Summary

Putting all together.mp4

The Impact of pH on Cell Culture in Bioreactors.mp4

The Impact of Aeration on Cell Culture in Bioreactors.mp4

The Impact of Sparging on Cell Culture in Bioreactors.mp4

Understanding the Role of Dissolved O_2 & CO_2 on Cell Culture in Bioreactors.mp4

Development of an Industrial Biotechnology Process

Process integration/ Scale-up

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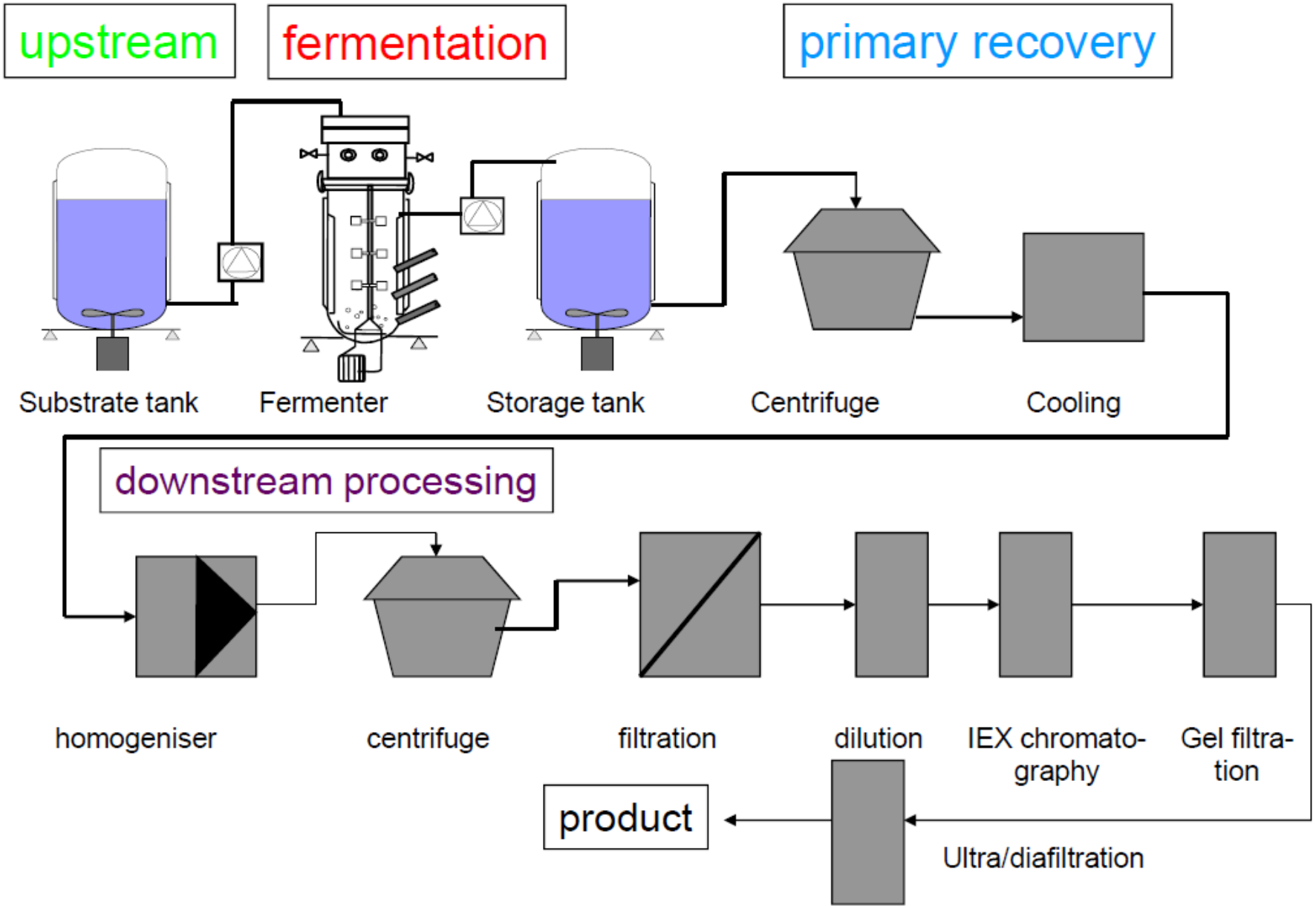
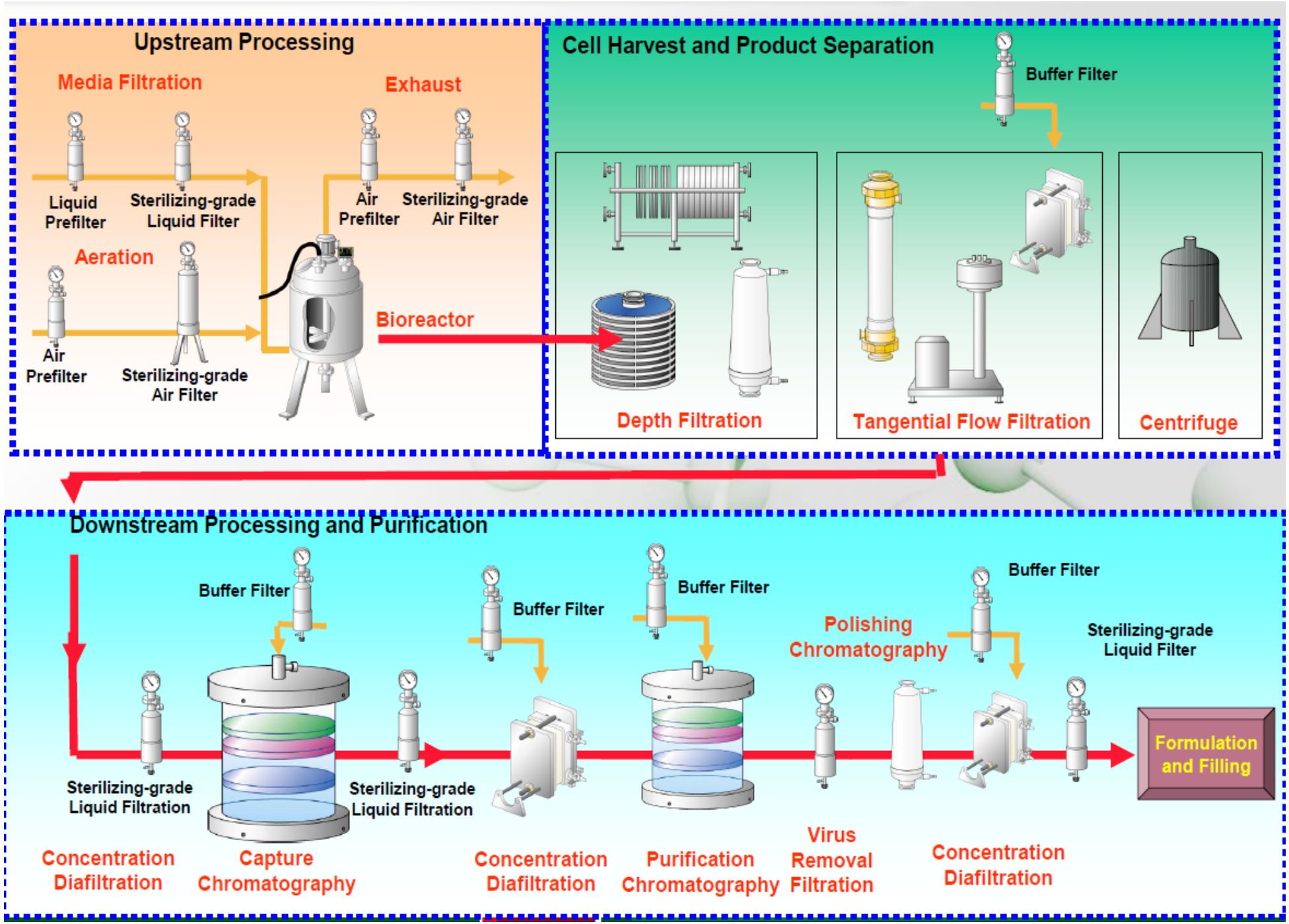
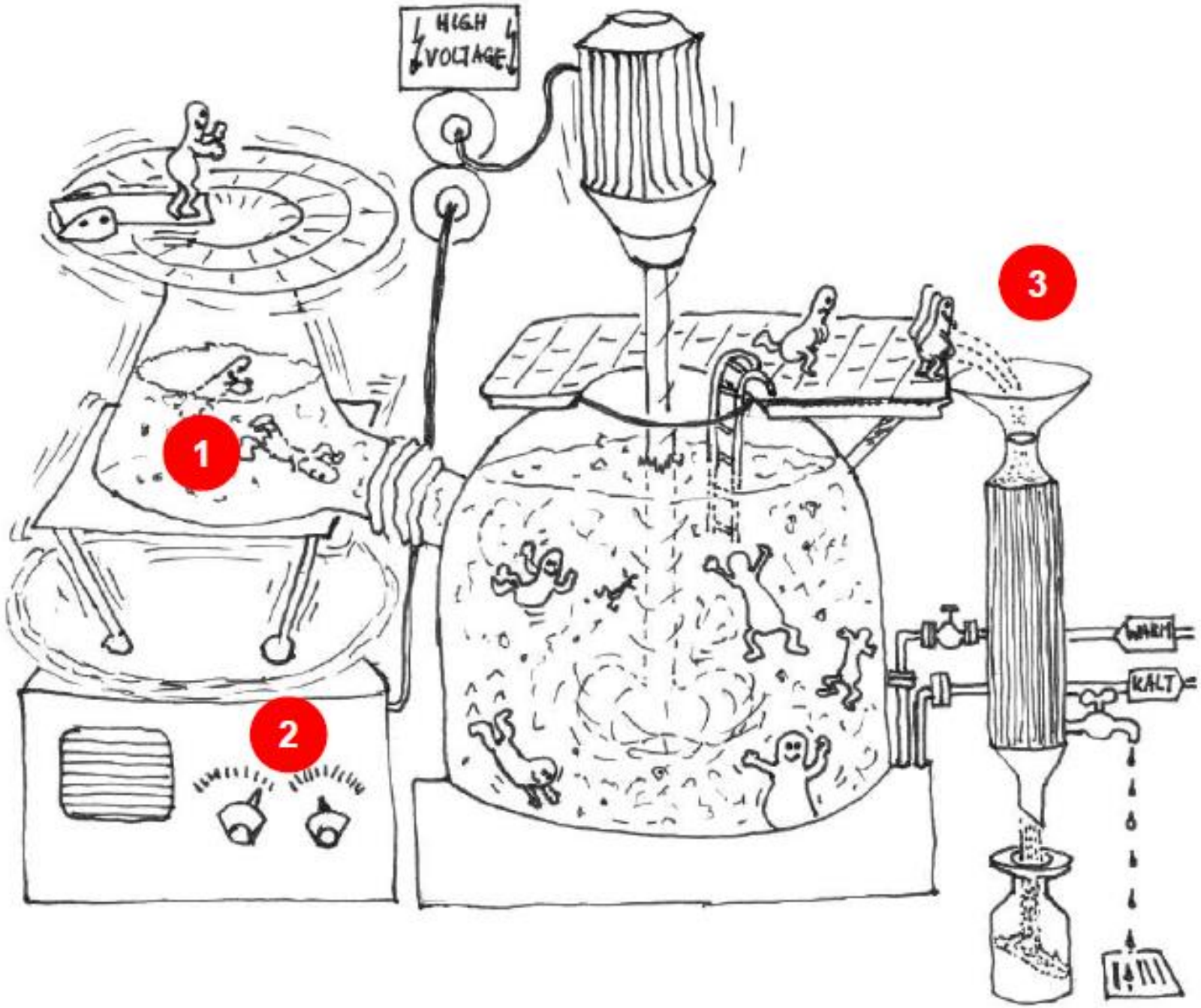
Principle configuration of a bioprocess (example)




