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Study of the particle formation and morphology of single mannitol-water droplets depending on the drying conditions

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Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG

Study of the Particle Formation and Morphology of Single Mannitol-Water Droplets Depending on the Drying Conditions

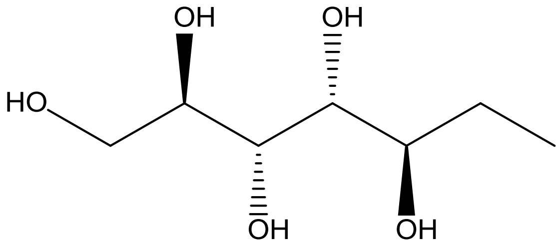
Design and Manufacture of Functional Microcapsules

T. Hellwig, M. Griesing, H. Grosshans, W. Pauer, E. Gutheil, H.-U. Moritz

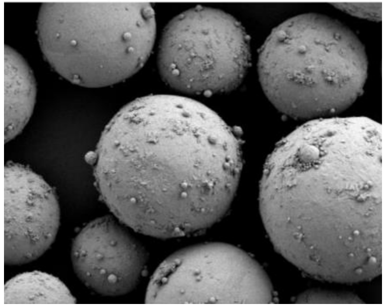
25.04.2016

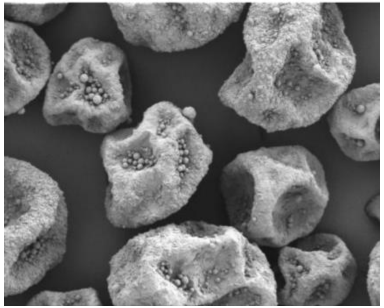
Type of Substance: Mannitol

Carrier for
dry powder inhalators (DPI)



Manufactured by spray process
with various morphologies

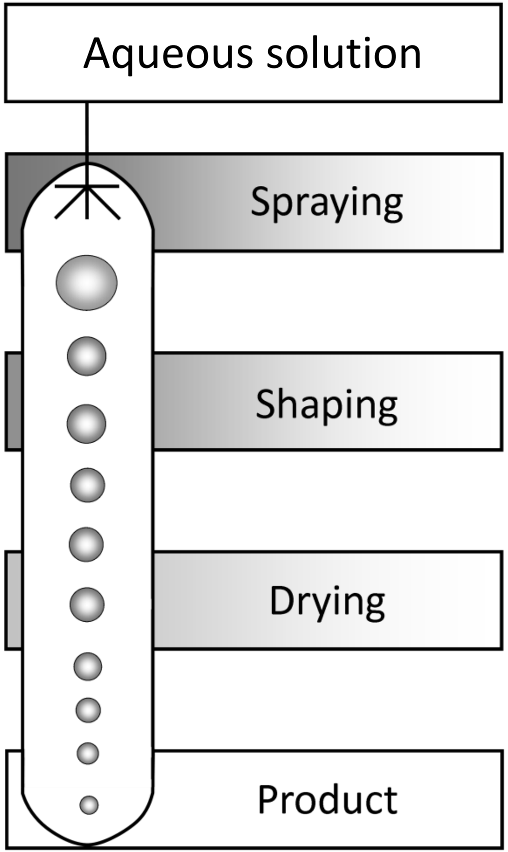


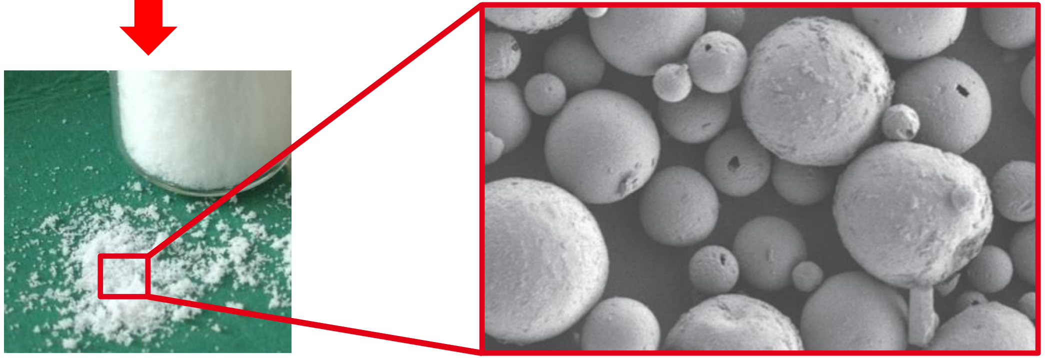


Challenging process design

M. Mönckedieck et al., Influence of particle shape of spray-dried mannitol carriers on powder flow and aerodynamic properties, DDL 25, Edinburgh, 2014

Advantage of Spray Drying Process





Multiple operations

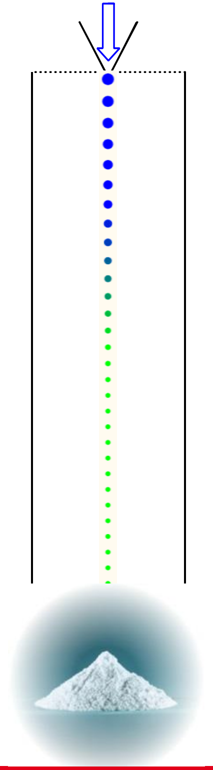
↓

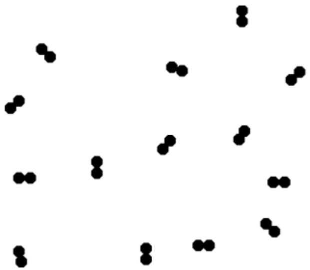
Single stage process

Process intensification

Observing Single Droplet Using Acoustic Levitation

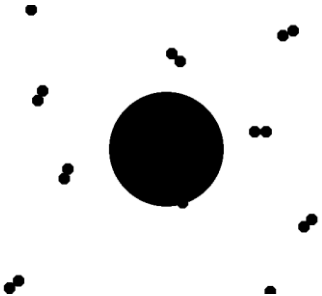
Spray process



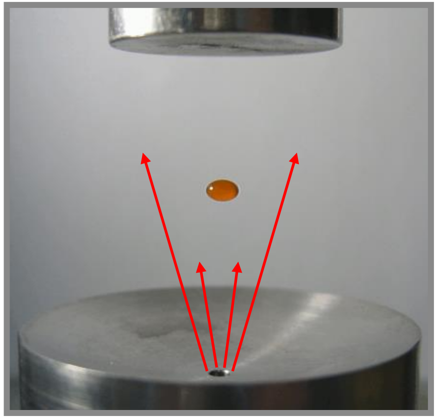


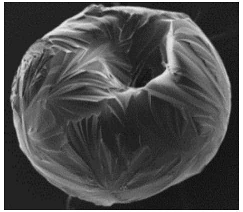
Disproportional effort to monitor single droplet

