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## **In situ X-ray for monitoring crystallization and phase transitions in suspension: In-situX®**

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# In situ X-ray for monitoring crystallization and phase transitions in suspension: In-situX®

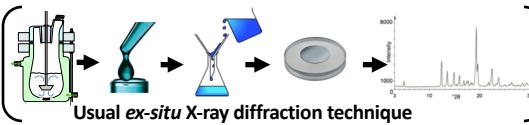


S. Clevers, A. Lafontaine, G. Baaklini, M. Schindler, M. Sanselme, Y. Cartigny, V. Dupray and G. Coquerel

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## Introduction



Usual ex-situ X-ray diffraction technique



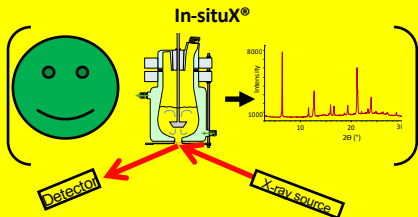
Not suitable for:

- In-situ analyses
- Metastable phase
- Efflorescent solvate
- Crystals in suspension
- Transient states

## Aim of the study

To highlight, through different examples, the possibilities of In-situX® as analytical tool able to solve academic as well industrial problems

## Conclusion



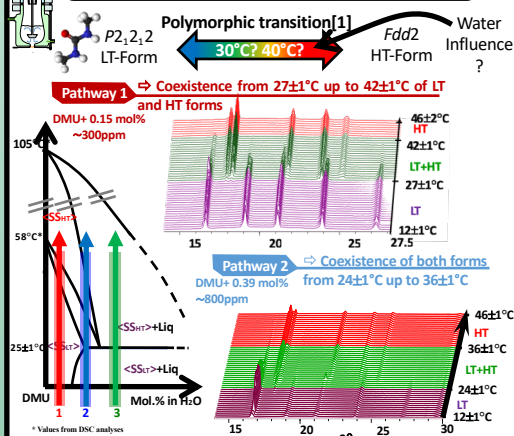
- No need for sampling (cytotoxic compounds, radioactive elements, low temperature crystallization, efflorescent solvates, CO<sub>2</sub>, O<sub>2</sub>, light, moisture sensitive compounds)
- Laboratory X-ray Source

Solid – solid transition studies of all sorts:

- Polymorphism (kinetics of transition during slurring)
- De/resolution (peritectic transitions in binary, ternary systems, etc.)
- Co-crystal formation
- Host Guest associations
- Clathrates

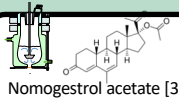
- Optimization of the resolution of chiral molecules
- Optimization of the filterability by means of temperature cycling

## DMU/H<sub>2</sub>O- Polymorphic transition



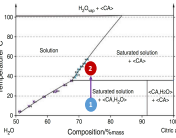
$\Rightarrow$  evidence of a metatectic invariant [2]  
 $\Rightarrow$  Water as impurity strongly impacts the phase transition of DMU  
 Dried DMU  $\rightarrow T_i = 58^{\circ}\text{C}$   
 ~300ppm + DMU  $\rightarrow T_i = 27^{\circ}\text{C}$ !

## Detection of solvate

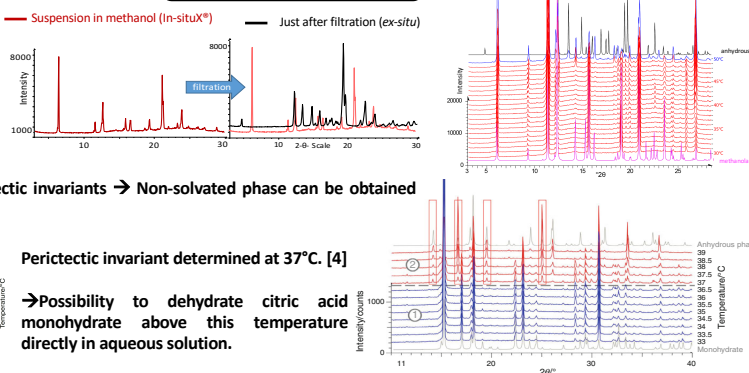


$\rightarrow$  Detection of highly efflorescent solvate

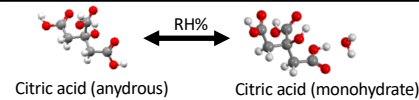
Determination of peritectic invariants  $\rightarrow$  Non-solvated phase can be obtained directly in suspension



$\rightarrow$  Possibility to dehydrate citric acid monohydrate above this temperature directly in aqueous solution.

