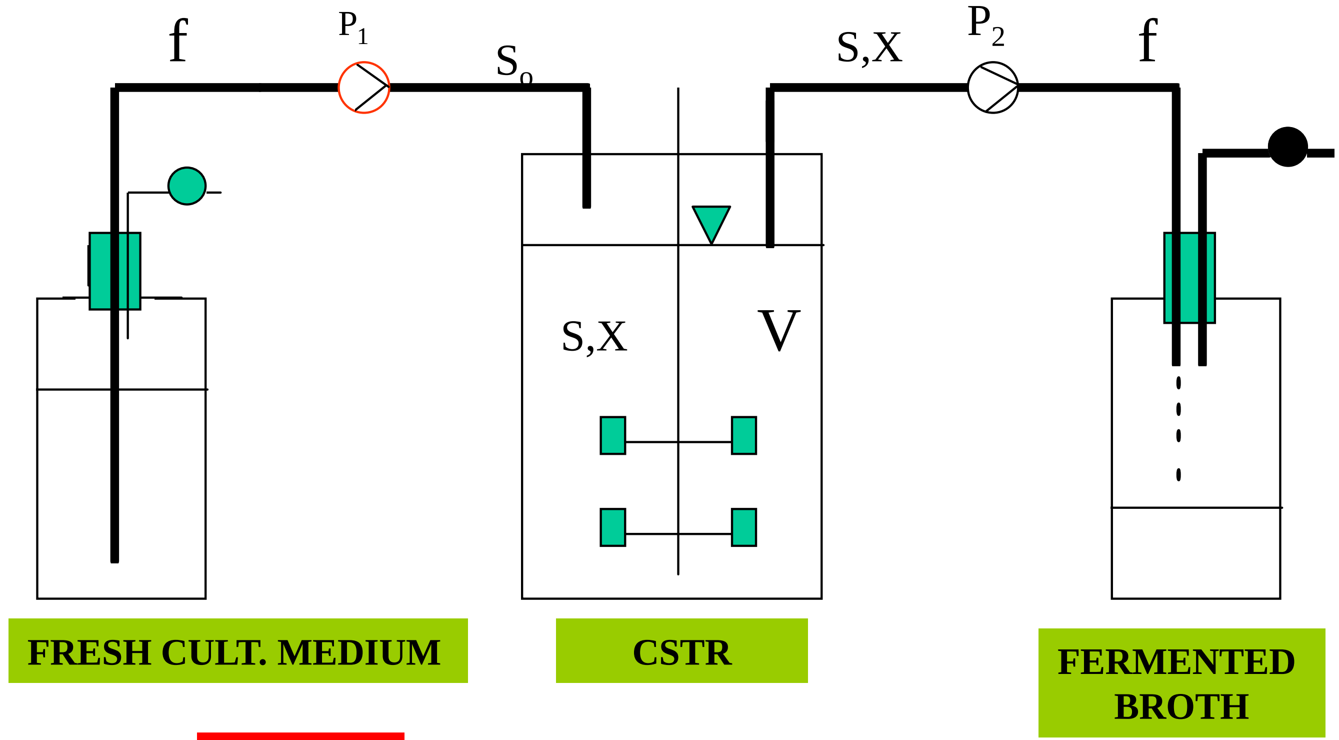
CONTINUOUS FERMENTATION



P-pump

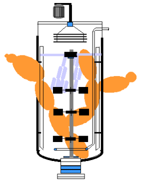
Cell mass:

$$V\frac{dx}{dt} = V\left(\frac{dx}{dt}\right)_{growth} - f.x$$

i^{th} substrate:

$$V\frac{dS_i}{dt} = fS_{i,0} - fS_i - V\frac{1}{Y_{x/S_i}}\left(\frac{dx}{dt}\right)_{growth}$$

$$\frac{f}{V} = D$$



CONTINUOUS FERMENTATION

$$\frac{f}{V} = D$$

f: $\mathbf{m^3/h}$

V: $\mathbf{m^3}$

D: $\mathbf{h^{-1}}$

Higítási sebesség
Dilution rate

$$\frac{1}{D} = \bar{t}$$

$\mathbf{h}$

Átlagos tartózkodási idő
Mean residence time

CONTINUOUS FERMENTATION

In the case of one limiting S (if MONOD model holds):

$$\frac{dx}{dt} = \mu x - Dx = (\mu - D)x = \left(\mu_{max}\frac{S}{K_S + S} - D\right)x$$

$$\frac{dS}{dt} = D(S_0 - S) - \frac{\mu x}{Y}$$

Necessary and enough condition of the steady state

$\mu = D$

In steady state

$$\frac{dx}{dt} = 0 \quad \text{and} \quad \frac{dS}{dt} = 0$$

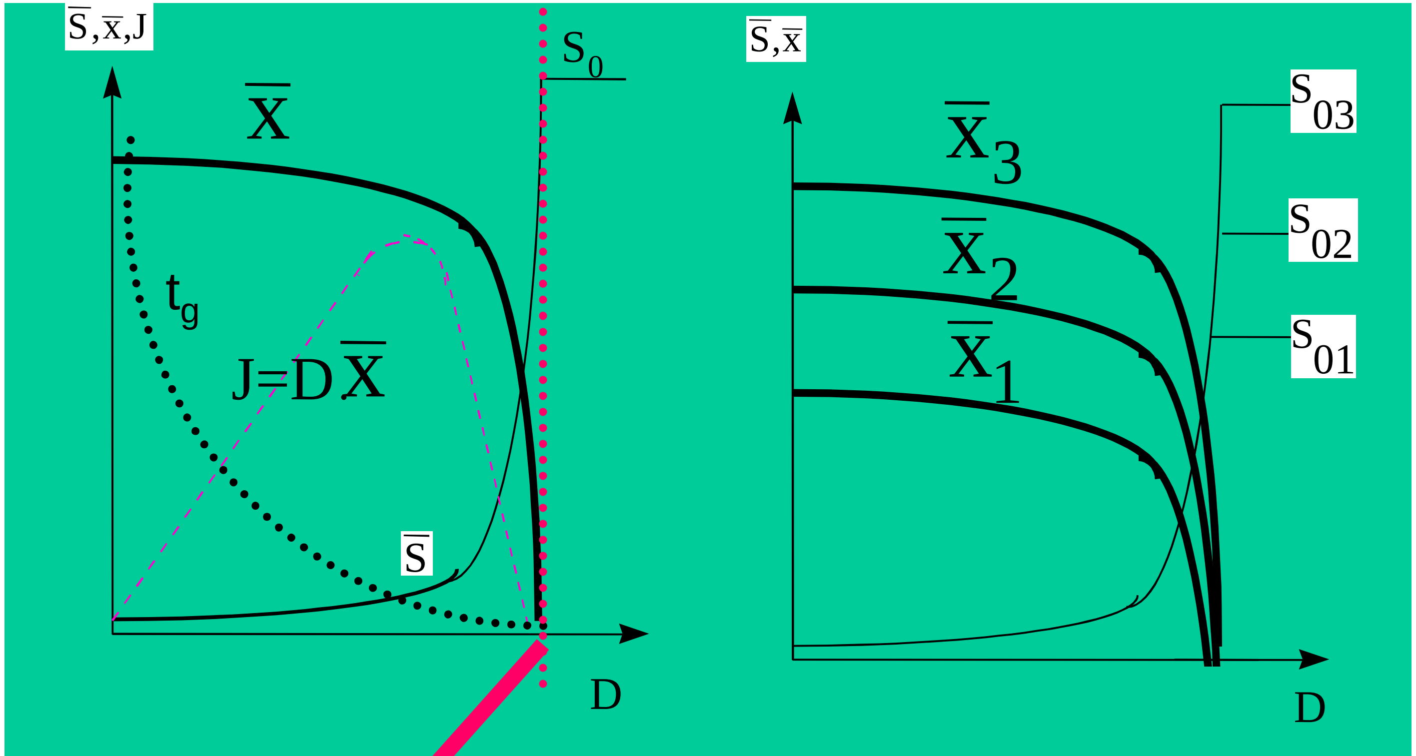
$$D = \mu_{max}\frac{S}{K_s + S} \Rightarrow \overline{S} = \frac{K_s D}{\mu_{max} - D}$$

CHEMOSTAT

$$D(S_0 - \overline{S}) = \frac{\mu x}{Y}$$

$$\overline{x} = Y(S_0 - \overline{S}) = Y\left(S_0 - \frac{K_S D}{\mu_{max} - D}\right)$$

CONTINUOUS FERMENTATION



$$\mu = D_{CRITICAL} = \mu_{max}\frac{S_0}{S_0 + K_S} \cong \mu_{max}$$

(corresponds to the declining phase)

CONTROLL VARIABLES OF THE CHEMOSTAT

V	**ONLY TECHNICAL CONSTRAINT**
f	
D	$< \mu_{max} = D_C$
S_0	**ONLY TECHNICAL CONSTRAINT: solublity**

