

III.1 - Introduction

III.2 - Heat transfer equipment

III.3 - Heat balance (1st approach)

III.4 - Heat balance (2nd approach): Thermal Balances

III.5 - Calculation of Heat Transfer Area

III.6 – Media sterilization

Different situations in Biochemical Engineering:

➤ **Temperature control** during process operation ⇒ heating / cooling

- Maintain optimal temperature for the microorganism

The metabolic activity of microorganisms generates heat



Reactors must be cooled to maintain the proper temperature for the reaction

- Heat release on substrate conversion
- Recovery processes

Different situations in Biochemical Engineering:

➤ **Sterilization** of culture media and equipment

Heating to sterilization temperature



Temperature is maintained for a certain period of time



Cooling down to reaction temperature

In bioprocesses, heat transfer takes place mainly between two fluids



Equipment used allows heat to be transferred between fluids without them coming into contact



Solid structure to separate fluids



heat transfer equipment

- Double chamber
- Coils
- Heat Exchangers

Double chamber

Structure **external** to the reactor, in which the fluid circulates to control the temperature



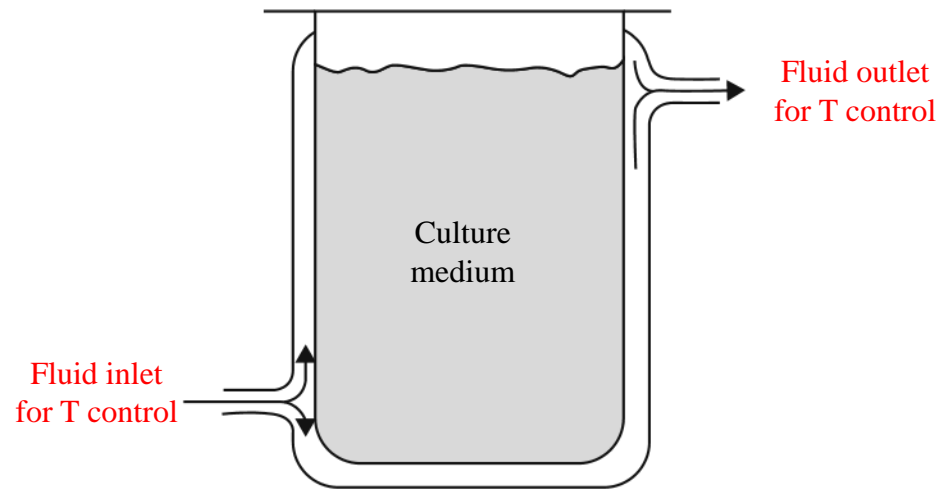
limited surface area



Suitable for **laboratory scale** or for small systems



They are hardly efficient on an industrial scale



Coils

Structure **external or internal** to the reactor, in which the fluid circulates to control the temperature

- **External coils** Fluid circulates inside the coil outside the reactor



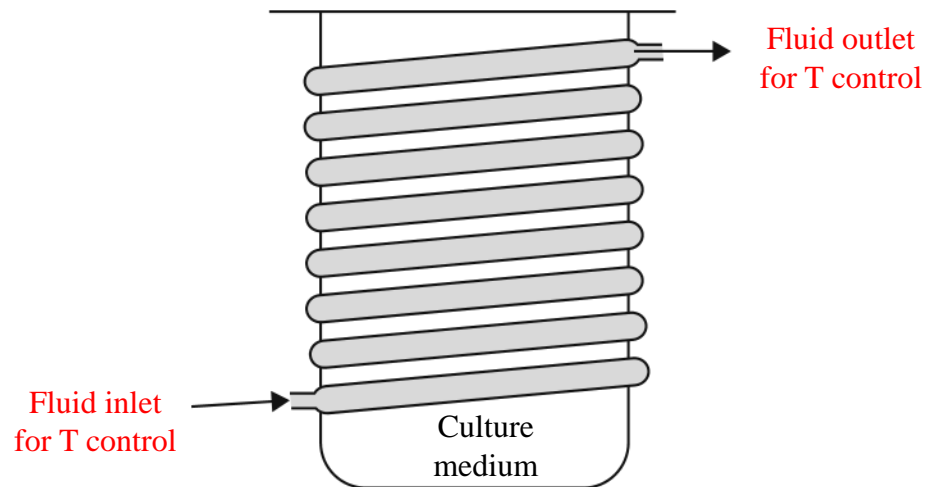
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Suitable for **laboratory scale** or for small systems