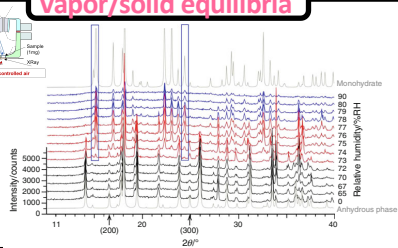


## Vapor/solid equilibria

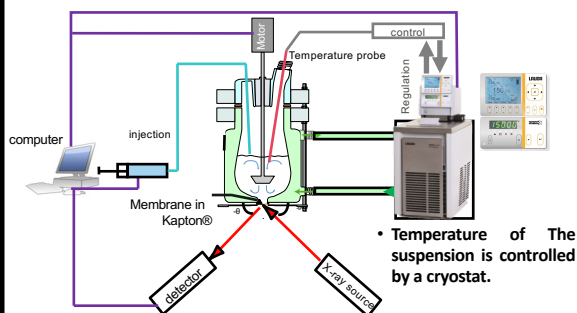


At 25°C [4]:

- $\rightarrow$  Hydration detected at 73%RH (DVS 73.4%) and completed at 78%
- $\rightarrow$  Above deliquescence: significant decrease of peak intensities
- $\rightarrow$  Useful information for the storage conditions

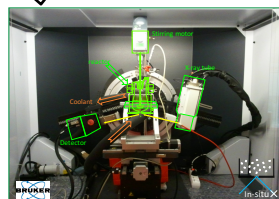


## In-situX® - Principle



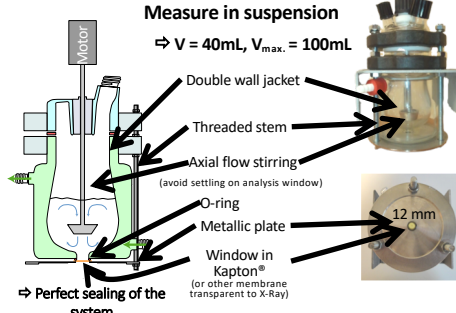
**Diffractionmeter [5]:**  
 Geometry:  $-\theta/-\theta$   
 Detector: Lynx eyes™  
 X-ray tube: anticathode in copper

Computer-controlled (stirring rate, chemical injection, temperature) by Labview® software

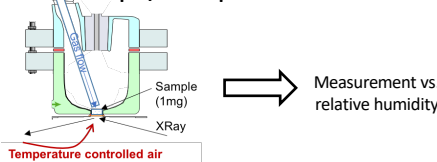


## Measure in suspension

$\Rightarrow V = 40\text{mL}, V_{\text{max}} = 100\text{mL}$



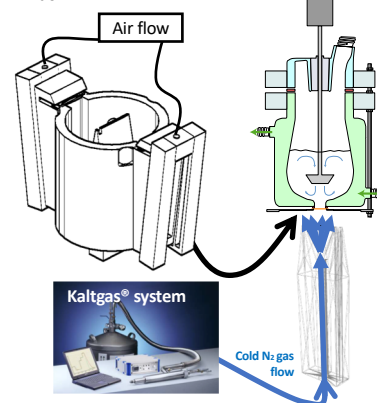
## Vapor/solid equilibria



## AFRODISM [6]:

-70°C  $\leftarrow$  Temperature range  $\rightarrow$  +70°C

- Temperature control of the exterior of the reactor
- Anti-frosting and anti-condensation on the Kapton window



## References

[1] C. Näther, C. Döring, I. Jess, P. G. Jones, and C. Taouss, Acta Crystallogr B Struct Sci, vol. 69, no. 1, 2012.  
 [2] G. Baaklini et al. "Depression of the polymorphic transition temperature of 1,3-dimethylurea (DMU) by insertion of hundreds of ppm of water in the crystal lattices and crystal structure determination of DMU monohydrate." to be published

[3] A. Lafontaine, PhD Thesis, Université de Rouen, 2013

[4] A. Lafontaine, M. Sanselme, Y. Cartigny, P. Cardinael, and G. Coquerel, Journal of Thermal Analysis, vol. 112, no. 1, pp. 307–315, Nov. 2012.

[5] G. Coquerel, M. Sanselme, and A. Lafontaine, US9255898B2 patent, 2014

[6] G. Coquerel, S. Clevers EP18305580.5 patent, 2018