

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

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Processes Group*



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

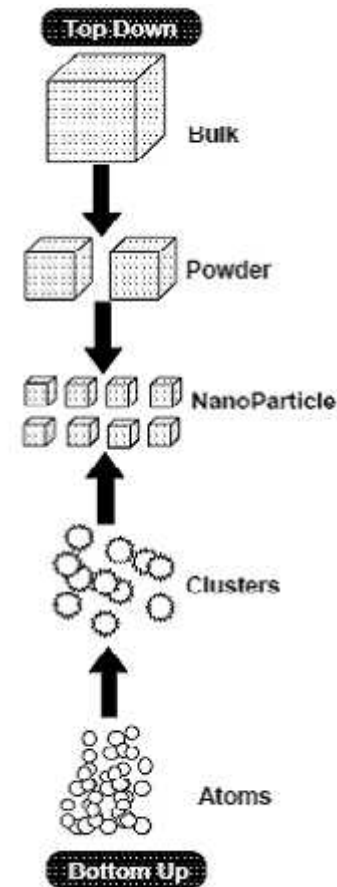


Electronics



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

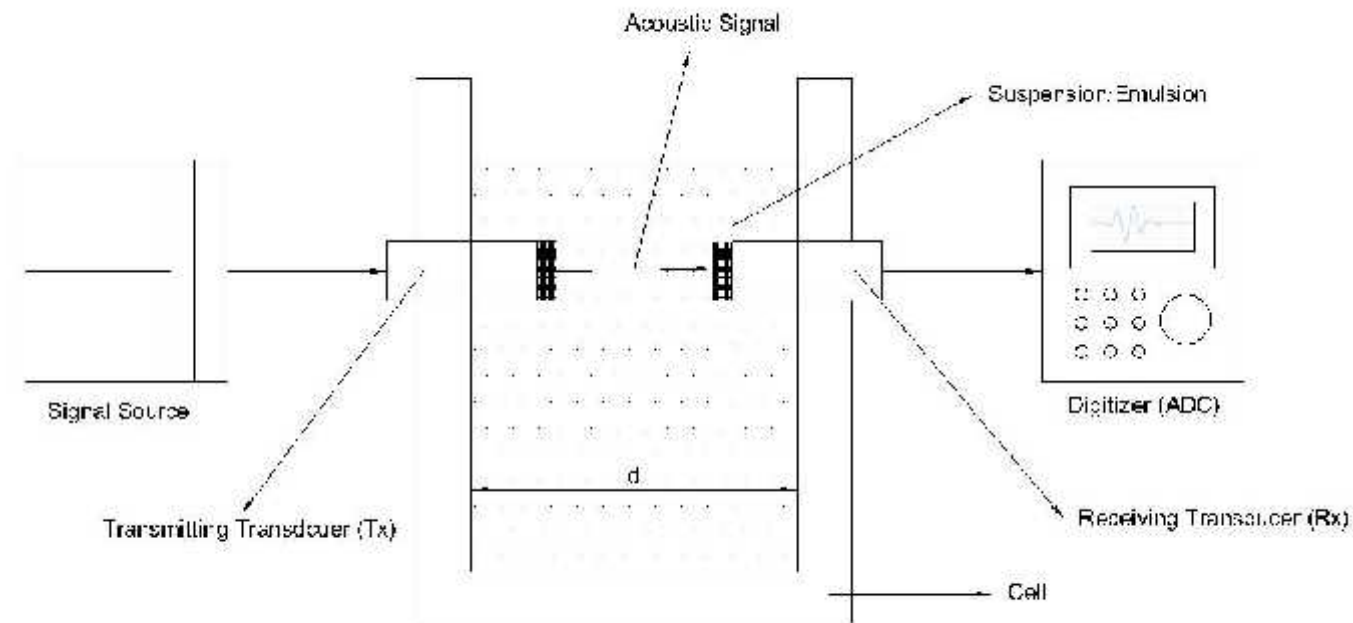
- Requirements?
 - Non-invasive i.e. the measurement should not affect the system
 - Requires no sampling (invasive and sometimes difficult to get a representative sample)
 - Requires no dilution: can affect the properties (such as PSD) of the suspension
 - Fast especially for purpose of control or for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



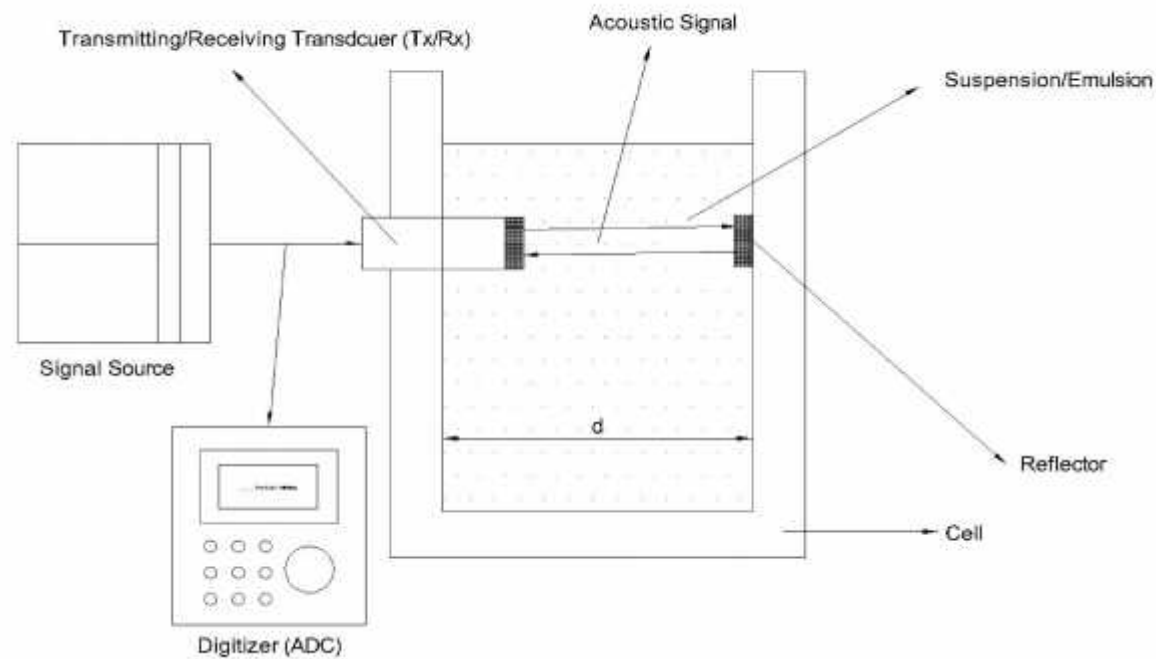
- Dynamic Light Scattering
 - Invasive: Requires dilution and sampling
 - Limited size range: 0.3 – 10 μm
- Light Scattering/Laser Diffraction
 - Invasive: Requires dilution and sampling
- Focused Beam Reflectance Method (FBRM)
 - Applicable only to non-opaque system
 - Limited size range: 0.3 – 10 μm
- 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



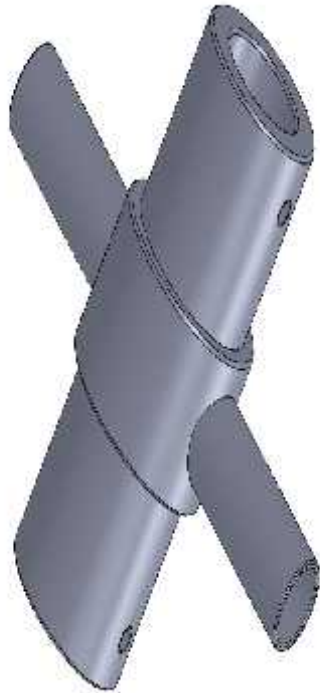
Basic Setup of An Acoustic Particle Measurement System in Through Transmission Mode



