

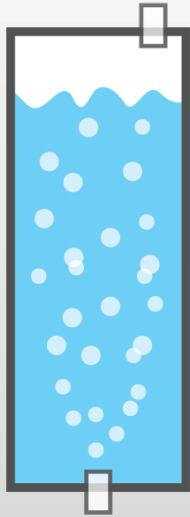
Fermenter operation

Technology for biobased products

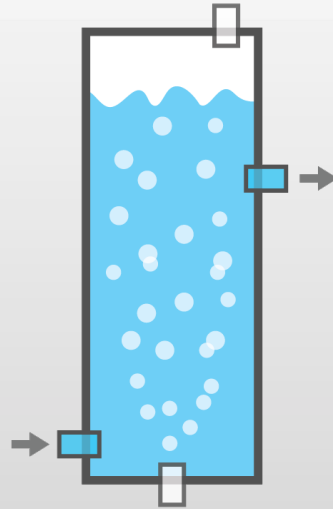
Henk Noorman, DSM / Department of Biotechnology, Faculty of Applied Sciences

Fermenter operation

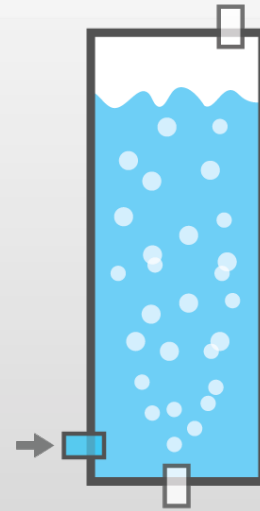
Different modes



Batch



Continuous
(chemostat)



