Micromeritics

What is Micromeritics?

The Science and Technology of small particles is known as Micromeritics.

Micromeritics deals with-

- **Particle size and Size Distribution**
- **Methods of Determining particles size**
- **Particle shape and surface area**
- **Pore size**

Importance of Study of Micromeritics

Knowledge and control of the size and the size range of particle is of profound importance in pharmacy.

Size and surface area can be related to the physical, chemical and pharmacological properties of a drug.

1.Particle size affect its release from dosage forms that are administered orally, parenterally, rectally and topically

2. Physical stability and pharmacologic response of suspensions, emulsion and tablets depends on particle size.

3. It is also important in flow properties and proper mixing of granules and. powders in tableting.

4. Both Tablets and capsules are produced using equipment which controls the mass of drug and other particles by volumetric filling. Therefore any interference with the uniformity of fill volumes may alter the mass of drug incorporated into the tablet or capsules. Thus reduce the uniformity of the medicine.

5. Powders with different particle sizes have different flow and packing properties which alter the volumes of powder during each encapsulation or tablet compression.

6. The rate of solution depends on the several factors. One factor is the particle size. Thus particles having small dimensions will tend to increase the rate of solution.

For example:

a). Griseofulvin has a low solubility by oral administration but is rapidly distributed following absorption. The solubility of Griseofulvin can be greatly increased by particle size reduction.

b). Reduction of particles size also increase the rate of absorption of tetracycline, Aspirin and Sulphonamides.

c). Reduction of particle size of nitrofurantoin increased the rate of absorption. Therefore the toxic effect due to rapid absorption.

Different means of expressing particle size.

There are different means of expressing particle size:

Millimeter (mm)……. 10^{-3} meter

Micro meter (μ m) ……. 10^{-6} meter

nano meter (nm)…….. 10^{-9} meter

pico meter ……10^{-12} meter

fanto meter…….. 10^{-15} meter

Particle Dimension in Pharmaceutical Disperse system

Particle size

Micrometer (μ m)	Millimeter (mm)	Disperse systems
0.5-10	0.0005 - 0.010	Suspension, fine emulsion
10-50	0.010- 0.050	Coarse emulsion, flocculated suspension
50- 100	0.50- 0.100	Lower range of sieve range, fine powder range
150-1000	0.150-1.000	Coarse powder range
1000- 3360	1.000- 3.360	Average granule size

Methods of determining particle size

- **Optical Microscopy**
- **Sieving Methods**
- **Sedimentation Methods**

Particle volume measurement:

- **Coulter Counter Method (Electrical stream sensing method)**
- **Laser light scattering methods.**

Methods of determining surface area:

- **Adsorption method**
- **Air permeability method**

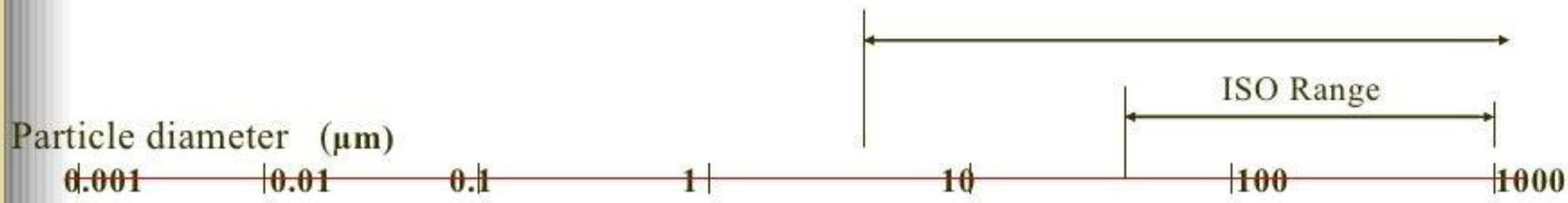
Sieving Method

Sieving method is an ordinary and simple method. It is widely used as a method for the particle size analysis.

Range of analysis:

The International Standards organization (ISO) sets a lowest sieve diameter of 45 µm and since powders are usually defined as having a maximum diameter of 1000 µm, this could be considered to be the upper limit.

