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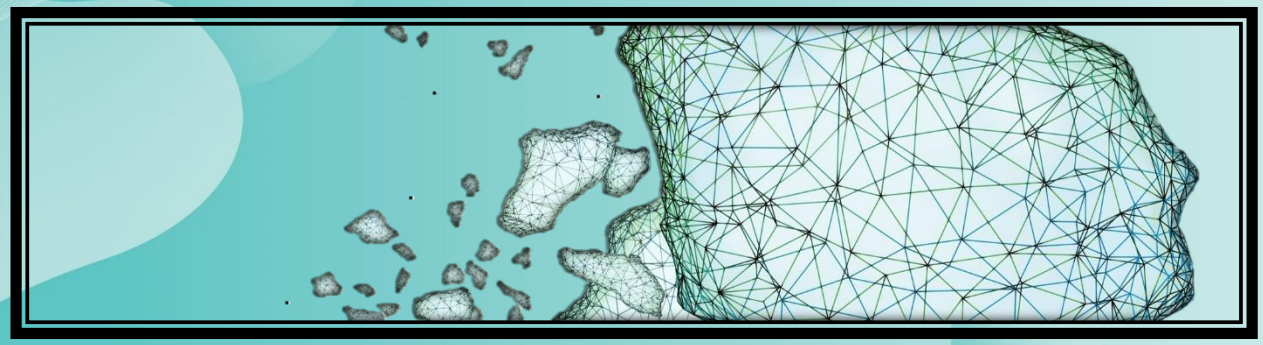

Which Particle Characterization Technique?

28/02/2022

Omer Shenkman
M.Sc. Chemical Engineering
Head of the Physical Characterization Dept.

Agenda

- Why size and shape?
- What do they mean?
- What are my options?
- Which option(s) for me?

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Why size and shape?

Why size and shape?

Product performance requirements could include

- Ability to stay in suspension
- Dissolution rate
- Reaction Rate
- Texture / Mouth feel
- Content uniformity
- Surface Area

- Flowability (of a powder)
- Viscosity (of a suspension)
- Packing density
- Color / Appearance
- Inhalation properties

Embedded Chemical Composition

Why size and shape?

During this lecture – size but also shape

Single particle

Agglomerate

Rough

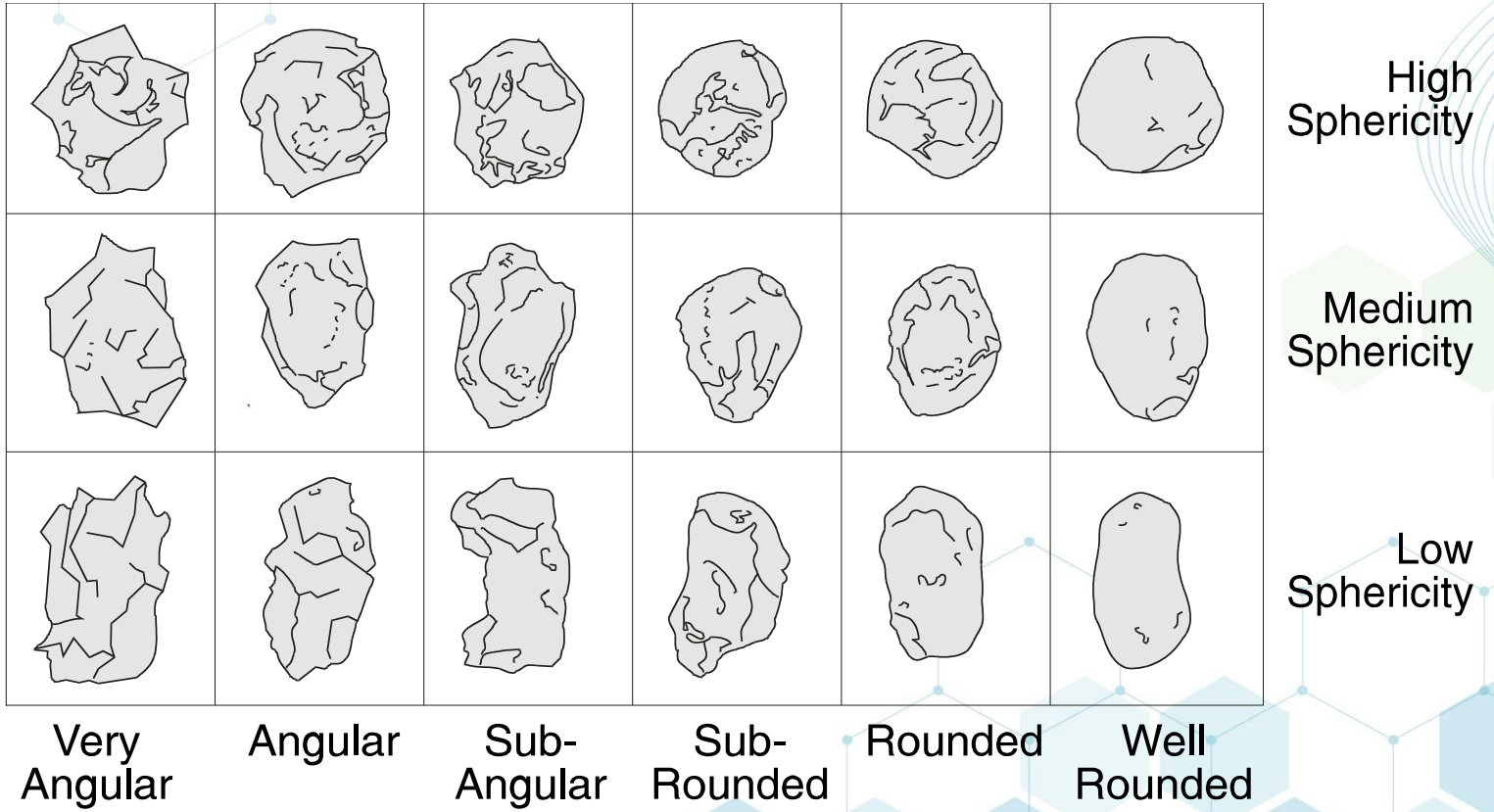
Smooth

Regular

Elongated

Why Size and Shape

- Flowability
- Compacting
- Surface Area
- Dissolution rate
- Polymorphism



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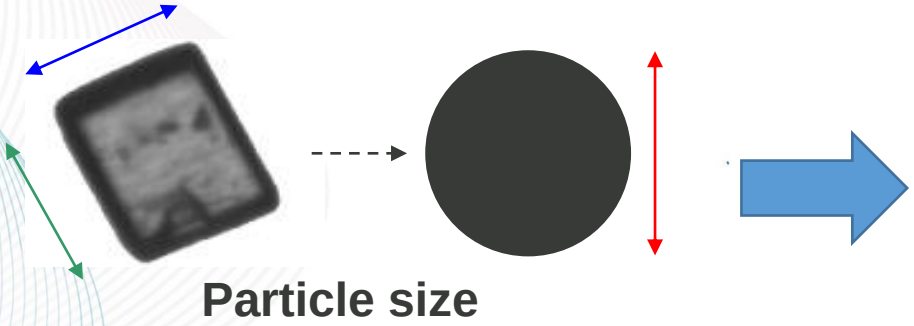
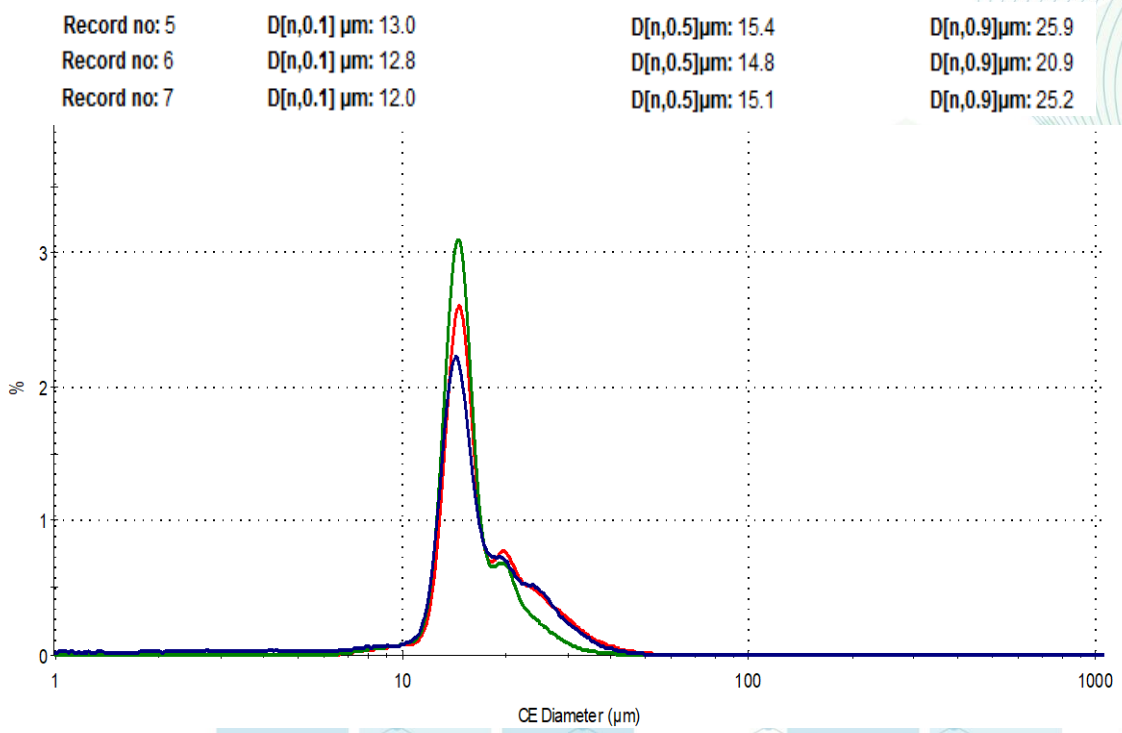
What Do Size and Shape Mean?

What do they mean?

Equivalent Circular\Spherical Diameter – **for size**

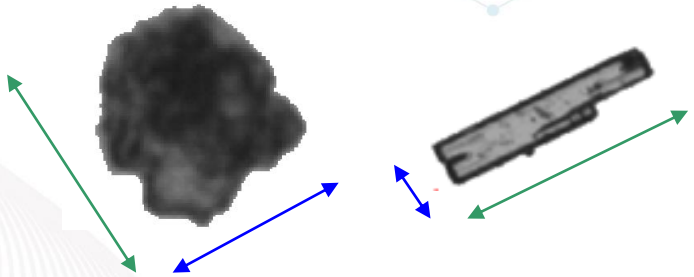


Particle size



What do they mean?

