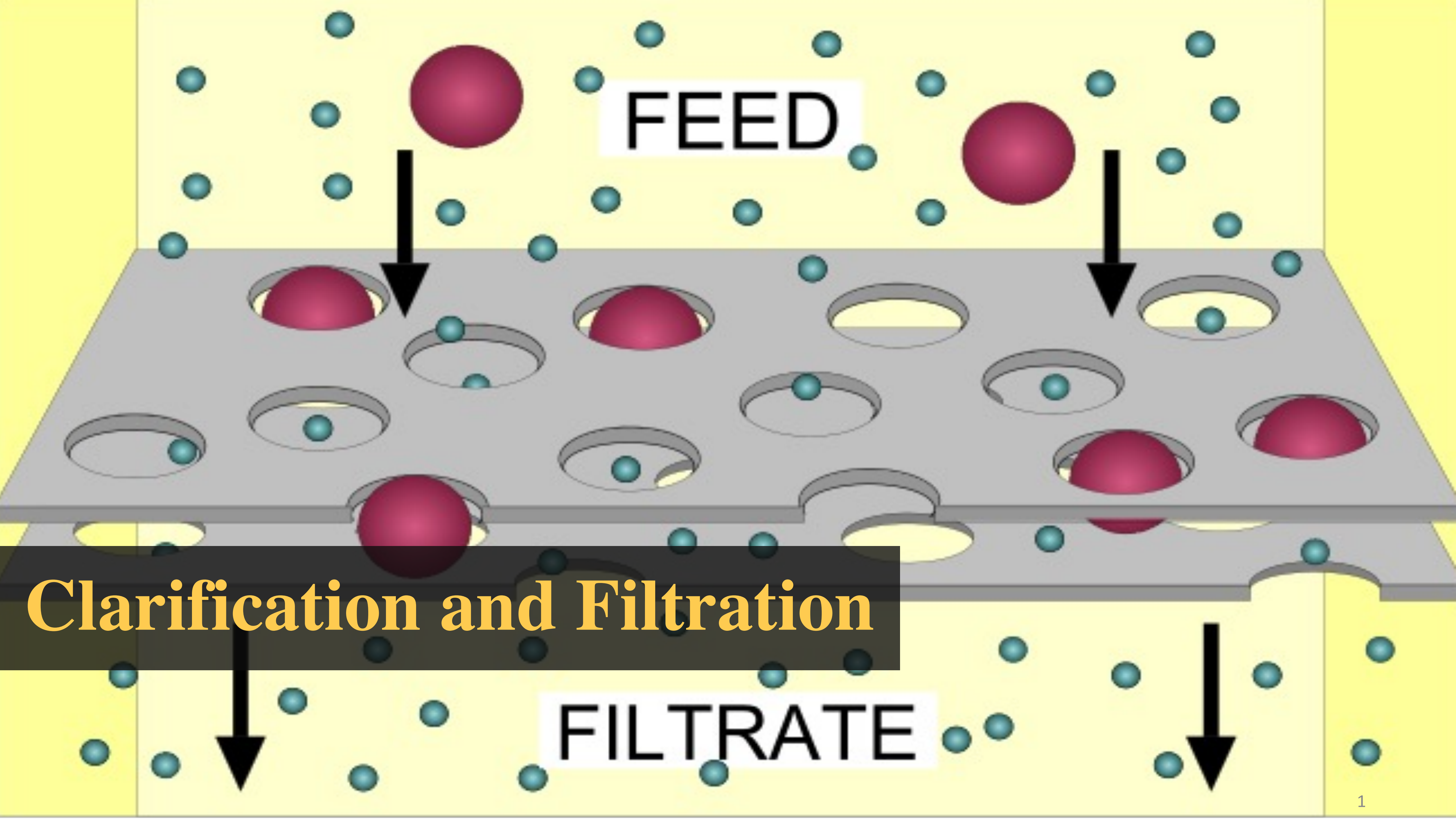
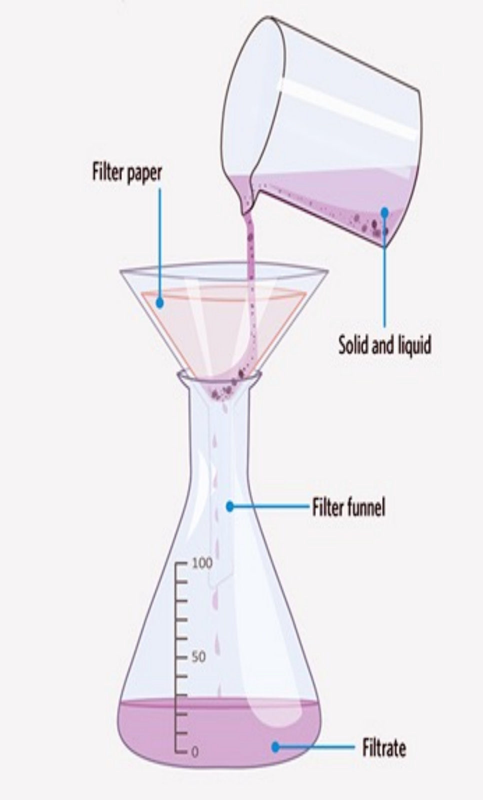
Clarification and Filtration