CONTINUOUS FERMENTATION

$$J = D.x \quad [g/l.h] \quad \text{or} \quad [kg/m^3h]$$

$$J = D.\bar{x} = D.Y\left(S_0 - \frac{K_S D}{\mu_{max} - D}\right) = \textbf{max!!!}$$

$$\frac{\partial J}{\partial D} = 0 \longrightarrow D_{max} = \mu_{max}\left(1 - \left(\frac{K_S}{S_0 + K_S}\right)^{1/2}\right)$$

$$\bar{x}_{max} = Y\left[S_0 + K_S - \sqrt{K_S(S_0 + K_S)}\right]$$

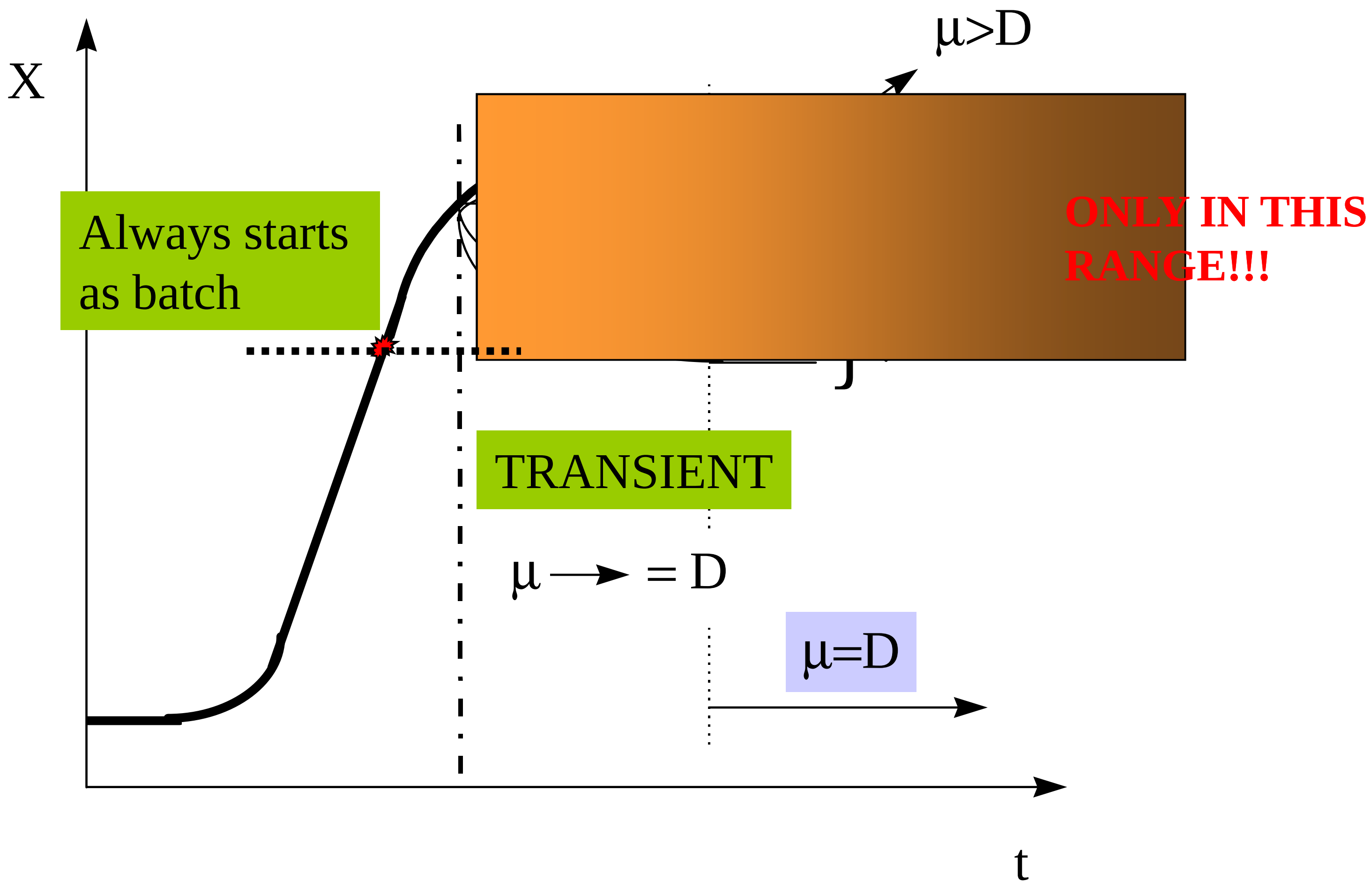
$$= D_{max}\bar{x}_{max} = \mu_{max} Y\left[1 - \left(\frac{K_S}{K_S + S_0}\right)^{1/2}\right].\left[K_S + S_0 - \sqrt{K_S(S_0 + K_S)}\right] =$$

$$= Y\mu_{max} S_0\left(\sqrt{\frac{K_S + S_0}{S_0}} - \sqrt{\frac{K_S}{S_0}}\right)^2$$

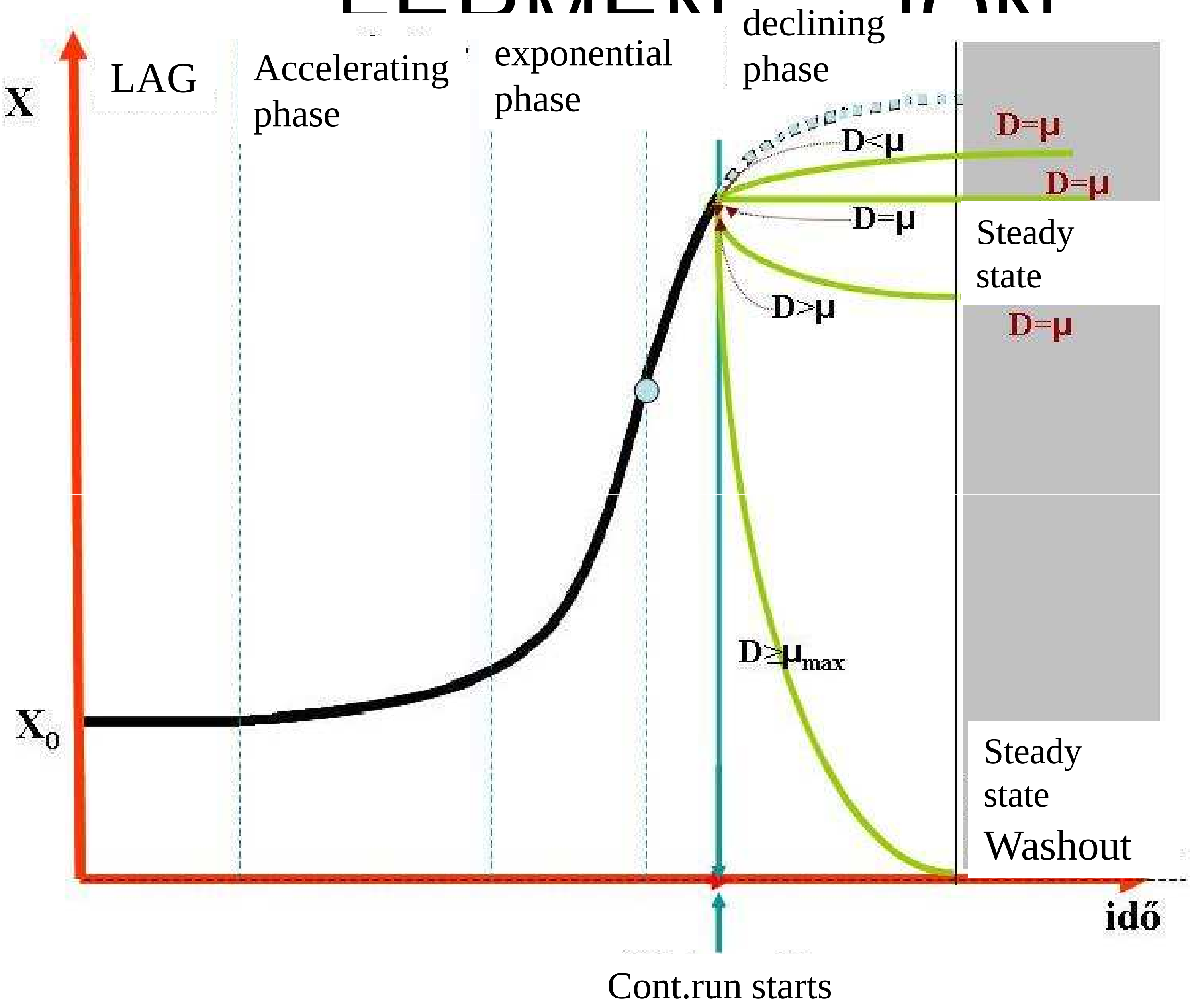
CONTINUOUS FERMENTATION

Transient behaviour

1.After start: transient from bach to continuous operation



CONTINUOUS FERMENTATION

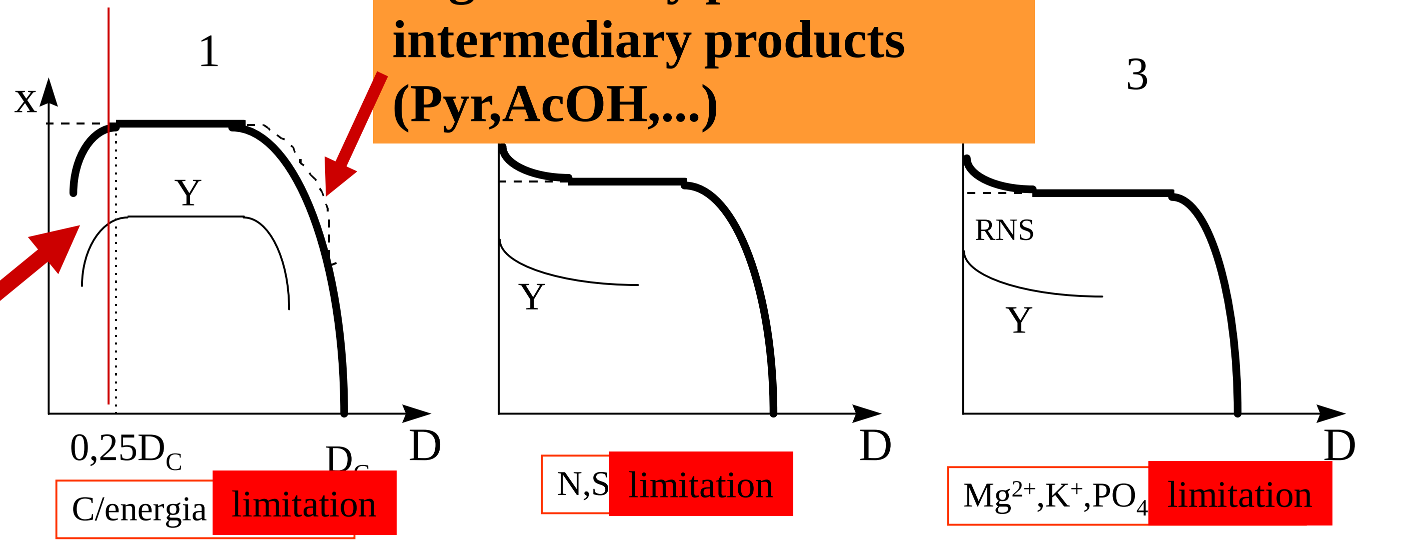


CONTINUOUS FERMENTATION

Alterations from ideal behaviour

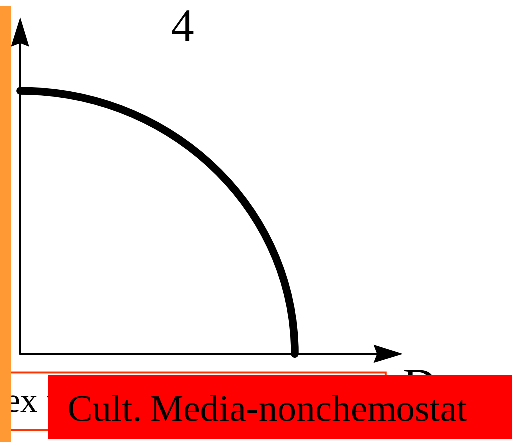
High velocity production of intermediary products (Pyr,AcOH,...)