Acoustic levitation



Acoustic levitation offers accessible analytics for single droplet





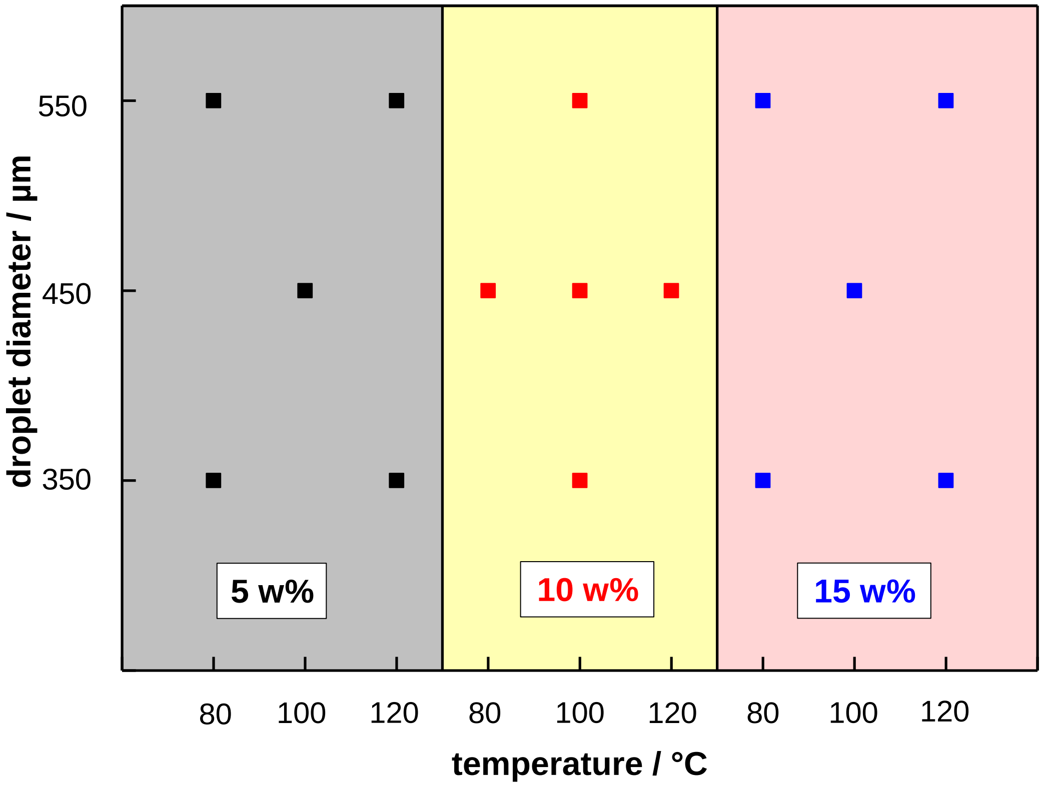
Levitation Aq. Mannitol Droplets - Experimental Design

Design of Experiment

- Factors: Temperature (80-120 °C)
  Mass fraction (5-15 w%),
  Droplet size (350-550 µm)
- 5 experiments for each condition
- Constant relative humidity (r.h.) 1 %

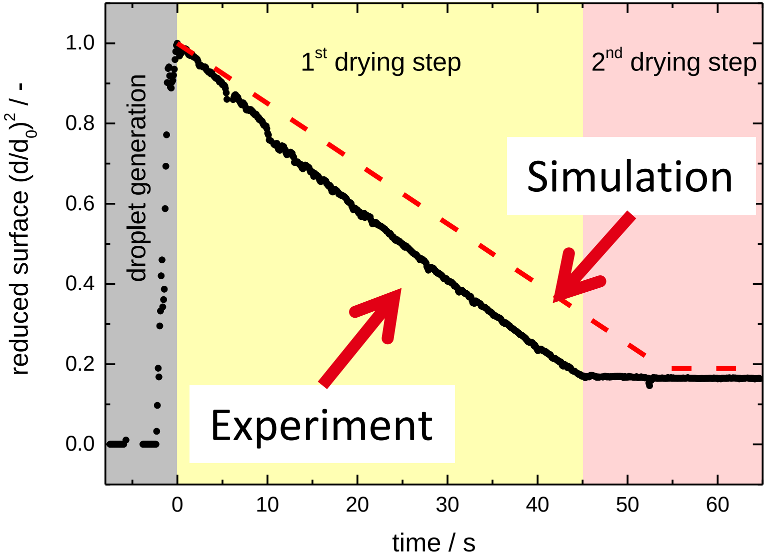
Outcomes

- Drying kinetics
  - Evaporation rate
  - Solid layer formation
- Porosity
- Surface texture (morphology)



Numerical Simulation for Drying of Single Aq. Mannitol Droplets

- Experimental determined drying kinetic via shadowgraphy
- Numerical simulation procedure by H. Großhans, S.R. Gopireddy and E. Gutheil (IWR, University of Heidelberg)



- Mass conservation

$$\frac{\partial w_i}{\partial t} = \frac{D_{12}}{r^2}\left[\frac{\partial}{\partial r}\left(r^2 \frac{\partial w_i}{\partial r}\right)\right]$$

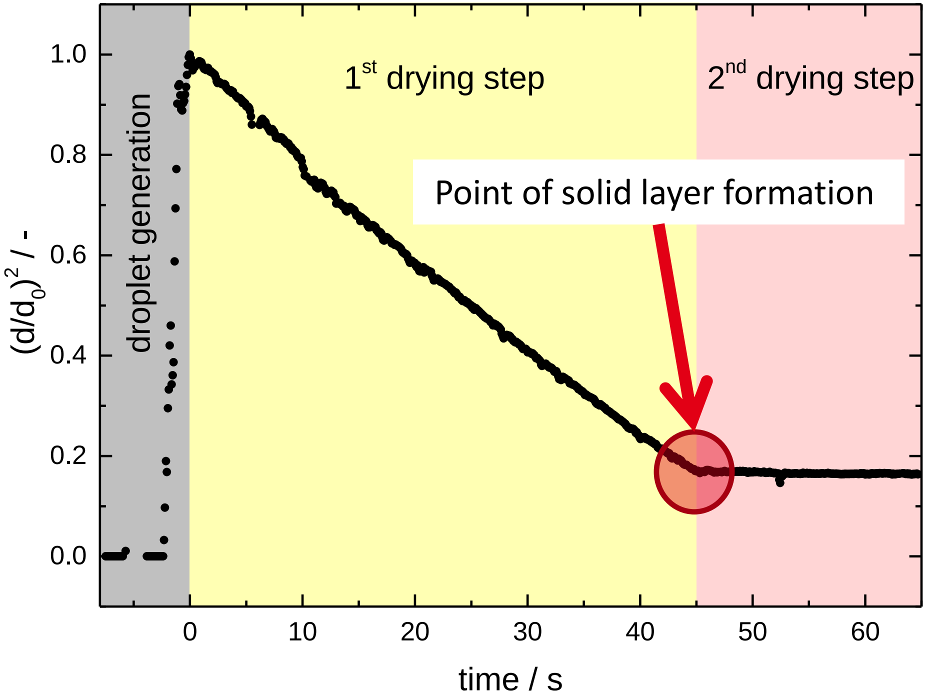
- Energy conservation

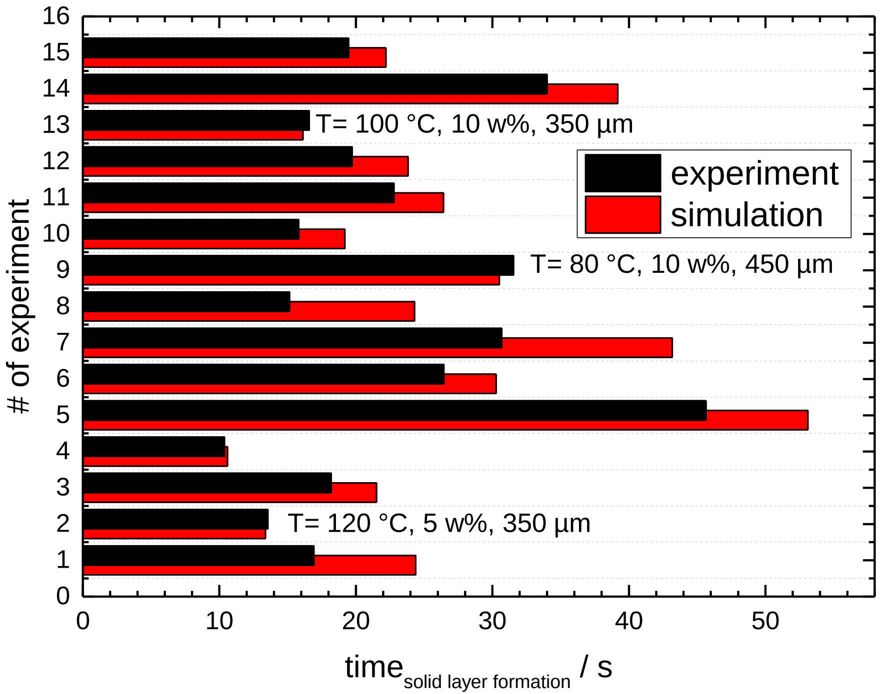
$$m c_{\mathrm{p,l}} \frac{dT_{\mathrm{d}}}{dt} = \frac{Q_{\mathrm{l}} + \dot{m} h_{\mathrm{L}}(T_{\mathrm{d}})}{1 + Nu^{*}\, k_{\mathrm{g,f}}\, \beta / (2k_{\mathrm{s}}(R-\beta))} - \dot{m}\, h_{\mathrm{L}}(T_{\mathrm{d}})$$

