Processing Nanoparticles in Suspension of High Solid Concentration: Online Characterisation and Process Modelling

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CONTENT

- **Background**
  - Nanotechnology
  - Why Size Matters?
  - Online Size Measurement System
- **NanoSonic**
  - Hardware
  - Software
  - System Validation
- **Conclusions**

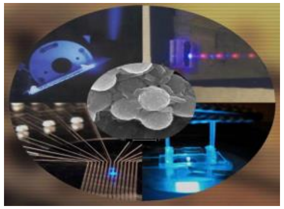
INTRODUCTION

- Applications of nanoparticles
  - Pharmaceutical and drugs delivery
  - Chemicals (including plastics)
  - Biosensors, transducers and detectors
  - Food and nanofood
  - Water and wastewater treatment
  - Electronics
  - Optics, jewellery, paints, energy, etc.

Drugs

Chemicals

Biosensors



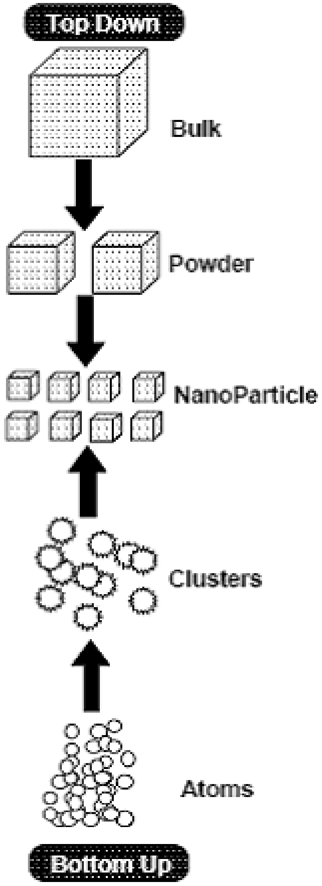
Food

Wastewater

Electronics

PRODUCTION OF NANOPARTICLES

- Bottom up approach
  - From single atoms or molecules
- Top down approach
  - Dry milling
  - Wet milling i.e. stirred media mill



MOTIVATIONS?

Size Matters

- Nanomaterial properties are size dependent
- Drug product performance and bio-availability depends on the particle size distribution
- Size distribution is the key for quality and stability of products
- Achieving consistent product quality is difficult

➢ This is mainly limited by lack of online monitoring systems for wet milling process especially at high concentration

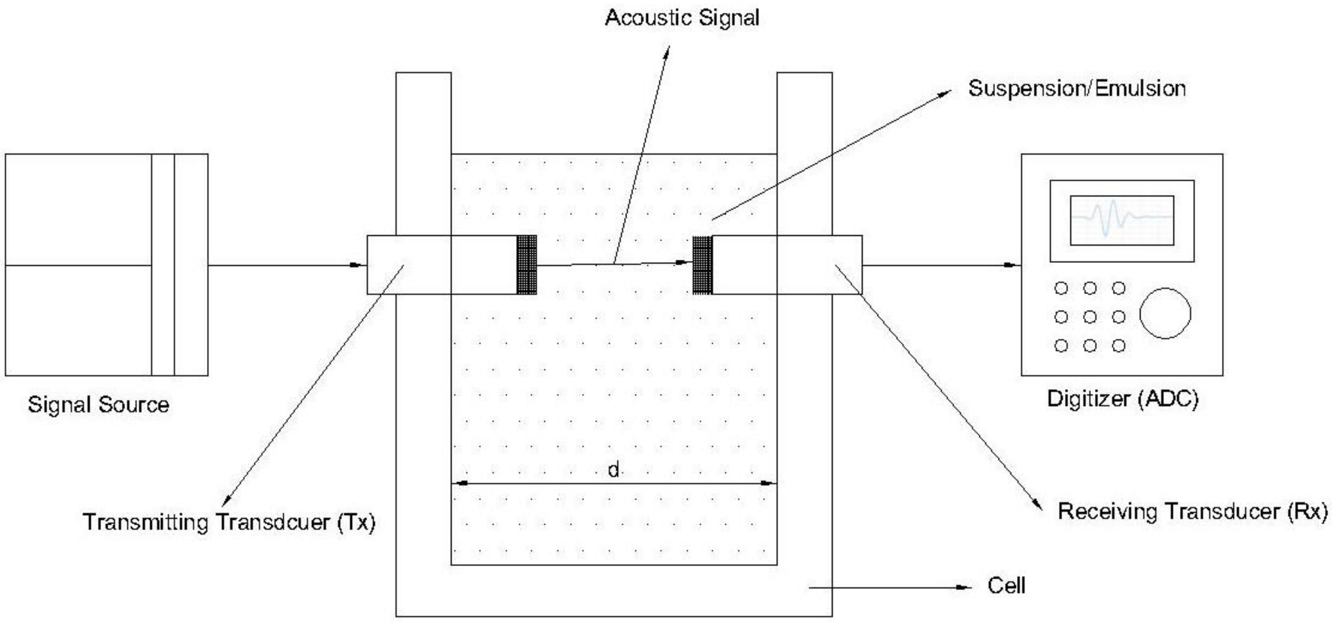
➢ Lack of mechanistic/quantitative understanding of the interactions between operational conditions/process design and product quality- **Population Balance Modelling**

ONLINE MEASUREMENT SYSTEM

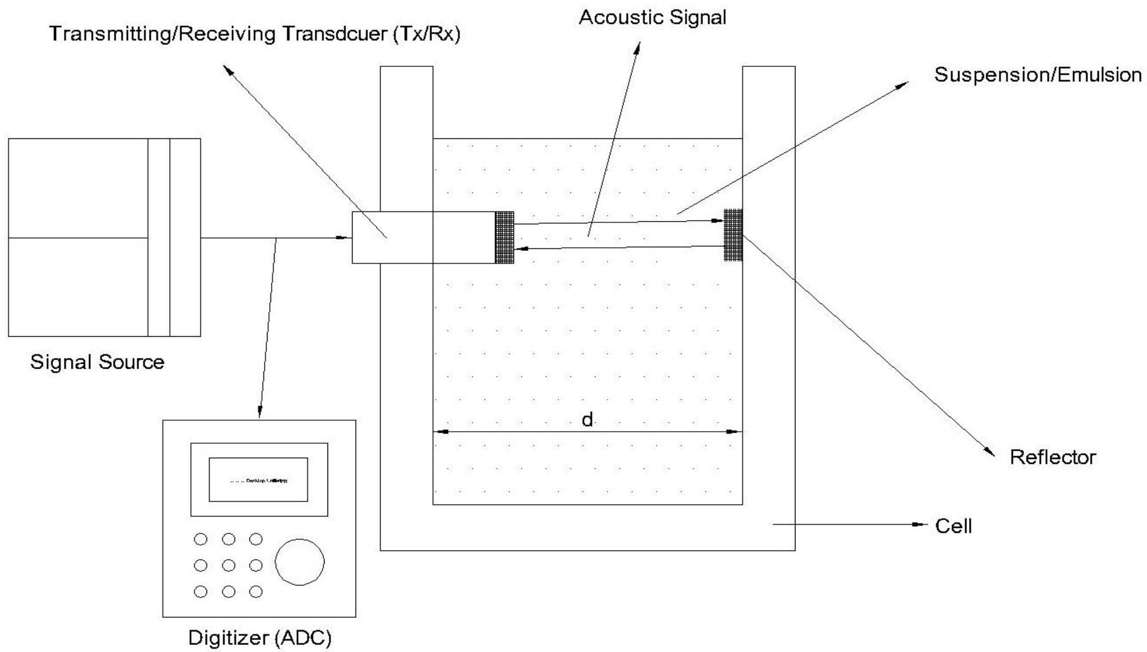
- Requirements?
  - Non-invasive i.e. the measurement should not affect the system
  - Requires no sampling (invasive and sometimes difficult to get a representative sample)
  - Requires no dilution: can affect the properties (such as PSD) of the suspension
  - Fast especially for purpose of control or for flowing system
  - Applicable to large particle range i.e. 0.010 – 100μm and volume concentration 0 – 50% v/v

- Dynamic Light Scattering
  - Invasive: Requires dilution and sampling
  - Limited size range: 0.3 – 10 µm
- Light Scattering/Laser Diffraction
  - Invasive: Requires dilution and sampling
- Focused Beam Reflectance Method (FBRM)
  - Applicable only to non-opaque system
  - Limited size range: 0.3 – 10 µm
- ➢ Ultrasonic Spectroscopy
  - ➢ Meets most of the requirements
  - ➢ Not well developed compared to DLS and Laser Diffraction methods

