Wurster Mass Flow Sensor: Using Microwave Technology To Monitor Wurster Coating Processes

Wurster Coating Technology

(White Paper)
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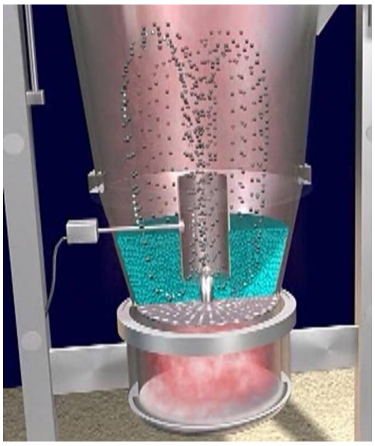
WURSTER MASS FLOW SENSOR

NEW TECHNOLOGY APPLIED TO WURSTERS TO OPTIMIZE FLUIDIZATION

1) BACKGROUND



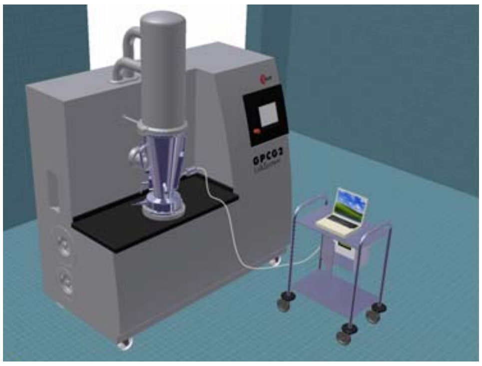
Wurster coating has long been a staple of solid dosage processing. It is well known that optimal coating efficiencies and film quality occur when the particle motion inside the partition (or coating zone) is dense and homogeneous. A need has been seen to quantify and reproduce the fluidization characteristics of the process, which up to this point, has usually been through subjective visual means.

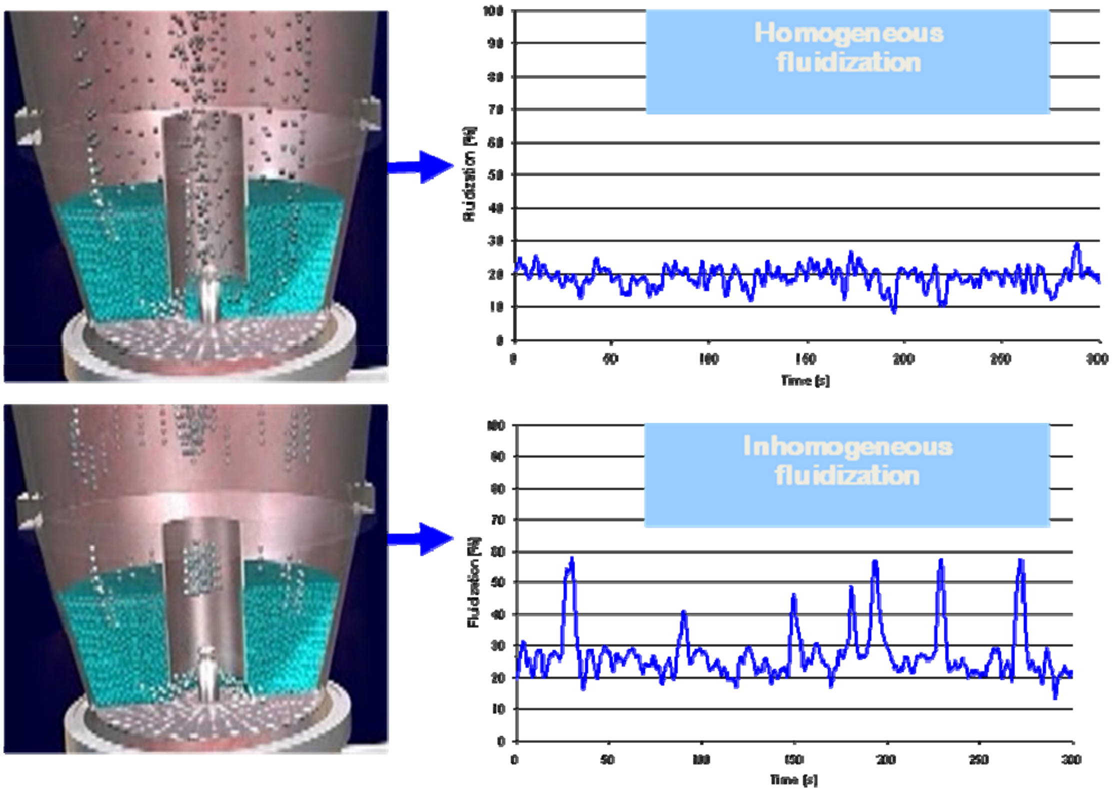
2) OVERVIEW

The Wurster Mass Flow Sensor is a device to control and monitor fluidization performance in a semi-quantitative fashion. This device creates a response based on the particle flow through the partition. The fluidization characteristics of particle density and homogeneity of flow are known in real time. The effects on fluidization by changing air flow and partition height is quantified and can also be observed in real time.

