

Module ChE 311 Biochemical Engineering

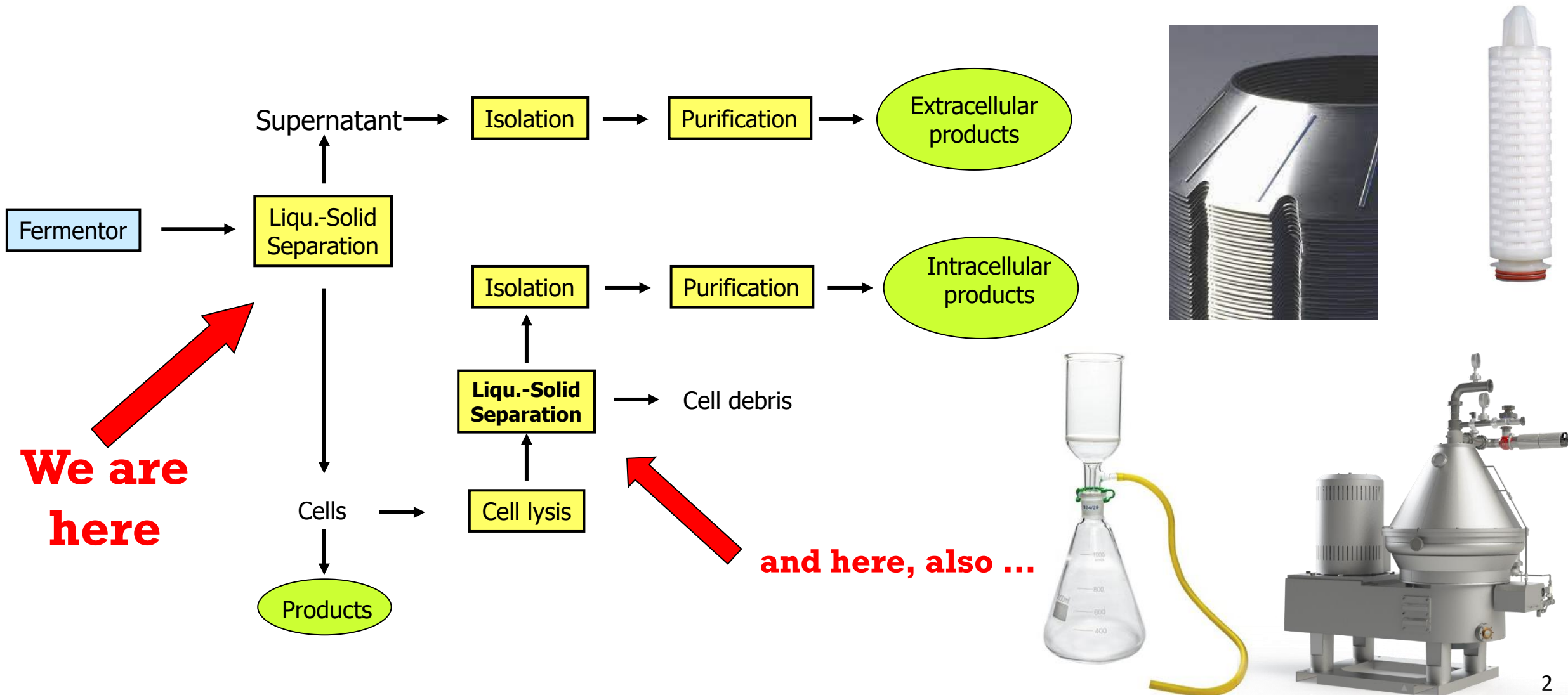
Downstream processing **Lecture 2 - Liquid-solid separation**

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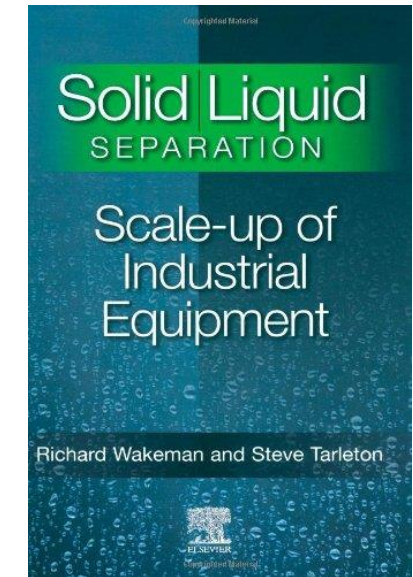
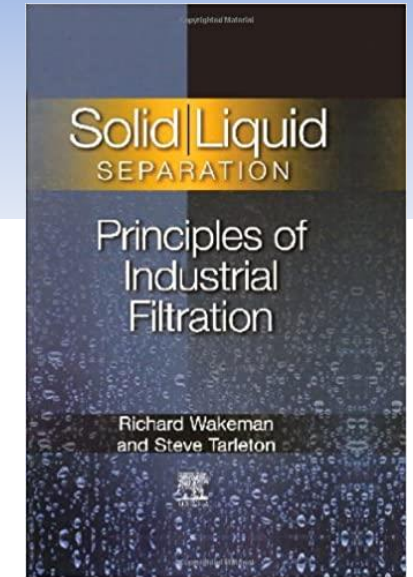
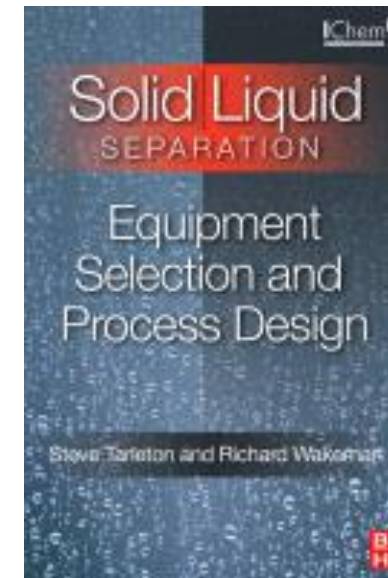
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Common pathway for a purification protocol

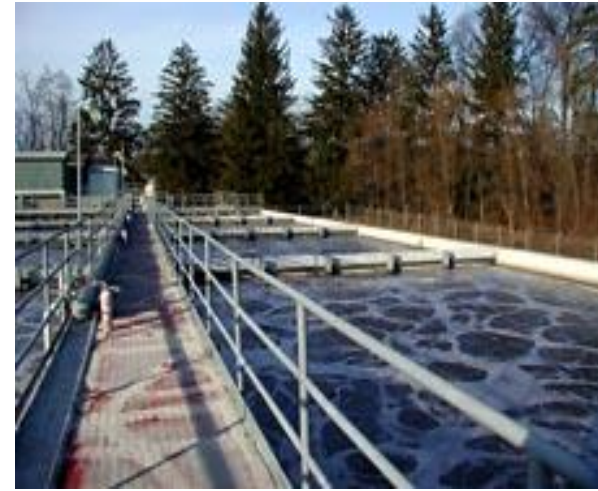
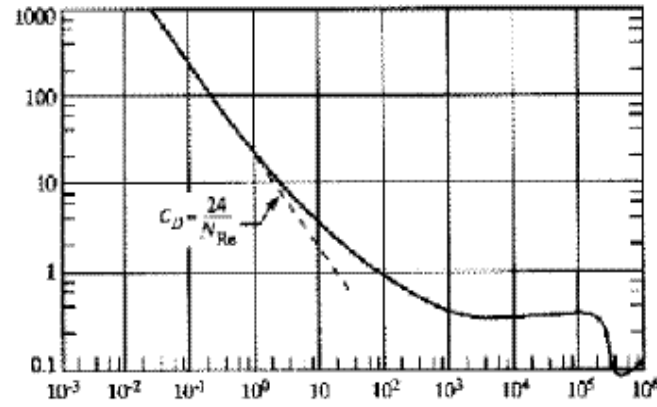


S/L separation: a limited choice of proven techniques

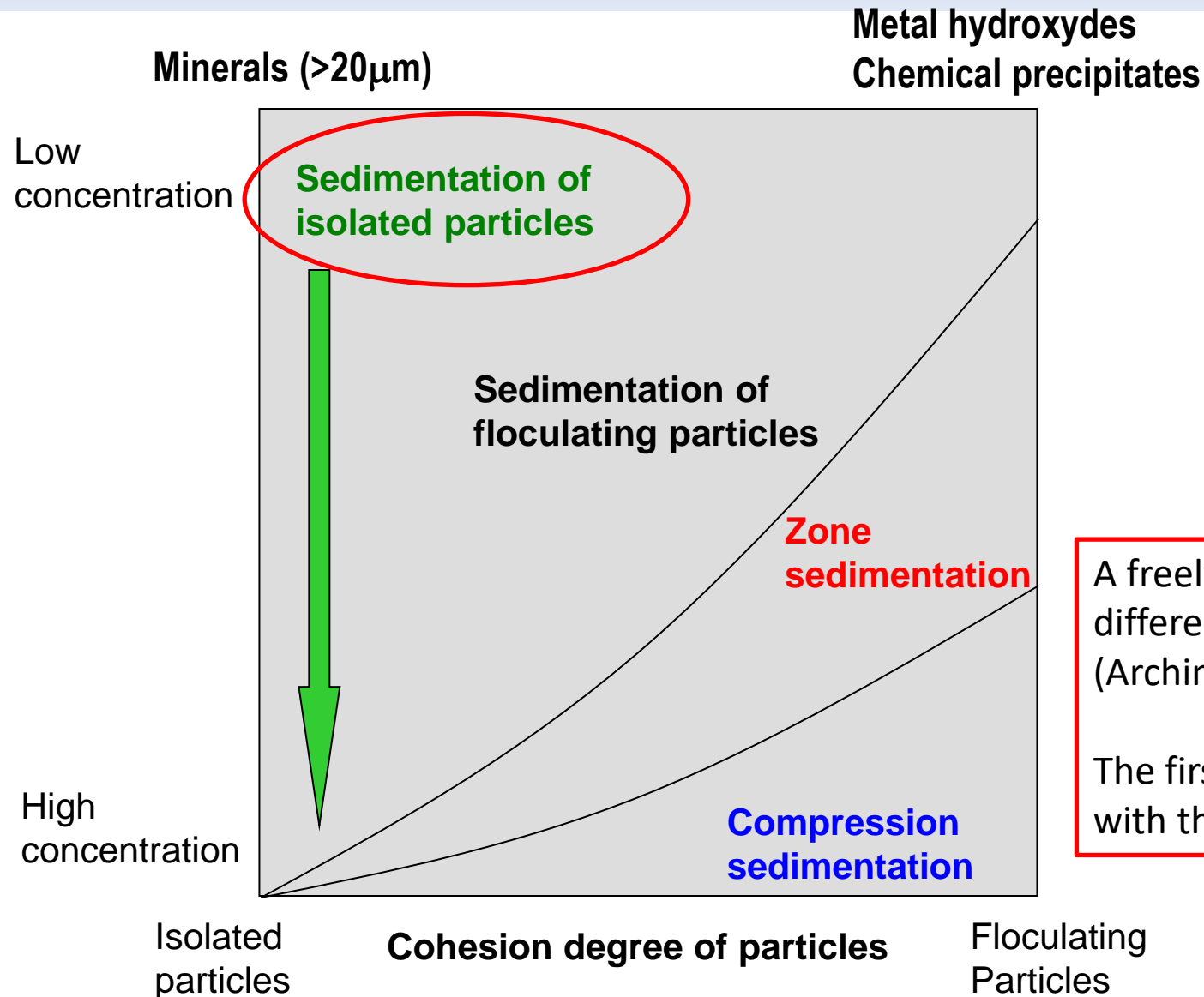
- **Sedimentation:** density difference-induced separation of solid particles from the liquid they are dispersed in (acceleration = $g = 9.81 \text{ m/s}^2$)
- **Centrifugation:** accelerated sedimentation of solid particles from a liquid phase thanks to a centrifugal force field (acceleration $G = f(r, \omega, \text{device geometry})$)
- **Filtration:** liquid/solid separation obtained by forcing the liquid phase through a retention device



2a. Sedimentation



2.1.1 There are four types of sedimentations



IMPORTANT:

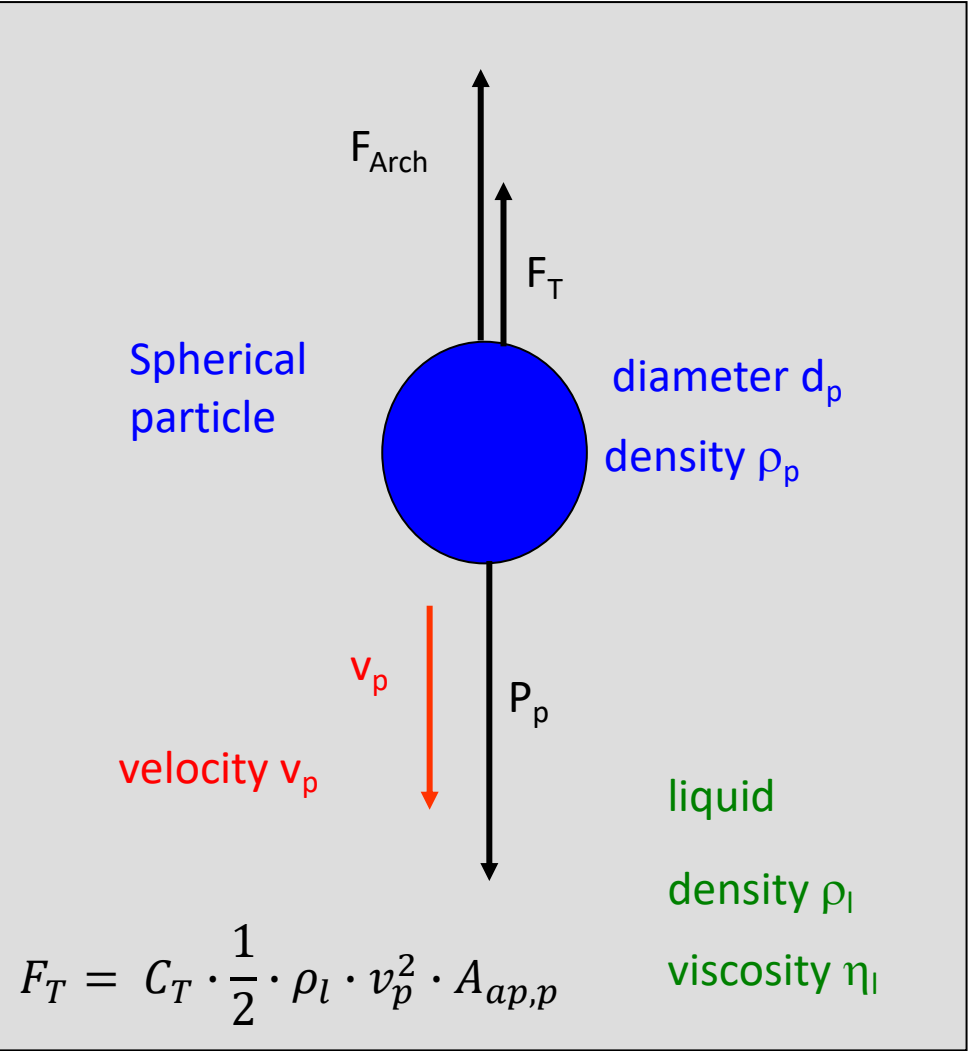
Only the **free sedimentation of isolated particles** will be covered here .

The behaviour of industrial sedimentation (e.g. in waste water treatment plants) is however much more complicated to describe.

A freely sedimenting particle is submitted to three different forces: its mass (gravity), the buoyant (Archimedes) force and the drag force.

The first two are constant, the drag force increases with the particle velocity

2.1.2 May the force (balance) be with us



m_p : particle mass [kg]
 F_{arch} : buoyant force [N]
 F_T : drag force [N]

$$P_p - F_{arch} - F_T = m_p \cdot dv_p/dt$$

What is the driving force for sedimentation (and centrifugation) ?

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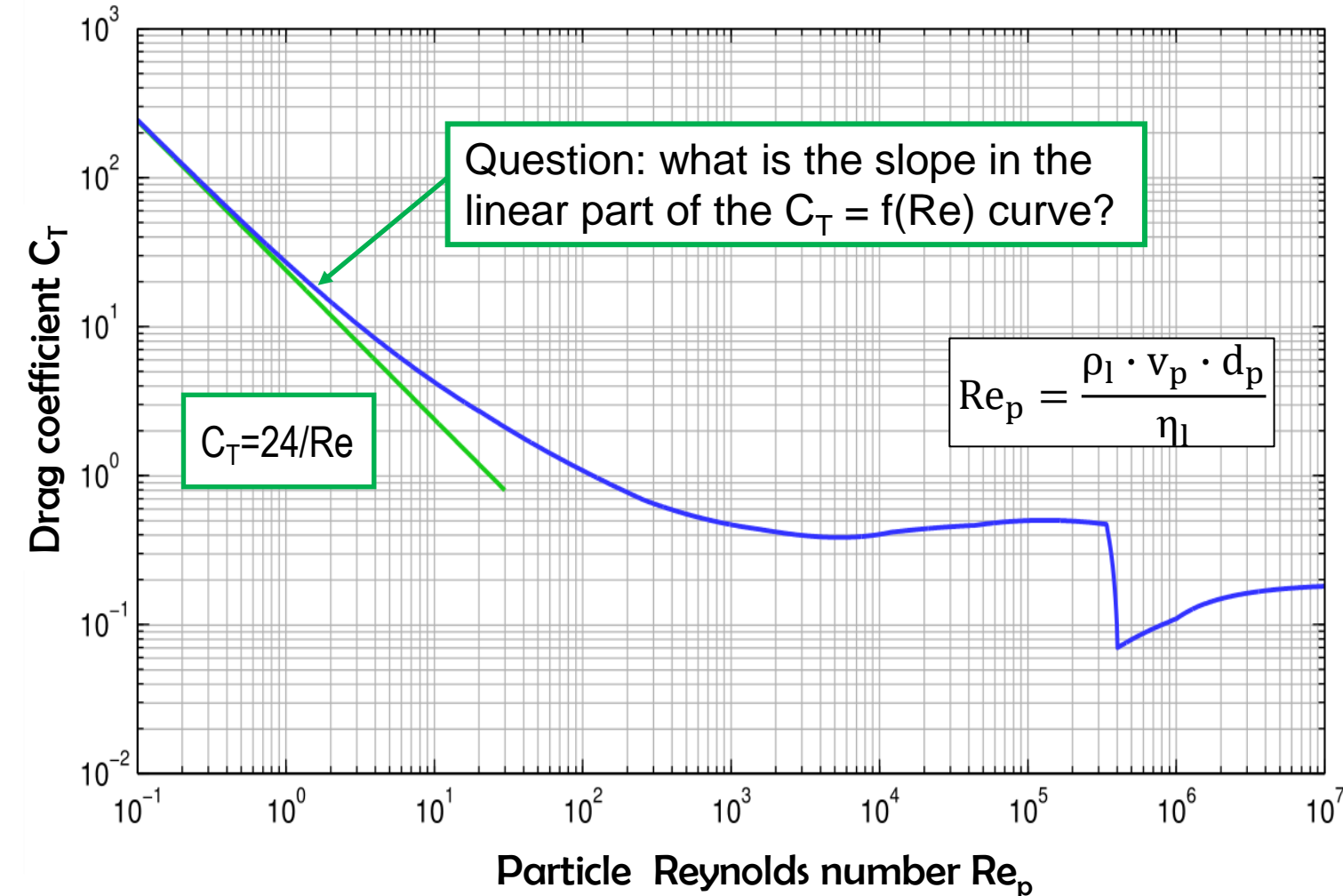
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TABLE 5.2
Measured Values of the Density of Representative Cells, Organelles, and Biomolecules

Cell, organelle, or biomolecule	Density, ρ (g/cm ³)
<i>Escherichia coli</i>	1.09 ^a
<i>Bacillus subtilis</i>	1.12
<i>Arthrobacter</i> sp.	1.17
<i>Saccharomyces pombe</i>	1.09
<i>Saccharomyces cerevisiae</i>	1.11 ^a
<i>Amoeba proteus</i>	1.02
Murine B cells	1.06 ^a
Chinese hamster ovary (CHO) cells	1.06
Peroxisomes	1.26 ^a
Mitochondria	1.20 ^a
Plasma membranes	1.15 ^a
Proteins	1.30 ^a
Ribosomes	1.57 ^a
DNA	1.68 ^a
RNA	2.00 ^a

^aAverage value.