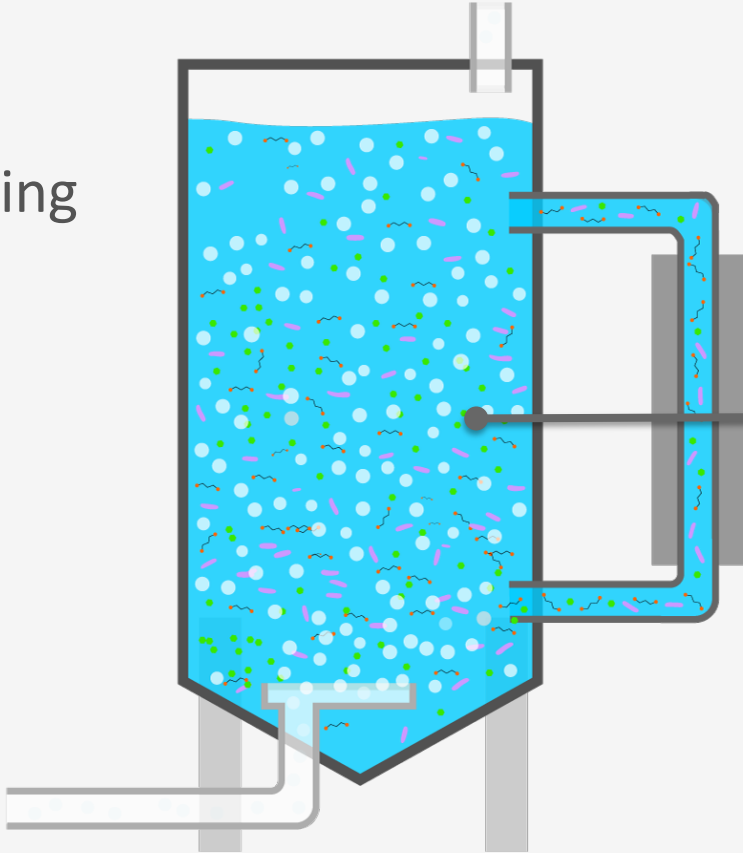
Fed-batch

Batch

No feeding

No removal

All nutrients
in excess



Batch

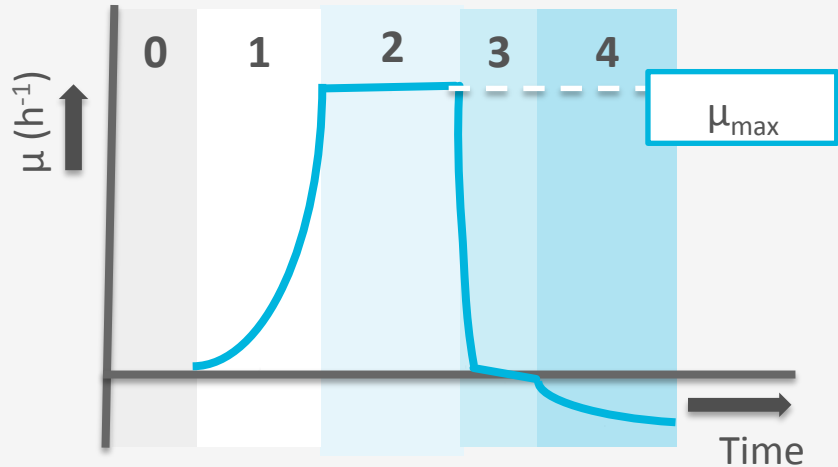
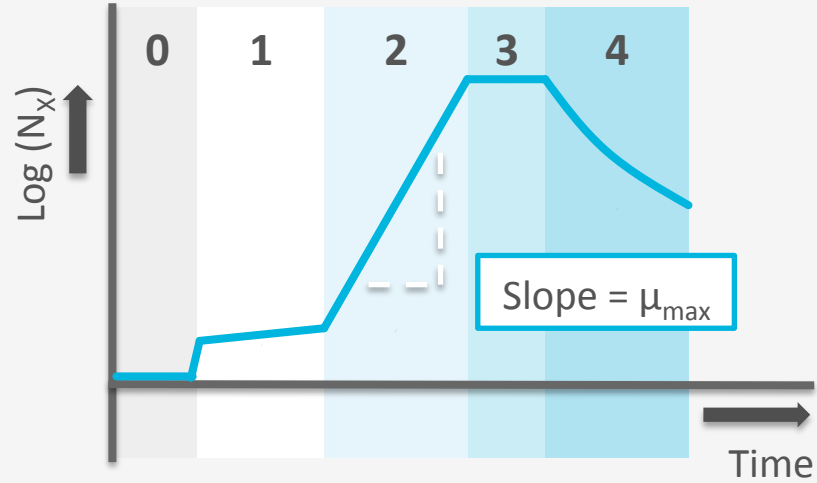
0 All nutrients in excess,
before inoculum

1 Inoculum added, lag phase
Adaptation period, $\mu < \mu_{\max}$

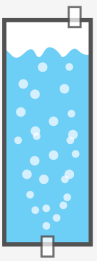
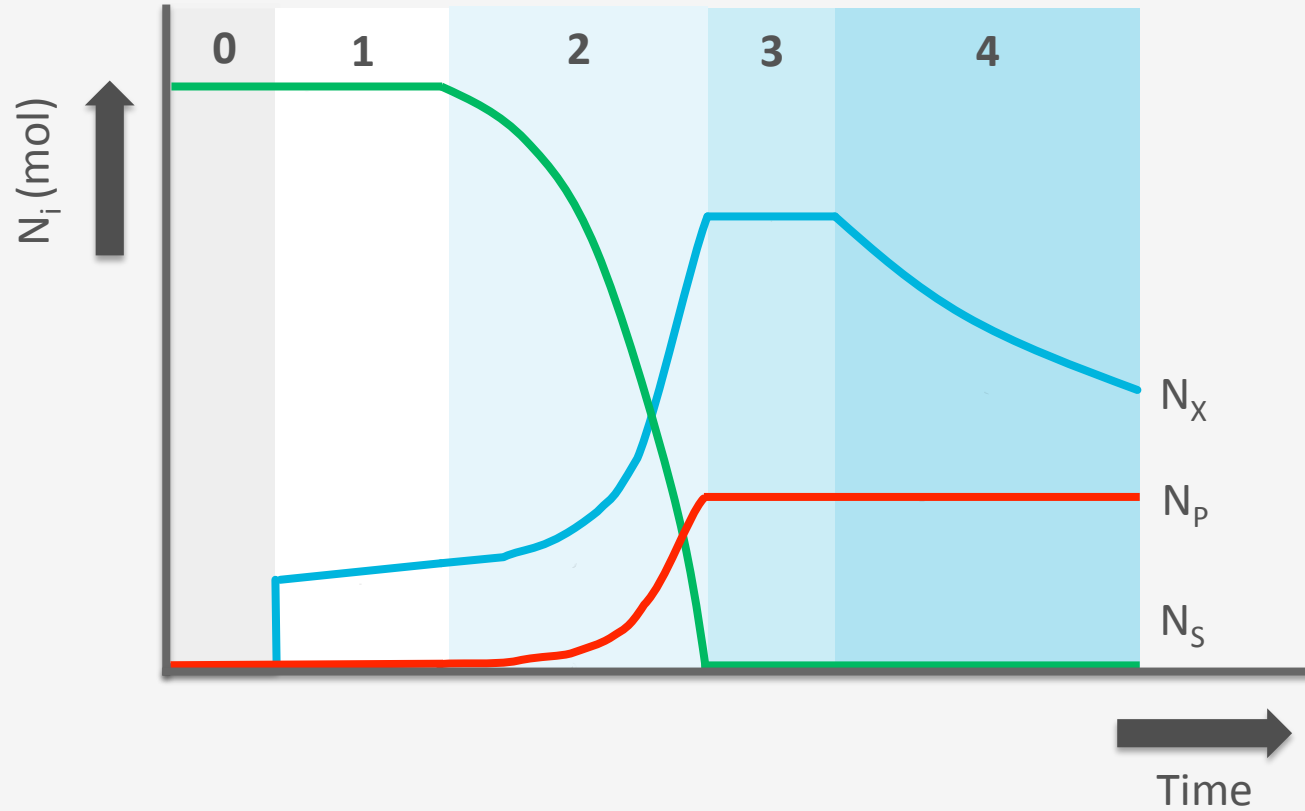
2 Exponential growth phase
Substrate in excess, $\mu = \mu_{\max}$