Developed numerical simulation is able to describe 1st drying step

H. Grosshans et al., Int. J. Heat Mass Trans. **2016**, 96, 97-109.

Solid Layer Formation of Single Aq. Mannitol Droplets

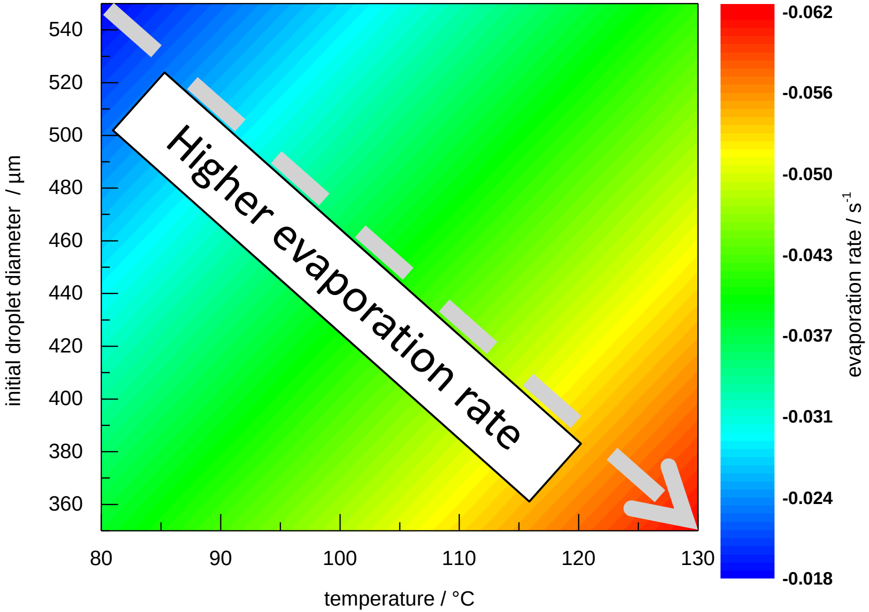




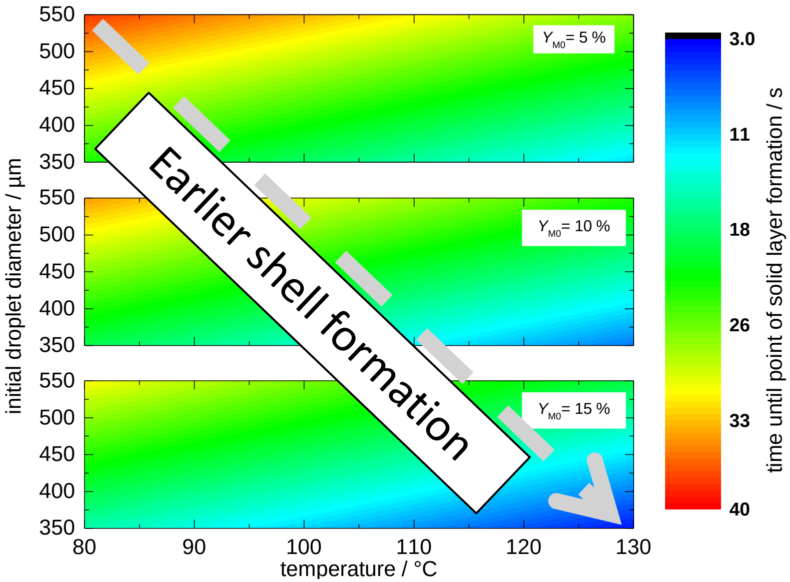
Numerical simulation can be used to determine point of solid layer formation

Influences on Drying Kinetic

Evaporation rate



Point of solid layer formation

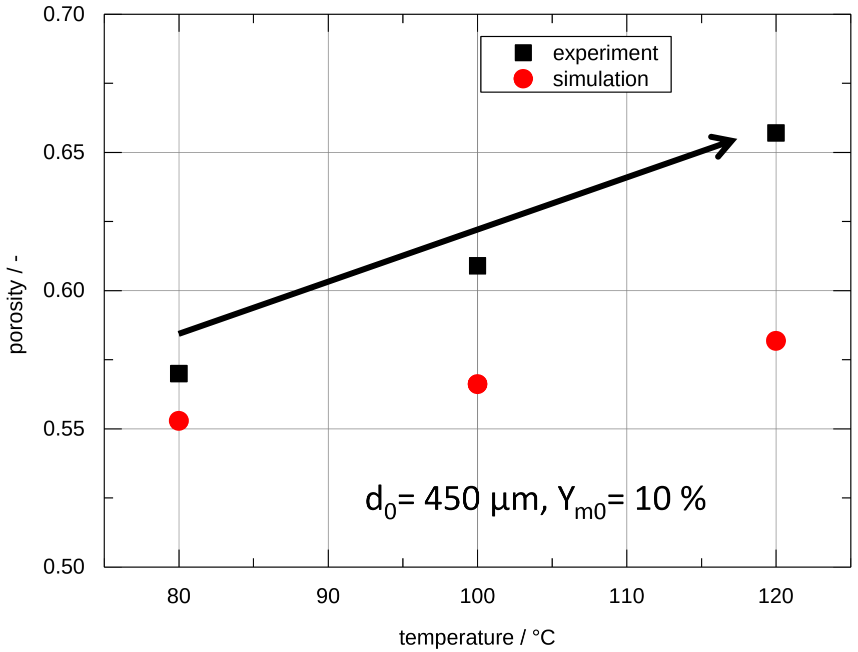


Mass fraction x
Temperature ✓
Starting droplet diameter ✓

Mass fraction ✓
Temperature ✓
Starting droplet diameter ✓

Porosity of Produced Single Mannitol Particles

- Porosity calculated based on shadowgraphy data



$$\phi = \frac{(V_{\mathrm{end}} - V_{\mathrm{m}})}{V_{\mathrm{end}}} \quad \text{with} \quad V_{\mathrm{m}} = \frac{V_{\mathrm{d0}} \rho_{\mathrm{d0}} Y_{\mathrm{m0}}}{\rho_{\mathrm{m}}}$$

- Higher deviation at higher temperatures:
  - Simulation does not take inner pressure into account

