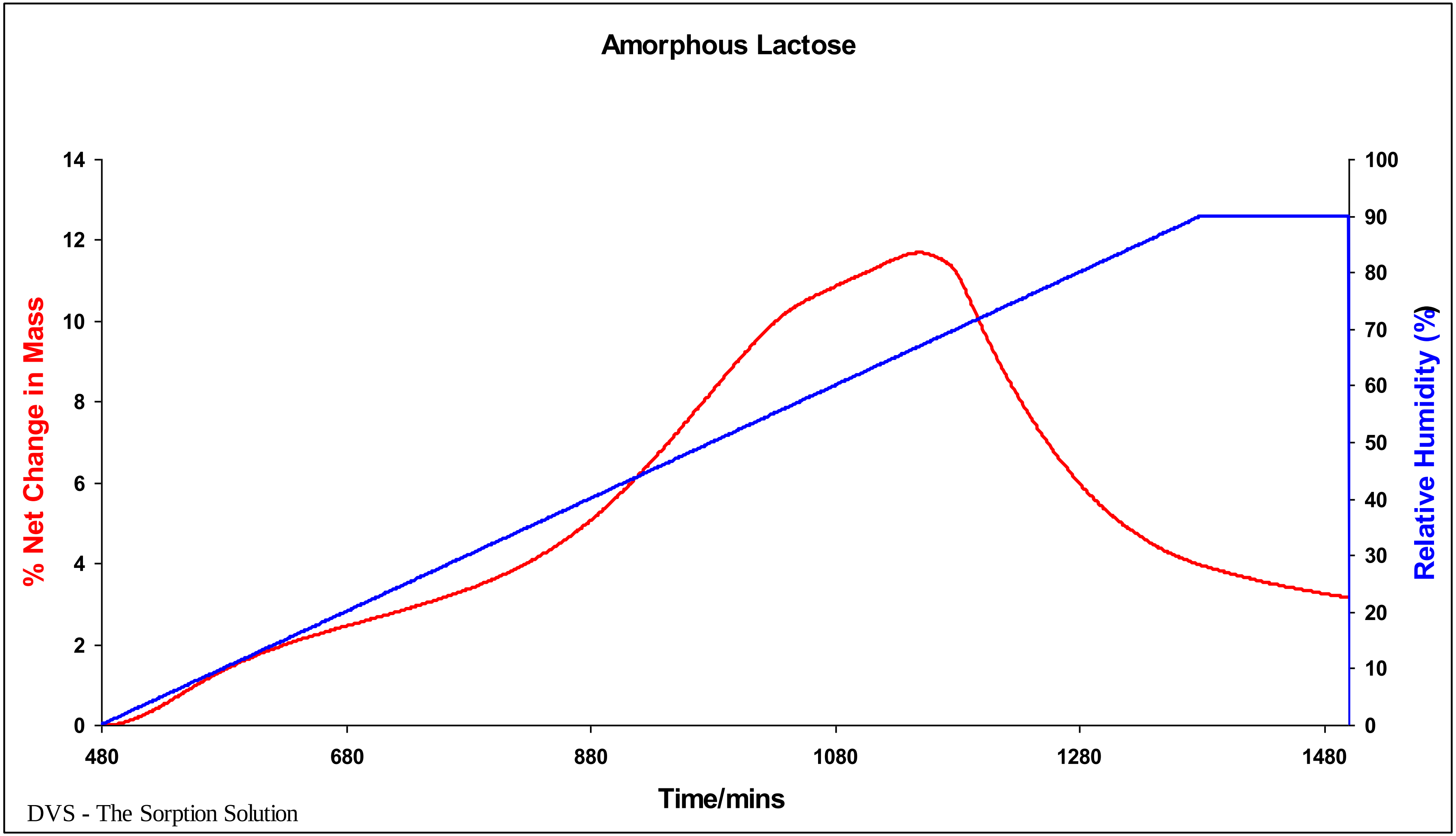
Adsorption Cycle 1



Desorption Cycle 1



Ramp Results for Spray Dried Lactose (25 °C, 6% RH/hour)