Upstream Processing
Media Filtration
Exhaust
Liquid Prefilter
Sterilizing-grade Liquid Filter
Air Prefilter
Sterilizing-grade Air Filter
Aeration
Air Prefilter
Sterilizing-grade Air Filter
Bioreactor
Cell Harvest and Product Separation
Buffer Filter
Depth Filtration
Tangential Flow Filtration
Centrifuge
Downstream Processing and Purification
Buffer Filter
Buffer Filter
Buffer Filter
Buffer Filter
Polishing Chromatography
Sterilizing-grade Liquid Filter
Sterilizing-grade Liquid Filtration
Sterilizing-grade Liquid Filtration
Formulation and Filling
Concentration Diafiltration
Capture Chromatography
Concentration Diafiltration
Purification Chromatography
Virus Removal Filtration
Concentration Diafiltration


HIGH VOLTAGE
1
2
3
WARM
KALT

Process integration

- Once a process has been defined, either a new process or an existing one, the next step is to define how to integrate each part of the process to make the most efficient and cost effective production process.

- Ideally process integration should not be something done after each part of the process has been optimized and defined but should start from the outset of any new process

Integration of USP and DSP

- USP involves all stages upto and including the cell culture and production phase
- DSP involves all stages from the product harvesting from the bioreactor, through cell separation and chromatographic steps to final product formulation
- The aim of any production process should be to facilitate the integration of the USP and DSP

Process integration

- Medium supply
- Medium preparation and feeding (continuous sterilization)
- USP- CIP and SIP
- Batch, fed- batch, continuous culture
- Single stage or multiple stage culture
- Cell separation
- Product concentration (capture)
- Intermediate purification
- Polishing
- Formulation
- Analytics- QA and QC

Process integration

When a cell line/organism is initially chosen it should be with respect to:

- FDA approval (retroviruses etc.)
- stability
- glycosylation profile (??)
- high productivity
- whether it is suspension (or anchorage dependent)
- whether it can be grown to high density or requires immobilization
- whether batch, fed- batch or continuous process will be supported
- shear sensitivity and growth on defined medium

USP

- Choose system based on concentration and product stability
- Avoid high perfusion rates- productivity high but concentration low- large volumes
- Define system which is scalable
- Define system with lowest labour costs- roller bottles to be avoided
- Define seed train

USP

- Define kinetics
- If production continuous will DSP be continuous or as series of batches (stability dependent)?
- If continuous how long can one run be operated with consistency of product?
- Risk of contamination or mutation higher with continuous

DSP

- All processes require the prior removal of cells from the product- containing medium
- Cells should be removed rapidly (even from continuous processes) to avoid cell lysis and product contamination by host cell proteins and proteases
- Viability within USP should be maintained high to avoid cell lysis
- Medium should be chosen to have the minimum of protein contaminants, while maintaining high cell viability

Introduction: Scale-up

- A knowledge-based scale-up and scale-down methodology is vital, regardless of the microorganism or target product, for the transfer of a bioprocess from the laboratory to the industrial production scale

- Such process knowledge must consider fluid dynamic aspects with regards to the specific type of bioreactor applied and the responses of the biological system to changes in physical and chemical process parameters

- One major issue in the scale-up of fed-batch processes is the formation of concentration gradients at high cell densities

- A robust scale-up should include the change of the type, size, or other construction parameters of the bioreactor

- Engineering parameters affected: power input, stirrer tip speed, dissolved oxygen concentration or oxygen transfer coefficient

- Other considerations: physiological conditions inside the cell and the space–time dynamics of the environmental parameters that determine the specific responses and response time constants (kinetics) in the biological system

- Case-specific, i.e. needs specific studies of the fluid phase and the complex responses of cells to fast environmental perturbations at heterogeneous cultivation conditions.

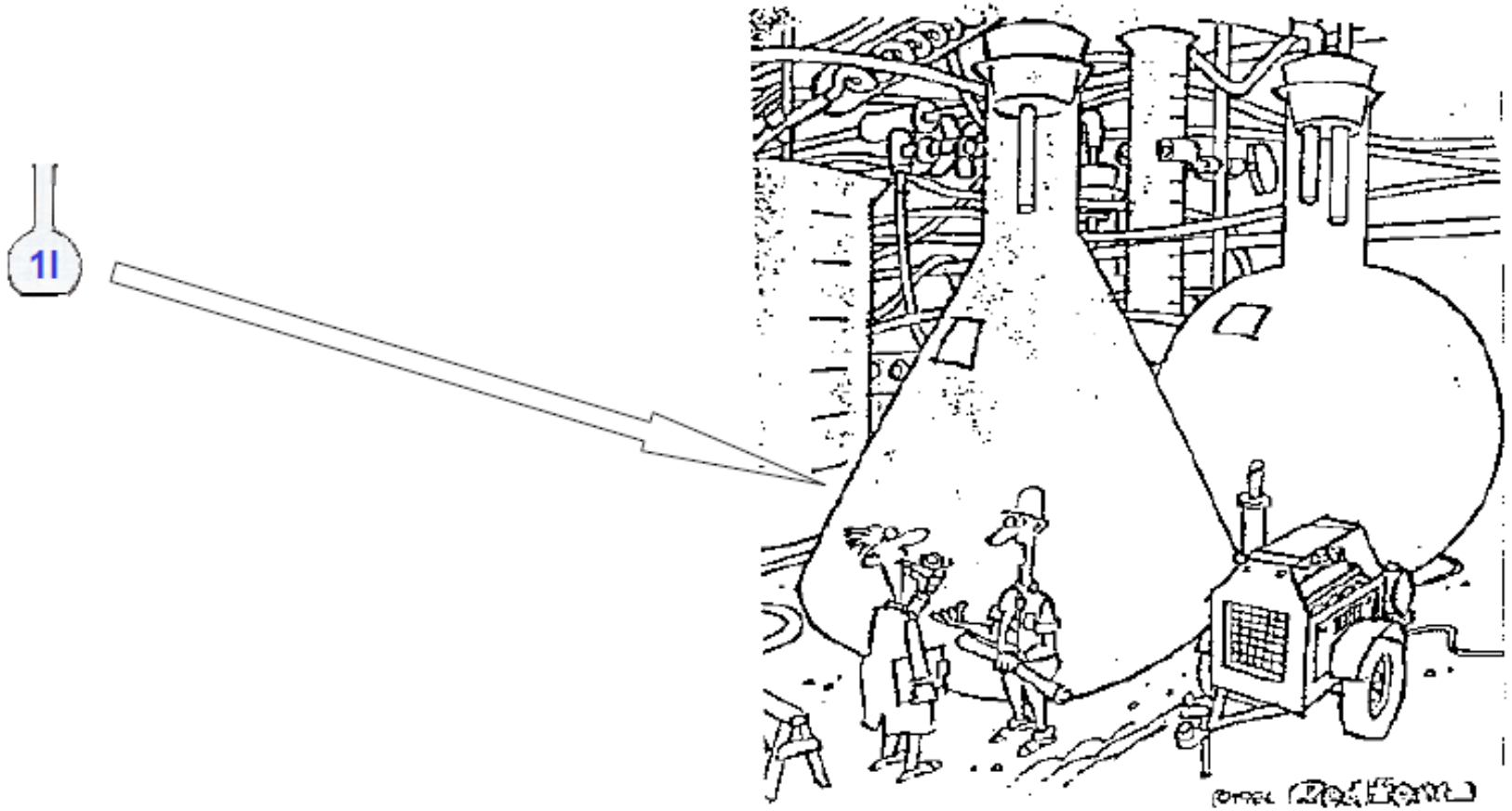
SCALING-UP:

"Operation and staringt-up of a **commercially-sized unit** whose design and operating procedures are based, in part, on experimentation and demonstration on a **smaller scale** of operation"

"Study of **problems associated with the transfer of experimental data** from laboratory and pilot-plant equipment to large scale industrial equipment."

The ideal scale-up criterion is that parameter which has the same numerical value as the volumes of the geometrically similar bioreactors increase in size

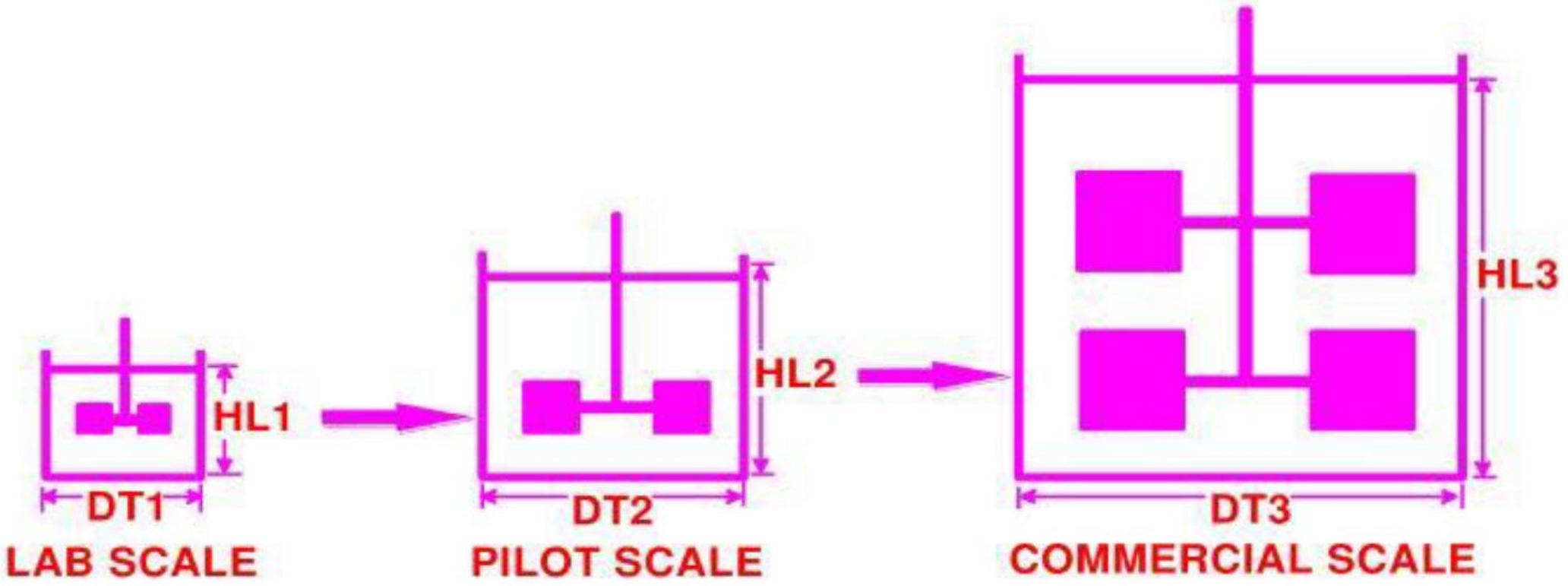
Scale-up: More an art than a science



"Got a few problems going from lab scale up to full-scale commercial."

