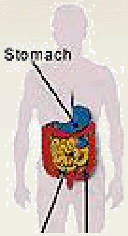
SIZE DISTRIBUTION ?

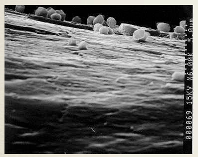
Denis poncelet

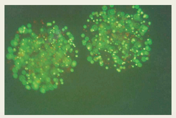
Size ?

- Diameter = first property of the capsules
- Define largelly
  - the membrane or coating surface, then quantity
  - the mechanical resistance
  - the fluidisation and flowing properties
  - the active loading and quantity
- Needed for most modelling of
  - the membrane formation
  - the release profile
  - the biocatalyst kinetics (mass transfer)

Size ?







From a few micrometers ... to a few millimeters

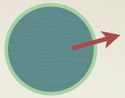
Size distribution ?

- Mono-dispersion ?
  - do not believe pictures
- Narrow size distribution allows
  - better microcapsule formation control
  - easier modelling
  - more homogeneous properties
- Narrow size distribution

  = higher cost & lower production

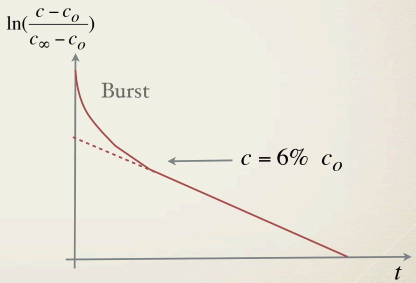
Size distribution ?

Controlled release



$$\frac{dc}{dt} = -D\frac{(c-c')}{e}$$

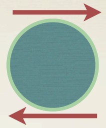
$$\ln\left(\frac{c-c_o}{c_\infty - c_o}\right) = -k \;\; t$$



Burst effect ?   ... no size distribution

Size distribution ?

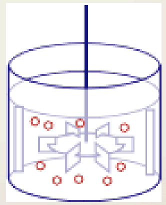
Mechanical resistance



$$v_{breakage} \div d^4$$

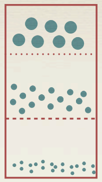
d = 500 to 1000 µm

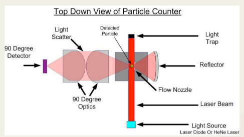
$V_{breakage}$ varies from 1 to 16

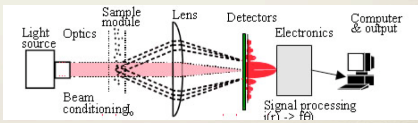


How to measure the size ?

- Sieving analysis
- Microscopy
- Counting
- Laser diffraction
- Acoustic spectroscopy