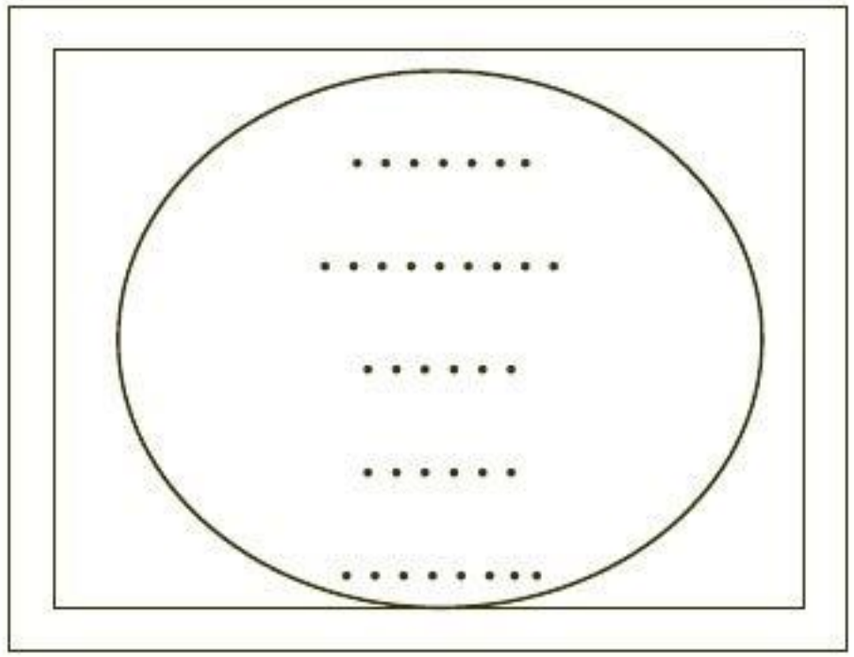
In practice sieves can be obtained for size analysis over a range from 5 to 125 000 µm.



Sample preparation and analysis condition

1. Sieve analysis is usually carried out using dry powders.

2. Although, for powders in liquid suspension or which agglomerate during dry sieving, a process of wet sieving can be used.



Principle of Measurement:

Sieve analysis utilizes a woven, punched or electroformed mesh often in brass, bronze or stainless steel with known aperture (hole) diameters which form a physical barrier to particles.

Most sieve analyses utilize a series, stack (Load /Mountain or nest (layer) of sieves which have the smallest mesh above a collector tray followed by meshes which get progressively coarser towards the top of the series.

A sieve stack usually comprises 6-8 sieves with a progression based on a $\sqrt{2}$ or $2\sqrt{2}$ change in diameter between adjacent aperture.

Powder is loaded on to the coarsest sieve of the assembled stack and the nest is subjected to mechanical vibration for, say 20 minutes

After this time , the particles are considered to be retained on the sieve mesh with an aperture corresponding to the minimu or sieve diameter.

A sieving time of 20 minutes is arbitrary and BS 1796 recommen sieving to be continued until less than 0.2% material passes a giv sieve aperture in any 5 minutes interval

Advantages: **1. This method is very simple.**
2. Not expensive
3. Easy to operate