« Commit your blunders on a small scale and make your profits on a large scale » H. Baekelands, 1916

Geometrical Scale-up of Bioreactors / Fermenters



First scale-up criterion is the

→ Preservation of Geometrical Similarity

REACTOR SCALEUP

Transport phenomena become increasingly important

Mixing, mass and heat transfer limitations?

Bioreactor scaling-up

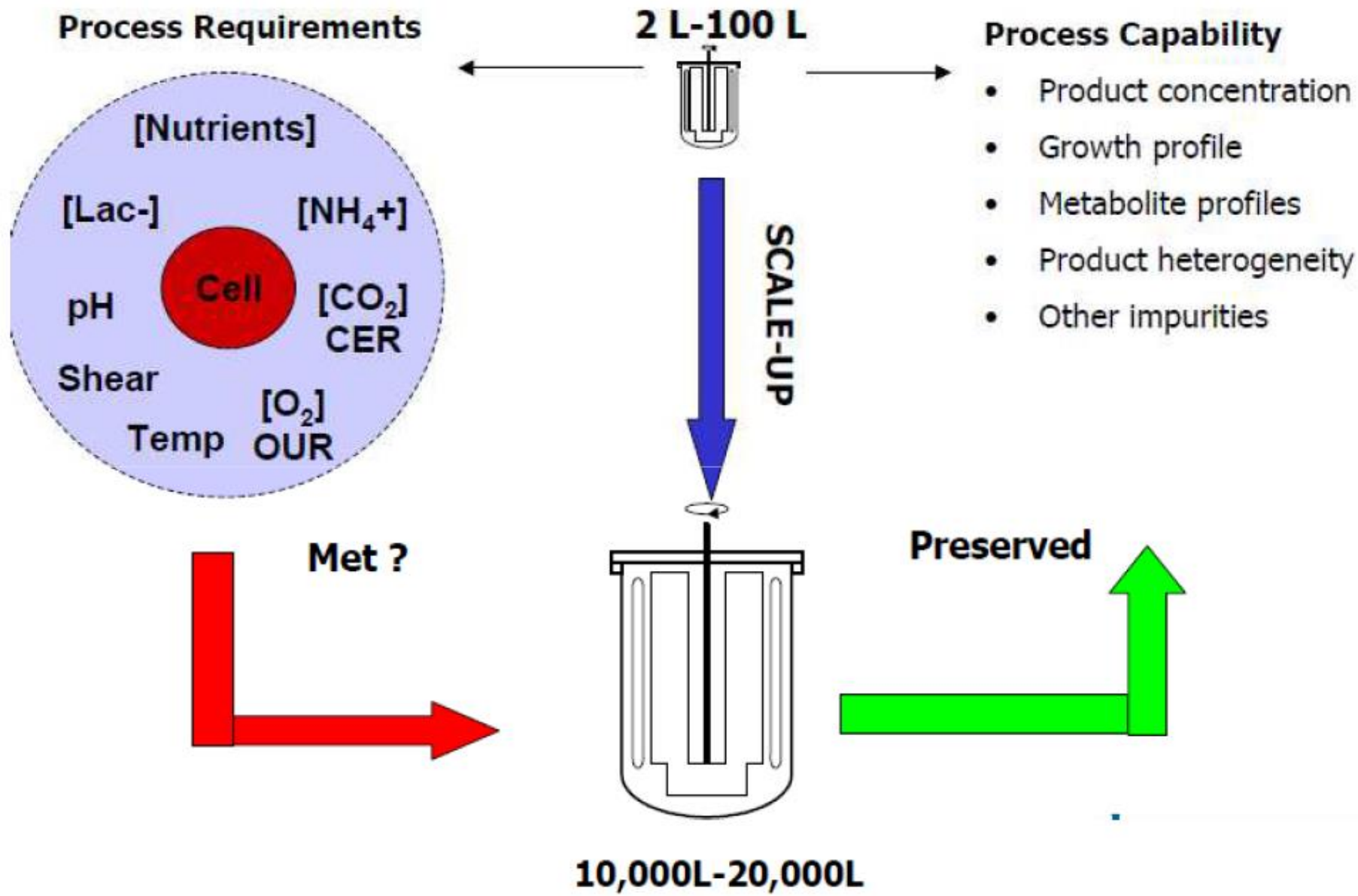
DIFFICULTIES:

- Scaling-up change **cannot be done directly.**
- It **doesn´t consist in increasing the number of small-scale units.**
- **Inaccuracy** in the model.
- Process is affected by changes within **response times**.
- **Some surface phenomena** are not considered.
- Change within the **hydrodynamic regime**.
- **Interactions between phenomena** of mass, energy and momentum transport along the scaling up.
- **Aeration and agitation** are the most complicated parameters.

- In reality, scale-up of laboratory and pilot plant to the commercial size industrial bioreactors is very difficult and complicated

- Scale-up is often facing problems due to the restrictions in the maintenance of key process parameters, which cannot be held constant for mechanical and economic reasons

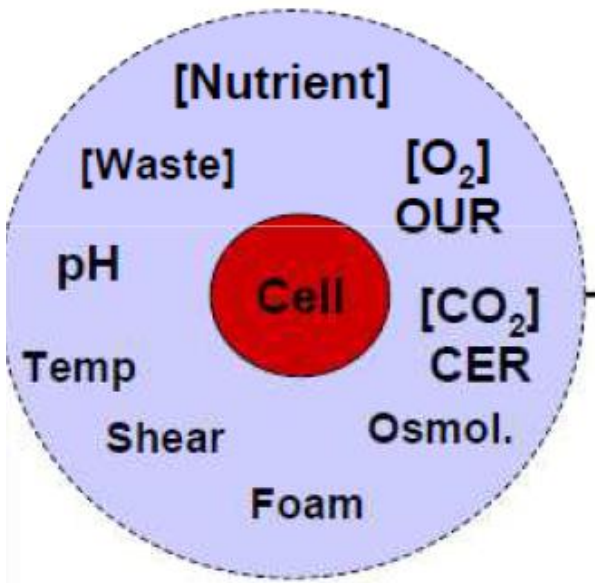
- A consideration of the rate of change of these parameters from the lab to the industrial scale allows an estimation of the change of the degree of homogeneity, to which the cells are exposed to


Process Requirements
2 L-100 L
Process Capability
Product concentration
Growth profile
Metabolite profiles
Product heterogeneity
Other impurities
[Nutrients]
[Lac-]
[NH4+]
Cell
pH
[CO2]
CER
Shear
[O2]
OUR
Temp
SCALE-UP
Met ?
Preserved
10,000L-20,000L

Define Process Requirements (10L-100L)

Establish Design Space Equipment Independent Parameters (10L-100L)

Determine Equipment Design and Operation Parameters (10,000L – 20,000L)

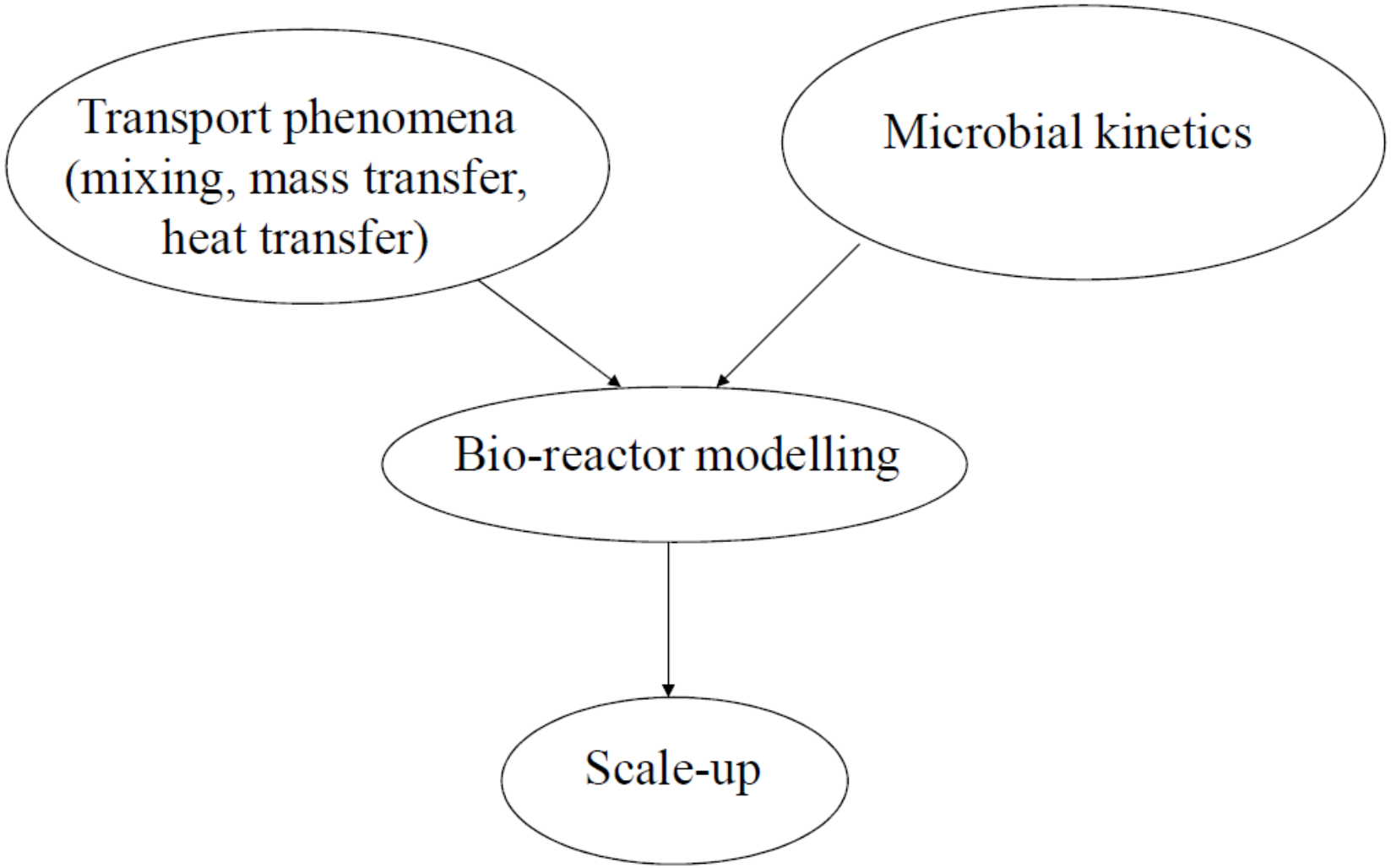


K_La
P/V
t_m
v_s
Tip speed
Others…

Equipment
Tank
Impellers
Sparger
Baffles

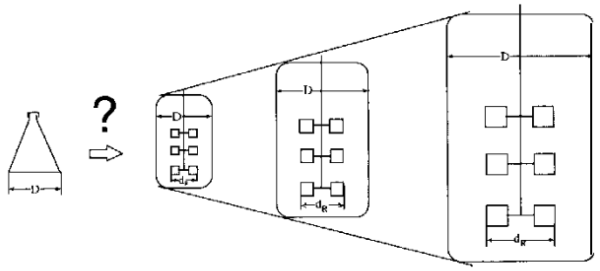
Operation
Volume
RPM
VVM
Gas compositions
Back pressure