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Coils

Structure **external or internal** to the reactor, in which the fluid circulates to control the temperature

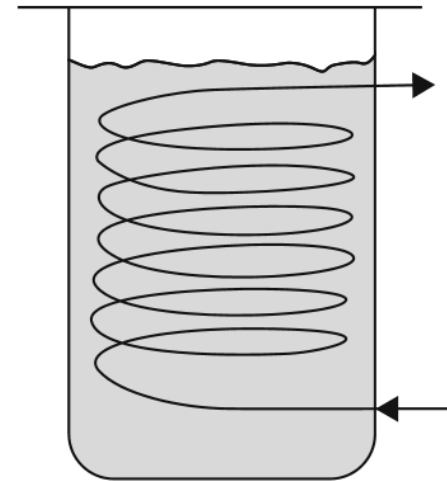
- **Internal coils** Fluid circulates inside the coil inside the reactor



More efficient than external coils

Disadvantages:

- may interfere with agitation
- make it difficult to clean the reactor
- biofilm formation may occur → reduces surface area



Heat exchangers

Equipment **external** and independent of the reactor

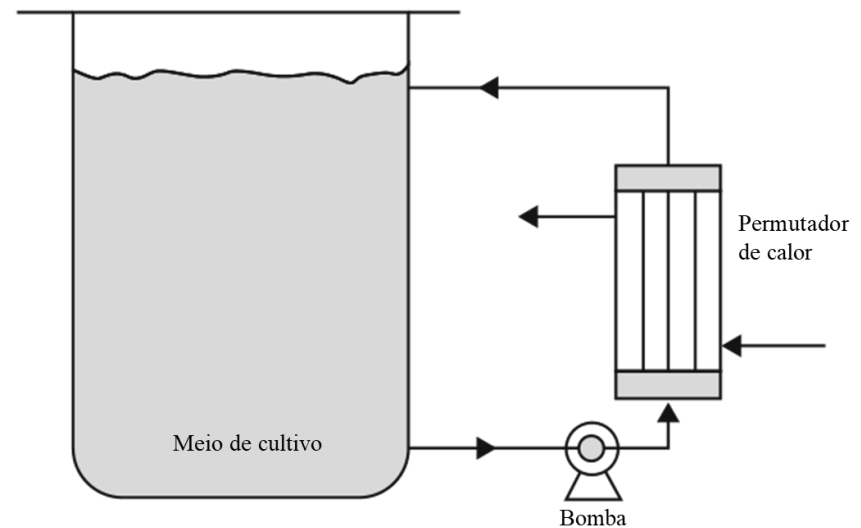
Allow good heat transfer



Used on an industrial scale

Requirements:

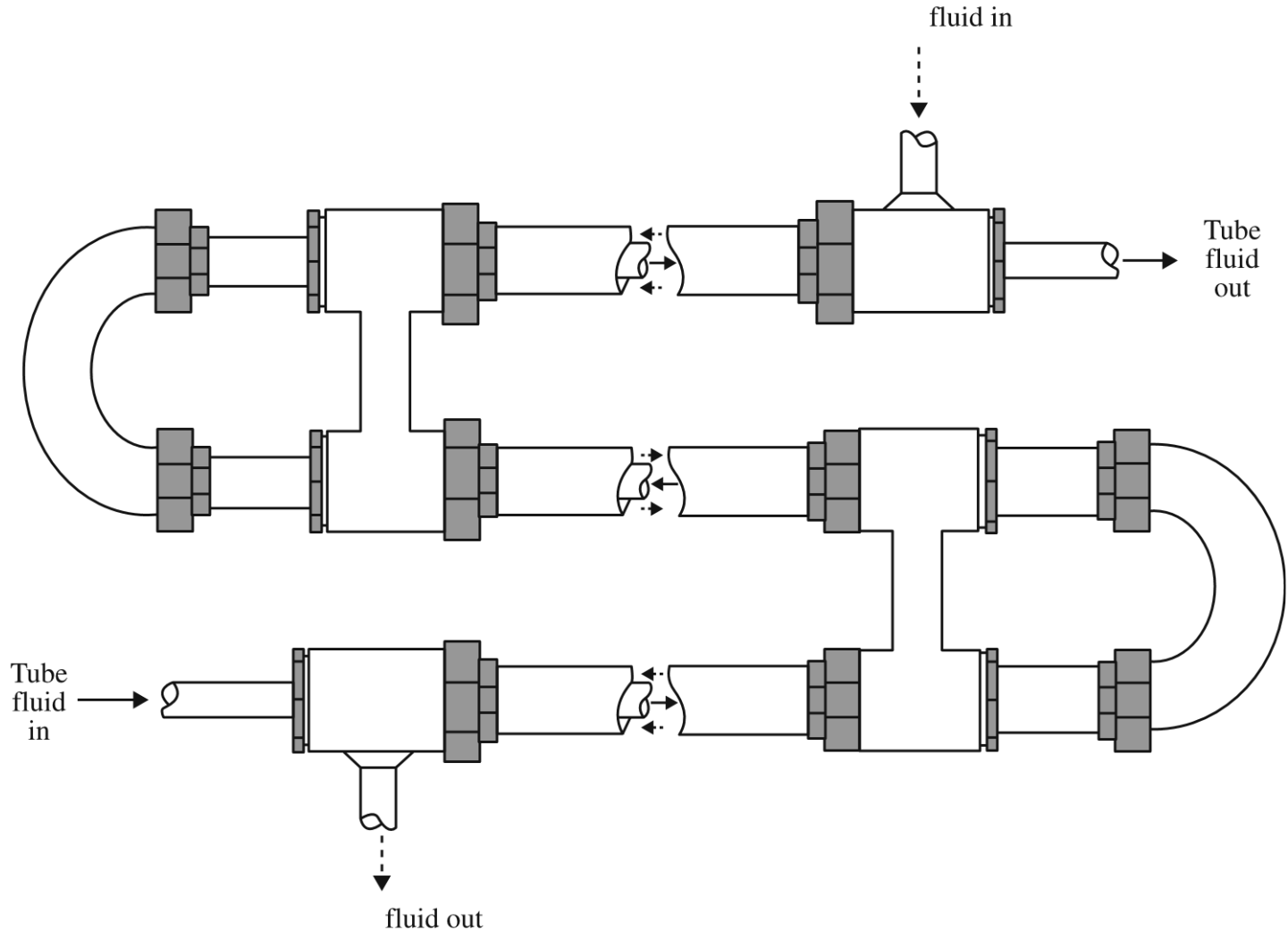
- maintain sterility
- residence time of the reaction fluid must be short to ensure that nutrients are not depleted while in the exchanger



Heat exchangers

Two types:

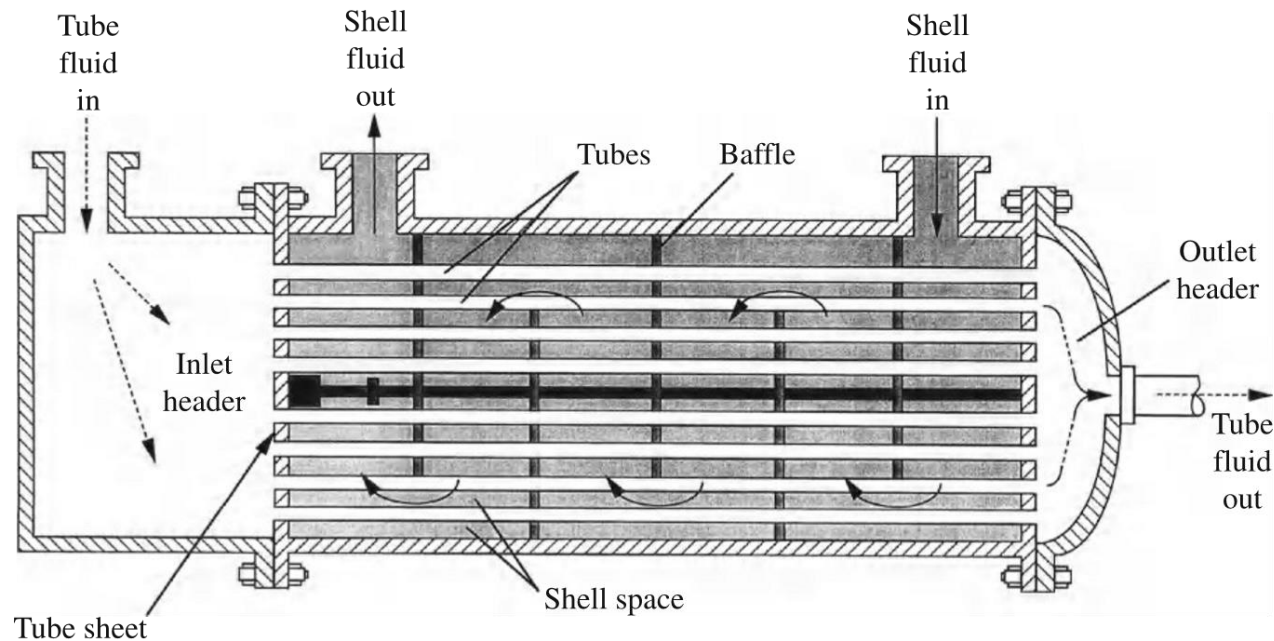
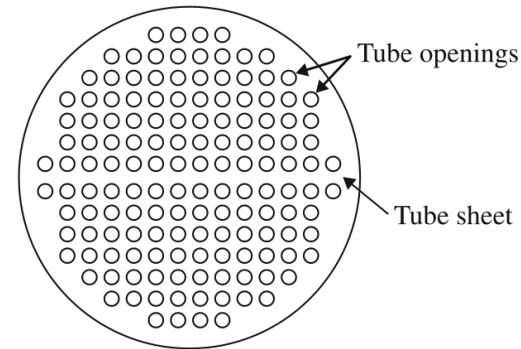
- **Tubular**