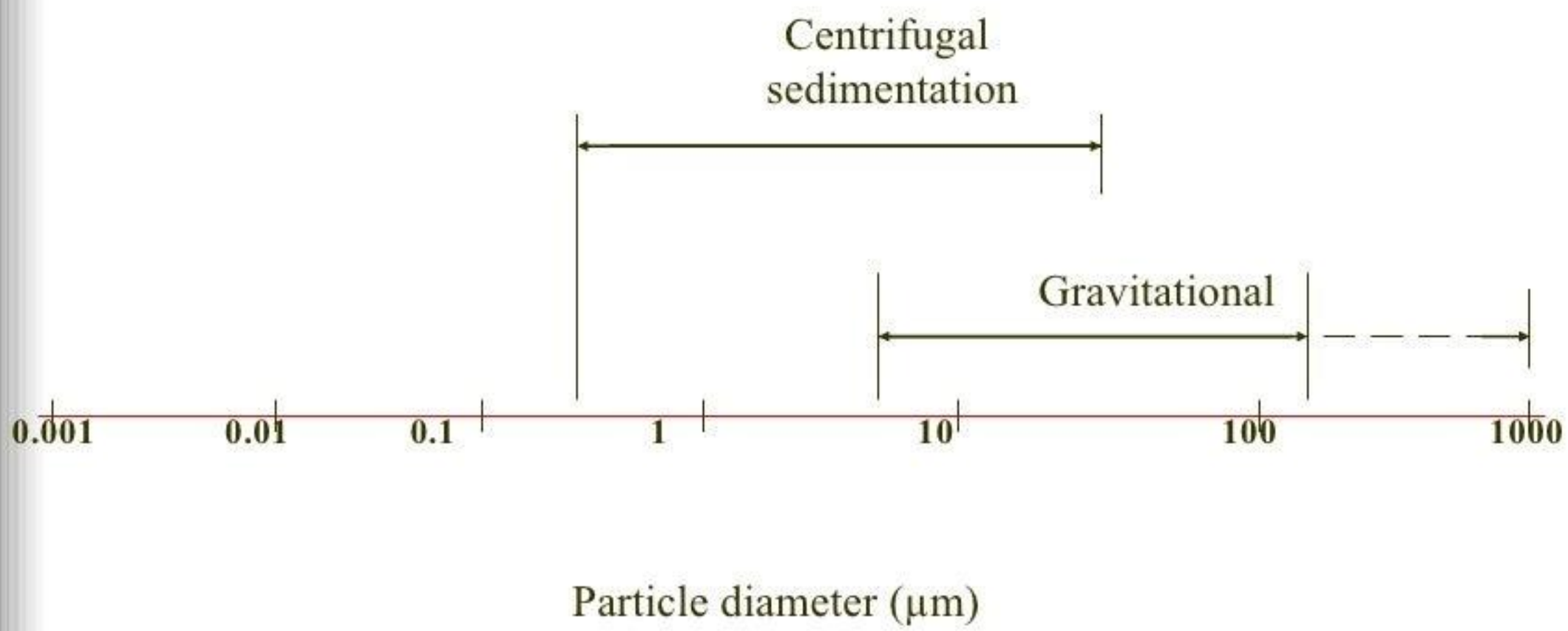
Disadvantages: **1. Not too much precise** method.
2. Not applicable for all disperse systems.

Sedimentation Methods

Sedimentation Method **is also an ordinary and simple method**

It is widely used as a method for the particle size analysis.

Range of analysis:



Sample preparation and analysis conditions

In this method particle size can be determined by examining the powder as it sediments out.

(a). In cases where the powder is not uniformly dispersed in a fluid it can be introduced as a thin layer on the surface of the liquid.

(b). If the powder is lyophobic, e.g. hydrophobic in water , it may be necessary to add dispersing agent to aid wetting of the powder.

(c). In case where the powder is soluble in water it will be necessary to use non- aqueous liquids or carry out the analysis in a gas.

Principle of Measurement

Particle size analysis by sedimentation method can be divided into two main categories according to the method of measurement used.

1. One of the type is based on measurement of particle in a retention zone.
2. Another type uses a non-retention measurement zone.

An example of a non-retention zone measurement is known as the pipette method.

In this method , known volumes of suspension are drawn off and the concentration differences are measured with respect to time.

One of the most popular of the pipette methods was that developed by *Andreasen and Lundberg and commonly called the Andreasen pipette.*

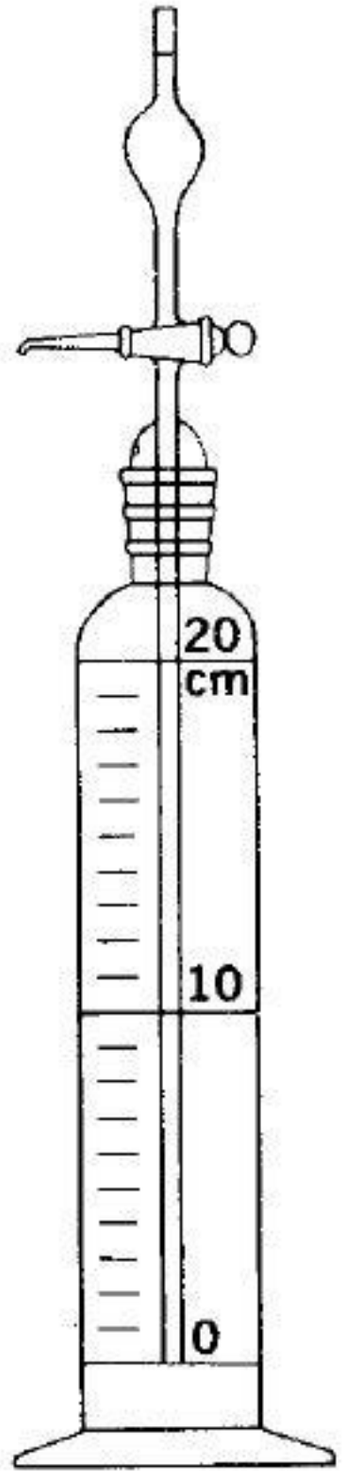


Fig. 16–8. Andreasen apparatus for determining particle size by the gravity sedimentation method.