Scale-up


Transport phenomena (mixing, mass transfer, heat transfer)
Microbial kinetics
Bio-reactor modelling
Scale-up

Scaling-up

- Scaling-up in practice
  - e.g. 100 ml shake flask → 3 L lab reactor, 100 L pilot plant → 3000 L production plant



Geometric similarity:
Prerequisite for scale up

- Bioprocesses are dependent on the scale
  - e.g. mixing time increases sharply with an increase in volume

- Aim of scaling-up
  - Similarity of geometrical and physical influence variables

Quelle: Storhas, Bioverfahrensentwicklung, S. 189 ff, S 232 ff

- Which similarity criteria are relevant?
  - Mass transport (O_2, CO_2)
  - Mechanical stress on the cells
  - Mixing time / Homogeneity

} **dependency** ⟺ power density *P/V*

Bioreactor scaling-up

HIGH COMPLEXITY:

EXAMPLE:

Broadly speaking, **height/diameter ratio** between **2:1** and **3:1**.

By **increasing the scale** and keeping this relationship constant, the **surface/volume ratio decreases rapidly.**

➔ The heat transfer with the exterior changes.

➔ The aeration and gas withdrawal requirements increase drastically.

Parameters are affected non-linearly by an increase in size while maintaining the aspect ratio.

Bioreactor scaling-up

HIGH COMPLEXITY:

ANALOGY:

A carpenter receives a client who wants to build a cubic box for a circus show. This client shows a wooden sample box presenting 25 cm each side.

He would like to build a 4 times bigger cube for a show.

Calculate dimensions, surface and volume for the structure to be built. If more than one solution is possible, do the calculations for everyone.

Bioreactor scaling-up

"**A Four times bigger cube**" can be understood in many different ways, so that the solution for the problem could consist in:

- Increasing the **cube side four times**.
- Increasing **total volume four times**.
- Increasinge **total area four times**. ➔ However, interest in this situation is only explained if the expenses of material used need to be controled.

Bioreactor scaling-up

Anyway, equations putting into relationship side, surface and volume of the cubic structure are the following ones:

$$S = 6L^2$$

$$V = L^3$$

Where,

L, in the side of the cubic structure,

S, is the total surface area of the structure and

V, the volume.

Bioreactor scaling-up

Initial situation

$L_0 = 25\ cm = 0{,}25\ m$

$S_0 = 6 \bullet (0{,}25)^2 = 0{,}375\ m^2$

$V_0 = (0{,}25)^3 = 0{,}016\ m^3$

Increasing the cube side four times

$L_1 = 4 \cdot 25\ cm = 100\ cm = \mathbf{1\ m}$
$S_1 = 6 \cdot 1^2 = \mathbf{6\ m^2}$
$V_1 = 1^3 = \mathbf{1\ m^3}$

$L_1/L_0 = 4$
$S_1/S_0 = 16 = 4^2$
$V_1/V_0 = 64 = 4^3$

Bioreactor scaling-up

Initial situation

$L_0 = 25\ cm = 0{,}25\ m$

$S_0 = 6 \bullet (0{,}25)^2 = 0{,}375\ m^2$

$V_0 = (0{,}25)^3 = 0{,}016\ m^3$

Increasing total volume four times

$V_2 = 4 \cdot V_0 = 4 \cdot 0{,}016 = 0{,}0625\ m^3$ ➔ $L_2 = \sqrt[3]{V_0 \cdot 4} = \sqrt[3]{4} \cdot L_0 = 0.397 m$

L_2 = **0,397 m**
$S_2 = 6 \cdot (0{,}397)^2$ = **0,945 m²**
V_2 = **0,0625 m³**

$L_2/L_0 = 1{,}587 = 4^{1/3}$
$S_2/S_0 = 2{,}520 = 4^{2/3}$
$V_2/V_0 = 4$

Bioreactor scaling-up

Initial situation

$L_0 = 25\ cm = 0{,}25\ m$

$S_0 = 6 \bullet (0{,}25)^2 = 0{,}375\ m^2$

$V_0 = (0{,}25)^3 = 0{,}016\ m^3$

Increasinge total area four times

$S_3 = 4 \cdot S_0 = 4 \cdot 0{,}375 = 1{,}5\ m^2$ ➔ $L_3 = \sqrt{\frac{S_0 \cdot 4}{6}} = \sqrt{\frac{6 \cdot L_0^2 \cdot 4}{6}} = 2 \cdot L_0 = 0{,}5m$

$L_2 =$ **0,5 m**
$S_2 = 6 \cdot (0{,}5)^2 =$ **1,5 m²**
$V_2 = (0{,}5)^3 =$ **0,125 m³**

$L_2/L_0 = 2 = 4^{1/2}$
$S_2/S_0 = 4$
$V_2/V_0 = 8 = 4^{3/2}$

Bioreactor scaling-up

TO SUM UP:

	Relationship Side / Initial Side	Relationship Surface / Initial Surface	Relationship Volume / Initial Volume
Increasing side	4	4^2	4^3
Increasing surface	$4^{1/2}$	4	$4^{3/2}$
Increasing volume	$4^{1/3}$	$4^{2/3}$	4

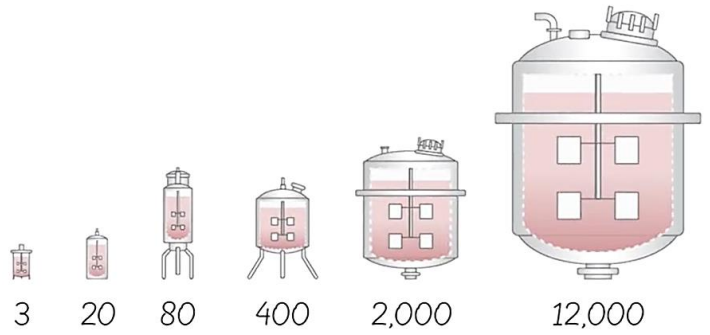
Scale-up Introduction

Scale-up ist the study of the problems associated with transferring data obtained in laboratory and pilot plant equipment to production level.

