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pvz Zentrum für Pharmaverfahrenstechnik

iPAT Institut für Partikeltechnik

Precision materials characterization and process modeling

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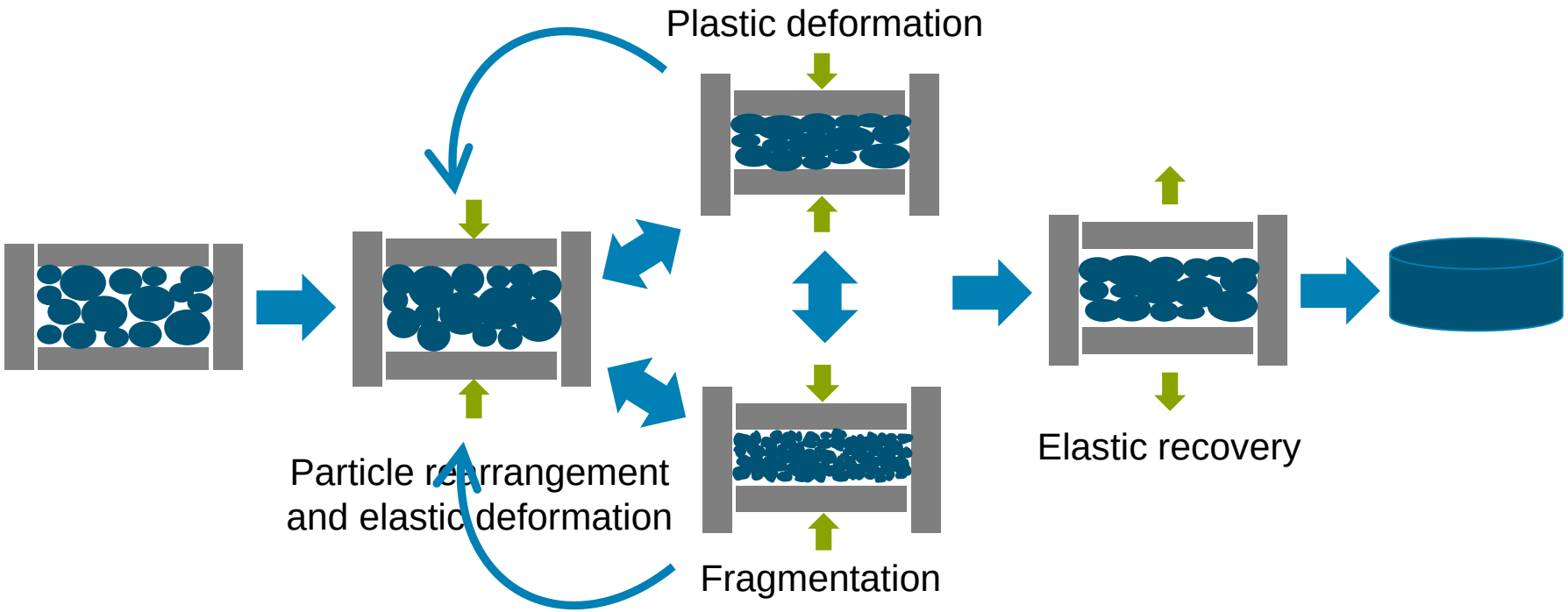
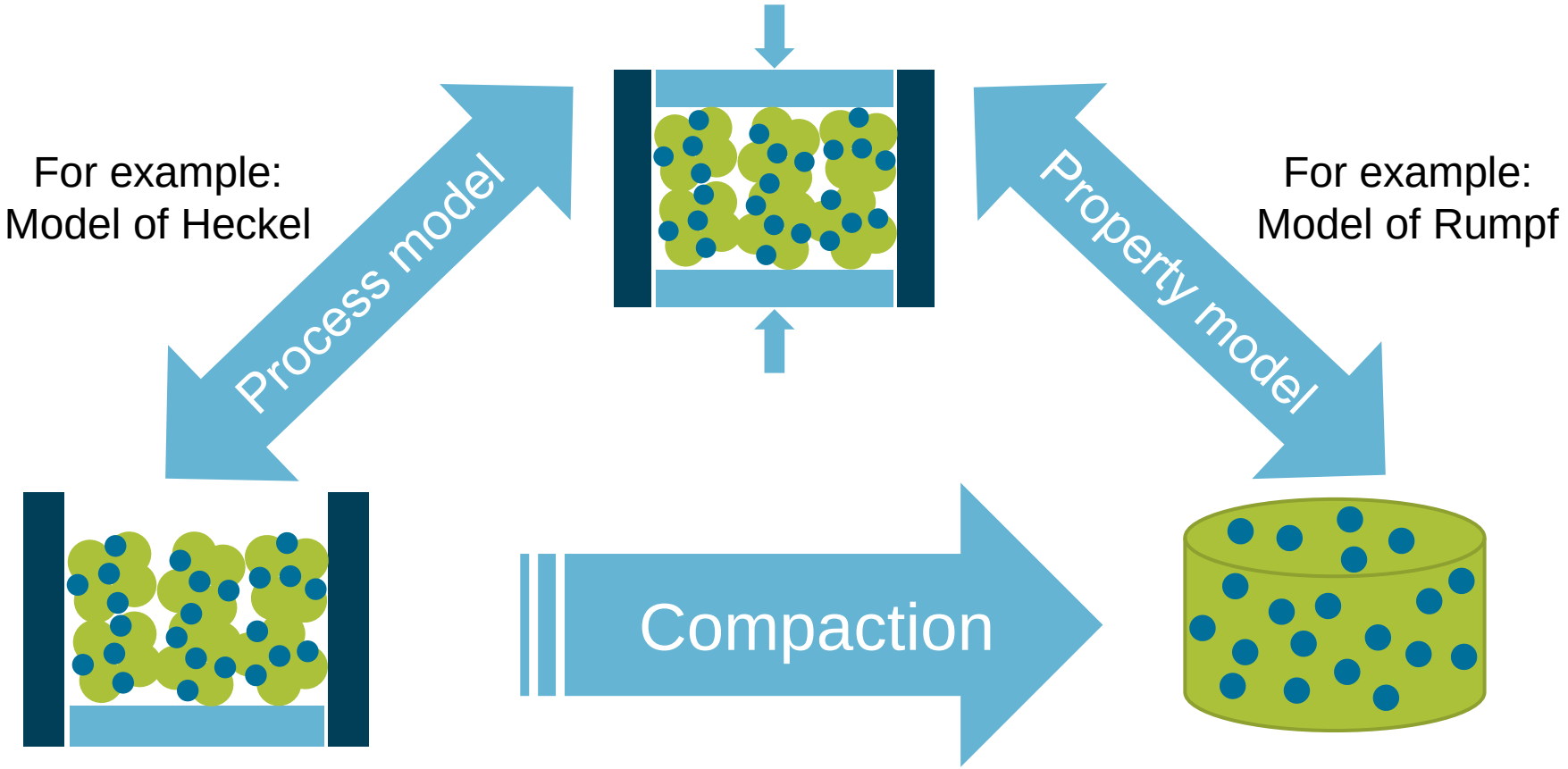
Motivation

- Powder compaction is an important production process in various industries
- A complete physical process understanding is still missing



Our approach – Necessary models



- Material deformation
- Particle size and shape
- Pretreatment / Mixture?

