APPLICATION NOTE 6

DFF Sensor as a PAT Tool for Pugmill Mixing: Identification of Under- and Over-Processed Powders

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Densification in solvent-free powders

DFF sensor has been shown to adequately monitor wet mass densification in pharmaceutical high shear wet granulation (HSWG) (Narang, A.S. et. al. 2015, 2016). Blending solvent-free powders in pugmills is another process where on-line real-time monitoring can provide benefits. For example, to produce a good quality carbon films, the powder needs to be granulated before calendared. An under-processed powder produces a weak film, but when it is over-densified, the powder becomes too tacky, can cause hard particles and bridging in hoppers. The densification time is adjusted based on the off-line analysis of powder characteristics. Introducing an in-line process analytical technology could significantly increase throughput and quality of the powder and thus the carbon film.

Experimental

Sample information

ENSACO® Carbon Black, by Imerys Graphite & Carbon Belgium SA, activated carbon, by Kuraray Chemical Co.,Ltd., Japan and Polytetrafluoroethylene (PTFE) fluoropolymer resin, by DuPont Fluoroproducts were blended in a Peter Pugger Pugmill. Three exemplary sample powders were collected just after the pug mill densifier:

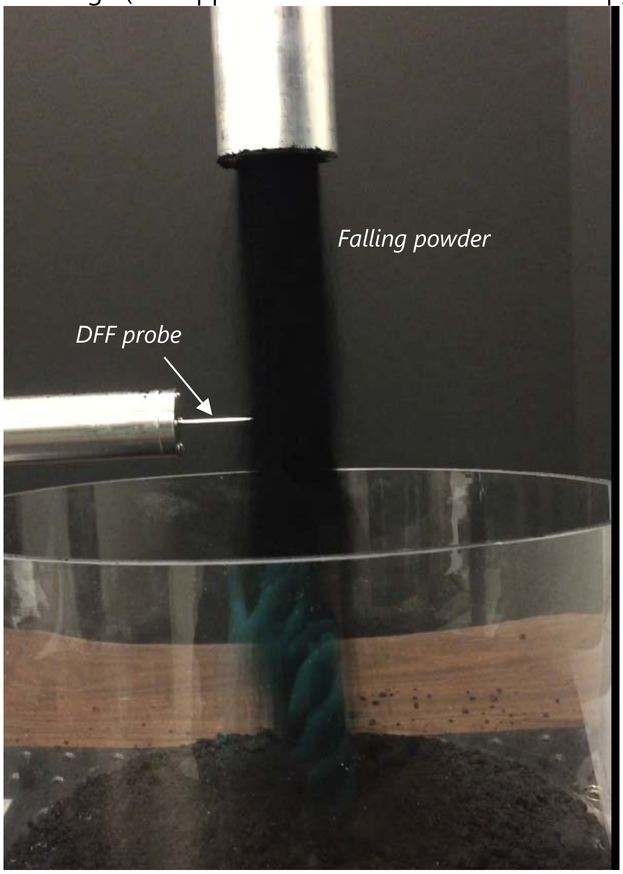
S1: Under-processed - produces a weak film when calendared

S2: Over-processed – over-densified, can produce hard particles

S3: Close to optimal mix

Method

The powders were analyzed in an apparatus where powder was loaded to a vertically held aluminum pipe and released to a DFF probe in a variation of hopper discharge (see Application 05 for details of the setup).



A photograph of the experiment.

Results and Discussion

Five consecutive runs for each sample powder were measured and analyzed. DFF sensor raw signals for two trials from each set are shown above in same scale for comparison. Horizontal axis represents time in seconds.

All signals show a background signal that is steadily rising from the beginning to the end of the run, where it reached its maximum level as expected from gravity considerations. The background level was below 0.04N for all trials. Randomly distributed peaks are also observed in all runs.

Peaks reflect impacts of large agglomerates in the powder, therefore their magnitude and frequency characterize the degree of densification and tackiness of the powder. Histograms of force pulse magnitudes (FPM, see Application Note 03) calculated for FPM frequency of