3) THE DEVICE

The Wurster Mass Flow Sensor operates like a particle counter. It utilizes a microwave signal radiated directly into the Wurster partition. The signal is back-scattered by the moving particles only and the diffraction of the signal is measured. This output is charted in real time to show particle density inside the Wurster partition. The amplitude of the output increases with increased particle density. The homogeneity of the particle flow increases with decreased variability of the sensor output. An example of the device output is illustrated below:



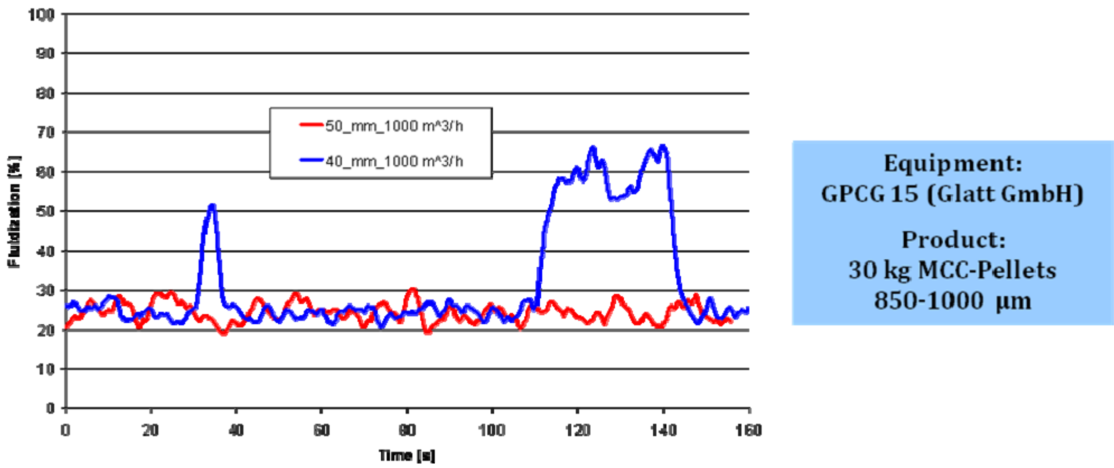


4) Examples of Use

The Wurster Mass Flow Sensor can be used to evaluate several different process parameters individually or grouped together. The following examples were conducted on a Glatt GPCG-15 using 30 kgs of 850 – 1000 µm MCC Pellets.

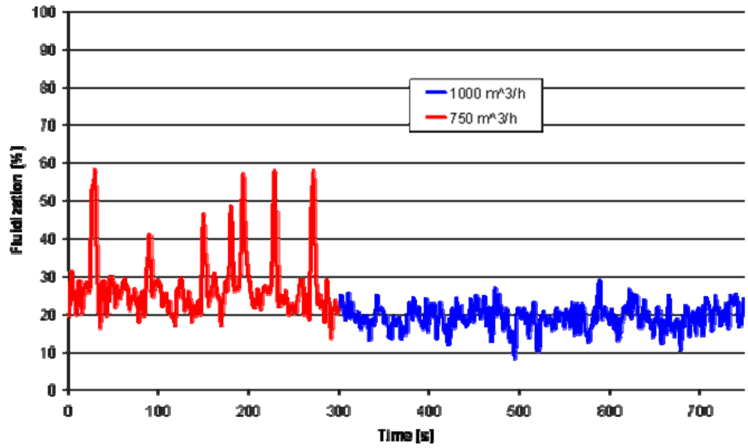
Example 1: Optimizing Wurster Partition Distance

The distance between the bottom plate and Wurster partition has influence on fluidization behavior. As seen below, the pellets move as "slugs" at higher partition height. This is evident as the blue line "spikes" at around 30 seconds and 120 seconds of processing. This effect can change while particles grow during coating/layering process.



Example 2: Optimizing Inlet Air Flow

Depending on particle size/shape, low or high inlet air flow values can cause inhomogeneous fluidization. The optimized air flow value may change during coating/layering process due to changing particle properties (size/shape/weight).