- Porosity
- Tensile strength
- Disintegration / dissolution

Process model for powder compaction

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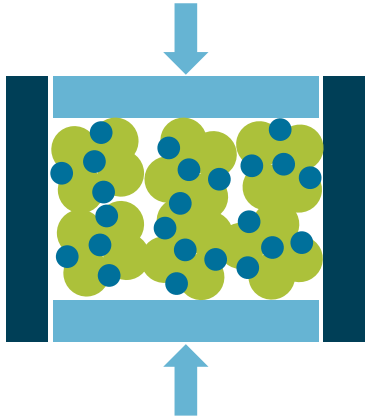
For example:
Model of Heckel

Process model



Property model

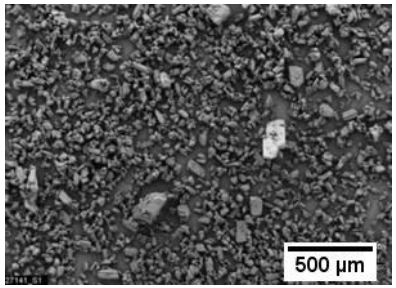
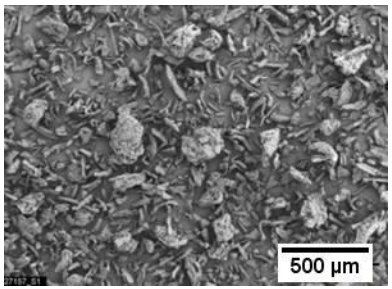
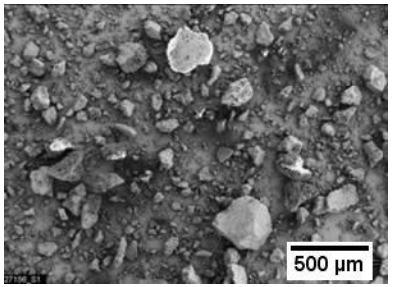
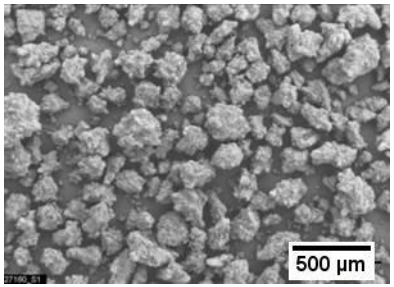
For example:
Model of Rumpf

Compaction

- Material deformation
- Particle size and shape
- Pretreatment / Mixture?

- Porosity
- Tensile strength
- Disintegration / dissolution

Materials and methods

Paracetamol	Microcrystalline Cellulose (MCC)	Lactose An. NF DT (Lactose)	DI-CAFOS A150 (DCPA)
			
($x_{50,3}$ = 43 µm)	Vivapur® 102 JRS Pharma AG ($x_{50,3}$ = 125 µm)	Foremost Farms ($x_{50,3}$ = 136 µm)	Budenheim ($x_{50,3}$ = 189 µm)

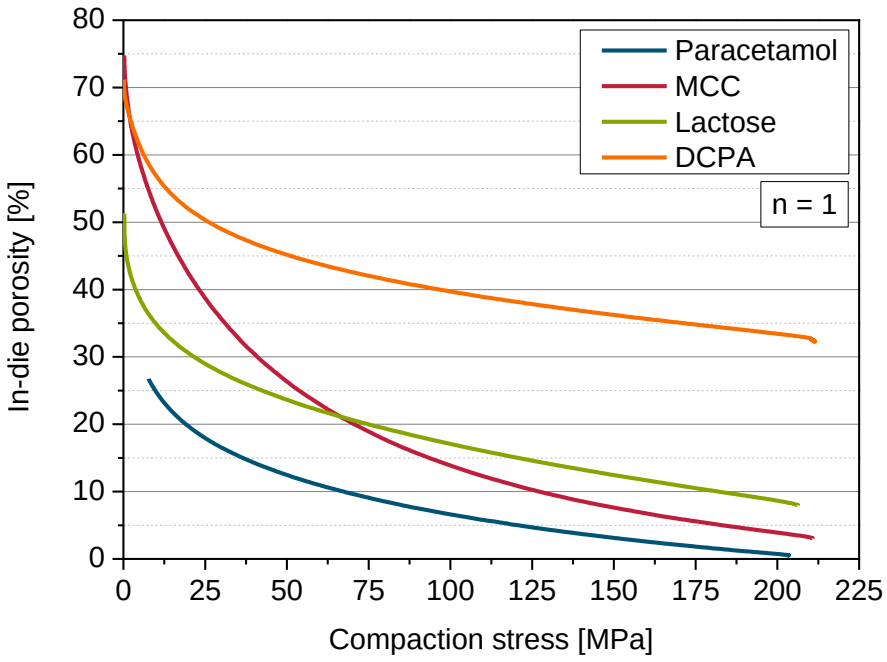
Direct compression using the compaction simulators Styl'Cam and Styl'One Evolution (Medel'Pharm, France)

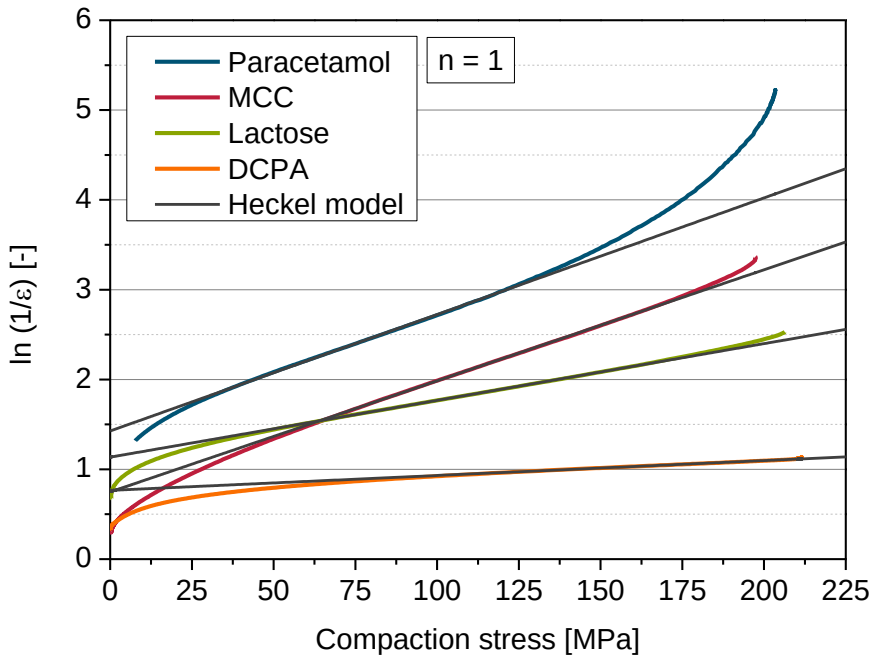
- Displacement driven mode
- External lubrication with magnesium stearate

[1]

[1] Source: Medel'Pharm (France)

Application of the Heckel model





$$\ln\left(\frac{1}{\varepsilon}\right) = k \cdot \sigma + A$$ [1]

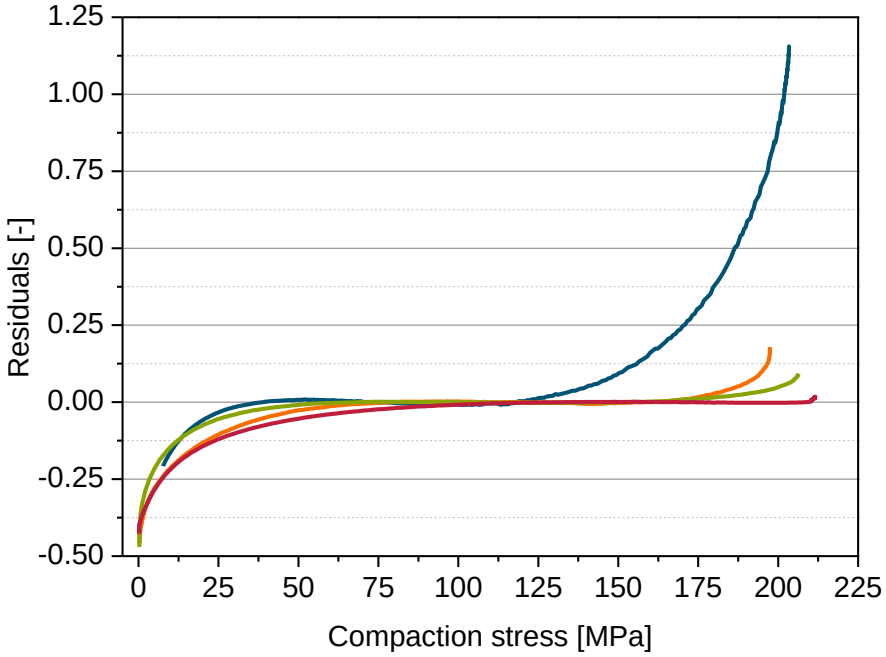
$$k = \frac{1}{3\sigma_0} = \frac{1}{P_y}$$