- Limitations of available acoustic instruments
  - **Long data acquisition time** – Malvern Ultrasizer can take 5 - 10 minute to acquire the full spectrum. Not specifically designed for online measurement
  - **Non-uniqueness of solution** – more than one PSDs fit the measured data well
  - **Lack of a single model** for all size ranges 0.001 – 1000 µm and volume concentration
  - **Long data processing time**
  - **Multiple scattering and particle-particle interaction issues at high solid concentrations**
  - User **need good understanding** of acoustic propagation and models



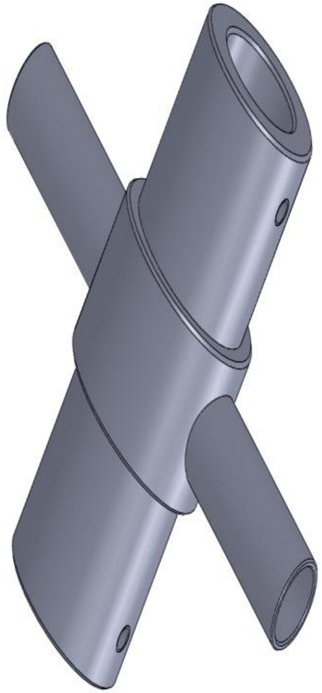
Basic Setup of An Acoustic Particle Measurement System in Through Transmission Mode



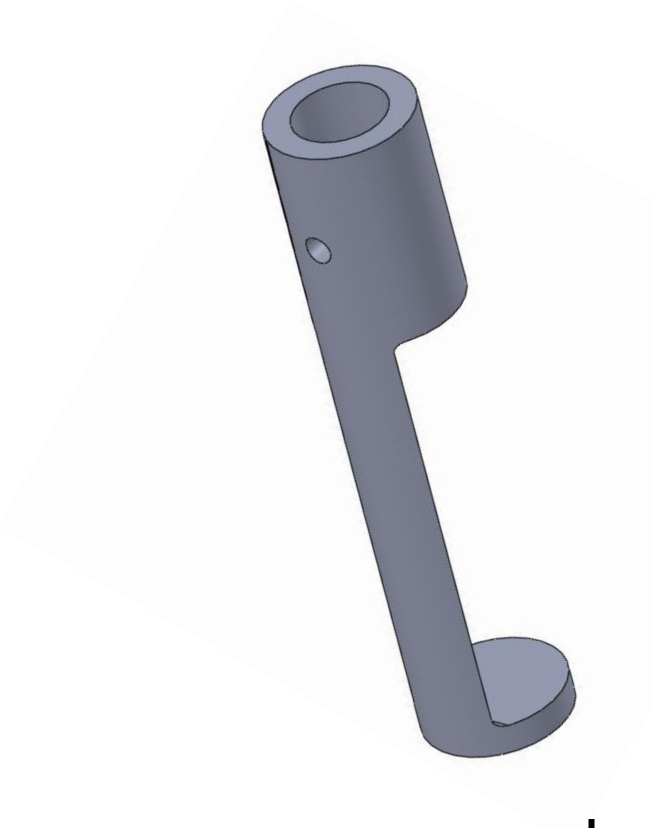
Basic Setup of An Acoustic Particle Measurement System in Pulse Echo Mode

Hardware design

- Minimalist
- Low volume

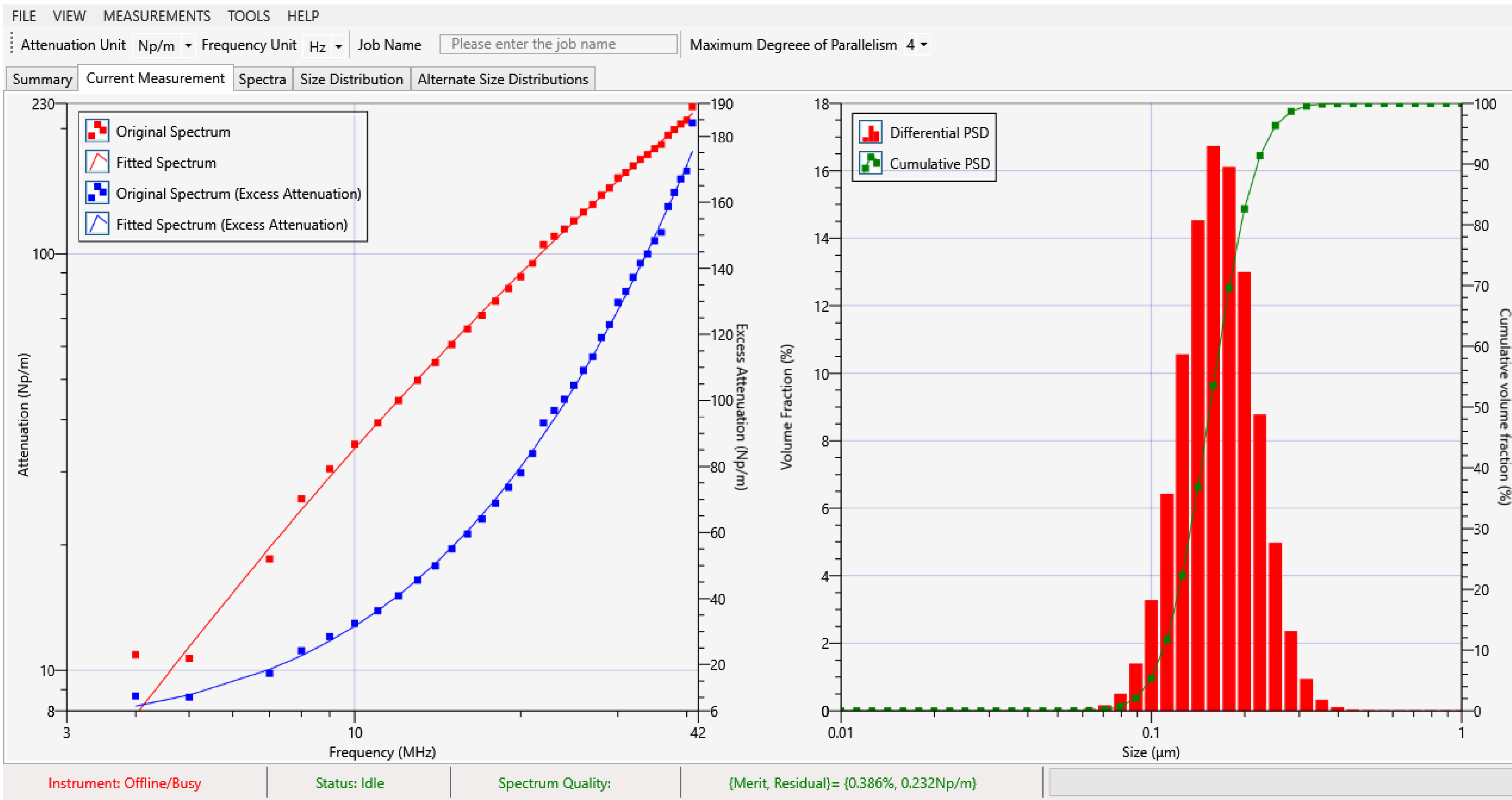


Flow through measurement cell



Insertion Probe

NanoSonic Software



NanoSonic Software

- Synchronise all the instrumentation
- **10 acoustic models implemented** - automatic model selection
- Powerful global optimisation algorithms
- Fast computation using parallel processing and high performance computing
- Designed for online measurement (can be used offline)
- Details too complex too describe here