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

Hardware design

- Minimalist
- Low volume



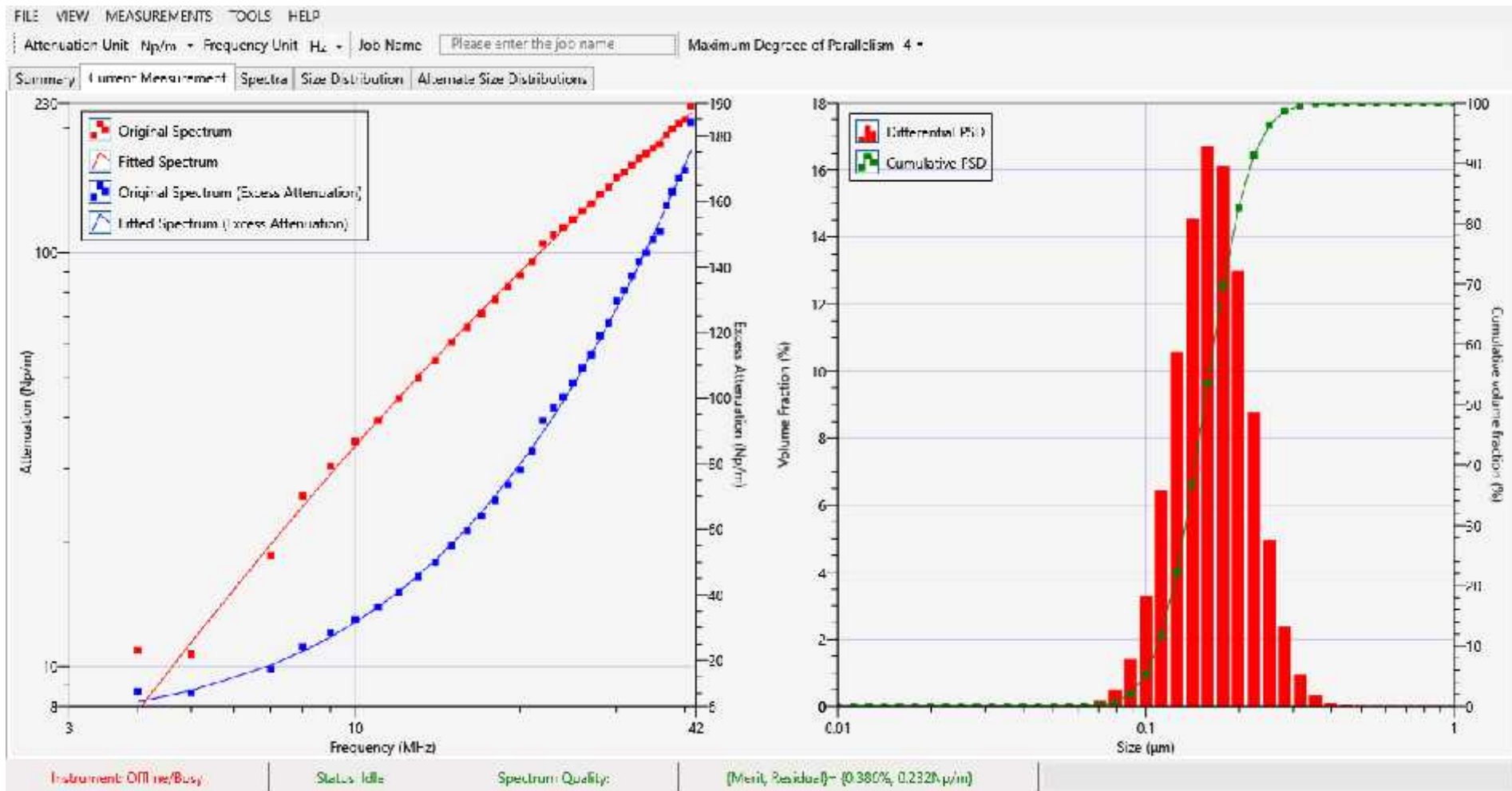
Flow through
measurement cell



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 Aqueous Silica Suspensions

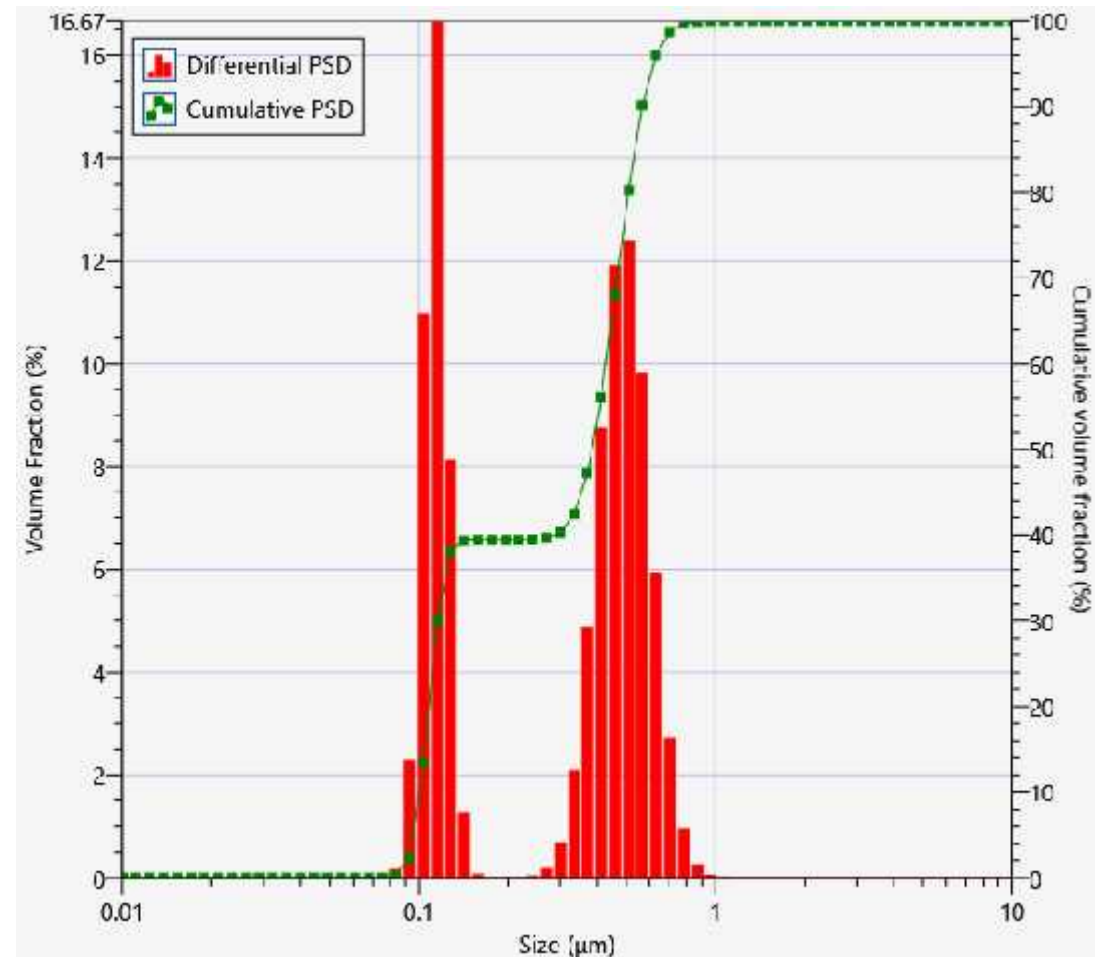
Manufacturer Specification	NanoSonic Measurement	% solid concentration
300nm	298nm	1.59
450nm	465nm	1.59
300nm	293nm	2.81
300nm	305nm	10.16
450nm	452nm	23.35
100nm	106nm	24.75
200nm	197nm	24.88
300nm	290nm	28.96