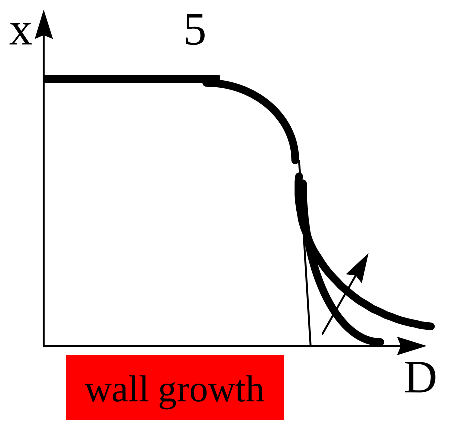
$D<0{,}25D_C$



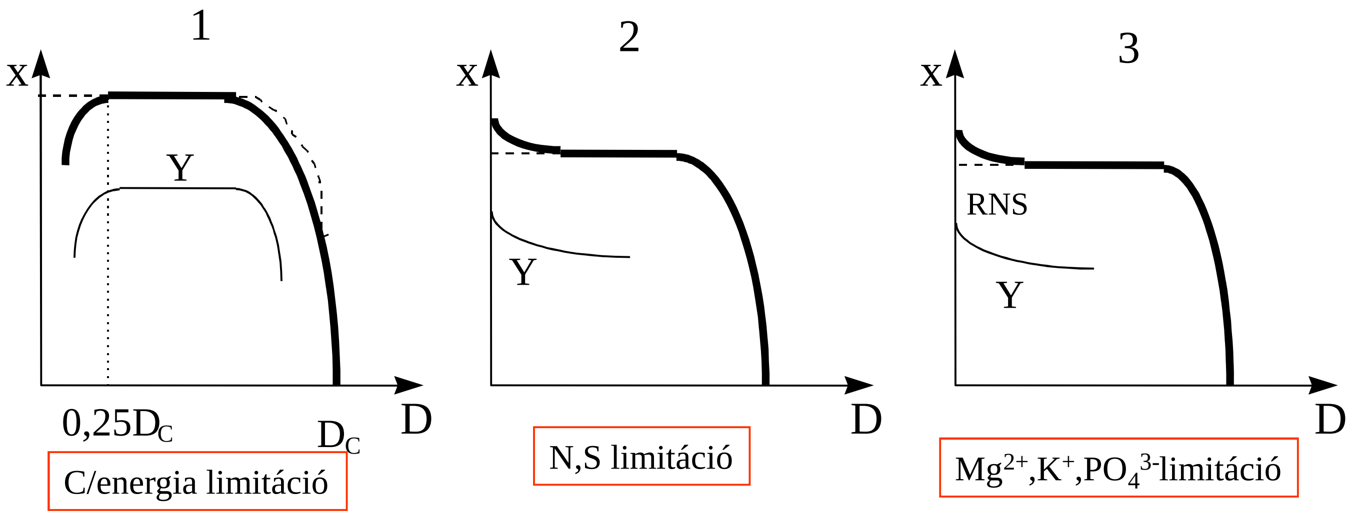
$$\frac{dS}{dt} = D(S_0 - S) - \left(\frac{1}{Y_C} - \frac{1}{Y_{EG}} - \frac{m}{\mu}\right)\mu x$$

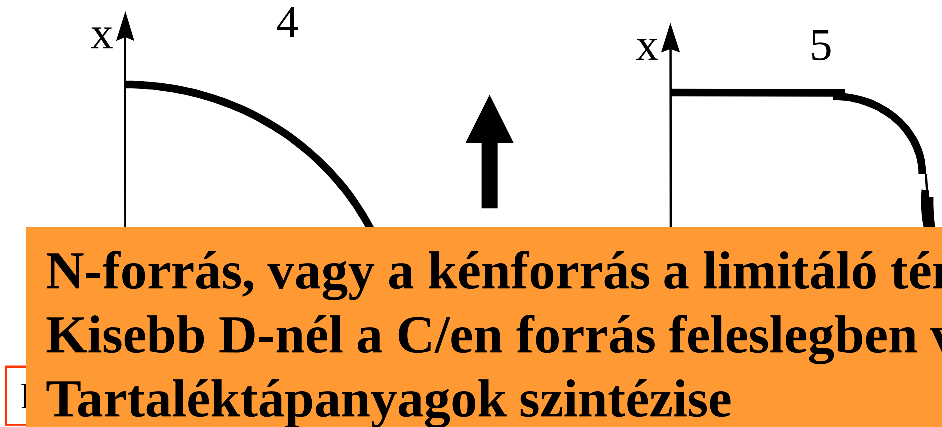
$$x = \frac{\left(S_0 - \dfrac{K_S D}{\mu_{max} - D}\right)}{\left(\dfrac{1}{Y_C} - \dfrac{1}{Y_{EG}} - \dfrac{m}{\mu}\right)}$$





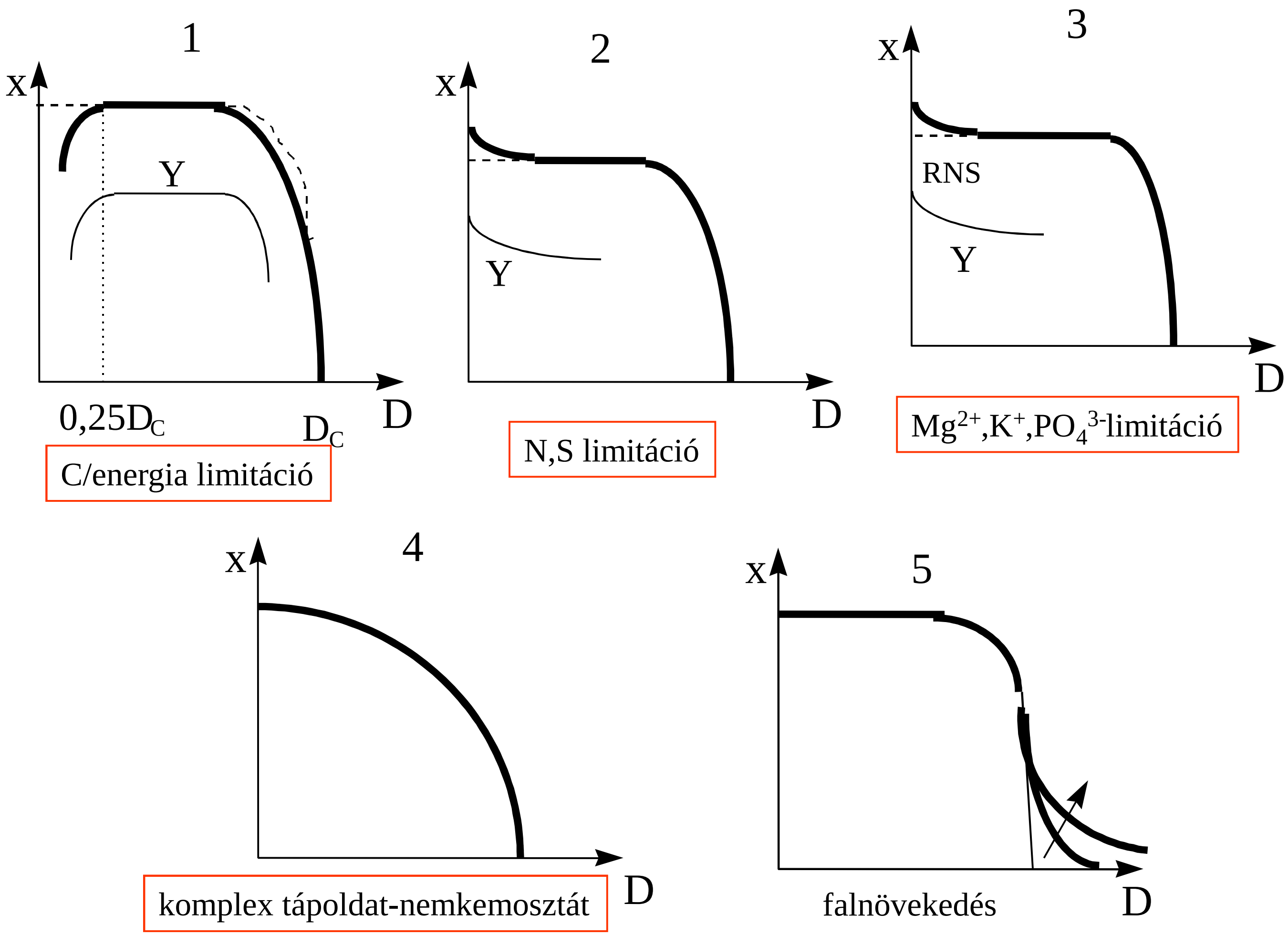
CONTINUOUS FERMENTATION



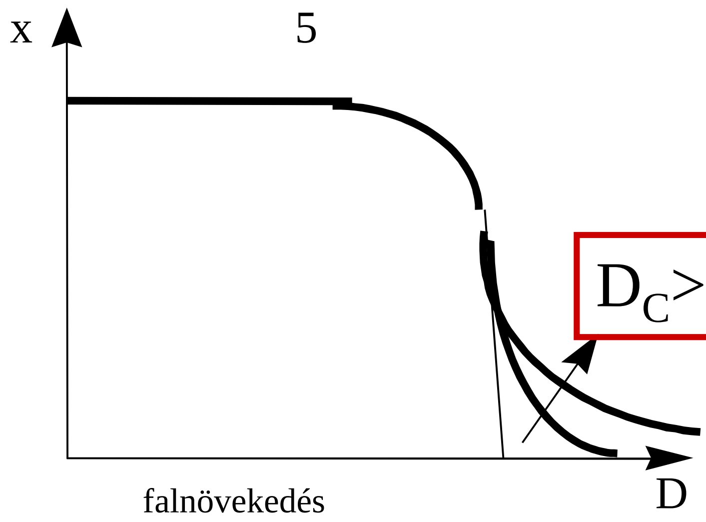


N-forrás, vagy a kénforrás a limitáló tényező
Kisebb D-nél a C/en forrás feleslegben van:
Tartaléktápanyagok szintézise
(poliszaharidok,lipidek, β-OH-butirát)

