تفريغ صيدلة صناعية 1

المحاضرة: Particel Size analys

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هذا التفريغ من شرح الدكتور نزال هي مراجعة المحاضرة
هي الدكتورة إسراء

Industrial Pharmacy 1
Introduction
Particle size analysis

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Credit: Prof. Nizar Al-Zoubi

Introduction

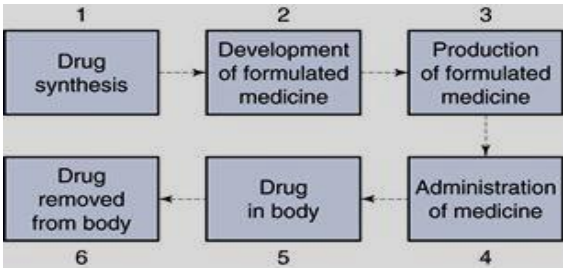
Categories of dosage forms

1. Solids: Powder, granulates, tablets, capsules

**** Powder, granules

1. Liquids: solutions, Suspensions, emulsions, etc
2. Semisolids: creams, ointments, etc.
3. Gaseous **

Particle size and the lifetime of a drug



Particle size and the lifetime of a drug

Particle size influence

- mixing (content uniformity for potent drugs, segregation)
- powder flow
- tabletability
- Bulk volume
- drug release into solution
  - (e.g. griseofulvin, tolbutamide, spironolactone, indomethacin and nifidipine)
  - Nitrofurantoin optimal particle size is 150 μm
  - ** **practically insoluble** in water

Particle size and the lifetime of a drug

Particle size influence

- The properties and behavior of various dosage forms:
  - suspensions: sedimentation rate, texture, taste, rheology
  - parenteral suspensions: *syringeability*, injectability and sustained release.
  - ophthalmic suspensions: irritation of the eye surface (small particle size is used)
  - inhalation aerosols: The position and retention of particles in the bronchopulmonary tract
  - topical formulation: grittiness (powder must be impalpable)

مثال على الـ content-uniformity:

نيجي لـ Panadol رح نشوف على الحبة 500mg من الـ Paracetamol بس بعد ما طلعت حبة وزنتها رح اشوف انه وزنها اعلى لشو؟ لانه الحبة ما فيها بس المادة الفعالة في مواد اضافية، مثلاً نعتبر انه حبة الـ Panadol فيها 200mg من الـ Lactose و 500mg من الـ Paracetamol (هذا مثال توضيحي فقط) فالمصنع لما بدو يصنع الدوا رح يصنع اعداد كبيرة، فهل رح يظل يوزن 500mg من الـ Para و 200mg من الـ lact لكل حدد الحبوب؟ لا بدو يصنعها كيف؟ لأ، طبيب شو بعملوا؟؟

بحكوا انه احنا اليوم بدنا نصنع مليون حبة Panadol، بحسبوا انهم بدهم بكلاخية 200mg lact / 500mg Para وبضربوا كل قوة بعدد الحبوب اي بدهم يعملوها (حكينا مليون) $200\text{mg} \times 10^6$ / $500\text{mg} \times 10^6$ و هيك بطلع معهم كم رح يحتاجوا ليصنعوا المليون حبة ويبلشوا يعملو Mixing منيح للدوا طبعاً لازم يكون الـ mixing منيح وإلا رح يطلع مي حبة كلها Para بحق كلها مادة فعالة (طبعاً ما بدي هذا الشي لانه الـ dose زادت) وحبة كلها lact بحق كلها inactive هيك صار آخذ الـ dose فإذا كانت الـ Partecl size مش مناسبة وإلا الـ Mixing لا يكون منيح.