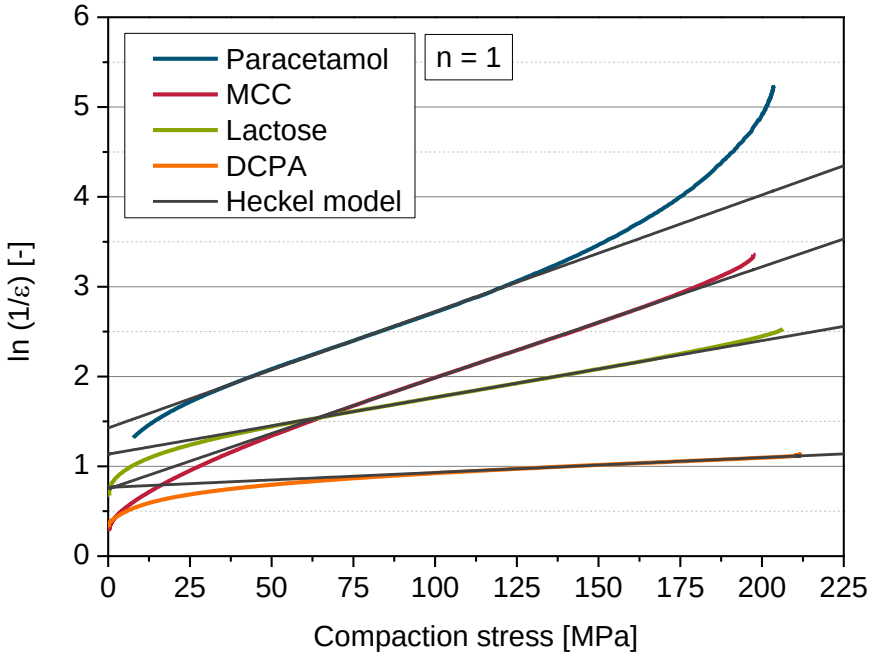
ε : Porosity
k : Heckel constant
σ : Compaction stress
A : Constant
P_y : Mean yield pressure
σ_0 : Yield strength

Krautstrunk et al. (2017): Fachausschuss für Schüttgut- und Agglomerationstechnik

[1] R.W. Heckel (1961): Density-pressure relationships in powder compaction, Transactions of the metallurgical society of aime 221, pp. 671-675

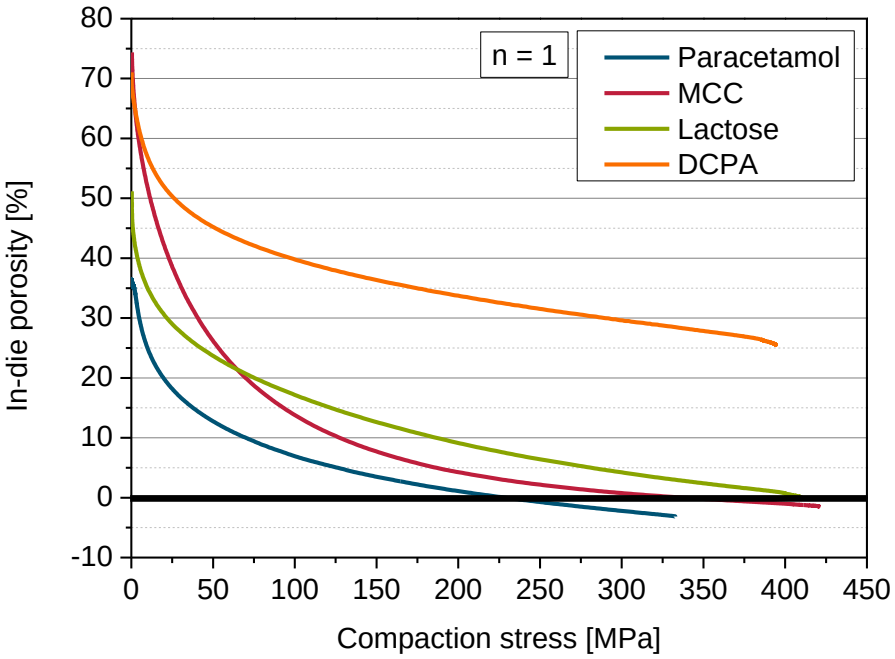
Application of the Heckel model

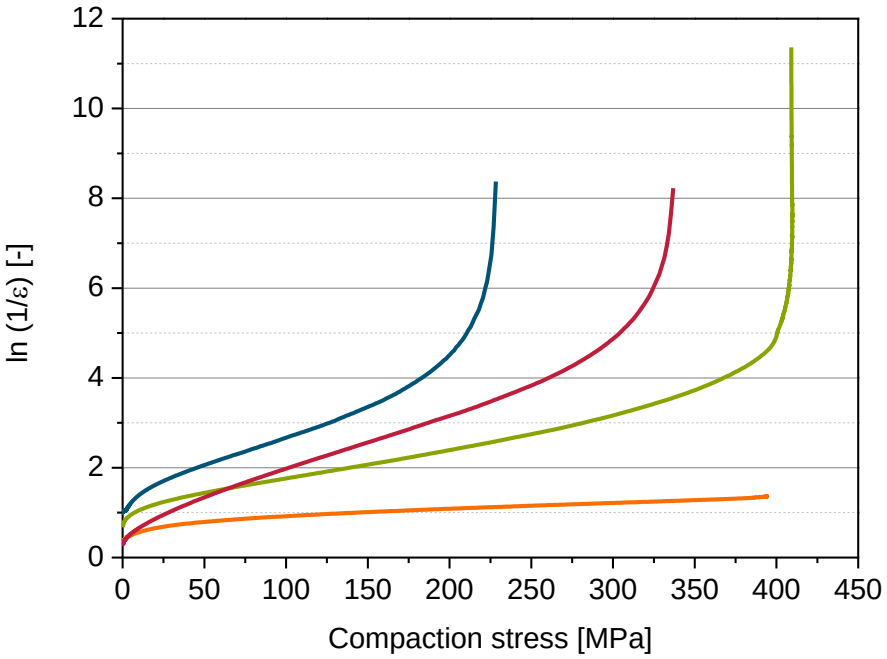




- Only description of the linear region of the compression curve
- Large deviations in the low and high compaction stress range