3 Stationary phase
Substrate depleted, $\mu = 0$

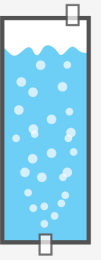
4 Death phase
Cells start to die, $\mu < 0$



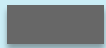
Batch



Batch



Simple
High growth rate cells
Short process



Limited control environment
Max growth rate is usually
not max production

Batch



Biomass balance:

$$\frac{d(V_L(t)c_x(t))}{dt} = \mu(t)V_L(t)c_x(t) + F_{in}C_{x,in} - F_{out}C_{x,out}$$

No in and outflow

$$\mu(t) = \mu_{max}$$

$$\frac{dN_x(t)}{dt} = \mu_{max}N_x(t)$$

$$N_x(t) = N_x(0)e^{\mu_{max}t}$$

Batch



Biomass balance:

$$\frac{d(V_L(t)c_x(t))}{dt} = \mu(t)V_L(t)c_x(t)$$

$$N_x(t) = V_L(t)c_x(t)$$

$$\mu(t) = \mu_{max}$$

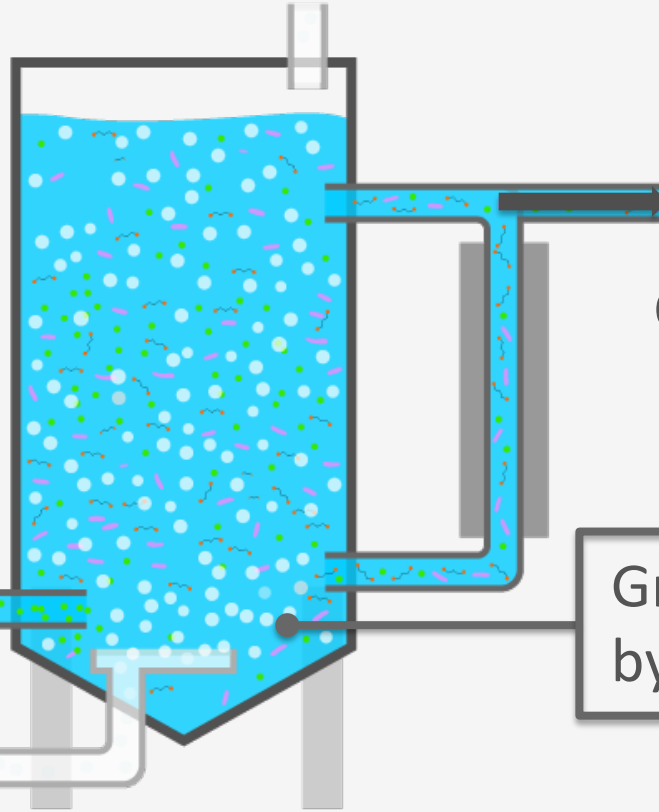
$$\frac{dN_x(t)}{dt} = \mu_{max}N_x(t)$$