* لا تنسوا زميلنا إلهم من دعائكم

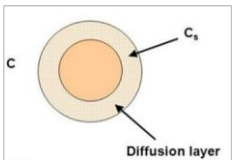
Effect of particle size on dissolution rate

Noyes & Whitney equation:

هاي المعادلة آخذناها بفيزكال 2

$$\frac{dM}{dt} = \frac{DS}{h}(C_s - C)$$

dM/dt: rate of dissolution
(Change of the dissolved amount with time)
C_S is the solubility of solute
C is the concentration of solute at time, t
Cs-C =concentration gradient
D is the diffusion coefficient of the solute in solution,
S is the surface area of the exposed solid ⇒ inversely proportional to particle size
h is the thickness of the diffusion layer.



Particle size

- When determining the size of large solid usually we need to measure at **least three dimensions**.

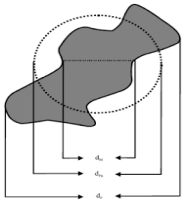
- When determining the size of regular particles like spheres or cubes, it is possible to describe the size using one dimension (diameter or length).

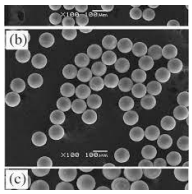
هذا الحكي Ideal لأنه مش كل الـ Particel اللي بشكل منتظم!

يعني بشكل منتظم

- If the particles are mono-sized (have the same size) then it is possible to describe the particle size by measuring one particle.

بما انه اللي نفس الـ size بقدر اطلع الحجم اللي كلهم عندهم عن طريق الـ size لـ Particel واحد

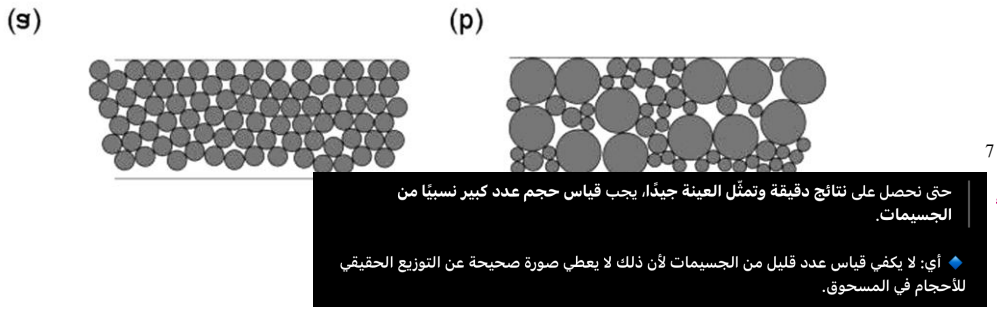




هون الشي الواقعي

Particle size

- However powders generally are composed of particles that are:
  - irregular in shape
  - with different sizes
  - Are very small in size to allow measuring of dimensions (الابعاد) حجم صغير لاقدر احسب الابعاد
- In order to give good representation the size of relatively large number of particles should be determined.

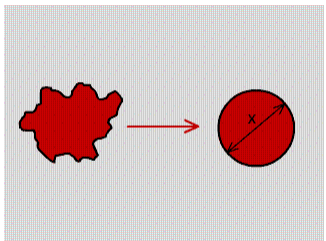


Particle size

غير عملي

- For these reasons it is impractical to measure more than one dimension.
- For this reason, solids are considered to approximate to a **sphere**, which can then be characterized by determining its diameter.
- This is an approximate representation of the particle size and is referred to as ***equivalent diameter*** of the particle.

يعني بقرب حجم الـ Particel لحجم الكرة وبدل ما اعبر عنها بالحجم بصير اعبر عنها باد diameter



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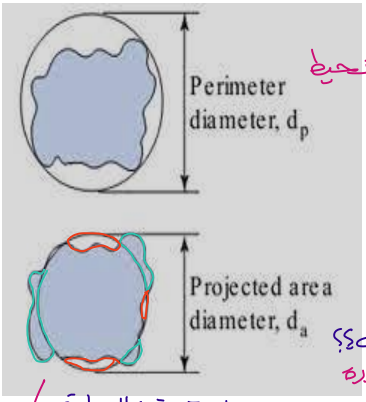
Equivalent diameters

Projected perimeter diameter (d_p)

- The diameter of a circle that has the same perimeter as the projected image of the particle.



