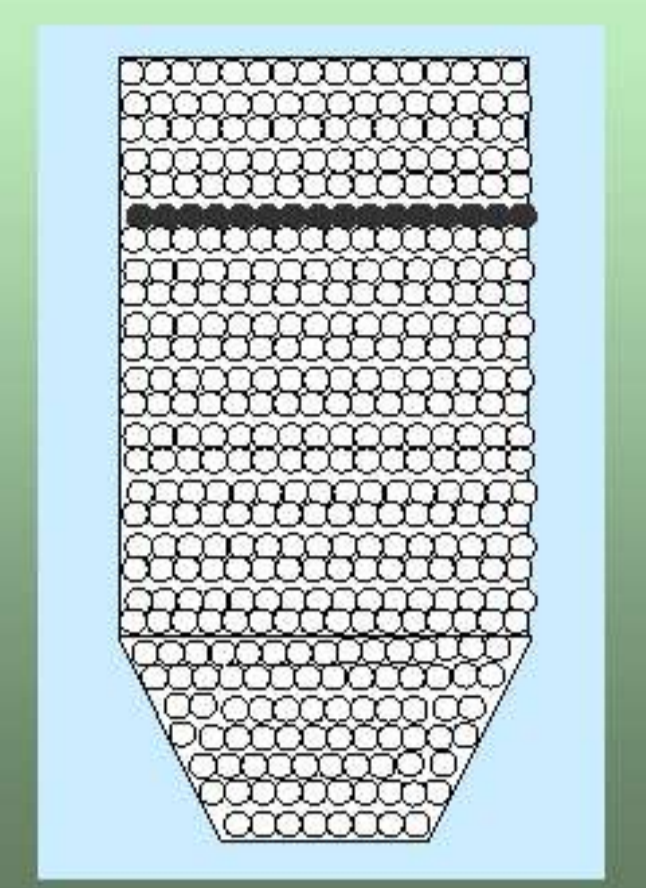


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Proposed Way to Study Segregation

- Bench Scale Silo of 16 kg (≈ 30L & 1:20)
- Use of a thin layer of an "active" ingredient in the silo. Similar to the method of the pulse used in reaction engineering
- Taking samples to measure the *conc.* at the outlet



Minimizing segregation tendency in pharmaceutical powder mixtures

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A phenomenological model for predicting segregation in particulate mixtures

Development of multivariable coefficients through statistical analysis

J.-S. Simard N. Abatzoglou

PPPI, Montreal, 2005

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Definition of N_{SAS}

Expression of the tendency to segregation

- Non-dimensional number that allow to compare the segregation tendency of different systems

$$N_{SAS} = \frac{[d_{p1} - d_{p2}]^2 * \left[\frac{\rho_{s1}}{1 - \epsilon_1} - \frac{\rho_{s2}}{1 - \epsilon_2} \right] * \left[\frac{1}{w} \right]^2 * [\psi_1 - \psi_2] * \left[\frac{M_1}{M_2} \right]^2 * [v] * [\mu]}{\rho g \frac{[6 \tan(\phi) d^2 H_{c,ij} + [d^3 - d_s^3]]}{[6 \tan(\phi) d_s^2]}}$$

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A Typical Example of a DOE

- Dry granular system, spherical and non cohesive
- 2³, partially replicated
- Apparatus : transport and the compression machine hopper

Conditions

- Two size ratio : ≈2:1 and ≈4:1
- Two density ratio : ≈1.5:1 and ≈2.5:1
- Two types of flow « Mass » and « Funnel »
- Measurement : C% vs t_{equivalent}

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The "Excipients"

- Cohesive systems**
 - Foremost Farm # 310 : 93 μm (average size), angular
 - Foremost Farm # 312 : 31 μm (average size), angular
 - Foremost Farm # 316 (Fast Flo) : 93 μm (average size), spherical
- Non Cohesive Systems**
 - Sugar spheres
 - Sphericity : ≈0.99
 - Size ranges
 - 500-600 μm
 - 600-710 μm
 - 710-850 μm
 - 850-1000 μm
 - 850-1150 μm
 - 1000-1180 μm
 - 1000-1400 μm