Definitions

- **Clarification**: a process that involves the **removal or separation** of a solid from a liquid, or a fluid from another fluid.
- The term "fluid" involves both **liquids and gases**.
- Clarification can be achieved using either **filtration or centrifugation techniques**.
- In **pharmaceutical processing** there are two main **goals** for such processes:

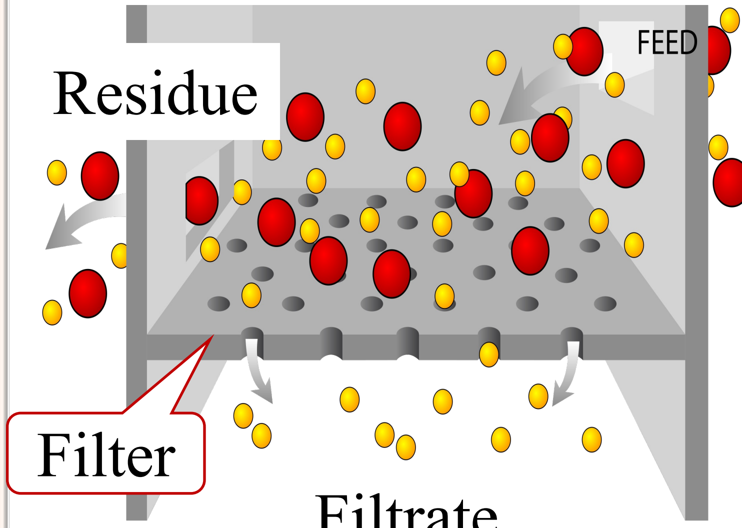
1. To **remove unwanted solid** particles from either a liquid product or from air
2. To **collect the solid** as the product itself (e.g. following crystallization). Also separation of fluid from another fluid (ex centrifugation)



Definitions

- **Filtration**: the process in which particles are separated from a liquid by passing the liquid through a permeable material.
- **The filter** is The permeable medium is a porous material that separates particles from the liquid passing through it.
- Thus, filtration is a unit operation in which a mixture of solids and liquid, **the feed**, suspension, dispersion, influent or slurry, is forced through a porous medium (**filter**), in which the solids are deposited or entrapped.
  - The solids retained on a filter are known as the **residue**.
  - The solids form a **cake** on the surface of the medium, and the clarified liquid known as **effluent or filtrate** is discharged from the filter.
- **If recovery of solids** is desired, the process is **called cake filtration**.

Filtration



Application of Filtration in Pharmaceutical Processing

1. Clarification of products to **improve** their appearance, i.e. to give them "sparkle" or "brightness".

2. **Removal** of **potential irritants**, e.g. from eye-drop preparation or solution applied to mucous membranes.

3. **Recovery of desired solid** material from a suspension or slurry, e.g. to obtain a drug or excipient after a crystallization process.