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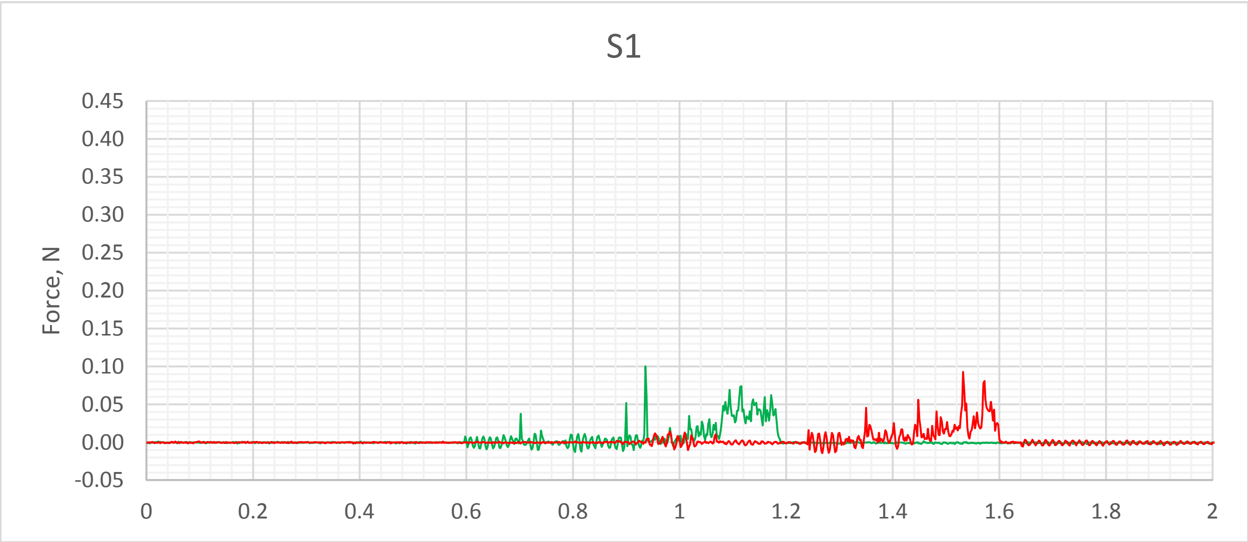
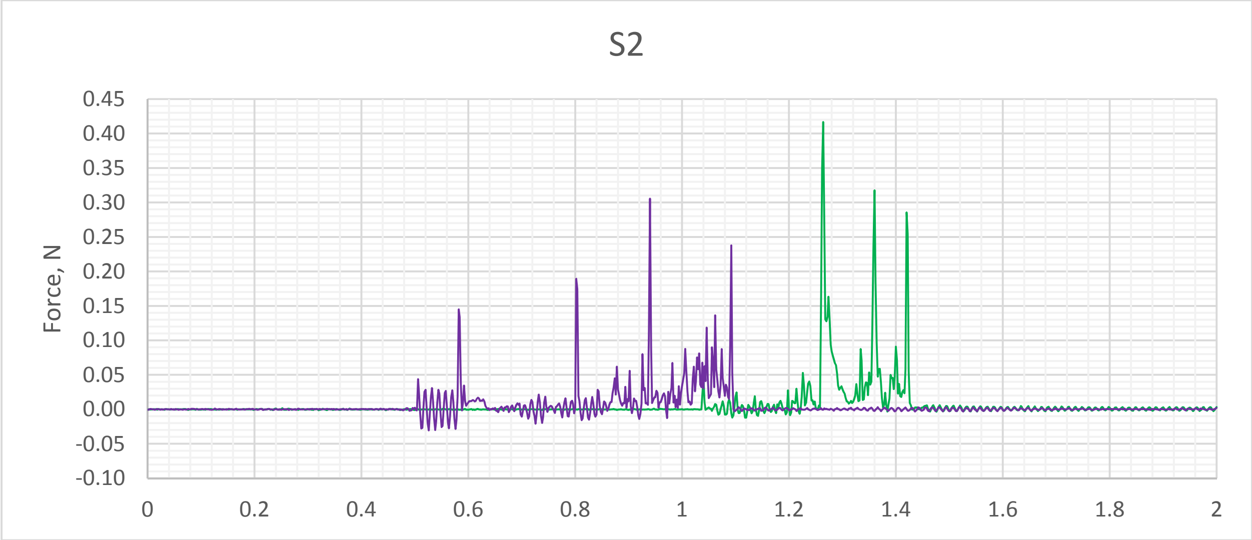