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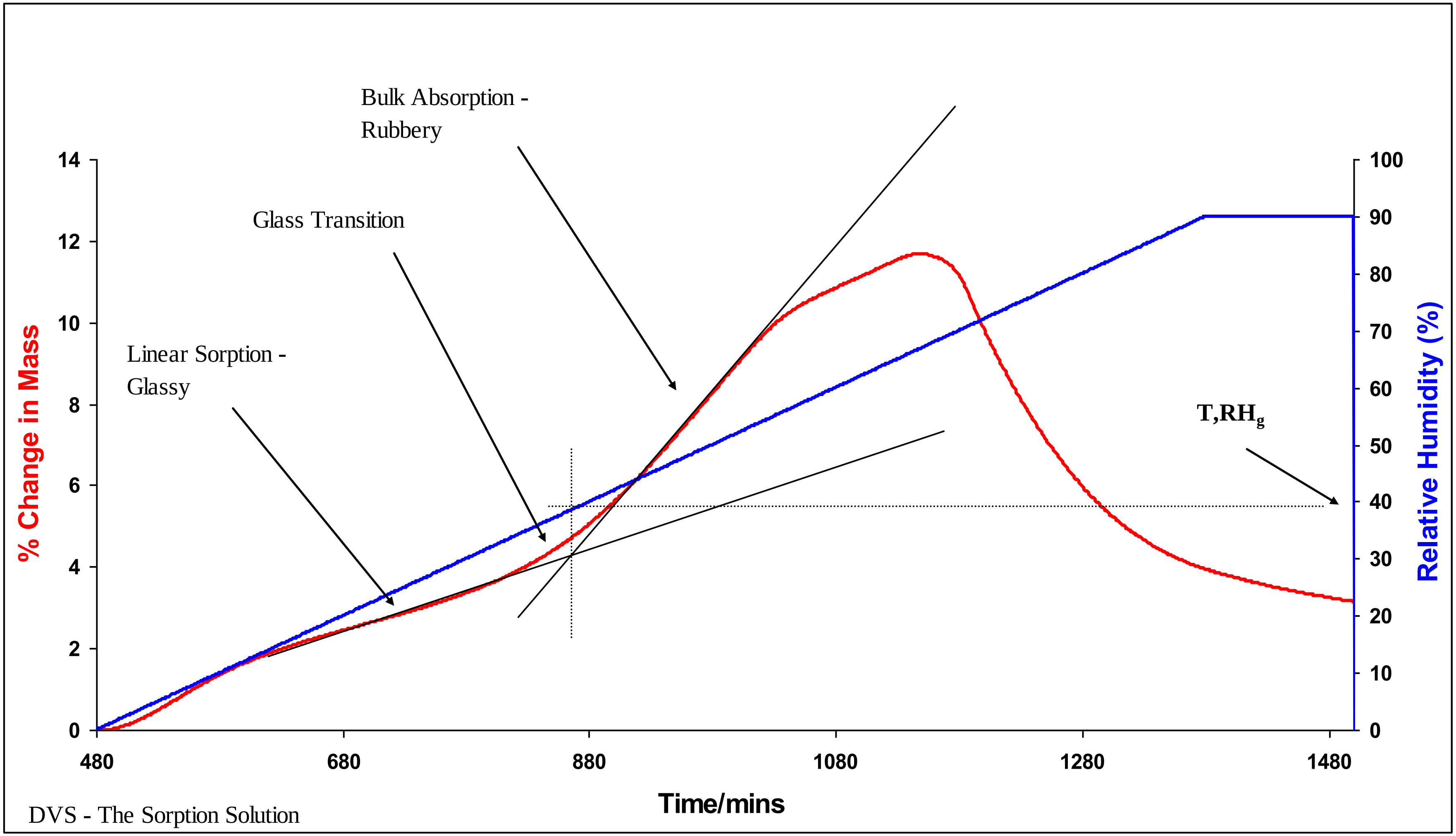