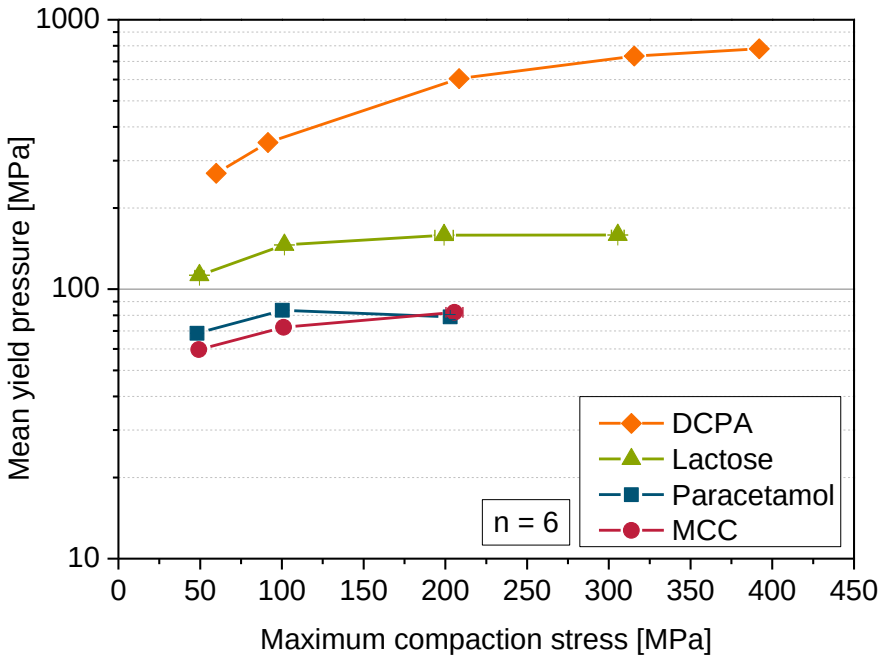
Application of the Heckel model

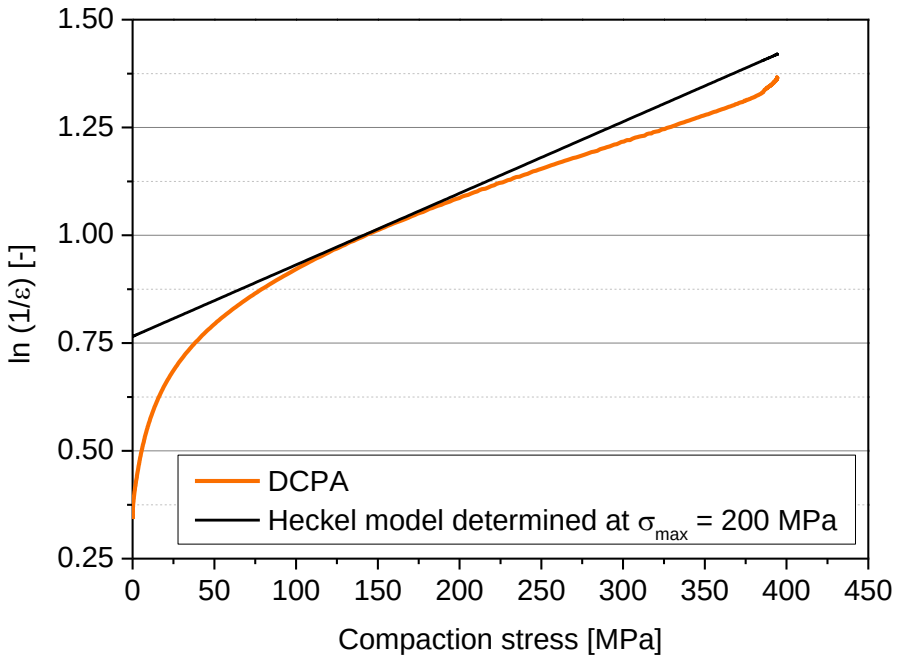




- Frequent phenomenon: negative porosities due to the wrong assumption of a constant solid density → Heckel model is not applicable
- Distortion of the data due to logarithmization

Application of the Heckel model

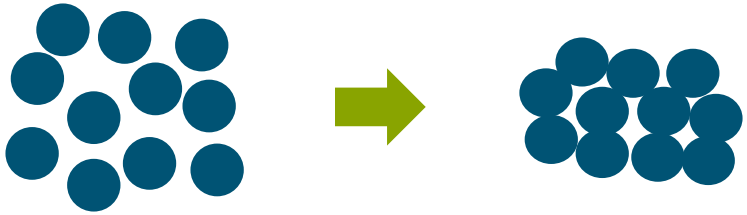




- P_y is pressure dependent → not a pure material constant
- Consideration of the compression curve at highest maximum compaction stress is necessary

Model of Cooper and Eaton

Filling of large pores



Filling of small pores

$$V^* = \frac{V_0 - V}{V_0 - V_\infty} = a_1 \, exp\left(-\frac{k_1}{\sigma}\right) + a_2 \, exp\left(-\frac{k_2}{\sigma}\right)$$

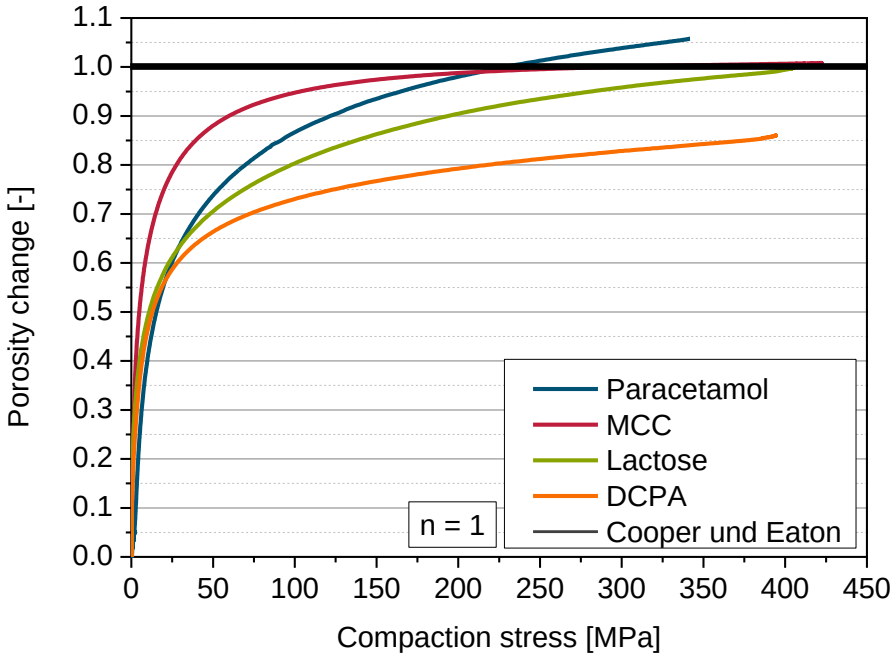
- Initial parameters: V_0 and V_∞
- a_1 and a_2: Measure of the volume change
- k_1 and k_2: Measure of the resistance against deformation

V_0 : Initial volume
V_∞ : Volume at infinite compaction stress
a_1, a_2, k_1, k_2: Constants

Krautstrunk et al. (2017): Fachausschuss für Schüttgut- und Agglomerationstechnik

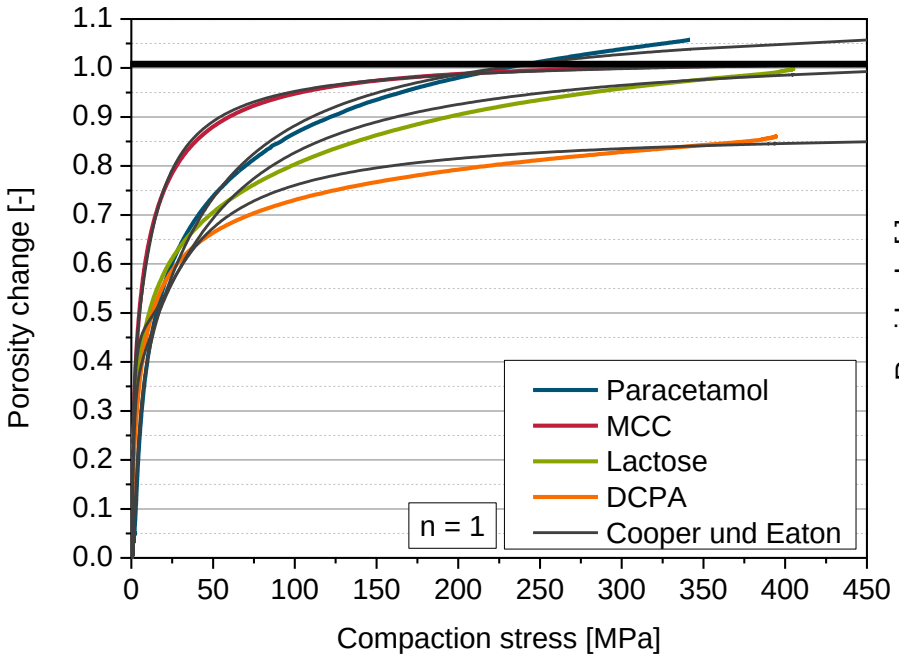
A.R. Cooper, L.E. Eaton, Compaction behaviour of several ceramic powders, Journal of the American Ceramic Society 45 (1962) 97-101.