The porosity is increased with increasing temperature at constant d_0 and Y_{m0}

Investigation of Particle Morphology by SEM

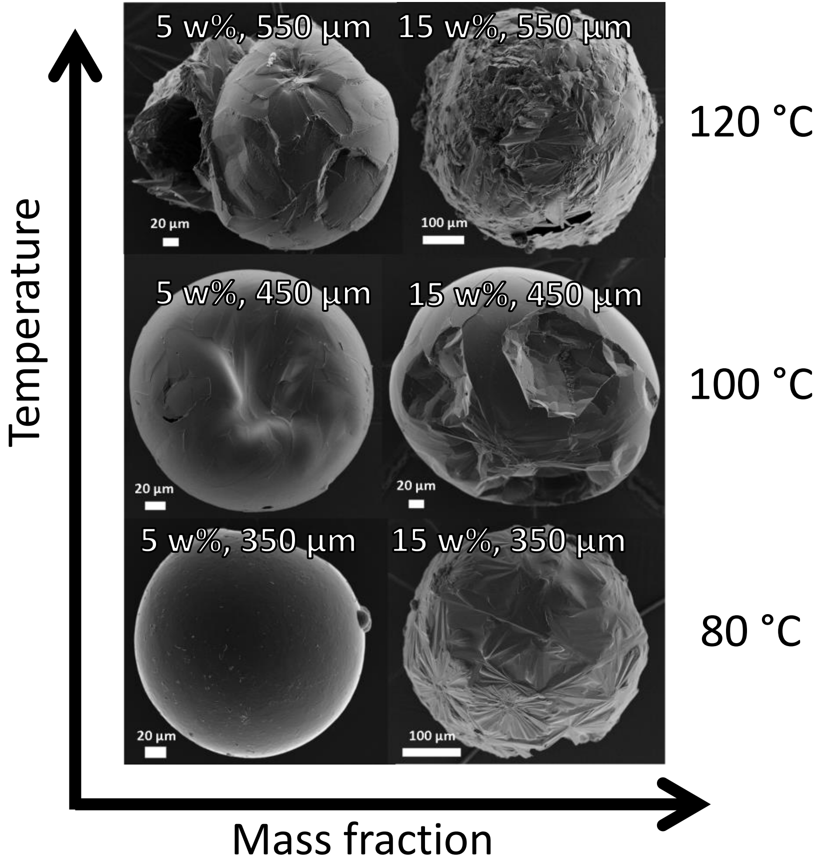
"Morphology map" by SEM

Tailor-made particles

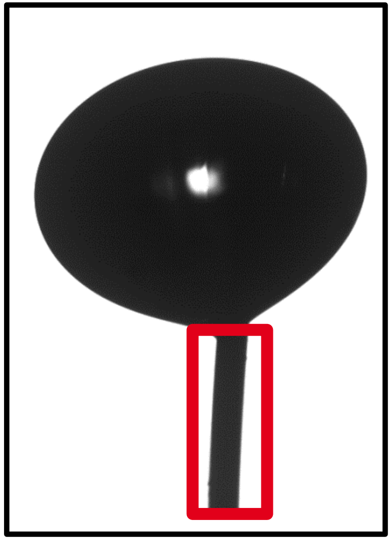
Influences onto particle surface

Mass fraction and temperature ✓

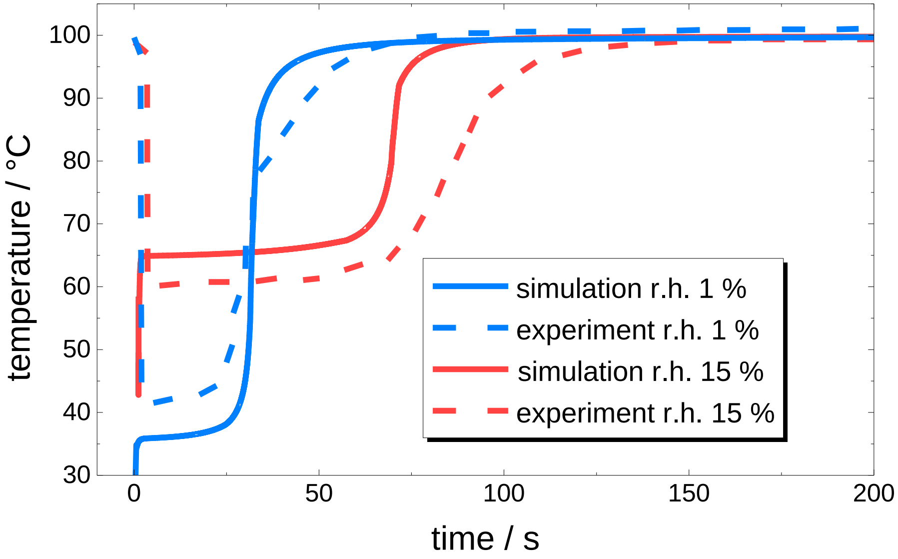
Starting droplet diameter X



Numerical Simulation of Temperature Profile



Thermocouple type K, Ø= 150 µm, ± 0.8 °C



Numerical simulation is able to describe whole droplet evolution at different rel. humidity

Effect of Relative Humidity on Structure Formation

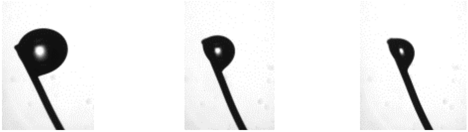
0 s 28 s 34 s 200 s

1 % r.h.

T = 100 °C, d_0= 480 µm, **dry, crystalline**

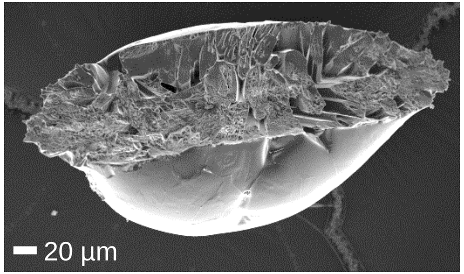
0 s 70 s 200 s

15 % r.h.



T = 100 °C, d_0= 501 µm, **remains liquid**

Quenching of droplet



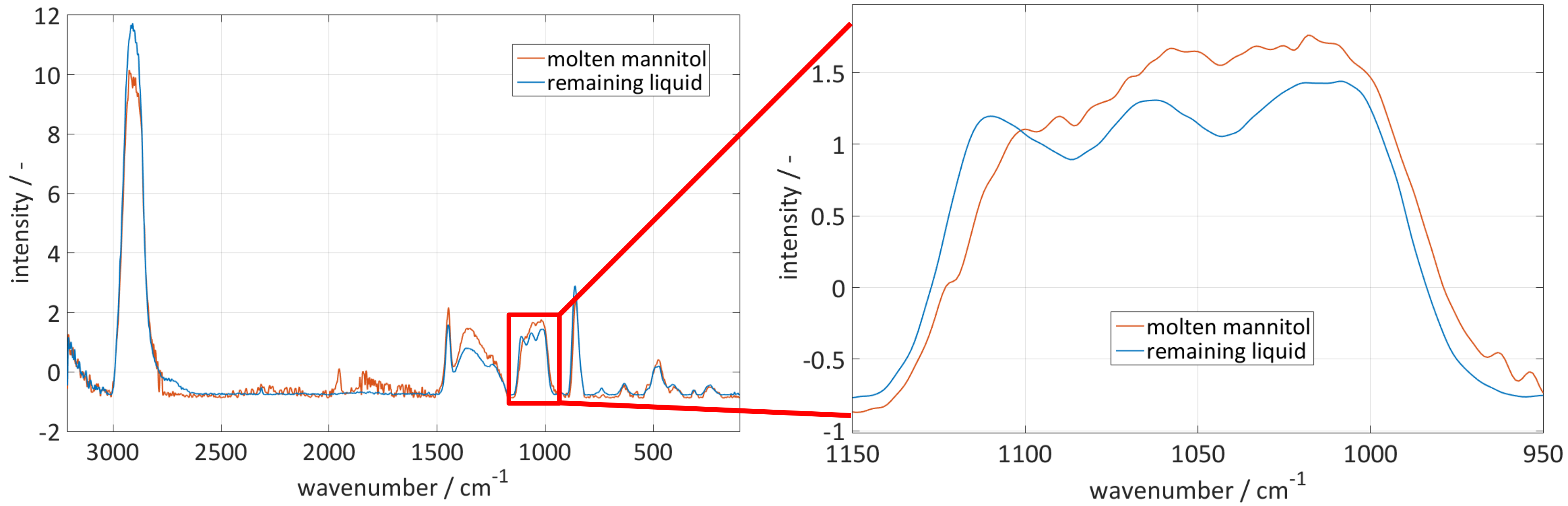
T = 100 °C
15 % r.h.