Validation - Monodispersed Aqeuous Silica Suspensions

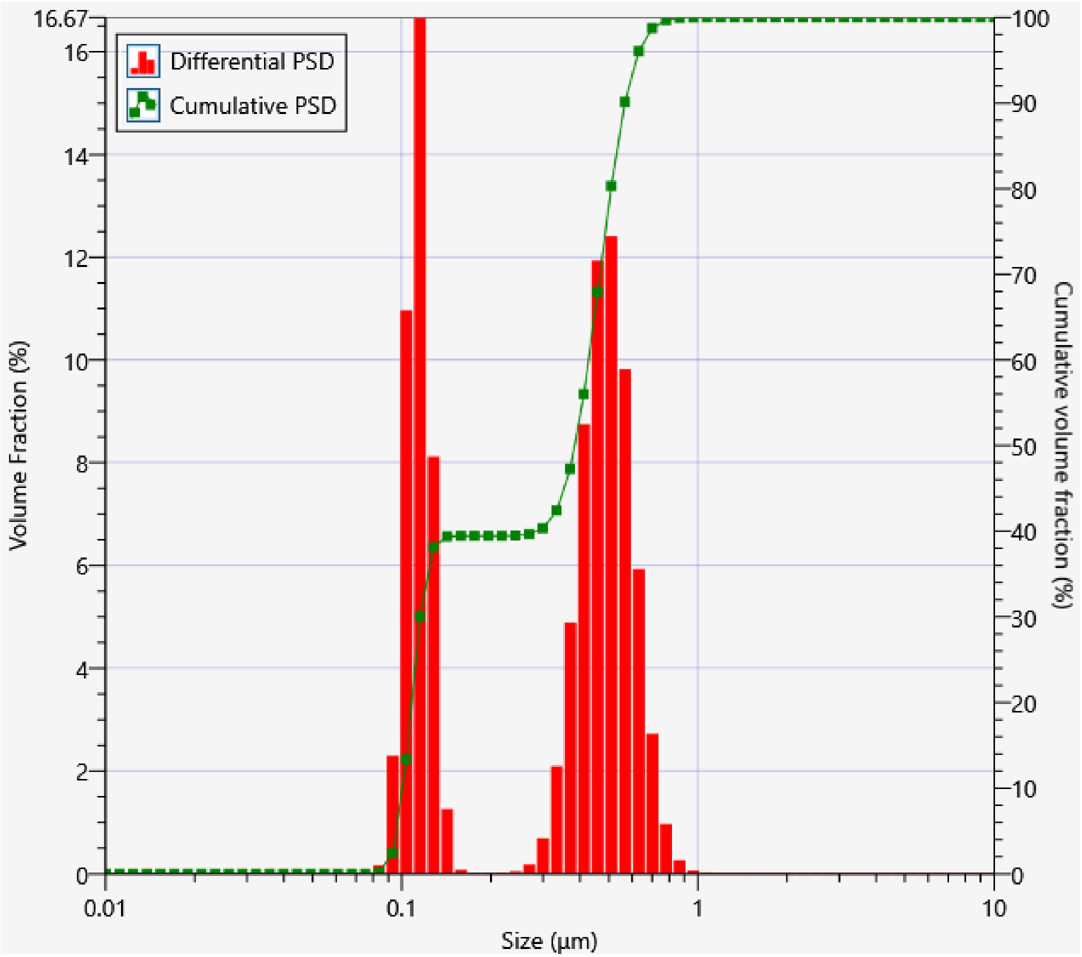
Manufacturer Specification	NanoSonic Measurement	% solid concentration
300nm	298nm	1.59
450nm	465nm	1.59
300nm	293nm	2.81
300nm	305nm	10.16
450nm	452nm	23.35
100nm	106nm	24.75
200nm	197nm	24.88
300nm	290nm	28.96

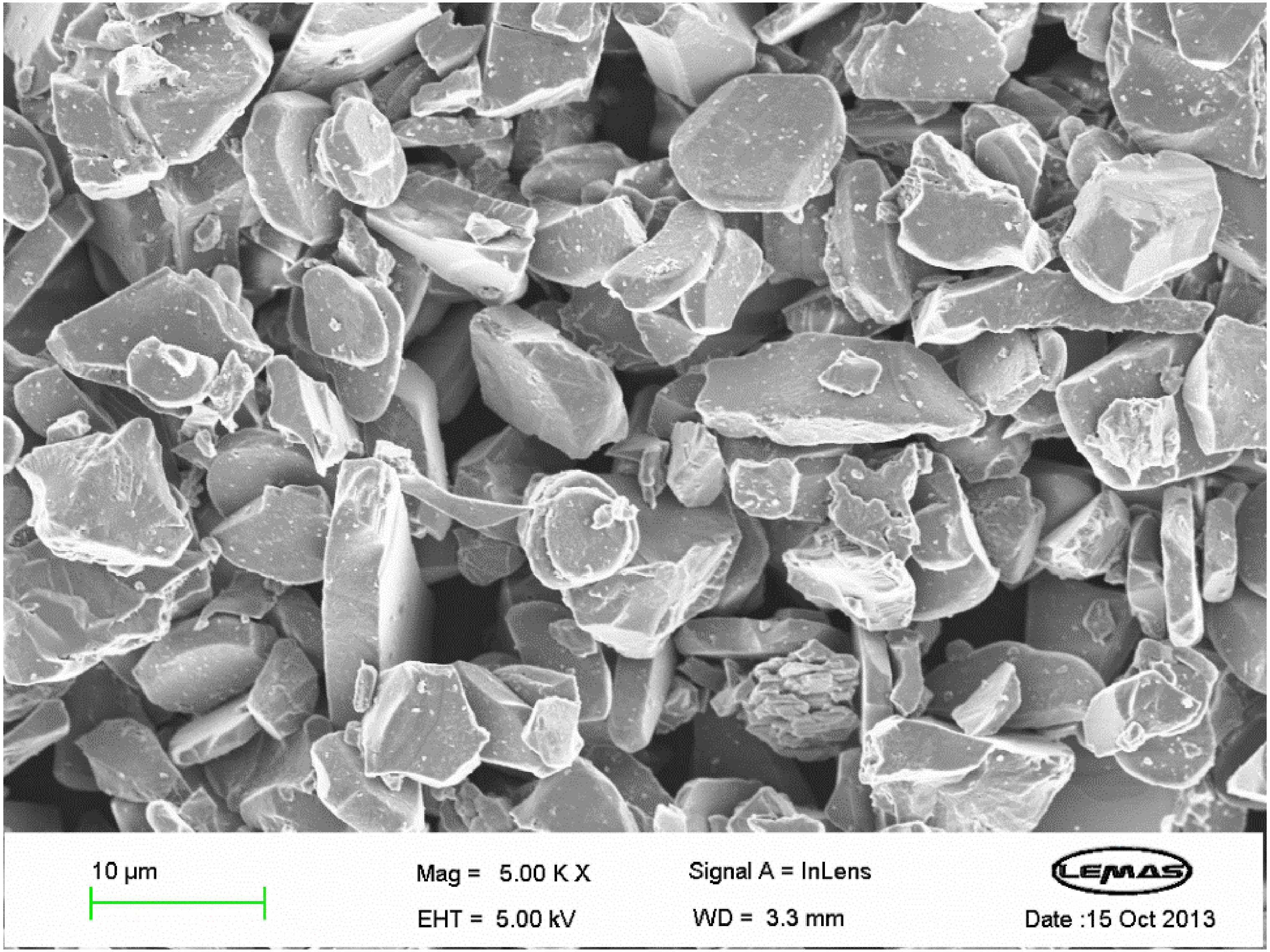
Mixture of 30% 100nm and 70% 450nm silica suspension (23.77% v/v)

Two peaks correctly predicted

- Peak 1: 114 nm, 39.5%
- Peak 2: 491nm, 60.5%

Correctly predict the bimodality of the size distribution, the location of the peaks as well as the relative proportion of each peaks.



