Nanostrukturierte Materialien: Gesundheit, Exposition, Materialeigenschaften

Light microscopy and computer based methods to analyse primary and agglomerated nanoparticles in liquids

GEFÖRDERT VOM
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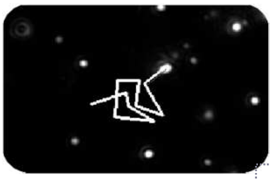
First Issue: Improving the interpretation of polydisperse size distributions: The Nanosight^{TM} Method is an optical tracking method that is increasingly employed to characterize the size of nanoparticles in suspensions. However, the separation of different particle populations in polydisperse suspension is still difficult (**Panel A**). Here we present a method which utilizes Box-Cox Transform combined with an automated cluster analysis to overcome this separation problem (**Panel B**).

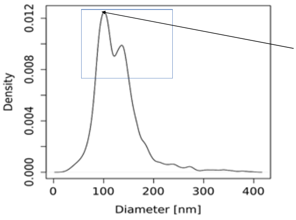
A:

Nanoparticle Tracking & Analysis (NTA)

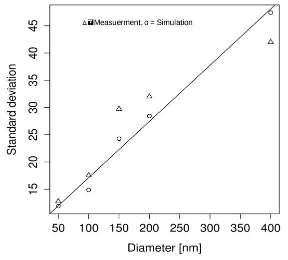


Hydrodynamic diameters
85 nm 99 nm
167 nm 120 nm
100 nm 139 nm
150 nm ...

Size Distribution (Measurement)



Are there more 100nm particles than 150nm particles?
Peaks are not comparable!
Because of constant *coefficient of variation*!

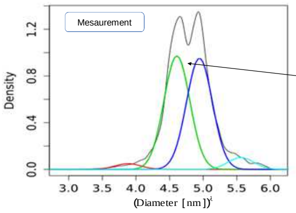


B:

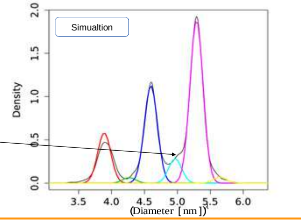
Hydrodynamic diameters
85 nm 99 nm
167 nm 120 nm
100 nm 139 nm
150 nm ...

Box-Cox-Transform

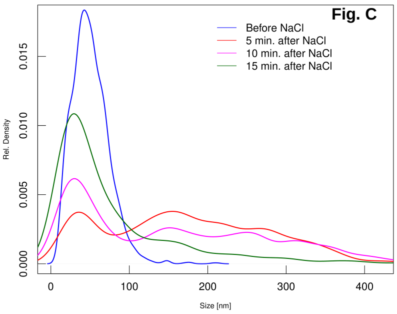
Clusteranalysis

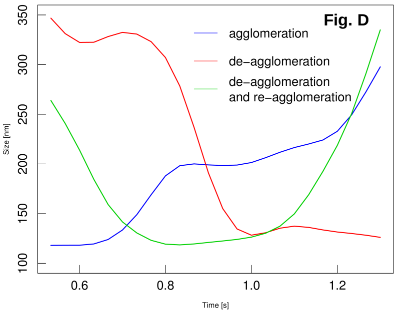


Benefits:
- Peaks are compareable
- Hidden subpopulations are uncovered



Second Issue: Analysis of agglomeration / de-agglomeration with NTA: SiO_2PEG was used at low ionic strength (0.45% NaCl) which induced agglomeration within minutes. While time elapsed, the number of size populations increased to four but declined to one population after 15 min (**Figure C**). The size analysis of three single tracks could be interpreted as to be due to a reversible agglomeration processes of SiO_2-PEG nanoparticles (**Figure D**).



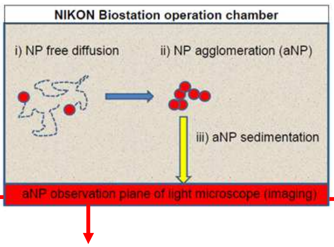


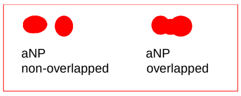
Conclusion First Issue: The procedure appears helpful to correctly interpreting the quantitative composition of a polydisperse particle suspension.

Conclusion Second Issue: Dynamic changes of particle agglomeration could be followed by calculating the diffusion coefficient for a single particle over an extended period. These changes were interpreted as either agglomeration and/or de-agglomeration.

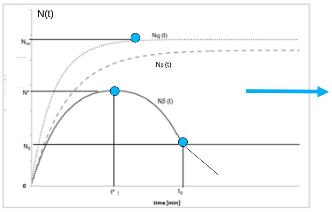
Third Issue: Sedimentation Kinetics under Cell Culture conditions

NIKON's Biostation©

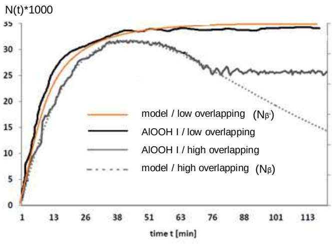




E) Particle counting: kinetic model



F) Particle counting: observation vs. model



Model:

$$N(t)=\begin{cases} N_\infty \cdot (1-e^{-q\cdot t})\cdot e^{-\beta\cdot t} & ,\ if\ 0\leq t<t_0 \\ N(t_0)=N_0 & ,\ if\ t\geq t_0 \\ 0 & ,\ if\ t<0 \end{cases}$$

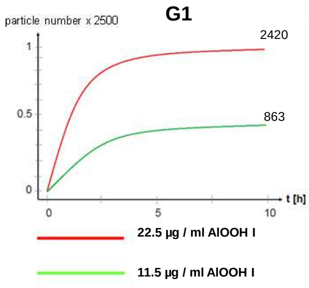
Number N(t) of agglomerated and sedimented particles (aNP) observed on chamber buttom:
- non-overlapping ($N_q(t)$)
- low overlapping ($N_{\beta'}(t)$)
- high overlapping ($N_\beta(t)$)

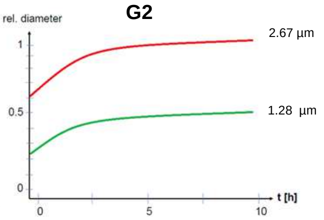
(N^* = maximum of N_β occurs at t=t*)

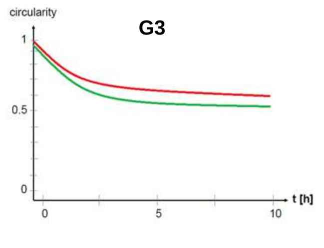
Test of model and imaging algorithms:

Example: real measurements of AlOOH I-aNP number (after NP in liquids were added to the Biostation with different concentrations) following agglomeration and sedimentation; observed on the bottom of the operation chamber by light microscopic imaging (time laps method) at time t.
The kinetic parameters q (sedimentation) and β (overlapping) were derived from the best fit of model and data.

G) Kinetics of agglomerated and sedimented AlOOH I-Nanoparticles (Example)







Example:
Influence of concentration on agglomerated and sedimented AlOOH I-nanoparticles:

-particle number (Figure **G1**)
-mean diameter (Figure **G2**)
-mean circularity (Figure **G3**)

Conclusion Third Issue: image based measurements of aNP during gravitational settling from liquids allow to

- **characterize the sedimentation by parameter q and the overlap of particles by parameter β;**
- **count particle numbers sedimented to the bottom;**
- **compute form parameters of sedimented aNP (e.g. diameter; circularity).**

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