S1
Force, N
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2


S2
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0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
0
0.2
0.4
0.6
0.8
1
1.2
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1.6
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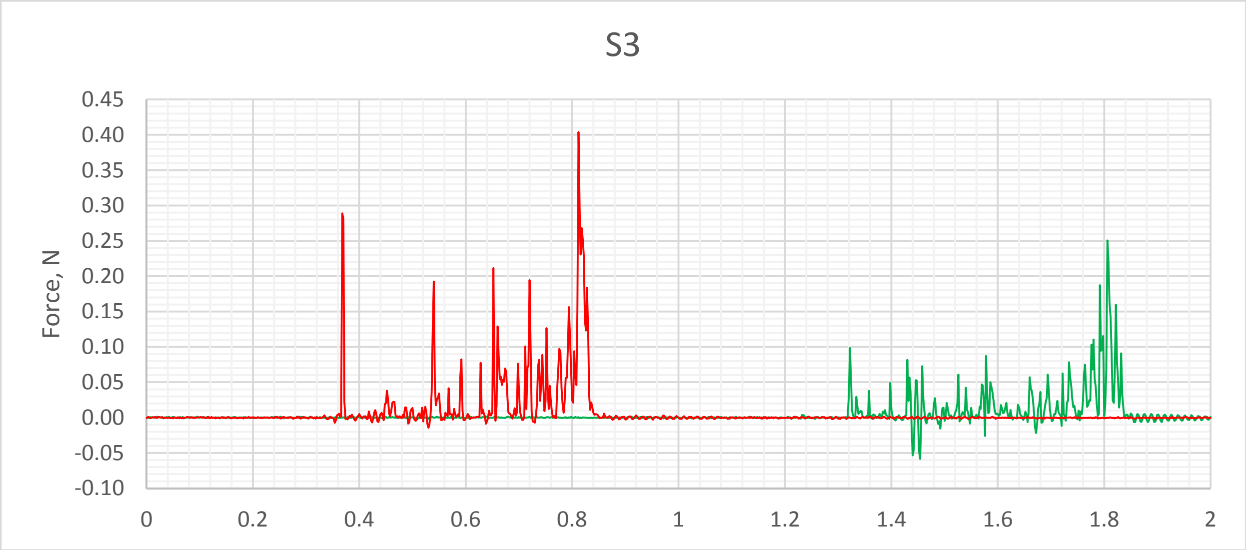
2


S3
Force, N
0.45
0.40
0.35
0.30
0.25
0.20
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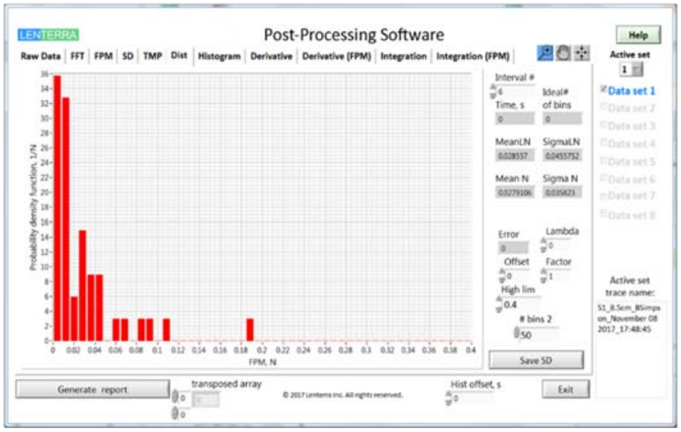
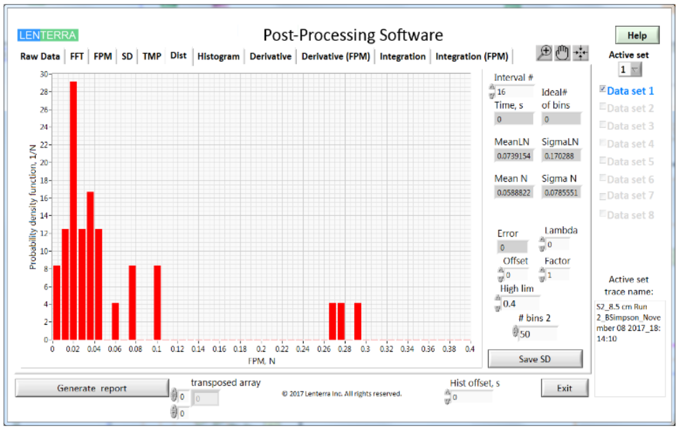
2