Projected area diameter (d_a)

- The diameter of a circle that has the same area as the projected image of the particle.

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Equivalent diameters

Feret's diameter (d_F)

- The mean distance between two parallel tangents to the projected particle perimeter

Martins diameter (d_M)

- The mean length of the chord separating the projected particle into two equal areas.

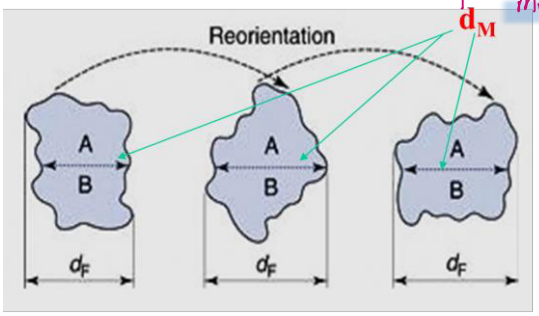
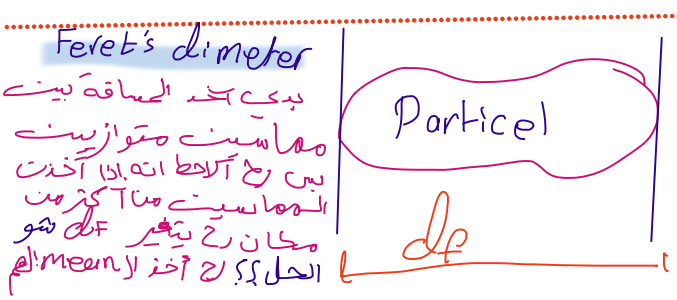
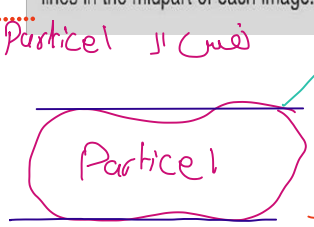


Fig. 10.3 Influence of particle orientation on statistical diameters. The change in Feret's diameter is shown by the distances, d_F; Martins diameter d_M corresponds to the dotted lines in the midpart of each image.





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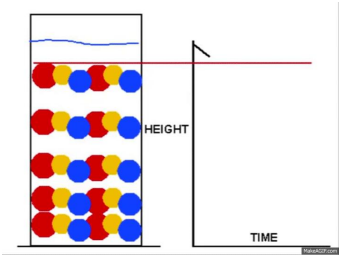
Equivalent diameters

Volume diameter (d_v)

- The diameter of a sphere that has the same volume as the particle.

Stokes diameter (d_{st})

- The diameter of a sphere that has the same sedimentation rate as the particles



Sieve diameter (d_s) ← زي المنخل

- The particle dimension that passes through a square aperture

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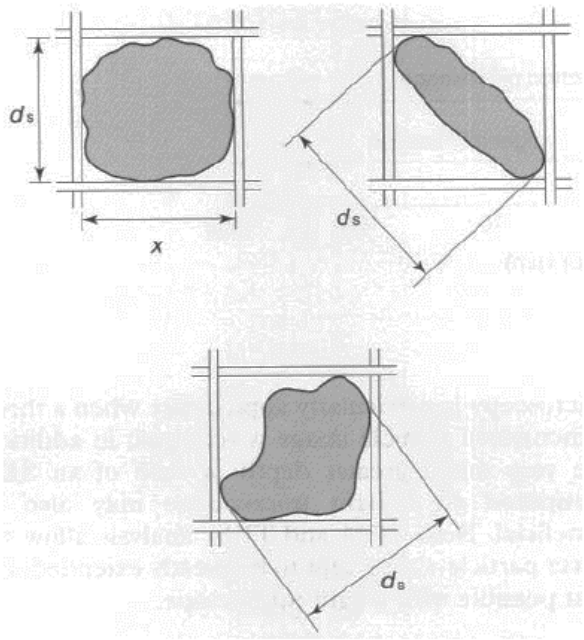