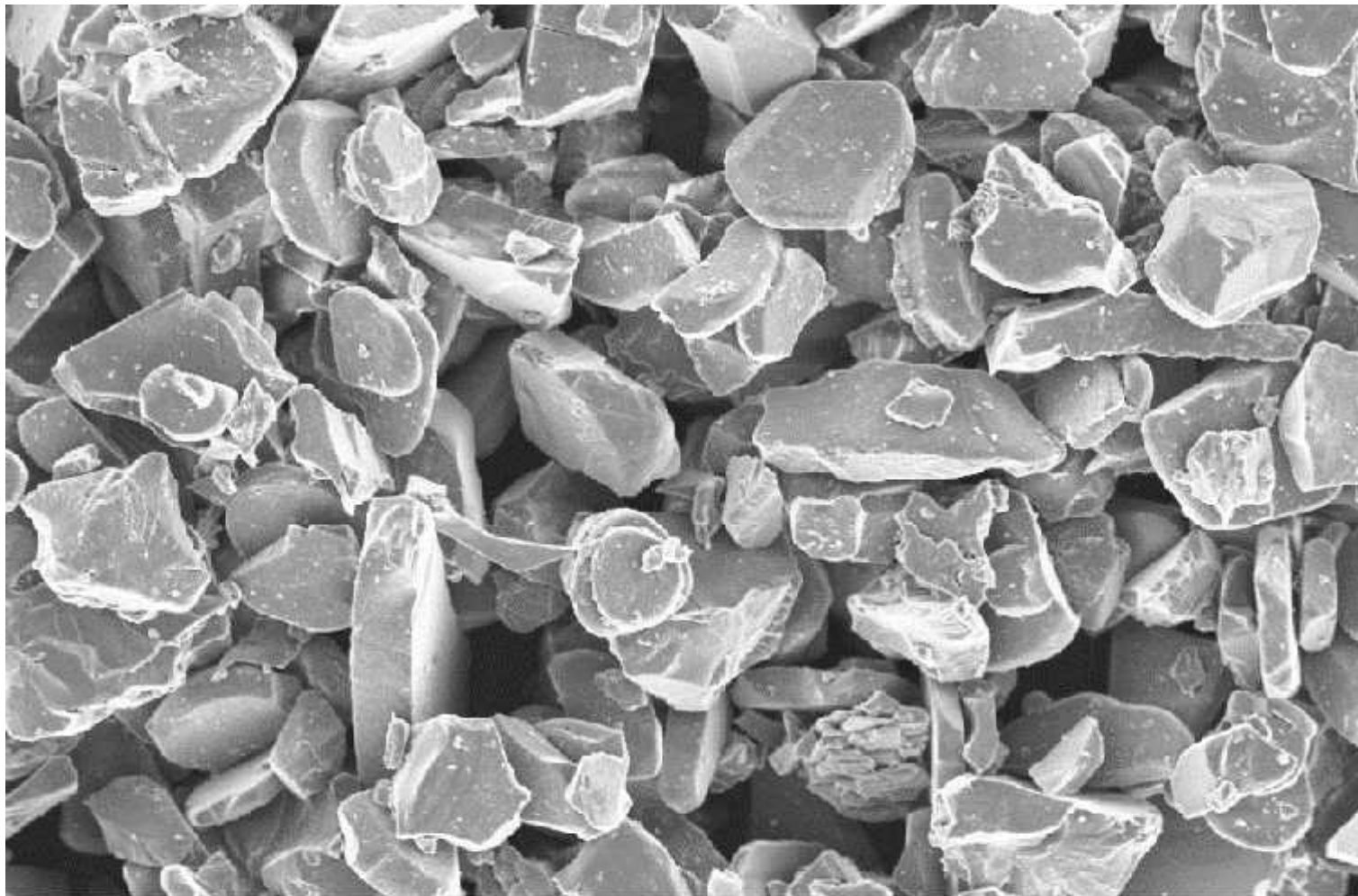
Mixture of 30% 100nm and 70% 450nm silica suspension (23.77% v/v)

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 μ m



Mag = 5.00 KX

EHT = 5.00 KV

Signal A = InLens

WD = 3.3 mm



Date :15 Oct 2013

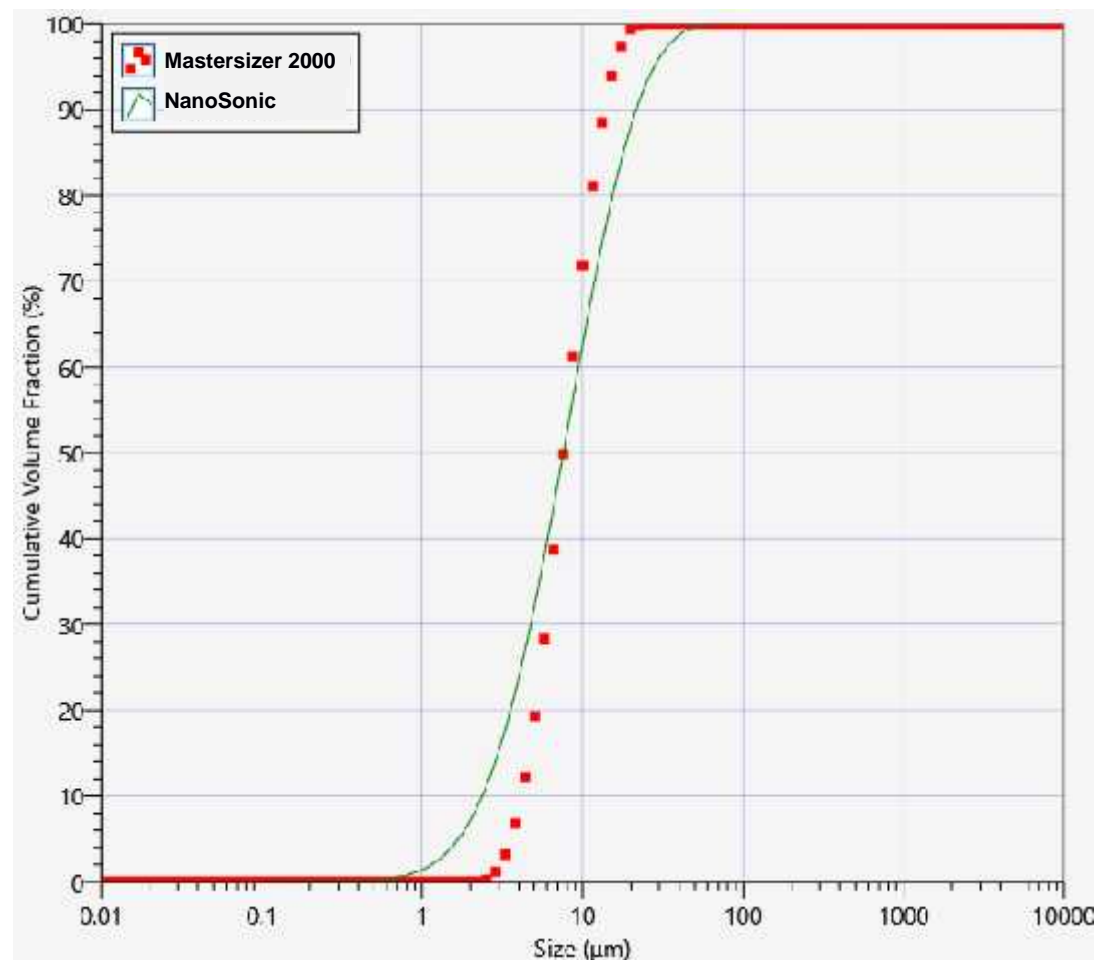


-Alumina 4% w/w, $D_{50} < 10 \mu\text{m}$

- NanoSonic: $D_{50} = 7.98\mu\text{m}$
- Mastersizer 2000: $D_{50} = 8.22\mu\text{m}$