Mannitol on heating plate

What is the difference between the dry crystalline particle and the remaining liquid?

Raman Spectroscopy of Remaining Liquid and Molten Mannitol

- Melting-point or freezing-point depression should lead to indifferent spectra

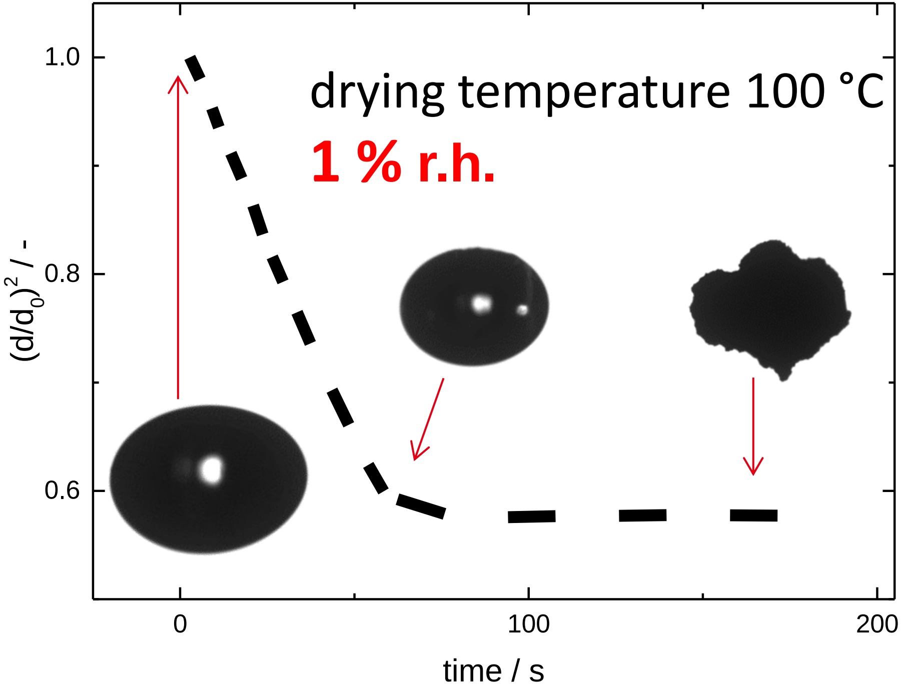


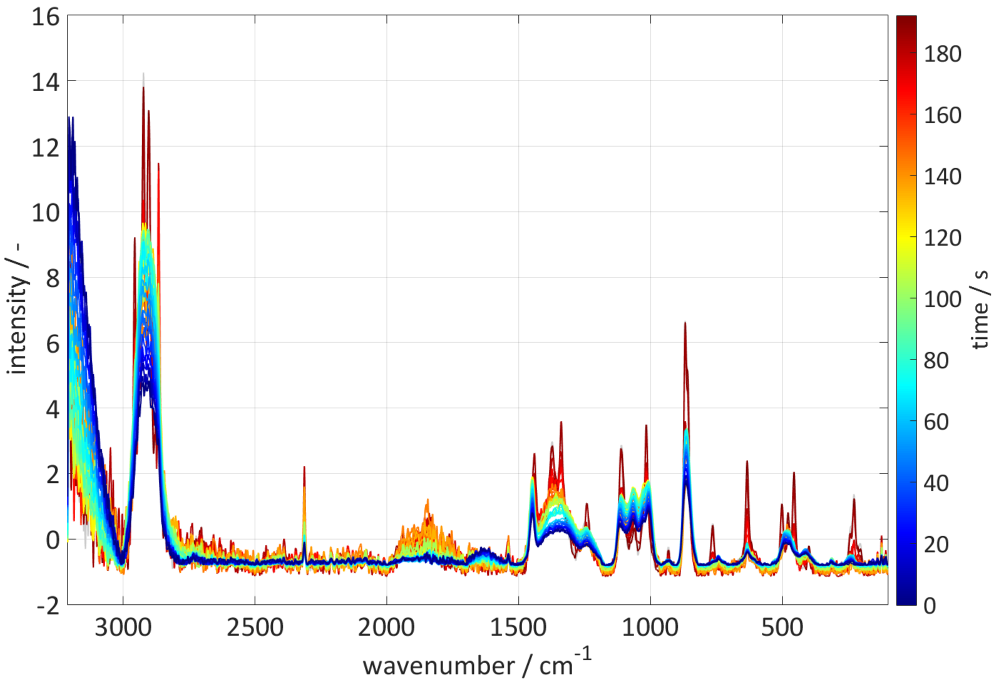
The remaining liquid is not molten mannitol

Study of Evaporation and Crystallization via Raman-Spectroscopy

Fachbereich Chemie

mass fraction mannitol 15 w%; initial droplet diameter 0.7 mm





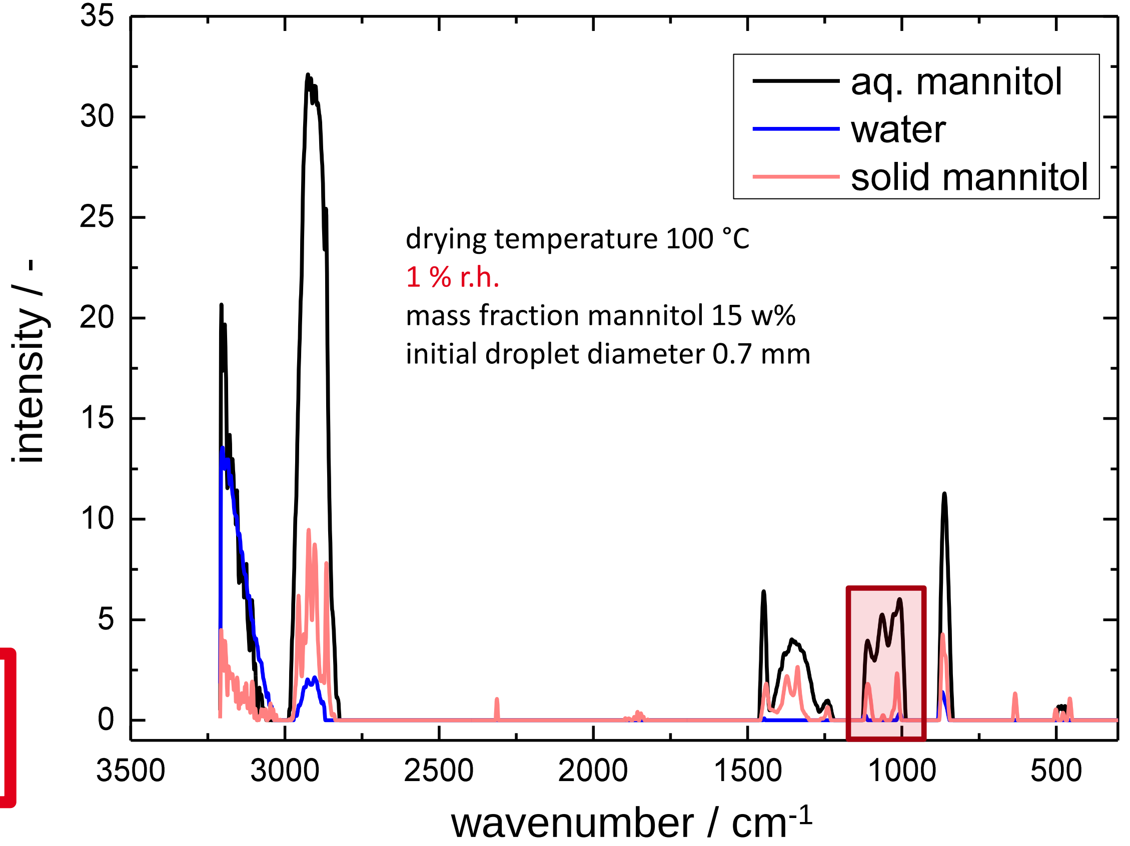
Drying and evaporation can be monitored using Raman spectroscopy

Analyzing the Spectra via Multivariate Curve Resolution (MCR)

MCR suggests 3 components within spectra:

- Aq. mannitol
- Water
- Solid mannitol

How do the concentration profiles evolve?