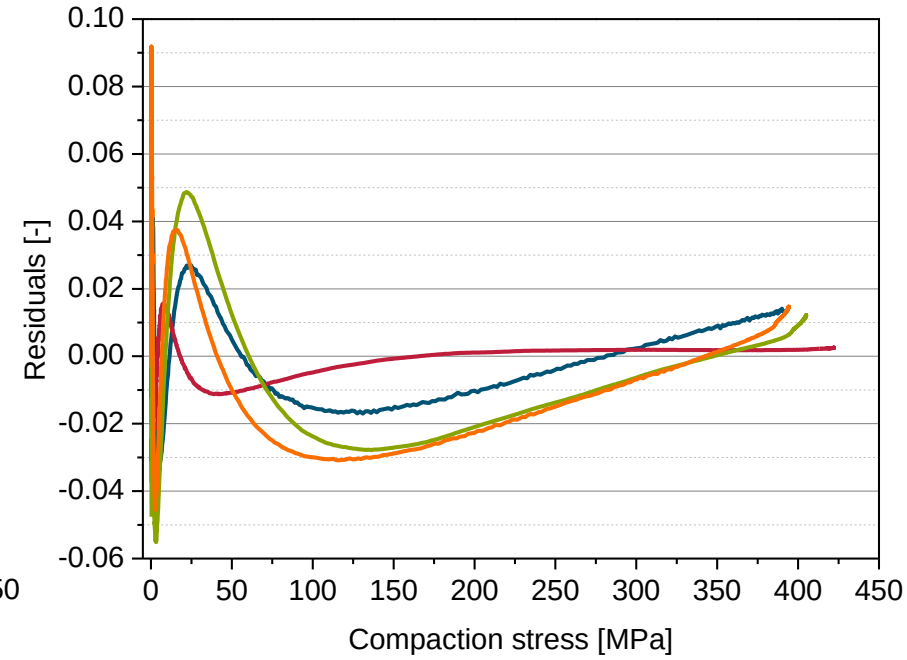
Application of the Cooper and Eaton model



Krautstrunk et al. (2017): Fachausschuss für Schüttgut- und Agglomerationstechnik

Application of the Cooper and Eaton model



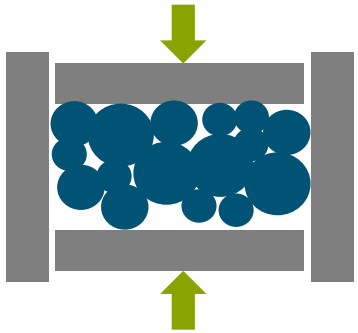


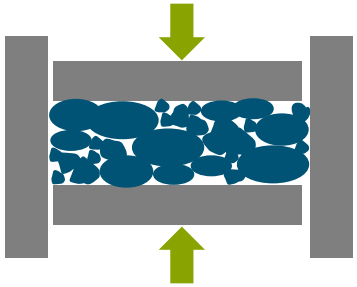
Negative porosities appear as unreasonable values > 1 porosity change

Comparison process functions

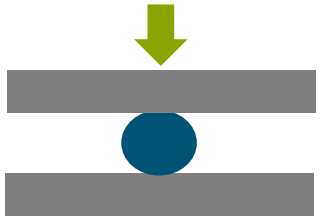
	Heckel	Cooper and Eaton
Description of the whole compression curve		
Correlation with measured data		
Correction of negative porosities		
R^2 [-] for Paracetamol	0.97099	0.99719

Improvement of the characterization of the fundamental deformation behaviour





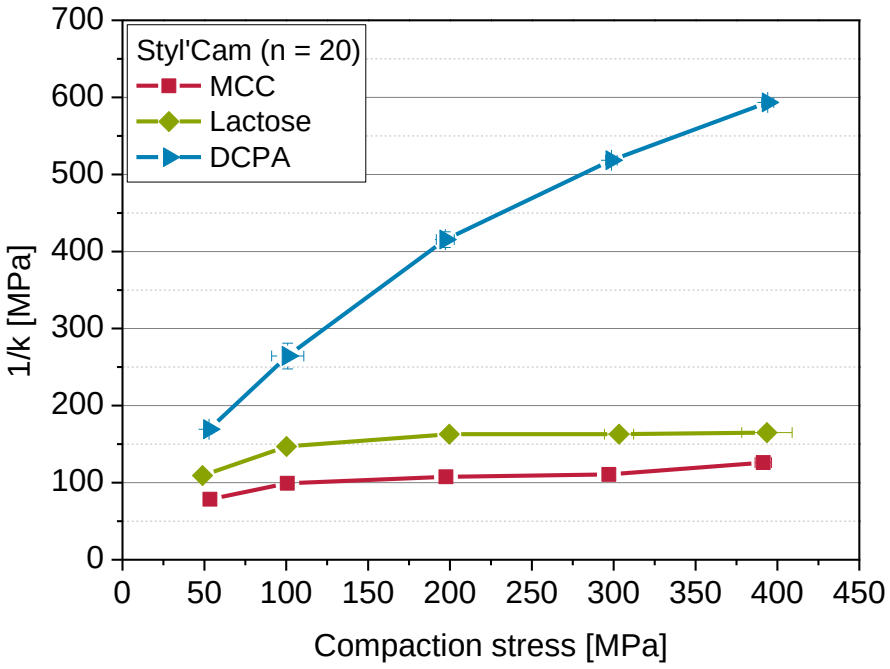
Experimental set-up
Unconfined single particle compression

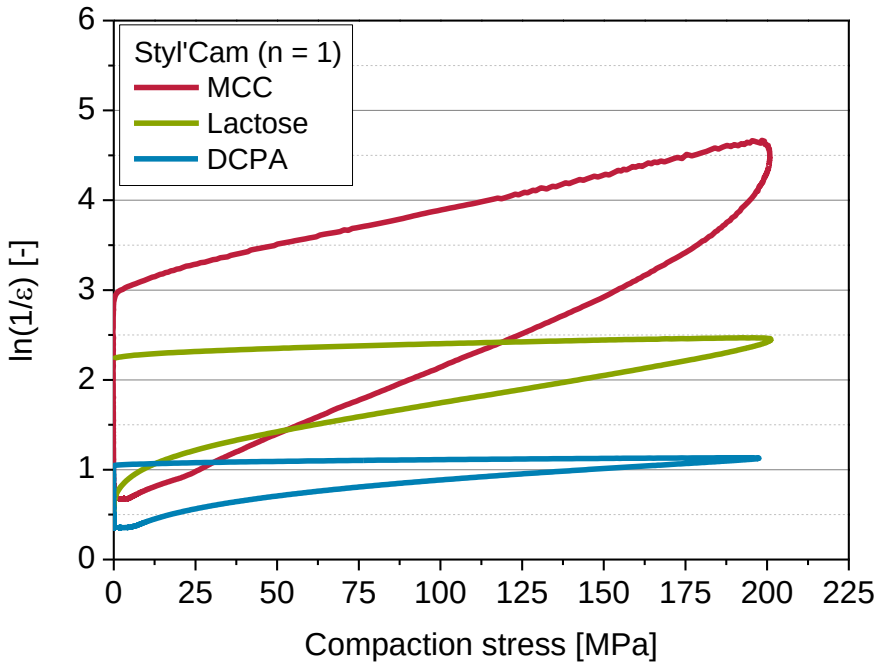


Unconfined single particle compression using the Triboindenter (Hysitron)

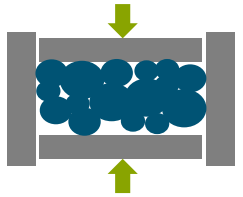
- Flat punch indenter (diameter:100/500 µm)
- Force driven mode
- Compression force: 100 mN
- Loading rate: 25 mN/s