The drag coefficient C_T strongly depends on the flow regime



General correlation for C_T

$$C_T = \frac{b}{(Re_p)^n}$$

Regime	b	n
Laminar ($Re < 2$)	24	1
Transition ($2 < Re < 500$)	10	0.5
Turbulent ($Re > 500$)	0.44	0

N.B. other, similar correlations have been published for intermediate values of Reynolds

Formulas for the terminal settling velocity



The most relevant equation for us

Laminar (Stokes) flow regime

$$v_{lim,p} = \frac{1}{18} \cdot \frac{d_p^2 \cdot (\rho_p - \rho_l) \cdot g}{\eta}$$

Transient (Allen) flow regime

$$v_{P,lim} = \sqrt[3]{\frac{4 \cdot (\rho_p - \rho_l)^2 \cdot g^2}{225 \cdot \eta \cdot \rho_l}} \cdot d_p$$

Turbulent (Newton) flow regime

$$v_{P,lim} \cong \sqrt{3 \cdot d_p \cdot \left(\frac{\rho_p}{\rho_l} - 1 \right) \cdot g}$$

Now you just wait a minute!

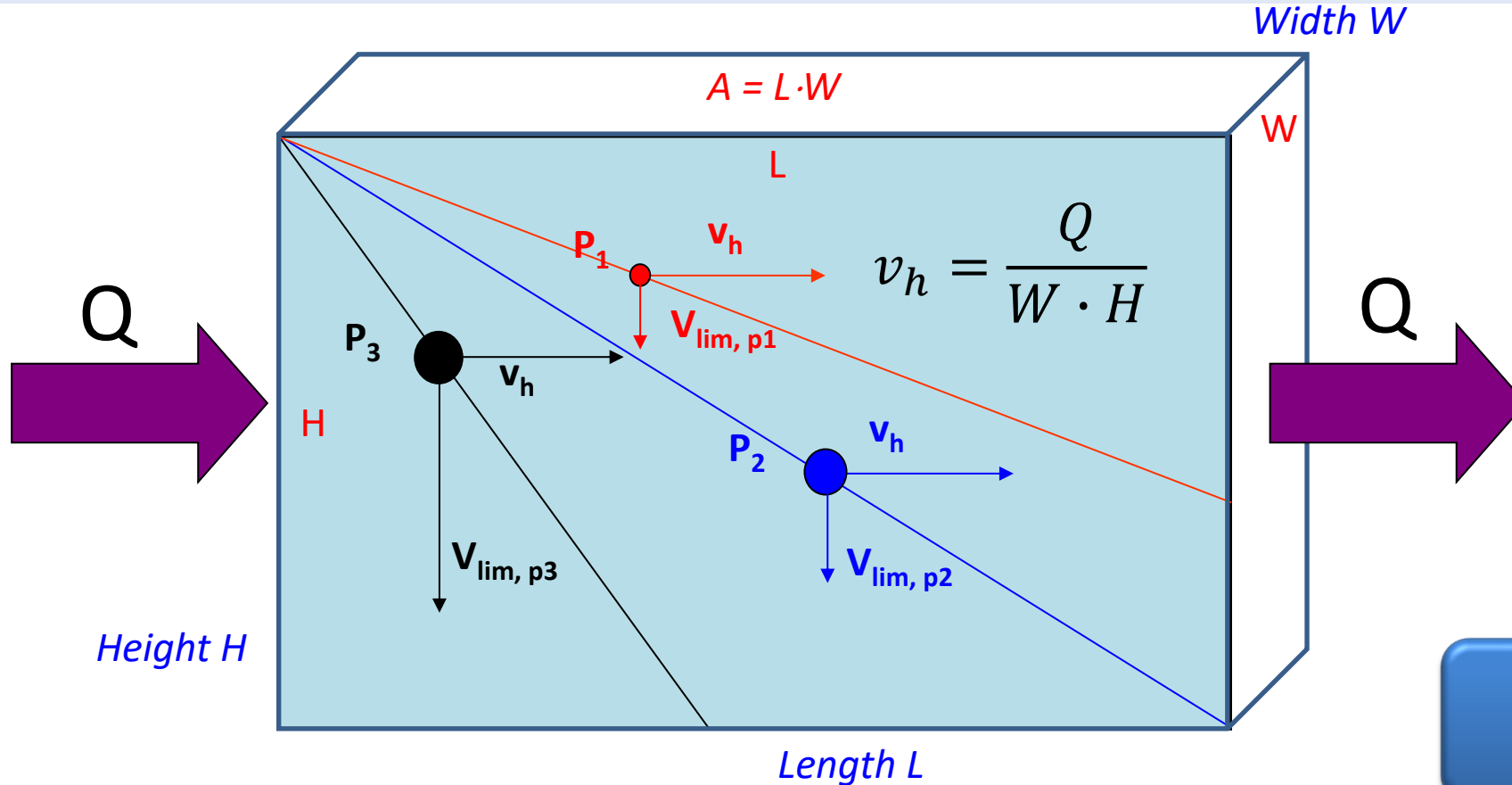
To calculate the sedimentation velocity we need the drag force, hence the drag coefficient. The latter depends on the Reynolds value, which itself depends on the flow velocity, which is exactly what we are trying to calculate. How can we escape this vicious circle?

The easiest approach consists in guessing a flow regime and calculating the terminal sedimentation velocity with the corresponding C_T value.

Once $v_{lim,p}$ has been obtained, calculate the corresponding Re value. If it matches the guessed flow regime, all right. If it does not, guess another flow regime and repeat the process.

What is the maximal flowrate my tank can handle?

(using the Camp-Hazen method)



$$v_{lim,p} = \frac{1}{18} \cdot \frac{d_p^2 \cdot (\rho_p - \rho_l) \cdot g}{\eta}$$

Using this oversimplified model of a sedimentation tank, it is quite easy to demonstrate that the maximum capacity of the tank for the sedimentation of particles with settling velocity $v_{lim,p}$ is given by

$$Q = v_{lim,p} \cdot A$$

- Both vertical and horizontal components of the particle velocity being constant, the resulting particle trajectory is a straight line
- The maximum capacity of the tank is achieved with particles P_2 (blue)

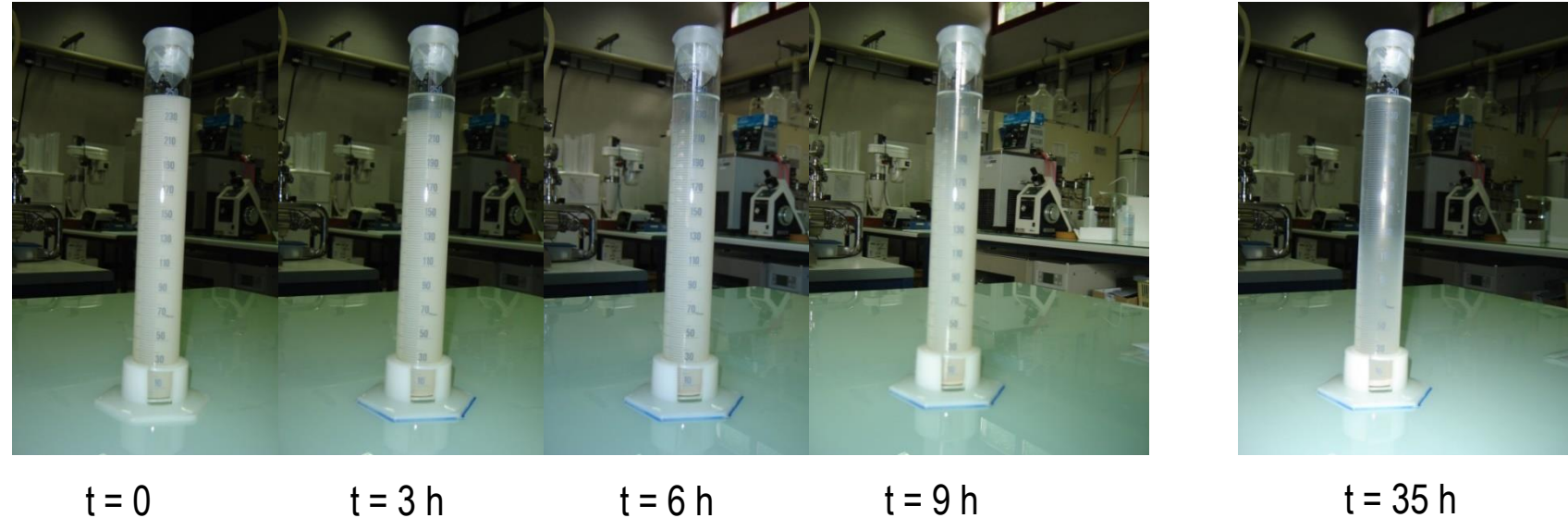
It is worth mentioning that this result does not depend on the tank's depth H

Why isn't sedimentation very useful for DSP?

Let us calculate the sedimentation velocity of *S. cerevisiae* in water at 20 °C

$d_p = 5.0 \mu\text{m}$
 $\rho_p = 1.100 \text{ g/cm}^3$
 $\rho_l = 0.998 \text{ g/cm}^3$
 $\mu_l = 1.0 \text{ mPa}\cdot\text{s}$

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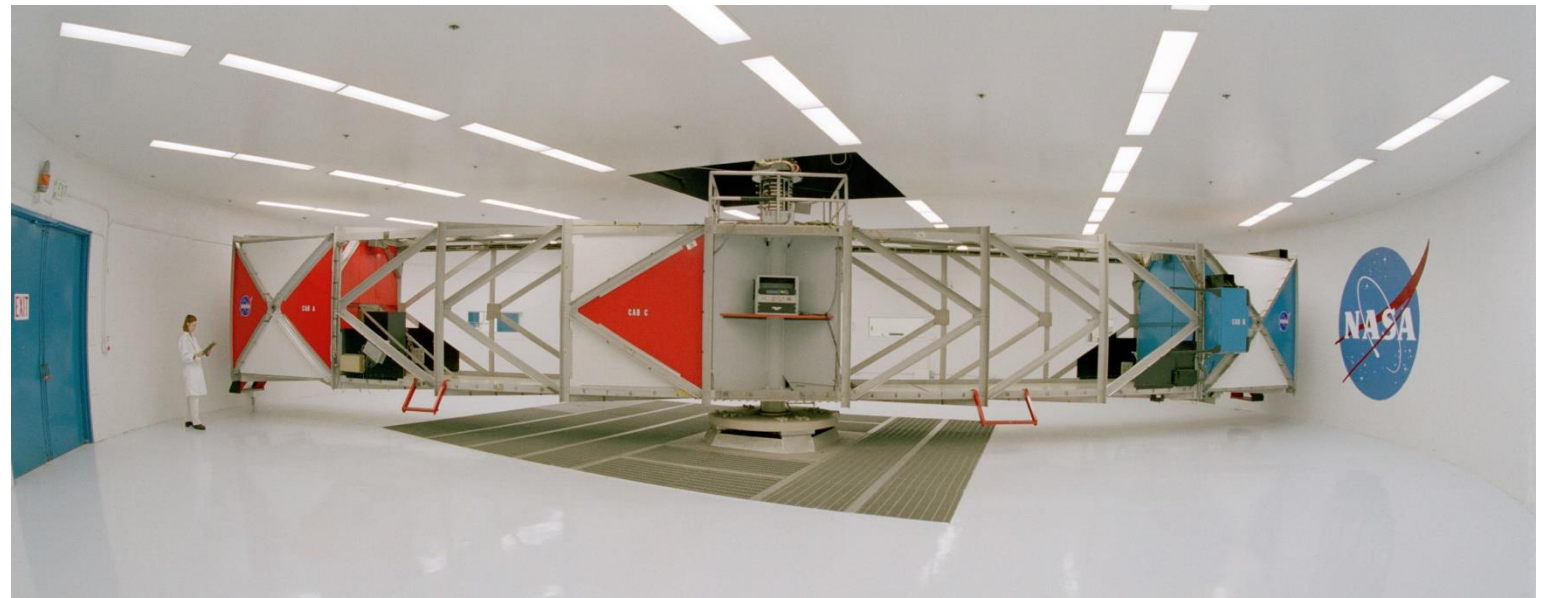
Based on the calculated velocity, how long would it take for a yeast cell to sediment from the surface liquid down to the bottom of a bioreactor containing a 1.0 m liquid height?

**I think you got the message
But don't forget that $Q = v_{\text{lim},p} \cdot A$**

A high-angle photograph of a large, circular wastewater treatment tank. The tank is filled with dark water. In the center, there is a rotating platform with a blue metal walkway and railings. The walkway has several blue support structures. The tank is surrounded by a concrete wall with a metal railing. In the background, there are other similar tanks, a grassy area, and some industrial buildings.

Needless to say that in real life, settling tanks look (and behave) differently ...

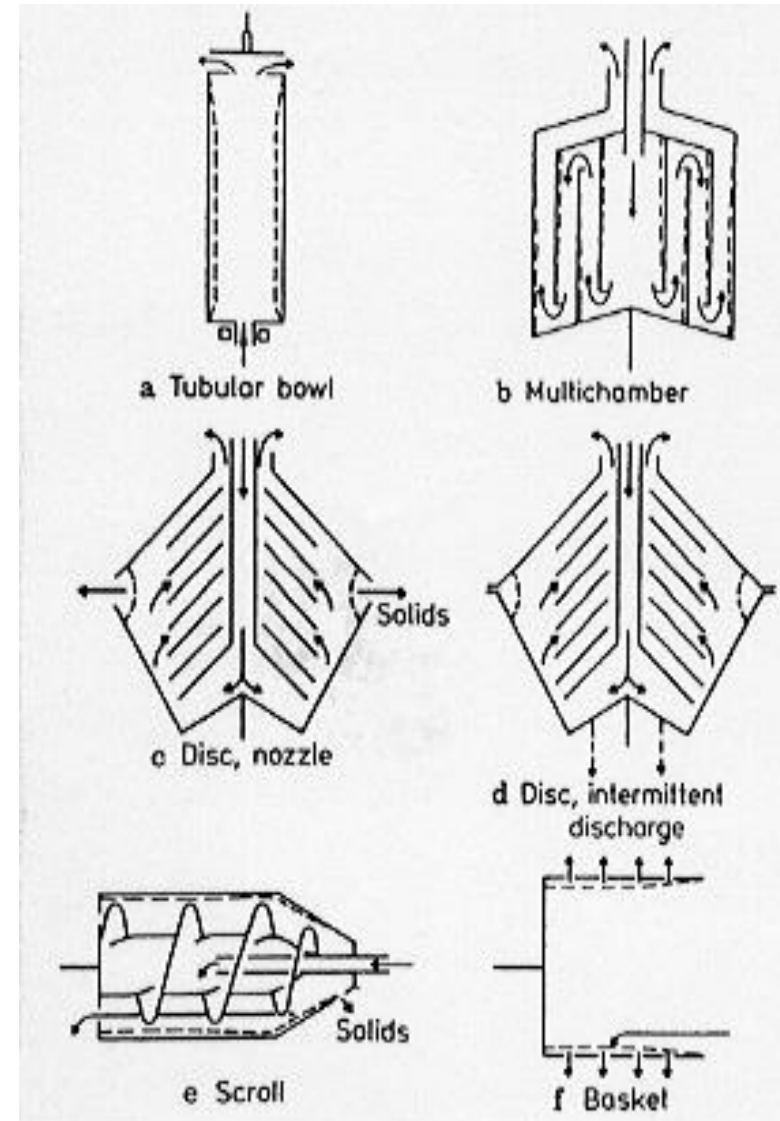
2b. Centrifugation



Rationale for centrifugation

- Sedimentation is way too slow for separations at production scale (few exceptions)
- Centrifugation becomes then most helpful for
 - Separation of cells from the fermentation medium
 - Clarification of a liquid before a chromatography step
 - Removal of cell debris after a lysis step
 - Recovery of an adsorbent which was dispersed in a fermentation beer
 - Quicker separation of two immiscible liquid phases
- The driving force of the separation is (again) the difference of density between the particles (or droplets) and the liquid

Designs for industrial centrifuges



These are continuous centrifuges which differ significantly from the batch, benchtop lab centrifuges

The path followed by the liquid phase through the machine is indicated by arrows.