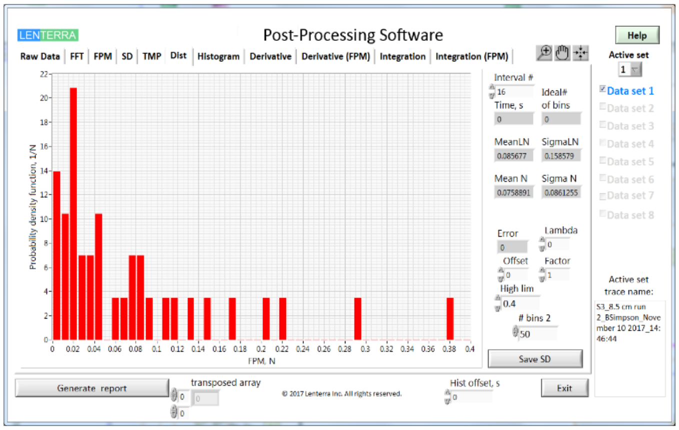
S1



S2



S3

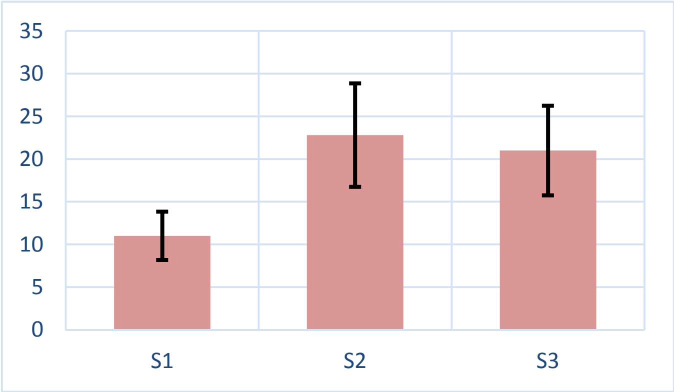


78 Hz, that is the natural mechanical frequency of the DFF probe used in the tests, are shown for one of the runs from each of the three powders.

The histograms indicate that the number of peaks with higher magnitudes increases from sample powder S1 to S2 and further to S3. A number of FPMs above a certain threshold may prove to be a good numerical characteristic for controlling the process. Charts below compare average number of peaks above FPM thresholds of 0.03N and 0.15N for the three sample powders:

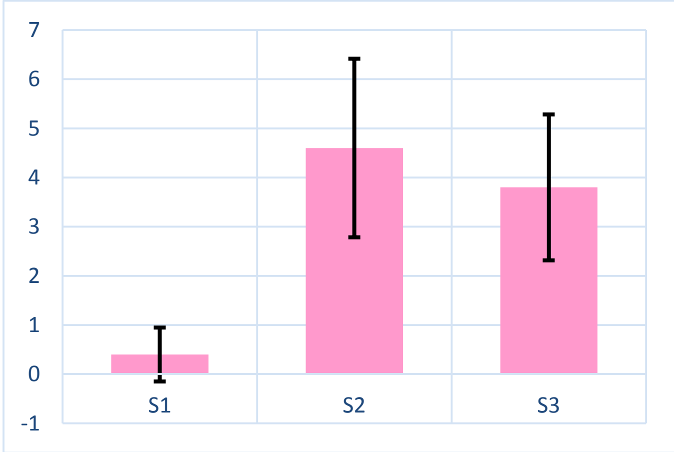
Number of FPM peaks above 0.03N

	Run 1	Run 2	Run 3	Run 4	Run 5	Mean	St.Dev
S1	13	14	8	8	12	11	2.83
S2	25	16	17	30	26	22.8	6.06
S3	22	21	29	18	15	21	5.24



Number of peaks above 0.15N

	Run 1	Run 2	Run 3	Run 4	Run 5	Mean	St. Dev
S1	1	1	0	0	0	0.4	0.55
S2	3	3	4	7	6	4.6	1.82
S3	2	6	4	4	3	3.8	1.48



Conclusions

Samples of under- and over-densified powders of a solvent-free carbon formulation processed using a pugmill mixer were successfully identified by allowing the powder to fall on the tip of a DFF probe. The agglomerates inside the powder manifested itself in the DFF signal as well-pronounced peaks with magnitudes noticeably lower in the under-densified sample as compared to over-densified sample of normal mix. The over-densified sample an average has greater number of samples above a certain magnitude than the normal mix. The test confirmed DFF sensor technology as a promising PAT tool for industrial processing, specifically those where powder densification is a critical parameter of the process.

References

Narang, A.S., Sheverev, V.A., Stepaniuk, V., Badawy, S., Stevens, T., Macias, K., Wolf, A., Pandey, P., Bindra, D., Varia, S., 2015. Real-Time Assessment of Granule Densification in High Shear Wet Granulation and Application to Scale-up of a Placebo and a Brivanib Alaninate Formulation. *Journal of pharmaceutical sciences* 104, 1019-1034.

Narang, A.S., Sheverev, V.A., Freeman, T., Both, D. Stepaniuk, V., Delancy, M., Millington-Smith, D., Macias, K., Subraumanian, G., 2016. Process Analytical Technology for High Shear Wet Granulation: Wet Mass Consistency Reported by In-Line Drag Flow Force Sensor Is Consistent With Powder Rheology Measured by At-Line FT4 Powder Rheometer®. *Journal of pharmaceutical sciences* 105, 182-187.

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