Compression of the powder

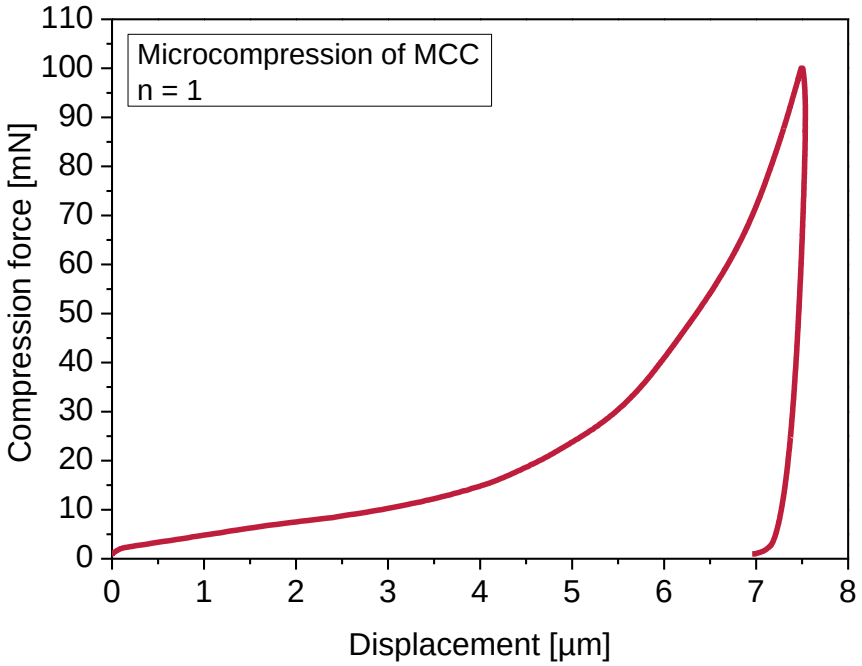


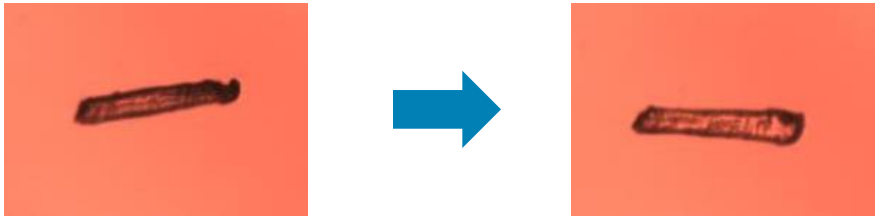


Characterization of the fundamental deformation behaviour by powder compression

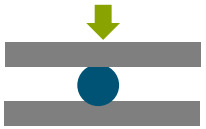


Compression of single particles



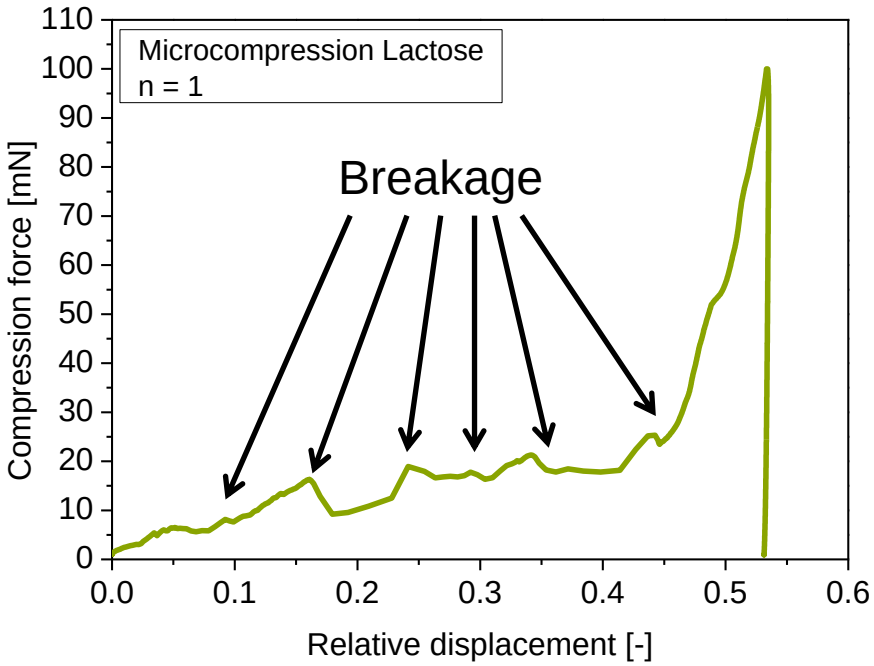


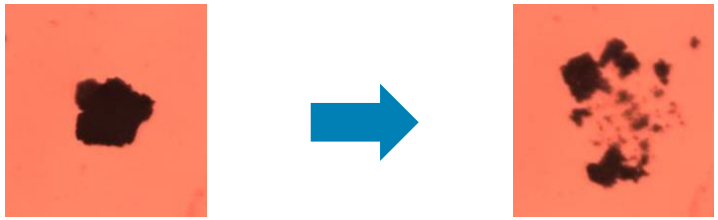
- A plastic deformation behaviour is determined for MCC
- Good correlation with the classification according to the Heckel model



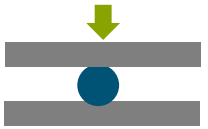
Krautstrunk et al. (2016): Fachausschuss für Schüttgut- und Agglomerationstechnik