Places where the solid phase is accumulating are indicated by dotted lines.

We need to replace g by the centrifugal acceleration

- As compared to gravity settling, the earth gravity constant g is simply replaced by the centrifugal acceleration $r\omega^2$ to calculate the sedimentation velocity
- Hence:

$$v_{\text{sed,p}} = \frac{1}{18} \cdot \frac{d_p^2 \cdot (\rho_p - \rho_l) \cdot r \cdot \omega^2}{\eta}$$

Reminder: $\omega = \frac{\text{rpm} \cdot 2\pi}{60}$

Case of a spherical particle in a laminar flow. That equation is usually sufficient to handle most bioprocess cell suspensions

Acceleration factor or relative centrifugal force (RCF)

$$G = \frac{r \cdot \omega^2}{g}$$

Hence: $v_{\text{sed,p}} = v_{\text{lim,p}} \cdot G$



Source: <https://www.hettweb.com>

2.2.1 Tubular bowl centrifuge

Main features

- $0 < \text{DMC}^{[1]} < 1\%$ (v/v)
- $5'000 < G < 50'000$
- $5 < \text{diam} < 75 \text{ cm}$
- $0.02 < Q < 2 \text{ m}^3/\text{h}$

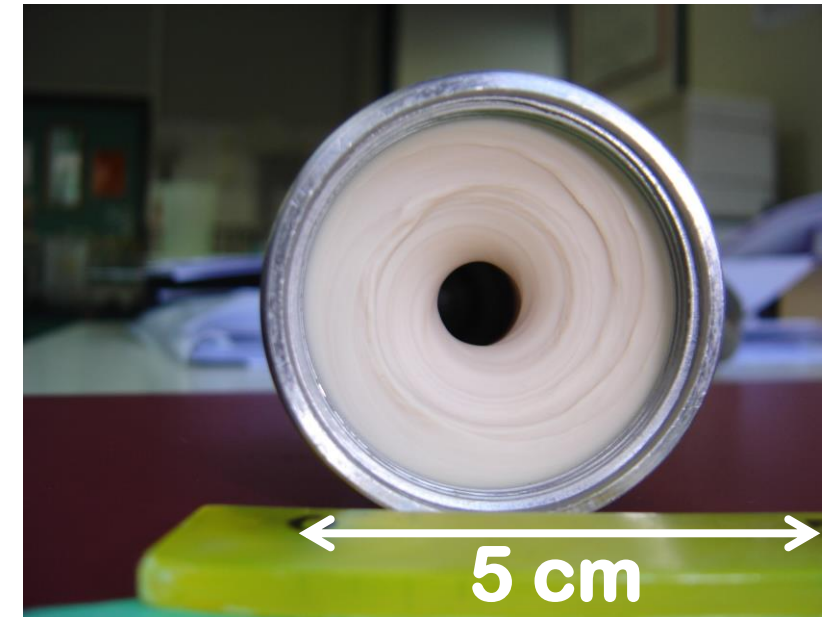
[1] DMC = Dry Matter Content

Drawbacks

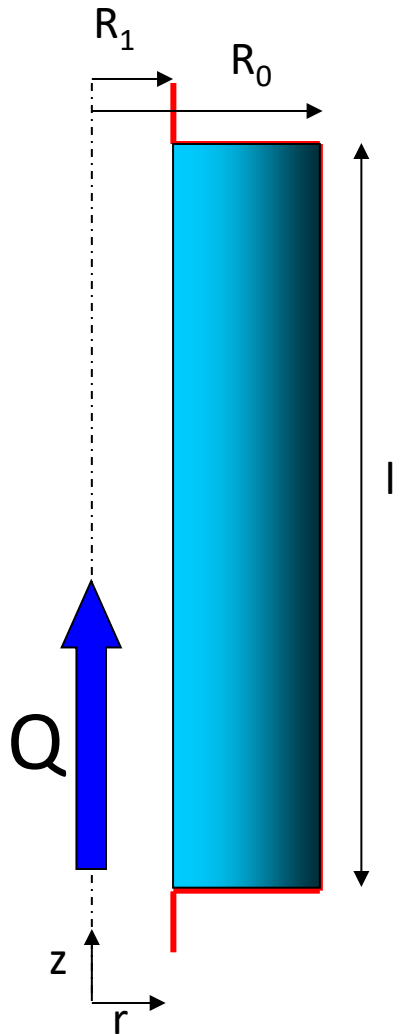
- ☹ Limited capacity for solids
- ☹ No discharge of solids
- ☹ Recovery of solids difficult
- ☹ Foaming a common problem

Advantages

- ☺ Large acceleration factors
- ☺ Concentrated sediment
- ☺ Easy cleaning and maintenance



The math of centrifugation in a tube (1/3)



- The particles move along the z as well as r directions
- Movement along the z axis (negligible impact of gravity)

$$\frac{dz}{dt} = \frac{Q}{\pi \cdot (R_0^2 - R_1^2)} \quad Q: \text{feeding flowrate [m}^3/\text{s]} \quad (\text{C-3})$$

- Movement along the r axis for a sphere with diameter $= d_p$

$$\frac{dr}{dt} = \frac{d_p^2}{18 \cdot \eta} \cdot (\rho_p - \rho_l) \cdot r \cdot \omega^2 = v_{\text{lim},p} \cdot \frac{r \cdot \omega^2}{g} \quad (\text{C-4})$$

NB: $V_{\text{lim},p}$ always refers to the terminal settling velocity in the earth gravitational field

The math of centrifugation in a tube (2/3)

- By combining the equations above, one gets:

$$\frac{dr}{dz} = \frac{dr/dt}{dz/dt} = v_{\text{lim},p} \cdot \frac{r \cdot \omega^2}{g} \cdot \frac{\pi \cdot (R_0^2 - R_1^2)}{Q} \quad (\text{C-5})$$

- From that equation it is possible to calculate the trajectory of a particle in the tubular bowl $r = f(z)$
- It is possible as well to determine the highest flow rate that allows the capture of particles having a terminal settling velocity $v_{\text{lim},p}$ (entering in the tube at $z=0$, $r=R_1$, and reaching $r=R_0$ for $z=l$)



The math of centrifugation in a tube (3/3)

Trajectory of a particle in the tubular bowl

$$r = R_1 \cdot \exp \left(\left(v_{\text{lim},p} \cdot \frac{\omega^2}{g} \cdot \frac{\pi \cdot (R_0^2 - R_1^2)}{Q} \right) \cdot z \right) \quad (\text{C-6})$$

Maximum flowrate that can capture particles with settling velocity $v_{\text{lim},p}$

$$Q = \frac{\pi \cdot l \cdot (R_0^2 - R_1^2) \cdot v_{\text{lim},p} \cdot \omega^2}{g \cdot \ln \left(\frac{R_0}{R_1} \right)} = v_{\text{lim},p} \cdot \frac{\pi \cdot l \cdot (R_0^2 - R_1^2) \cdot \omega^2}{g \cdot \ln \left(\frac{R_0}{R_1} \right)} \quad (\text{C-7})$$

What are the units in this block?

Does the general form of the above equation look familiar?

2.2.2 Disc stack centrifuge

Drawbacks

- ☹ Cleaning is complicated
- ☹ Thin, diluted sediments

Main features

- $0.2 < \text{DMC} < 20\%$ (v/v)
- $5'000 < G < 50'000$
- $5 < \text{diam} < 75 \text{ cm}$
- $4.5 < Q < 45 \text{ m}^3/\text{h}$ (batch)
- $9.0 < Q < 90 \text{ m}^3/\text{h}$ (nozzles)

Advantages

- ☺ Discharge of solids is possible
- ☺ Discharge under pressure reduces foaming problems
- ☺ Cooling of bowl possible

Clarificateurs	Type	Débits nominaux jusqu'à*	
		l/h	lbs/h
MSA	20-06-076	10 000	22 000
MSD	45-06-076	20 000	44 000
MSA	45-06-076	17 500	38 000
MSD	60-96-076	25 000	55 000
MSD	140-96-076	35 000	77 000
MSD	300-96-777	45 000	100 000

* Le débit réel à l'alimentation est fonction du type de sérum.
Les débits indiqués sont les débits max.

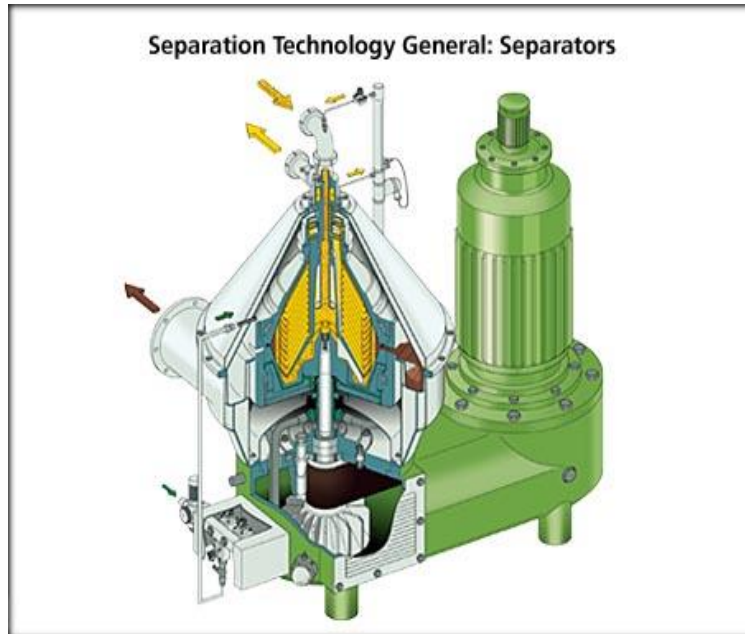
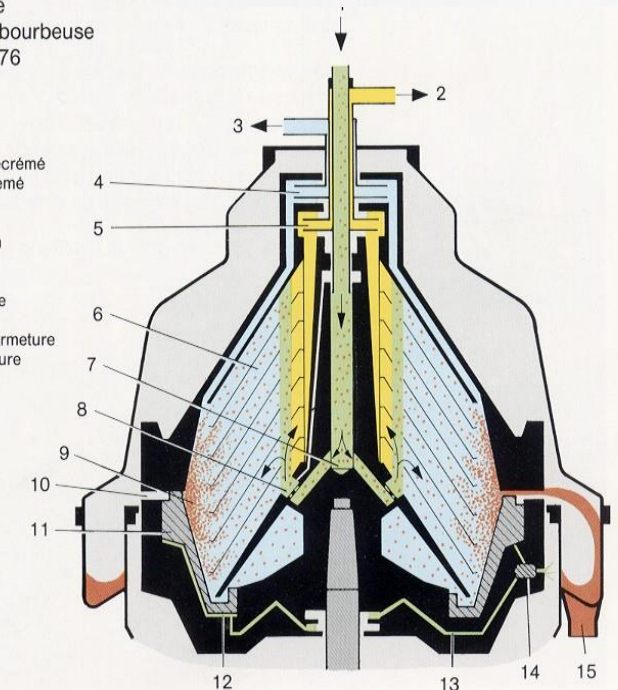
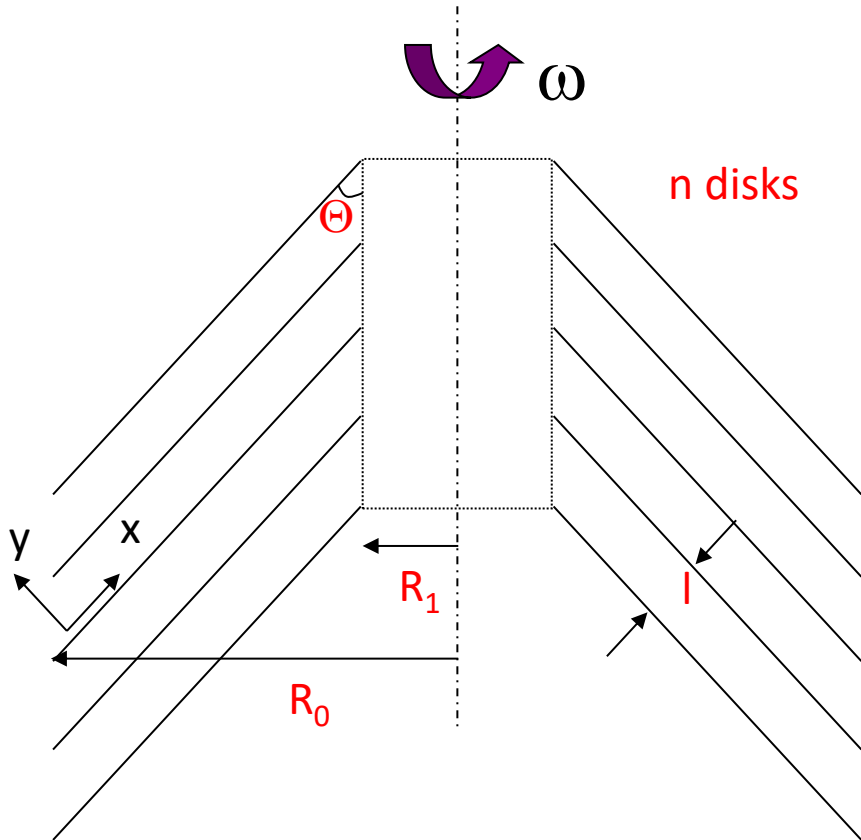


Fig. 60 Coupe d'une écrémeuse auto-débourbeuse type MSD 200-01-076

- 1 Alimentation
- 2 Refoulement crème
- 3 Refoulement sérum écrémé
- 4 Turbine à sérum écrémé
- 5 Turbine à crème
- 6 Pile d'assiettes
- 7 Système Soft-Stream
- 8 Canaux de montée
- 9 Chambre à boues
- 10 Outils de débouillage
- 11 Piston
- 12 Chambre d'eau de fermeture
- 13 Canal d'eau d'ouverture
- 14 Vanne à piston
- 15 Sortie des boues



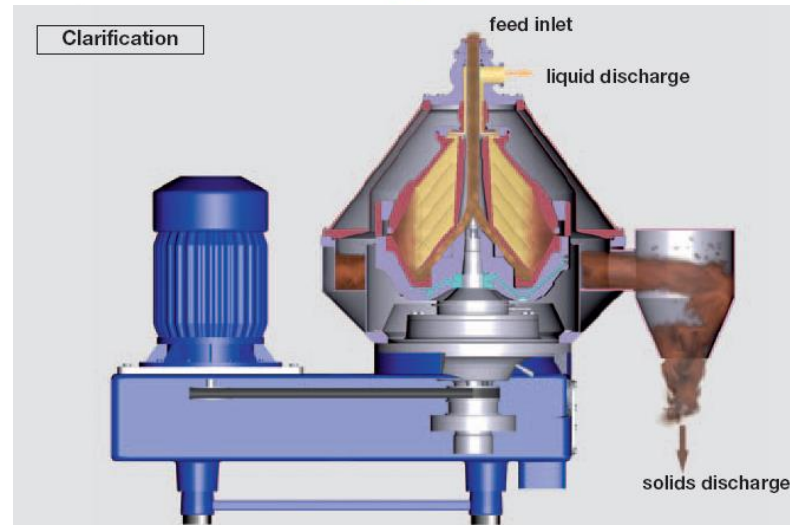
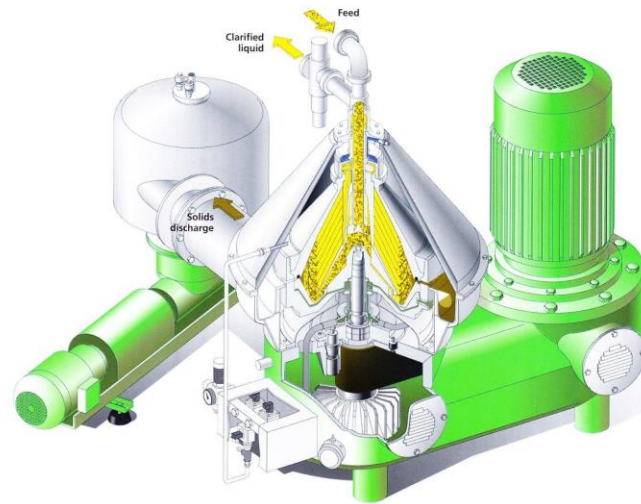
Geometric features of a disc stack centrifuge



x,y system of reference:

x : distance from the external edge of the disk toward the center, along the space between two disks

y : normal distance from the surface of the inferior disk



FLOTTWEG DISK STACK CLARIFIER for the separation of solids from liquids

The disc stack centrifuge is by far the most commonly used clarifying equipment in the biopharmaceutical industry

Sedimentation & centrifugation: THE equation



- For a sedimentation tank

$$Q = v_{\text{lim},p} \cdot \boxed{A}$$

$\Sigma = \text{Sigma factor}$

- For a tubular centrifuge

$$Q = \frac{\pi \cdot l \cdot (R_0^2 - R_1^2) \cdot v_{\text{lim},p} \cdot \omega^2}{g \cdot \ln\left(\frac{R_0}{R_1}\right)} = v_{\text{lim},p} \cdot \boxed{\frac{\pi \cdot l \cdot (R_0^2 - R_1^2) \cdot \omega^2}{g \cdot \ln\left(\frac{R_0}{R_1}\right)}}$$

$\Sigma = \text{Sigma factor}$

- For a disk stack centrifuge

$$Q = v_{\text{lim},p} \cdot \boxed{\left(\frac{2\pi \cdot n \cdot \omega^2}{3g}\right) \cdot (R_0^3 - R_1^3) \cdot \cot \Theta}$$

$\Sigma = \text{Sigma factor}$

2.2.4 Solid bowl scroll centrifuge

Main features

- $5 < \text{DMC} < 80\% \text{ (v/v)}$
- Particules $> 3 \mu\text{m}$ diam.
- $1'000 < G < 5'000$
- $15 < \text{diam} < 100 \text{ cm}$
- $1 < Q < 200 \text{ m}^3/\text{h}$