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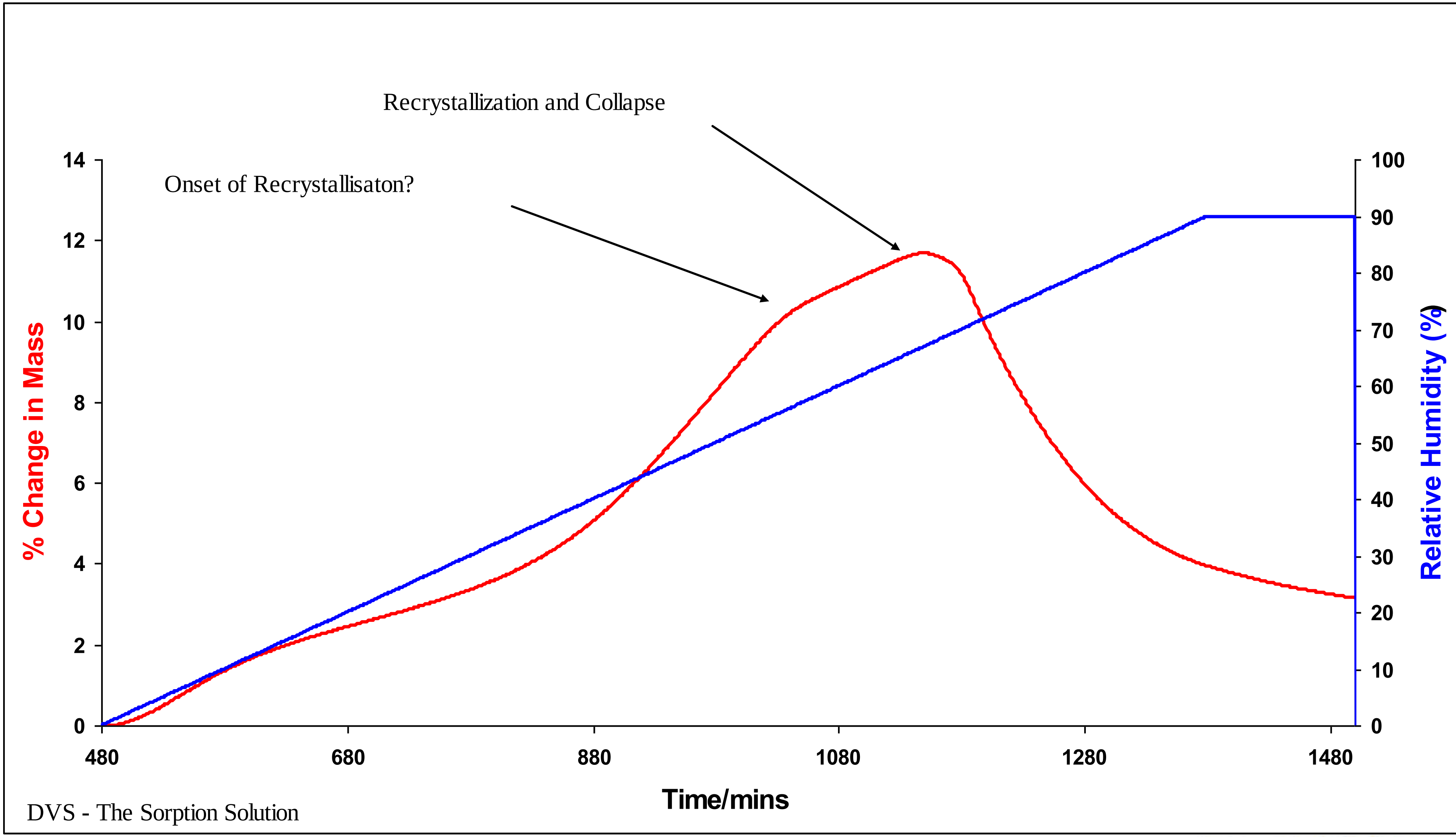

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