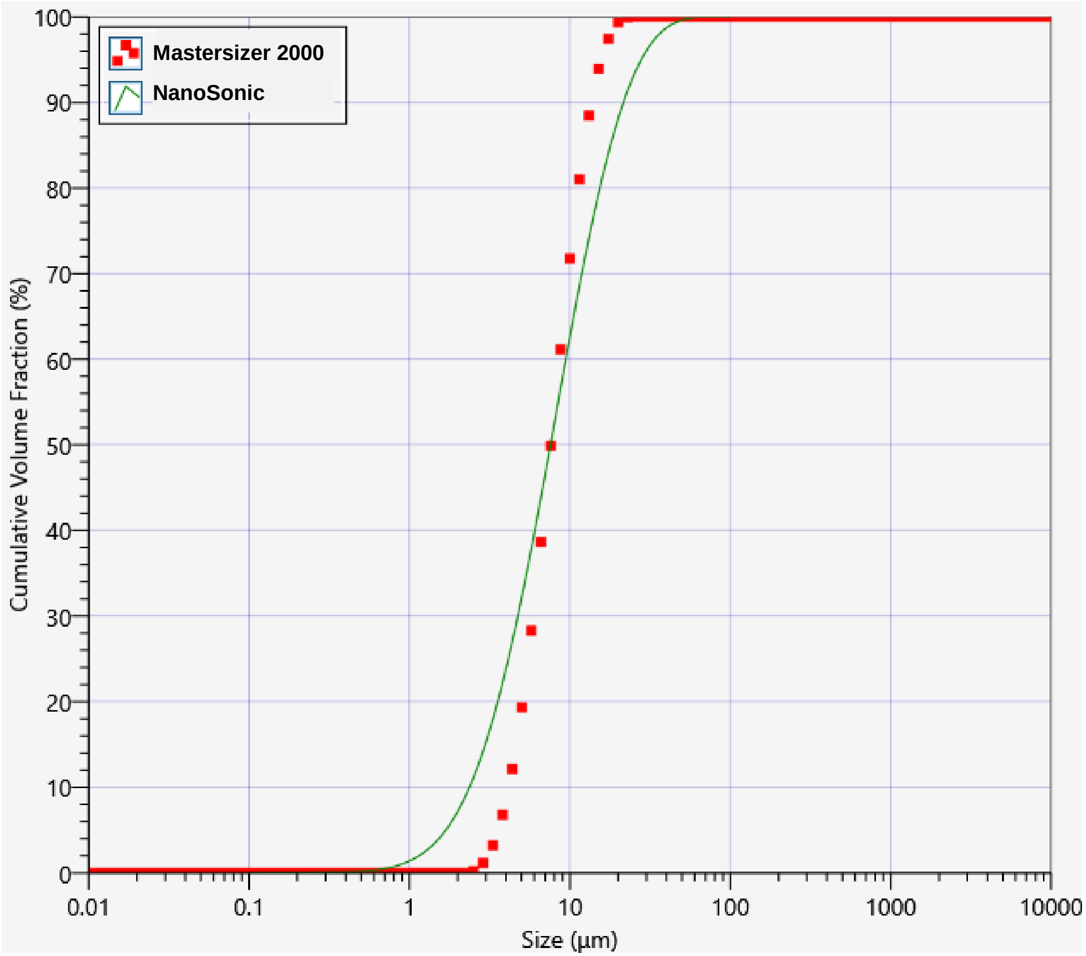

10 µm
Mag = 5.00 K X
EHT = 5.00 kV
Signal A = InLens
WD = 3.3 mm
LEMAS
Date :15 Oct 2013

α-Alumina 4% w/w, D_{50} < 10 µm

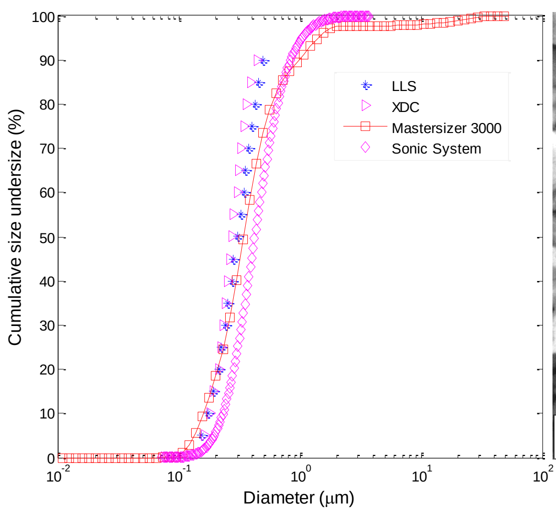
- NanoSonic: D_{50} = 7.98µm
- Mastersizer 2000: D50 = 8.22µm

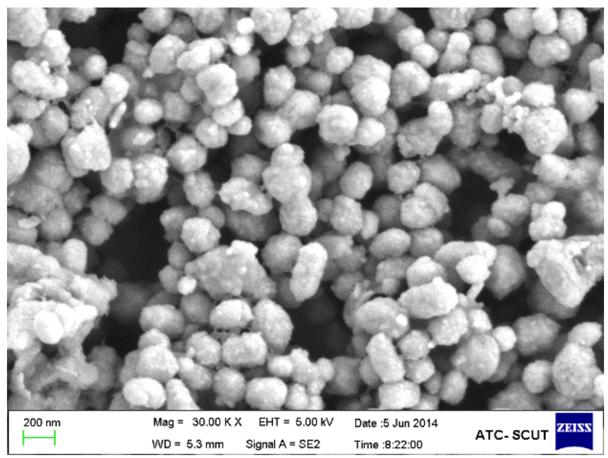
Mastersizer 2000 predicts much narrower size distribution but the D50 shows very good agreements.

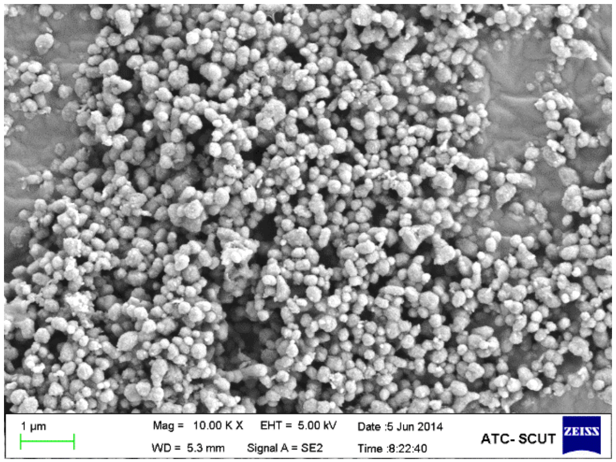
Difference can be because the Mastersizer 2000 is very dilute while the Nanosizer is measured in 4% w/w.