CONTINUOUS FERMENTATION



CONTINUOUS FERMENTATION



$D_C > \mu_{max}$ is elérhető!

$$D\bar{x} = \mu\bar{x} + \mu\bar{x}_f$$

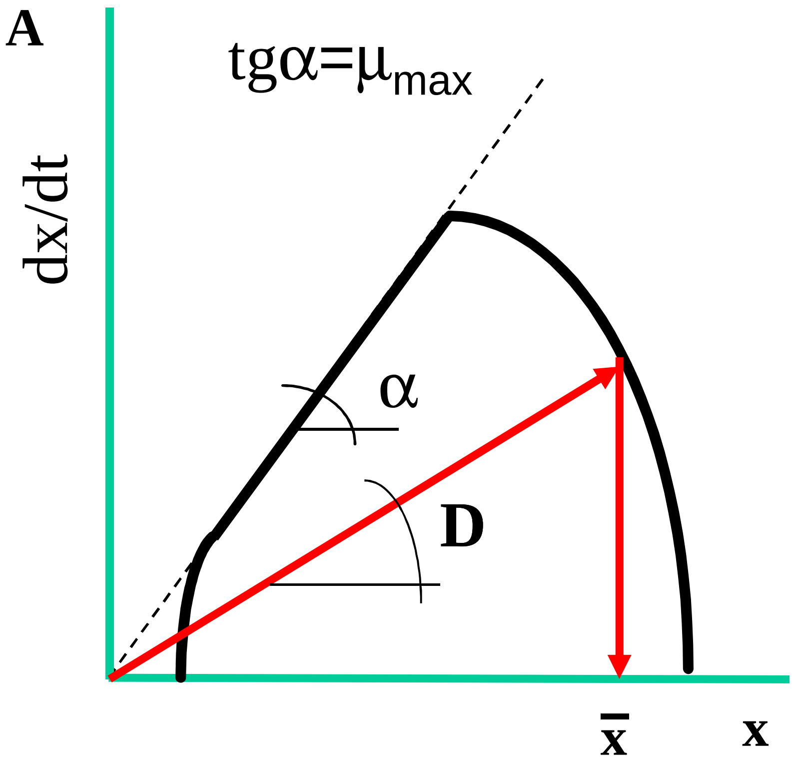
$$D\left(S_0 - \bar{S}\right) = \left(\mu\bar{x} + \mu\bar{x}_f\right) / Y_{x/S}$$

$$\bar{x} = Y_{x/S}\left(S_0 - \bar{S}\right)$$

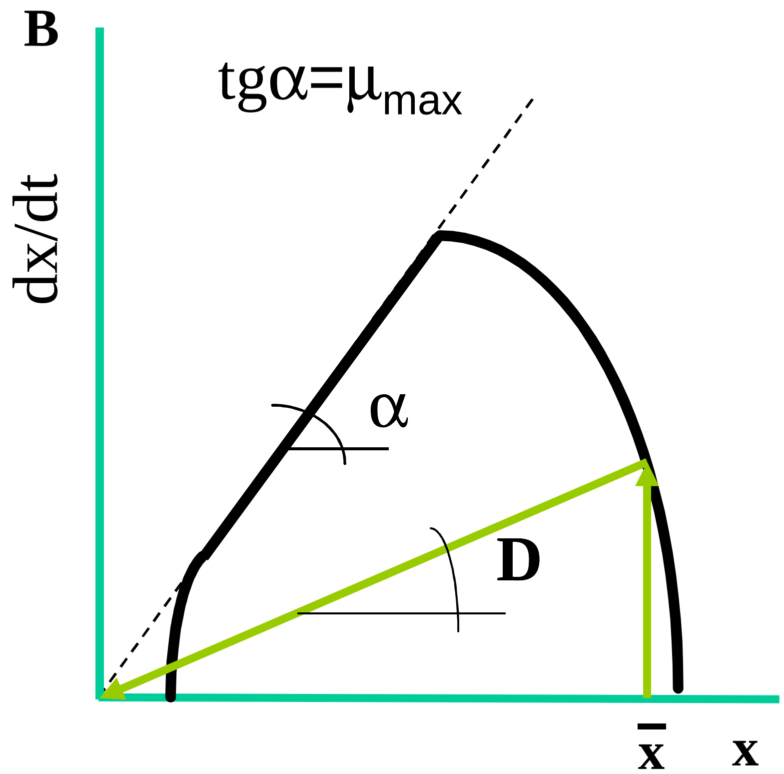
$$D = \mu\left(1 + \frac{\bar{x}_f}{\bar{x}}\right)$$

Design of the chemostat

1.Known batch kinetics: μ_{max}, Y, K_S D
2.Known batch growth curve (and derivative)



choose D-t, what is x?



Choose x,
What is the necessary D?

CONTINUOUS FERMENTATION

Problems

Volume control **aeration,foaming**

USE OF CHEMOSTAT?

ADVANTAGES: higher productivity
balanced, limited growth
measurment and control

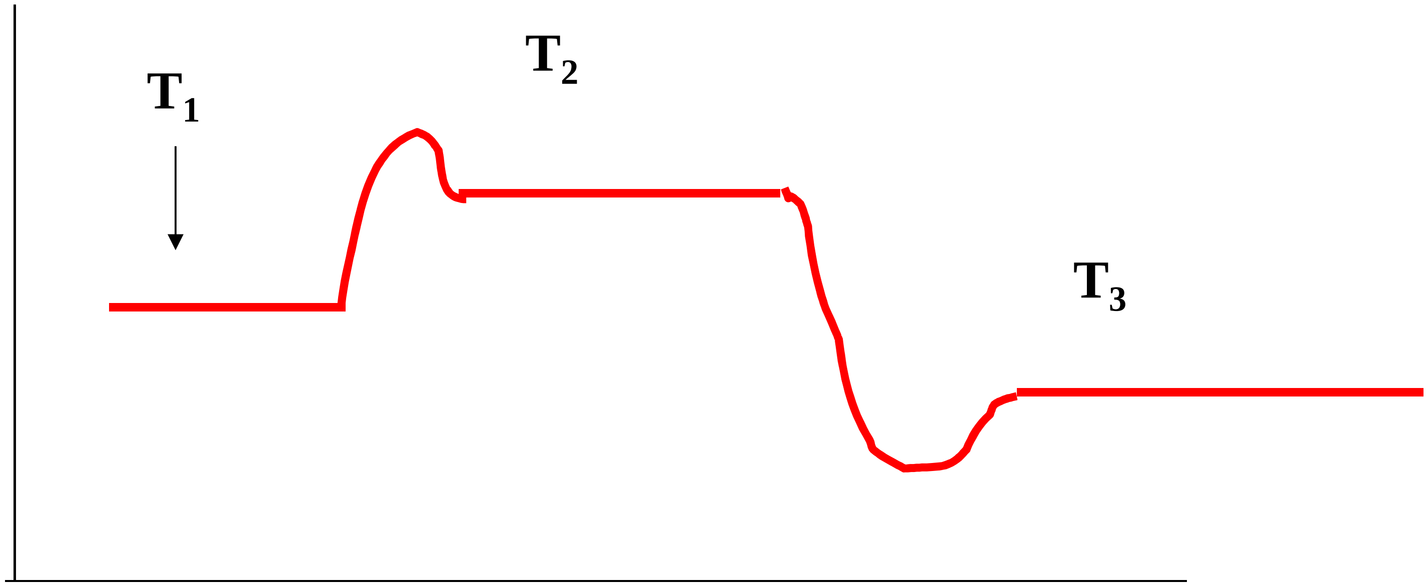
SCP, bakers yeast, fodder yeast, (cell mass), primery metabolites:
alcohol, beer