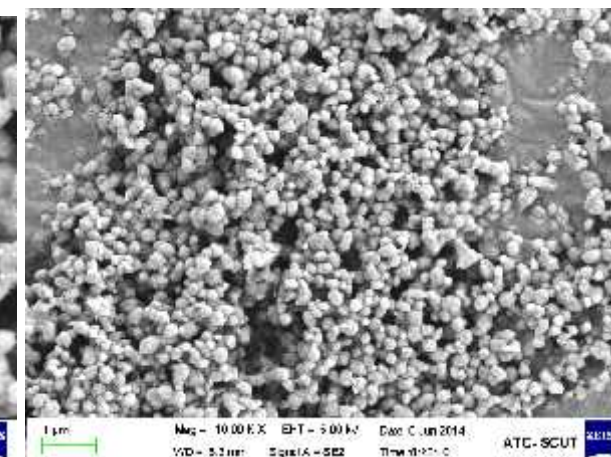
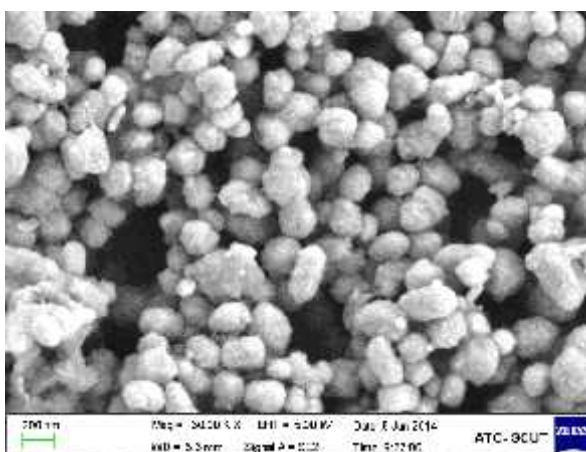
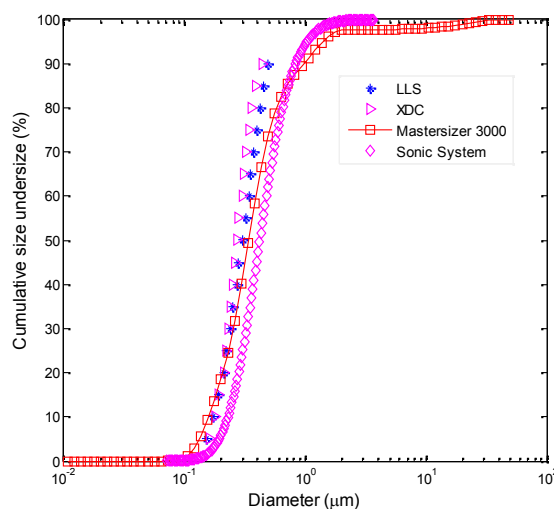
Mastersizer 2000 predicts much narrower size distribution but the D_{50} shows very good agreements.