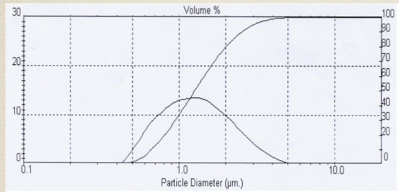


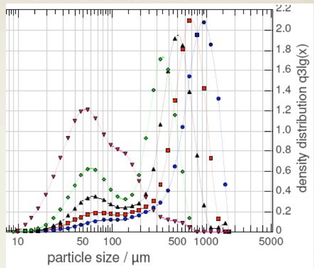


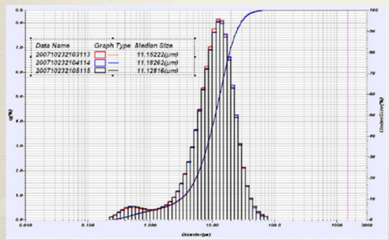


http://en.wikipedia.org/wiki/Particle_size_distribution

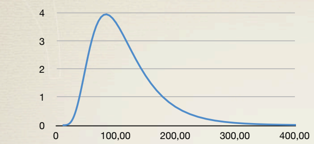
Size distribution







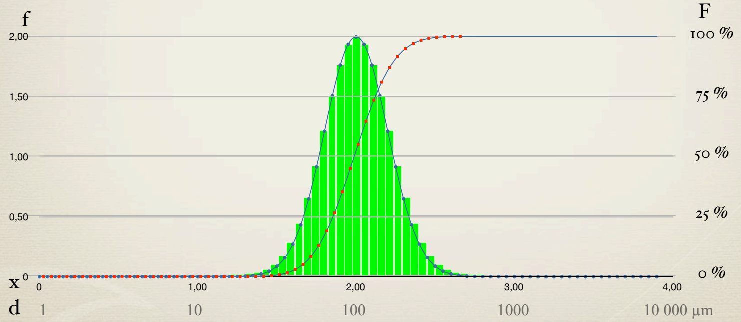
Histograms



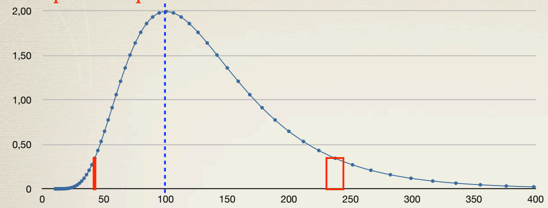
$$f = \frac{dF}{dx} = \frac{1}{\sigma\sqrt{2\pi}} \exp^{-\frac{(x-\bar{x})^2}{2\sigma^2}}$$

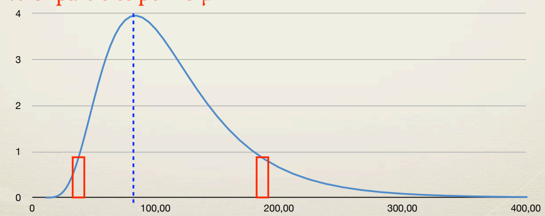
x = log(d)

$$F_x = \int_0^x f\,dx \quad or \quad \sum_0^x f\,\Delta x$$



Histograms



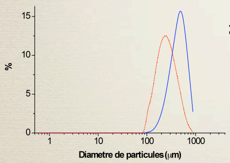


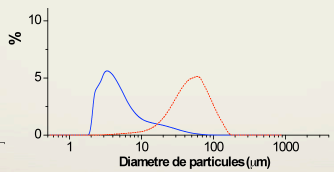
Frequency !

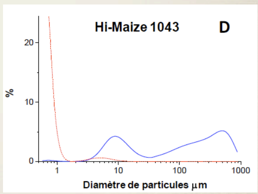
Frequency

- Numeric, f_n (microscope)
- Volumic, f_v (Malvern)
- Massic, f_m (sieving)
- ...

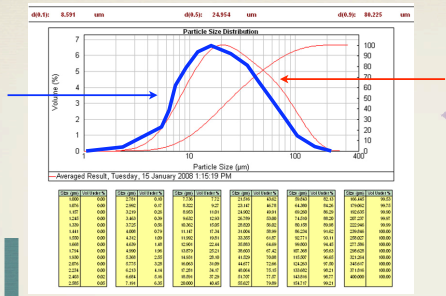
$$f_s = k\ x^3\ f_n$$

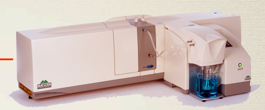


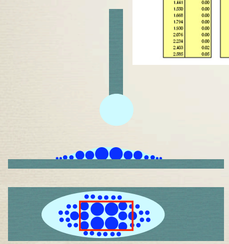




Fv versus Fn

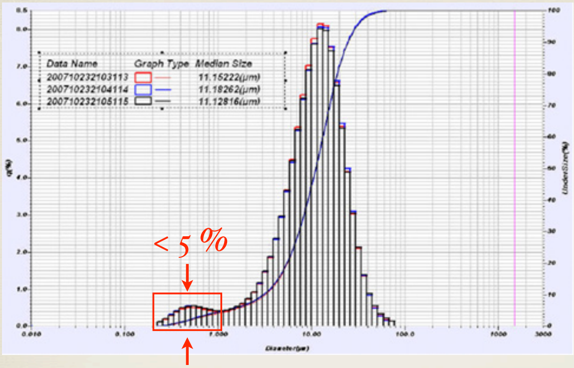






- Sampling is the key point
- Use raw data, avoid conversion
- Make tendencies not absolute values

Artefacts

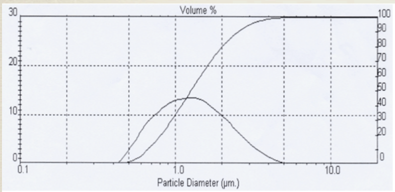


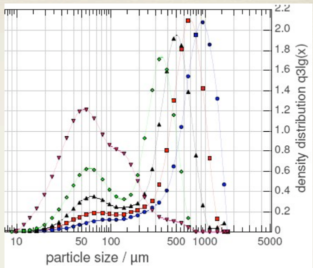
Most probably defaults assimilated to particles

Mean size ?