research: kinetics, optimization,

but: secondery no, though penicillin...in lab scale

CONTINUOUS FERMENTATION

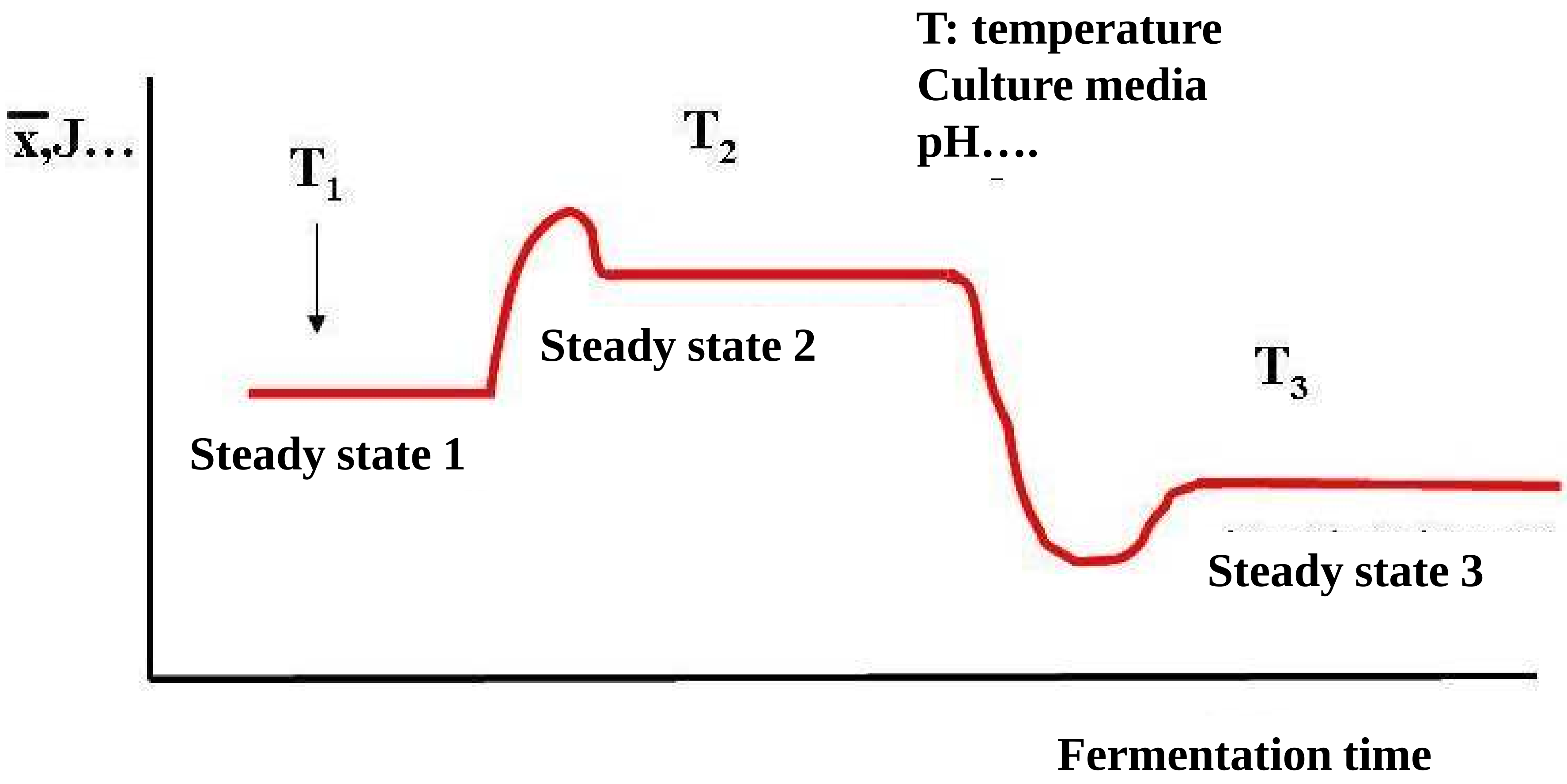
OPTIMIZATION



T: TEMPERATURE
CULTURE MEDIA...

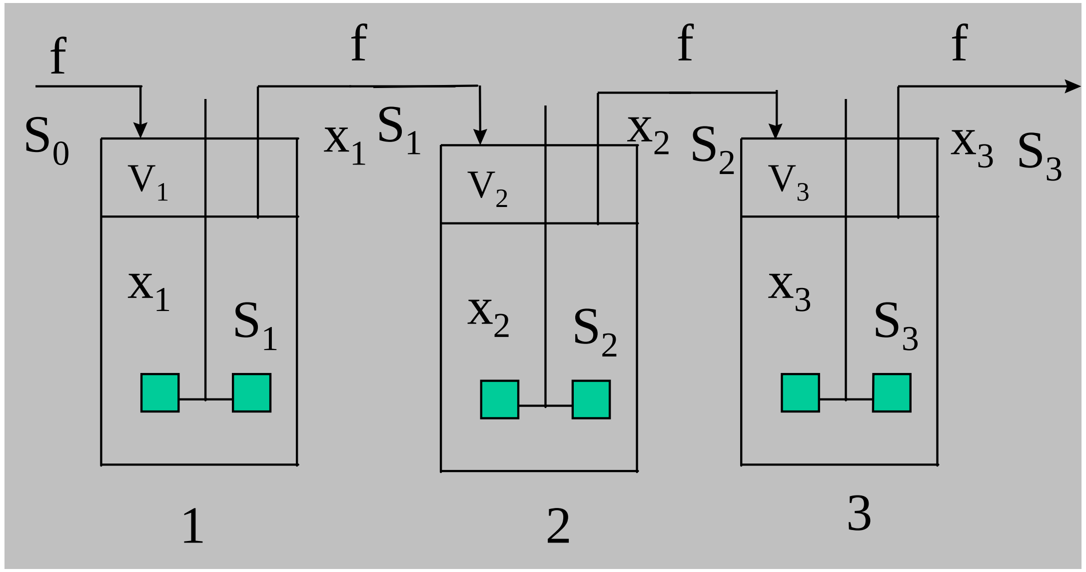
CONTINUOUS FERMENTATION

CONTINUOUS FERMENTATION

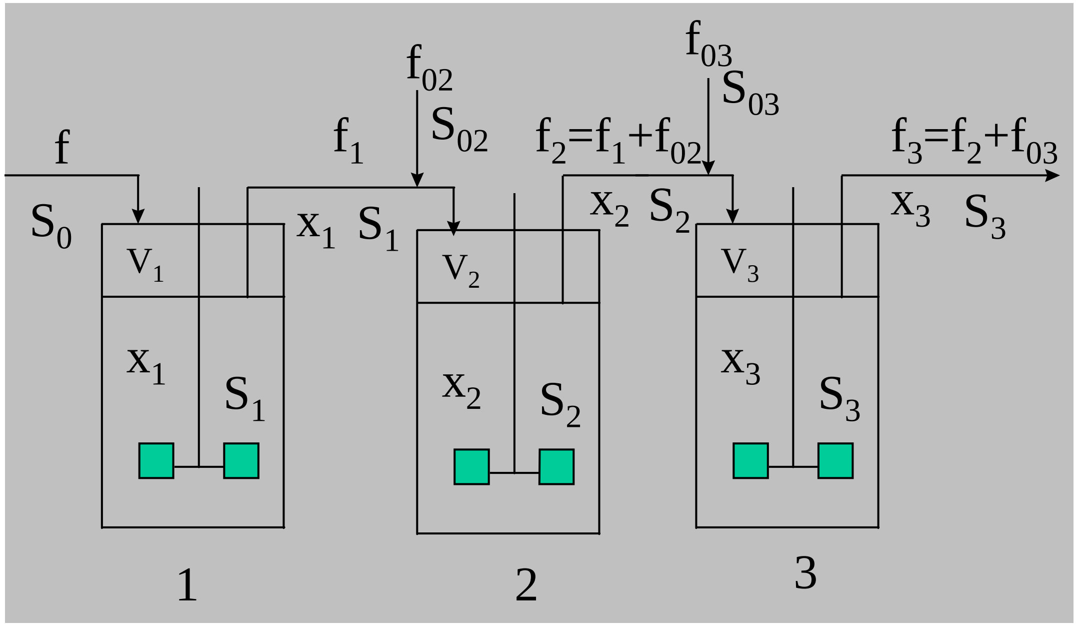


CONTINUOUS FERMENTATION

One stream, multiple stage

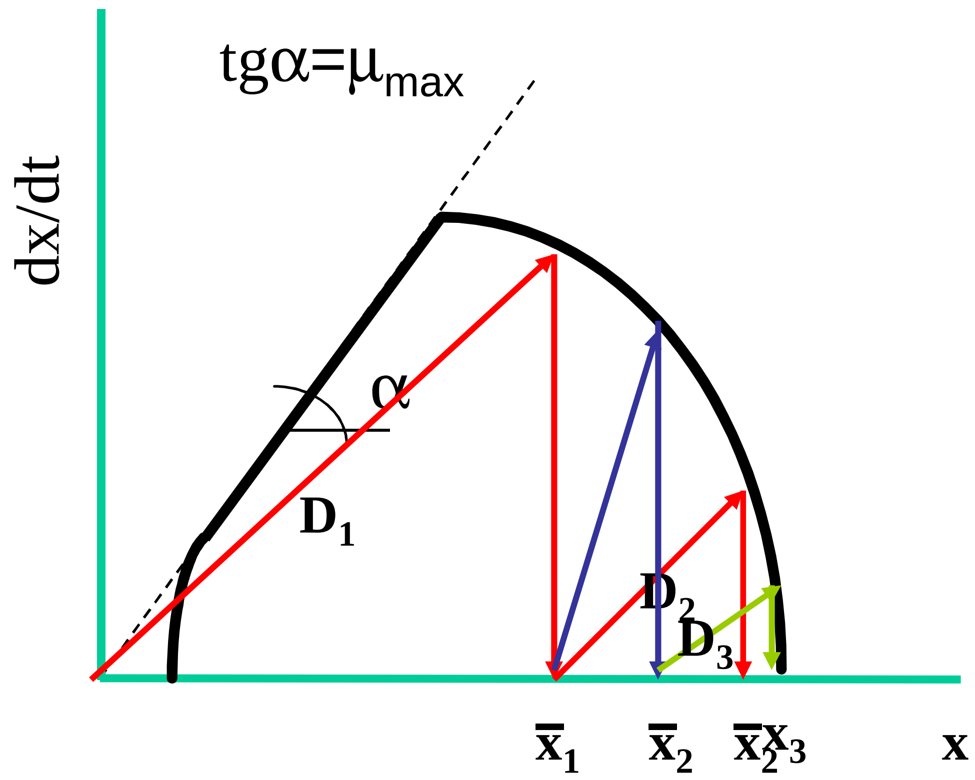


Multiple stream, Multiple stage



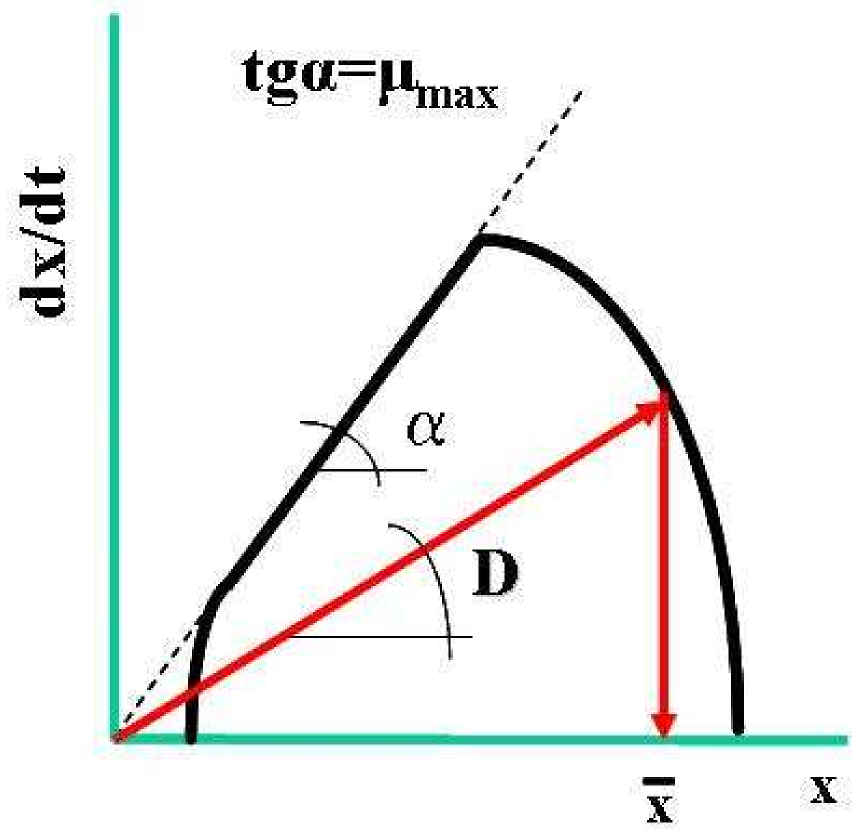
CONTINUOUS FERMENTATION

design:



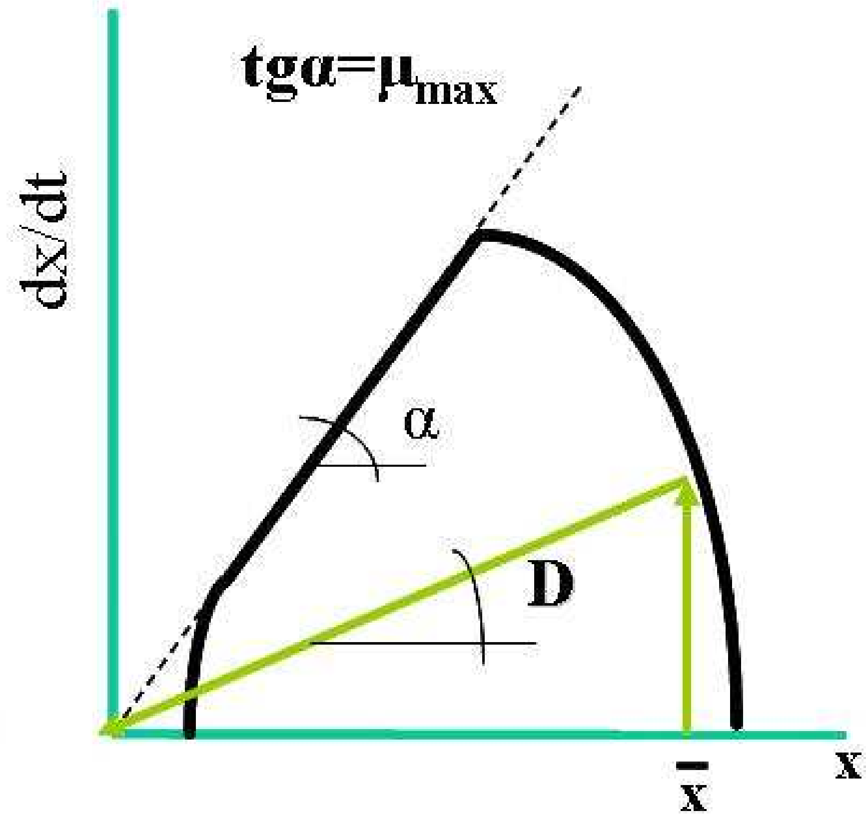
CONTINUOUS FERMENTATION

A



Choosing D
What the outlet will be?

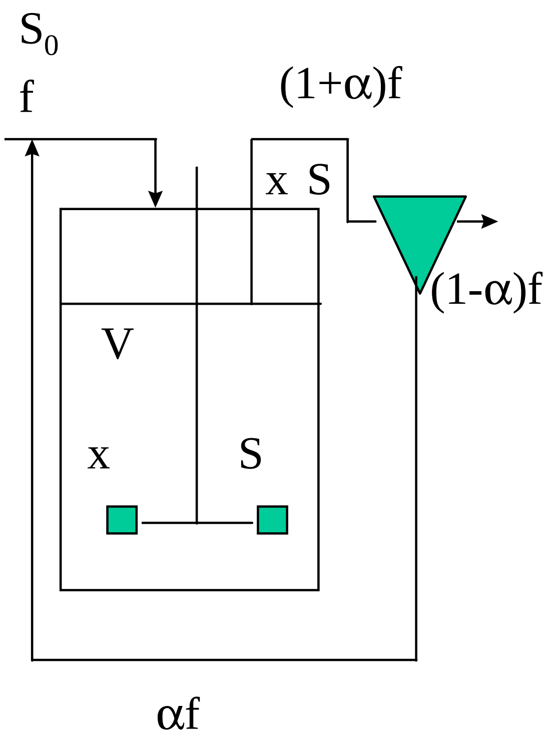
B

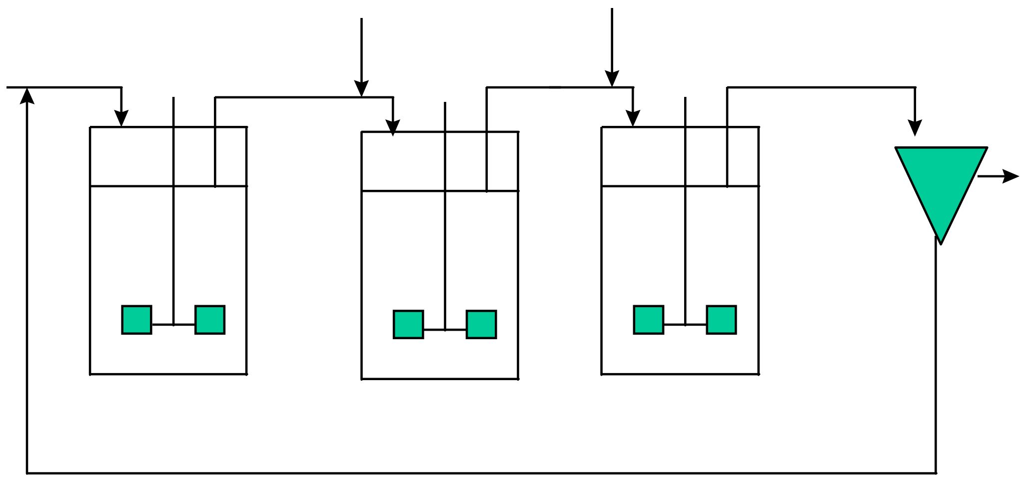


Choosing outlet
What the D will be?