$$N_x(t) = N_x(0)e^{\mu_{max}t}$$

Chemostat

Continuous feeding

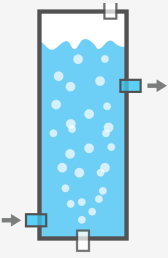
Nutrients
and feedstock



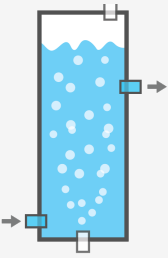
Continuous removal

Fermentation
broth

Growth rate determined
by dilution rate



Chemostat



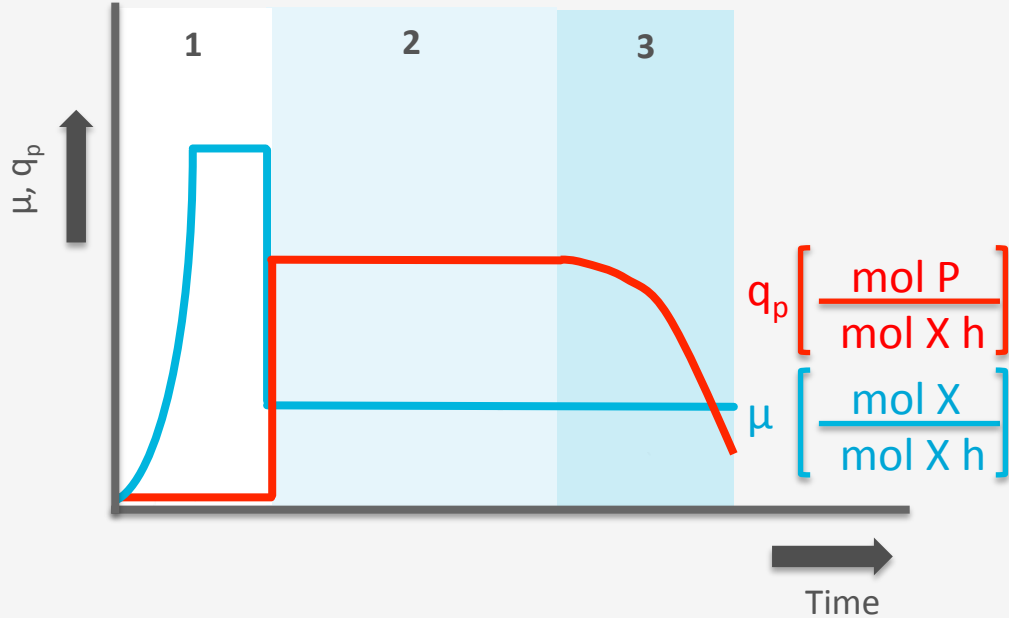
1 **Start-up phase (batch)**

$$\mu = \mu_{\max}, q_p = \text{low}$$

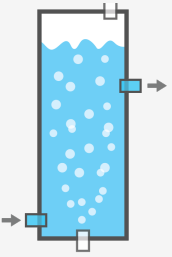
2 **Steady state phase**

$$\mu = \mu_{\text{opt}}, q_p = q_{p,\text{opt}}$$

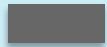
3 **$q_{p,\text{opt}}$ decreases**



Chemostat

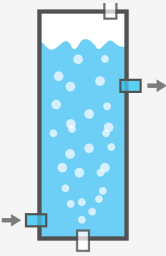


- Steady state
- Controlled environment
- Optimal production conditions



- Takes time to start up
- Loss of production capacity
- Contamination risk

Chemostat



Biomass balance:

Steady state

$$\frac{dV_L(t)c_x(t)}{dt} \left[\frac{\text{mol}}{\text{h}} \right] = \underbrace{\mu V_L c_x}_{V_L c_x} \left[\frac{\text{mol}}{\text{h}} \right] + F_{in} c_{x,in} \left[\frac{\text{mol}}{\text{h}} \right] - F_{out} c_{x,out} \left[\frac{\text{mol}}{\text{h}} \right]$$