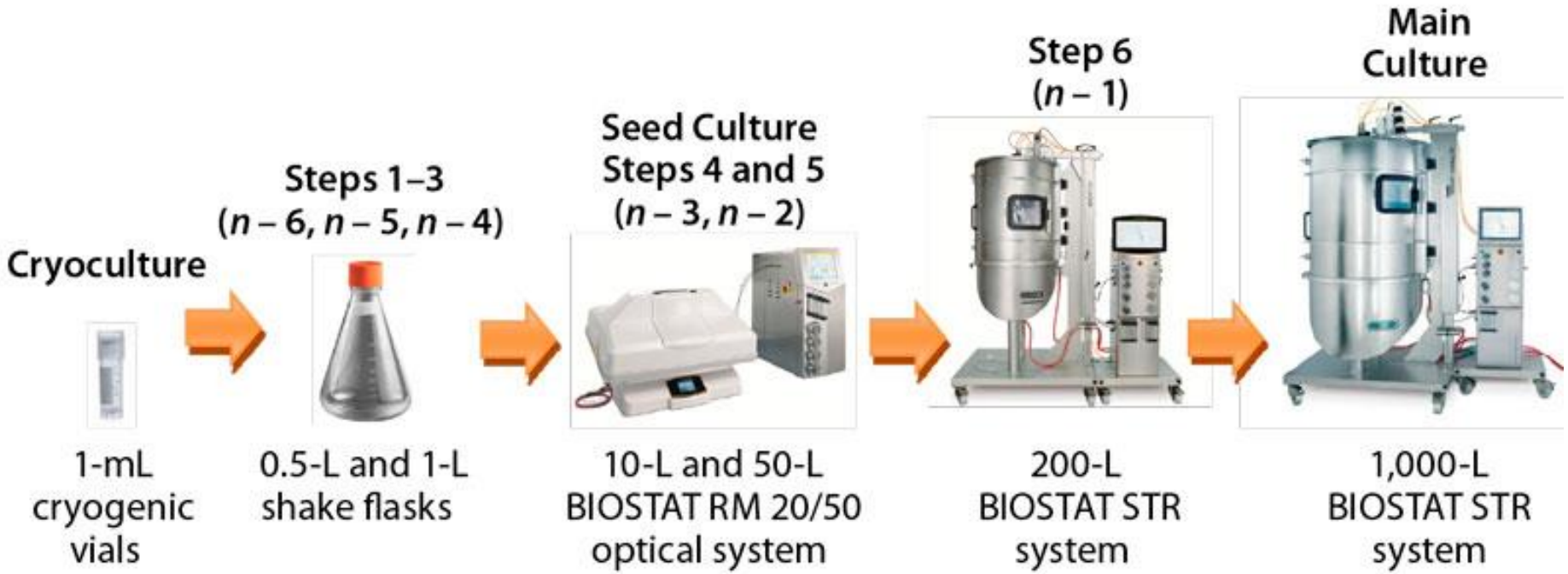
See video: bioreactor scale-up

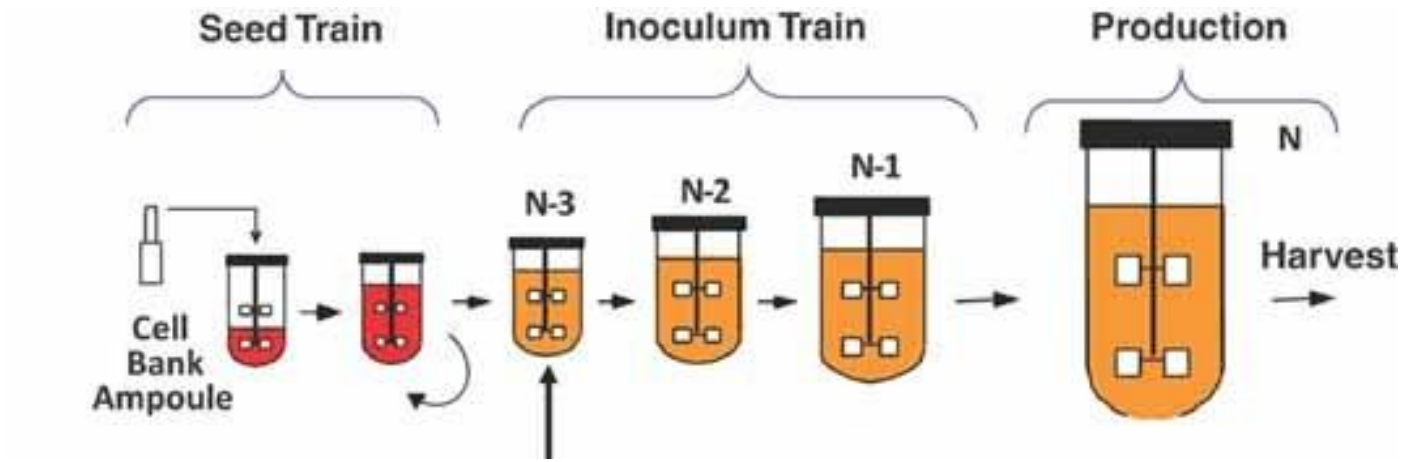
Power per unit volume is scalable

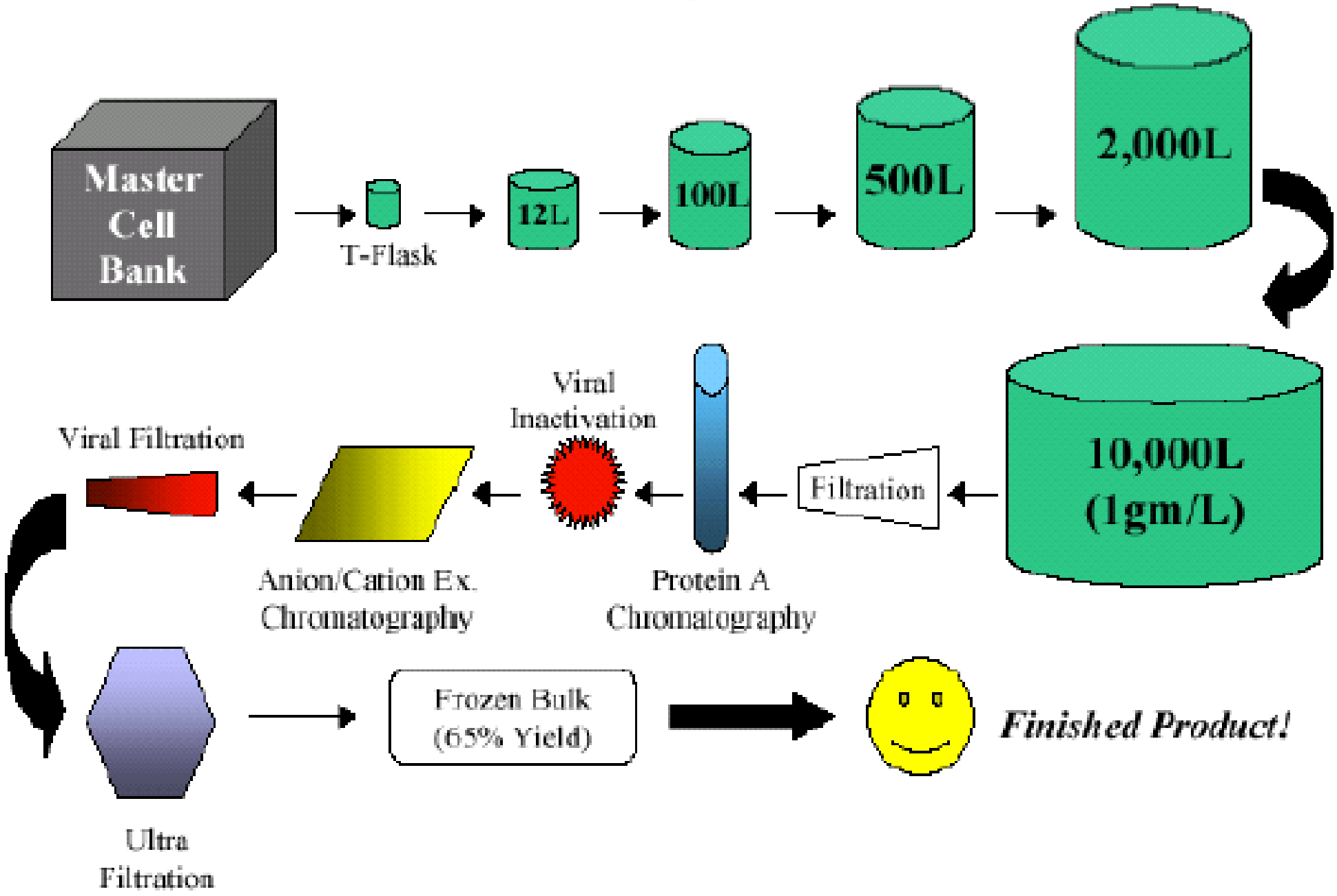
Agitation is not scalable




1 mL
100 mL
1 L
10 L
100 L
1000 L


Cryoculture
Steps 1–3
(n – 6, n – 5, n – 4)
Seed Culture
Steps 4 and 5
(n – 3, n – 2)
Step 6
(n – 1)
Main
Culture
1-mL
cryogenic
vials
0.5-L and 1-L
shake flasks
10-L and 50-L
BIOSTAT RM 20/50
optical system
200-L
BIOSTAT STR
system
1,000-L
BIOSTAT STR
system


Seed Train
Inoculum Train
Production
Cell
Bank
Ampoule
N-3
N-2
N-1
N
Harvest

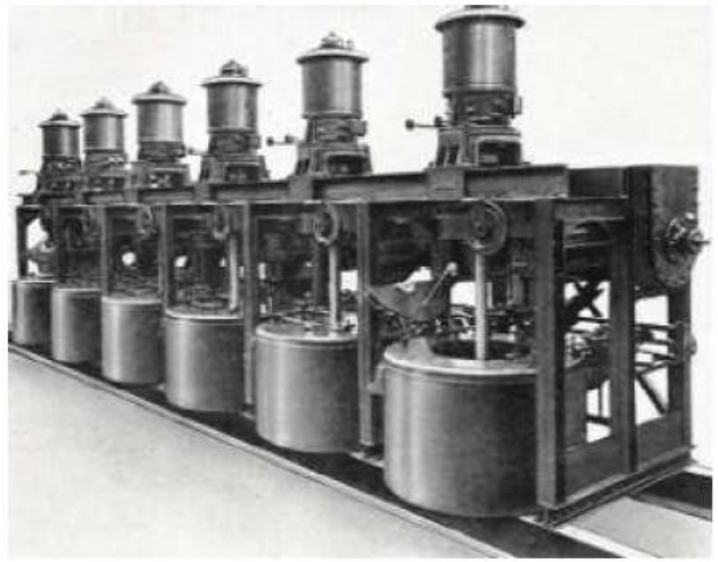

Master Cell Bank
T-Flask
12L
100L
500L
2,000L
10,000L (1gm/L)
Filtration
Protein A Chromatography
Viral Inactivation
Anion/Cation Ex. Chromatography
Viral Filtration
Ultra Filtration
Frozen Bulk (65% Yield)
Finished Product!

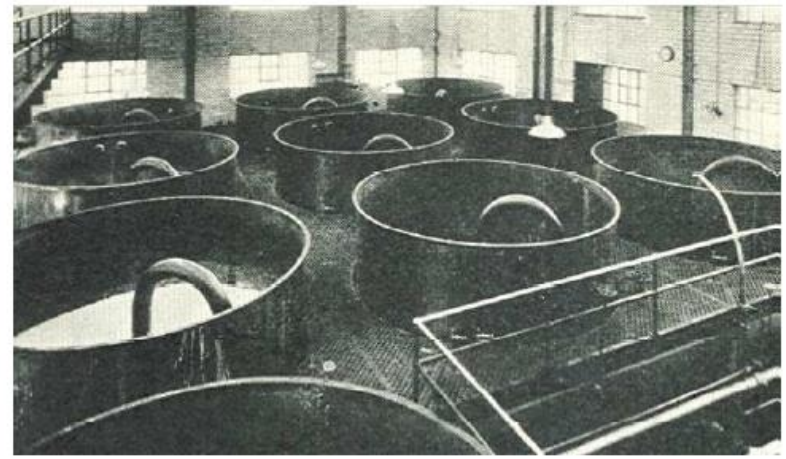
Scale-up methods in use

- *Multiplication*
- Fundamental approach
- *Rules of thumb*
- Dimensional analysis
- Similarity
- *Regime analysis and scale-down*

and often: « Trial and error » - approach

Scale-up by multiplication

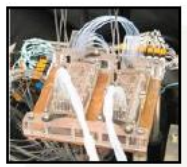




Bioreactor scaling-up

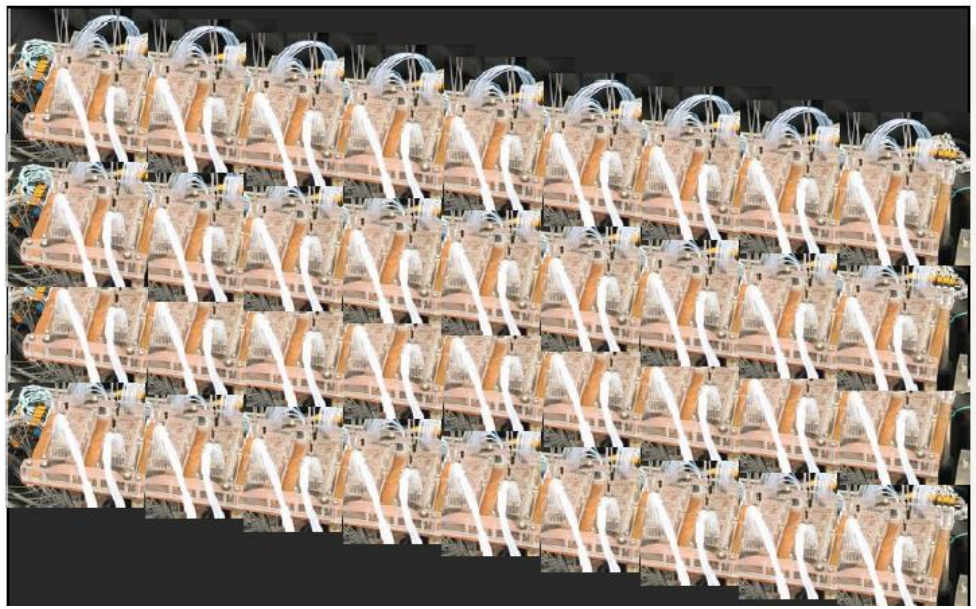
DIFFICULTIES:

- A protocol developed in a miniature bioreactor should be used for the production of antibiotics.