CONTINUOUS FERMENTATION

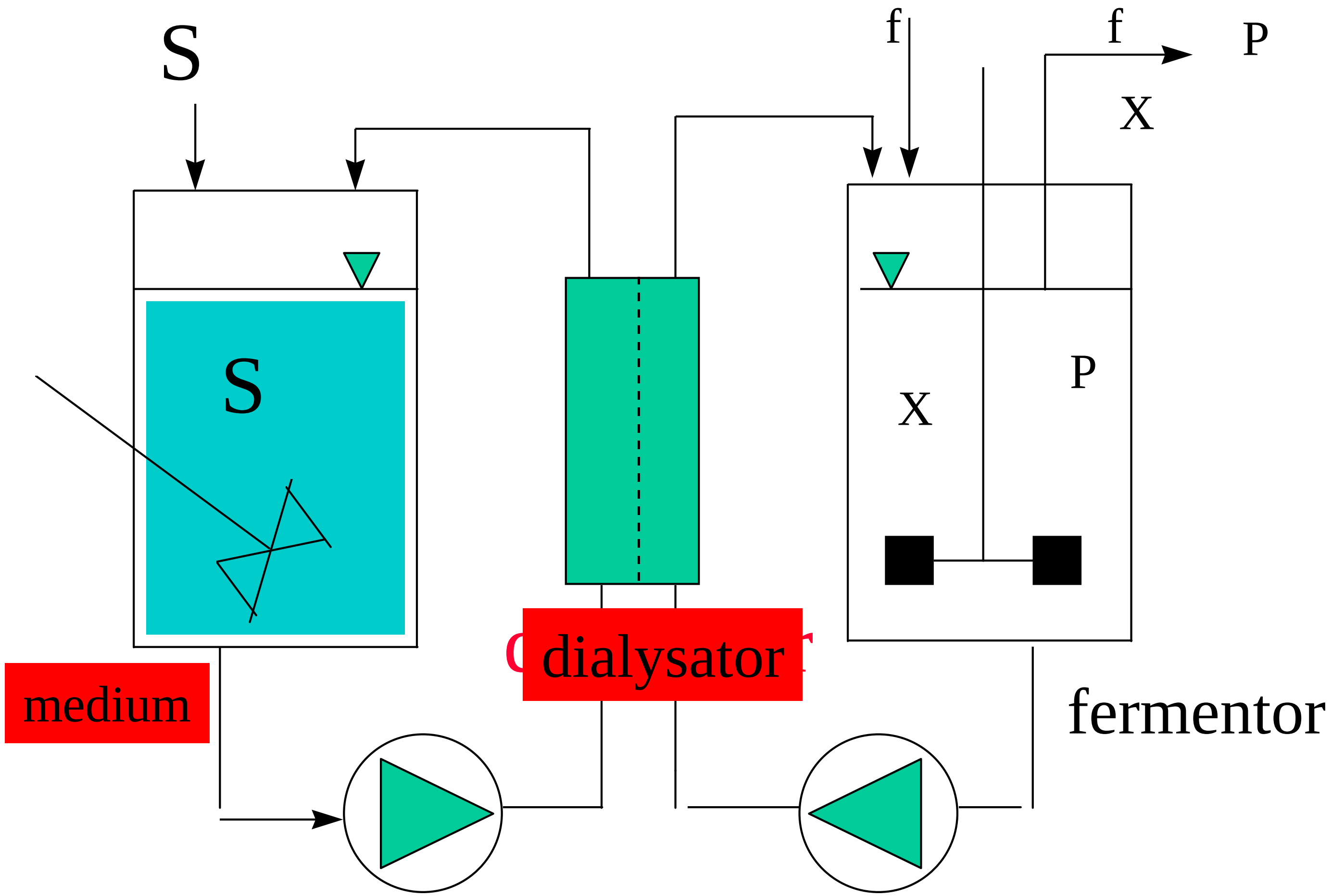
Chemostats with recycle





CONTINUOUS FERMENTATION

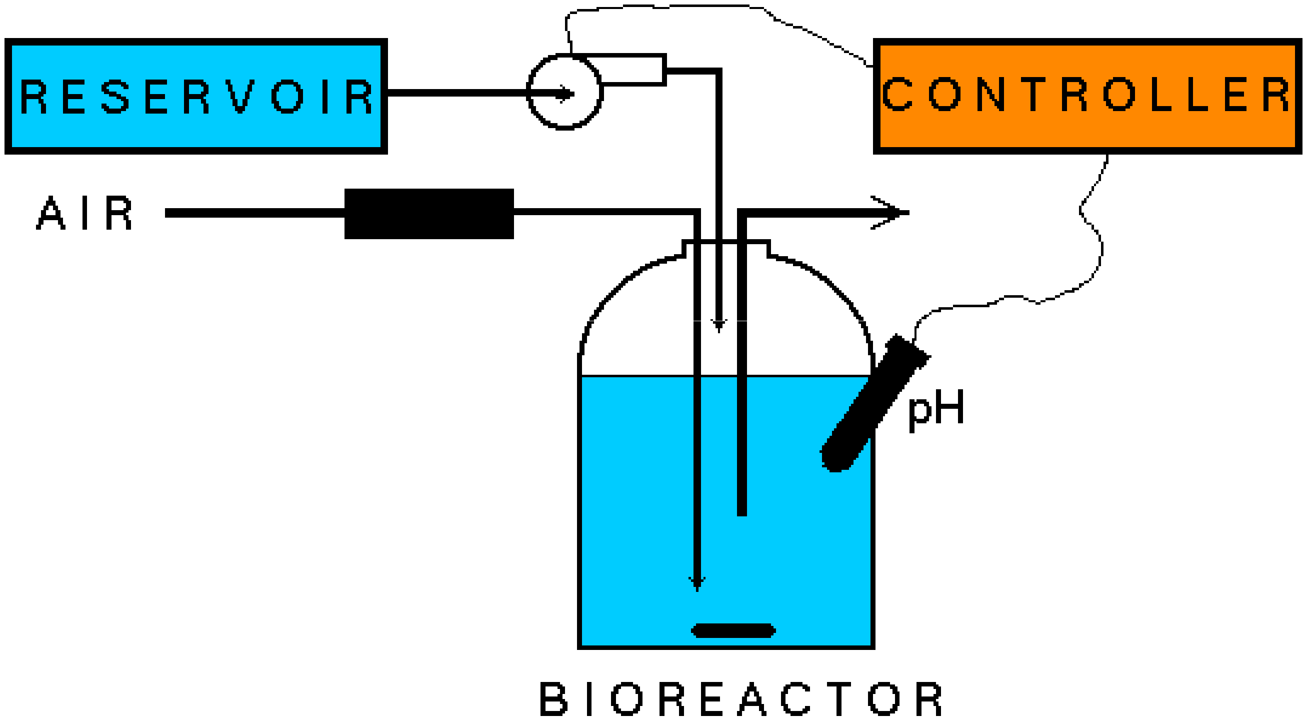
Special chemostat: dialysis culture



CONTINUOUS FERMENTATION

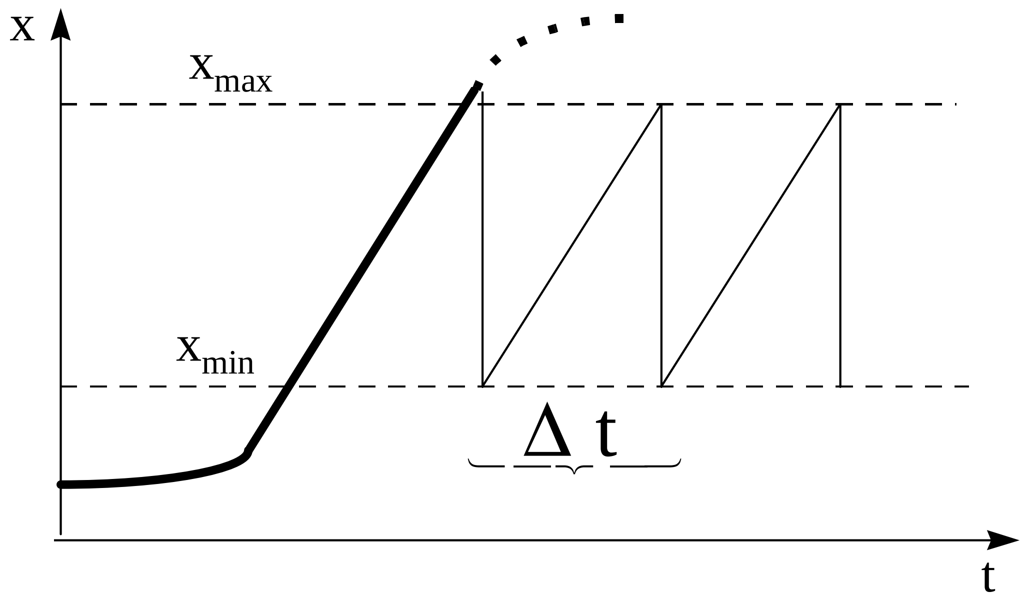
Auxostats

pH-auxostat



Semicontinuous fermentation

$$x_{max} = x_{min} e^{\mu \Delta t} \quad \text{vagy} \quad \ln \frac{x_{max}}{x_{min}} = \mu \Delta t$$

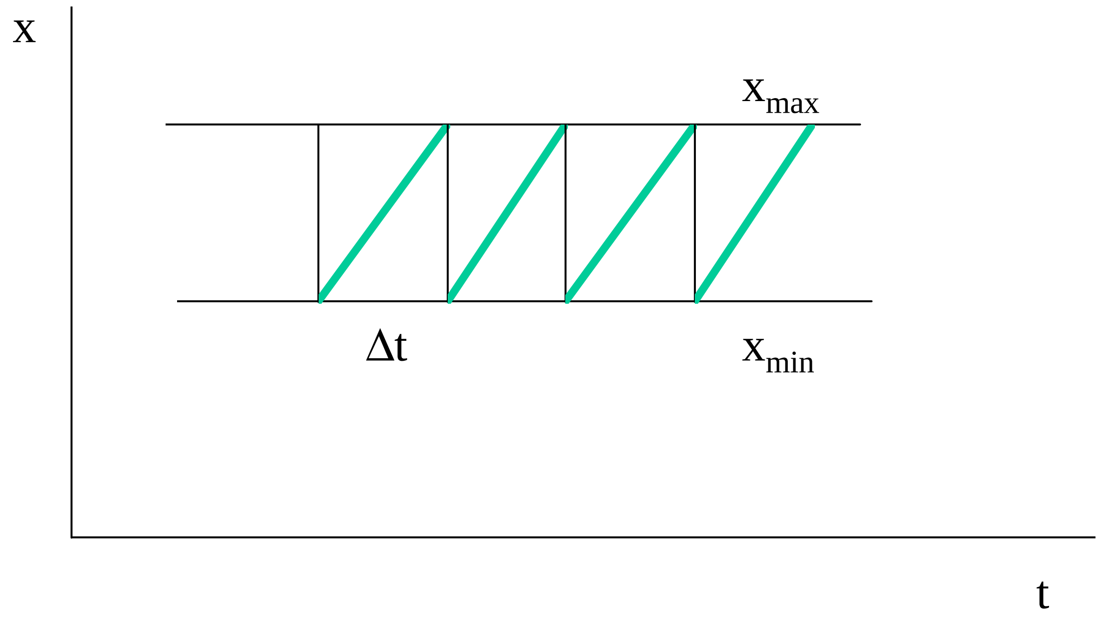


$$D = \frac{\alpha V}{\Delta t} \frac{1}{V} = \frac{\alpha}{\Delta t} = \frac{\alpha \mu_{max}}{\ln \frac{x_{max}}{x_{min}}}$$