Fig. 10.7 Sieve diameter d_s for various shaped particles

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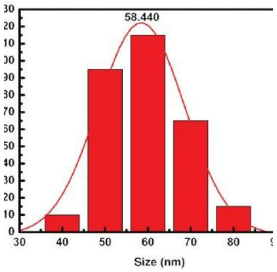
Description of particle size

(1) Mean particle size

- The mean particle size of an analyzed sample can be considered as a rough description for the size of sample.



(2) Particle size distribution

- The distribution of particles into different size ranges can be plotted in the form of histogram.
- A histogram presentation allows different particle size distributions to be compared.
- The value of the peak is the ***mode*** (highest frequency)

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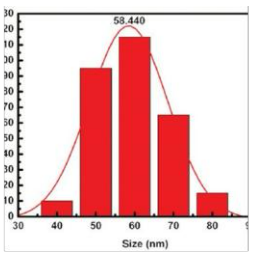
Presentation of size distribution

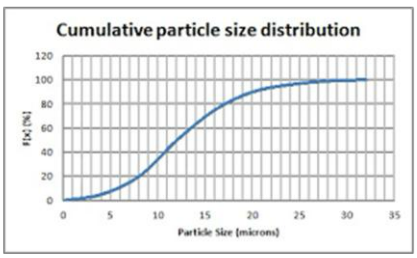
1) Frequency distribution data

2) Cumulative frequency distribution data

They are either under size or oversize



1) Frequency distribution data



2) Cumulative frequency distribution data

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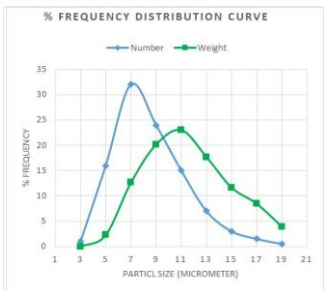
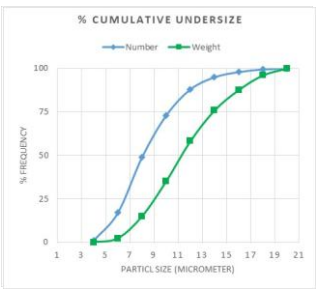
Presentation of size distribution

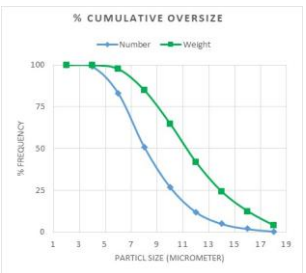
Number and weight distributions

- Frequently, we are interested in obtaining data based on a weight, rather than a number distribution.
- This can be obtained directly by methods such as *sieving* and *sedimentation*.
- Number distribution can be **converted** to weight distributions and vice versa.

(1) size range	(2) Mean of size range, d (μm)	(3) Number of particles in each size range, n	(4) Percent n	(5) nd3	(6) Percent nd3 (Weight)	(7) Cumulative percent frequency undersize (Number)	(8) Cumulative percent frequency undersize (Weight)	(9) Cumulative percent frequency oversize (Number)	(10) Cumulative percent frequency oversize (Weight)
2.0-4.0	3	2	1	54	0.03	1	0.03	100	100
4.0-6.0	5	32	16	4000	2.31	17	2.34	99	99.97
6.0-8.0	7	64	32	21952	12.65	49	14.99	83	97.66
8.0-10.0	9	48	24	34992	20.16	73	35.15	51	85.01
10.0-12.0	11	30	15	39930	23.01	88	58.16	27	64.85
12.0-14.0	13	14	7	30758	17.72	95	75.88	12	41.84
14.0-16.0	15	6	3	20250	11.67	98	87.55	5	24.12
16.0-18.0	17	3	1.5	14739	8.49	99.5	96.04	2	12.45
18.0-20.0	19	1	0.5	6859	3.95	100	99.99	0.5	3.96
		Σ n = 200	100	173534	99.99				