4. Production of **water of appropriate quality** or pharmaceutical uses such as Nanopure® water.

Application of Filtration in Pharmaceutical Processing

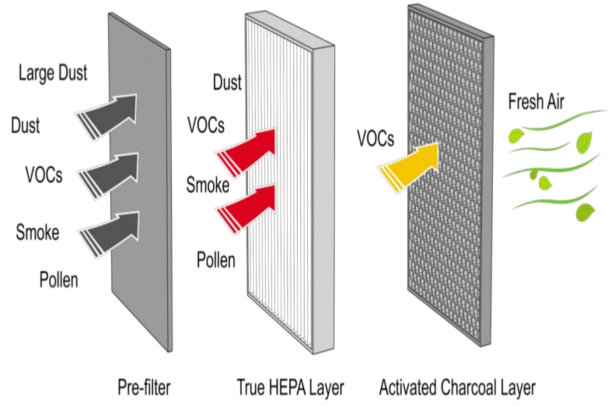
5. To meet the sterility specification (removal of microorganisms) required for some products using *sterile filtration or aseptic filtration*

6. **Sterilization** of solution and vehicle of suspension that are chemically or physically unstable under heating conditions.

7. **Detection of microorganisms present** in liquids by analyzing a suitable filter on which the bacteria are retained.

8. To assess the **efficiency of preservatives** added to the pharmaceutical product.

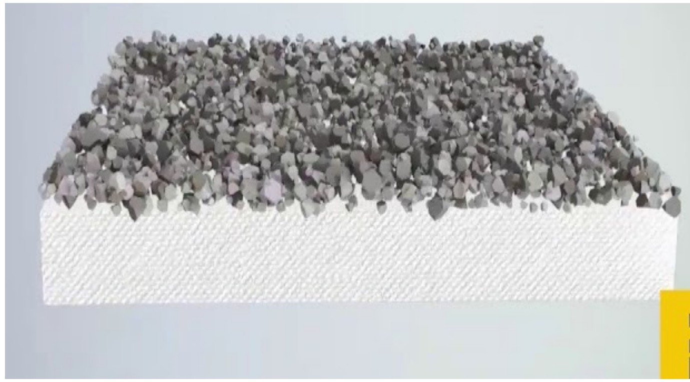
- Recently, techniques such as nanofiltration, ultrafiltration, and microfiltration have been used to recover colloidal delivery systems from mother liquor.



Mechanisms of Filtration

- **Four** different mechanisms of filtration according to how the suspended material is trapped by the filter medium:

1. **Surface straining/ sieving**: any particle that is larger than the pores of the medium deposits on the surface, and stays there until it is removed.
   - Particles that are smaller in size than the pores pass quickly through the medium.