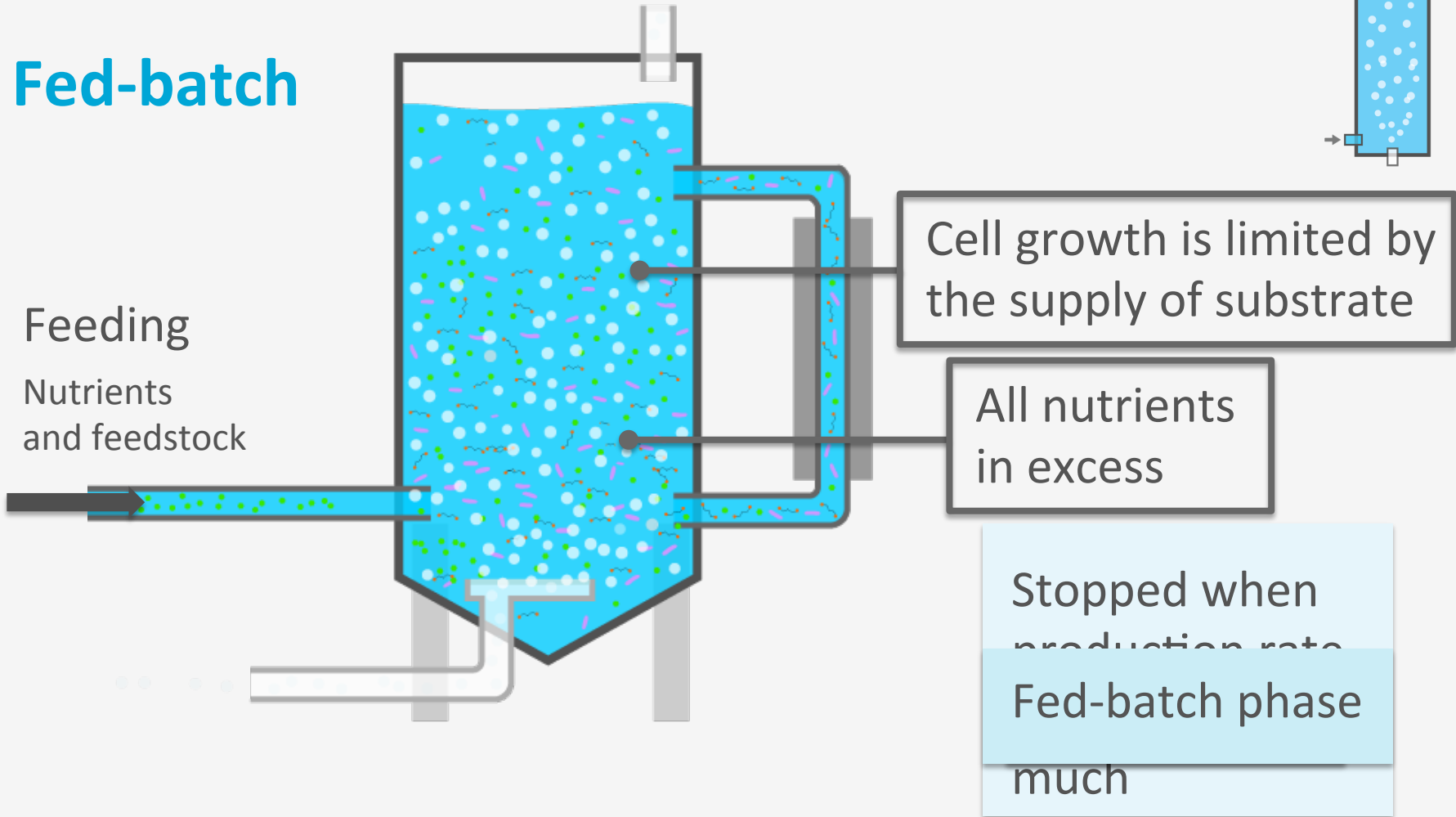
[mol X present in the vessel]

Ideal broth outflow: $c_{x,out} = c_x$
Biomass concentration inflow: $c_{x,in} = 0$