Shape parameters

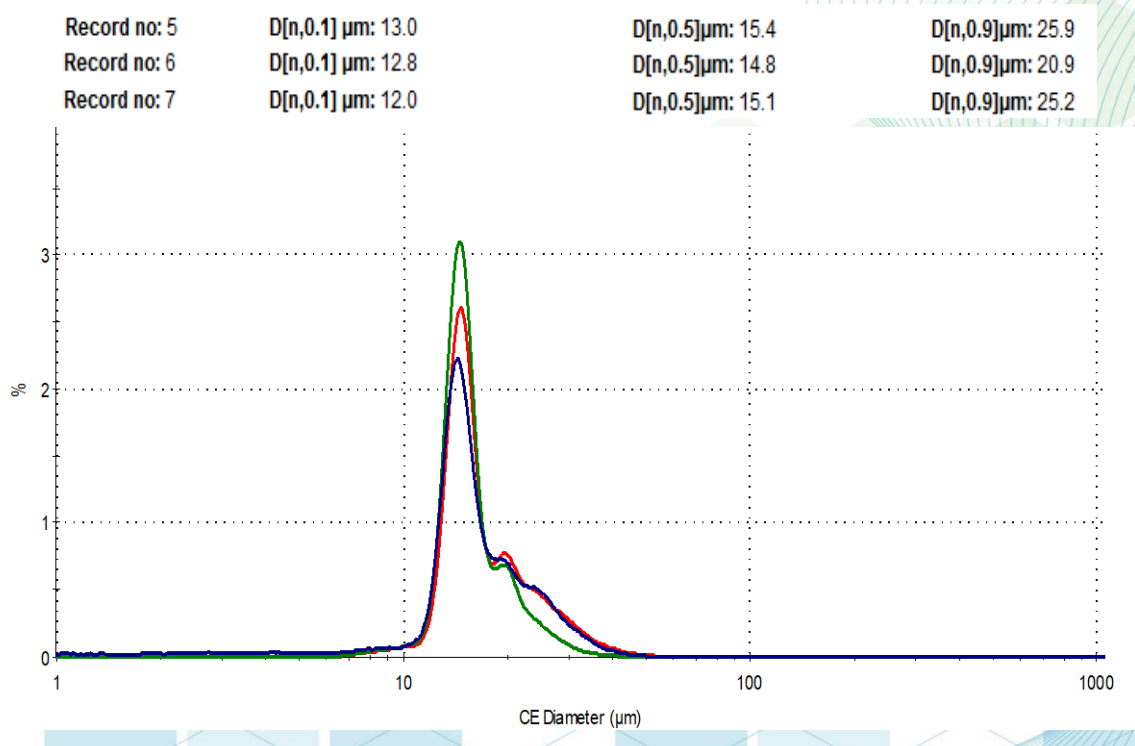


Particle shape

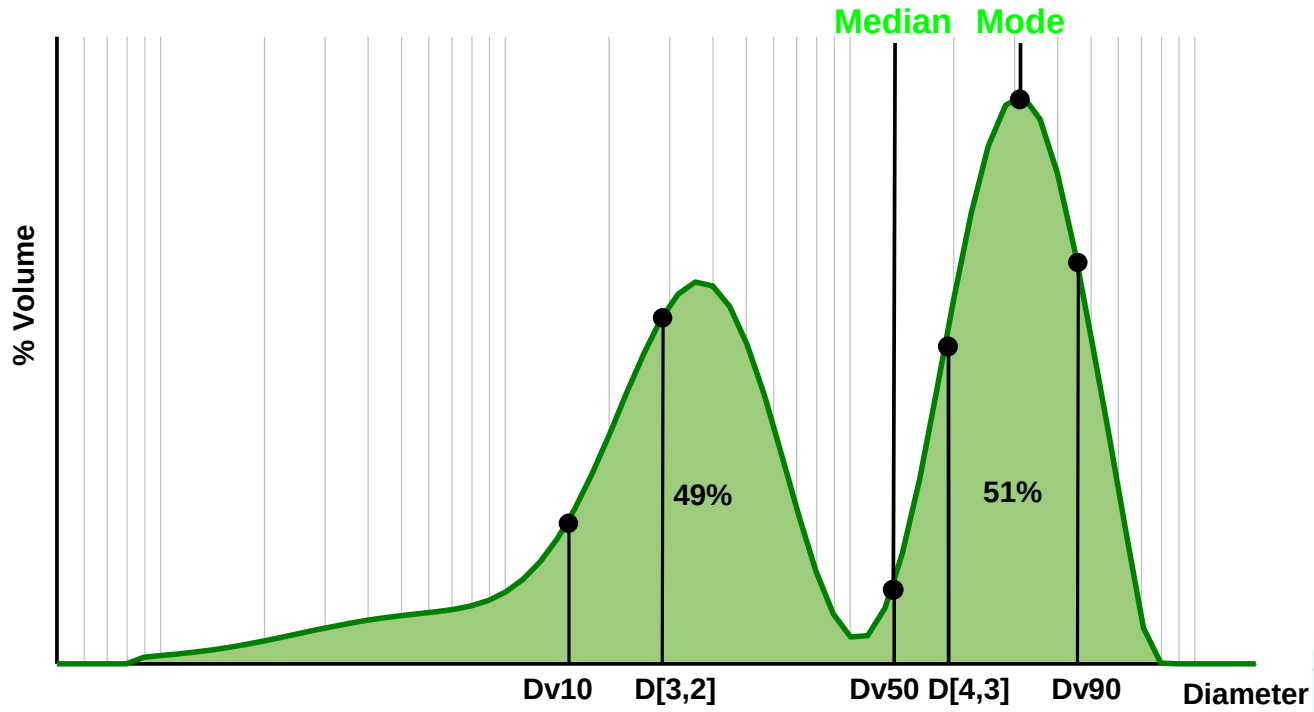
$$Aspect\ ratio = \frac{width}{length}$$

$$Elongation = 1 - \frac{width}{length}$$

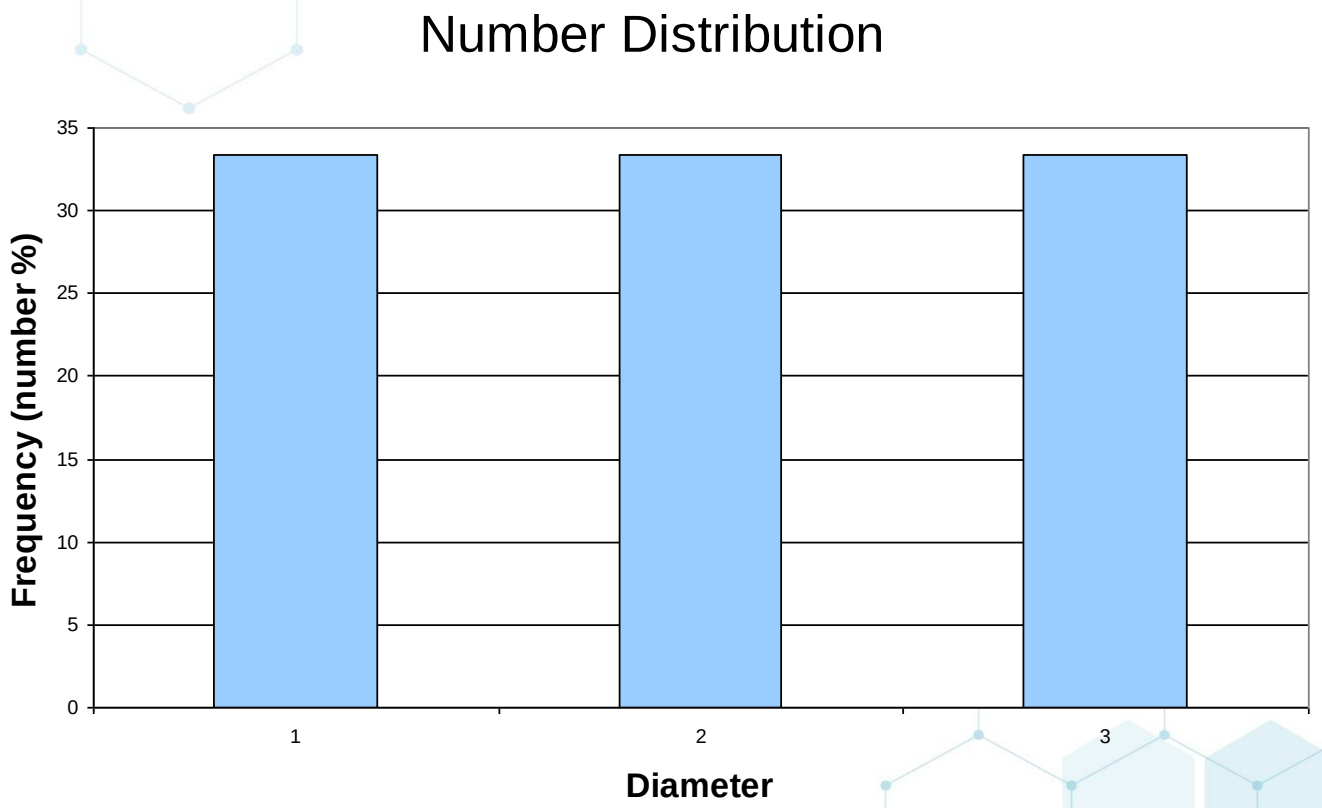
Convexity



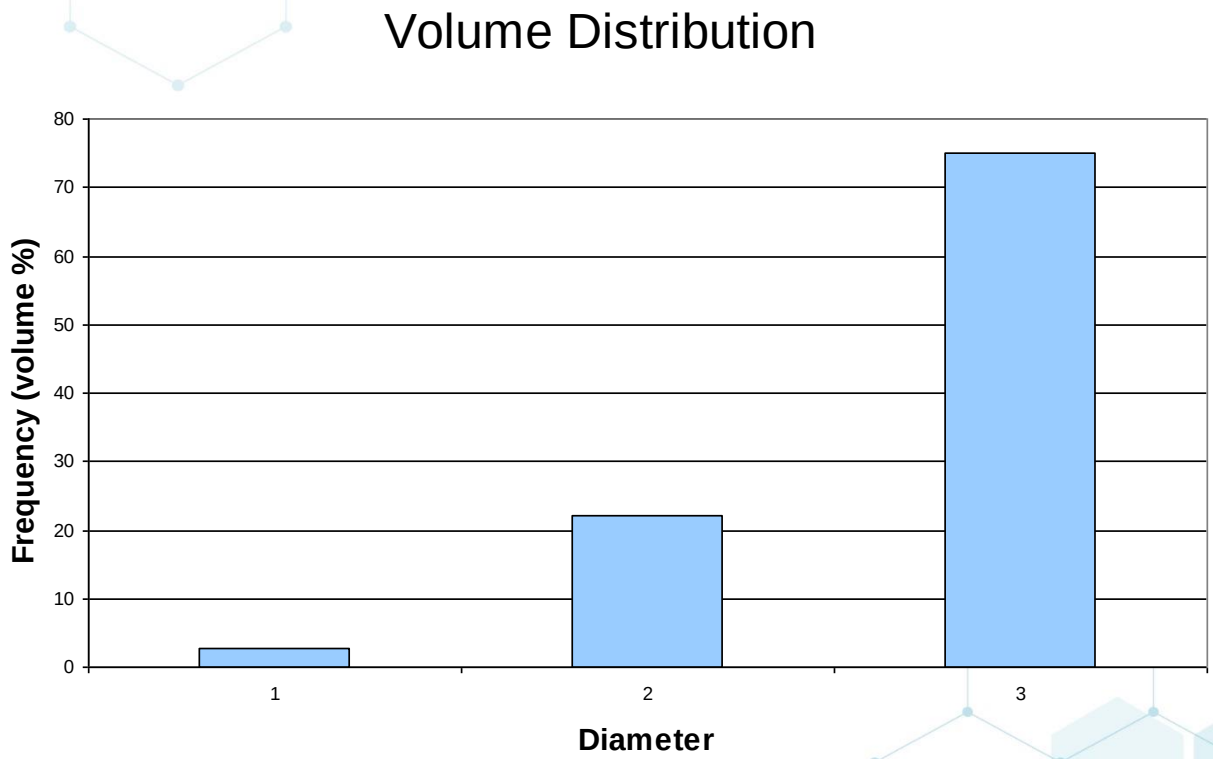
What do they mean?



What do they mean?

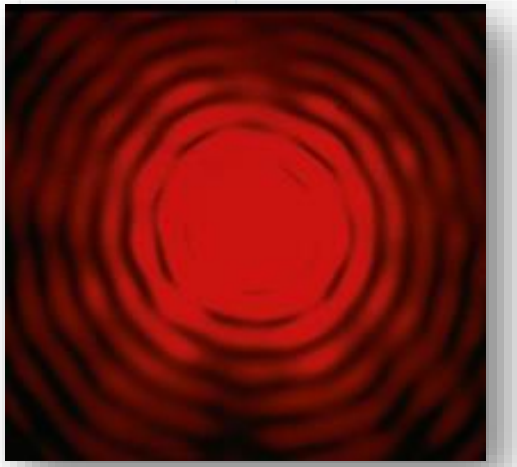


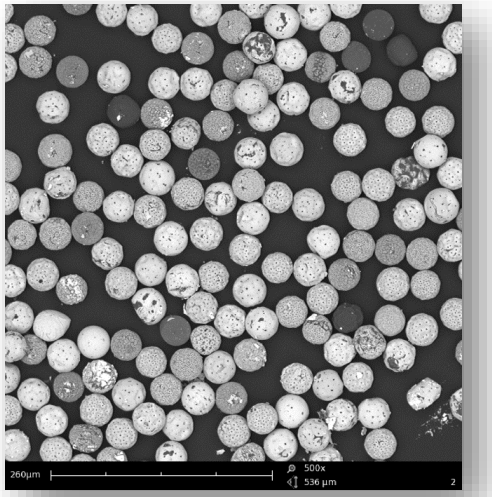
What do they mean?