Cornel, J., Kidambi, P., Mazzotti, M., 2010. Ind. Eng. Chem. Res. 49, 5854–5862.

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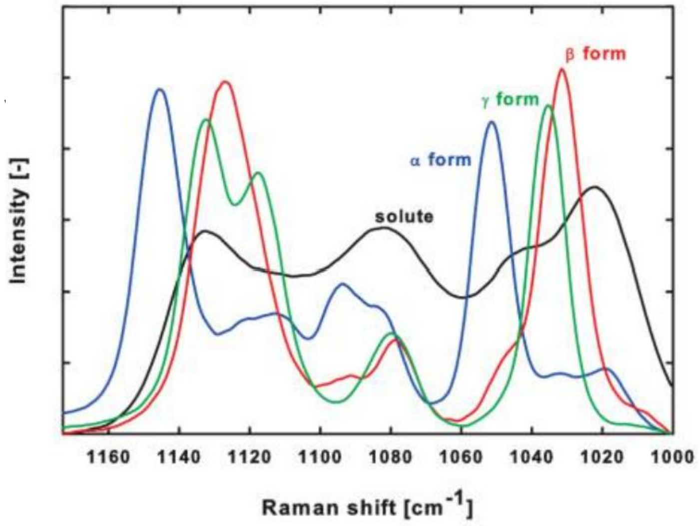

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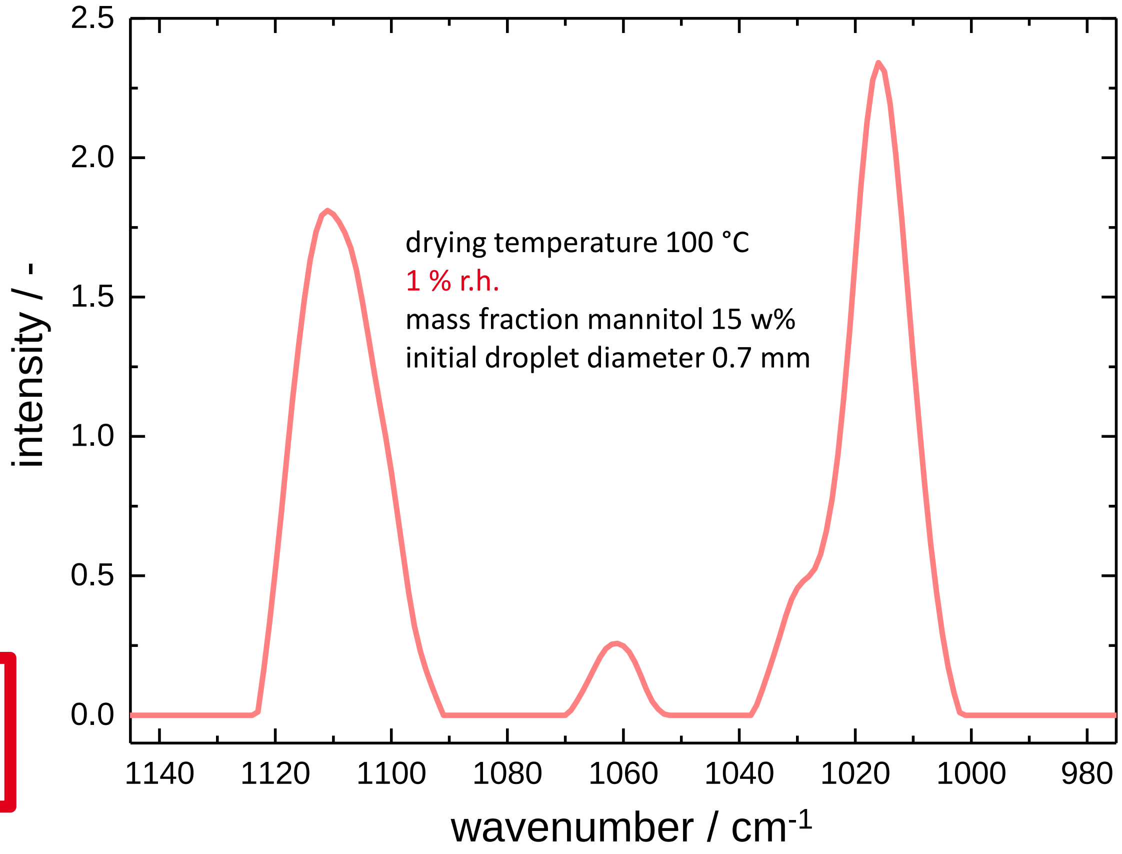

