



Size analysis by laser diffractometry – how valid are the data?

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Purpose: Laser diffractometry is frequently used for particle sizing. For proper analysis of the nanometer range Mie analysis is required. However, the problem is that Mie analysis requires the input of real refractive index and imaginary refractive index, where the problem starts. Both values are very difficult to determine. Purpose of this study is to evaluate which errors can occur when using incorrect indices.

Results: In the first instance only Mie theory was applied to analyse the Fraunhofer diffraction spectra. The analysed particle size and particle size distribution is strongly influenced by the optical parameters used. With a systematic increase of the imaginary and the real index of refraction the results vary dramatically and irregular due to the complicated Mie formula (Fig.1, Tab.1). The increase of the imaginary index reduces the influence of the real compound. These “averaged” results may underestimate small and/or larger particles (Fig.2).

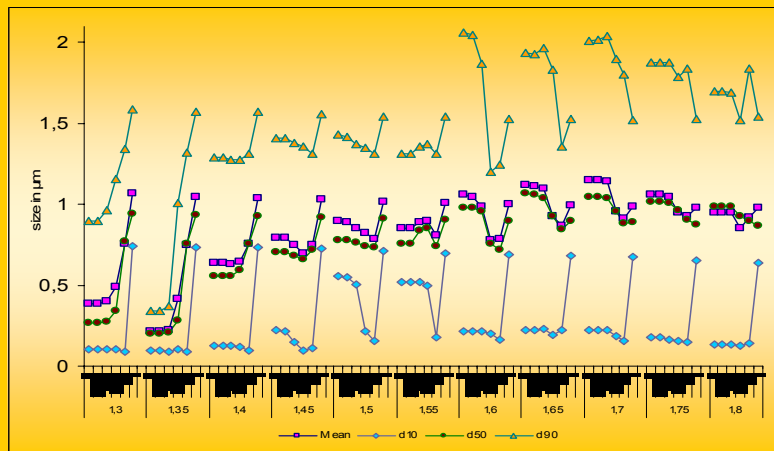


Figure 1: particle sizes of one LD- measurement obtained by analysing the data with increasing values of the real index of refraction (1,3-1,8) each correlated with increasing imaginary indices of refraction (0-1)

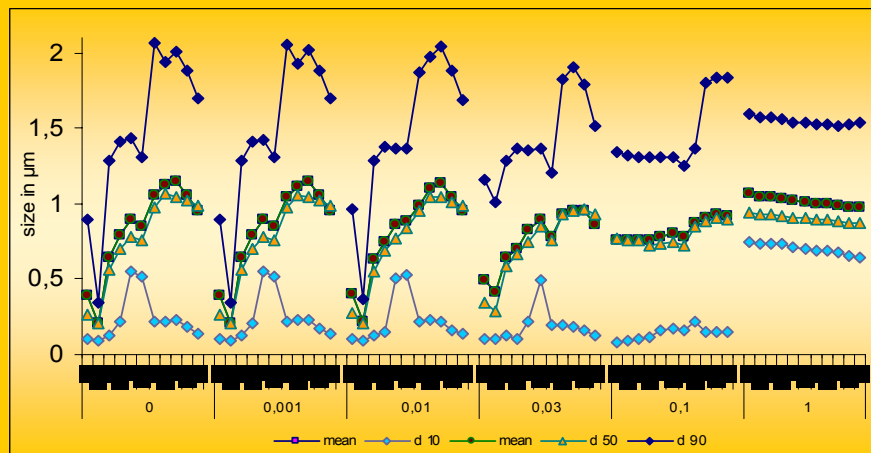


Figure 2: particle sizes of one LD- measurement obtained by analysing the data with increasing values of the imaginary index of refraction (0-1) each correlated with increasing real indices of refraction (1,3-1,8)

Methods: A cyclosporine nanosuspension was produced by high pressure homogenisation using a Micron LAB 40 (APV Systems, Unna, Germany). Particle size analysis was performed using a Coulter LS 230 (Beckmann-Coulter, Krefeld, Germany). The obtained raw data were modelled using the Beckman-Coulter Software Version 3.19. The Fraunhofer spectra were analysed using the Mie theory and additionally the PIDS technology (polarisation intensity differential scattering). Different values for the real refractive index and the imaginary refractive index were used.

Table 1: minimal, maximal and averaged results of the modelled data

	Min	max	average
Mean	0,212 µm	1,15 µm	0,847 µm
S.D.	0,095 µm	0,647 µm	0,429 µm
C.V.	30,3%	94,9%	53,1%
d10	0,086 µm	0,743 µm	0,286 µm
d50	0,202 µm	1,07 µm	0,785 µm
d90	0,345 µm	2,06 µm	1,48 µm

Conclusion: The importance of using correct or at least very close values of imaginary and real refractive indices has been shown. Only the knowledge of the correct optical parameters of a system will lead to accurate particle size and size distribution values, being important for the characterisation of the system, i.e. stability, crystal growth, aggregation etc.. Laser diffractometry data based on Mie analysis without using and publishing the refractive correct indices can be considered being rather a rough estimation than a correct measurement, to avoid the expression of “meaningless” or “false” data.