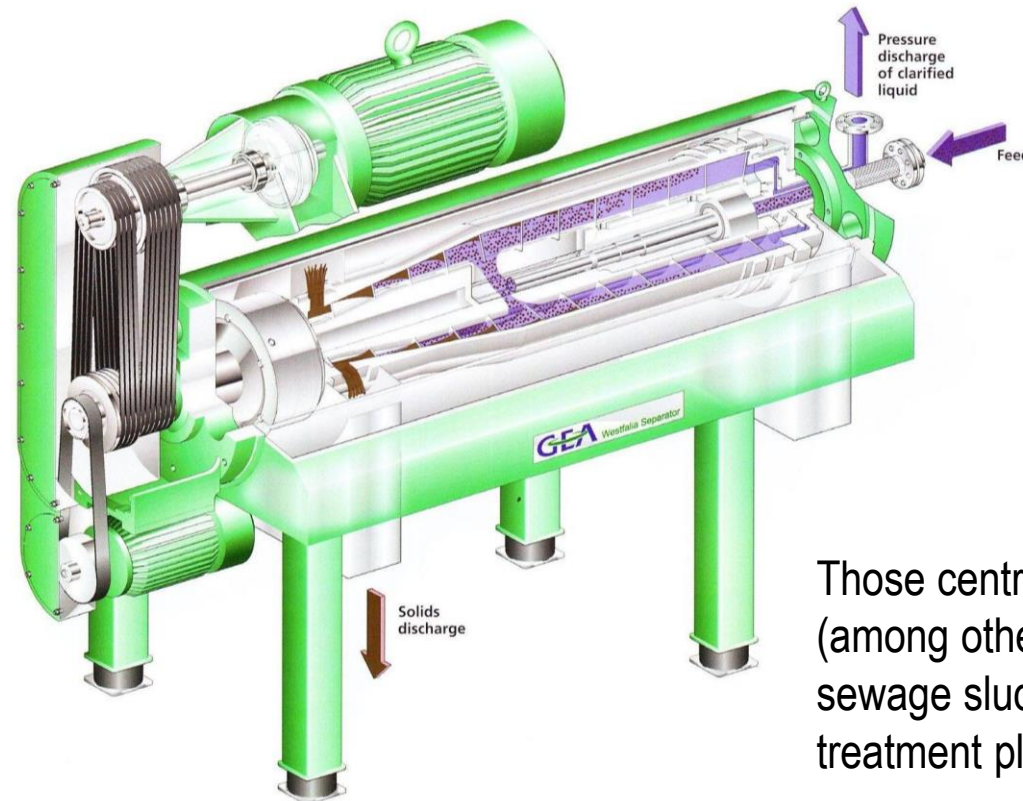
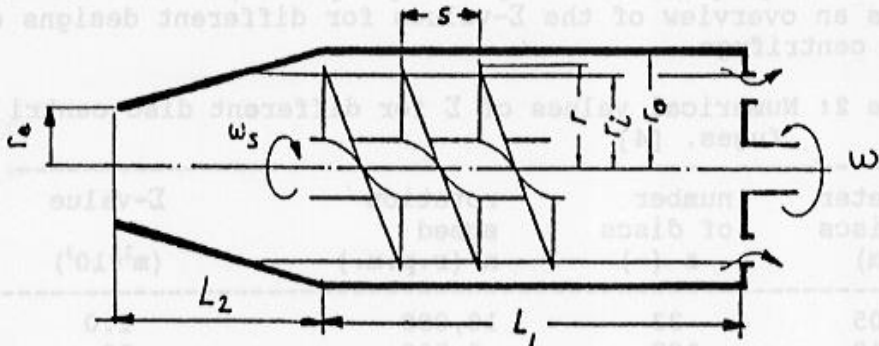
Drawbacks

- ☹ Low acceleration factors
- ☹ Turbulences caused by the screw

Advantages

- ☺ Continuous discharge of solids
- ☺ Treatment of highly concentrated suspensions

The geometric features below can be chosen, adapted or adjusted to meet the requirements of the desired separation

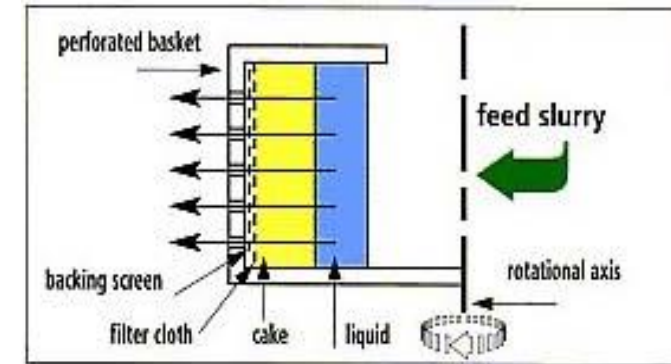


Those centrifuges are commonly used (among others) for the dewatering of sewage sludge from wastewater treatment plants (WWTP)

2.2.4 Filter centrifuge: half, centrifuge, half filter

Main features

- $0 < \text{DMC} < 40\% \text{ (v/v)}$
- $500 < G < 1'500$
- $30 < \text{diam} < 90 \text{ cm}$
- $0.1 < Q < 20 \text{ m}^3/\text{h}$



This type of centrifuge is very useful for the recovery of crystallized compounds from a liquid slurry

Batch Quadramatic 120
Western States Machine Co



Advantages

- ☺ Can handle concentrated suspensions
- ☺ Easy discharge and cleaning
- ☺ Very efficient for rigid particles such as crystals (sugar, citric acid, antibiotics, ...)

Drawbacks

- ☹ Low accelerations
- ☹ Limited bowl capacity (batch)
- ☹ Maximal flowrate strongly depends on cake properties

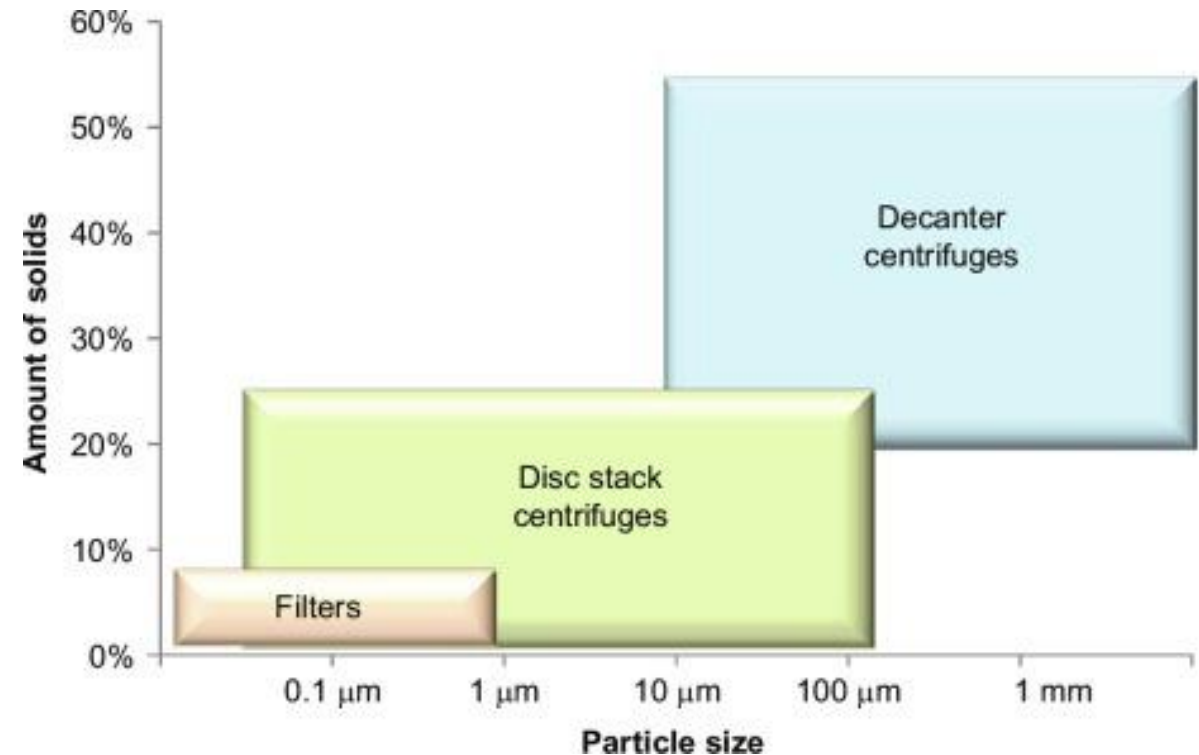
For comparison purposes ...

TABLE 1. G-FORCES GENERATED BY VARIOUS TYPES OF CENTRIFUGES ($\times g$, m^2/s)

Single-chamber bowl centrifuge	600 –1,200
Decanter centrifuge	2,000–5,000
Multichamber bowl centrifuge	5,000–9,000
Disk stack centrifuge	5,000–15,000
Laboratory bottle centrifuge	2,000–20,000
Tubular centrifuge	12,000–62,000
Ultracentrifuge	20,000–1,000,000

TABLE 2. SIGMA FACTORS FOR VARIOUS COMMERCIAL CENTRIFUGES

Batch solid bowl centrifuge	20 – 200 m^2
Decanter centrifuge	150 – 2,500 m^2
Tubular centrifuge	2,000 – 3,000 m^2
Disk stack centrifuge	400 – 120,000 m^2



Source: H. M. Amaro et al., 2017

<https://doi.org/10.1016/B978-0-08-101023-5.00016-9>

2c. Filtration

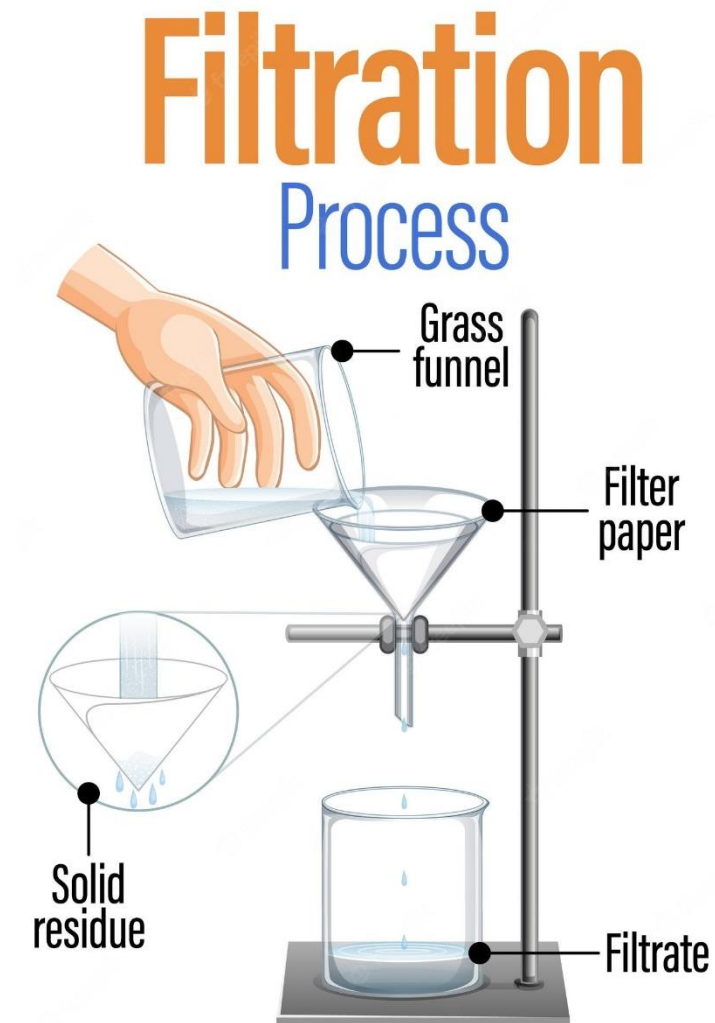


Filtration: basic, proven, efficient

- Liquid/solid separation obtained by forcing the liquid phase (using a pressure gradient) through a retention element
- Well-characterized and controlled process for the separation of rigid particles of sufficient size
- Deformability and small size of micro-organisms slow the process down in a significant manner

A few words of caution:

1. This section will deal mostly with the theory of classical filtration and its fundamental practical aspects
2. Theoretical and mathematical developments will be kept to a minimum. More advanced models can be found in a large selection of textbooks

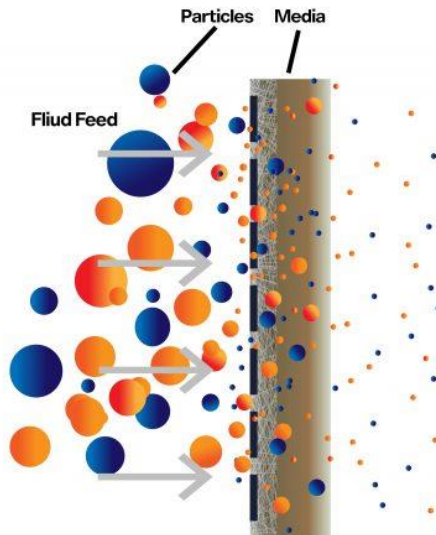


Two modes of retention



Lots of filters in a bioprocess

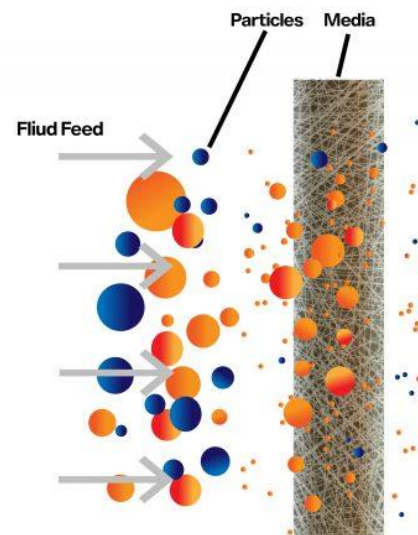
Surface Filtration



Surface filtration

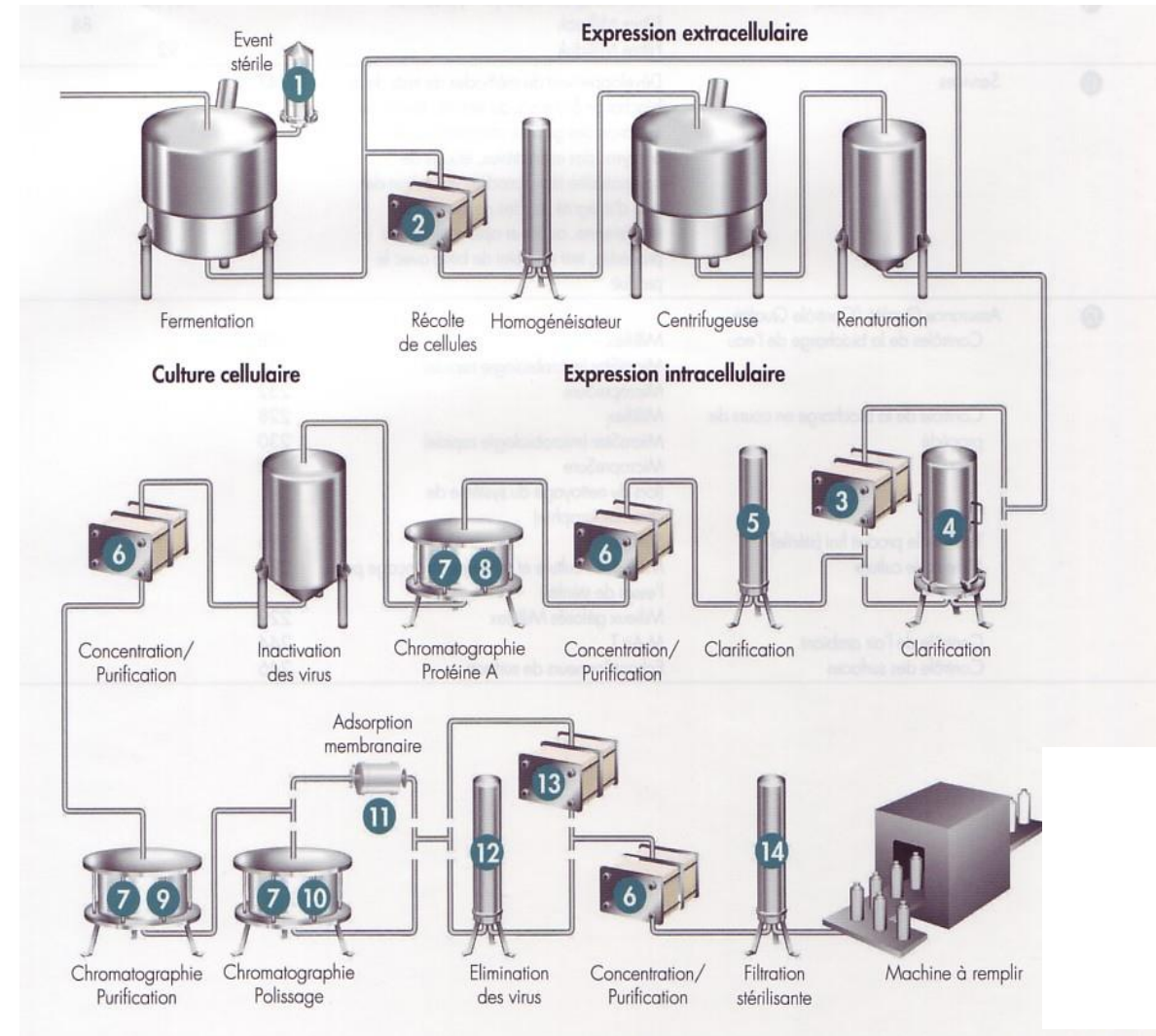
Typical of membrane filters, which are characterized by a precisely defined porosity. Particles larger than the pores are retained at the surface, smaller ones go through

Depth Filtration



Depth filtration

Typical of paper filtration; the filter internal structure is made of randomly organized fibres. Separation is caused either by mechanical retention or adsorption



Filtration: it is about liquid flow in a porous medium

Darcy !
$$v = \frac{k \cdot \Delta p}{\mu \cdot h}$$

v : velocity of the fluid flow

k : Darcy permeability constant

Δp : pressure drop through the particle bed

h : thickness of particle bed

μ : liquid viscosity

Darcy's equation is valid for $(Re)_{\text{particle}} < 5$

$$Re_{\text{particle}} = \frac{d_p \cdot v \cdot \rho_l}{\mu \cdot (1 - \varepsilon)} < 5 \quad \text{Reynolds !}$$

d_p : diameter of the porous bed particles

ε : porosity or void fraction of the bed (typically 0.4)