(1) size range	(2) Mean of size range, d (μm)	(3) Number of particles in each size range, n	(4) Percent n	(5) nd3	(6) Percent nd3 (Weight)	(7) Cumulative percent frequency undersize (Number)	(8) Cumulative percent frequency undersize (Weight)	(9) Cumulative percent frequency oversize (Number)	(10) Cumulative percent frequency oversize (Weight)
2.0-4.0	3	2	1	54	0.03	1	0.03	100	100
4.0-6.0	5	32	16	4000	2.31	17	2.34	99	99.97
6.0-8.0	7	64	32	21952	12.65	49	14.99	83	97.66
8.0-10.0	9	48	24	34992	20.16	73	35.15	51	85.01
10.0-12.0	11	30	15	39930	23.01	88	58.16	27	64.85
12.0-14.0	13	14	7	30758	17.72	95	75.88	12	41.84
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18.0-20.0	19	1	0.5	6859	3.95	100	99.99	0.5	3.96
		Σ n = 200	100	173534	99.99				

العامود رقم "1"

رح يكون في Particel size rang ورح احيد اتعامل معه Eqavelant dimeter ك .

العامود رقم "2"

رح آخذ ال mean لل Rang بالعامود 1 مثلاً $\frac{2+4}{2} = \frac{6}{2} = 3$

او $\frac{4+6}{2} = \frac{10}{2} = 5$

العامود رقم "3"

رح يكون فيه عدد ال Particel الموجودة بال Rang (لما اعمل منحنى رح يكون X-axis) وآخر اشي رح اجمع القيم الموجود بهذا العامود وهي بعدين لحتى بعطيني عدد كل ال Particel وهذا المثال بطلع 200

عامود رقم "4"

رح يكون نسبة ورح احسبها من عامود 3 (مثلاً 2) واقسمها على المجموع من العامود 3 (200)

مثلاً $\frac{2}{200} \times 100 = 1$ / $\frac{32}{200} \times 100 = 16$

عامود رقم "7"

لما بدي احسب ال Cumulative undersized Percent frequency رح اشوف العامود 4 واشوف شو اول قيمة اي هي 1 بحطها زي ما هي بعدين رح اروح لل 16 واجمعها مع اي قبلها (1) ورح يصير المجموع 17 وبحطه وبعد هيك بروح لل 32 و بجمعها مع ال 1 وال 16 ورح يصير المجموع 49 وبكمل

عامود رقم "9"

لما بدي احسب الـ Percent Frequency الـ Cumulative oversize رح ابلش من آخر رقم من عامود 4 (100 هيك) وبعد هيك بنقص منه الرقم الأول من نفس العامود (1) 100 - 1 = 99 بعدين

الـ 99 رح اطرح منها الـ 1 والـ 16 ← 99-1-16 = 83 وهكذا

* هيك لما يكون مطلوب منا نغير حسب الـ Particel size الـ Frequency Number 1 بس مرات بطلب منا حسب الوزن وهيك رح نعمل متحن جديد ورح نعمل جدول في قيم مختلفة

رح يكون في عامود رقم 5 و 8 و 10

عامود رقم "5"

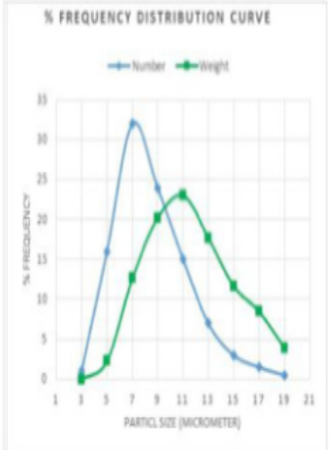
رح آخذ الـ n من عامود 4 واضربها بمكعب الـ d من عامود 2 (n=2 و d=3) ← 2 x 3^3 = 54