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Classification of materials tested

- Based on literature and observations
 - Type of flow
 - Type of inter-particle forces

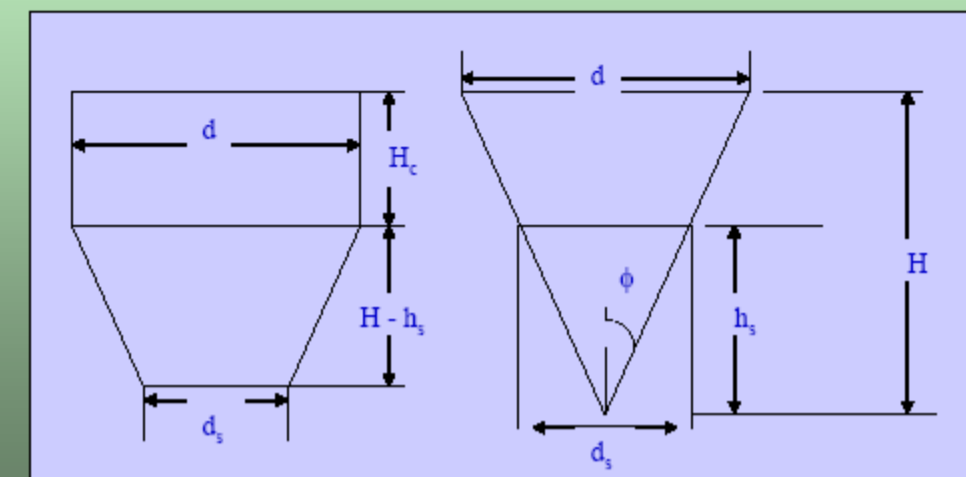
Mass Flow + Cohesive	Mass Flow + Non Cohesive
Funnel Flow + Cohesive	Funnel Flow + Non Cohesive

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Use of N_{SAS} for the scale-down