Numbering up

Scaling up



Numbering-up

- Parallel connection of the miniature bioreactors

- **Nature's principle**

  Unicellular→ Multicellular

  Leaves ➔ Tree ➔ Forest

- **Advantages**

  No risks and compromises through scaling-up

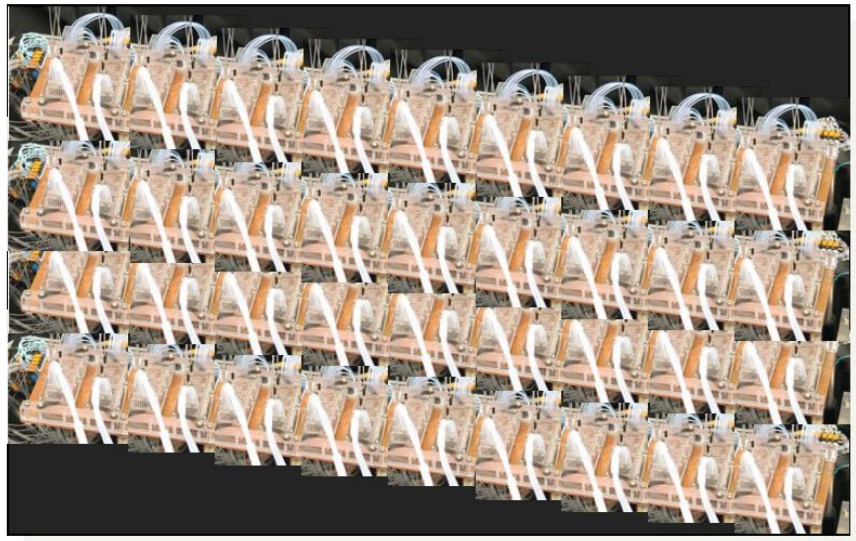
  „Process Intensification":

  good energy and material exchange

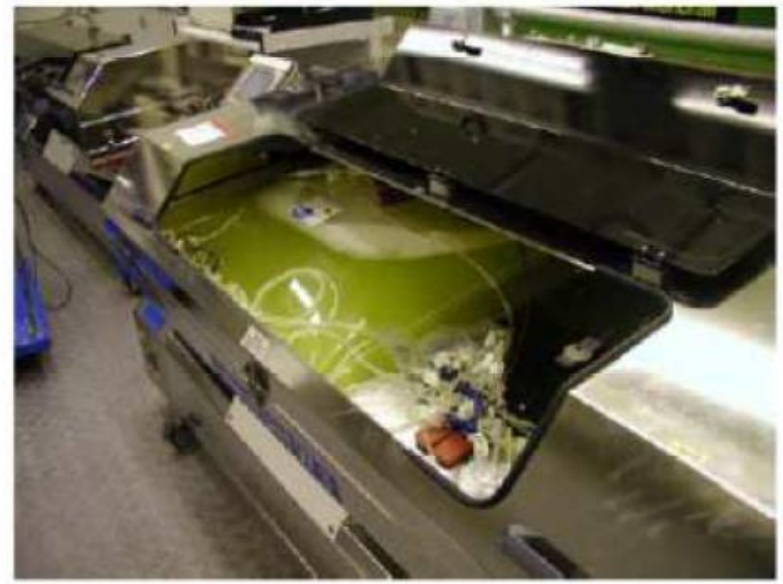
  (short diffusion distance)

- **Disadvantages**

  Individual process guidance and control for every single miniature reactor necessary



Multiplication =>
in biopharmaceutical production



Fundamental approach

- Use of balances:
  - Mass
  - Heat
  - Momentum

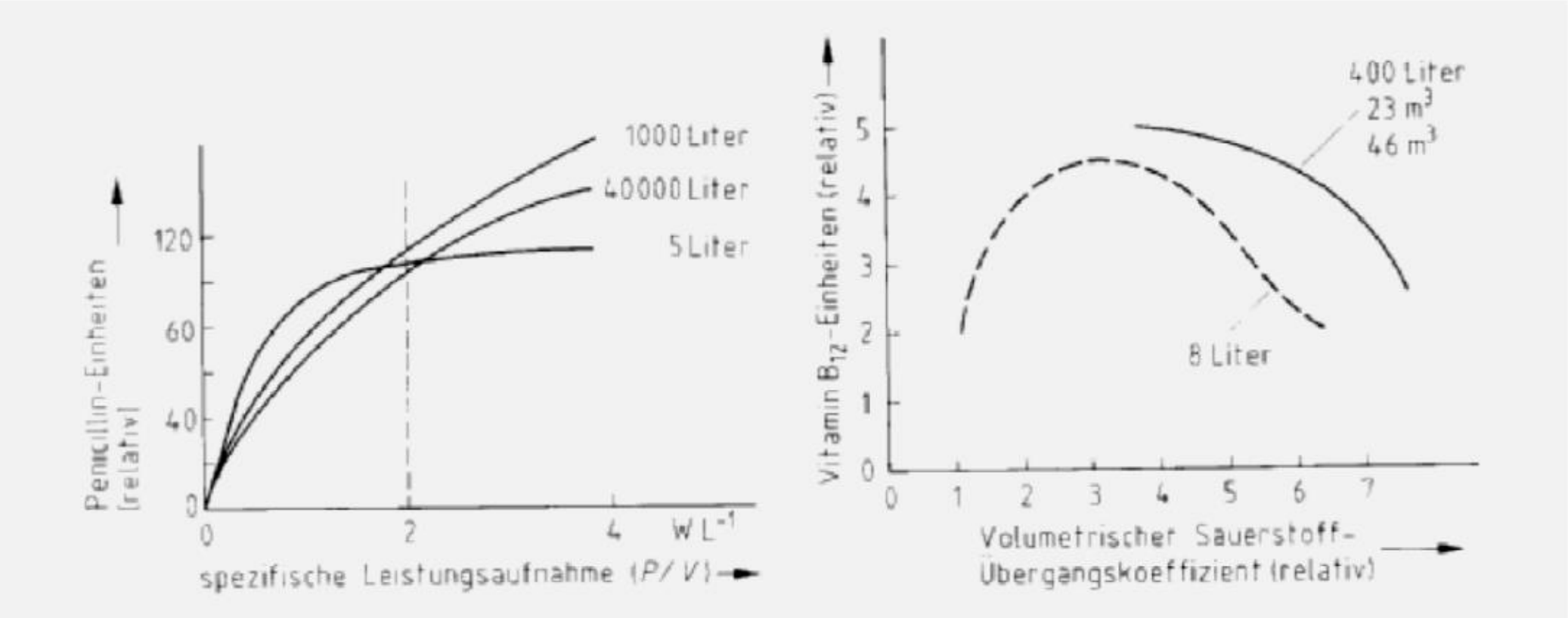
- Not easy applicable to heterogeneous systems

Basics for scaling-up

- Important questions:

1) Which criterion or parameter has the biggest influence at lab-scale
   → "biological concept"
2) Is it possible to scale-up the reactor under found conditions from 1)
   → " physical concept"
3) Has this criterion also the biggest influence at large - scale?

Biological concept



Basics for scaling-up

Physical concept

- from chemistry
- Based on similarity theory

Assumptions:

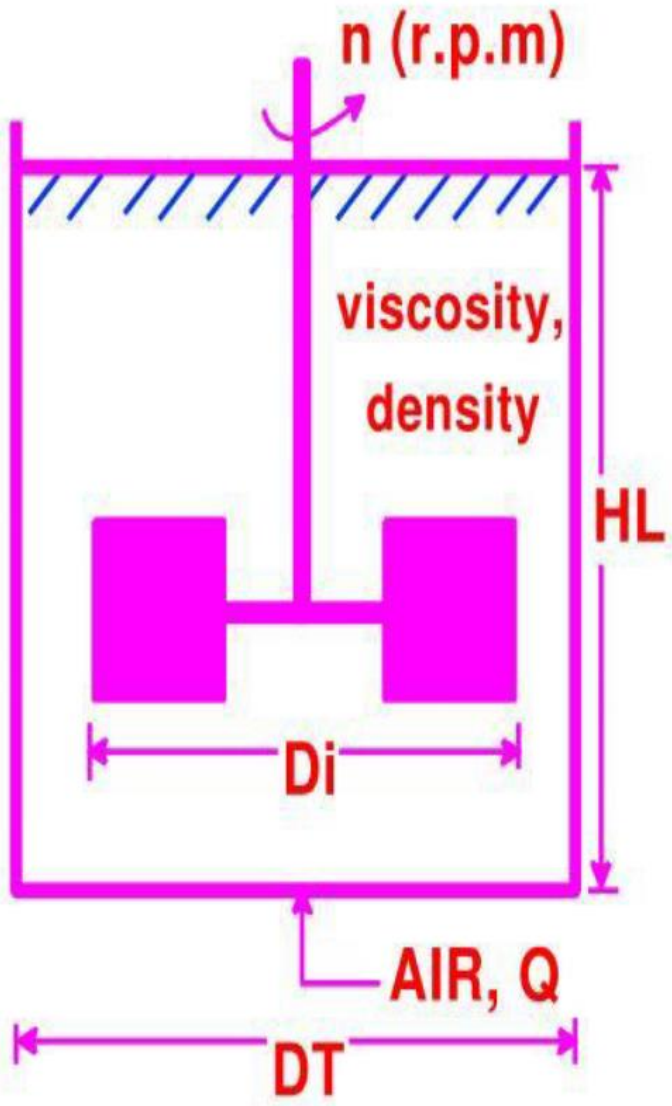
geometric similarity remains

Nutrient composition and also cultivation parameters keep constant during scale-up (T, pH, …..)

Homogeneity over the whole reactor

In general, scale-up criteria are a function of independent variables:

i. Rotational speed, *n or N*
ii. Diameter of impeller, *D*i
iii. Diameter of tank, *D*T
iv. Height of liquid, *H*L
v. Gas flow rate, *Q*g
vi. Liquid viscosity, μ
vii. Liquid density, □



Scale-up criteria for small bioreactor is the same for the large scale bioreactor

The choice of scale-up criteria depends on two considerations:

a) Nature of the fermentation and morphology of the microorganism:

- Aerobic or anaerobic condition
- Single cell microorganisms
- Fungi
- Mammalian or plant cells
- Exothermic fermentation
- Thermophilic microorganisms
- Viscous or non-viscous fermentation broth
- Newtonian or non-Newtonian broth

b) During scale-up, what is the objective parameter of fermentation to be optimized or maximized?