ρ_l : density of the liquid phase

Filtration: Symbols and units

A	Filter surface	$[m^2]$
C_{ms}	Dry matter concentration	$[kg \cdot m^{-3}_{\text{filtrate}}]$
h	Cake thickness	$[m]$
k	Darcy's bed permeability	$[m^2]$
R_F	Filter resistance	$[m^{-1}]$
s	Cake compressibility ($0 < s < 1$)	$[-]$
V_f	Filtrate volume	$[m^3]$
$A \cdot t / V_f$	Variable for linearisation	$[s \cdot m^{-1}]$
V_f / A	Variable for linearisation	$[m]$
α	Cake specific resistance	$[m \cdot kg^{-1}]$
α'	Constant	$[units=f(s)]$
ε	Cake Porosity	$[-]$
μ	Liquid viscosity	$[kg \cdot m^{-1} \cdot s^{-1}]$

Filtration of incompressible particles (1/2)



The velocity of the fluid through the cake and filter is given by:

$$\frac{1}{A} \cdot \frac{dV_f}{dt} = \frac{\Delta p}{\mu \cdot \left(R_F + \alpha \cdot c_{ms} \cdot \frac{V_f}{A} \right)}$$

Where

$$\alpha \cdot c_{ms} \cdot \frac{V_f}{A} = R_C$$

The integration of the above equation is subject to the following boundary condition: $t=0 \rightarrow V_f = 0$

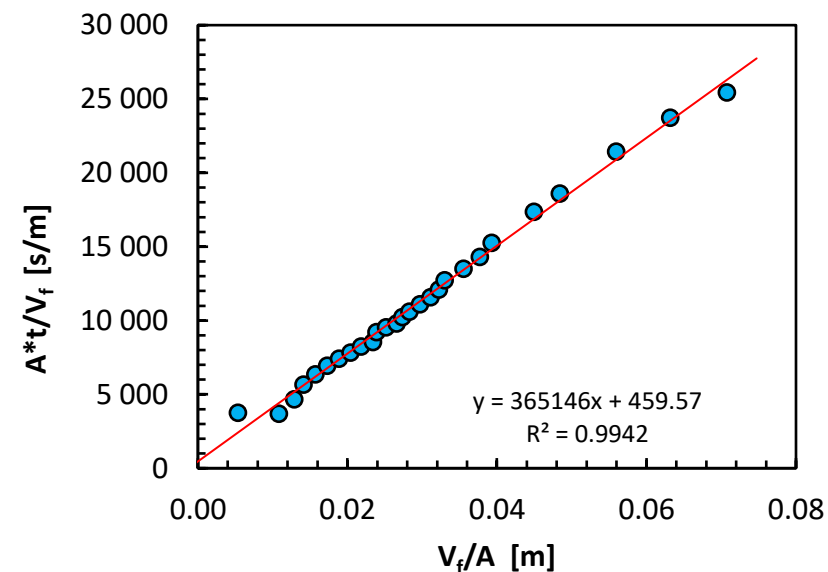
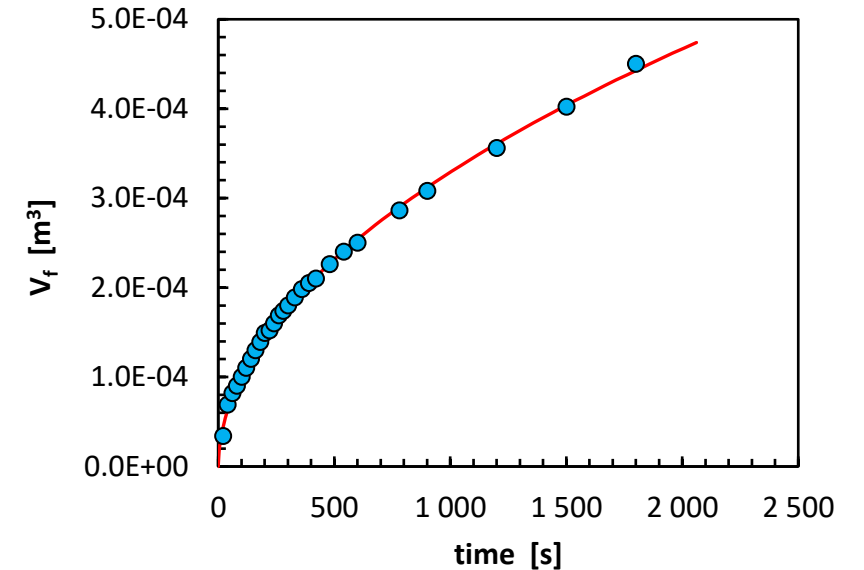
Following integration and rearrangement, one gets the following expression for a **filtration with constant pressure drop**:

$$\frac{A \cdot t}{V_f} = \left(\frac{\mu \cdot \alpha \cdot c_{ms}}{2\Delta p} \right) \cdot \left(\frac{V_f}{A} \right) + \left(\frac{\mu \cdot R_F}{\Delta p} \right)$$

Filtration of incompressible particles (2/2)

- For the filtration of incompressible particles, a plot $A \cdot t / V_f$ as a function of V_f / A yields a straight line
- The latter's intercept and slope are inversely proportional to Δp (all other parameters being kept constant)
- The intercept is directly related to R_F . If its value is low, i.e. if the straight line passes close to the origin, R_F can be considered negligible as compared to the resistance generated by the cake

Filtration of a 0.15 kg/L_{water} suspension of CaCO₃ particles on a paper filter (9 cm diameter) at 1.2 bar overpressure



Filtration of compressible particles (1/3)

- The most frequent situation when dealing with biological media.
- When the cake gets compressed its porosity closes down, pressure drop Δp rises and the filtration rate decreases.
- The behaviour of such cakes cannot be described with the previously developed models.
- Starting assumption: specific cake resistance α is a (simple) function of pressure drop Δp .

$$\alpha = \alpha' \cdot (\Delta p)^s$$

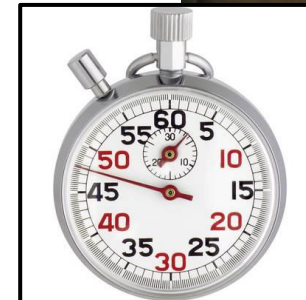
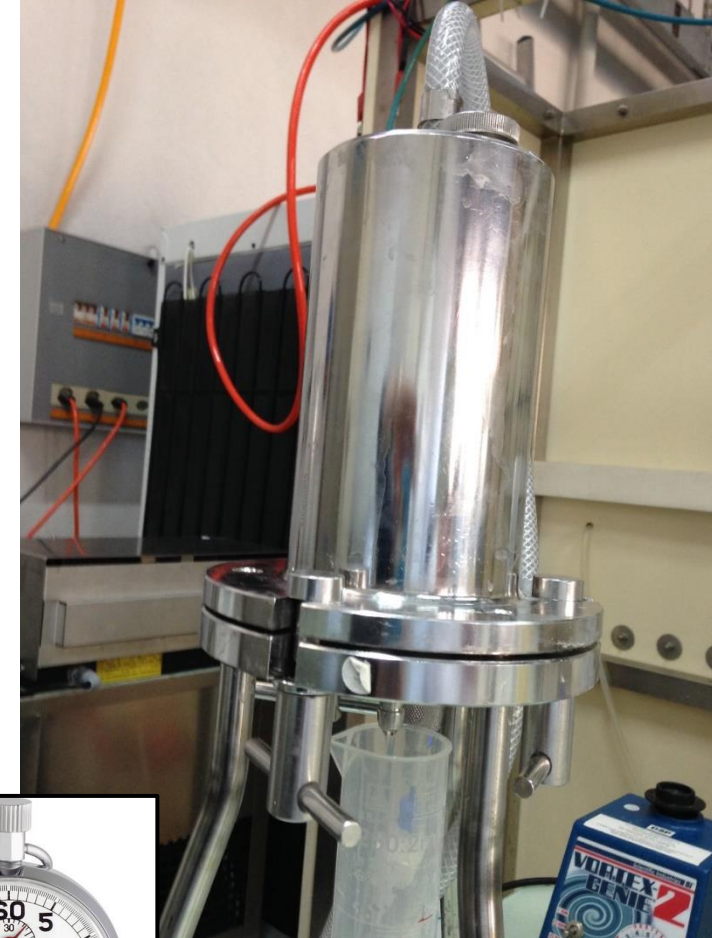
α' : constant (linked to size and shape of cake particles)
 s : cake compressibility
 s varies between 0 (incompressible) and 1 (very compressible).
In practice, s is most commonly varying between 0.1 and 0.8

How can α' and s be determined ?

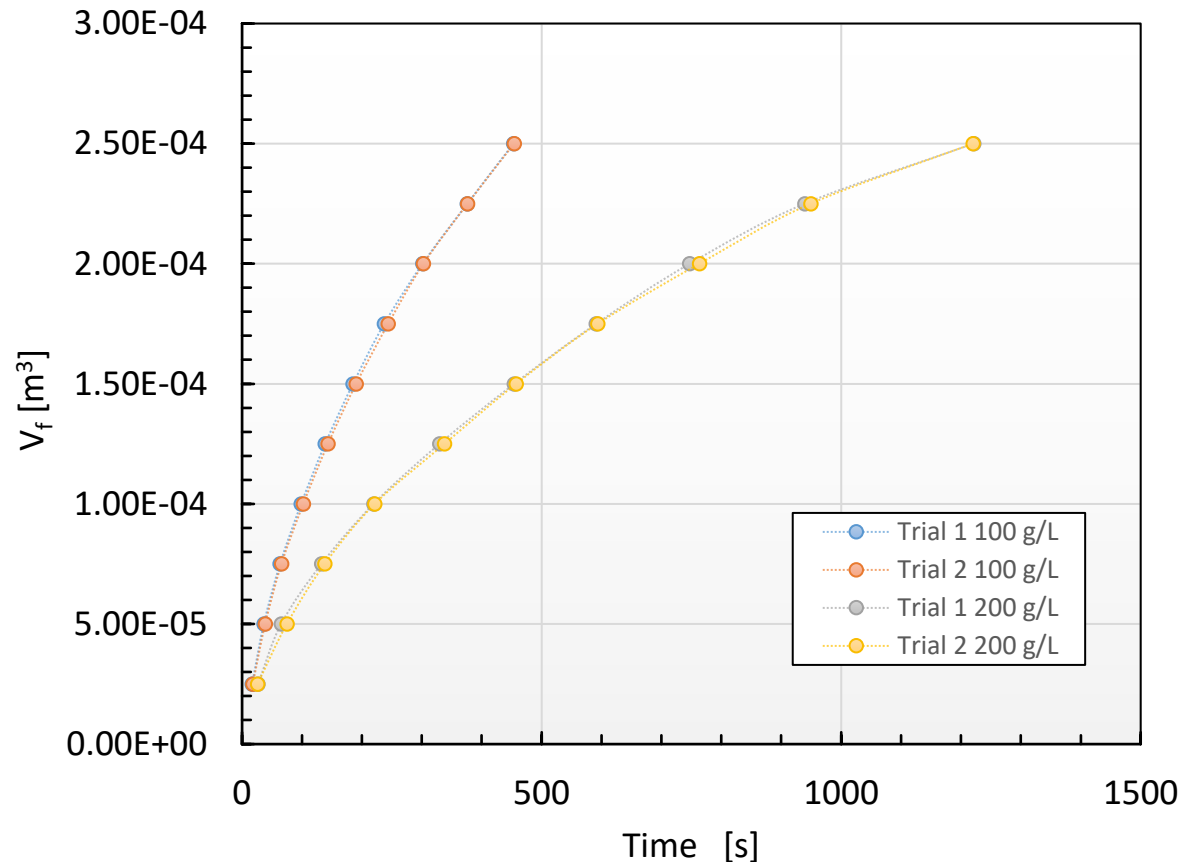
- By estimating the α for different values of Δp
- $\ln(\alpha)$ is then plotted as a function of $\ln(\Delta p)$
- A straight line is obtained, which slope corresponds to s and intercept to $\ln(\alpha')$

Experiment: depth filtration of yeast cells

- Cubes of baker's yeast have been dispersed in water at different concentrations
- The yeast suspensions have been filtered at constant Δp on industrial depth filters (9 cm diameter) with various porosities
- Different Δp values were applied using compressed air
- All trials were performed at room temperature (ca. 20 °C)
- Filtrate volume was measured as a function of time
- Some typical results are shown hereafter



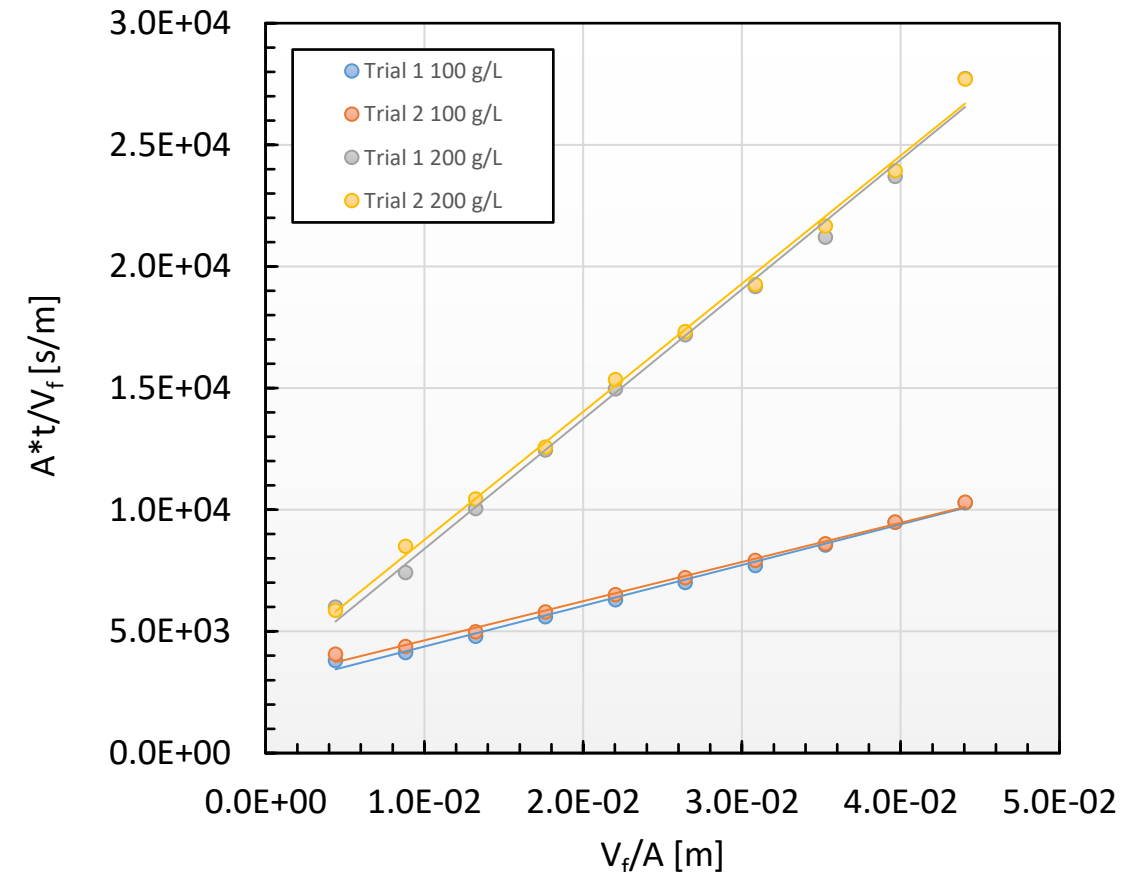
Results: Filtration volume as a function of time



Look at these results and tell me:
is the filtration cake compressible?