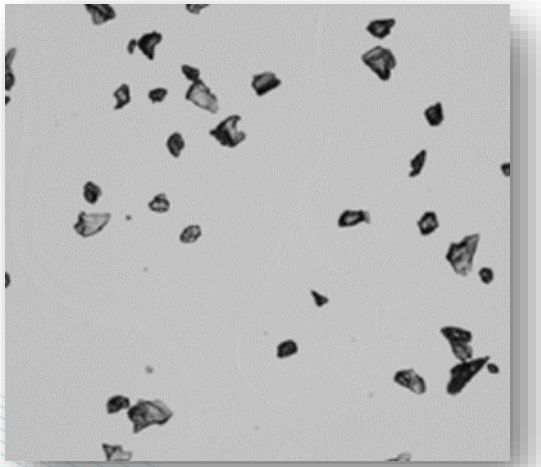


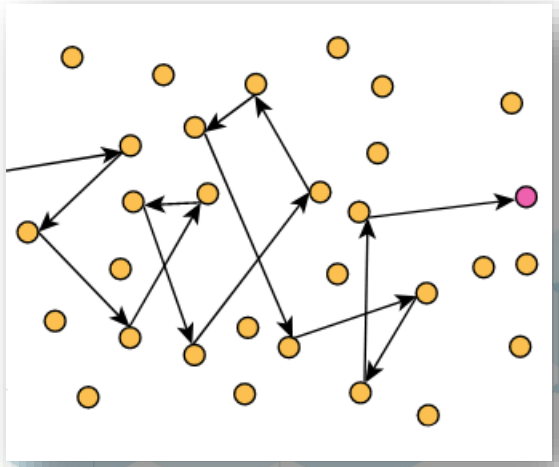
What are my options?

Different Techniques

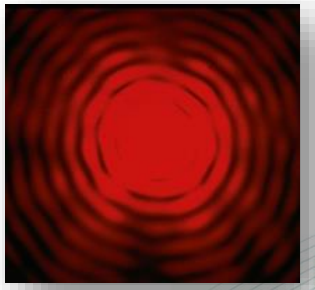








Laser Diffraction



- Size
- Range 10nm -3,500microns
- Wet suspension and dry powder
- Suspension and emulsions
- Very fast measurement
- Little sample preparation
- High statistics – millions of particles
- Per volume (can be converted)

Applications:

Almost any industry or Academy which uses particles

More than 150 systems in Israel

Mastersizer 3000

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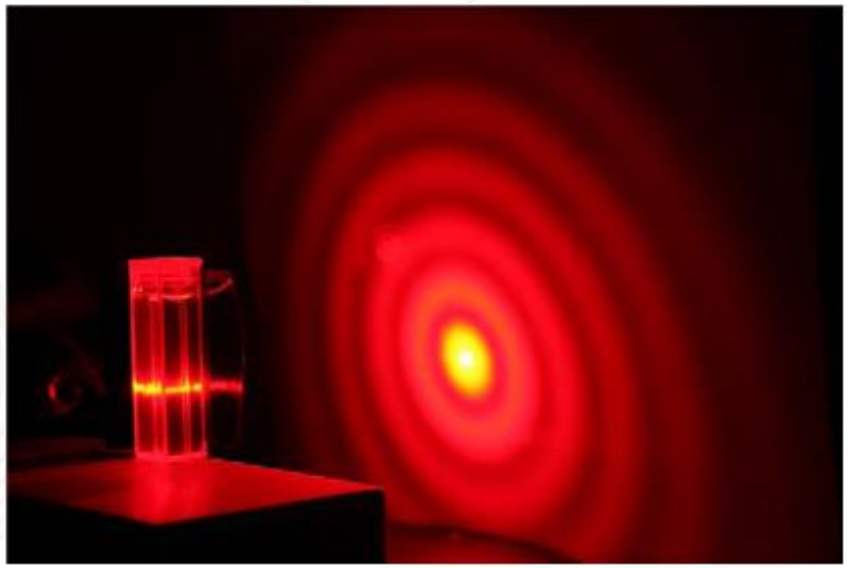
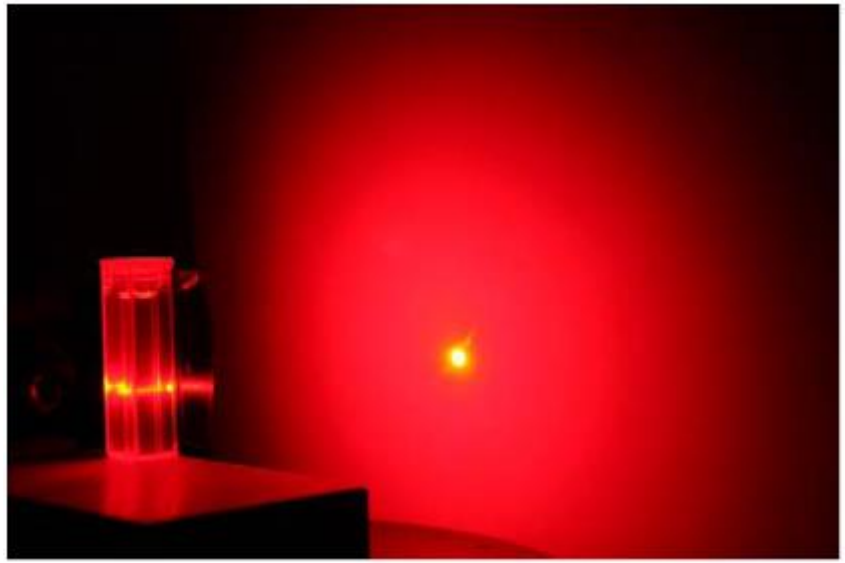
Laser Diffraction



5 microns



800 nanometres

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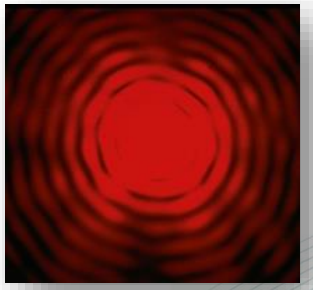
Laser Diffraction



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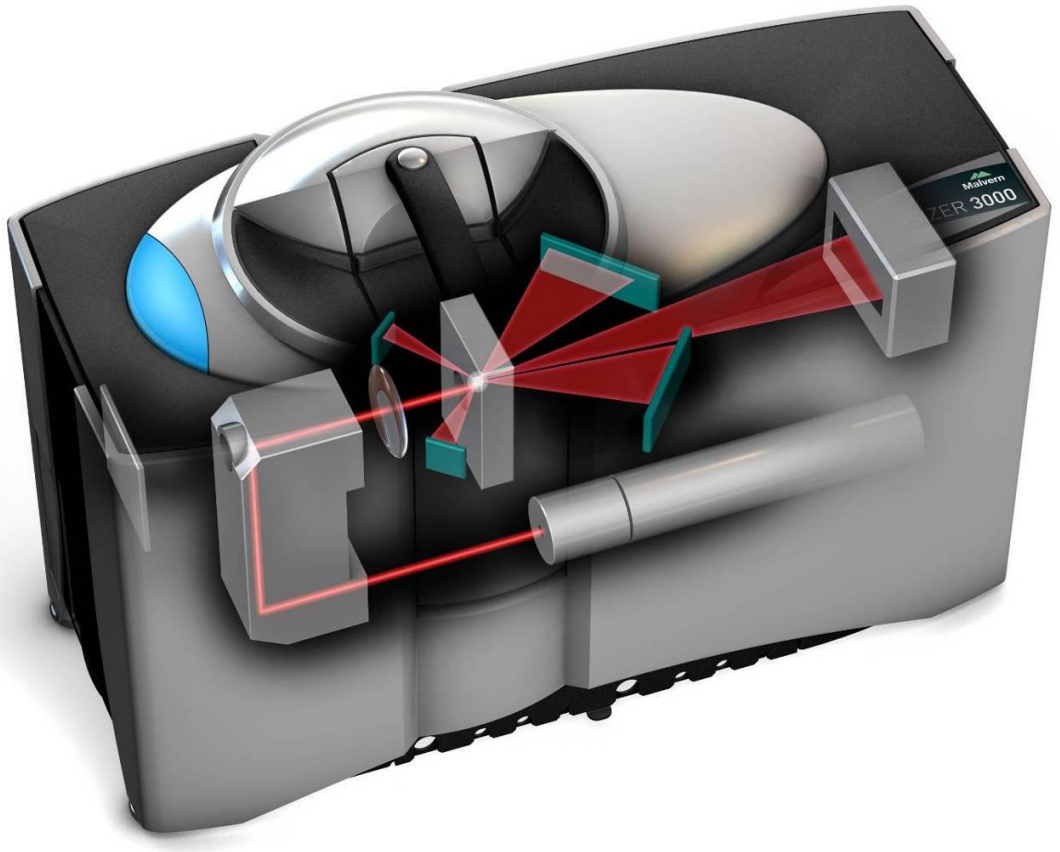

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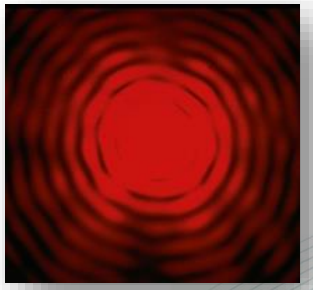
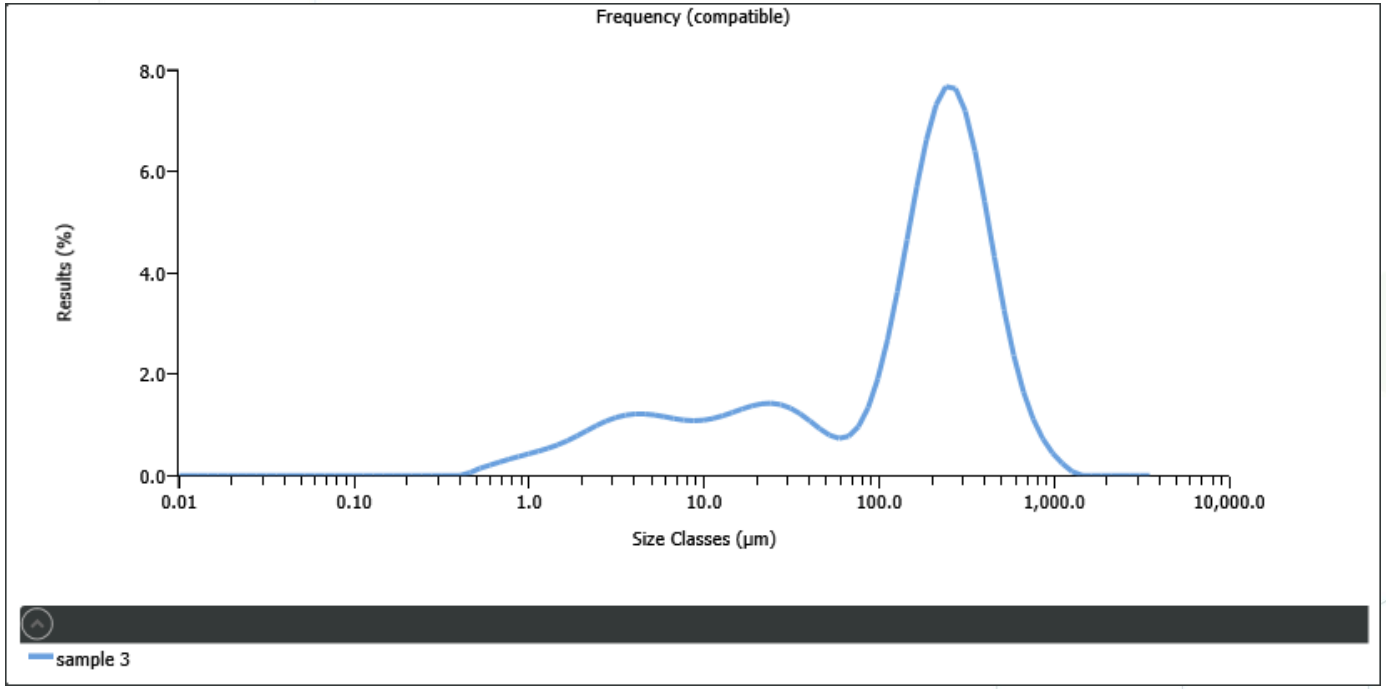
Laser Diffraction