The principle of geometric and dynamic similarity was used for the scale-down

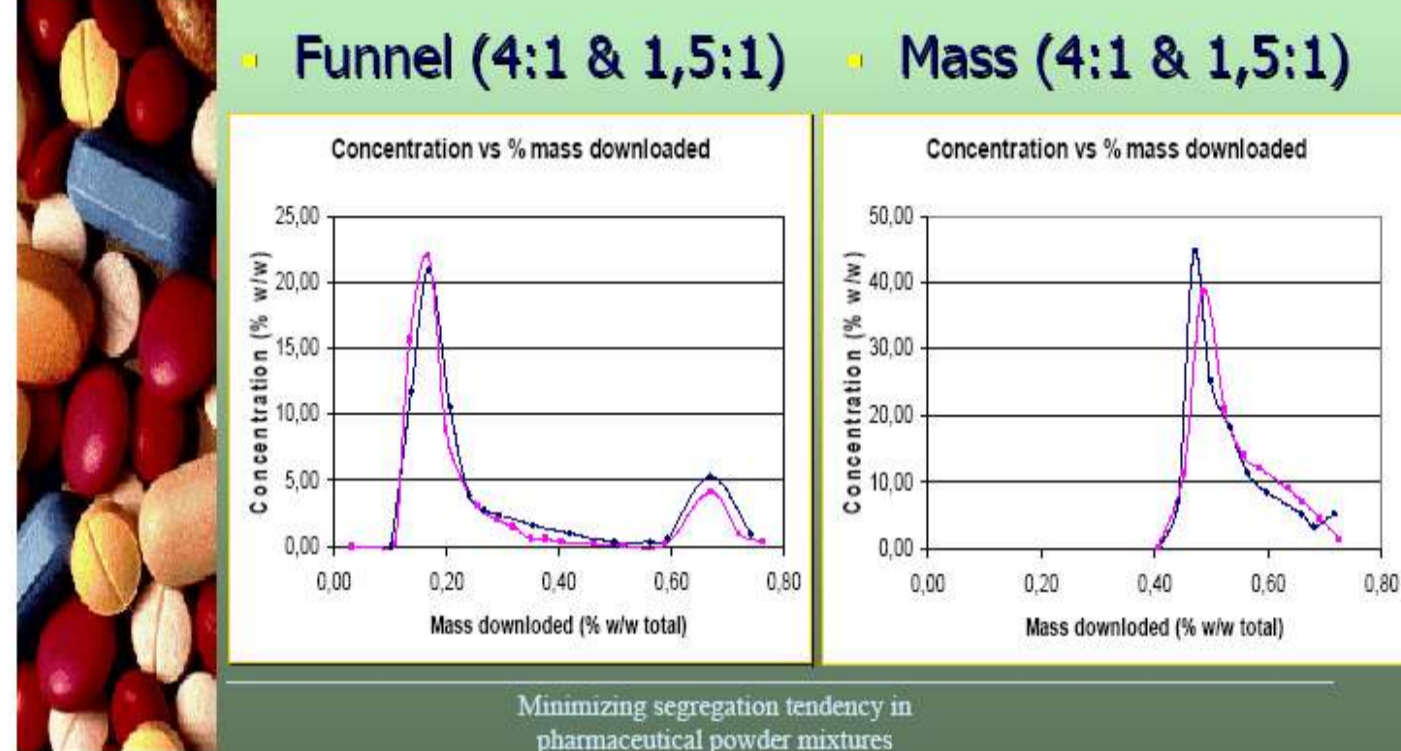


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Typical readings

- Funnel (4:1 & 1,5:1)
- Mass (4:1 & 1,5:1)



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Usefulness of method and models

Analysis of Non-Cohesive Systems

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Statistically significant parameters

- Average time, t_m
- Type of flow
- Size Ratio
- Density Ratio
- Variance σ
- Type of flow
- Size Ratio
- Bin Geometry

Storage Time and Components Conc. were not proven conclusive at the range tested

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Modeling for t_m

$$t_m = \frac{E}{(D * d)^{0.2}} = E * (D * d)^{-0.2}$$

- E : Flow factor (=18 for Funnel Flow and 30 for Mass Flow)
- D : Ratio of diameters of the two components
- d : Ratio of densities of the two components

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Modeling for σ

$$\sigma = EG * D^{0.2}$$

E-G Form factor

Geometry	Flow	Funnel	Mass	
		Prismatic	80	8
		Cylindro-conic	8	6

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Comparison Table

If	$t_m \uparrow$	$\sigma \downarrow$	Then:
			Dispersion speed and propagation are lower. The system is more stable and segregation tendency is lower.
	$t_m \downarrow$	$\sigma \uparrow$	Dispersion speed is lower but propagation is faster. The system is less stable and segregation tendency increases.
			Dispersion speed is faster but propagation is lower. Our conclusion is uncertain. More work is needed by playing with variables.
			Dispersion speed and propagation are faster. The system is less stable and segregation tendency is higher.

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How to apply the method

- Take a granular system which gives a marginally "acceptable" RSD of its product and apply the method
- Take the new system under study and apply the method
- Compare results (in terms of t_m and σ)
- Use the "Comparison Table" to decide whether the system under study has a higher or lower tendency to segregation

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Analysis of Cohesive Systems

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Statistically significant parameters

- Average time, t_m
- Type of flow
- Size Ratio
- Density Ratio
- Variance σ
- Type of flow
- Size Ratio
- Bin Geometry

Storage Time and Components Conc. were not proven conclusive at the range tested

Minimizing segregation tendency in pharmaceutical powder mixtures

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Statistically significant parameters

- Average time, t_m
- Size Ratio
- Concentration
- Variance σ
- Concentration

All other parameters were not proven significant but due to high level variability in the experimental observations definite conclusions are not possible

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Modeling for Cohesive Systems

$$t_m = 40 * D^{-0.5} * C^0.2$$

$$\sigma = 250 * D^{0.5}$$

- D : Ratio of diameters of the two components
- C% : Concentration of Active component

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