NIST TiO_2 Reference Materials 8988

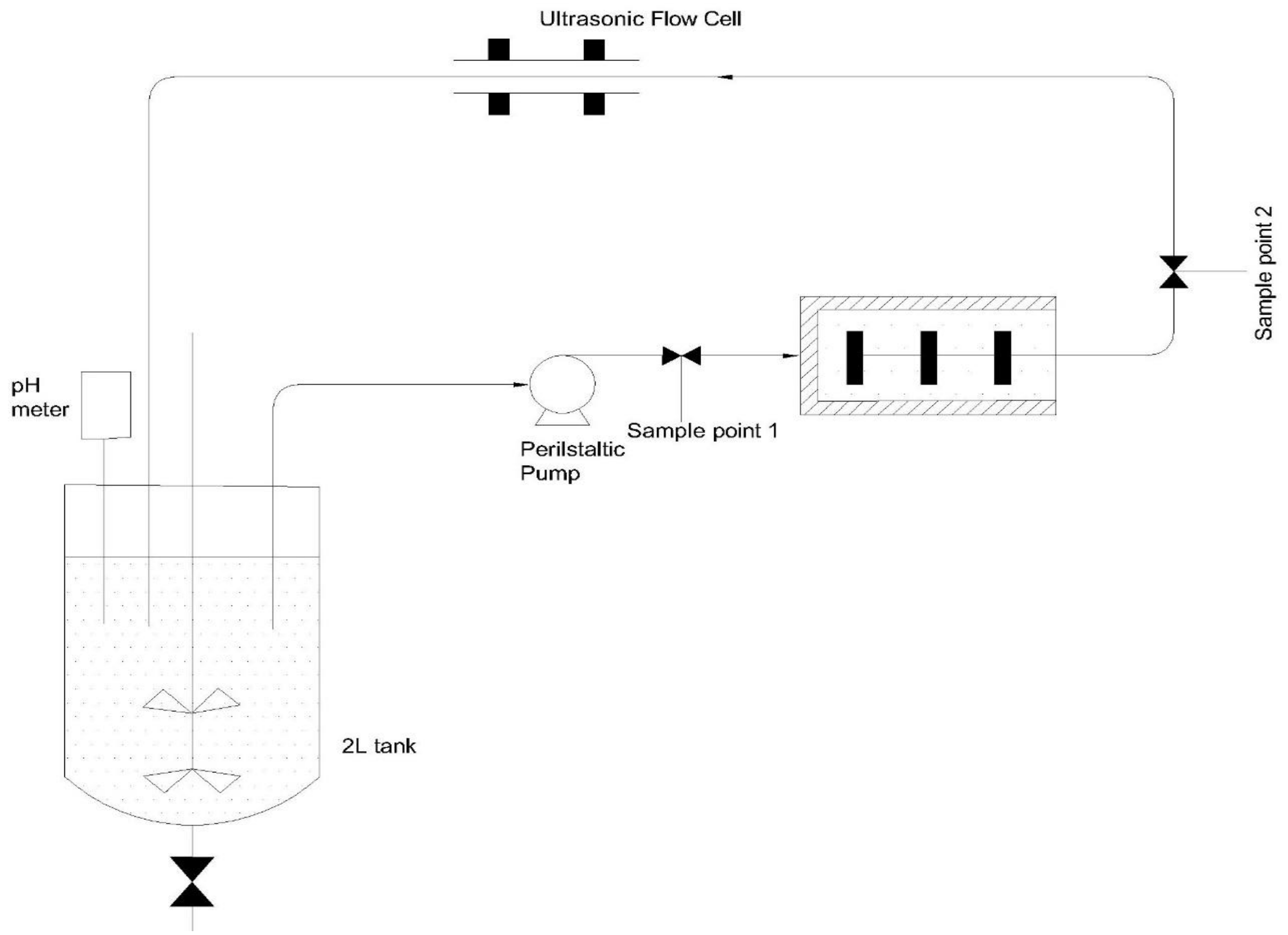




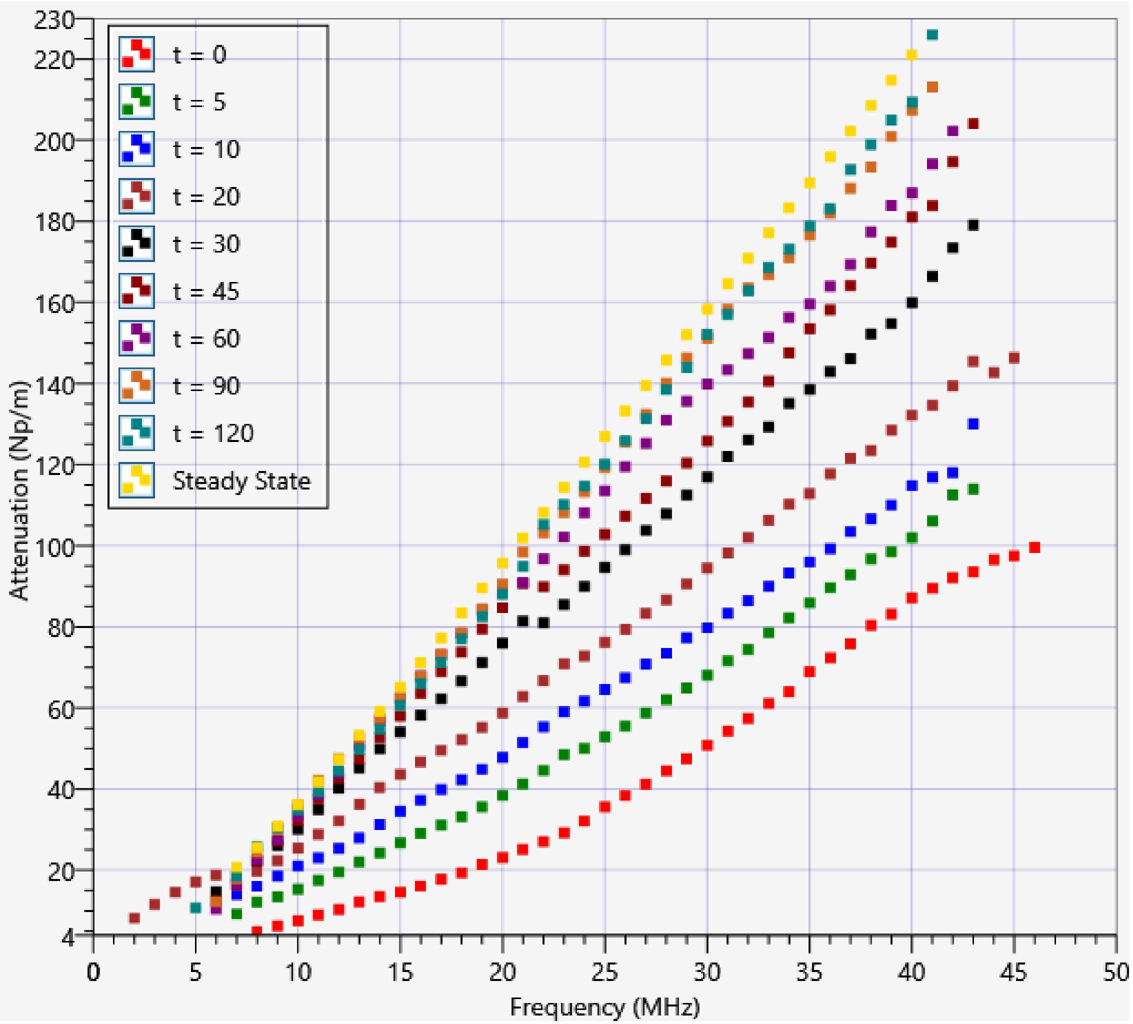


	D10 (nm)	D50 (nm)
NIST LLS	170±20	300±30
NIST XDC	180±20	270±30
Mastersizer 3000	165±7	356±13
NanoSonic	246±3	406±5