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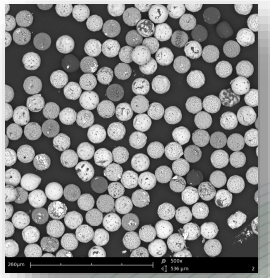
Automated Scanning Electron Microscopy



Phenom Desktop SEM

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Scanning Electron Microscopy

- Size and Shape
- Range 100nm -0.1mm
- Dry and wet
- Solid particles
- Sample preparation
- Can separate the distributions of two components in formulation
- Elemental analysis
- 21CFR11 – for microscope

Applications:

Any industry or academy with solid particles

Phenom Desktop SEM

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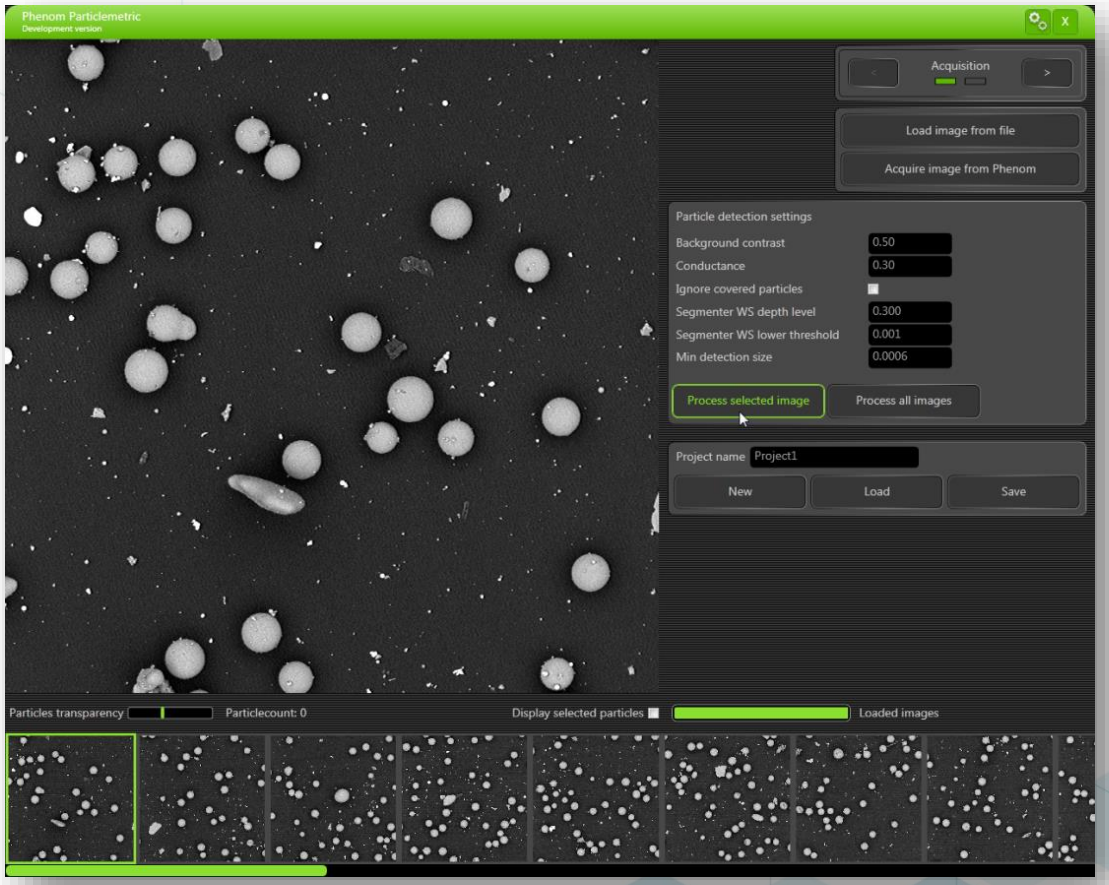
Scanning Electron Microscopy



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Phenom Desktop SEM

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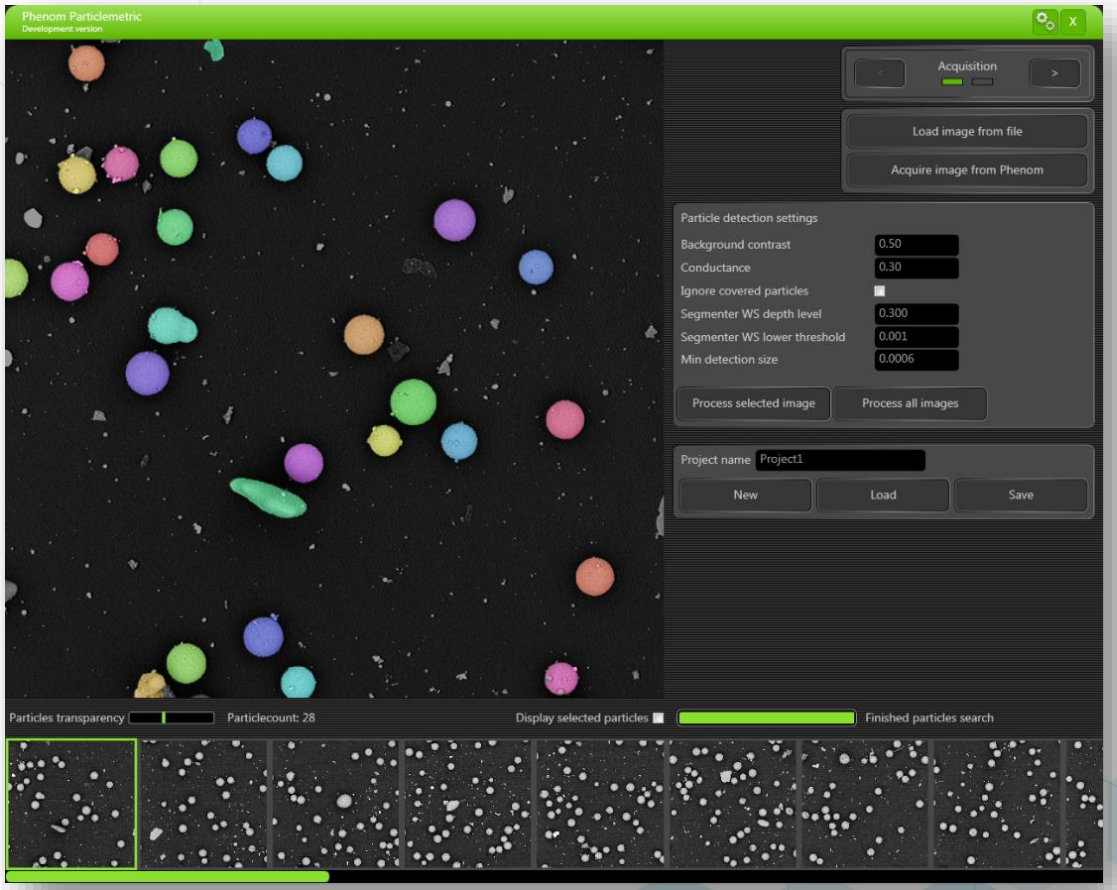
Scanning Electron Microscopy



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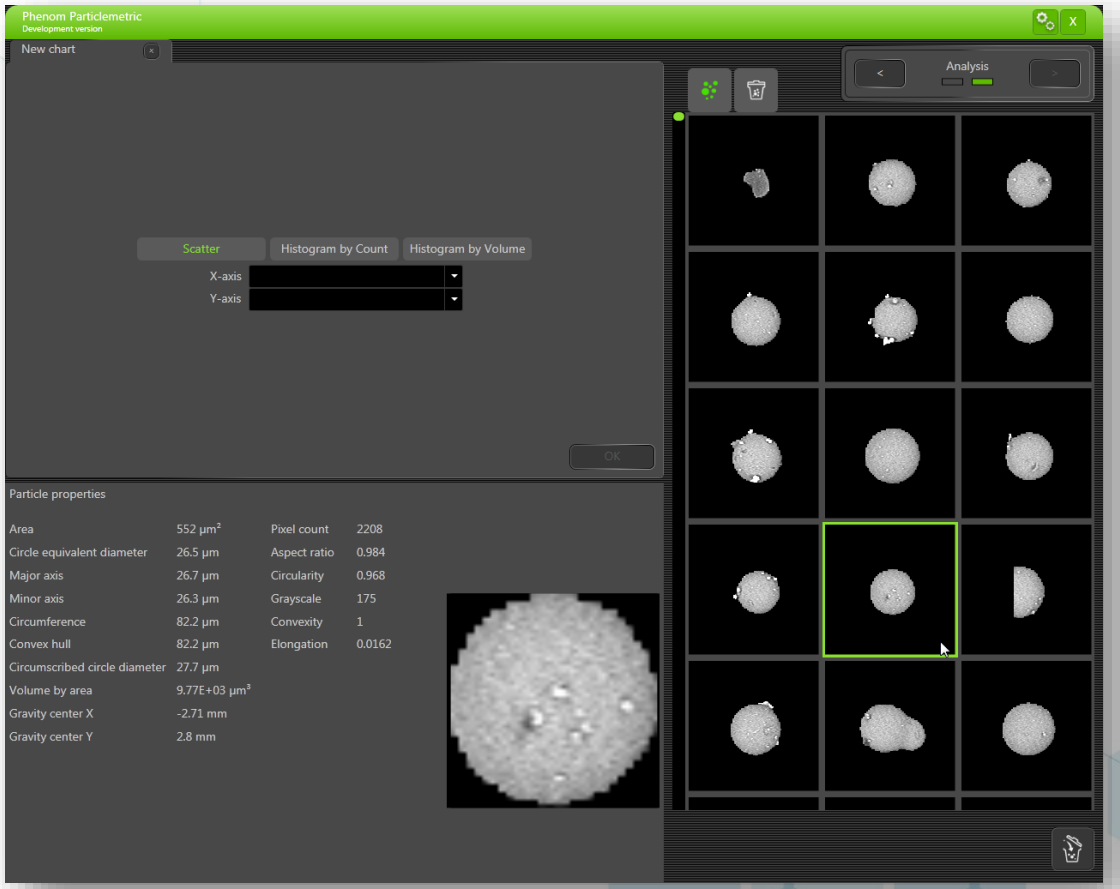
Scanning Electron Microscopy