The Andreasen fixed-position pipette consists of a 200 mm graduate cylinder which can hold about 500 ml of suspension fluid.

A pipette is located centrally in the cylinder and is held in position by a ground glass stopper so that its tip coincides with the zero level.

A three way tap allows fluid to be drawn into a 10 ml reservoir which can then be emptied into a beaker or centrifuge tube.

The amount of powder can be determined by weight following drying or centrifuging.

The weight of each sample residue is therefore called the weight of undersize and the sum of the successive weight is known as the cumulative weight of undersize. It can be expressed directly in weight units or percent of the total weight of the final sediment..

The data of cumulative weight of undersize is used for the determination of particle weight distribution, number distribution,

The largest particle diameter in each sample is then calculated from *Strokes' Law.*

The particle size may be obtained by gravity sedimentation as expressed in *Strokes' law.*

$$v = \frac{h}{t} = \frac{d_{st}^2 (\rho_s - \rho_o)\, g}{18\eta_o}$$

or

$$\mathbf{d_{st}} = \sqrt{\frac{18\eta_o\, h}{(\rho_s - \rho_o)\, gt}}$$

Where ,

v = rate of settling

h = Distance of the fall in time , t

d_{st} = the mean diameter of the particles based on the velocity of sedimentation

ρ_s = density of the particles

ρ_o = density of the dispersion medium

g = Acceleration due to gravity

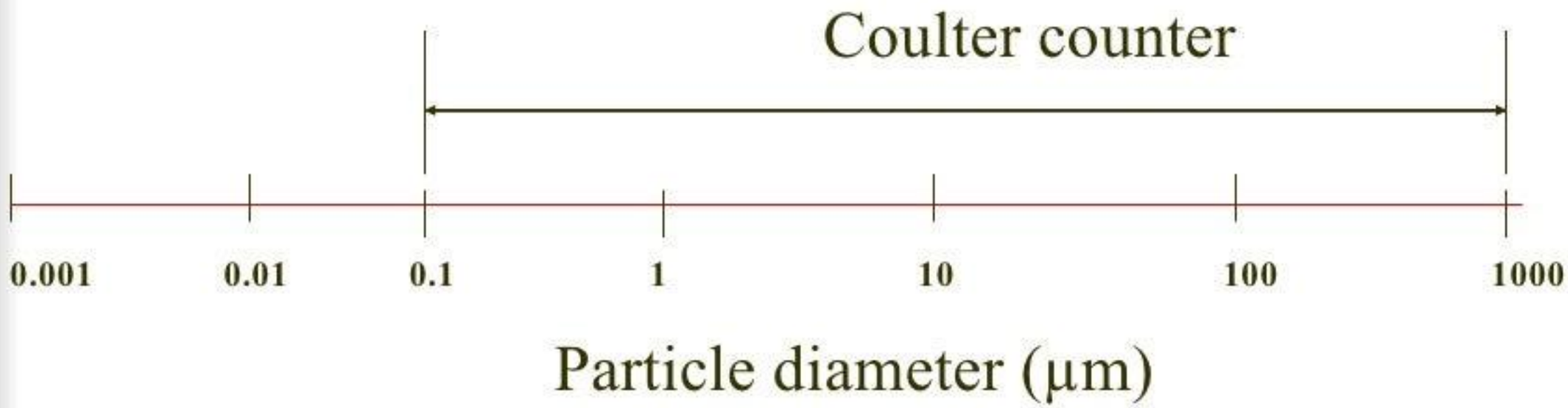
η_o = Viscosity of the medium

Note: The question holds spheres falling freely without hindrance and at a constant rate.

Coulter Counter Method (Electrical stream sensing zone method)

Coulter Counter Method (Electrical stream sensing zone method) is a sophisticated method. It is a precise and accurate method.