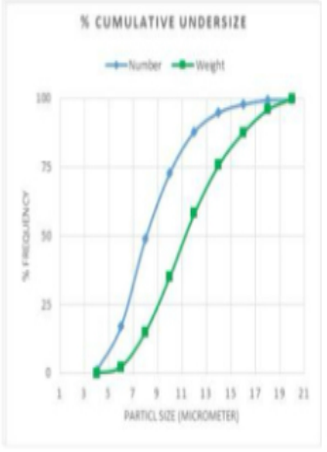
عامود رقم "8"

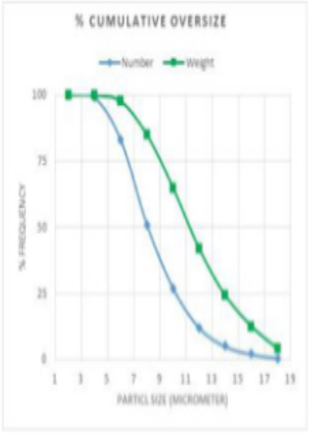
نفس عامود 7 بس رح آخذ القيم من عامود 5

عامود رقم "10"

نفس عامود 9 بس رح آخذ القيم من عامود 5

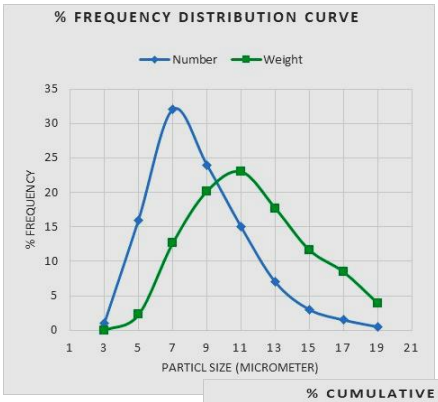


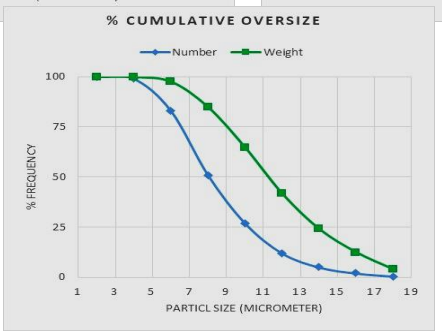




* الـ Cumulative ما في Peak

رح آلاحظ انه الـ Peak قيمها اعلى لما اشتغل حسب الوزن





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Description of particle size

Types of distributions

- ***Normal distribution***: The mode separates the curve into two symmetrical halves.
- ***Positively skewed***: A frequency curve with an elongated tail towards the higher size range.
- ***Negatively skewed***: A frequency curve with an elongated tail towards the lower size range.
- ***Bimodal***: The frequency curve containing two peaks (two modes)

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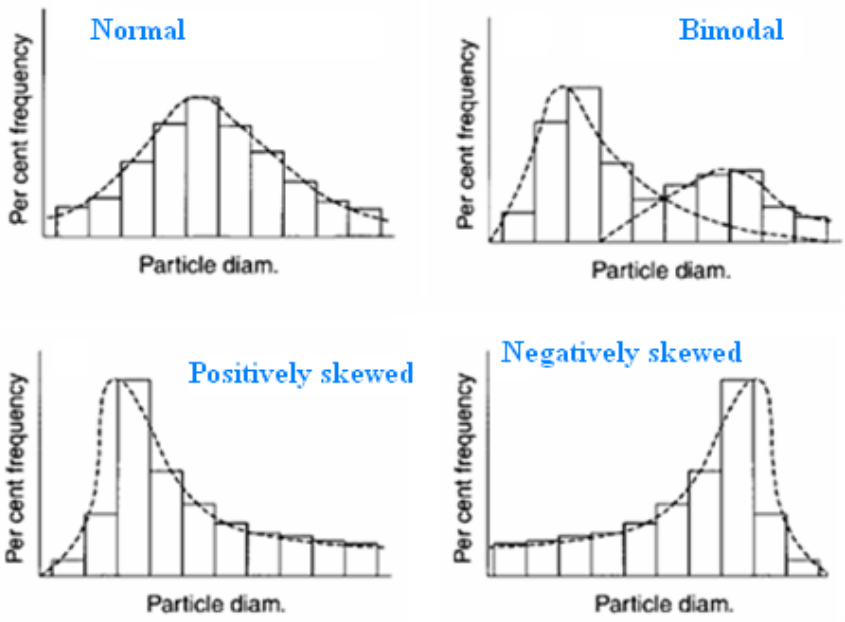