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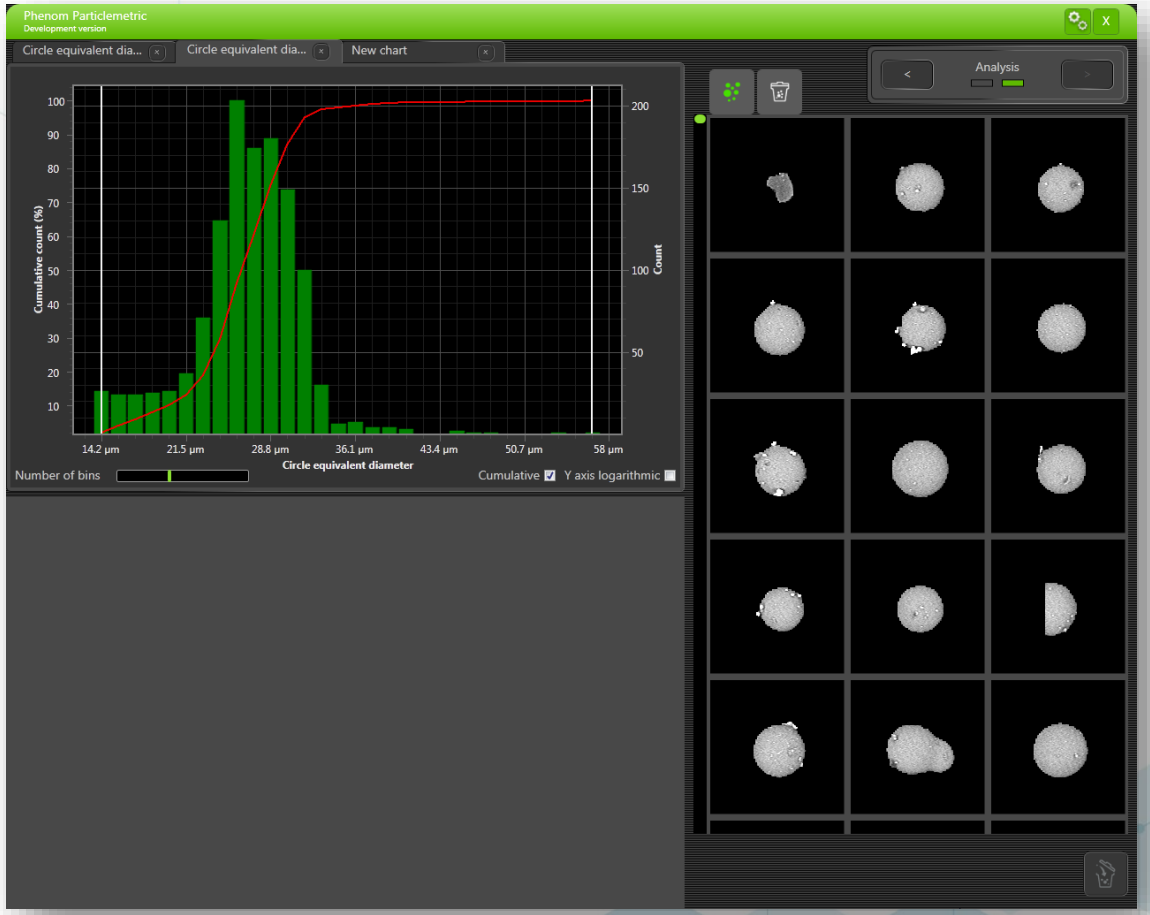
Scanning Electron Microscopy



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Scanning Electron Microscopy

Phenom Desktop SEM

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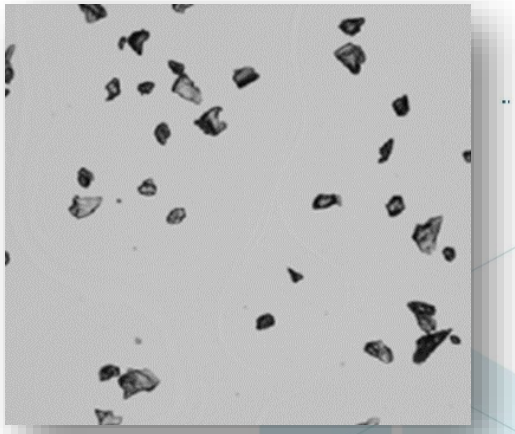
Automated Light Microscopy



Automated Light Microscopy

- Size and Shape
- Range 500nm -1mm
- Dry and wet
- Solid particles and emulsions
- Sample preparation
- Can separate the distributions of two components in formulation
- Chemical Identification
- 21CFR11

- Nasal spray
- Topicals
- Additive manufacturing
- Inhalers
- Polymorphs
- Metal powders
- Batteries
- Forensic

Dr. Bing Li
Acting Director
Office of Generic Drugs

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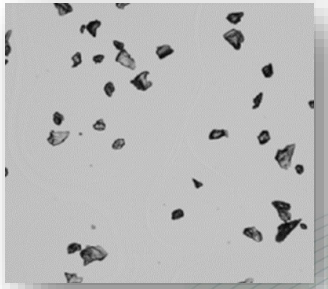
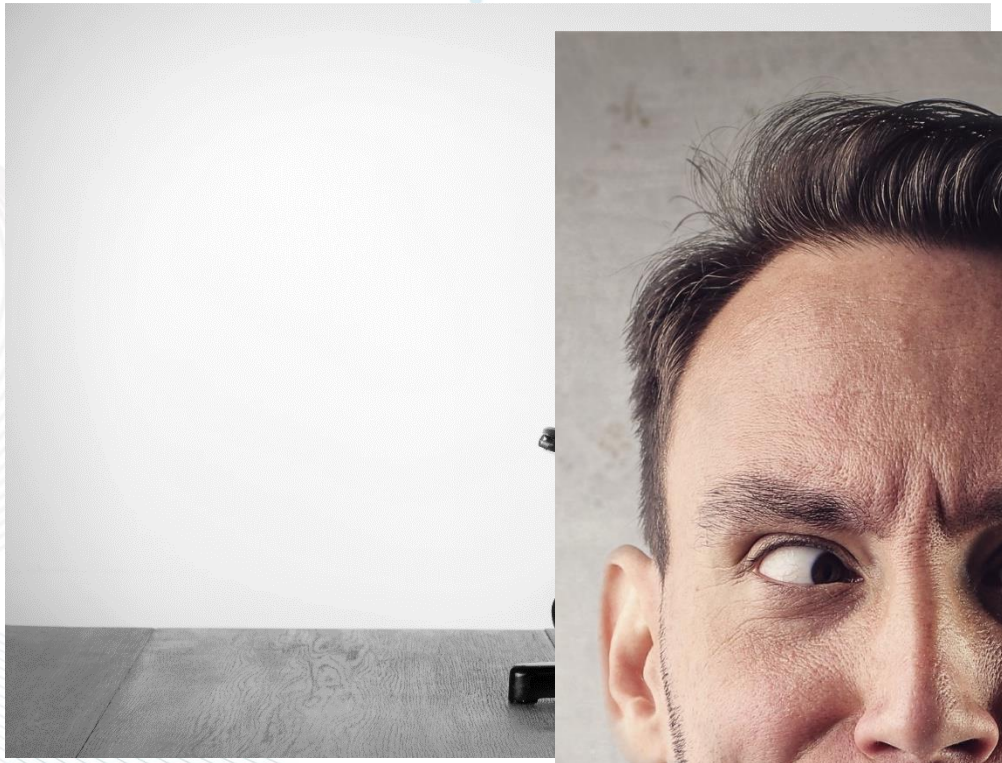
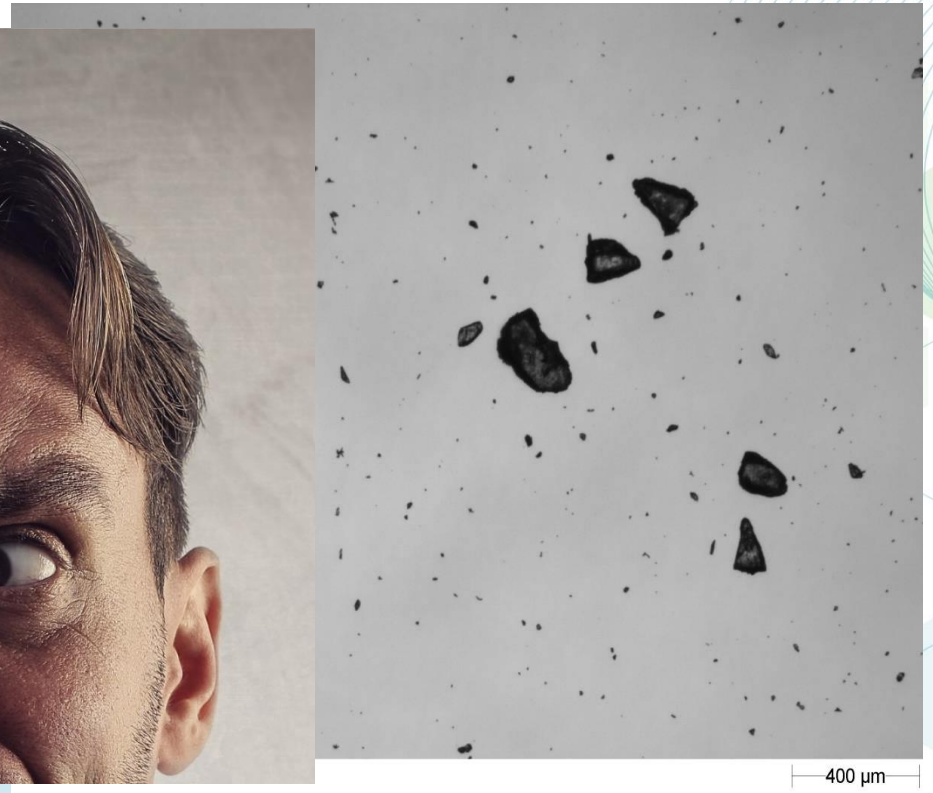
Traditional Methods

Manual Microscopy







Subjectivity of the method

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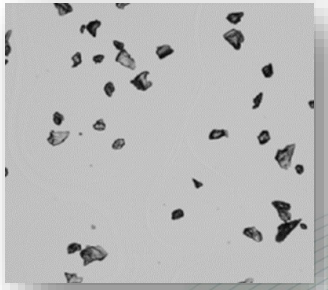

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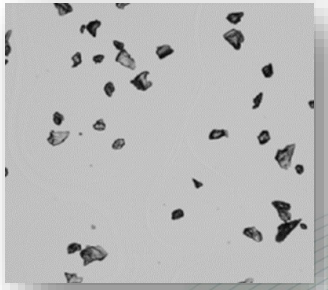

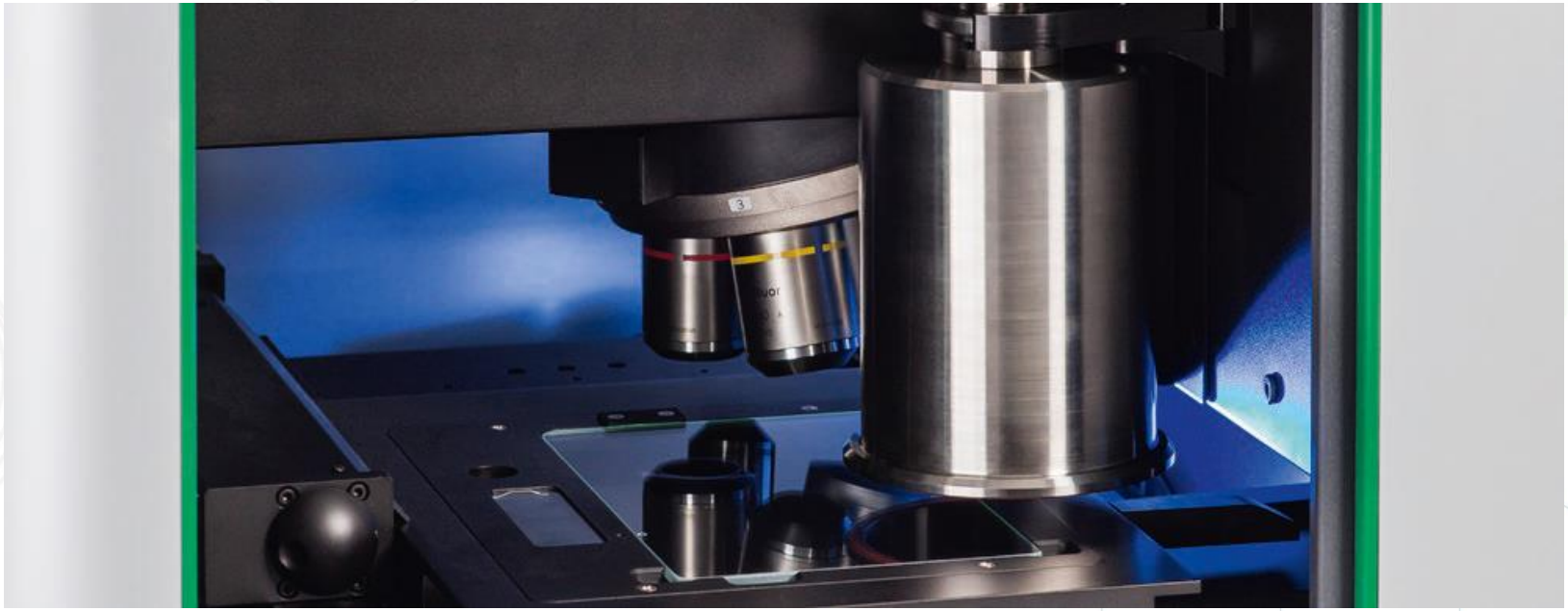

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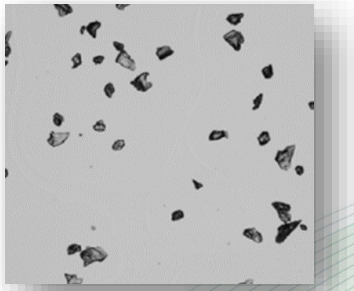
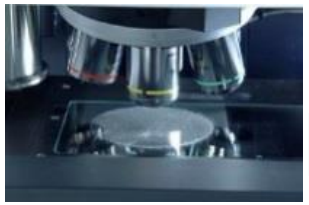
Automated Light Microscopy