α.V volume taken off

$$J = D.x = \frac{\alpha \mu_{max}}{\ln \frac{x_{max}}{x_{min}}} x_{max}$$

Other…. TURBIDOSTAT

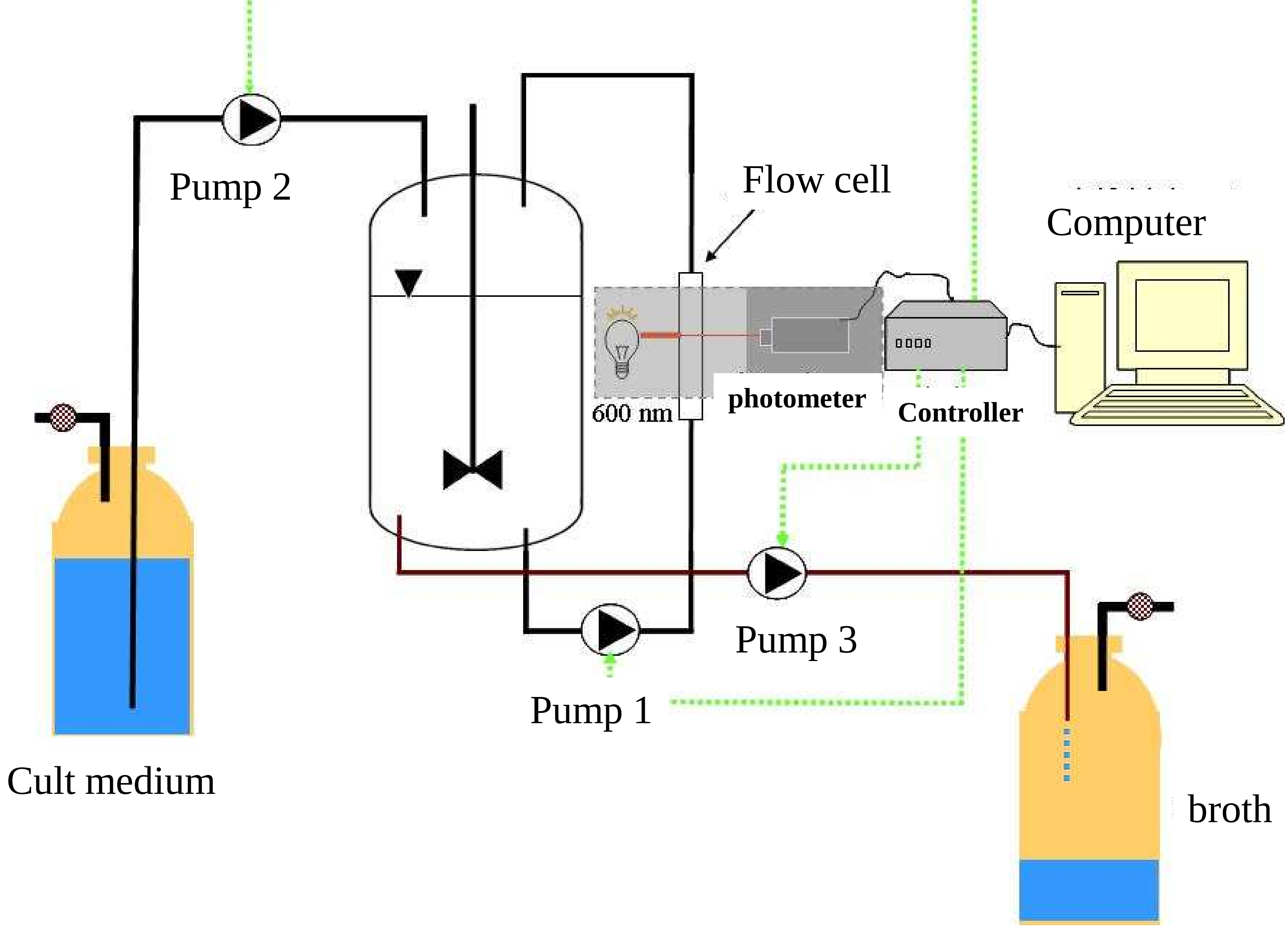


$$\frac{dx}{dt} \cong \frac{\Delta x}{\Delta t} = \frac{x_{max} - x_{min}}{\Delta t}$$

$\mu = \mu_{max}$ is possible!!!

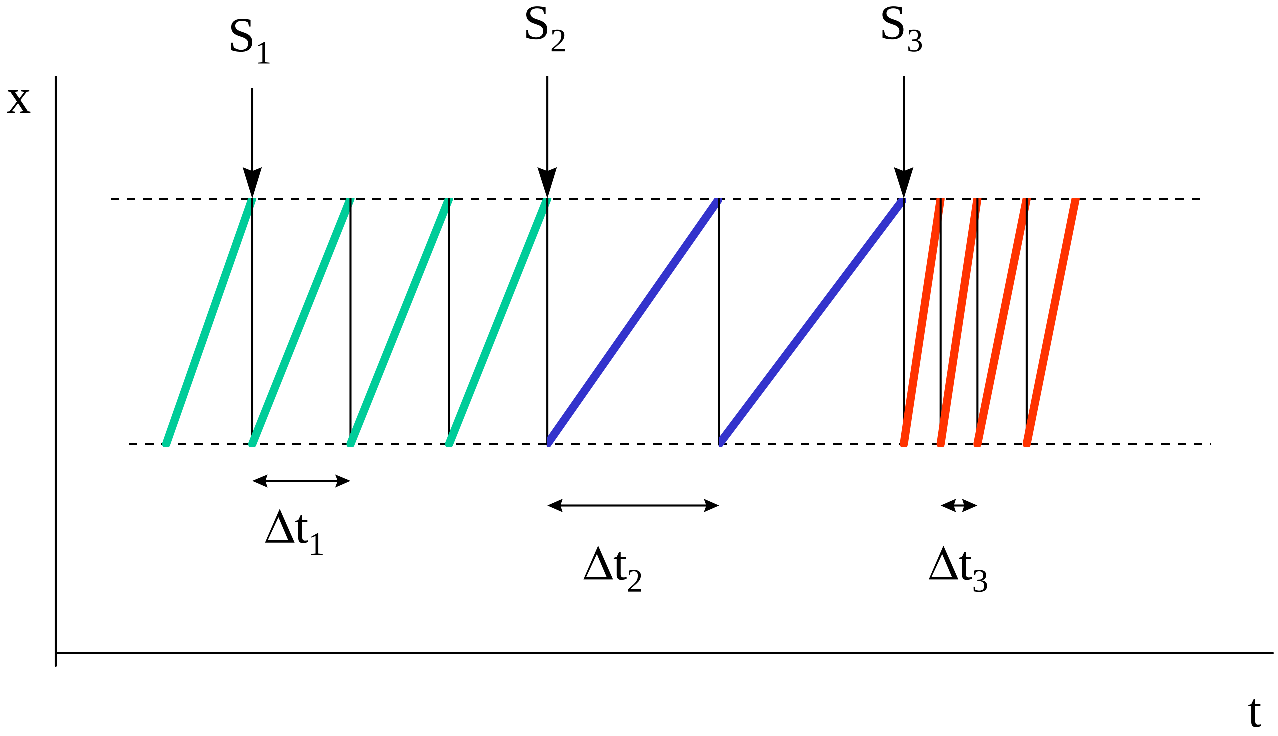
$$\mu = \frac{1}{x}\frac{dx}{dt} \cong \frac{1}{x}\frac{\Delta x}{\Delta t} = \frac{2}{x_{max} + x_{min}} \frac{x_{max} - x_{min}}{\Delta t}$$

Other….: TURBIDOSTAT



Other…. TURBIDOSTAT

Application for research: optimization



Other…….fed batch fermentation

Fed batch fermentation

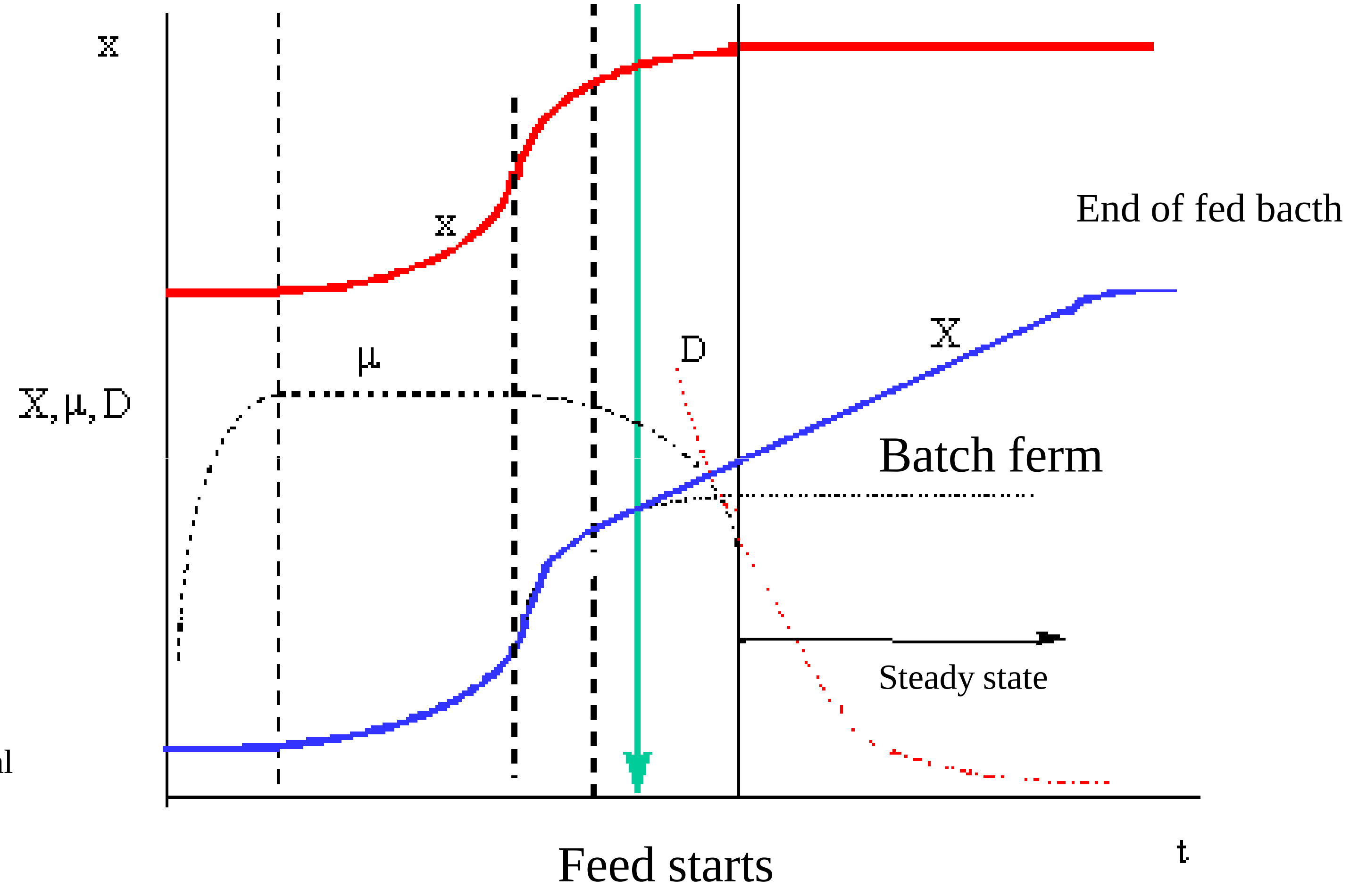
Continuation of the declining phase, constant, variable or periodic addition of fresh cult. medium, **no broth removal.**

*keeping low, constant S concentration (Baker's yeast: glucose repression, Crabtree effect),
*high constant S concentration (citric acid fermentation)
*precursor continuous addition (penicillin: phenyl-acetic-acid,)

pH control!!

Varying volume, f(t)

Other…….fed batch fermentation



$V_{start} \cong 0{,}5\text{-}0{,}6\ V_{total}$

$V_{end} \cong 0{,}7\text{-}0{,}85\ V_{total}$