

Characterization of Particle Size Distribution in Process Monitoring

R. R. Retamal Marín, F. Babick, M. Stintz

Motivation

PAT focusses on process monitoring, which is driven by industry for economic reasons and legal authorities for the sake of consumer safety (e.g. Hazard analysis and critical control points (HACCP) in food industry). Its application focusses on observing the progression of reactions and processes (in batches) as well as controlling process stability (continuous processes).

An overview of the state of the art related to research about on-line analytic processes is important in order to understand and compare the advance of the techniques for the determination of physico-chemical properties of matter (e.g. zeta potential). For the characterization of micro- and nanostructured materials targeting the improvement of PAT, the present study contains information about the relevant research and implementation of important measurement methods and project such as ProPAT [1] who aims the developing of novel sensors and analysers for on-line measurement and control of the process parameters in the industry.

PAT on sizing techniques

It is important for the PAT that applications of the process analyzer concentrate on real time measurement (on-line, in-line and in-situ [2]) in the process and not on measuring situation with time delay or separated from process in time and location (off-line, at-line). This different measuring situation requires measuring methods based on different measurands, for particle size and material composition, i.e. equivalent diameters, and also on different types of quantity of particle size distribution (PSD).

Common sizing techniques for on-line methods in process monitoring are listed as a follow:

- Spectroscopic methods
 - Laser diffraction spectroscopy
 - Ultrasonic / Acoustic spectroscopy
- Imaging methods
 - Dynamic imaging: Particle Vision and Measurement (PVM)
 - Dynamic image analysis (DIA)

State of the art in on-line measurement

Spectroscopic methods

- **Laser diffraction spectroscopy:**
 - Even though the working range of laser diffraction instruments is below 0.1 vol.-% they are frequently employed in monitoring high-throughput wet or dry product streams (e. g. cement or pharmaceutical industry [3] [4]).
- **Ultrasonic / Acoustic spectroscopy:**
 - Acoustic spectroscopy is a classic tool in process monitoring. Yet its performance depends to a large degree on the material (thus on temperature) and size range. Preferable applications concern aqueous suspensions of sub-micrometre particles [5] and all systems with particles $\gg 1 \mu\text{m}$ [6].

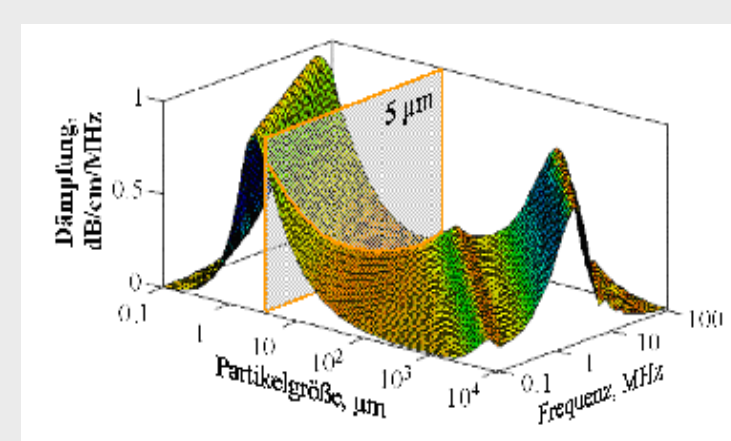
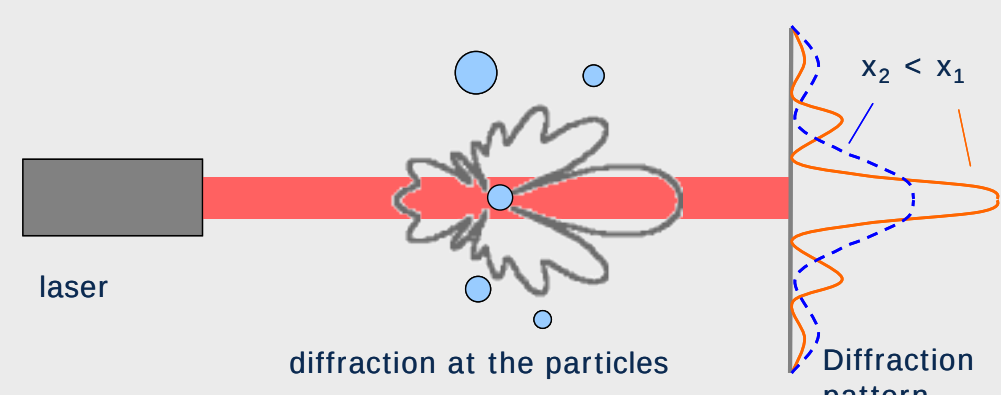