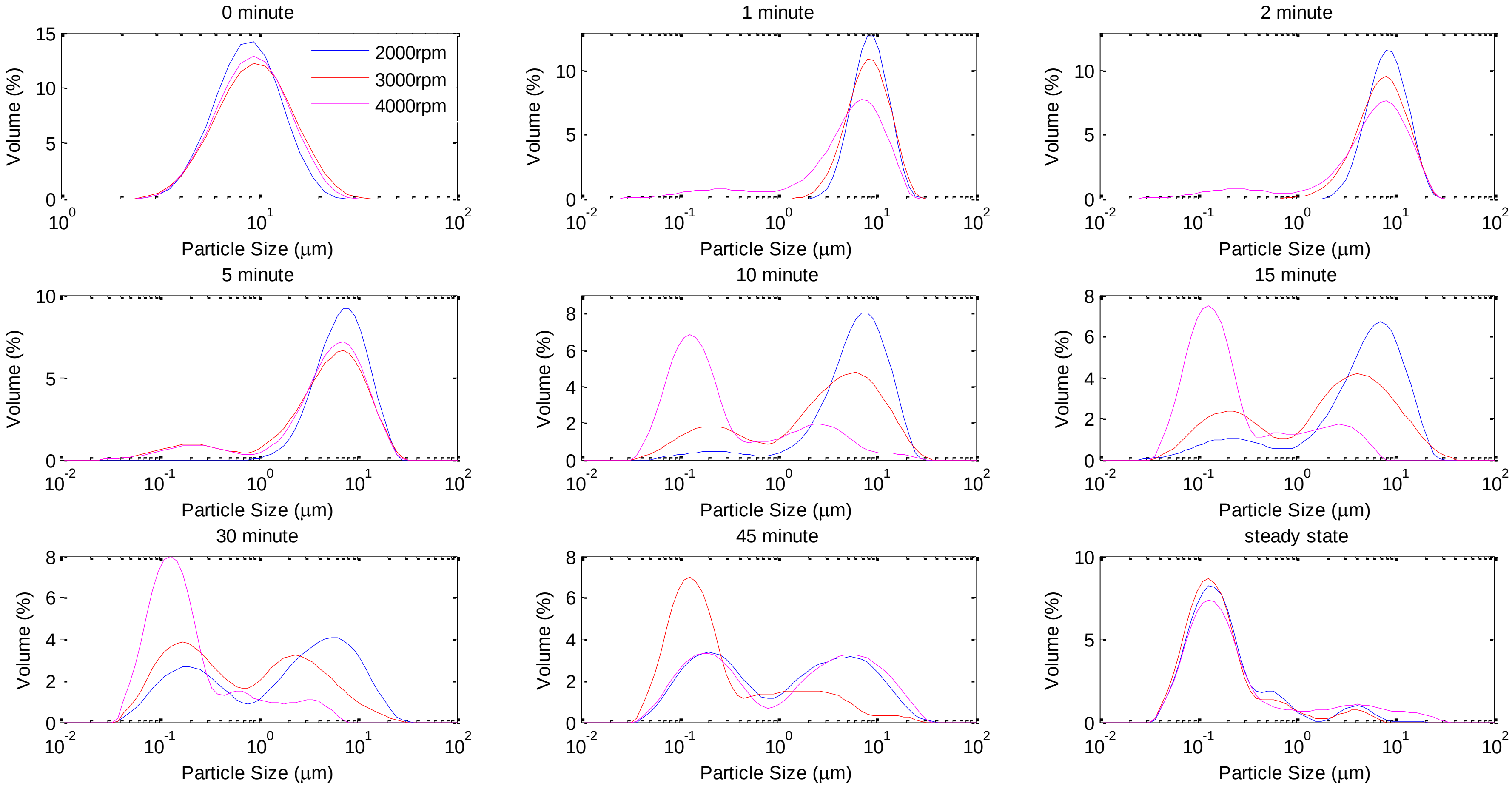
EXPERIMENTAL SETUP: nano-milling system

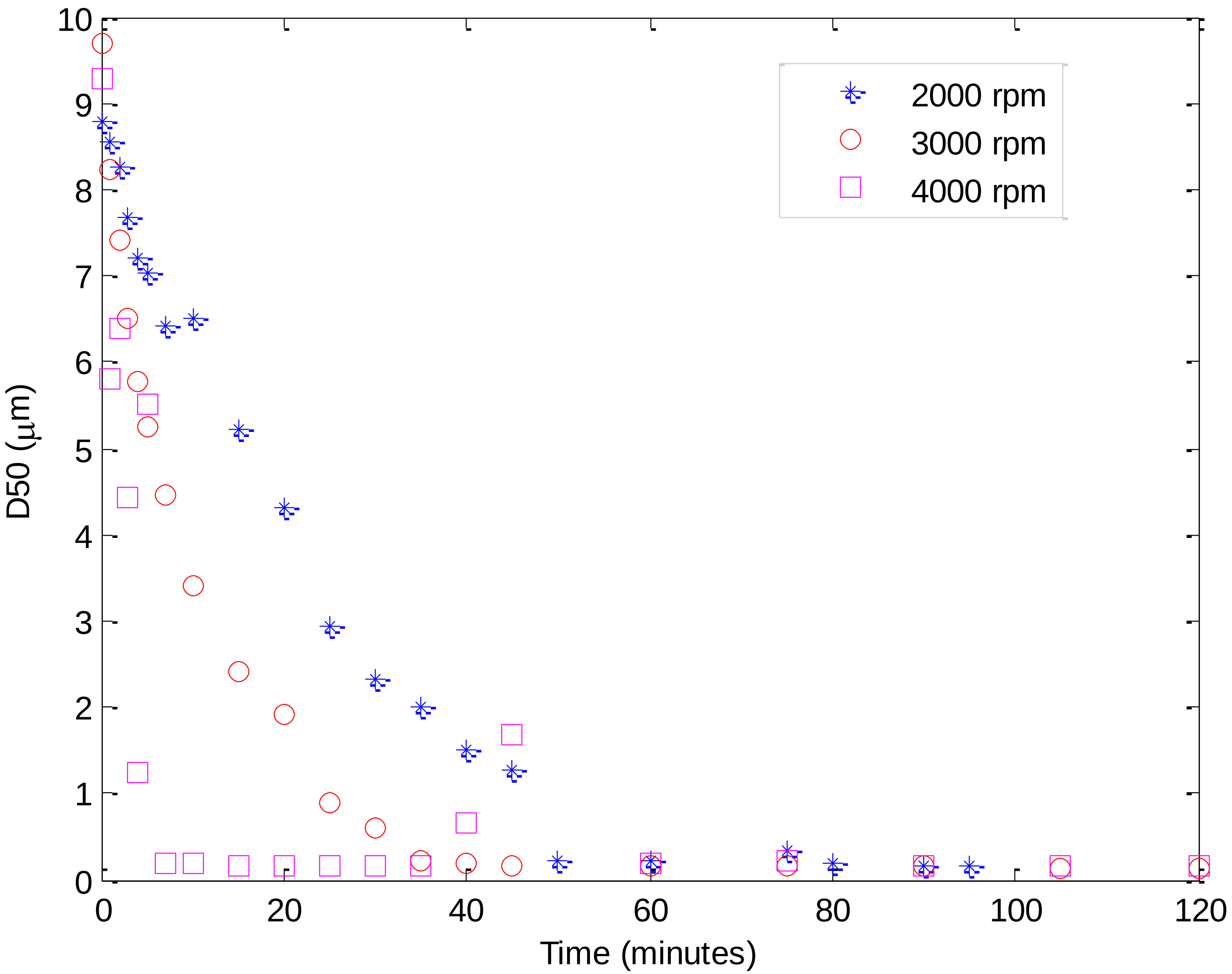


RESULTS – Attenuation Spectra



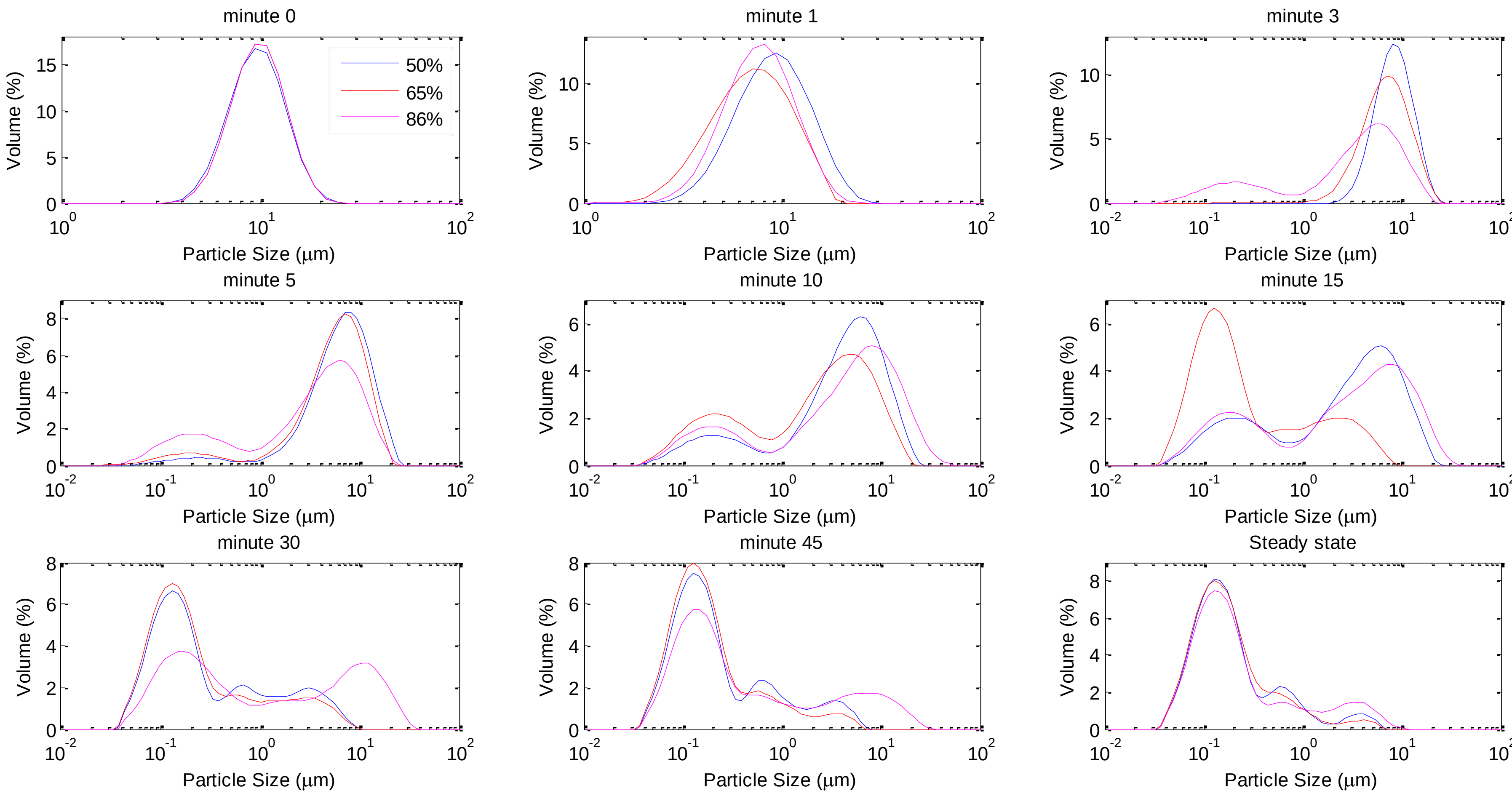
VARYING MILL SPEEDS

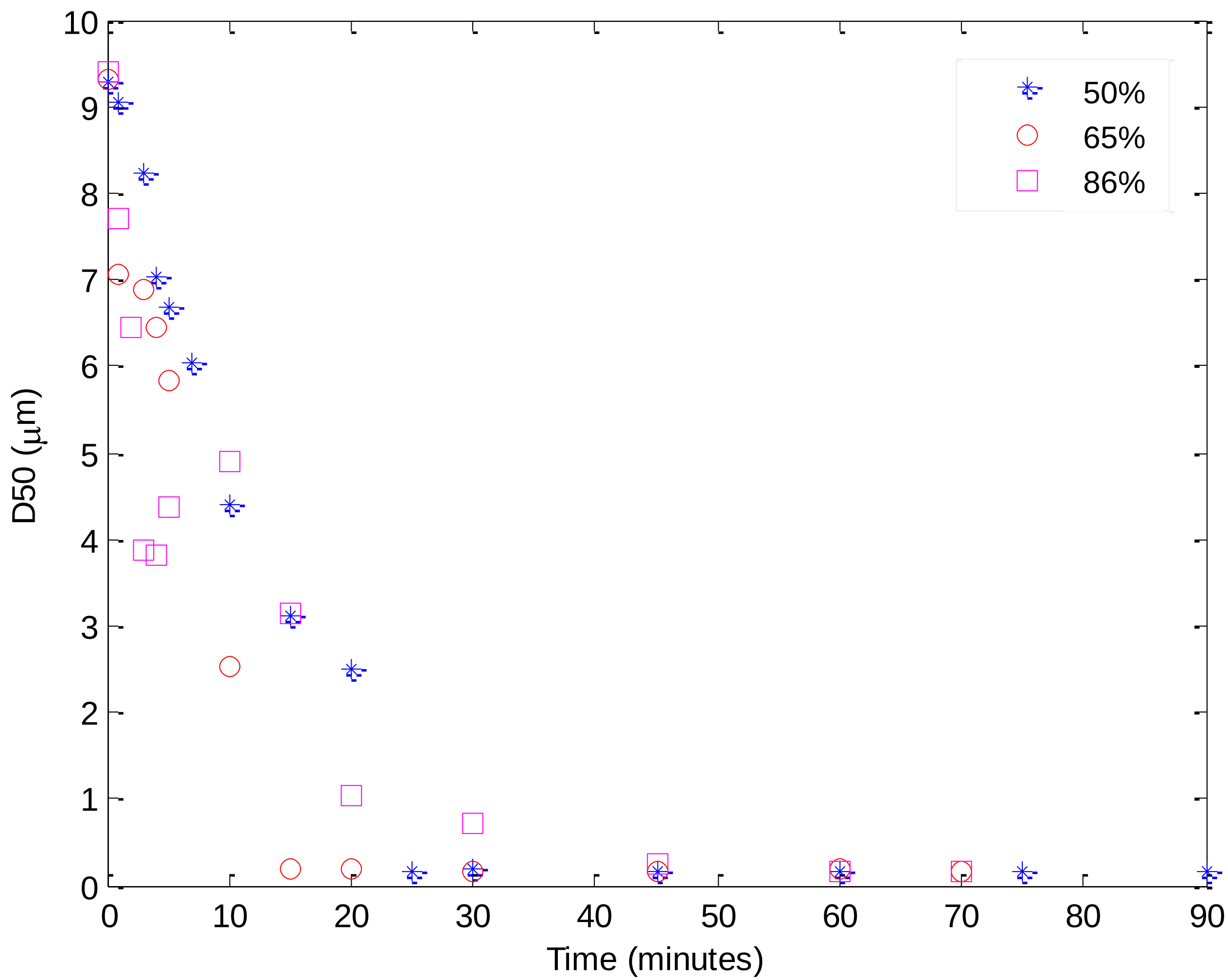




2000 rpm
3000 rpm
4000 rpm
D50 (μm)
Time (minutes)
0
1
2
3
4
5
6
7
8
9
10
0
20
40
60
80
100
120

VARYING GRINDING MEDIA LOADING





10
9
8
7
6
5
4
3
2
1
0
D50 (μm)
0
10
20
30
40
50
60
70
80
90
Time (minutes)
50%
65%
86%

POPULATION BALANCE MODELLING

- Process modelling required for process design and online control
- Population balance modelling predict evolution of PSD

$$\frac{dn(v;t)}{dt} = \int_{v}^{\infty} S(\varepsilon)b(v\,|\,\varepsilon)n(\varepsilon;t)d\varepsilon - S(v)n(v;t) +$$

$$\frac{1}{2}\int_{0}^{v} \beta(\varepsilon;v)n(\varepsilon;t)n(v-\varepsilon;t)d\varepsilon - n(v;t)\int_{0}^{v} \beta(v;\varepsilon)n(\varepsilon;t)d\varepsilon$$

- Widely applied to several particulate processes (e.g., granulation and dry milling)
- Limited application to wet milling

➢ Due to lack of breakage and aggregation kernels

- No phenomenological breakage model for stirred media milling
  - Empirical kernels employed

$$b(v) = kv^n$$

➢ Difficult for design and scale-up

➢ Provides little insight into the milling process