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



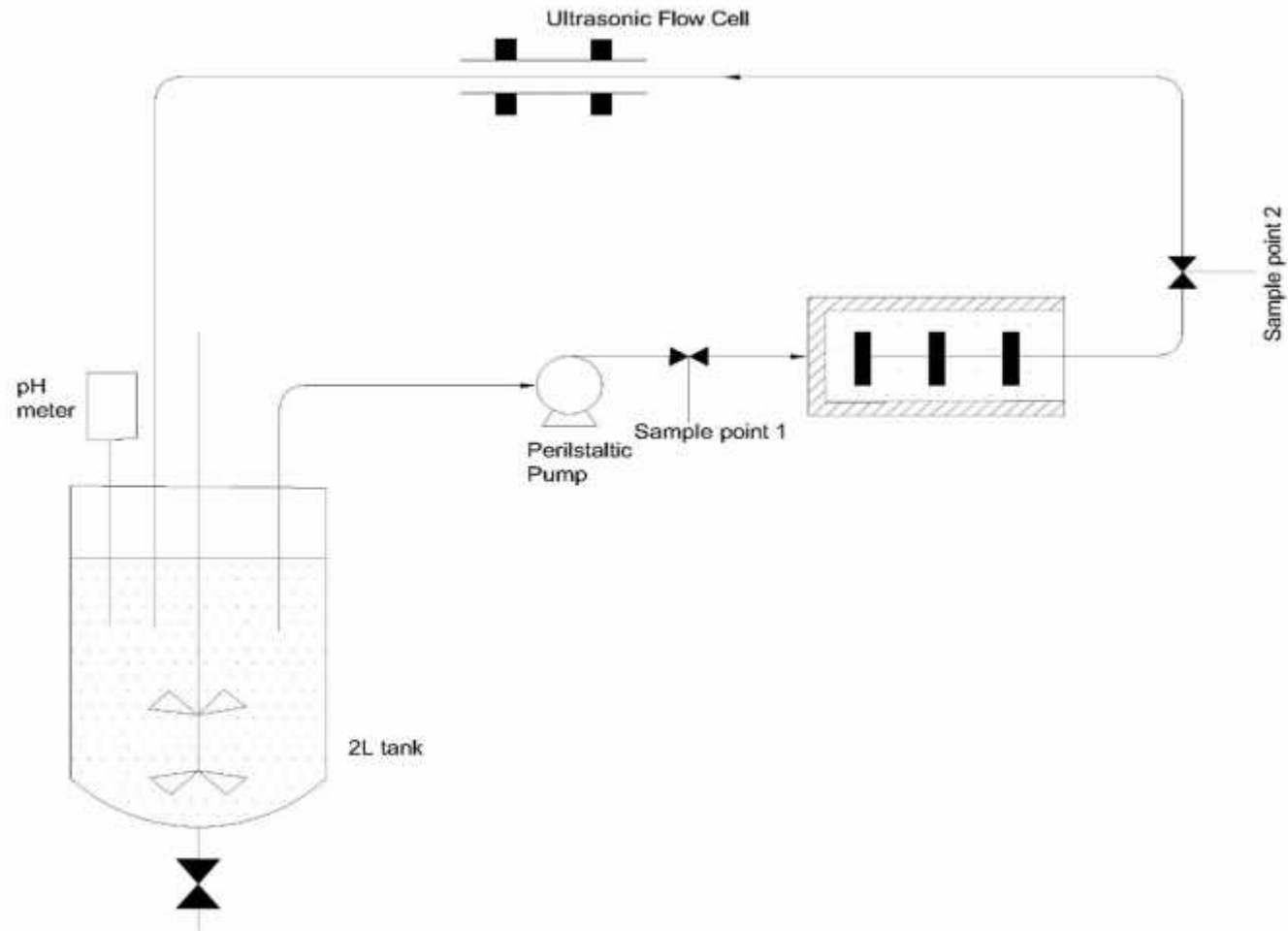


NIST TiO₂ Reference Materials 8988



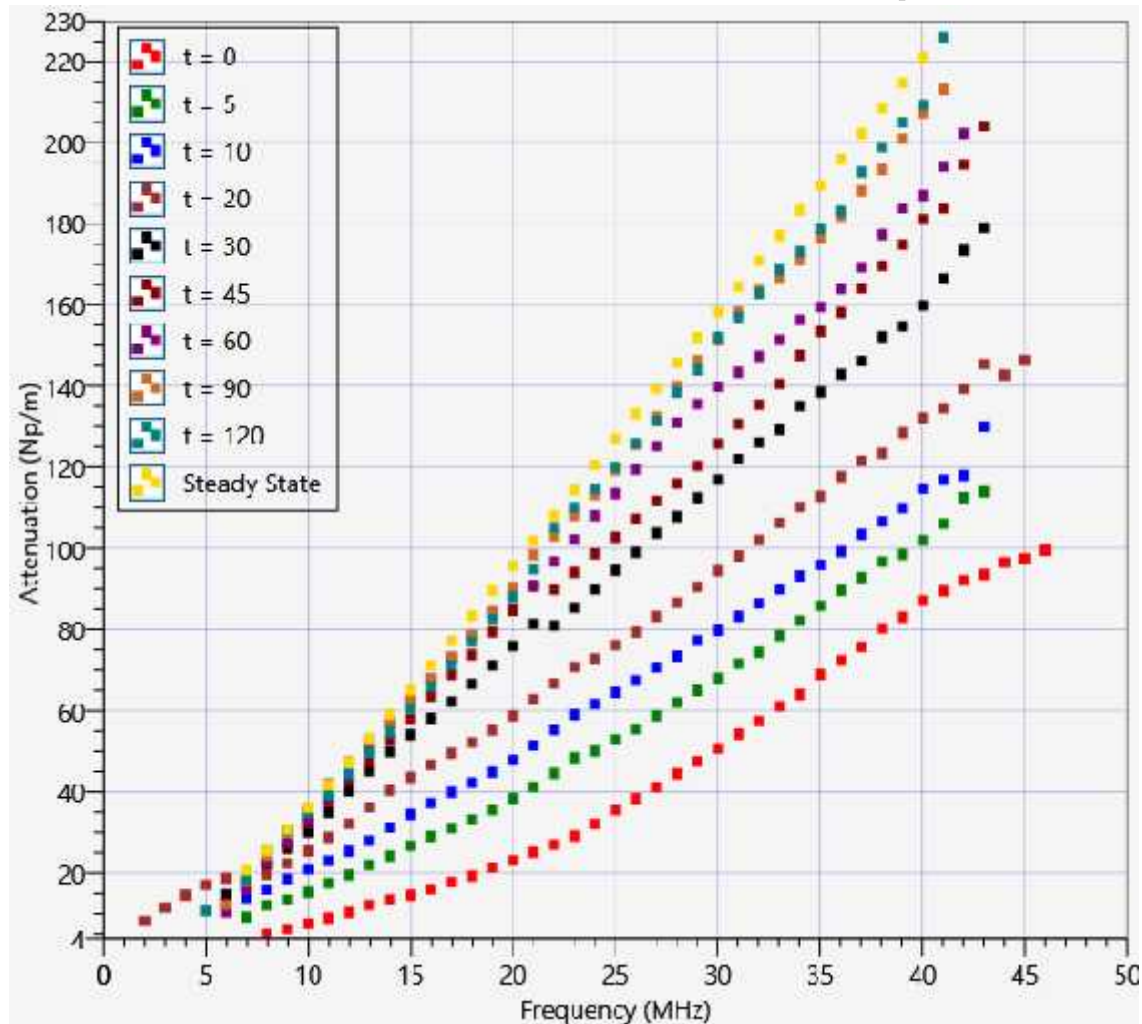
	D10 (nm)	D50 (nm)
NIST LLS	170±20	300±30
NIST XDC	180±20	270±30
Mastersizer 3000	165±7	356±13
NanoSonic	246±3	406±5