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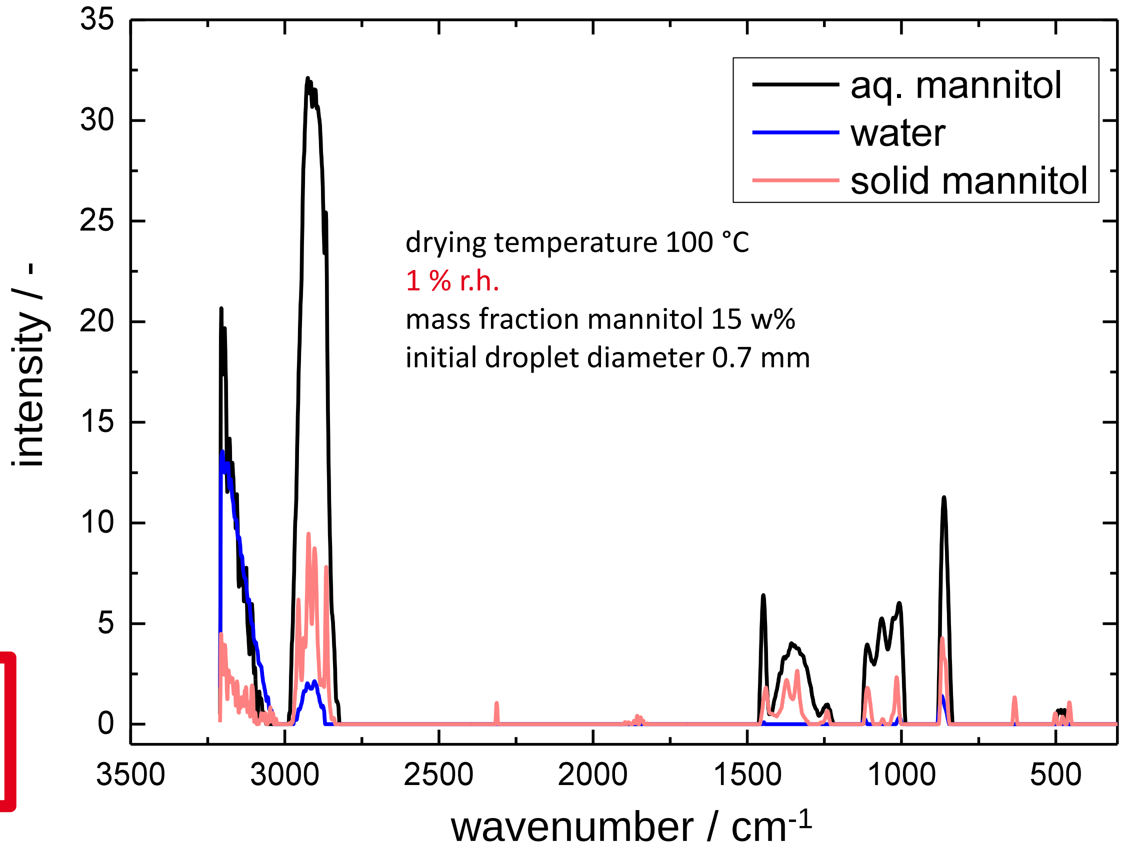
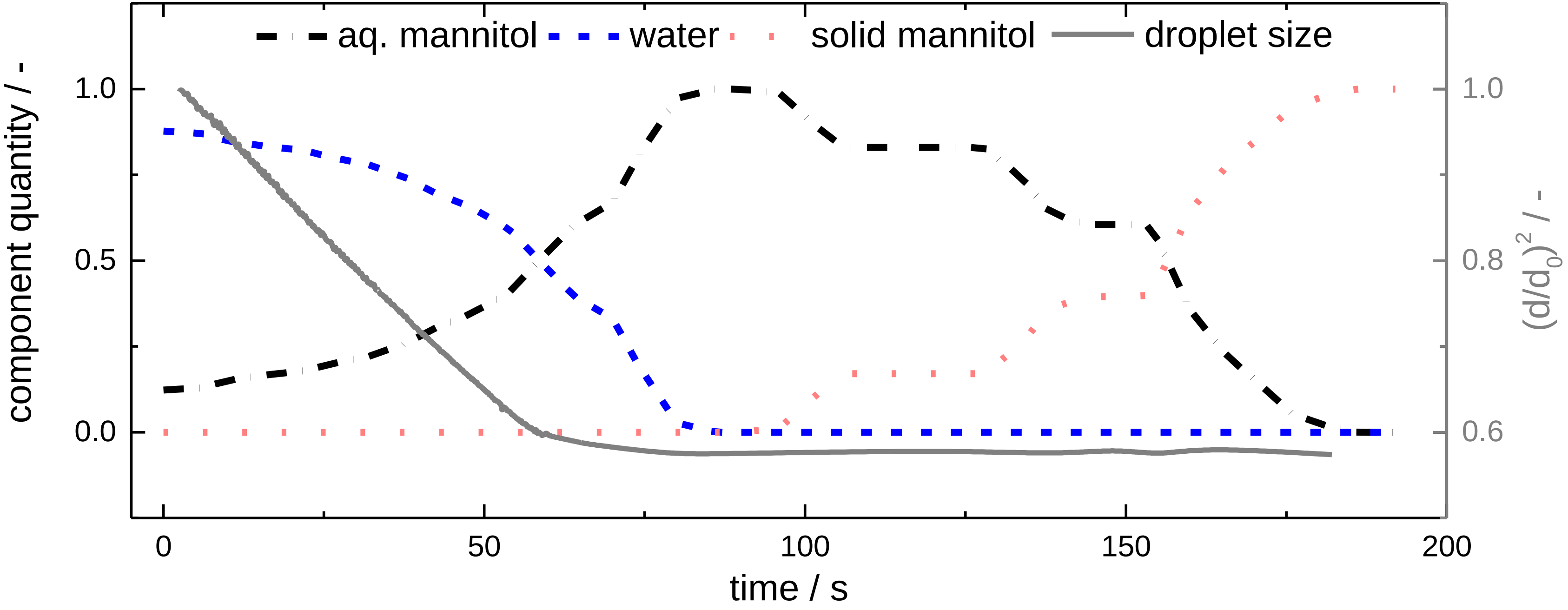


Cornel, J., Kidambi, P., Mazzotti, M., 2010. Ind. Eng. Chem. Res. 49, 5854–5862.

Analyzing Components and Crystallization via MCR

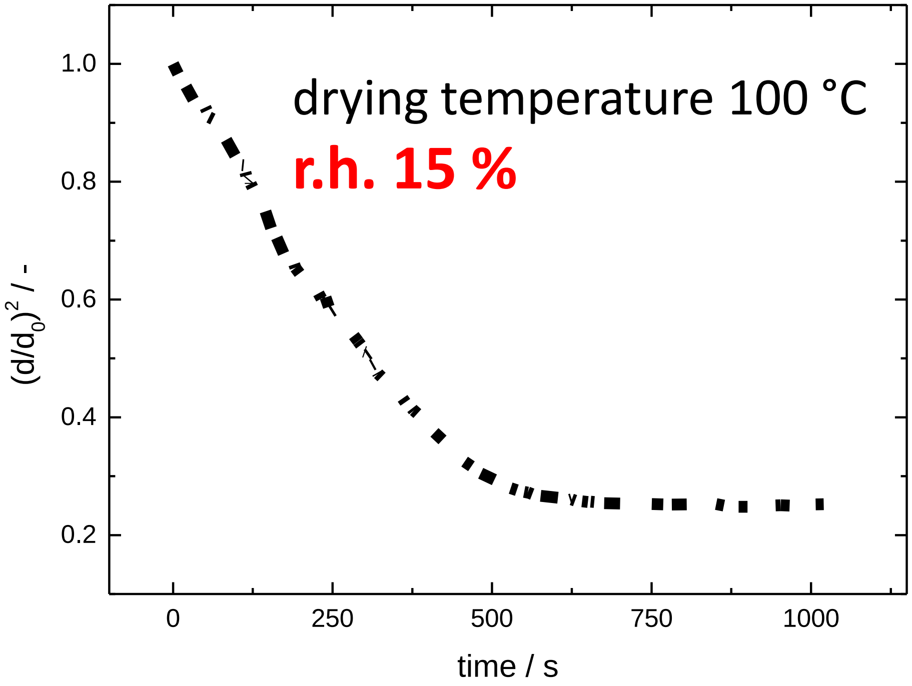
drying temperature 100 °C, 1 % r.h., mass fraction mannitol 15 w%, initial droplet diameter 1 mm