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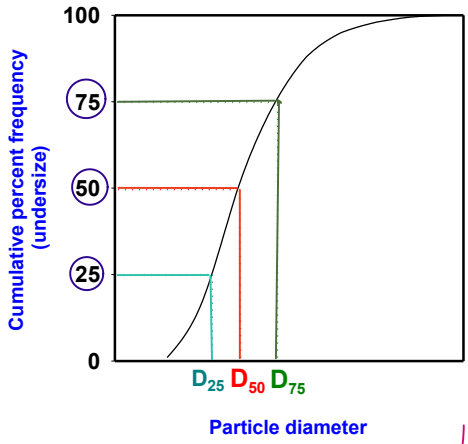
هون بحكي انه حجم الـ Particel
من الكبير ← الصغير

Presentation of size distribution

Evaluation of degree of skewness

- The degree of skewness can be estimated by determining interquartile coefficient of skewness (*IQCS*)



$$IQCS = \frac{(D_{75} - D_{50}) - (D_{50} - D_{25})}{(D_{75} - D_{50}) + (D_{50} - D_{25})}$$

القيمة المقابلة لـ 75٪
القيمة المقابلة لـ 25٪
القيمة المقابلة لـ 50٪

Cumulative frequency distribution curves.

Point D_{50} corresponds to the median diameter; D_{25} is the lower quartile point and D_{75} is the upper quartile point.

IQCS → + → +skewed
→ Zero → normal
→ − → −skewed

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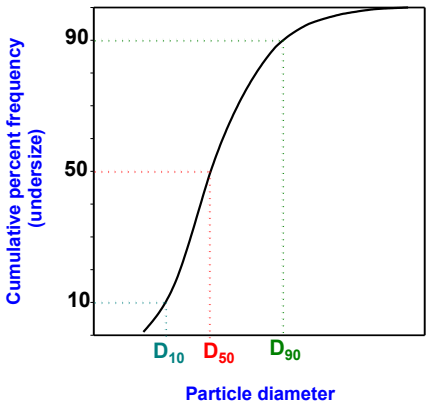
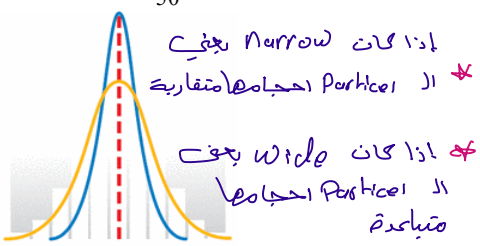
Presentation of size distribution

Evaluation of distribution width

- The size distribution width can be estimated by determining **Span**



$$Span = \frac{D_{90} - D_{10}}{D_{50}}$$



- **Note**: D_{90}, D_{50}, D_{10} are values corresponding to 90, 50 and 10% in the cumulative undersize curve.

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Particle size analysis methods

Microscope methods

Equivalent diameters

d_a, d_p, d_F and d_M can be determined

Range of analysis

- Light microscope (1 - 1000 μm)
- Scanning electron microscope (0.05 - 1000 μm)
- Transmission electron microscope (0.001 - 0.05 μm)

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