EXPERIMENTAL SETUP: nano-milling system



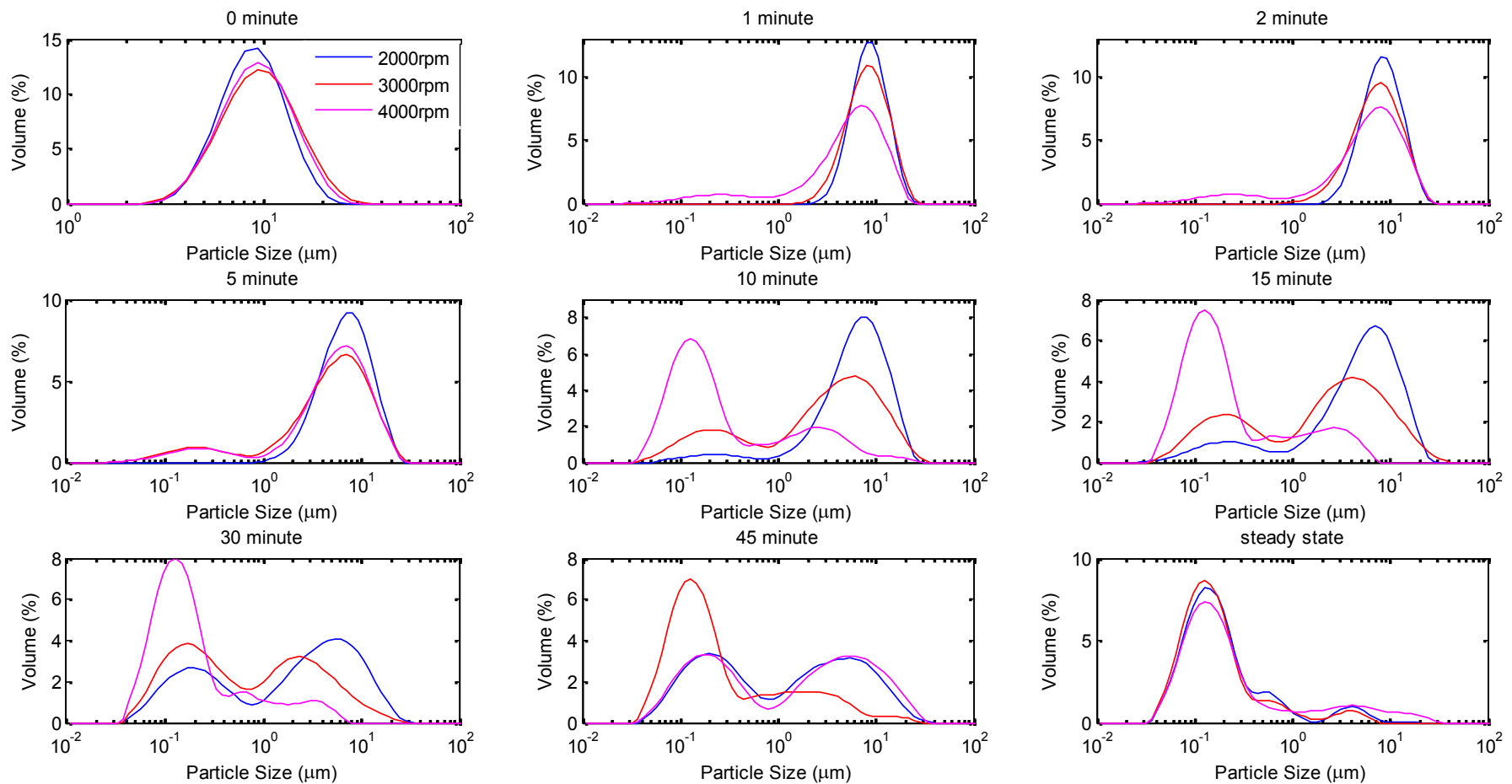


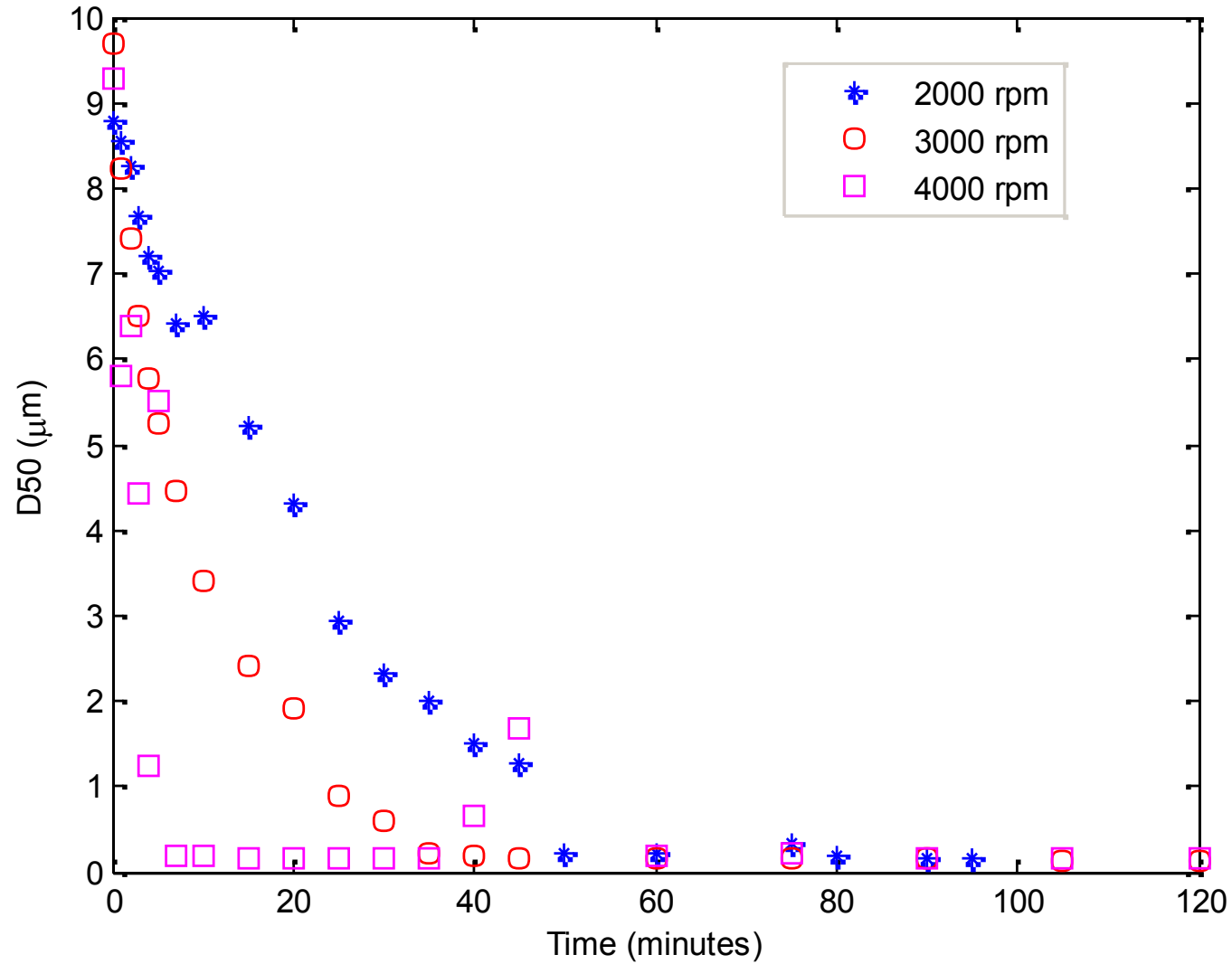
RESULTS – Attenuation Spectra





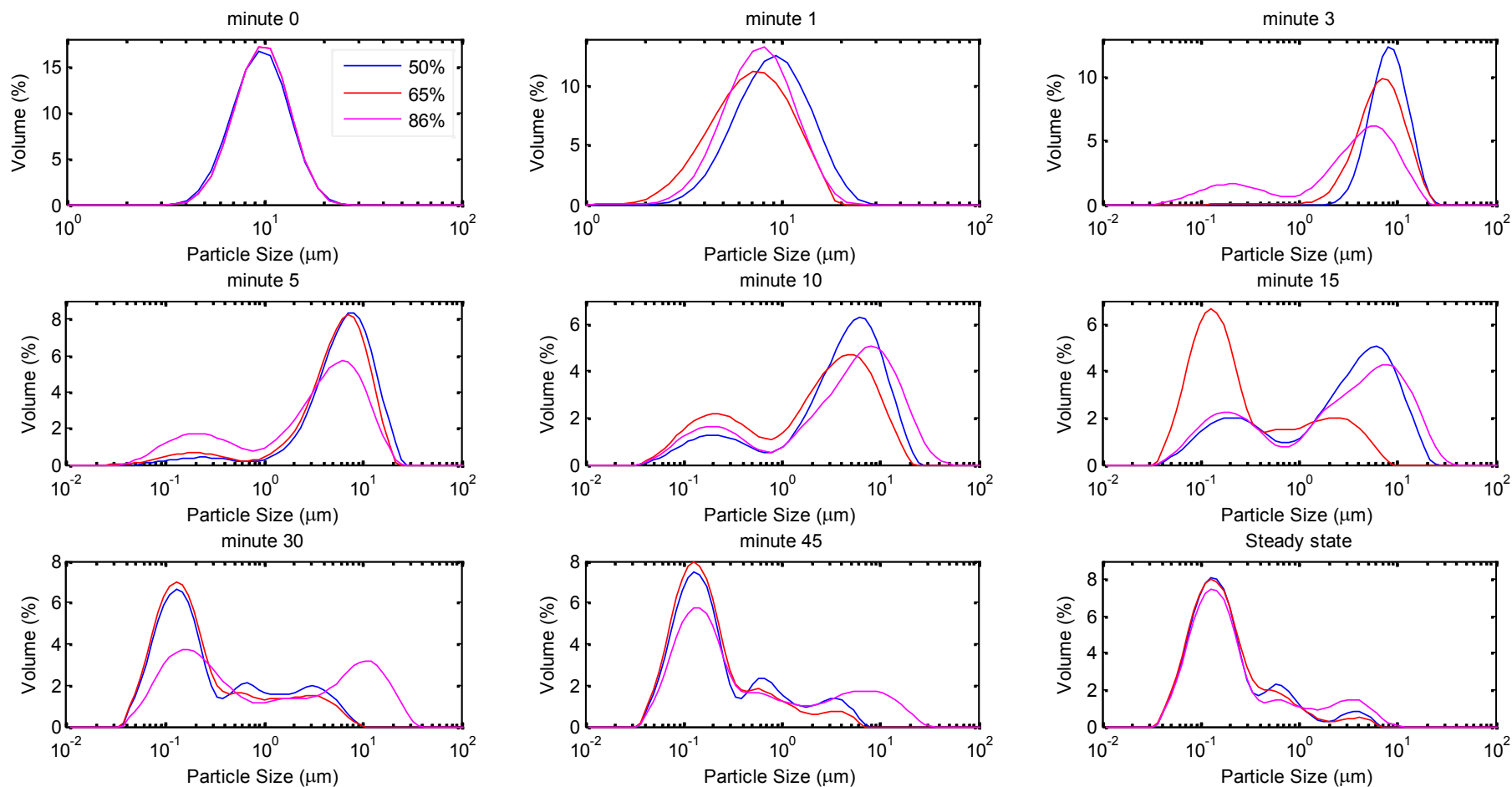
VARYING MILL SPEEDS

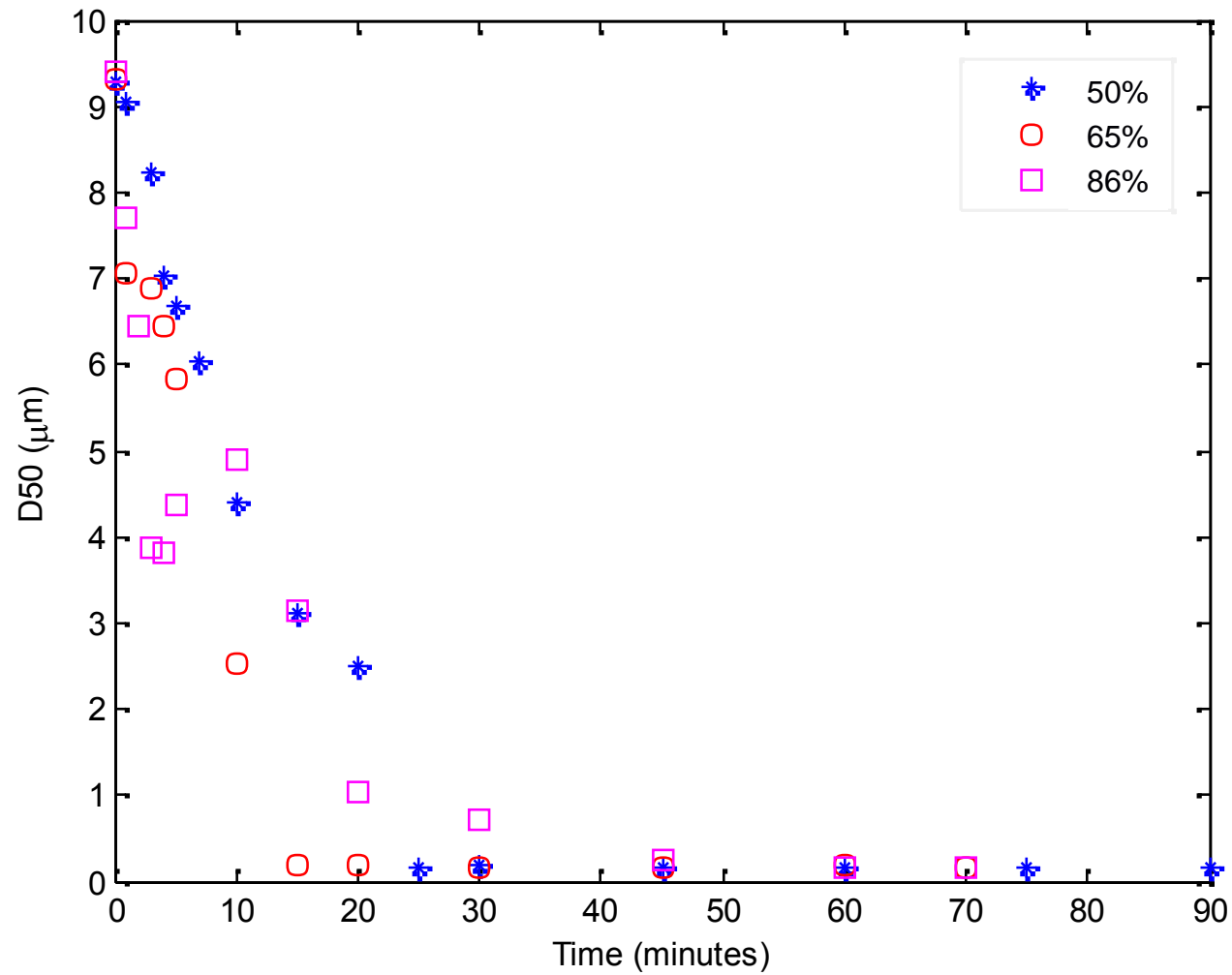






VARYING GRINDING MEDIA LOADING







POPULATION BALANCE MODELLING

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

$$\frac{dn(v;t)}{dt} = \int_v^{\infty} S(v) b(v|v) n(v;t) dv - S(v) n(v;t) + \frac{1}{2} \int_0^v S(v;v) n(v;t) n(v-v;t) dv - n(v;t) \int_0^v S(v;v) n(v;t) dv$$

- 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 \longrightarrow breakage