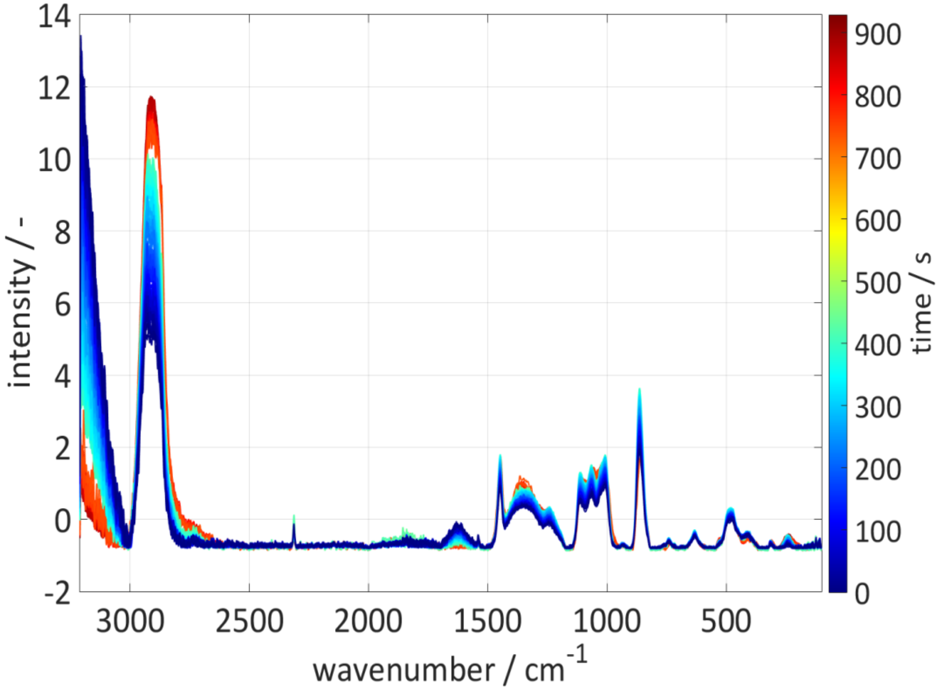


Qualitatively model for evaporation and crystallization accessible

Using Raman Spectroscopy to Resolve “liquid” Mannitol

mass fraction mannitol 15 w%; initial droplet diameter 1 mm





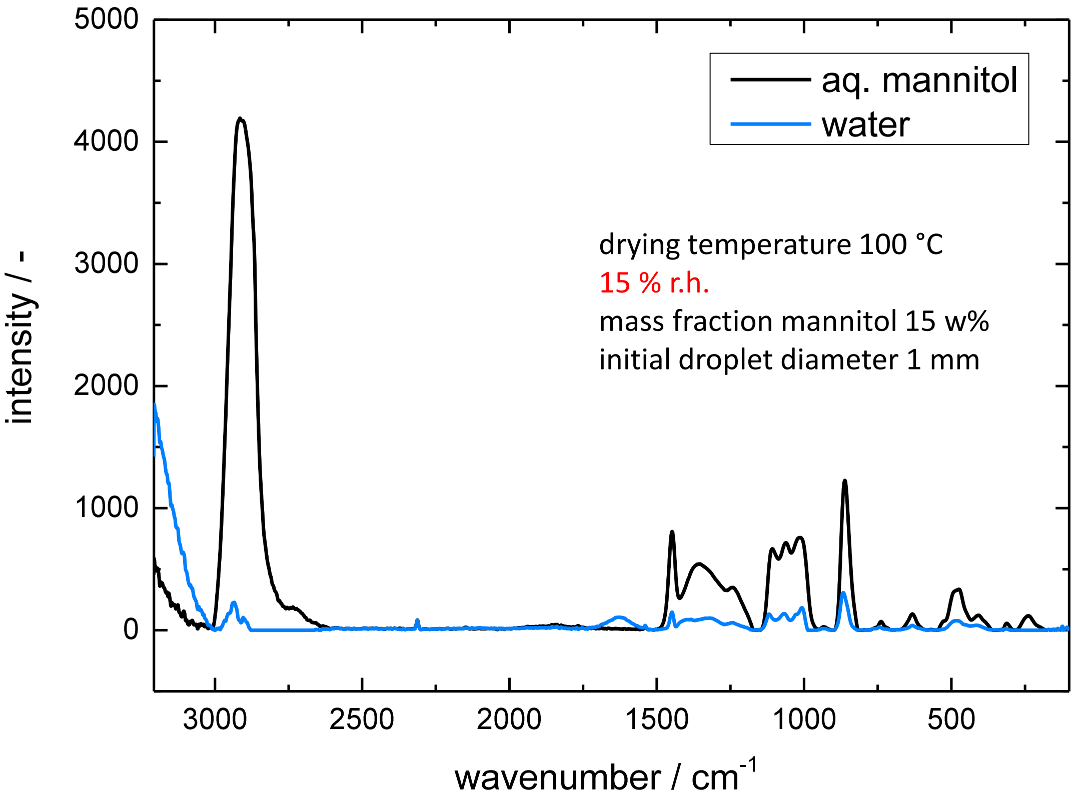
Raman spectra reveal no crystallization

Resolving “liquid” Mannitol out of Spectra via MCR

MCR suggests 2 components within spectra:

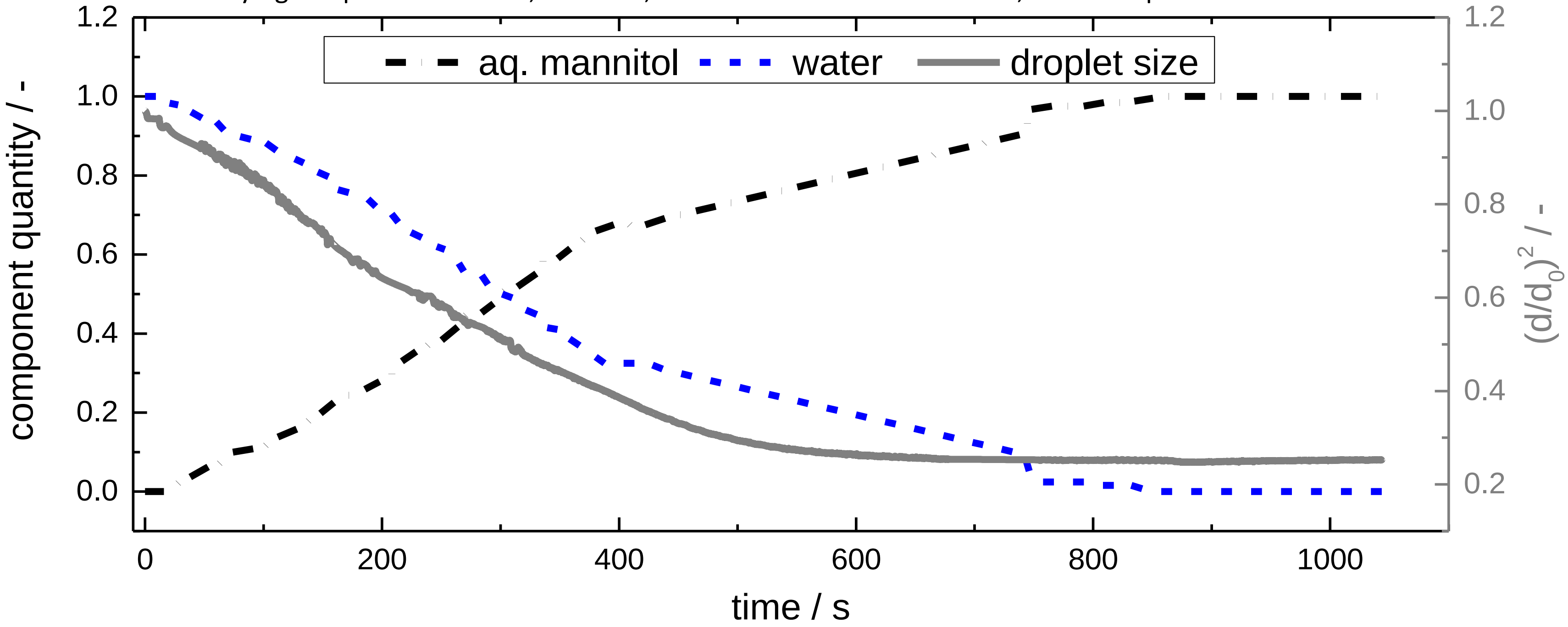
- Aq. mannitol
- Water

R.h. ≥ 15 % prevents crystallization



Calculated Concentration Profile at Relative Humidity 15 %

drying temperature 100 °C, r.h. 15 %, mass fraction mannitol 15 w%, initial droplet diameter 1 mm



Small amount of water prevents crystallization of mannitol

Conclusion and Future Prospects

- Easy accessible „Morphology Map“
- Tailor-made particle structures
  - Solid-layer formation
  - Particle porosity
  - Structure formation
- Numerical model in good agreement with experimental results
- Raman spectroscopy was utilized to monitor evaporation and crystallization
  - At relative humidity above 15 % droplets consist of a oversaturated mannitol solution
  - Remaining water prevents crystallization of mannitol
- Next step: validate results via spray process

Thank you for your attention!