Sample preparation

Manual dry dispersion



Dry sample dispersion unit

Evaporative dispersion

Wet cell

Thin path wet cell

Wet (slide and coverslip)

100nm | 1µm | 10µm | 100µm | 1mm | 10mm

Particle size

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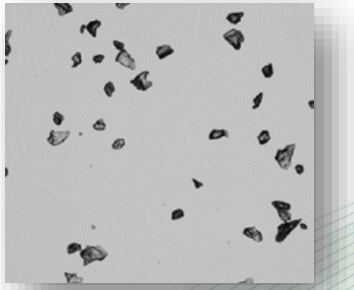

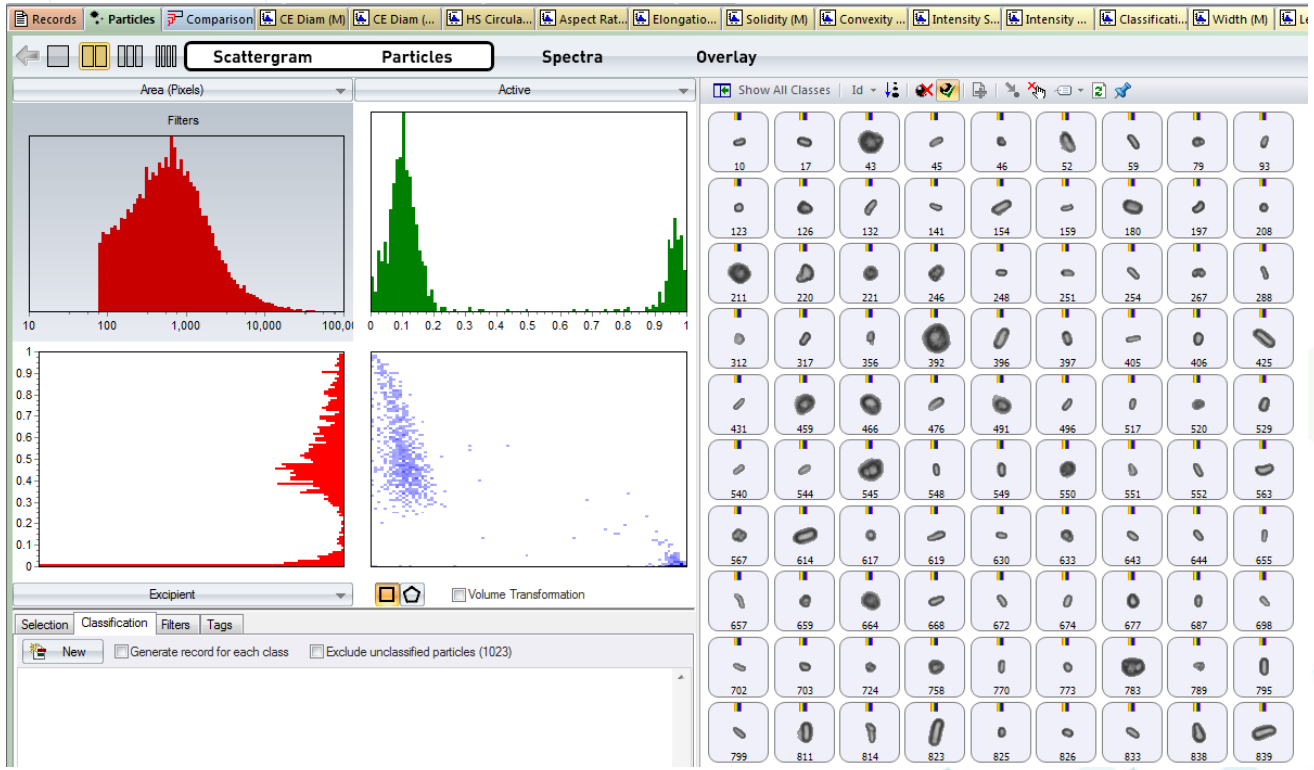

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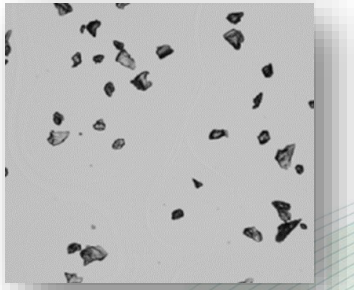

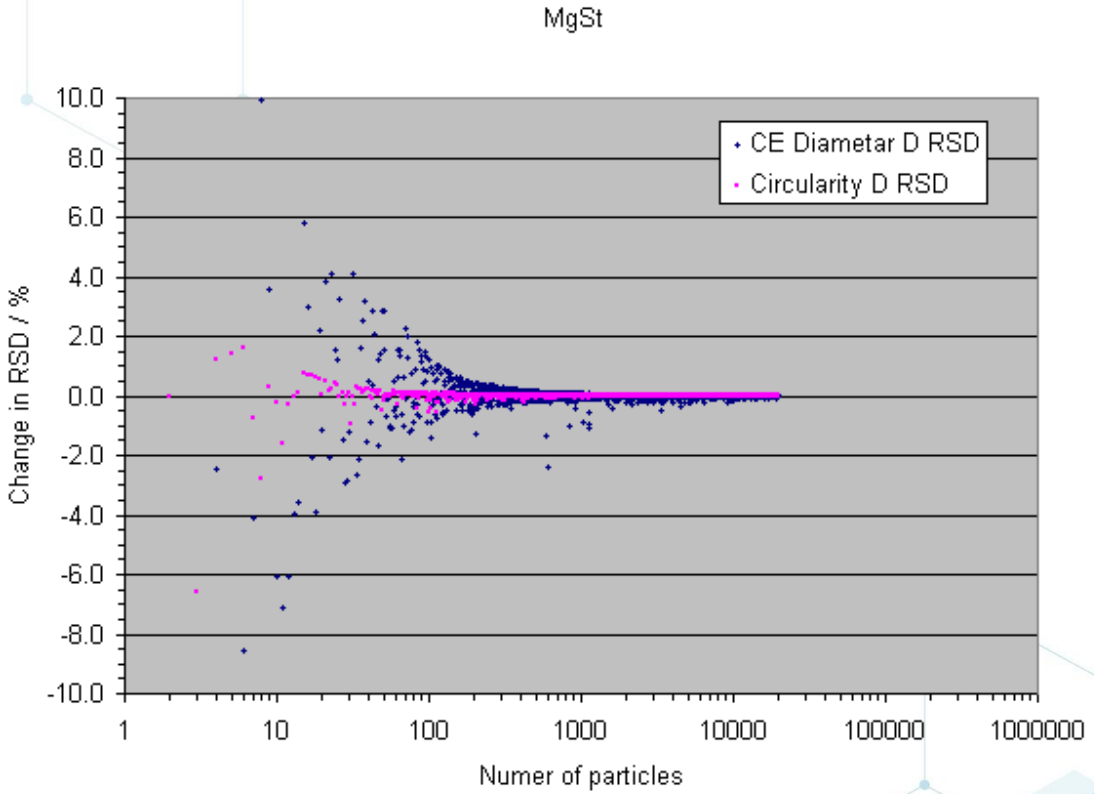

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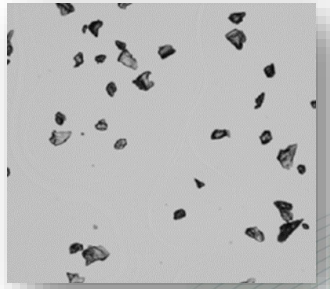
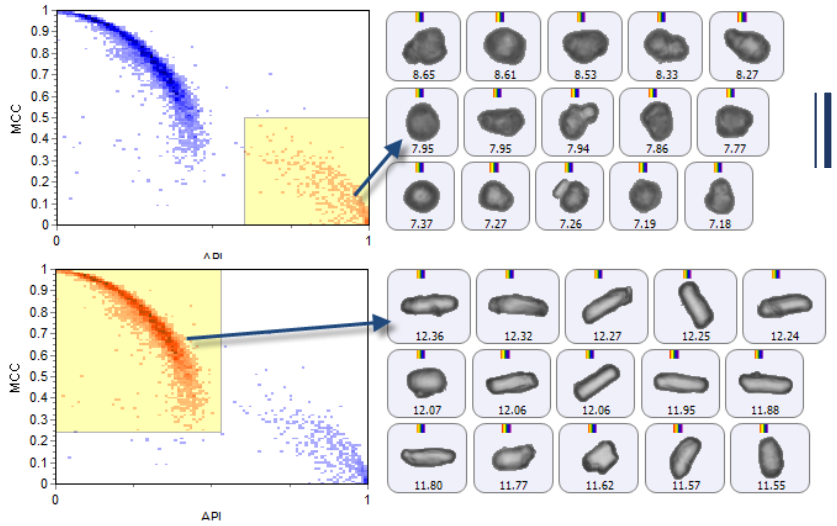
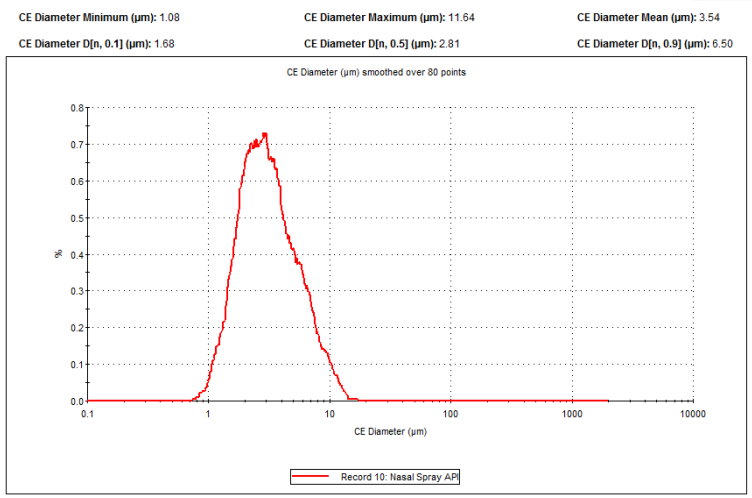
Automated Light Microscopy