Fig. 1: Measurement principle spectroscopic methods: Measurement principle of laser diffraction (left) and functional dependency of sound attenuation on particle size and frequency (right)

Imaging methods

- **Particle Vision and Measurement (PVM):**
 - PVM is employed in process monitoring – either in-line or on-line with appropriate sampling systems. These images help validate particle shape and give an indication of particle dimension and structure following nucleation and during dissolution [7]. A field of application is monitoring crystallization processes as a FBRM technology [8].
- **Dynamic image analysis (DIA):**
 - DIA is employed in process monitoring – either in-line or on-line with appropriate sampling systems. A typical application area is in pharmaceutical (GMP) [9] [10]

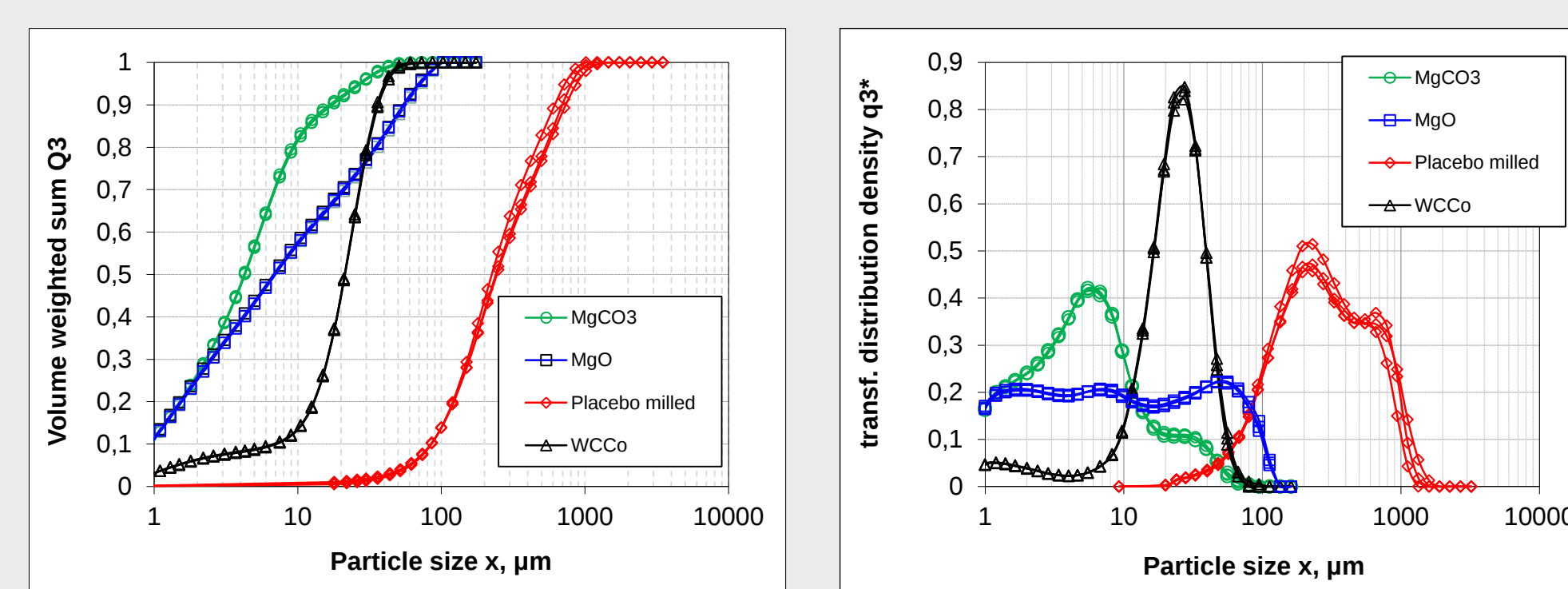
ProPAT on particle size

Project overview

- ProPAT aims to develop novel sensors and analysers for providing measurements on composition, particle size and local bulk properties, as well as more traditional but smart sensors for measuring other process parameters, and integrate them into a versatile global control platform for data acquisition, data processing & mining and User Interface in order to measure properties of process streams and products, accurately and in real-time [1].

Challenges of PSD in process monitoring

- Off-line procedure (e.g. LD, DLS) are currently used for the characterization of micro- and nanostructured materials
- Graphical representation of time dependency of quantile parameter of particles sizes distribution ($x_{10,3}$, $x_{50,3}$ and $x_{90,3}$) is often used in industrial examples of process monitoring in LD.
- Frequently high concentration for high space-time-yield; high polydispersity (broad PSD) and multiple particle species (physical-chemical condition: dry or wet measurement) (fig. 2)



	$x_{10,3}$	$x_{50,3}$	$x_{90,3}$
	μm	μm	μm
MgCO ₃	0,9	4,3	17,2
MgO	0,9	7,0	55,4
Placebo milled	84,9	236,9	685,1
WCCo	8,5	22,1	37,8

Fig. 2: Analysis of PSD with off-line procedure (LD) of different samples materials. Volume weighted sum $Q_3(x)$ (left), trans. distribution density $q_3^*(x)$ (middle) and relevant quantile parameter (right)