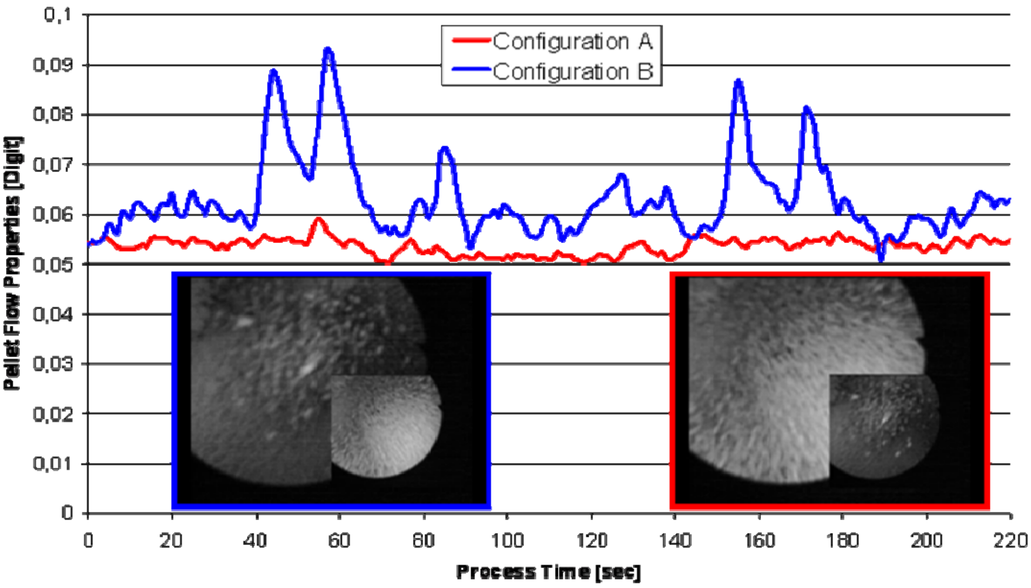


Equipment:
GPCG 15 (Glatt GmbH)

Product:
30 kg MCC-Pellets
850-1000 µm

Example 3: Optimizing Plate Configuration

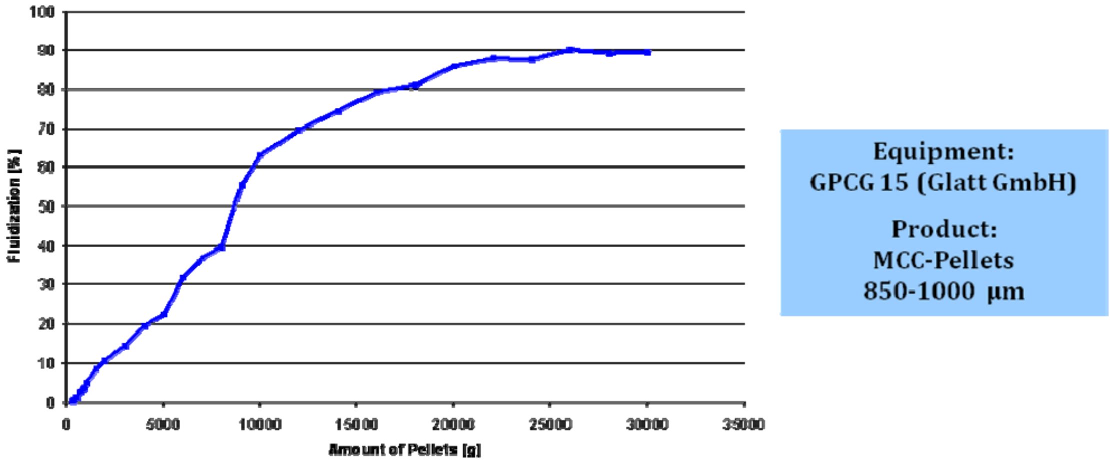
Depending on particle size and shape, the bottom plate configuration can cause inhomogeneous fluidization. A proper choice of bottom plates can be determined in the pilot phase with the help of the microwave monitoring system.



Equipment:	GPCG 15 (Glatt GmbH); 1250 m3/h inlet air flow
Product:	MCC-Pellets 850-1000 µm

Example 4: Minimum Filling Volume of Product Bowl

The lowest possible filling volume of the product bowl is important to know for scale-up considerations. Here, at least 20 kg of pellets should be used to gain optimum fluidization in Wurster partition.



5) Use of the Wurster Mass Flow Sensor in a Design of Experiments to Determine Optimum Fluidization Conditions

The Wurster Mass Flow Sensor was used in a GPCG-2 6“ Wurster to determine the optimal Air Flow, Partition Height and Orifice plate to fluidize 1 kg of ~10 micron MCC pellets by means of a 2^3 full-factorial Design of Experiments.

<u>Variables:</u>

Plate	Air Flow (CMH)	Partition Height (mm)
	20	10
	20	40
A	50	25
	80	10
	80	40
	20	10
	20	40
B	50	25
	80	10
	80	40

The ranges were determined during several preliminary scouting experiments. The centerpoint experiment (50 m^3/hr Air Flow and 25mm Partition Height) was conducted for each orifice plate.