PSD of API in nasal spray





Particle Size Distribution of one chemical entity



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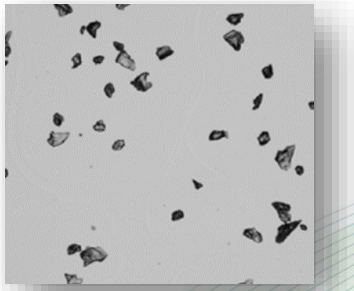
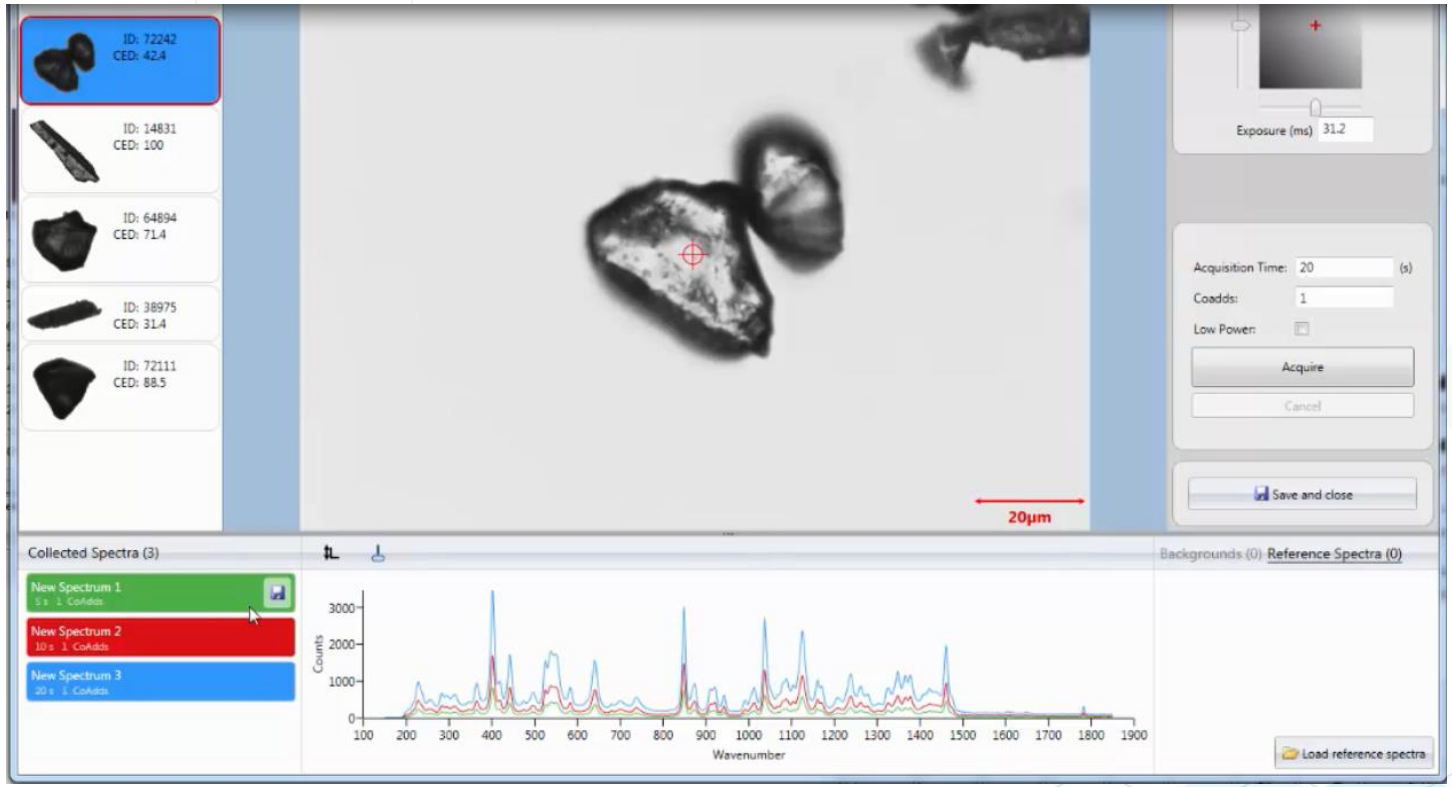
Automated Light Microscopy





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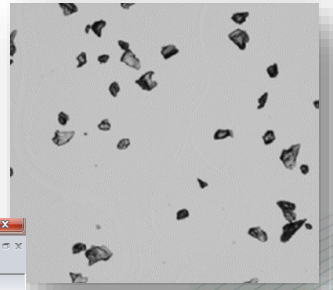

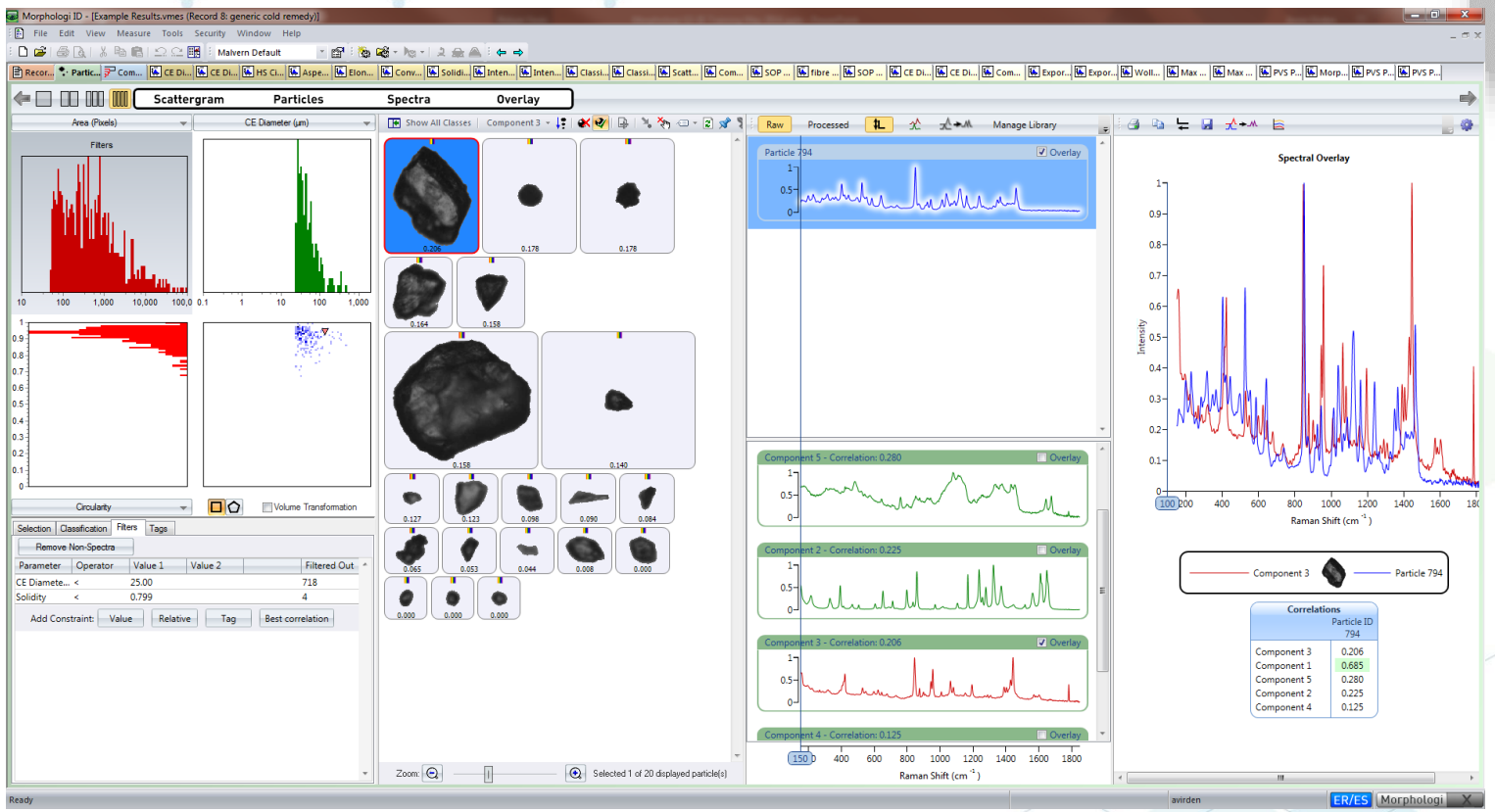

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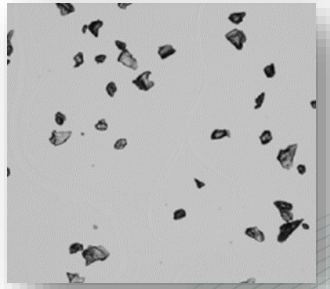
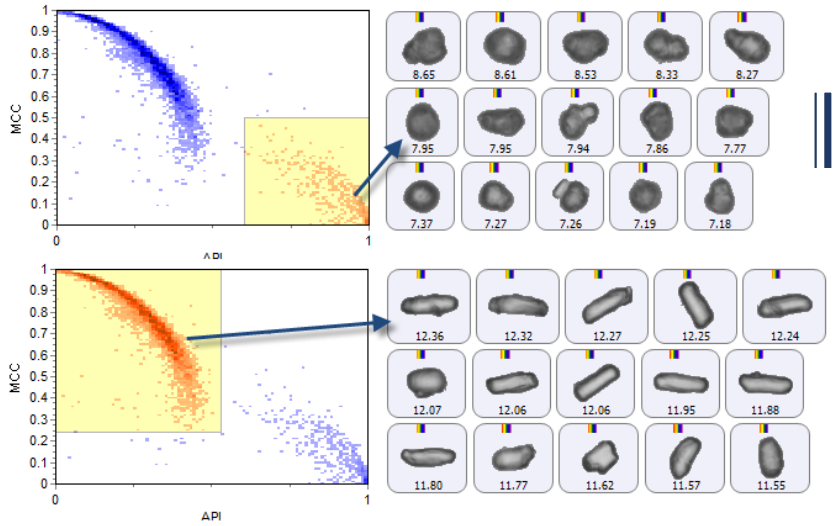
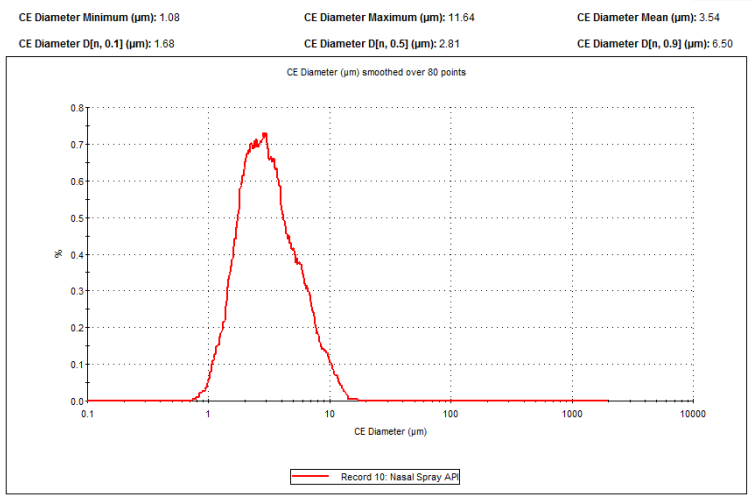
Automated Light Microscopy

PSD of API in nasal spray





Particle Size Distribution of one chemical entity



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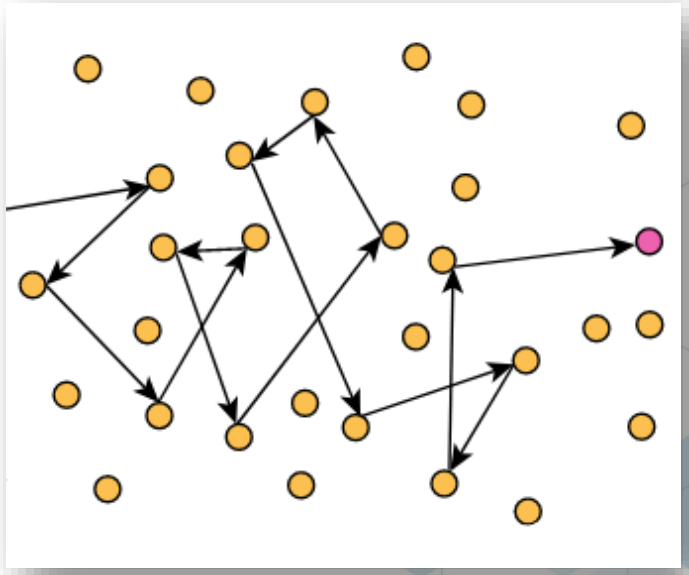
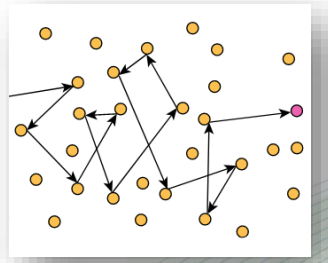
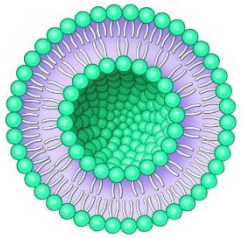
Dynamic Light Scattering and Nanoparticle Tracking Analysis



Dynamic Light Scattering (DLS)



- Size
- Range 0.3nm -10micron
- Wet
- Solid particles and emulsions
- Sample preparation
- Size
- Fluorescence Filter
- Concentration
- Zeta Potential
- 21CFR11



Applications:

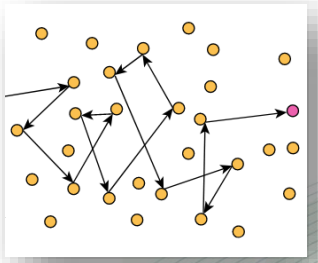
Mostly submicron particles. For example:

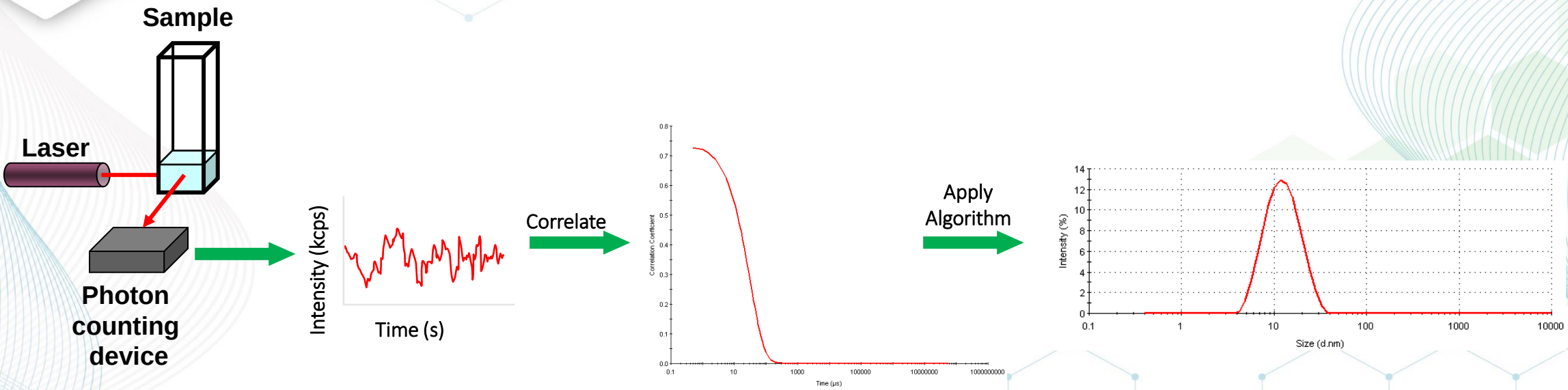
- Inks and pigments
- Liposomes
- Biomolecular research
- And much more

More than 70 systems in Israel

Zetasizer

Dynamic Light Scattering (DLS)





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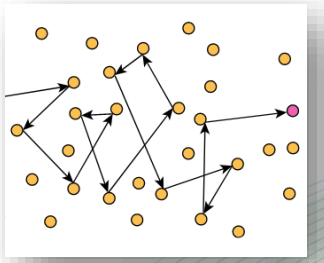
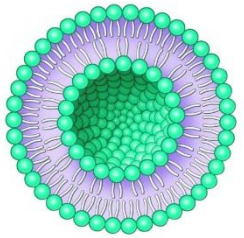
Zetasizer

Nanoparticle Tracking Analysis (NTA)



- Size
- Range 10nm -1micron
- Wet
- Solid particles, emulsions and nano bubbles
- Sample preparation
- Size
- Fluorescence Filters
- Increased resolution
- Concentration
- 21CFR11



Applications:
Mostly submicron particles:

- Lyposomes
- Exosomes
- Protein aggregation
- VLP
- Polymers and colloids
- And more..

Nanosight

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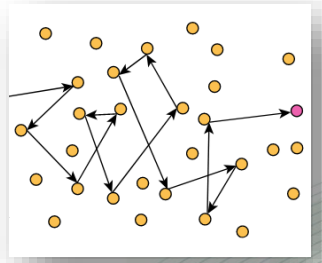
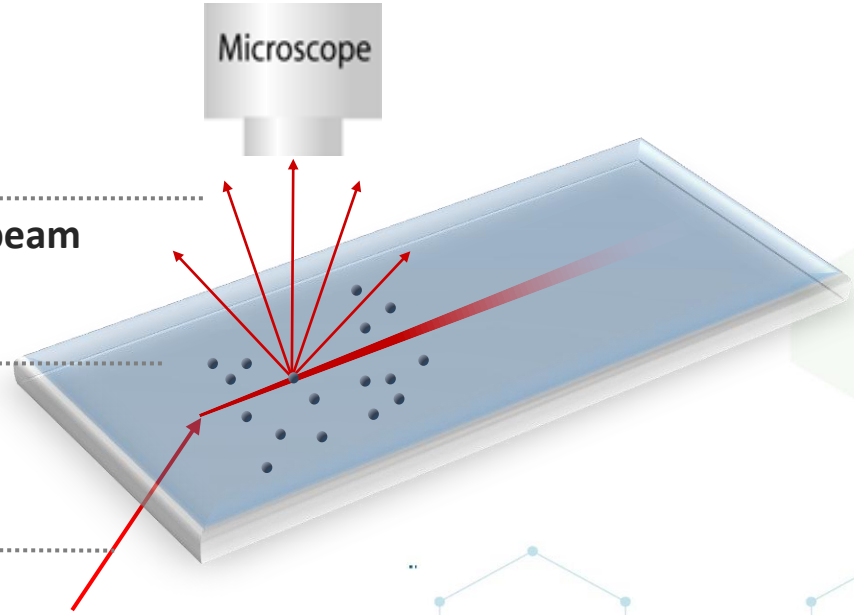
Nanoparticle Tracking Analysis (NTA)





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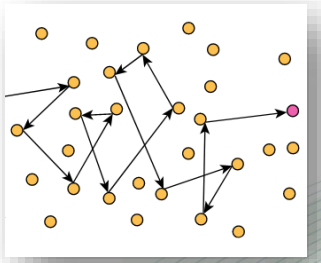
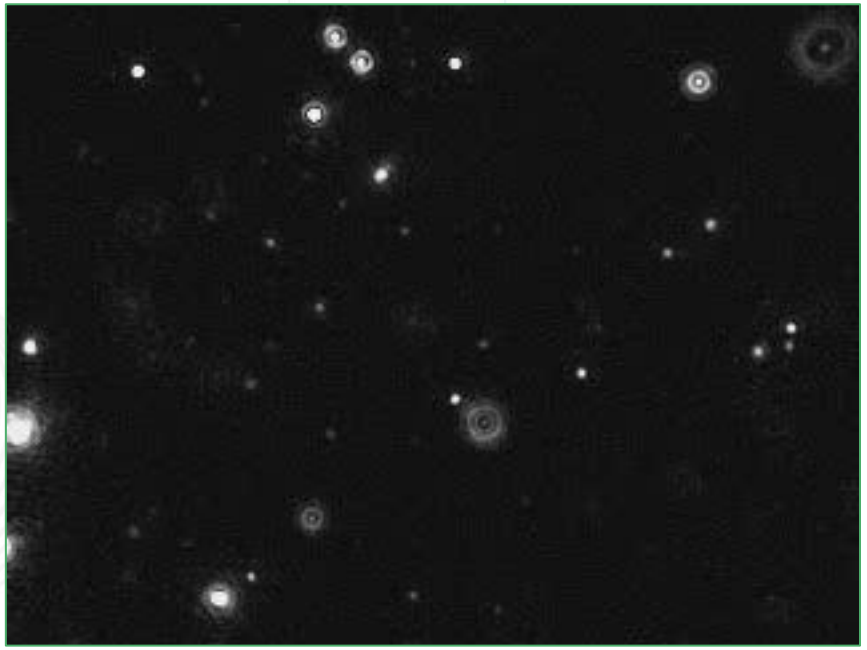
Nanosight

Nanoparticle Tracking Analysis (NTA)

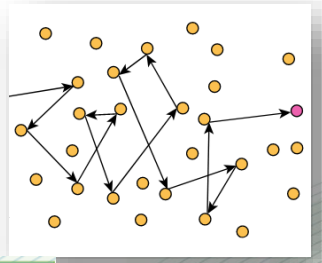




- Particles are too small to be imaged with a microscope
- Small particles are visualised as point scatterers
- Larger particles scatter significantly more light

Nanosight

Comparing DLS with NTA



Size

❖ Minimum size limit

NTA	Zetasizer
10 nm – 40 nm (Related to Wavelength and power of illumination source)	**0.3 nm**

❖ Maximum Size limit:

NTA	Zetasizer
1000 – 2000 nm (Related to Limited Brownian motion and Viscosity of solvent)	**10000-15000 nm** (Related to Zetasizer advance model- detection angle of the detector)

Concentration

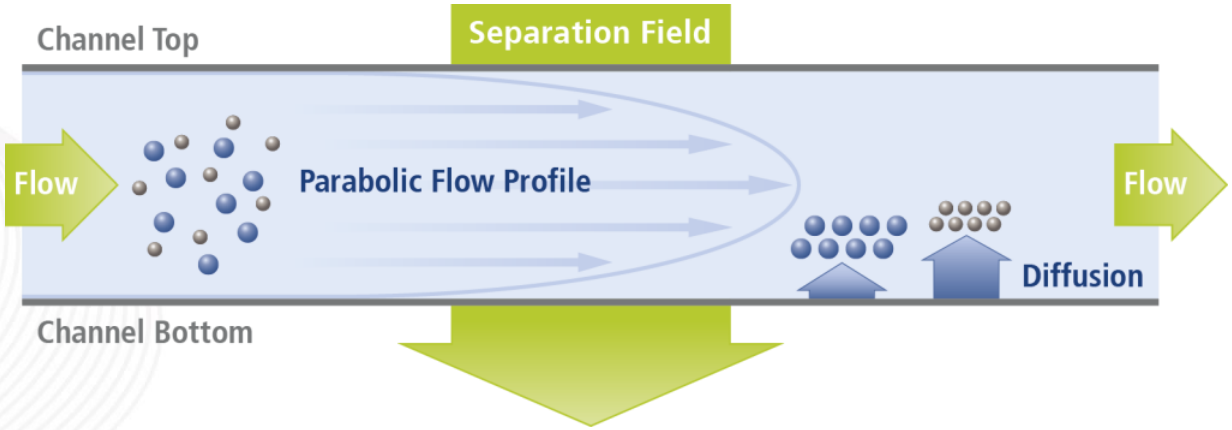
- ❖ Zetasizer- 10^{8} - 10^{12} particles / mL
- ❖ NTA- Approx 10^{6} - 10^{9} particles / mL

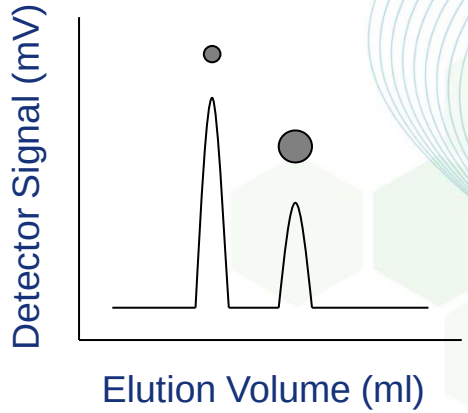
Zeta Potential

- ❖ Zetasizer- 3.8-10000 nm

Bonus Technique

Field Flow Fractionation (FFF)





- Fraction can be used for further analysis

FFF

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Which option is for me?

Which option is for me?

Technology	Instrument	Size range	Samples	Comments
Laser Diffraction (LD)	Mastersizer 3000	10nm-3,500 micron	Wet and Dry	Size
Dynamic Light Scattering (DLS)	Zetasizer Advanced Series	0.3nm-10micron	Wet	Size, Fluorescence
Nanoparticle Tracking Analysis	Nanosight	10nm-1micron	Wet	Size, Fluorescence
SEM with Particle Metric	Phenom Desktop SEM	100nm-0.1micron	Wet and Dry	Size, Shape, Composition
Automated Light Microscopy	Morphologi 4	500nm-1,000micron	Wet and Dry	Size, Shape, Composition

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Before summing up:
Any Questions?

To Sum it up!

- Why size and shape?
  - → many properties
  - → Adi Ben-Yaakov
- What do they mean?
  - → how they are calculated
- What are my options?
  - → many techniques
- Which option is for me?
  - → there is an optimal method for each application

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Thank you

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