Compression of single particles

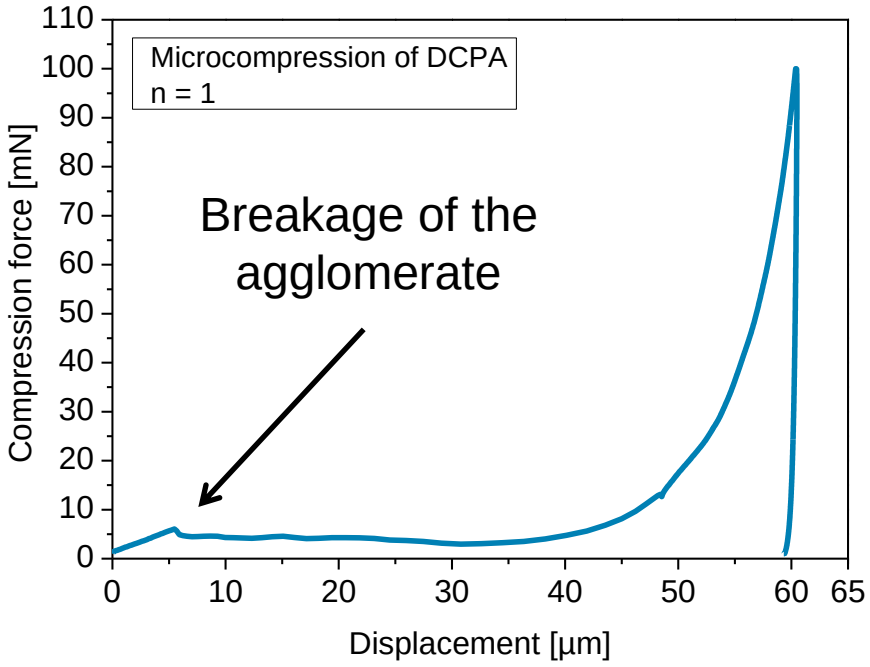


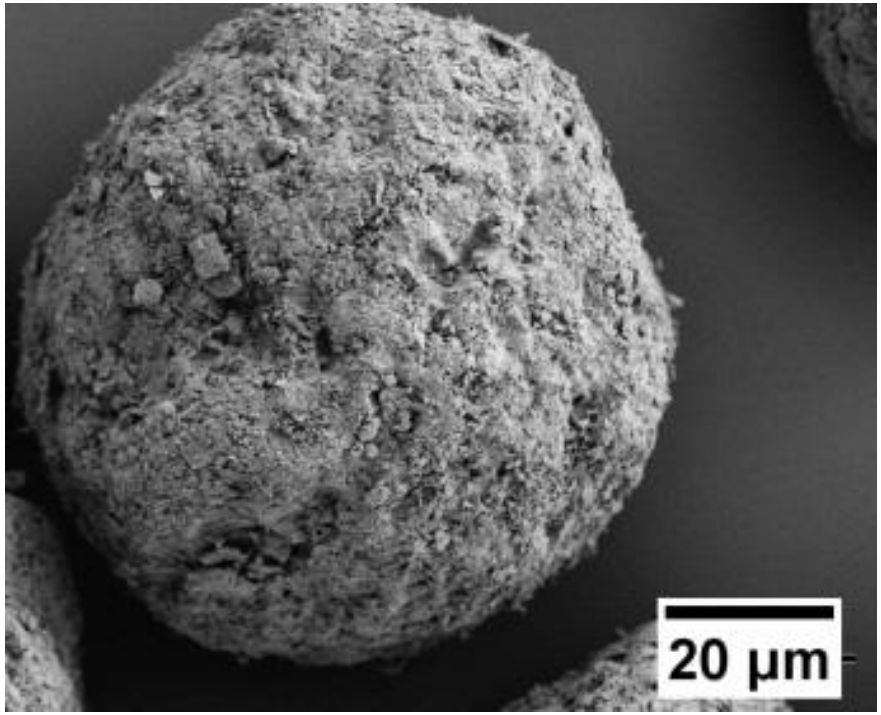


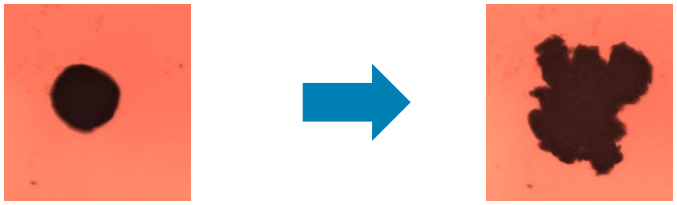
- Breakage of the Lactose agglomerate can be observed → brittle deformation behaviour
- Plastic deformation of the primary particles
- Sharp distinctions between the particles due to their different morphologies



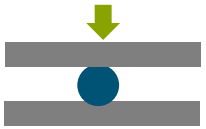
Compression of single particles



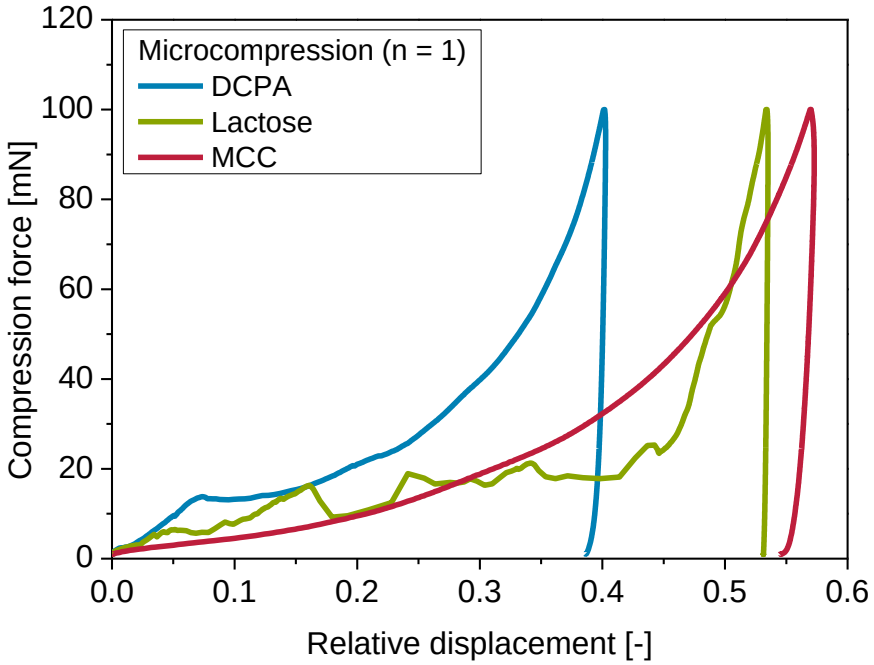


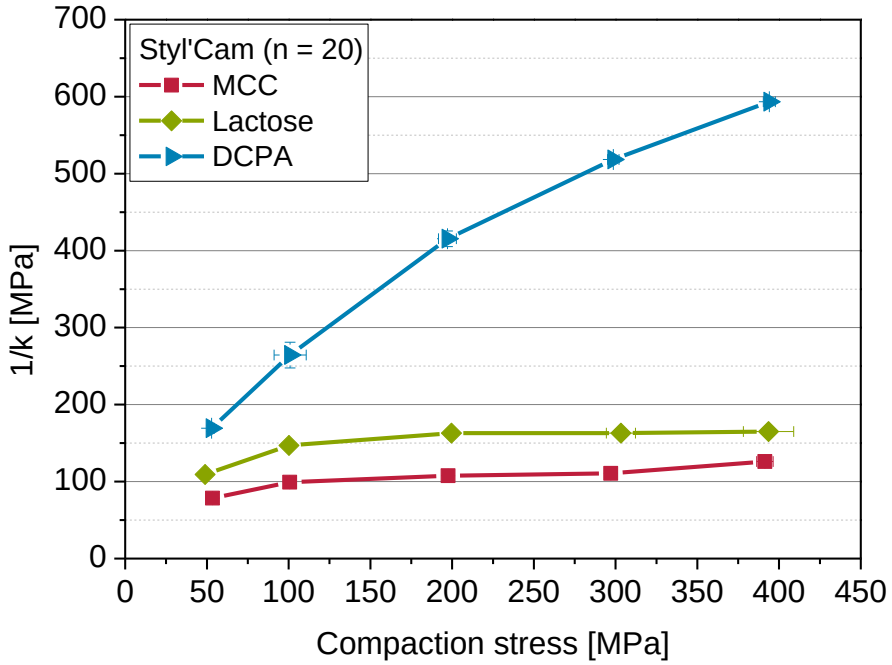


Breakage of the agglomerates at low compression force is observed for all tested particles

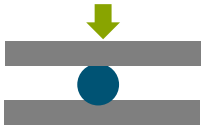


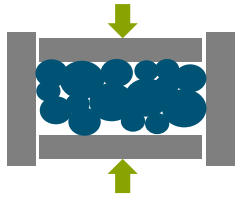
Comparison - powder and single particle compression