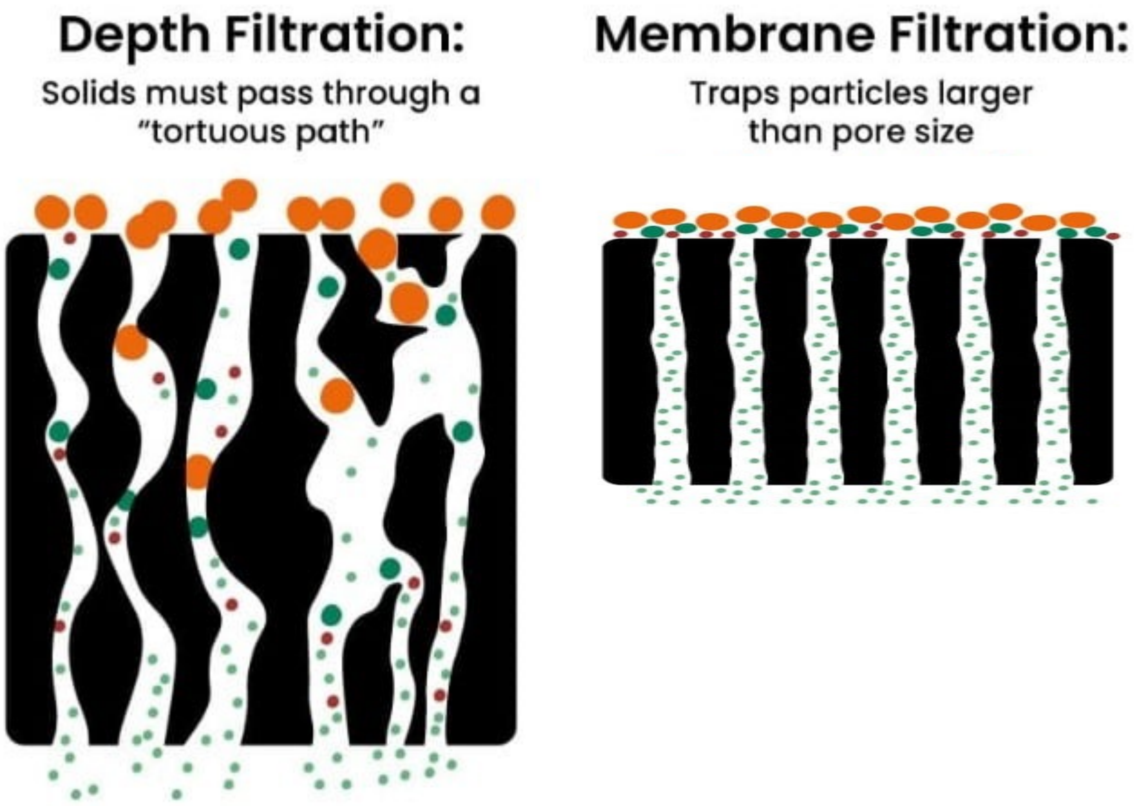


- Filtration occurs on the surface of the filter so-called **membrane filter.**
- Because filtration occurs on the surface, there is a tendency for them to become **blocked** unless the filter is carefully designed.
- Used where the **contaminant level is low** or small volumes need to be filtered.

Mechanisms of Filtration

2. **Depth straining**:

- Similar to the previous mechanism in which it is governed by the particle size or shape.
- However, the filter medium here is **thick** in comparison with the pore diameter ➔ particles **will travel along the pore** until they reach a point where the pore narrows down to a size too small for the particle to go any further so they become trapped.



3. Depth filtration (impingement):

- The particles become entrapped in the **depth of the medium**, even though they are smaller in diameter, and possibly much smaller than the pore at that point. →
- They become **attached to the pore wall**, or to another particle already held through van der Waals and other surface forces (*entanglement*).

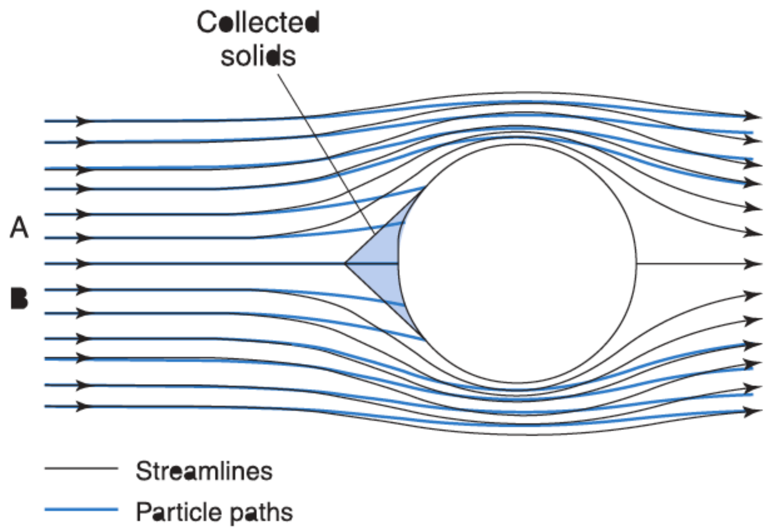
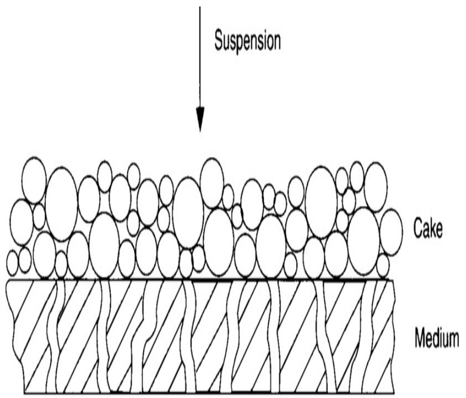


Fig. 25.1 • Filtration by impingement.

4. Cake Filtration (auto filtration):

- Cake filtration (which is a development of surface filtration) **begins** with the formation of a layer of particles on the surface of the filter medium, with larger pores bridged by a group of smaller particles.
- On this layer, **a cake of particles accumulates** to **act as the filter medium** for subsequent filtration.
- Cake filtration in which **solid recovery** is the goal.
  - These definitions emphasize that the mechanisms of filtration may result in the trapping of far smaller particles than might be expected from the size of the pores in the medium.
- The actual mechanism or combination of mechanisms in any specific instance is dependent on the characteristics of both the medium and the suspension being filtered
- This is **widely used in pharmaceutical** processing.