- Median = diameter of 50 % cumulative frequency = $d_{50\%}$
- Mode = diameter of maximum frequency
- Mean size ?
  - numeric (microscope) $d_n = d_{10} = \frac{\sum n_i \ d_i}{\sum n_i} = f_n \ d_i$
  - volume (Malvern) $d_{43} = \frac{\sum n_i \ d_i^4}{\sum n_i \ d_i^3} = \frac{\sum v_i \ d_i}{\sum v_i} = f_v \ d_i$
    $d_v = d_{30} = \sqrt[3]{\frac{\sum n_i \ d_i 3}{\sum n_i}}$
  - surface $d_s = d_{32} = \frac{\sum n_i \ d_i^3}{\sum n_i \ d_i^2} = \frac{\sum s_i \ d_i}{\sum s_i} = f_s \ d_i = \frac{1}{a_s}$

Mean size ?





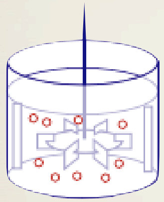
Mean size could be computed for all distributions

Multi-peaks ? multi-means ?

Which mean ?

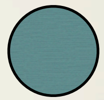
- Function of the applications / model

d_{32} d_{10} d_{30}



Emulsification
Mass transfer

Fluidisation

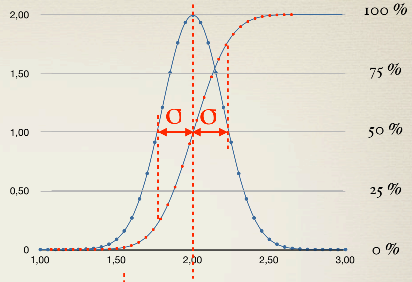


Loading
Yield

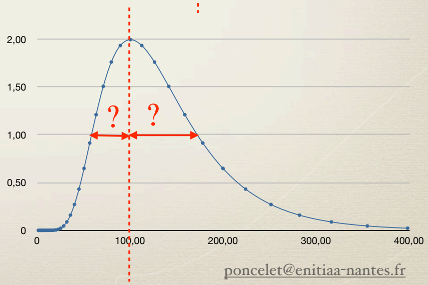
Sometime, mix of mean diameters

Size dispersion ?

- standard deviation, σ
  - graphically (!)
  - $\sigma = (d_{64\%}-d_{16\%})/2$ (!)
  - $$\sigma^2 = \frac{\sum f_i (x_i - \bar{x})^2}{\sum f_i}$$

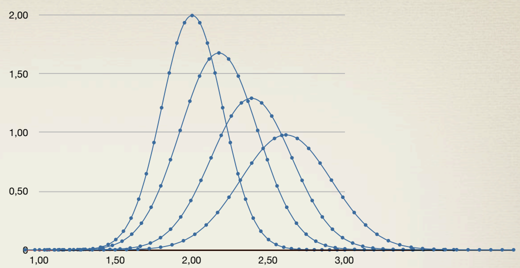


- Distribution
  - numeric or volumic
  - normal or log-normal

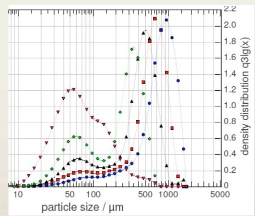


Standard deviation ?

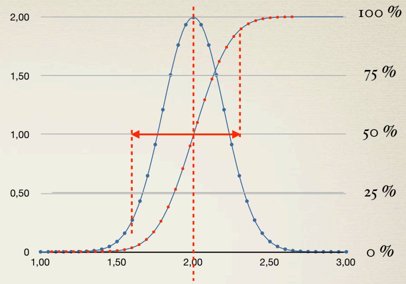
- $\sigma' = \sigma / d_{50\%}$



- multi-peaks ?



Span ?



- Span = = $(d_{90\%}-d_{10\%})/d_{50\%}$
- relative dispersion
- could be applied to all distributions
- take into consideration most particles
- deviations often under $d_{10\%}$ and over $d_{90\%}$

Conclusions

- Even (apparently) simple measurement needs standard
- Use simplest tool to measure the size
- Beware of the sampling
- Define your mean value
  - mode or median are easier
  - avoid conversion between distribution
- Use span to define dispersion
- Size distribution are not absolute value