References:

- [1] www.pro-pat.eu
- [2] M. Stieß, Mechanische Verfahrenstechnik - Partikeltechnologie 1, Springer (Berlin, Heidelberg)
- [3] M. Puckhaber, S. Röthele, Particle sizing – latest technology. *Eur. Cement Mag.*, 2000.
- [4] M. Heuer, M. Schaller, W. Witt, In- and on-line particle size analysis with representative sampling for pharmaceutical applications (GMP)., PARTEC 2007
- [5] D. M. Scott, A. Boxman, C. E. Jochen, In-line particle characterization. *Part. Part. Syst. Charact.*, 1998
- [6] M. Li, D. Wilkinson, K. Patchigolla, P. Mougin, K. J. Roberts, R. Tweedie, On-line crystallization process parameter measurements using ultrasonic attenuation spectroscopy. *Cryst. Growth Des.*, 2004
- [7] M. Kempkes, J. Eggers, M. Mazzotti, Measurement of particle size and shape by FBRM and in situ microscopy. *Chem Eng Sci.*, 2008
- [8] Ahmed S. Zidan, Ziyaur Rahman, and Mansoor A. Khan, On-line Monitoring of PLGA Microparticles Formation Using Lasentec Focused Beam Reflectance (FBRM) and Particle Video Microscope (PVM), The AAPS Journal, 2010
- [9] Yu W., Hancock B.C., 2008. Evaluation of dynamic image analysis for characterizing pharmaceutical excipient particles. *Int. J. Pharm.*, 2008
- [10] V. R. Nalluri, P. Schirg, X. Gao, A. Viridis, G. Imanidis, M. Kuentz, Different modes of dynamic image analysis in monitoring of pharmaceutical dry milling process, International Journal of Pharmaceutics, 2010

Glossary for different measuring situation

off-line → measurement separated from process in time and location (e.g. Laboratory), sampling, sample conservation and preparation required

at-line → measurement close to process line at distinct samples with time delay, sampling required, maybe with sample preparation (e. g. dilution)

on-line → measurement close to process line (e.g. by-pass), in real-time (time to get measurement results allows process control), maybe with sample preparation (e.g. dilution)

in-line → sensor is placed in pipe or reactor, specific on-line measurement, no sample preparation, „sampling“ by sensor location and possible impact on flow field

in-situ → sensor is not inserted into the process zone (e.g. Tomography), specific on-line measurement, no sample preparation