- This process requires the **solution to contain a large amount** of suspended solids (usually 3-20%).

Theory of Filtration

- The flow of liquid through a filter follows the basic rules that govern the flow of any liquid through a medium offering resistance.
- The Flow rate may be expressed as:

$$rate = \frac{driving\ force}{resistance}$$

- The **rate** may be expressed as **volume per unit time (rate change dV/dT)** and Driving force (**pressure differential**).

- The apparent complexity of the filtration equations arises from the expansion of the resistance term
- **But**: **Resistance** is **not constant** since it increases as solids are deposited on the filter medium.

Theory of Filtration

- An expression for this changing resistance involves a material balance as well as factors expressing the permeability or coefficient of resistance of the continuously expanding cake.
- These factors have been taken into account in the formation of **Darcy's equation** that counts for the change in resistance to flow during filtration as follows:

$$\frac{dV}{dT} = \frac{KA\,\Delta P}{\eta L}$$

- Where (dV/dT rate change, A= filter area, P= pressure **drop** through the filter medium, η =filtrate viscosity, L bed thickness, K permeability coefficient, and depends on the nature of the precipitate to be filtered and filter medium itself.
- So $$rate\ of\ filtration = \frac{(Area\ of\ filter)\,x\ (pressure\ difference)}{(viscocity)\ x\ (resistance\ of\ cake\ and\ filter)}$$

Interpretation of Flow Rate Equation

- **How to Change the Flow Rate**

$$rate\ of\ filtration = \frac{(Area\ of\ filter)\ x\ (pressure\ difference)}{(viscocity)\ x\ (resistance\ of\ cake\ and\ filter)}$$

a. **Pressure increases** → increase in flow unless the cake is highly compressible.

- Pressure increase on highly compressible, flocculent, or slimy precipitated may decrease or terminate flow.

- **Change the pressure difference** by using a **vacuum** (pull) on the far side (under) of the filter which will increase the pressure difference up to atmospheric pressure.
- **Note**: this **also** can be done by **pumping** the fluid into the filter (industrial scale).

Theory of Filtration

$$rate\ of\ filtration = \frac{(Area\ of\ filter) x\ (pressure\ difference)}{(viscocity)\ x\ (resistance\ of\ cake\ and\ filter)}$$

b. **An increase in the area →** increases flow since cake thickness and thus resistance is also **reduced**).

- This can be done by using a **larger filter** of several small units in parallel.
- **Note:** flow is proportional to A^2 because the **L** term has an area in its equation → small increase in the area will result in a bigger increase in flow rate.

Theory of Filtration

$$rate\ of\ filtration = \frac{(Area\ of\ filter)x\ (pressure\ difference)}{(viscocity)\ x\ (resistance\ of\ cake\ and\ filter)}$$

c. **Viscosity is inversely** proportional to the flow rate, increase in viscosity will decrease the flow rate. → so, filtration efficiency also may be affected by changes in temperature.

- The viscosities of most liquids **decrease** with an **increase in temperature**.→
- Increasing the temperature of heavy pharmaceutical syrups lowers the viscosity and increases filtration rates.

- Note: dilution may also decrease the viscosity

Theory of Filtration

$$rate\ of\ filtration = \frac{(Area\ of\ filter)x\ (pressure\ difference)}{(viscocity)\ x\ (resistance\ of\ cake\ and\ filter)}$$

d. **Cake resistance:** is a function of cake thickness, therefore, the average flow rate is inversely proportional to the **amount of cake deposited**.

- **Note: Decrease the cake thickness**: this can be decreased by removing some of the cake periodically.

Theory of Filtration

e. **The permeability coefficient** may be examined in terms of its two variables: **1) porosity and 2) surface area:**

1. The **cake porosity** depends on how particles are deposited and packed.→

- A fast deposition rate, **given by** concentrated slurries or high flow rates, may give a **higher porosity** because of the greater possibility of bridging and arching in the cake.

2. **Surface area** unlike porosity, is markedly affected by **particle size** and is inversely proportional to particle diameter.→

- Hence, a **coarse precipitate** is **easier** to filter than a fine precipitate even though both may pack with the same porosity.

- ➔ Most clarification problems can be resolved empirically by varying one or more of the 5 factors above.