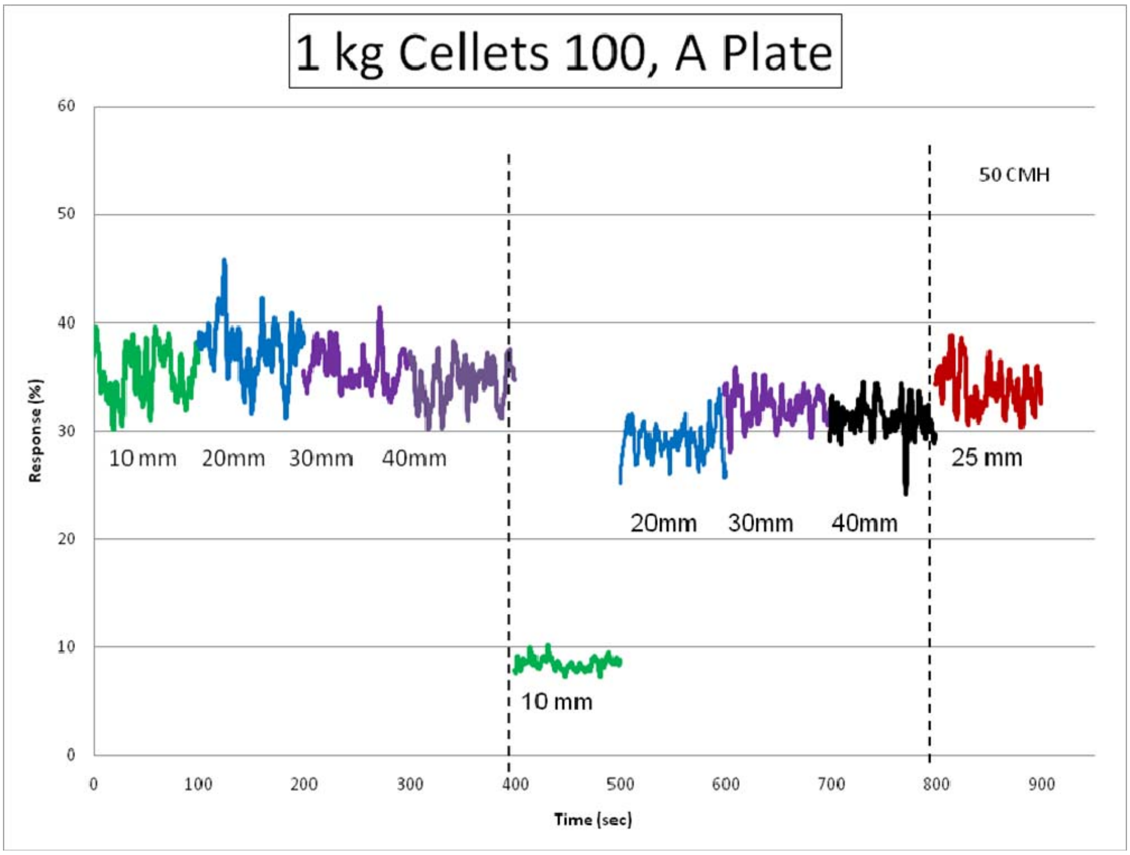
<u>Responses:</u>

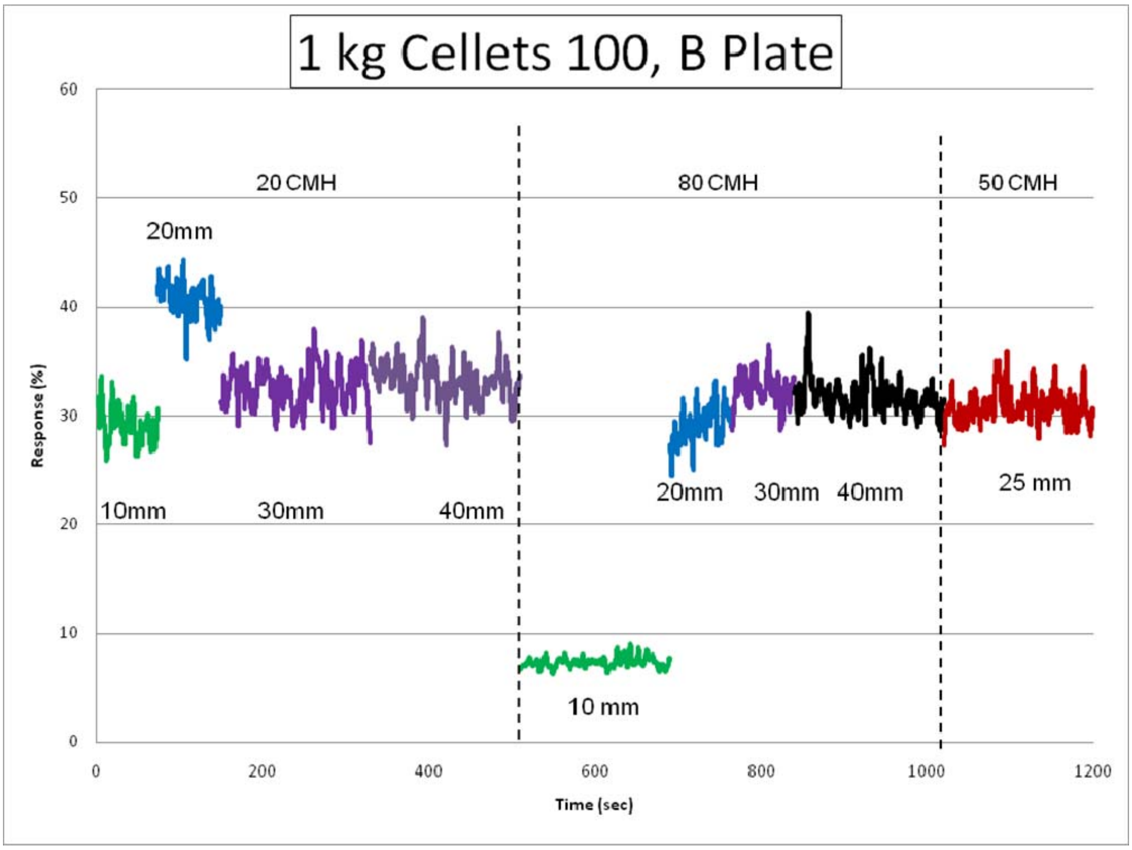
- AVG (Particle Flow Density):
    - Average Response % over a given time interval (~3 minutes)
- STDEV (Particle Flow Homogeneity):