Depth filter Pall EKS P
Diameter = 9.0 cm
 $\Delta p = 1$ bar

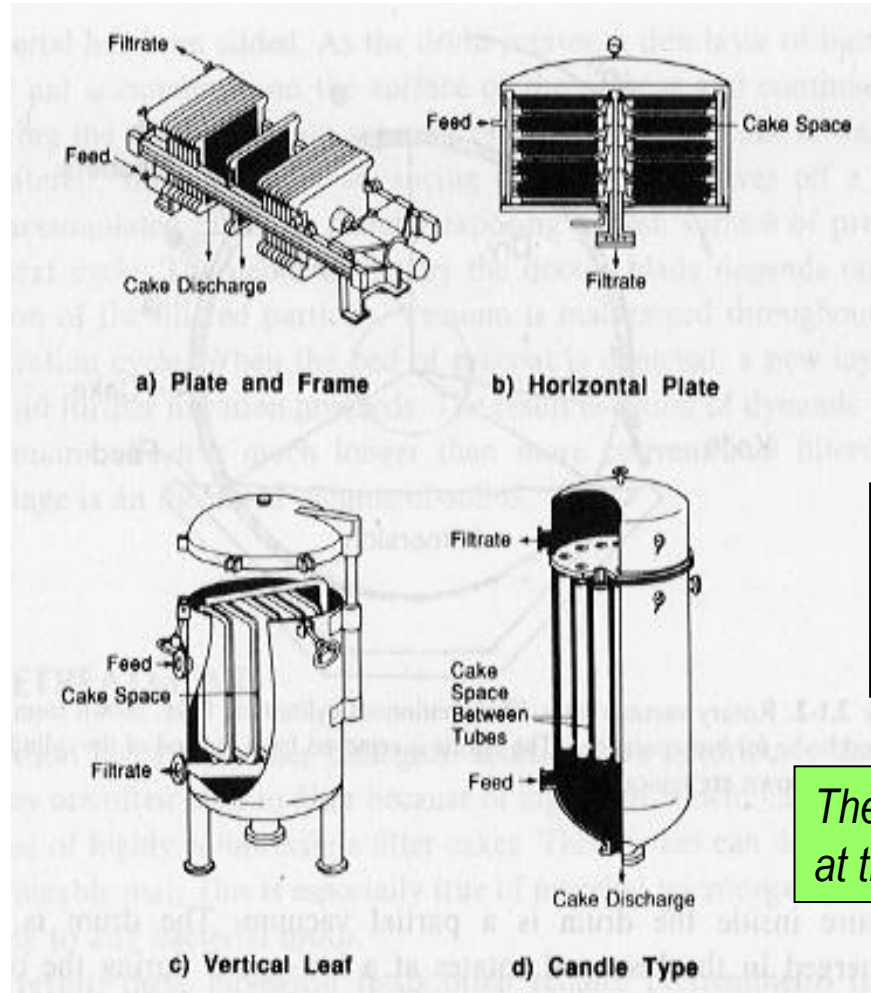
Trial	Intercept [s/m]	Slope [s/m ²]	R ² [-]
1 / 100 g/L	2700	$1.67 \cdot 10^5$	0.994
2 / 100 g/L	3020	$1.61 \cdot 10^5$	0.995
1 / 200 g/L	3060	$5.33 \cdot 10^5$	0.994
2 / 200 g/L	3500	$5.27 \cdot 10^5$	0.996



Pressure filters



Nutsche filter



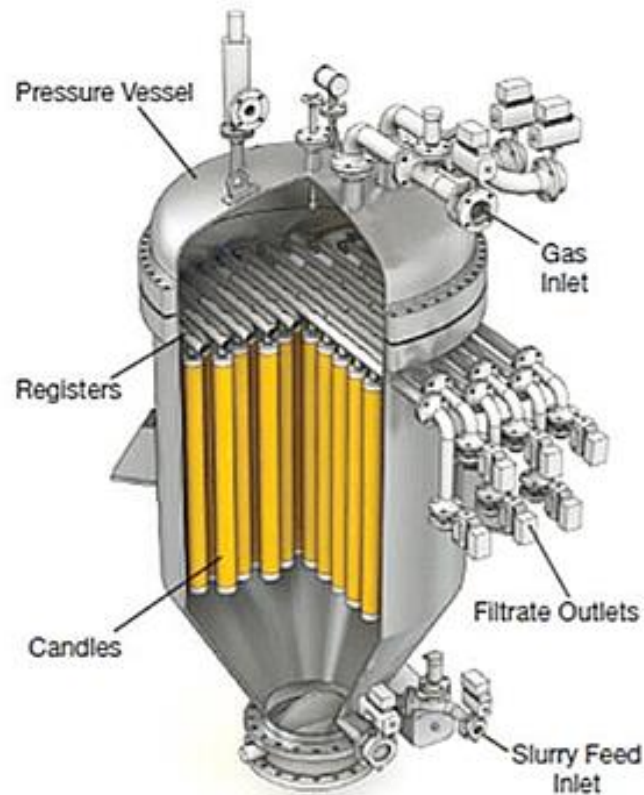
Pressure filters

- Plate-and-frame filters
- Candle filters
- Vertical or horizontal leaf filters

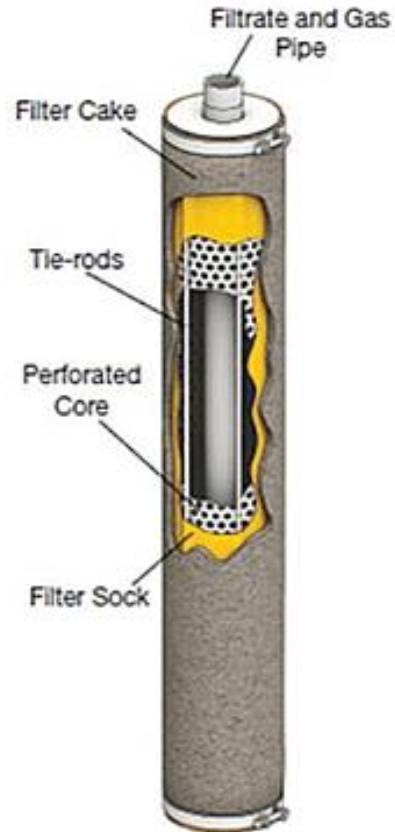
These filters commonly have a limited capacity for solids. They are used to treat rather diluted suspensions

These various designs and geometries all aim at the same thing: what do you think it is?

Candle filter and backflushing



▲ Figure 1. In a candle filter, the slurry enters through the bottom of a pressure vessel and flows across the filter media. The filter candles are attached to registers that collect the filtrate. Gas is fed into the top of the pressure vessel for cake drying and discharge.



▲ Figure 2. During operation, filtrate exits from the top of the candle, while the solids collect on the synthetic filter sock.



▲ Figure 3. During discharge, gas is fed into the top of the candle, which expands the flexible filter sock. This causes the dry cake to crack and break away from the filter. The solids are collected at the bottom of the pressure vessel.

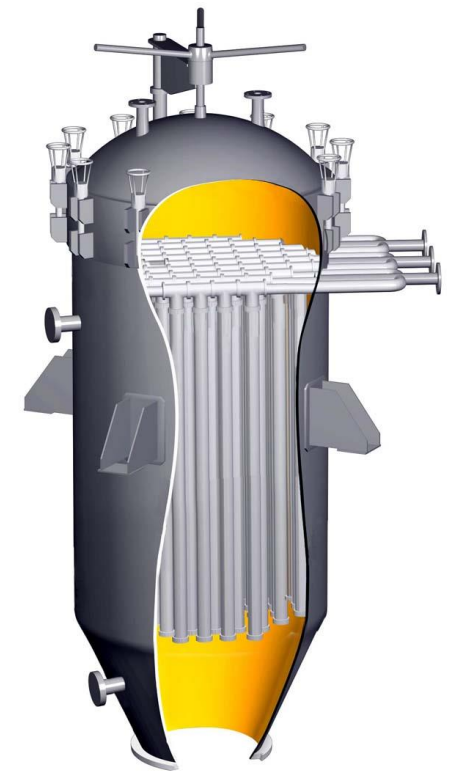


Plate and frame press filter

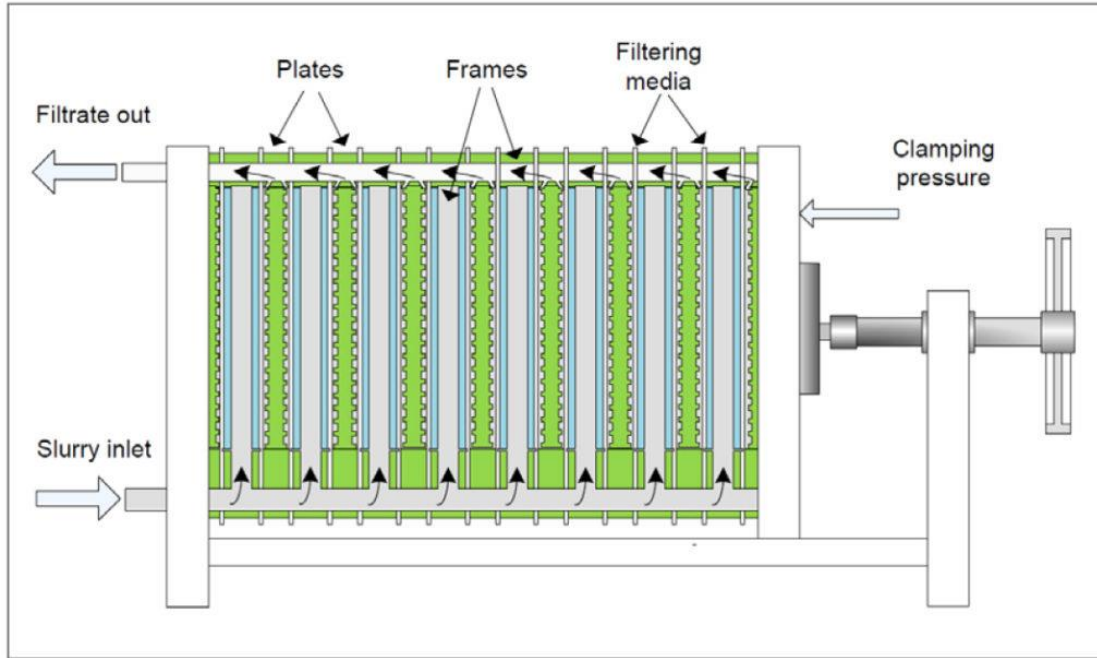
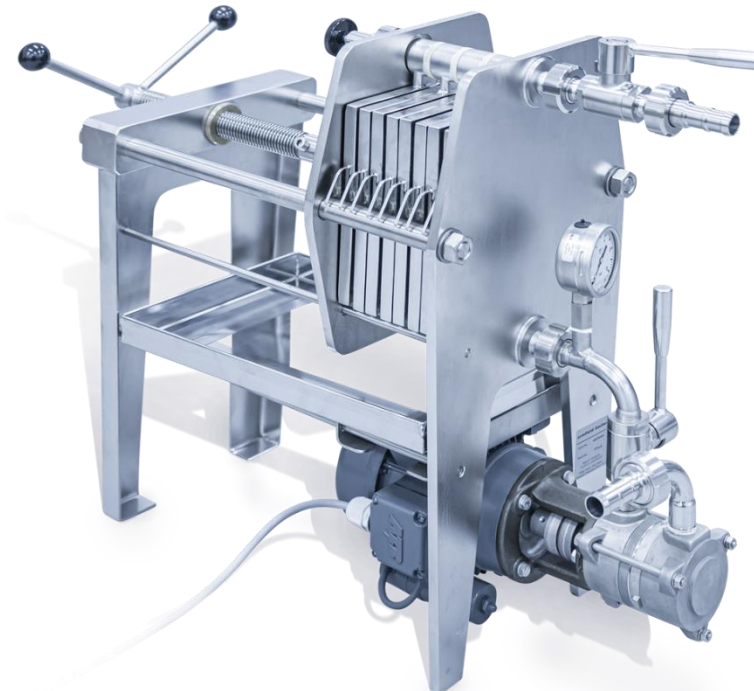
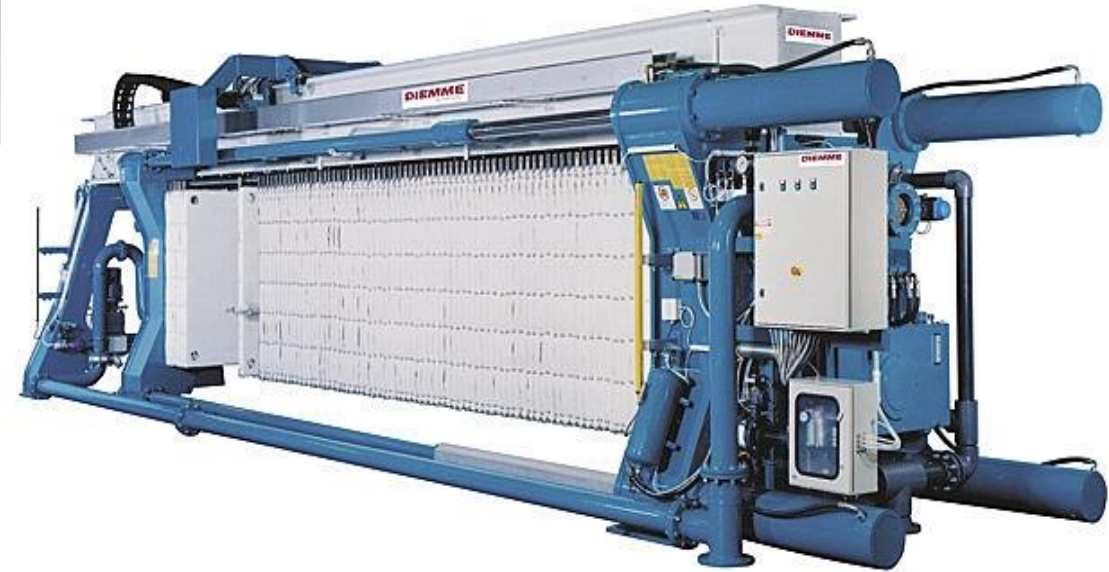
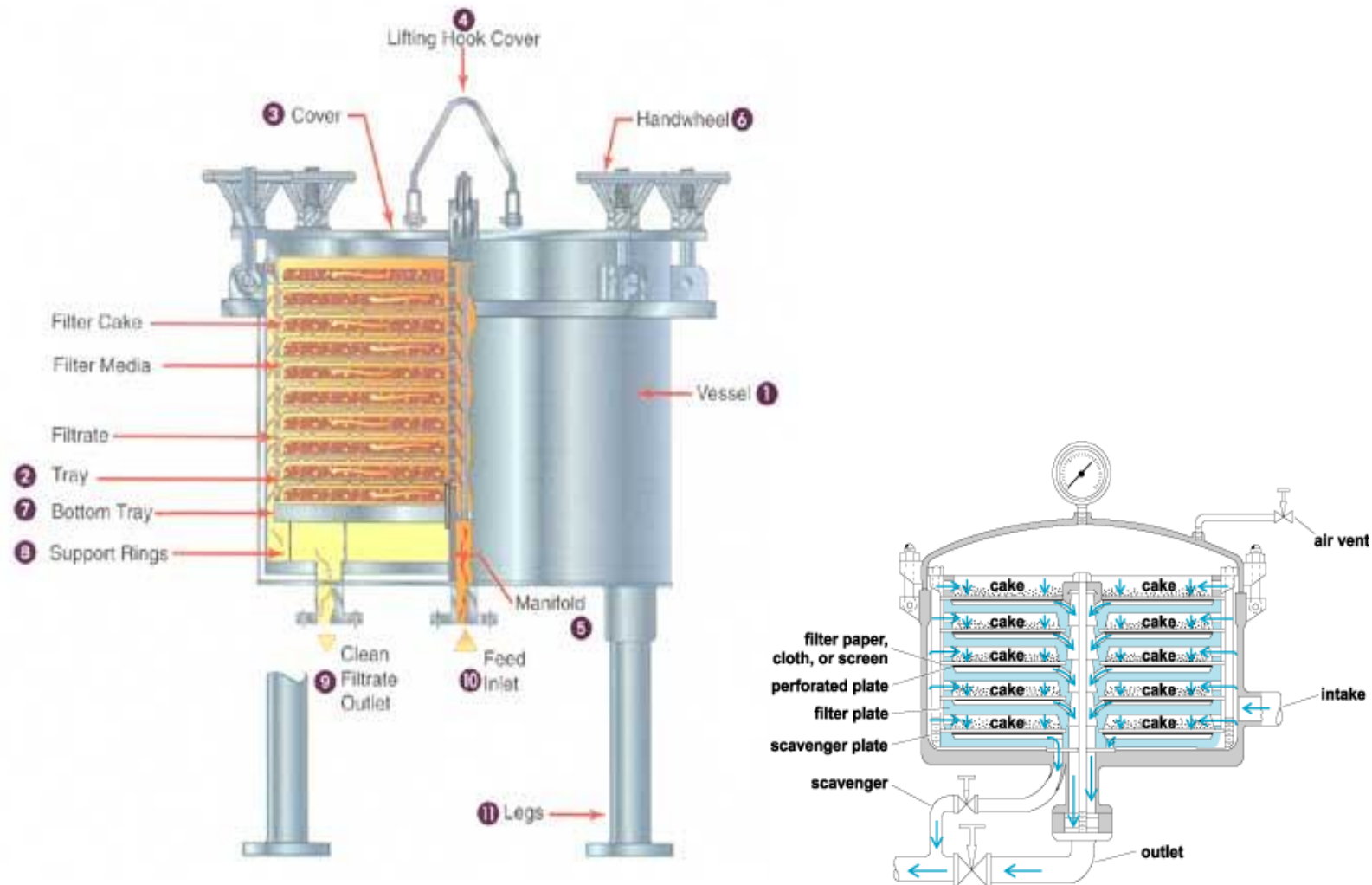


Figure 1 • Section of a plate and frame filter press

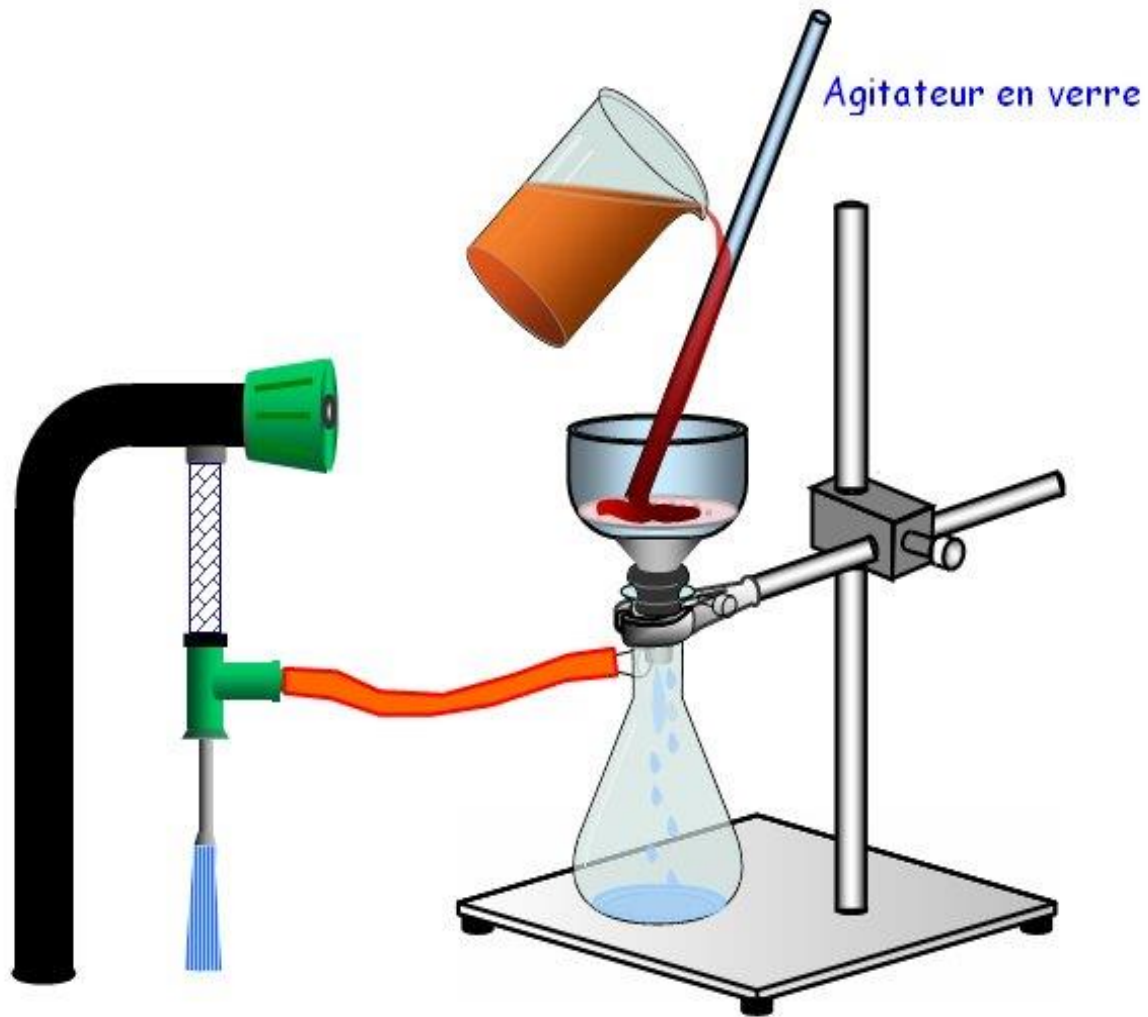
This kind of filter is a dead end for the unfiltered suspension
Only the clear liquid can be pressed through the filter cloth or plates and eventually get out.