- Therefore

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

(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

$$\begin{aligned} \frac{dn(v;t)}{dt} = & \int_v^\infty S(v)b(v|v)n(v;t)dv - S(v)n(v;t) + \\ & \frac{1}{2} \int_0^v S(v;v)n(v;t)n(v-v;t)dv - n(v;t) \int_0^v S(v;v)n(v;t)dv \\ & + \frac{m(v,t) - n(v,t)}{\tau_{mill}(t)} \end{aligned}$$

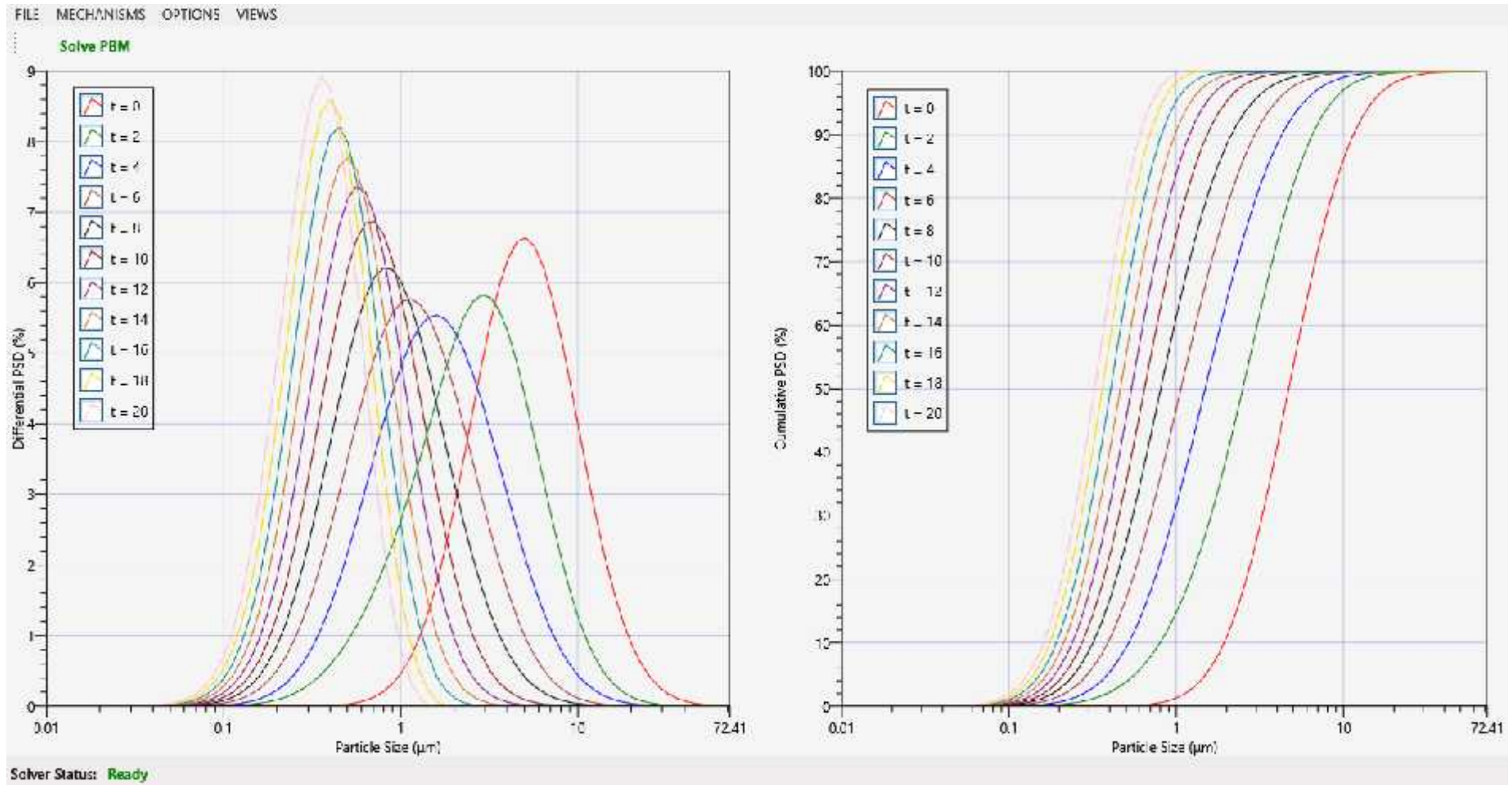
$$\begin{aligned} \frac{dm(v;t)}{dt} = & \frac{1}{2} \int_0^v S(v;v)m(v;t)(v-v;t)dv - m(v;t) \int_0^v S(v;v)n(v;t)dv \\ & + \frac{n(v,t) - m(v,t)}{\tau_{tan k}(t)} \end{aligned}$$