- Yield of product or biomass
- Cell concentration
- Product concentration
- Product activity
- Volumetric bioreactor activity

Basics for scaling-up

Based on this assumptions:

$P_0 \sim N^3 D^5$

$V \sim D^3$

$F \sim N D^3$

P_0 : Stirring power
F: pump capacity of stirrer

Scale-up criteria:

a) $P_0/V \sim N^3 D^2$

b) $F/V \sim N$

c) $v \sim N D$ (velocity of stirrer: tip speed)

d) $Re \sim N D^2$

e) $k_L a \sim (N^3 D^2)^{0.4\text{-}0.7} \sim (N^3 D^2)^{0.5}$

f) $t_m \sim 1/N$

Parameter	Definition	Scale-Up Factor	Why is this Important?
Mixing Time	Amount of time it takes the bioreactor to create a homogeneous environment	$N_2=N_1(D_1/D_2)^{1/4}$ N_2 agitation speed in scale-up N_1 agitation speed in scale-down D_1 impeller diameter of scale - down D_2 impeller diameter of scale-up	•Want to ensure that the materials are well-mixed in a timely manner
Power Input per Volume (P/V)	Amount of power transferred to a volume of cell culture through the agitator shaft and impellers	$P/V \approx N^3/D^2$ P- power supplied V- Volume of Bioreactor N- Agitation Speed D- Impeller Diameter	•Mammalian cells cannot handle a lot of power introduced into the culture media as it can cause small eddies that will shear the fragile cell membranes
Tip Speed	Related to the shear rate produced from the impellers moving through the cell culture media	$N_2=N_1(D_1/D_2)$ N_2 agitation speed in scale-up N_1 agitation speed in scale-down D_1 impeller diameter of scale - down D_2 impeller diameter of scale-up	•High shear rates can cause the cell membrane to tear and the cells to die. •If scale-up based on constant tip speed is attempted, P/V and mixing time will decrease

Basics for scaling-up

Comparison of different strategies for up-scaling with factor 125
Linear factor is 5

Strategy	**P**	**P/V**	**$k_L a$**	**N**	**t_m**	**N D**	**N D^2**
P/V =const	125	1	1	0,34	2.9	1,7	8,5
N = const	3125	25	5	1	1	5	25
v = const	25	0,2	0,4	0,2	5	1	5
Re = const	0,2	0,002	0,04	0,04	25	25	1

Increase of volume: factor 125 (at constant geometric ratio)

Interdependence of scale-up parameters

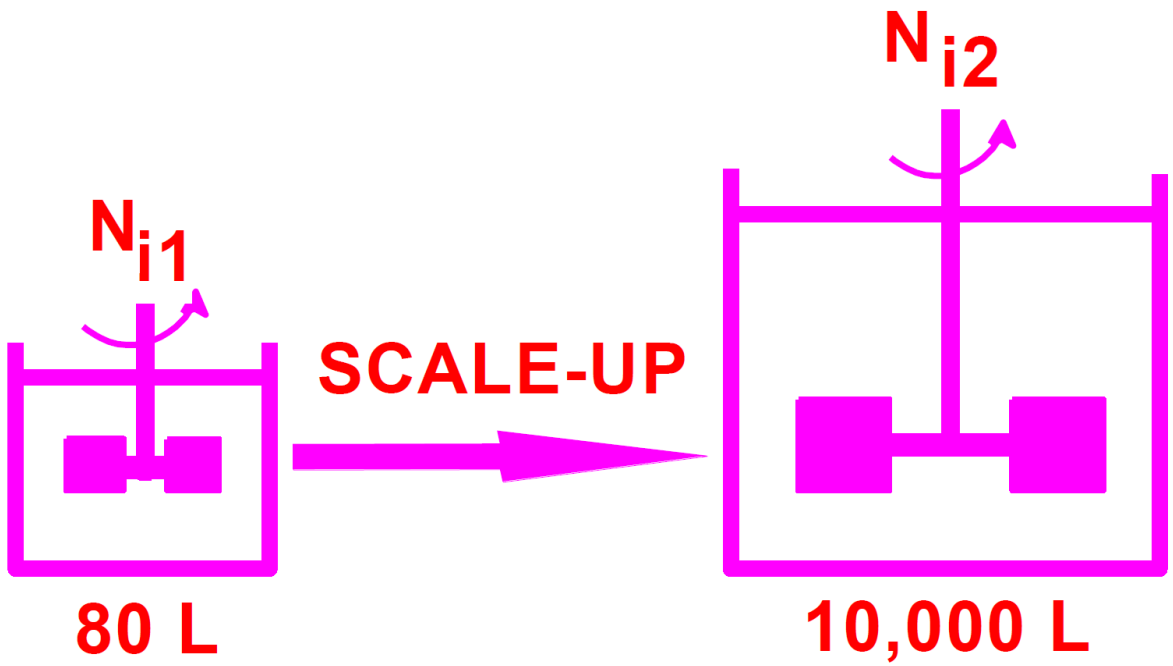
			Production fermenter: 10,000 L			
Scale-up riterion	Designation	Pilot-scale Fermenter 80 L	Constant, P_0/V	Constant, N	Constant, $N.D_i$	Constant, Re
Energy input	P_0	1.0	125	3125	25.0	0.2
Energy input/ volume	P_0/V	1.0	1.0	25	0.2	0.0016
Impeller rpm	N	1.0	0.34	1.0	0.2	0.4
Impeller diameter	D_i	1.0	5.0	5.0	5.0	5.0
Pump rate of impeller	Q	1.0	42.5	125	25.0	5.0
Pump rate of impeller /volume	Q/V	1.0	0.34	1.0	0.2	0.04
Max. impeller speed (max. shear stress)	$N.D_i$	1.0	1.7	5.0	1.0	0.2
Reynold number	$ND_i^2\rho/\mu$	1.0	8.5	25.0	5.0	1.0

Standard geometry vessel was used
and geometric similarity was applied.

- Volumetric scale-up ratio = V2/V1 = 10,000/80 = 125
- Impeller diameter scale-up ratio = Di2/Di1 = 5

As the Table indicates, if the
impeller speed is maintained constant,
the energy input of the impeller(s)
will be 3,125 times higher in the large-scale
fermenter.

It is safe to presume that such a significant
increase can change markedly the
performance of the larger fermenter,
e.g., with oxygen
transfer rates, temperature gradient,



(1) Scale-up Criterion:

$$(P/V_L)_1 = (P/V_L)_2$$

Property	80 L bioreactor	10,000L bioreactor
P (ungassed power)	1.0	125.00
N_i (r.p.m)	1.0	0.34
D_i (imp. diameter) 1.0		5.00
F (pumping rate)	1.0	42.50
F/V_L (liquid circ. rate)	1.0	0.34
N_iD_i (imp. tip speed)	1.0	1.70
N_{Re} (Reynolds No.)	1.0	8.50

Note: $N_{Re} = (N_iD_i^2\rho)/\mu$

Scale-up

Generally bioreactors maintain height to diameter (H/D) of 2:1 or 3:1 (note for STR ideal is 1:1 with respect to liquid height)

If H/D maintained constant during scale-up- surface to volume ratio decreases dramatically (i.e. m^2/m^3)

Result: less important effect of surface aeration, lower heat transfer surface etc.

Wall growth: becomes very important, since at small scale, cells with altered metabolism are common, whereas at larger scale smaller surface area means less important effect, but productivity lower.

If geometrical similarity is maintained then physical conditions must change since N and D_i define all quantities (cf.Table slide 34)

Scale-up

Different scale-up criteria have been used depending on the type of fermentation and the objective of optimization

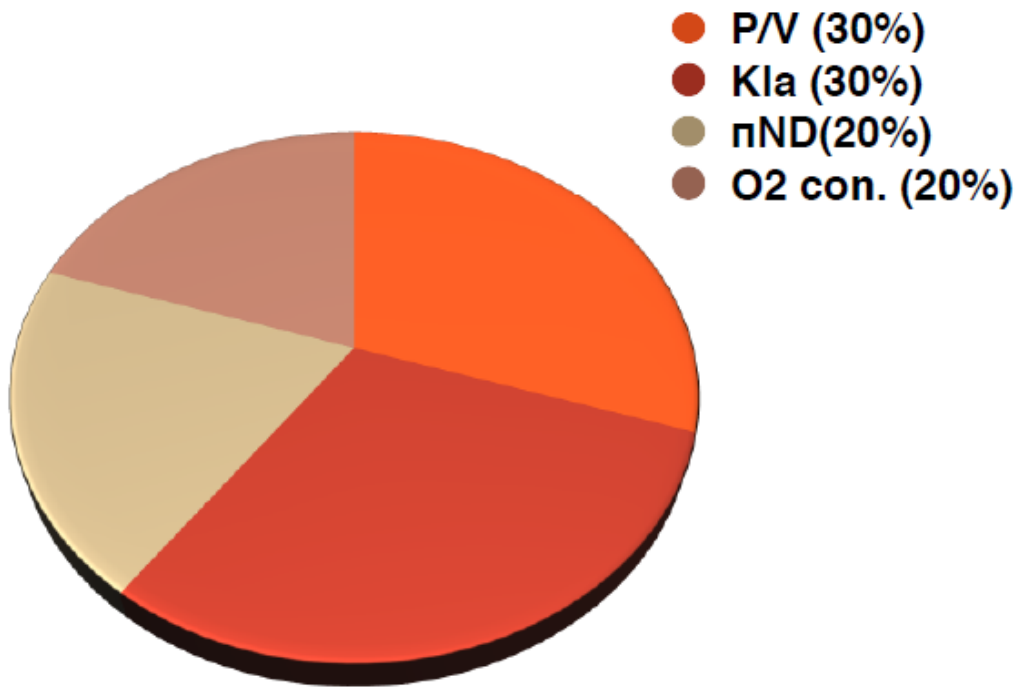
Different scale-up rules can give different results:

Constant P_0/V provides constant OTR
Constant Re provides similar flow patterns
Constant N gives constant mixing times
Constant tip speed gives constant shear

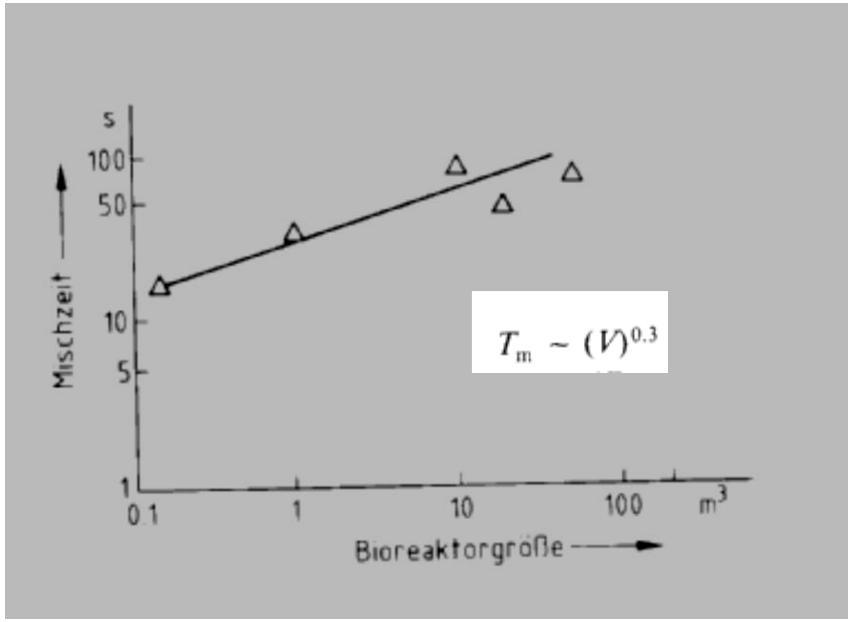
All scale- up problems are linked to transport processes