BREAKAGE KERNEL DEVELOPMENT

- Applied stress > fracture strength → breakage
- Therefore

$$Breakage\ rate\ \alpha\ Rate\ of\ particle\ stress \cdot \left(\frac{applied\ stress}{particle\ fracture\ strength} \right)^{a}$$

(RAMACHANDRAN et. al., 2009)

$$\frac{dn(v,t)}{dt} = K\,R_{GM}^{2-3a/2} N_{GM}^{2} u_{t}^{1-3a/5} v^{-k_2} \cdot n(v,t)$$

Therefore, the breakage kernel is:

$$b(v) = K\,R_{GM}^{2-3a/2} N_{GM}^{2} u_{t}^{1-3a/5} v^{-k_2} = K_{eff} v^{-k_2}$$

Allows the parameters fitted at one process condition to be applied to other process conditions i.e. for changing mill loading:

$$\frac{K_{eff,2}}{K_{eff,1}} = \left(\frac{N_{GM,2}}{N_{GM,1}}\right)^2$$

POPULATION BALANCE MODELLING

- Applied the PBM to our set up
- For circuit mode

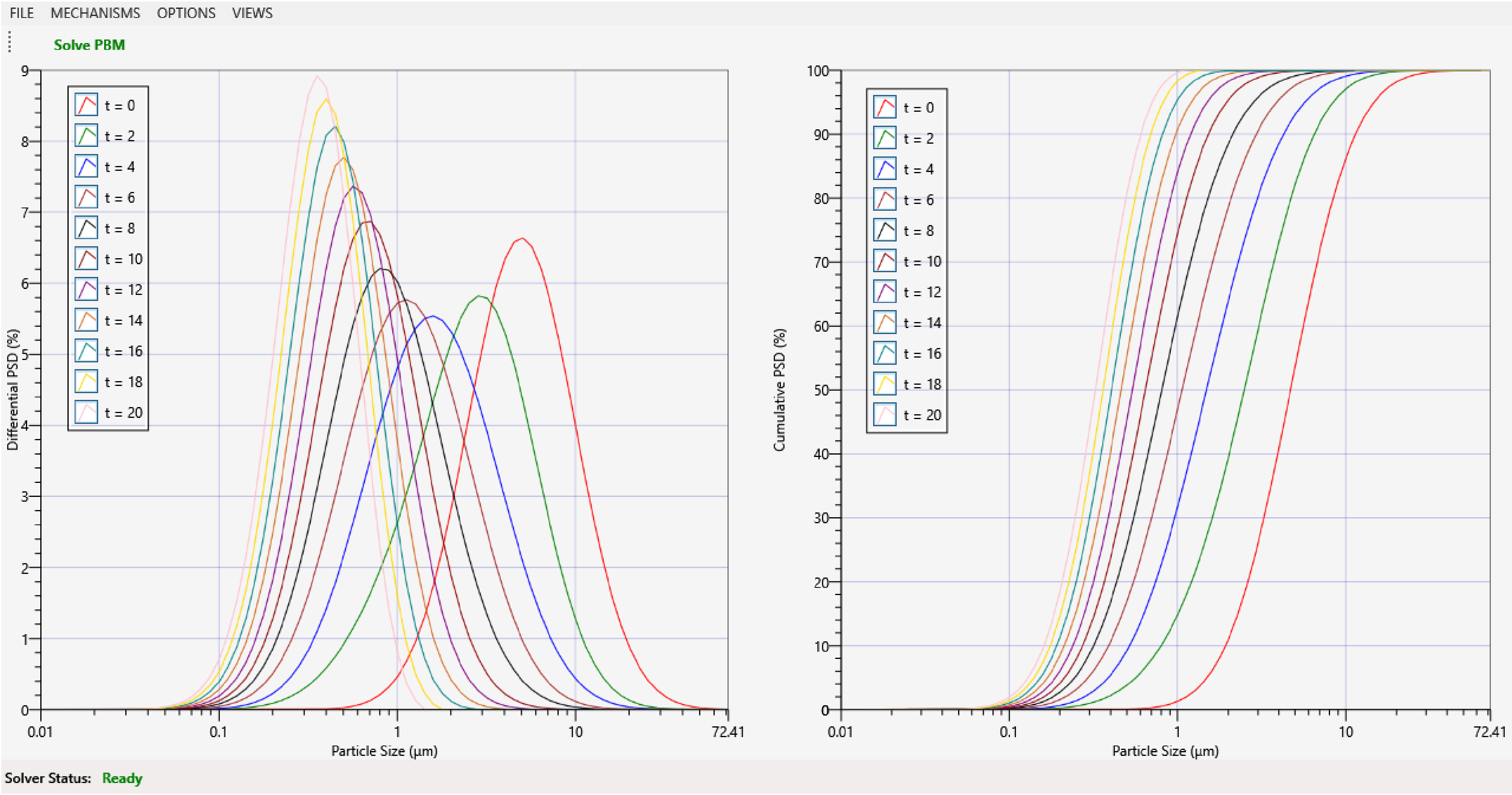
$$\frac{dn(v;t)}{dt} = \int_v^\infty S(\varepsilon)b(v \mid \varepsilon)n(\varepsilon;t)d\varepsilon - S(v)n(v;t) + \frac{1}{2}\int_0^v \beta(\varepsilon;v)n(\varepsilon;t)n(v-\varepsilon;t)d\varepsilon - n(v;t)\int_0^v \beta(v;\varepsilon)n(\varepsilon;t)d\varepsilon + \frac{m(v,t)-n(v,t)}{\theta_{mill}(t)}$$

$$\frac{dm(v;t)}{dt} = \frac{1}{2}\int_0^v \beta(\varepsilon;v)m(\varepsilon;t)(v-\varepsilon;t)d\varepsilon - m(v;t)\int_0^v \beta(v;\varepsilon)n(\varepsilon;t)d\varepsilon + \frac{n(v,t)-m(v,t)}{\theta_{\tan k}(t)}$$