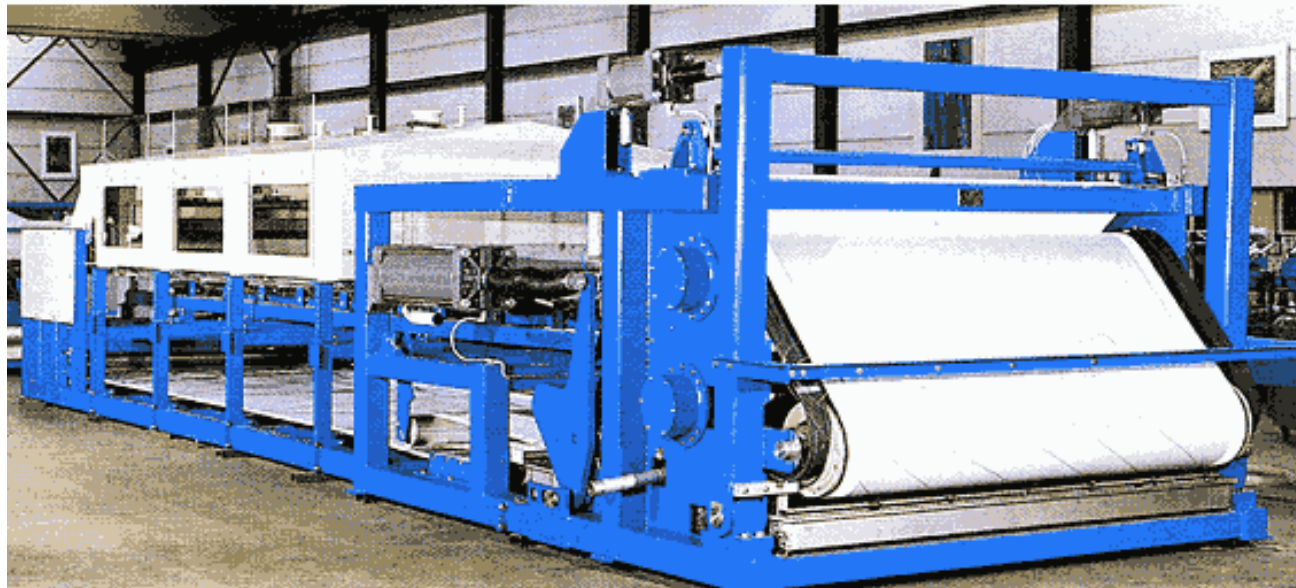
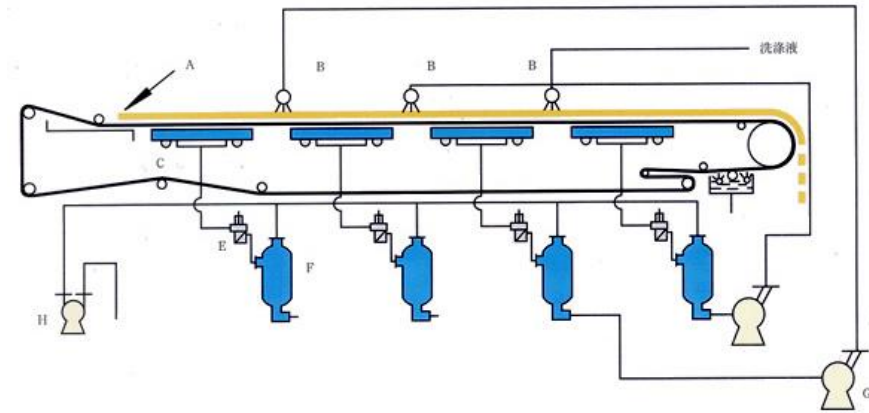
Horizontal plate filter



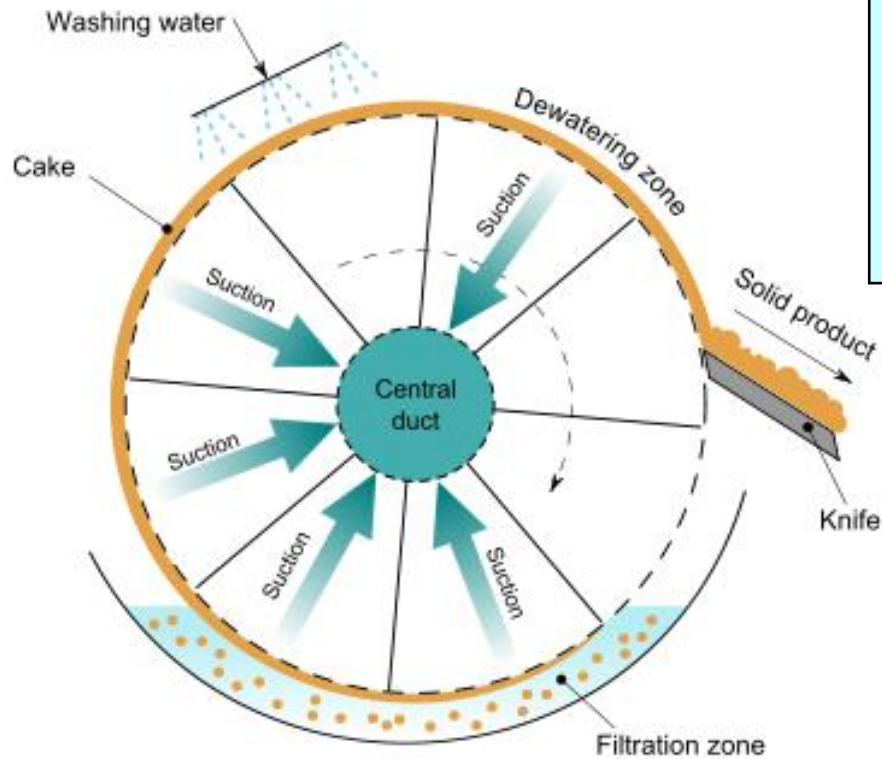
Vacuum filters



The reciprocating tray vacuum filter

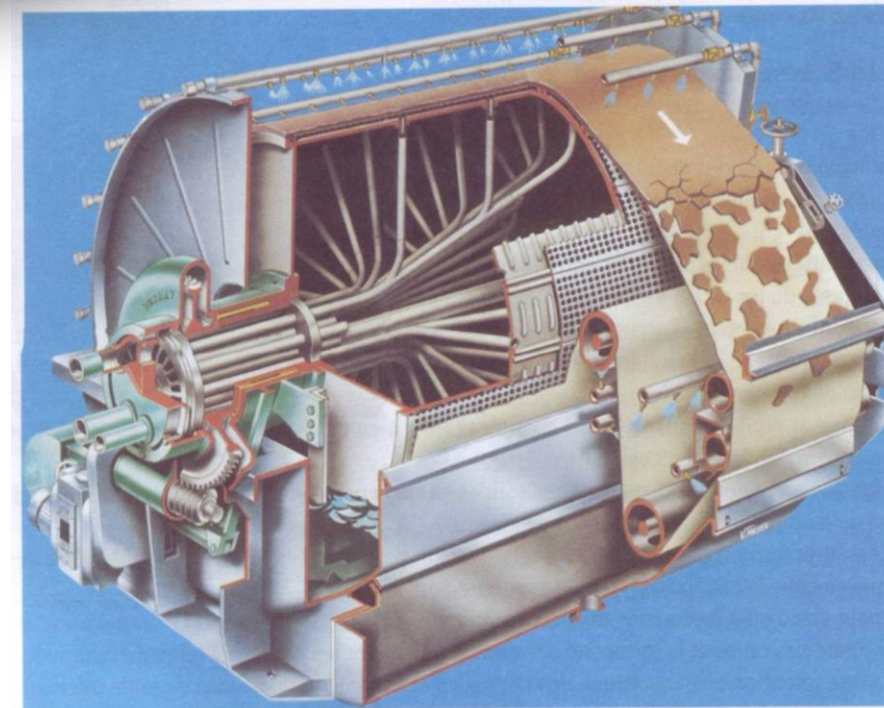


Rotating drum filter (Vernay)



3 main steps:

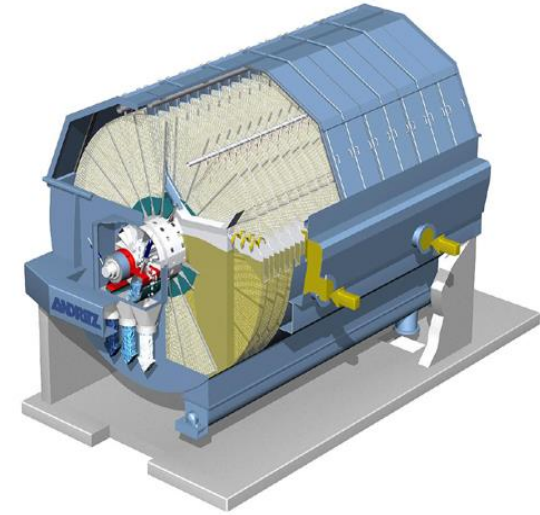
1. Cake formation
2. Cake washing
3. Cake discharge



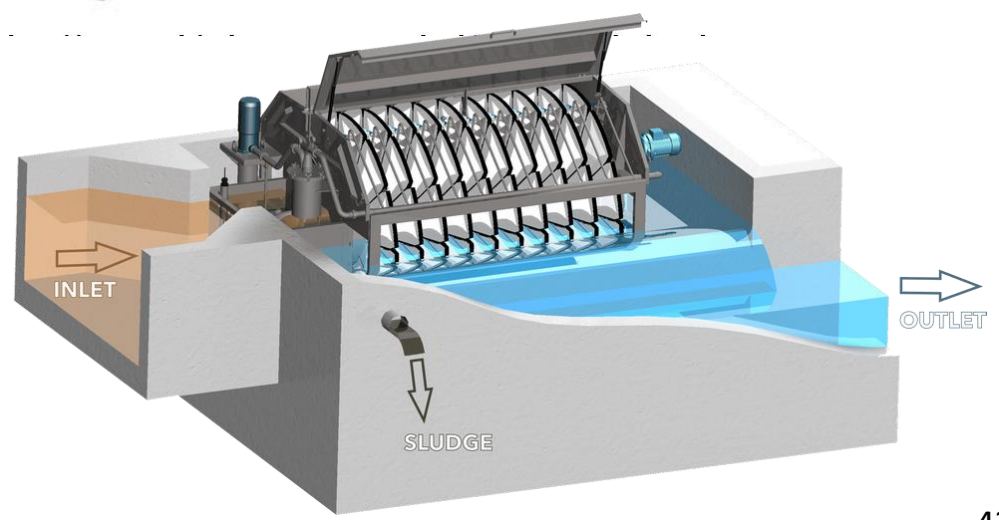
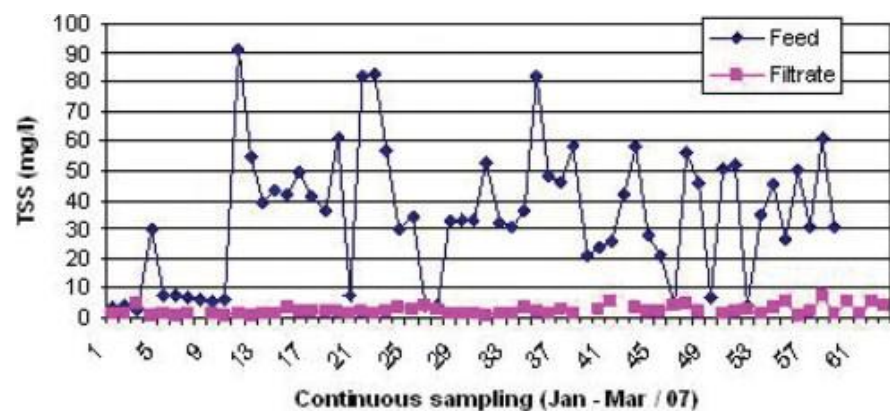
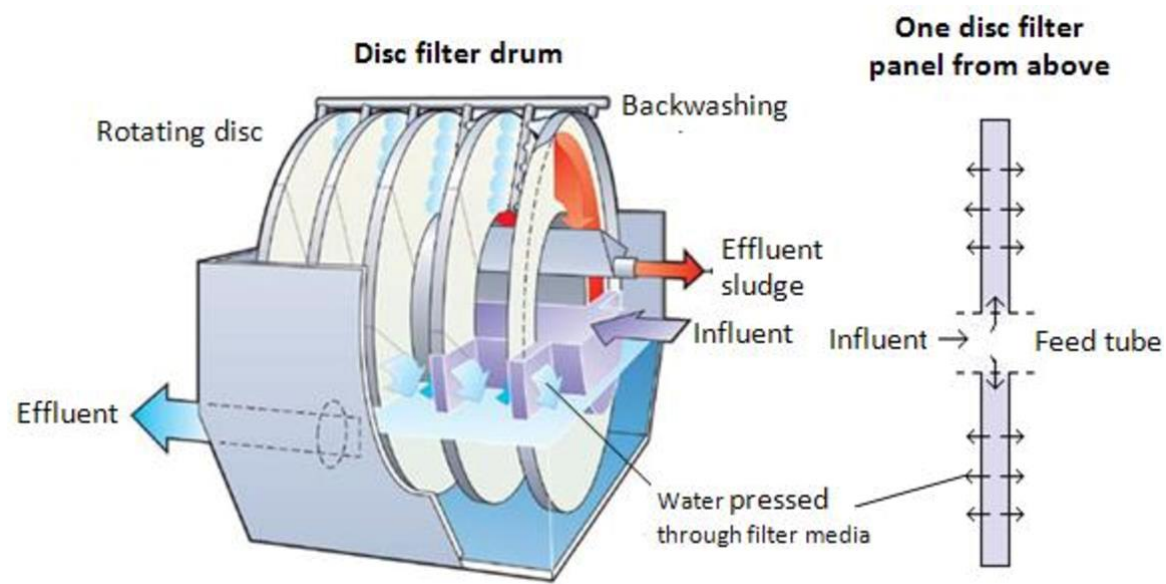
Commonly used (among many other applications) in the industrial production of antibiotics

The rotating disc filter works in a similar way

- The **rotating disc filter** is very similar to the drum filter
- It also allows the continuous treatment of a suspension
- Most of the time it works with vacuum suction of the liquid through the filtering element
- The cake is continuously scraped off the surface of the filter



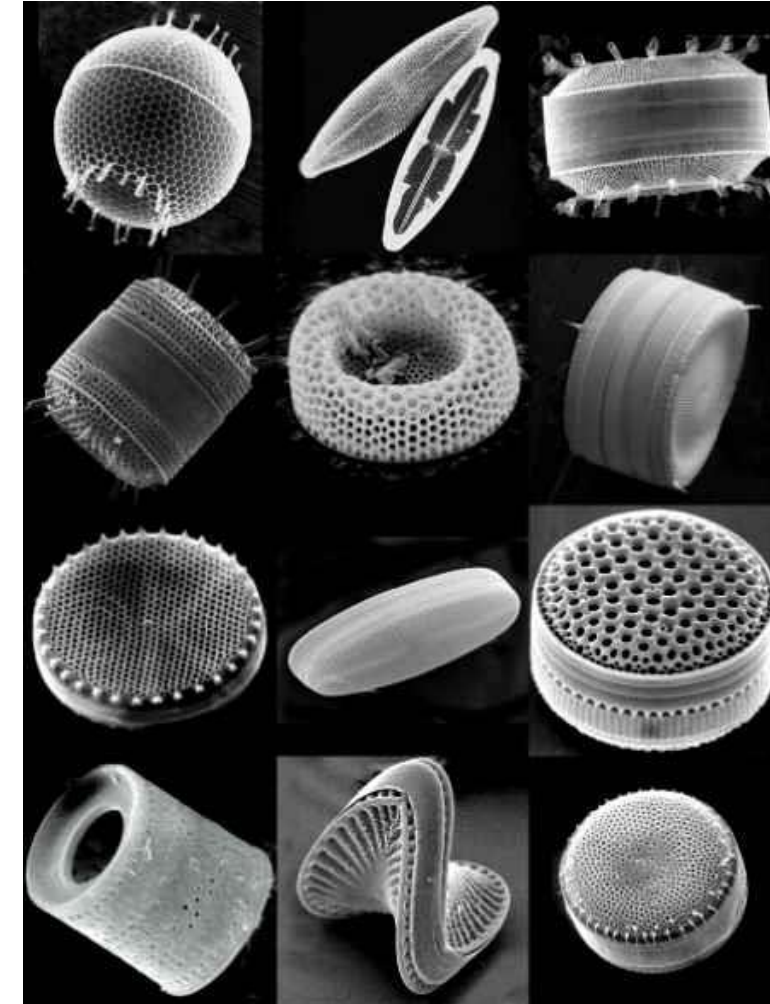
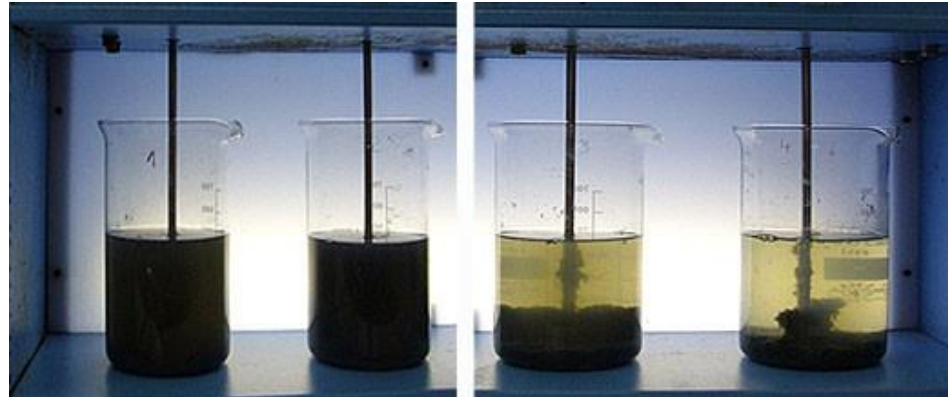
The rotating disc filter at work in a WWTP



How to accelerate the filtration process ?