    - Standard Deviation of Response % over the given time interval

<u>Goal:</u>

- Maximize AVG while Minimizing STDEV

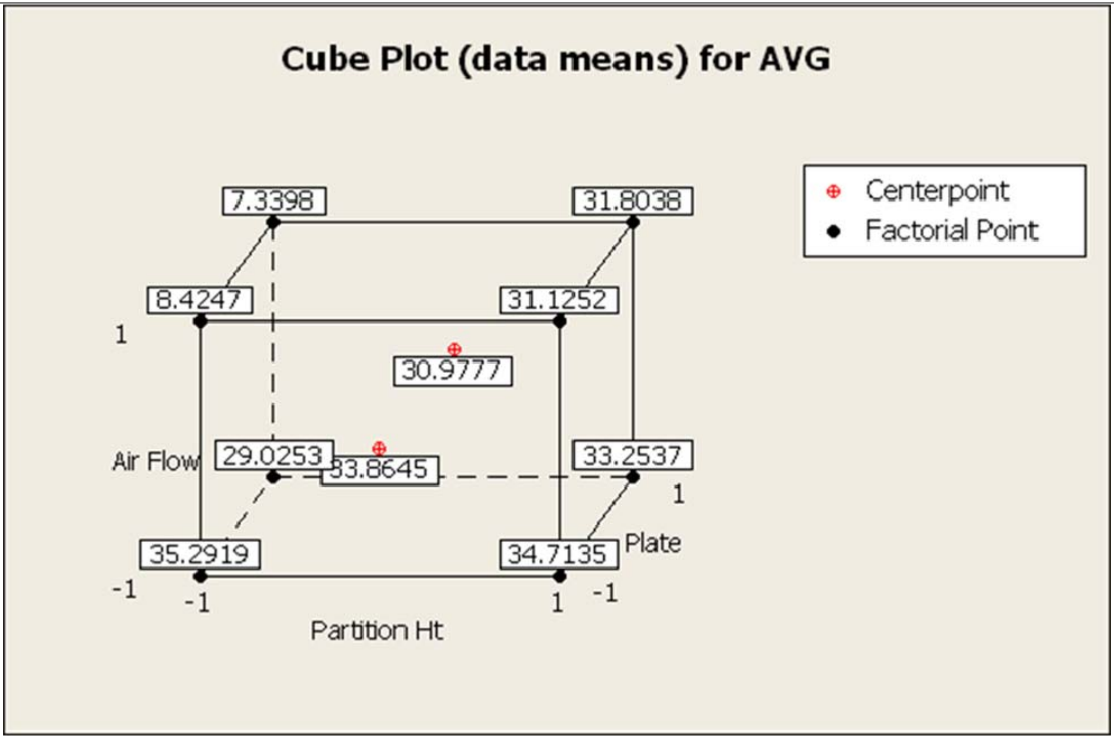
The data collected for each orifice plate is shown graphically below:



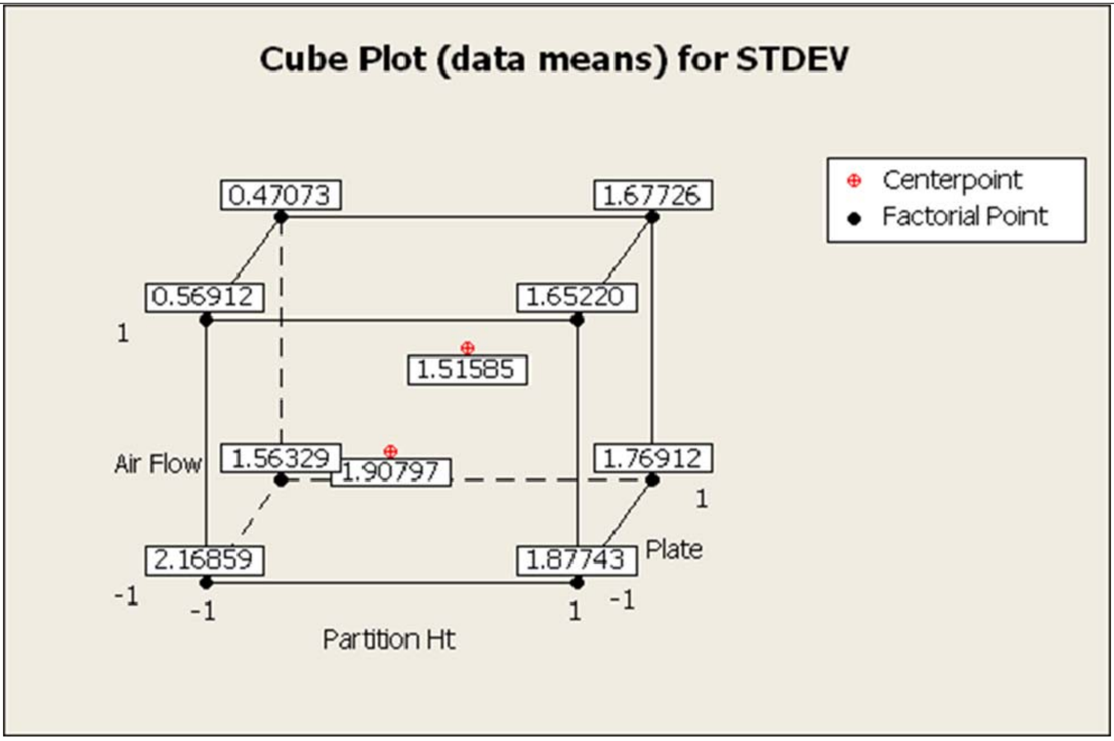


The data shows some changes to the fluidization based on varying partition height, air flow and orifice plate. The changing amplitude of the response variable at different conditions represents the change in density of particle flow at those conditions. The change in variability of the response at each condition represents the change in homogeneity of particle flow at those conditions. The Average and Standard Deviation of the response were calculated for each variable design point and plotted below:

100 micron 1 kg Data



100 micron 1 kg Data



Observations

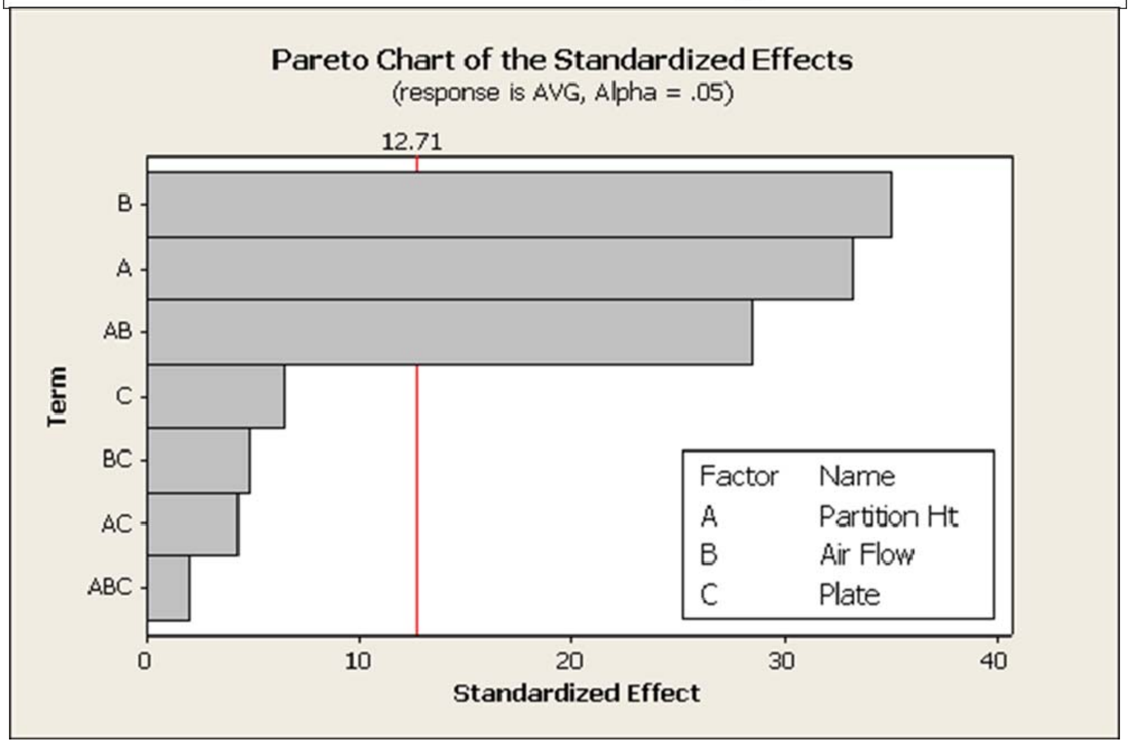
- A low Partition Height of 10mm and a high Air Flow of 80 m^3/hr is unacceptable for either orifice plate chosen due to a low density of particles fluidizing.
- A higher airflow of 80 m^3/hr seems to result in more homogeneous fluidization (lower peak-to-trough spread).
- Orifice Plate shows only a minor influence in the fluidization within the range of airflow studied.

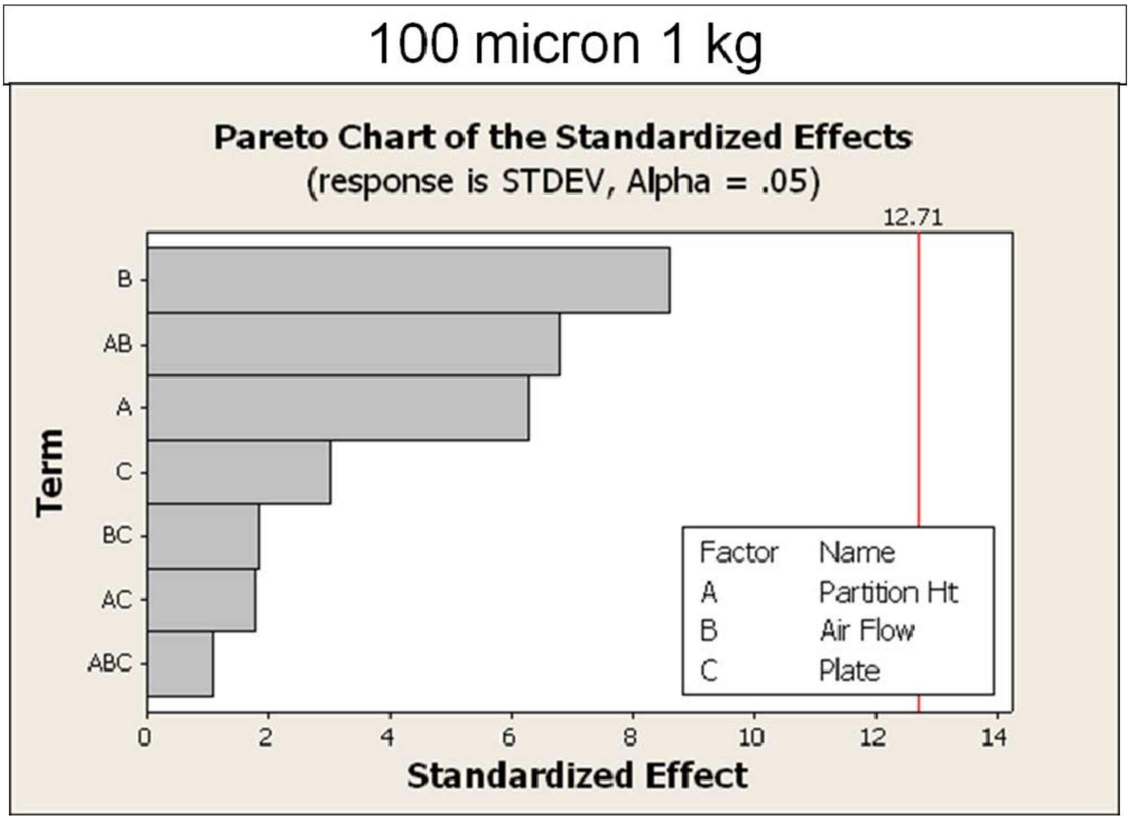
Effect Determination

Based on the Pareto Charts shown below:

- Air Flow and Partition Height have the greatest effect:
  - Particle Flow Density
  - Homogeneity
  - Confirms visual interpretation of the data
- Orifice Plate had little effect on fluidization in this example
  - Confirms visual interpretation of the data

100 micron 1 kg

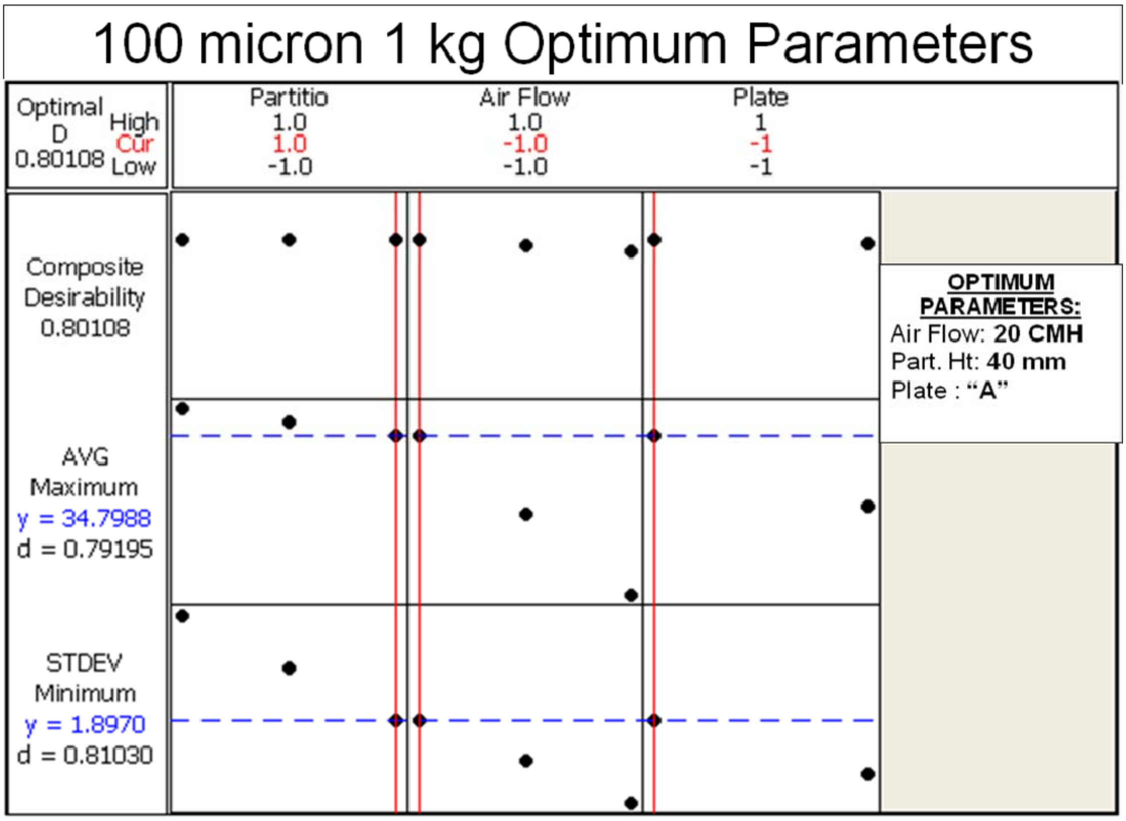




Optimum Parameters:

The data collected in this DoE was analyzed using MiniTab statistical software to determine optimum parameters that will maximize the average response (Fluidization Density) and minimize the standard deviation of the response (Homogeneity). The following MiniTab chart shows the results of this analysis. Based on this, the optimum parameters to use for this example are:

- Orifice Plate: “A”
- Partition Height: 10mm
- Air Flow: 20 CMH



6) Conclusions

The Wurster Mass Flow Sensor is a useful tool to aid scientists and engineers to better determine optimal equipment set-up and processing parameters to ensure dense and homogeneous fluidization in Wurster process development. In a manufacturing function, it provides usable data to insure process repeatability that can be used in troubleshooting. The Wurster Mass Flow Sensor response can also be utilized to control partition height and/or air flow during processing, especially during drug layering operations, where the batch size and particle size can change tremendously during a batch.

In summary, the Wurster Mass Flow Sensor

- Aids scientists and engineers in developing a robust process
- Provides recordable data that can be used to monitor fluidization without relying on an operator's visual observations
- Affords additional data that can be used during troubleshooting
- Can be used to adjust/control partition height and air flow during long drug layering processes where batch size and particle size significantly increase over the batch time