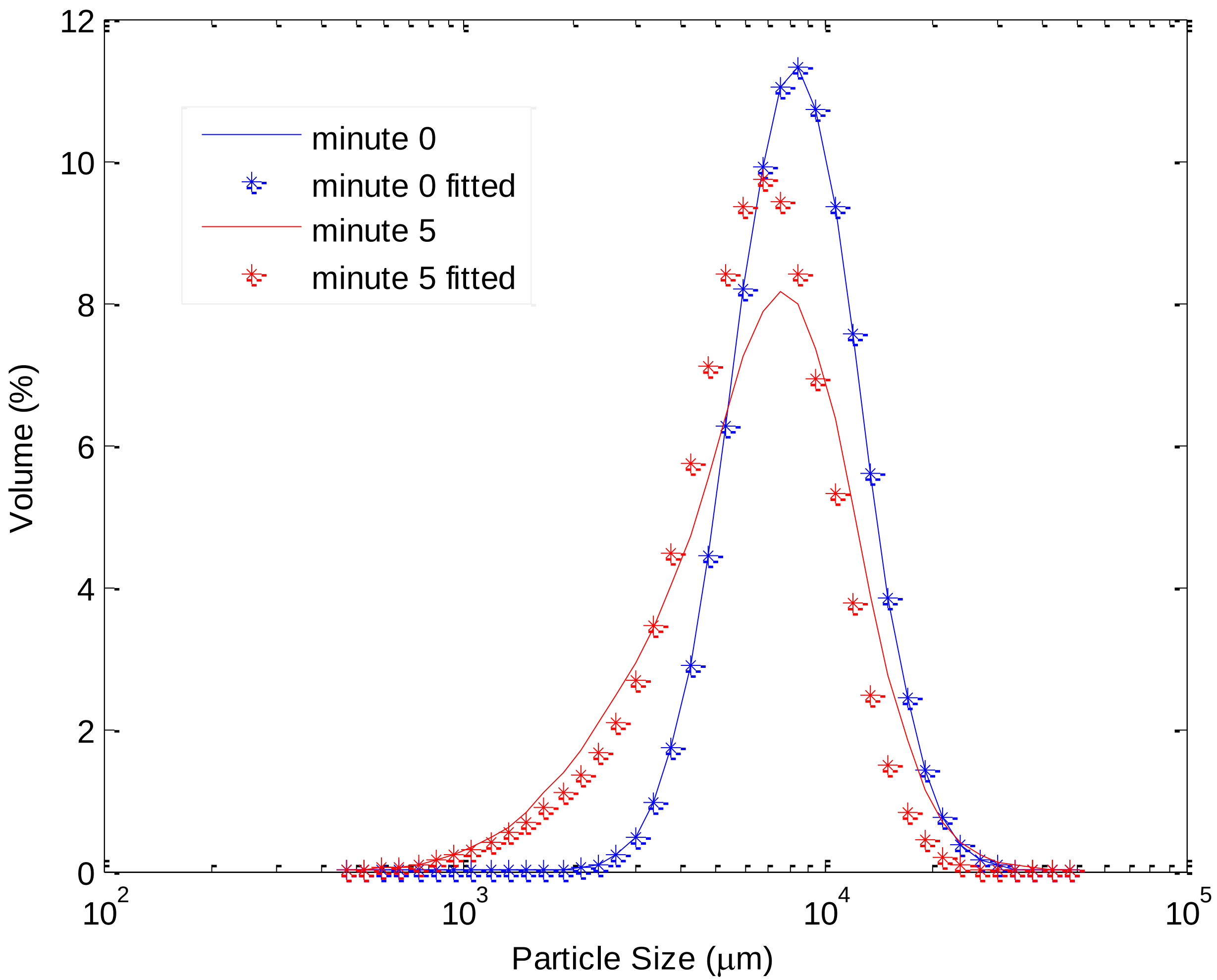
SOLUTIONS OF PBE

- Discretised Population Balance (DPB) method
  - Hounslow et al (1988)
  - Litster et al. (1995)
  - Kumar and Ramkrishna (1998)
  - Wynn et al (1998)
- Moment methodologies
  - QMOM: McGraw (1997), Marhisio et al. (2003, 2005)
  - EMOM: Falola et al. (2013)

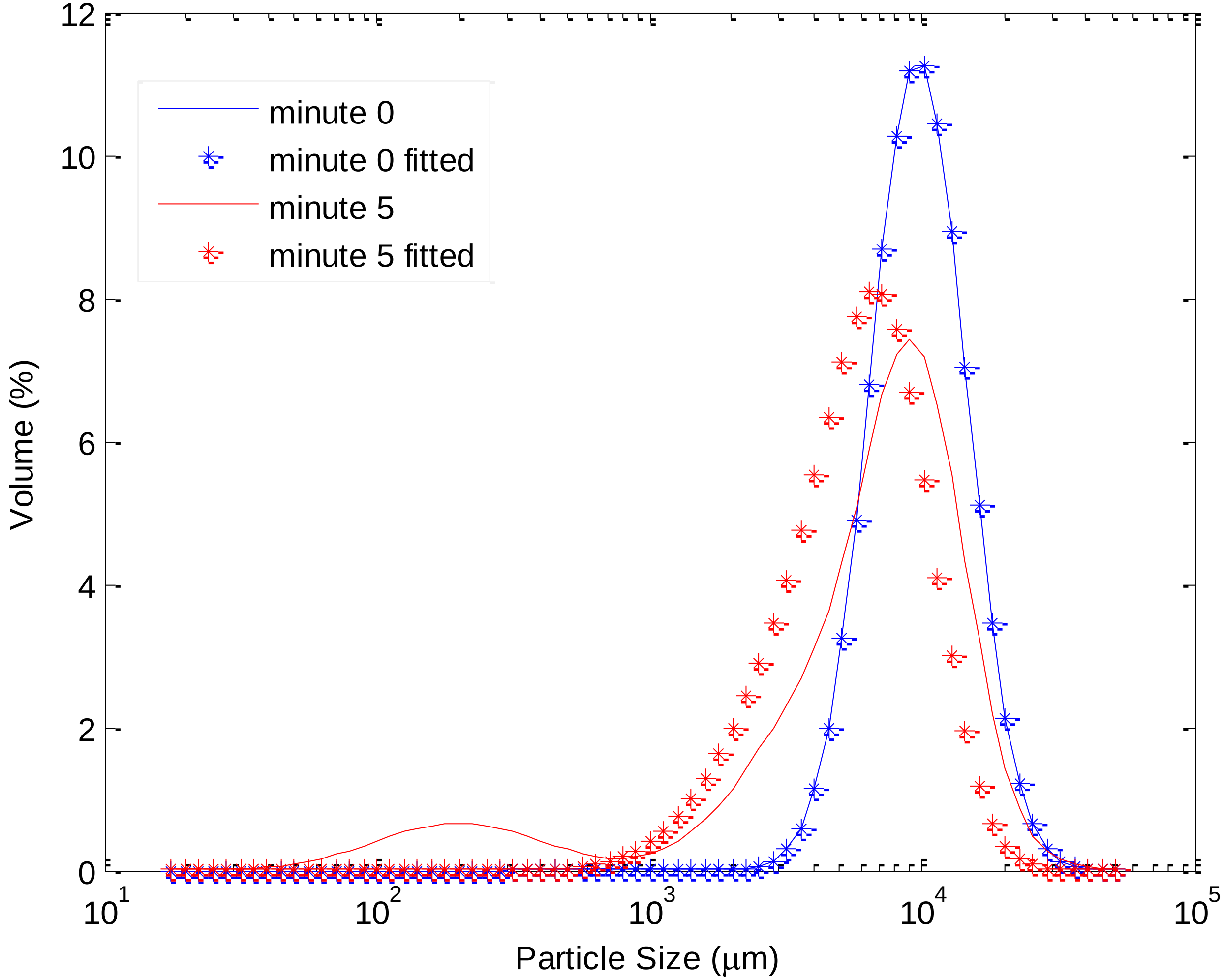
POPULATION BALANCE SOLVER



Process Identification – 0.8mm GM



Prediction/Simulation - 0.6mm GM



CONCLUSIONS

Our group have developed tools for:

- Particle size measurement
- Population balance modelling

- Successful applications

THANK YOU