- Remove the cake as it is formed (been there, done that)
- Pre-treat the suspension (electrolytes, pH, heat)
- Use filtration aids
- Use flocculation agents
- Avoid cake formation



Pre-treatment of the suspension

- **By heating**

- May improve things (both viscosity and density of the liquid decrease)
- Can have a positive pasteurisation effect
- May induce some aggregation or coagulation of solid particles
- Watch for the impact on target molecule, though!



- **By pH modification**

- Sometimes has a spectacular effect on filterability of biomass suspensions (classical example of *Streptomyces griseus*)



Filtration aids

- Often used in biotechnology processes to improve filtration performance
- They are dense, highly porous and incompressible granulated materials
- While capturing larger particles at their surface and smaller fragment inside their pores, they help maintain the cake porosity and rigidity and guarantee an easier filtration of otherwise compressible cakes
- The most common filter aids are diatomaceous earth (p.ex. Celite), some sorts of cellulose or Perlite (p.ex. Dicalite)

NB: The use of filtration aids implies it is the filtrate you are interested in, and not the solid phase



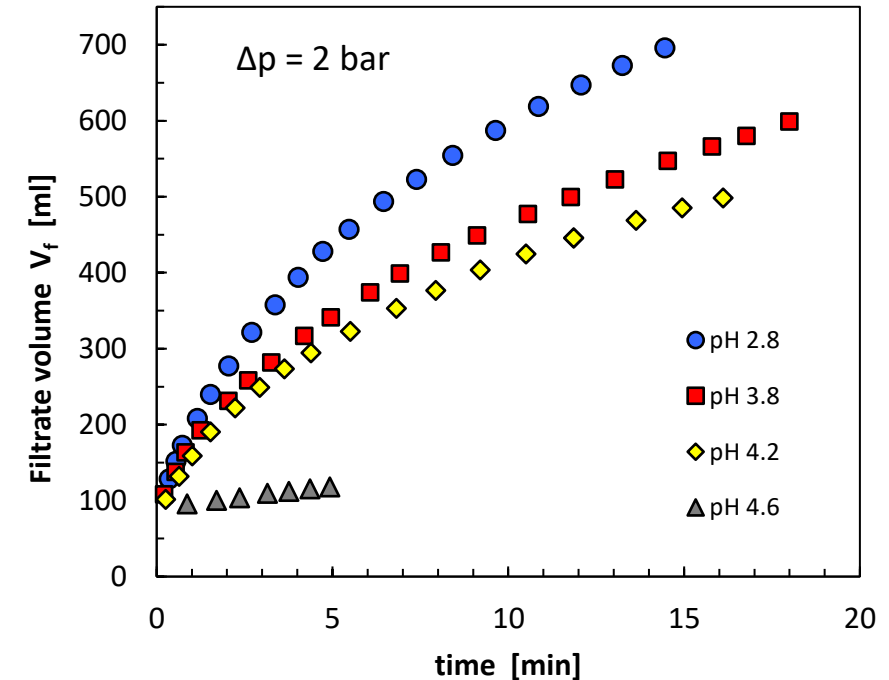
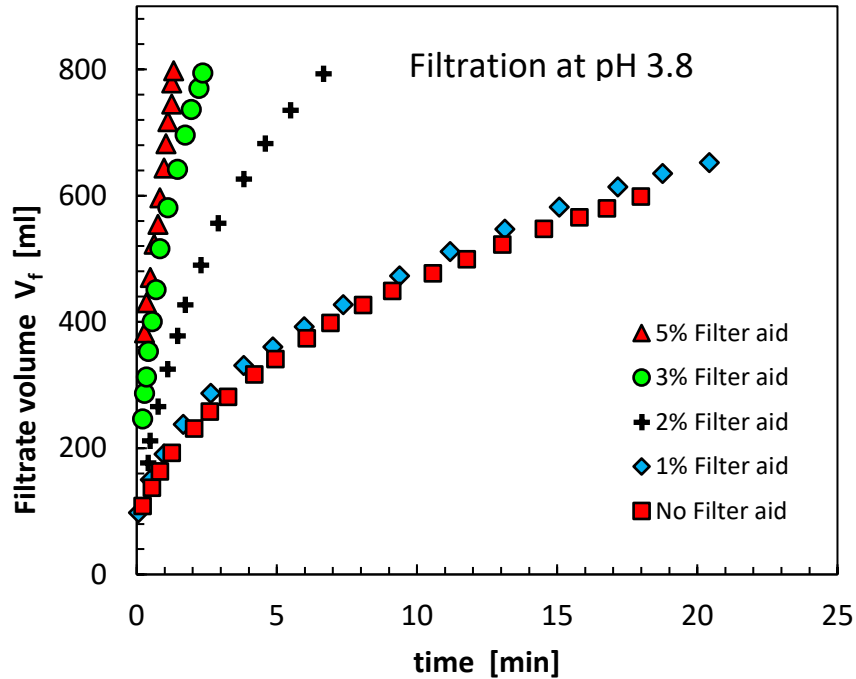
Diatomaceous earth (diatomite), and Celite, the corresponding commercial product



Perlite particles, after thermal expansion of the amorphous volcanic glass it is derived from



Effect of pH and filtration aid: the example of *S. griseus*

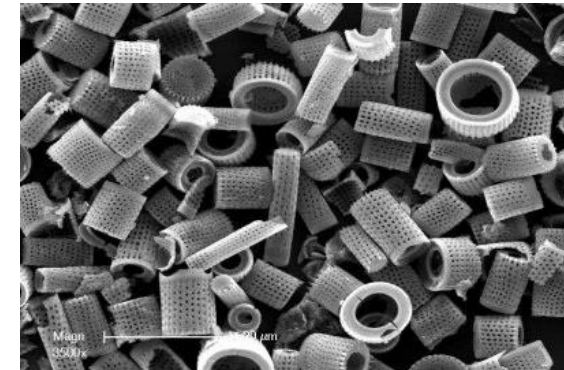
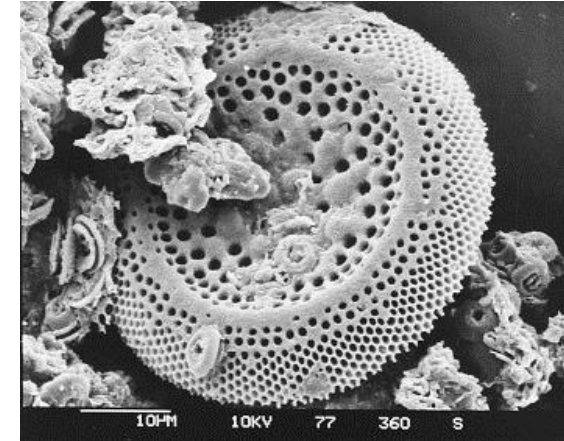
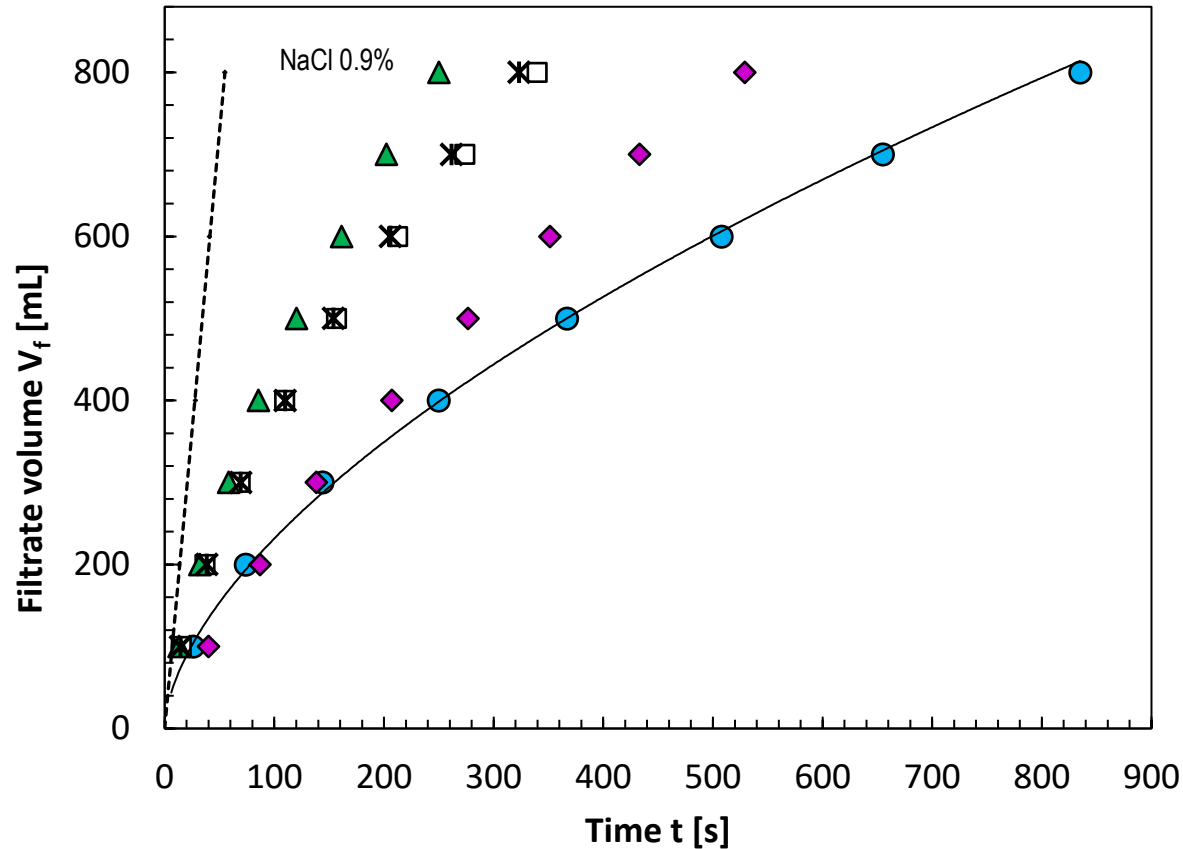


Filtration of a Streptomyces griseus suspension in the presence of filter aid at different dosages

*Filtration of *S. griseus* at different pH values*

Source: S. Shirato & S. Esumi. Filtration of a culture broth of *Streptomyces griseus*, J. Ferment. Technol (Japan) 41, 87 (1963)

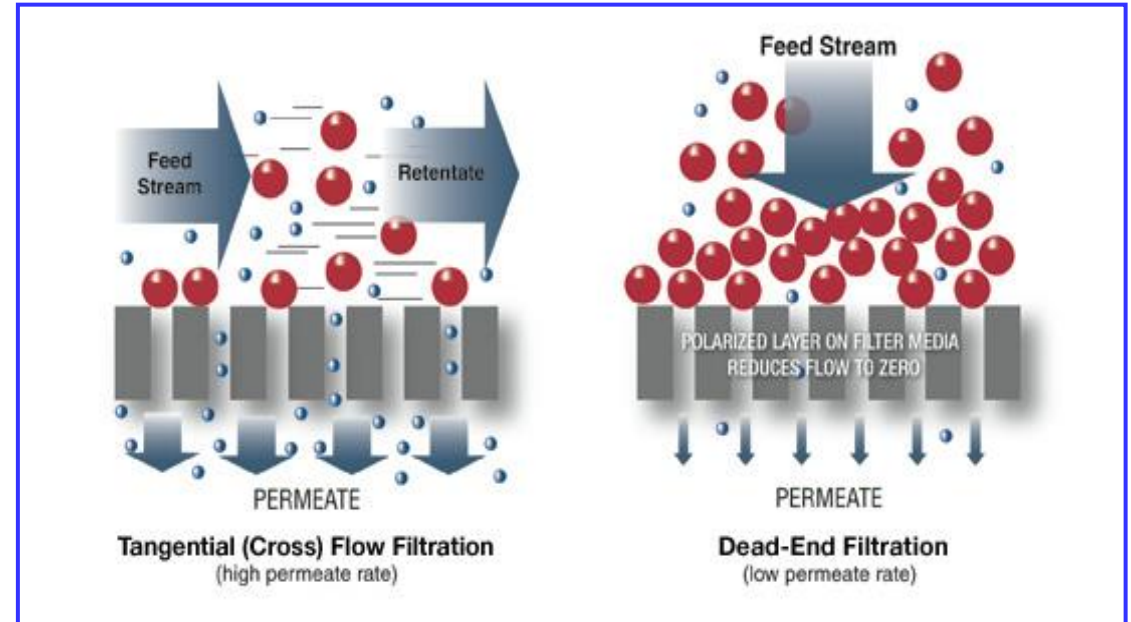
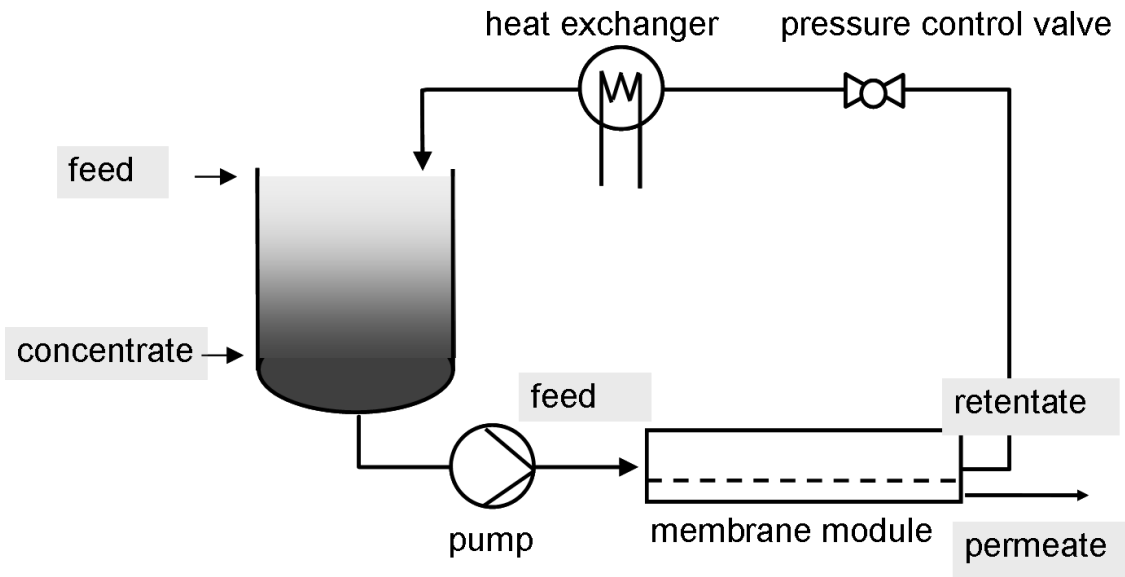
Kieselguhr: suspended or as a pre-coating?



How to avoid cake formation?



Cake thickness can be reduced by pumping the suspension to be filtered at high velocity parallel to the filtration element. The particles thus remain in suspension and less cake is formed. This is known as TFF (Tangential Flow Filtration) or CFF (Cross Flow Filtration)



Principle of tangential flow filtration (TFF) or cross flow filtration (CFF)

There is more in the catalog of S/L separation techniques

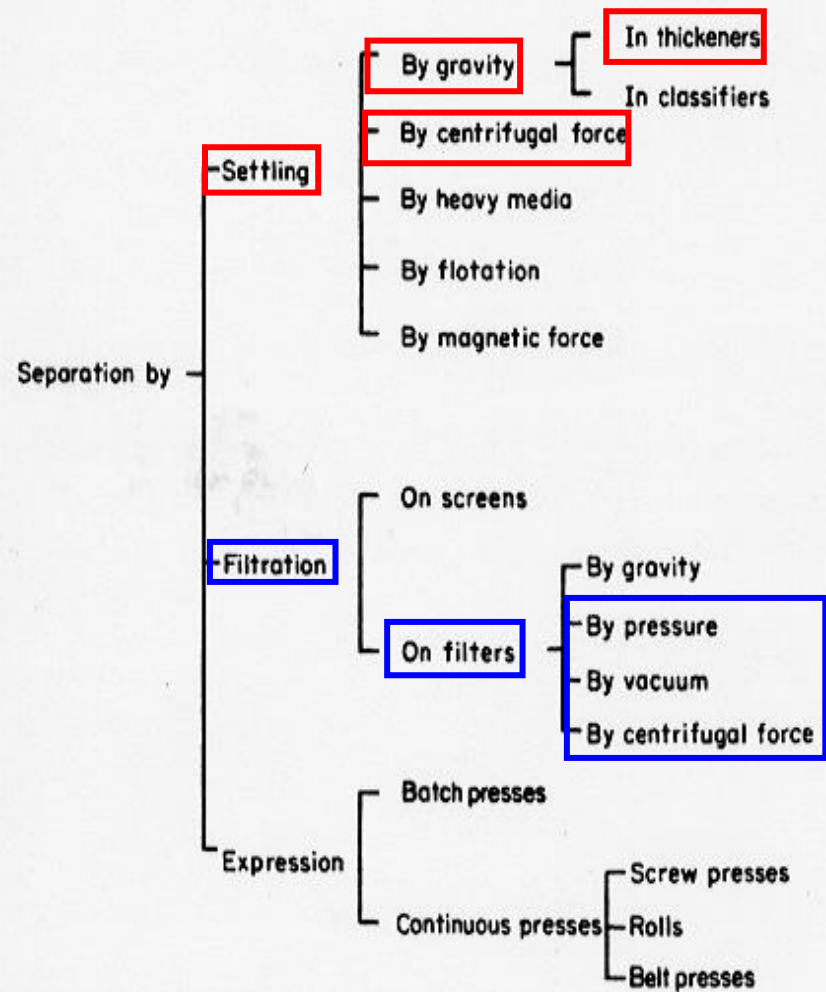


FIG. 19-133 Main paths to solids-liquid separation.