Range of analysis:



Sample preparation and analysis conditions

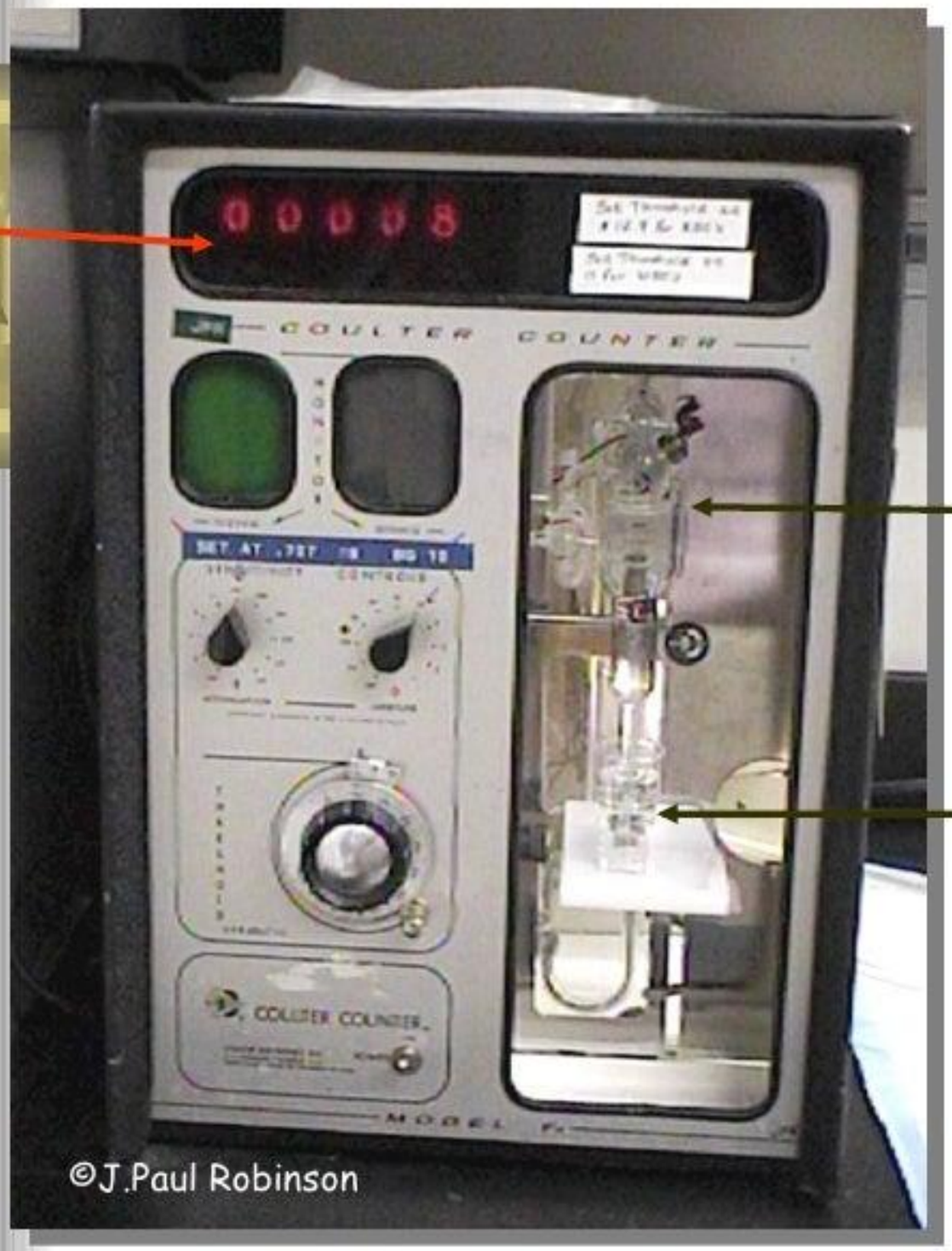
1. Powder samples are dispersed in an electrolyte to form a very dilute suspension.

2. The suspension is usually subjected to ultrasonic agitation for a period to break up any particle agglomerates.

3. A dispersant may also be added to aid particle deagglomeration.

Wallace Coulter - Coulter orifice - 1948-1956

Cell counter



vacuum

orifice