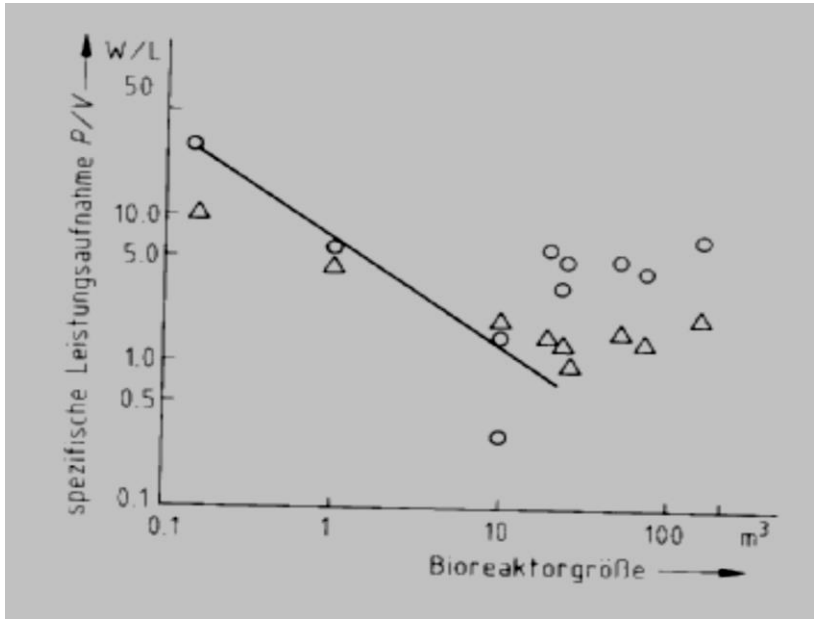
Scale-up criteria

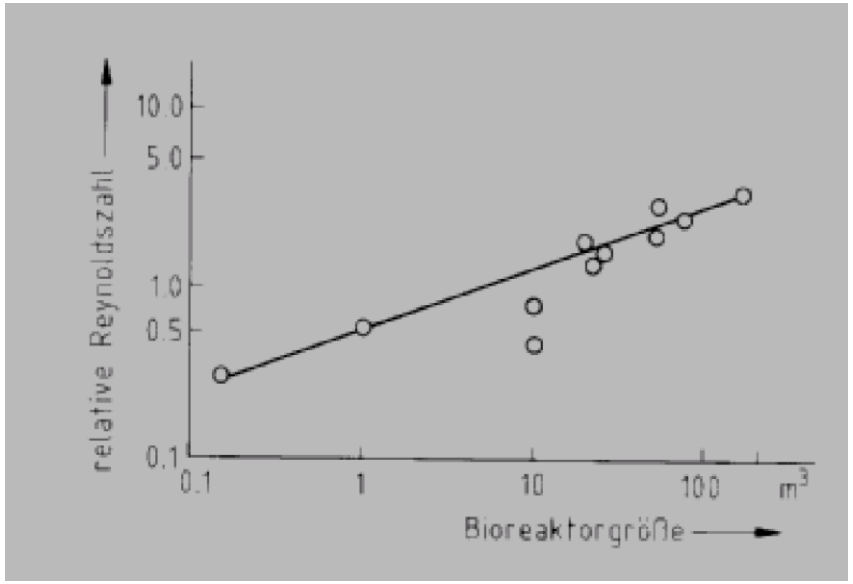
- Constant volumetric mass transfer coefficient(K_La)
- Constant power consumption per unit volume(P/V)
- Constant impeller tip speed(πND)
- Constant Reynolds number(Re)
- Constant dissolved oxygen concentration (pO2)

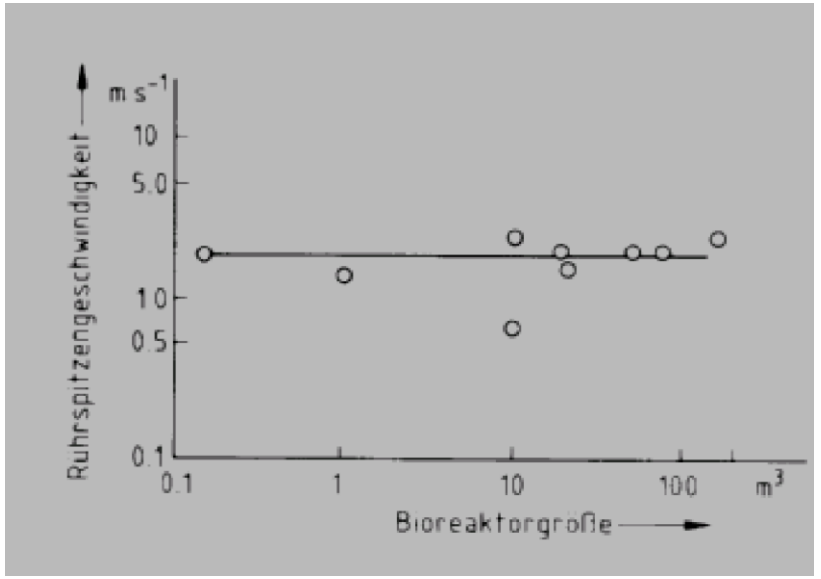


Garcia and Gomez, Biotechnology Advances, 2009


s
100
50
10
5
1
Mischzeit
$T_m \sim (V)^{0.3}$
0.1
1
10
100
m³
Bioreaktorgröße


W/L
50
10.0
5.0
1.0
0.5
0.1
spezifische Leistungsaufnahme P/V
0.1
1
10
100
m³
Bioreaktorgröße


10.0
5.0
1.0
0.5
0.1
relative Reynoldszahl
0.1
1
10
100
m³
Bioreaktorgröße


m s⁻¹
10
5.0
1.0
0.5
0.1
Ruhrspitzengeschwindigkeit
0.1
1
10
100
m³
Bioreaktorgröße

Impeller Reynolds Number

- The Reynolds number based on impeller diameter, D_i is given by:

$$Re = \frac{\rho N D_i^2}{\mu}$$

- Therefore, for a given fermentation broth of given constant physical properties μ und δ

$$Re \propto N D_i^2$$

Constant Power Consumption per unit volume of liquid, P/V

- For power consumption in an agitated vessel, there is a fixed relation between impeller speed (N) and impeller diameter (D_i):

$$\frac{P}{V} = \frac{\rho N^3 D_i^5}{D_i^3} \quad \text{for } Re \geq 10^4$$

- The power per unit volume is constant

- The relations for the impeller size and agitation rate in small and large bioreactors/ fermenters:

$$N_1^3 D_{i,1}^2 = N_2^3 D_{i,2}^2$$

Constant impeller tip velocity, ND_i

- Scale-up calculation is based on constant shear forces, where shear is directly related to impeller tip velocity
- Maximum shear rate is allowed to prevent possible irreversibel shear damage to the cells growing inside the bioreactor
- In some cases where the cells have a tendency to form flocs, it is necessary to provide at least the minimum shear rate required to break-up these flocs

- The impeller is a device where shear forces are transmitted to the fermentation broth

- Since the process is sensitive to high agitation rate, it is necessary that the bioreactor be scaled up, based on shear forces for maximizing product yield

- This is the main reason for keep impeller tip speed constant; in practice , it is recommended that this is in the range of 0.25 – 0.5 m/s

Scale- up of DSP

Rule:

Maintain column height constant, vary diameter to maintain constant linear flow rate

e.g. 10 cm/h

Example 1: Scale - up

After a batch fermentation, the system is dismantled and approx. 75% of the cell mass is suspended in the liquid phase (2 l), while 25% is attached to the reactor walls and internals in a thick film (ca. 0.3 cm). Work with radioactive tracers shows that 50% of the target product (intracellular) is associated with each cell fraction. The productivity of this reactor is 2 g product / L at the 2 L scale.

What would be the productivity at 20000 L scale if both reactors had a heigh-to-diameter ratio of 2 to 1?

Class - Example 2: Scale - up

Consider the scale-up of a fermentation from 10 L to 10000 L vessel. The small fermenter has a height-to-diameter ratio of 3. The impeller diameter is 30% of the tank diameter. Agitator speed is 500 rpm and three Rusthon impellers are used.

Determine the dimensions of the large fermenter and agitator speed for:

a) Constant P/V
b) Constant impeller tip speed
c) Constant Reynold number

Assume geometric similarity

Help: $V = (\pi /4)\, Dt^2\, H$

** ADDITIONAL NOTE:

- **Scale-up based on constant power per unit volume:**

$$\left.\frac{P}{V}\right|_{Small} = \left.\frac{P}{V}\right|_{Large}$$

$$N_1^3 D_{i,1}^2 = N_2^3 D_{i,2}^2$$

- **In scale-up for constant power, the proportional factor for scale-up would be D_i^2:**

$$\frac{P_2}{P_1} = \frac{N_2^3 D_{i,2}^5}{N_1^3 D_{i,1}^5} \qquad \frac{P_2}{P_1} = \left(\frac{D_{i,1}}{D_{i,2}}\right)^2 \left(\frac{D_{i,2}}{D_{i,1}}\right)^5 = \left(\frac{D_{i,2}}{D_{i,1}}\right)^3$$

- **The scale-up for power ratio ends up to be the same scale-up factor for volumetric proportion, i.e.:**

$$\frac{V_2}{V_1} = \left(\frac{D_{i,2}}{D_{i,1}}\right)^3$$

Example 2: The scale-up factor is the cube root of the ratio of tank volumes

Example 3: Scale-down

A stirred-tank bioreactor is to be scaled down from 10m3 to 0.1m3. The dimensions of the large tank are:

D_t = 2 m; D_i = 0.5 m; N = 100 rpm

a) Determine the dimensions of the small tank (D_t, D_i and H by using geometric similarity

b) What would be the required rotational speek of the impeller in the small tank if the following criteria were used?
   i. Constant impeller speed
   ii. Constant impeller Reynolds number

Outlook

- Economics :BioprocessEconomicsEPFL2024 not part of exam.ppt
- DSP: Vorlesung 1 & 2\2022\Bioprocessing Part 2- Separation.mp4
- DSP: Vorlesung 1 & 2\2022\Bioprocessing Part 3- Purification.mp4