Dilution rate:

$$\mu_{SS} = D = \frac{F_{out}}{V_L} \left[\frac{\text{m}^3/\text{h}}{\text{m}^3} \right]$$

Fed-batch



Fed-batch

1

Start-up phase (batch)

$$\mu = \mu_{\max}$$

2

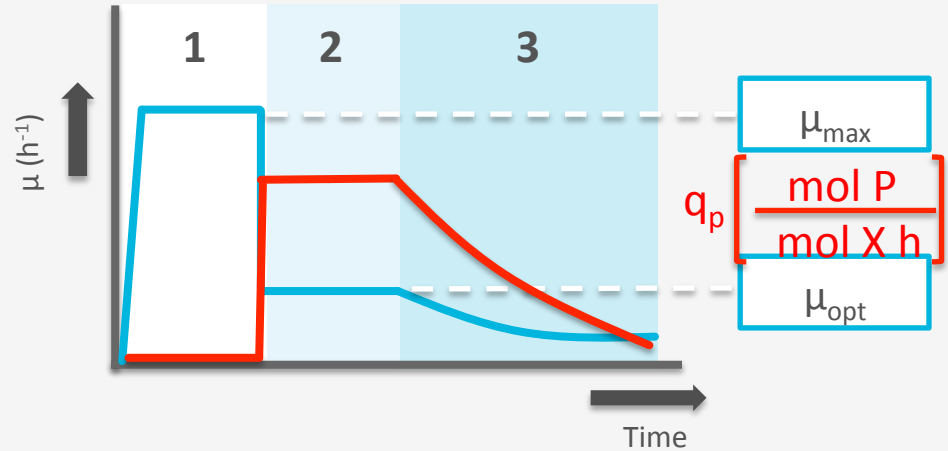
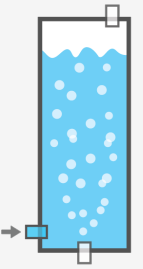
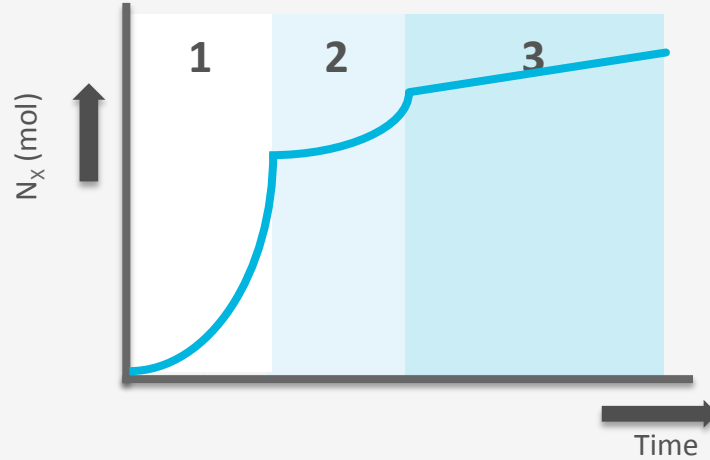
Feed phase

$$\mu = \mu_{\text{opt}}$$

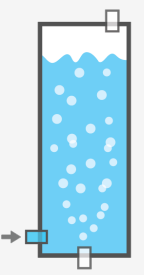
3

Transport limitation

$$\mu < \mu_{\text{opt}}$$



Fed-batch

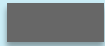


Simple set-up

Long cycles

Good conditions for production

High product titer

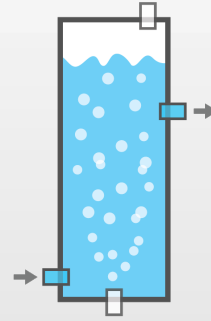


Not as optimal as chemostat

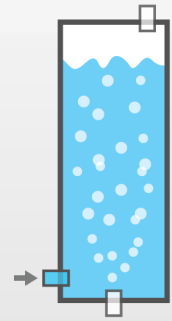
Operation in industry



Batch



Chemostat



Fed-batch

Operation time	+	+++	++
Maintaining sterility	+++	+	++
Product titer	+	++	+++
Productivity	+	+++	++
Employed in industry	++	+	+++

See you in the next unit!