SOLUTIONS OF PBE

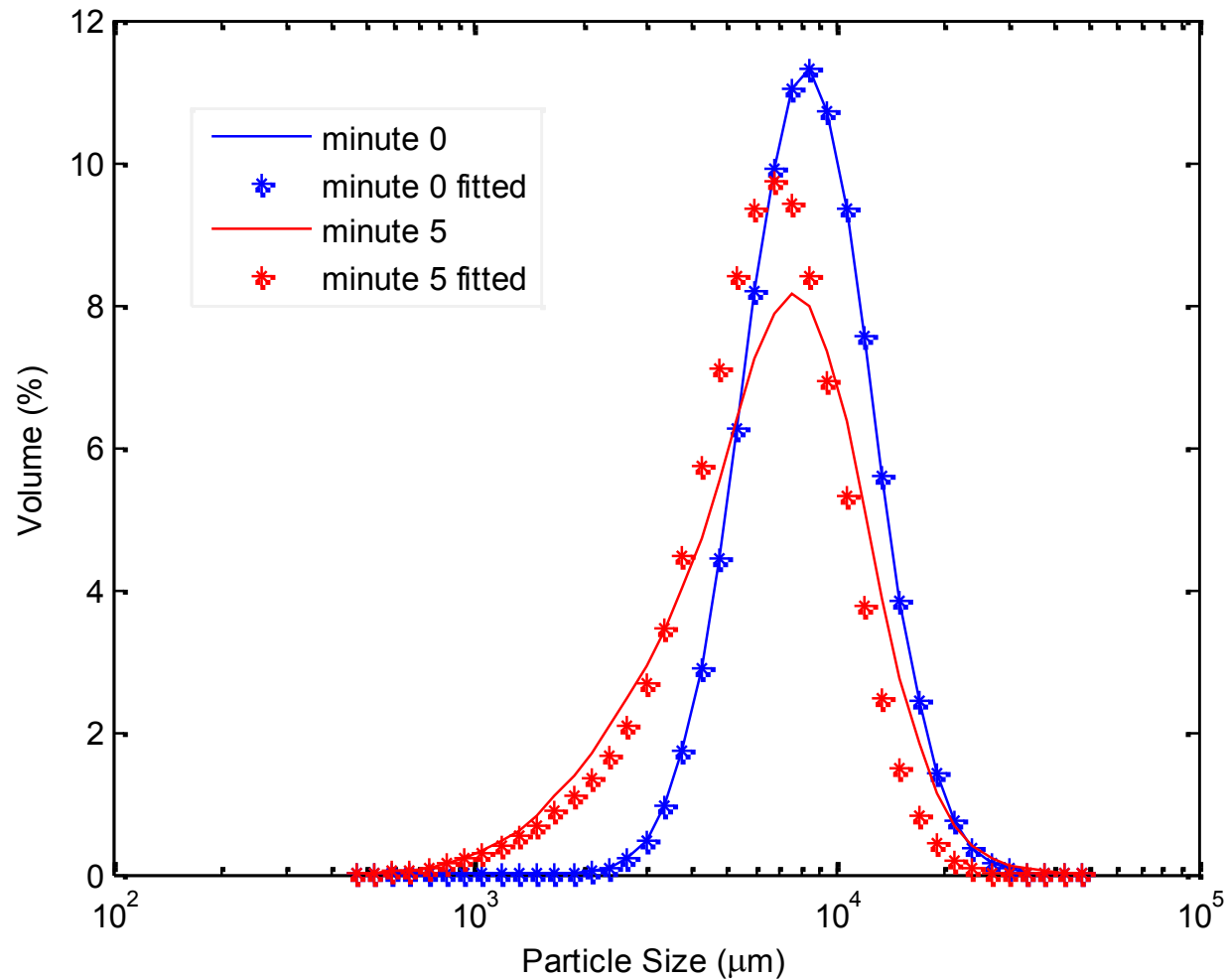
- Discretised Population Balance (DPB) method
 - Hounslow et al (1988)
 - Litster et al. (1995)
 - Kumar and Ramkrishna (1998)
 - Wynn et al (1998)
- Moment methodologies
 - QMOM: McGraw (1997), Marhisio et al. (2003, 2005)
 - EMOM: Falola et al. (2013)

POPULATION BALANCE SOLVER

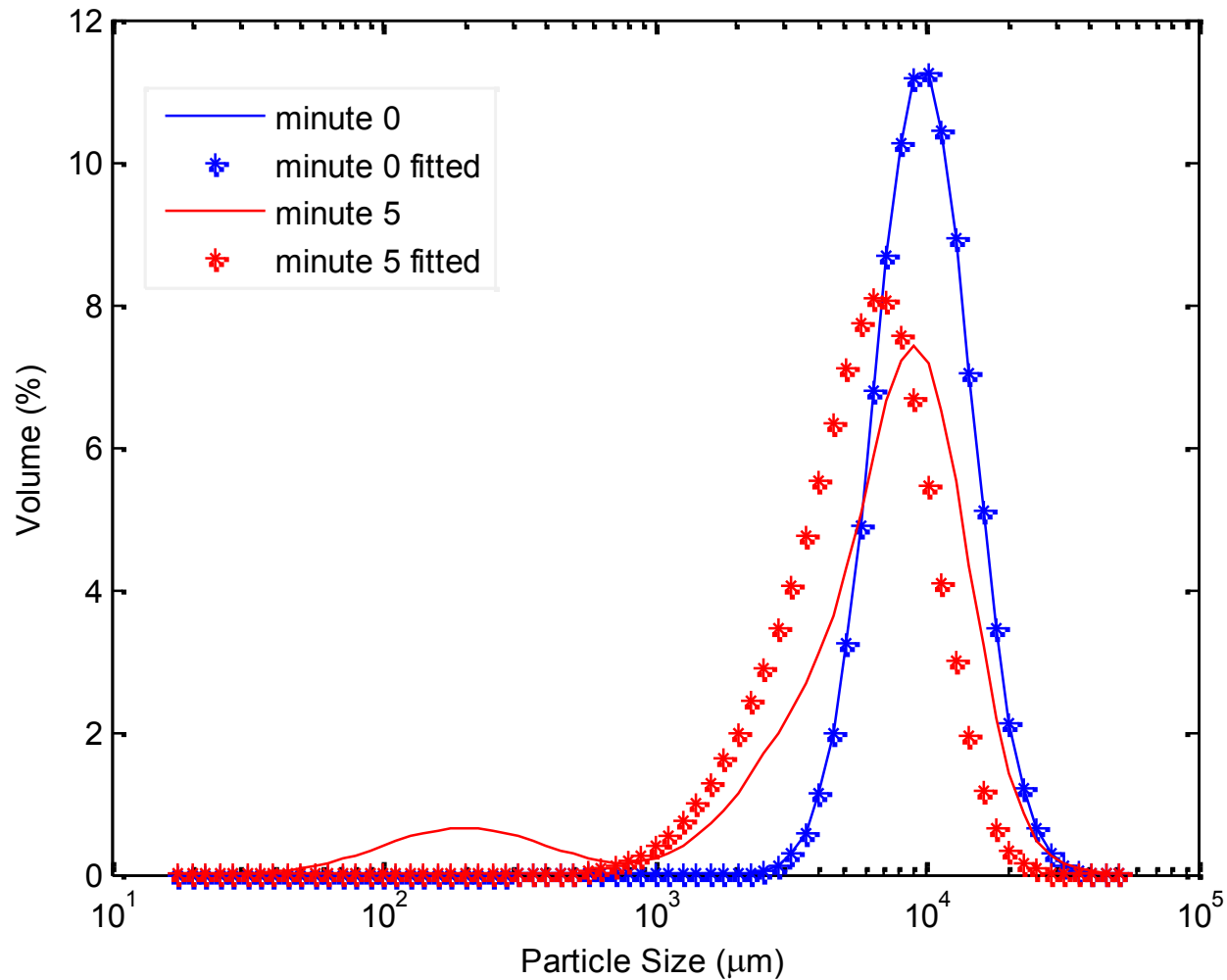




Process Identification – 0.8mm GM



Prediction/Simulation - 0.6mm GM





CONCLUSIONS

Our group have developed tools for:

- Particle size measurement
- Population balance modelling

- Successful applications

Institute of Particle Science & Engineering
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THANK YOU