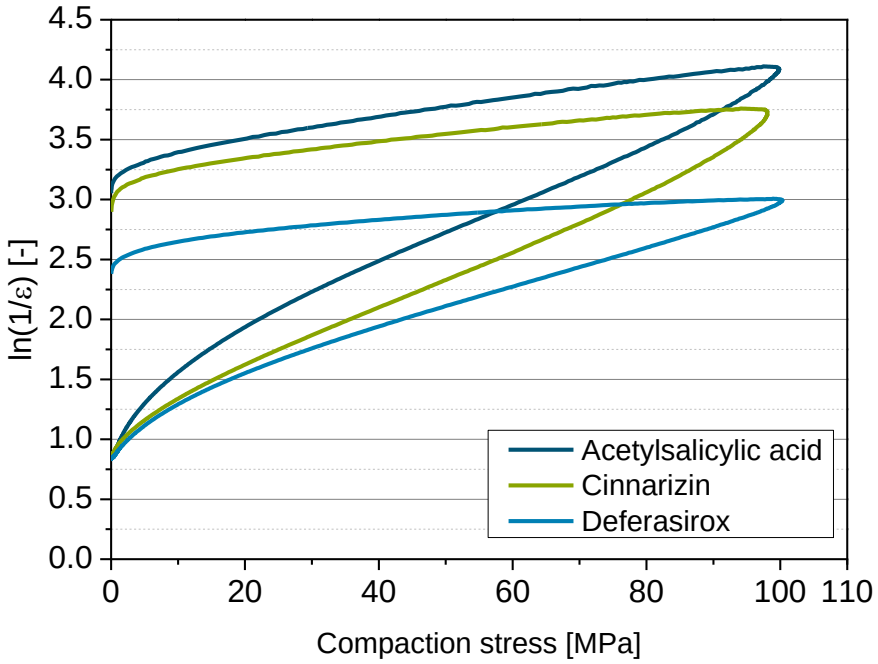


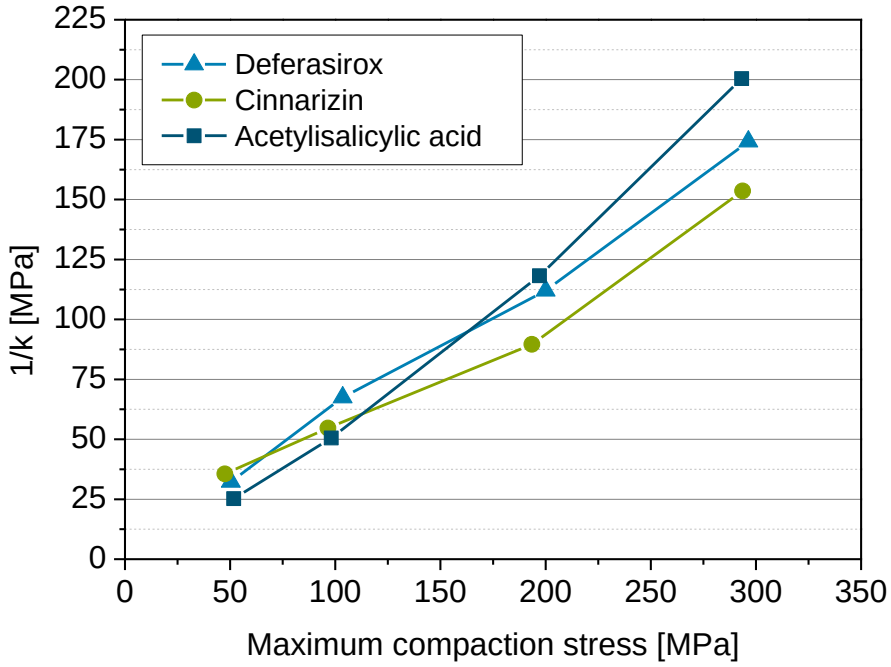
- Correlation between powder and single particle compression
- Challenge: confined vs..unconfined compression





Compression of the powder APIs

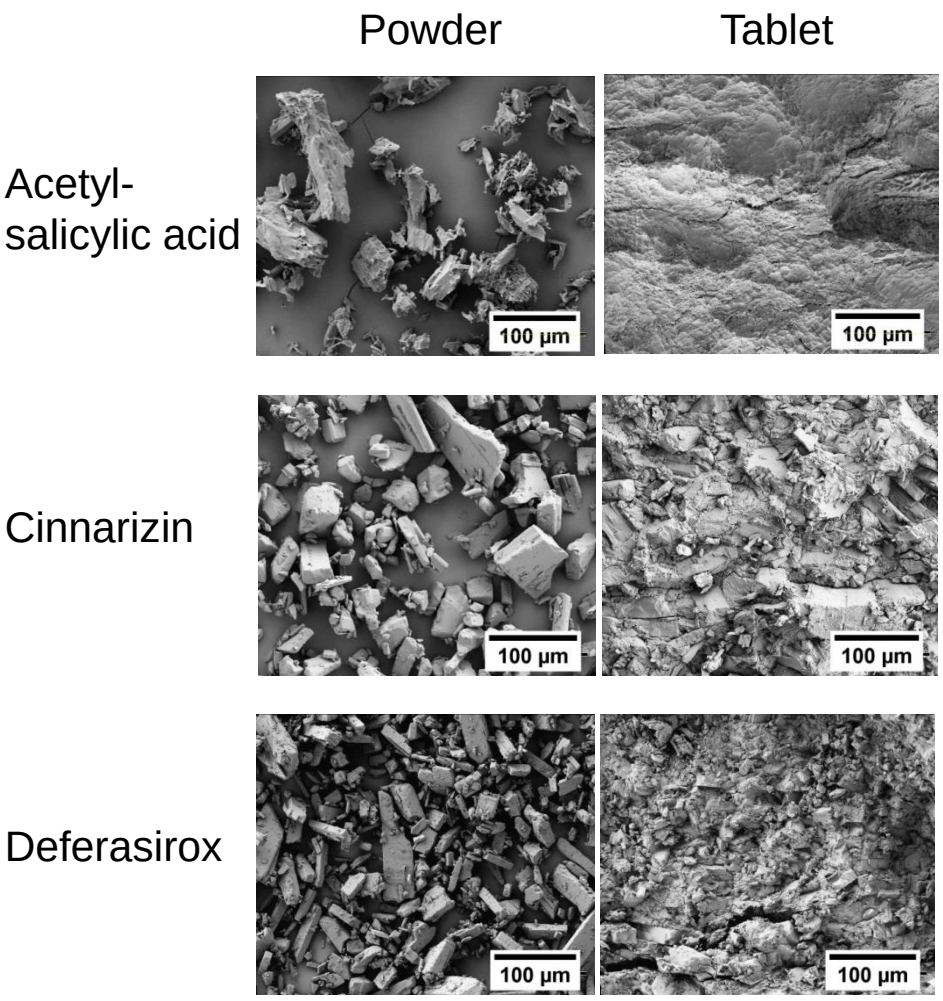


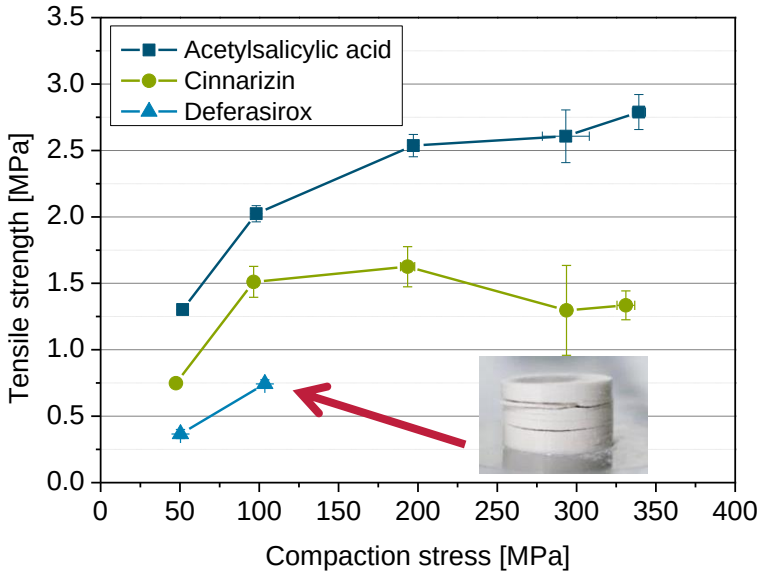


- Different compression behaviour is observed, but comparable mean yield pressures are determined
- Heckel analysis does not capture these differences

Krautstrunk et al. (2016): 10th PBP World meeting

Compaction behaviour APIs





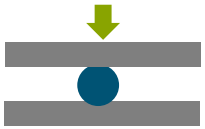
- SEM reveals different deformation behaviour of APIs
- The deformation behaviour affects the resulting tablet properties

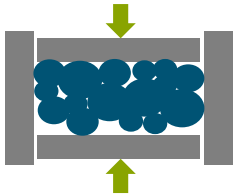
Conclusion and outlook

- The fundamental deformation behaviour affects structural and mechanical properties of tablets
- Comprehensive process understanding is important for prospective work and scale-up
- Mathematical models can contribute to the improvement of the process understanding

Outlook

- Direct correlation between powder and single particle compression
- Investigation of the physical meaning of the modified process function





Thank you very much for your attention!

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