Heat exchangers

Two types:

- **Plates**



To size the equipment:

determine the amount of heat per unit of time (heat transfer rate) needed to maintain a certain temperature (heat/cool)

- Calculate required heat transfer area
- Equipment design

Heat Balance

$$\sum Q_{in} - \sum Q_{out} = Q_{acc}$$

$$Q_{acc} = \sum_{\text{the stream in}} \text{enthalpy of} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap} - Q_{perm} - \sum_{\text{the stream out}} \text{enthalpy of}$$

Q_{acc} = heat accumulated along the process

Heat Balance

$$\sum Q_{in} - \sum Q_{out} = Q_{acc}$$

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Q_{acc} = heat accumulated along the process

Q_{ger} = heat generated by the microorganisms' activity

Heat Balance

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Q_{ger} = heat generated by the microorganisms' activity

Q_{agi} = heat generated by mechanical agitation

Heat Balance

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Q_{agi} = heat generated by mechanical agitation

Q_{gas} = heat generated by aeration

Heat Balance

$$\sum Q_{in} - \sum Q_{out} = Q_{acc}$$

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Q_{acc} = heat accumulated along the process

Q_{ger} = heat generated by the microorganisms' activity

Q_{agi} = heat generated by mechanical agitation

Q_{gas} = heat generated by aeration

Q_{evap} = heat lost by evaporation

Heat Balance

$$\sum Q_{in} - \sum Q_{out} = Q_{acc}$$

$$Q_{acc} = \sum_{\text{the stream in}} \text{enthalpy of} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap} - Q_{perm} - \sum_{\text{the stream out}} \text{enthalpy of}$$

Q_{acc} = heat accumulated along the process

Q_{ger} = heat generated by the microorganisms' activity

Q_{agi} = heat generated by mechanical agitation

Q_{gas} = heat generated by aeration

Q_{evap} = heat lost by evaporation

Q_{perm} = heat transferred to the environment or to the exchanger

Heat Balance

$$\sum Q_{in} - \sum Q_{out} = Q_{acc}$$

$$Q_{acc} = \sum \text{enthalpy of the stream in} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap} - Q_{perm} - \sum \text{enthalpy of the stream out}$$

$$Q_{sens} = \sum \text{enthalpy of the stream in} - \sum \text{enthalpy of the stream out}$$

Q_{sens} = sensitive heat

$$Q_{acc} = Q_{sens} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap} - Q_{perm}$$

III.3 - Heat balance (1st approach)

$$Q_{acc} = Q_{sens} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap} - Q_{perm}$$

For constant temperature $\Rightarrow Q_{acc} = 0$

$$0 = Q_{sens} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap} - Q_{perm}$$

$$Q_{perm} = Q_{sens} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap}$$

Typical values for Q (KJ l⁻¹ h⁻¹):

$$Q_{ger} = 36.16$$

$$Q_{ag} = 13.84$$

$$Q_{acum} = 47.34$$

$$Q_{perm} = 2.72$$

$$Q_{evap} = 0.188$$

$$Q_{sens} = 0.042$$

$$Q_{perm} = Q_{sens} + Q_{ger} + Q_{agi} + Q_{gas} - Q_{evap}$$

generally:

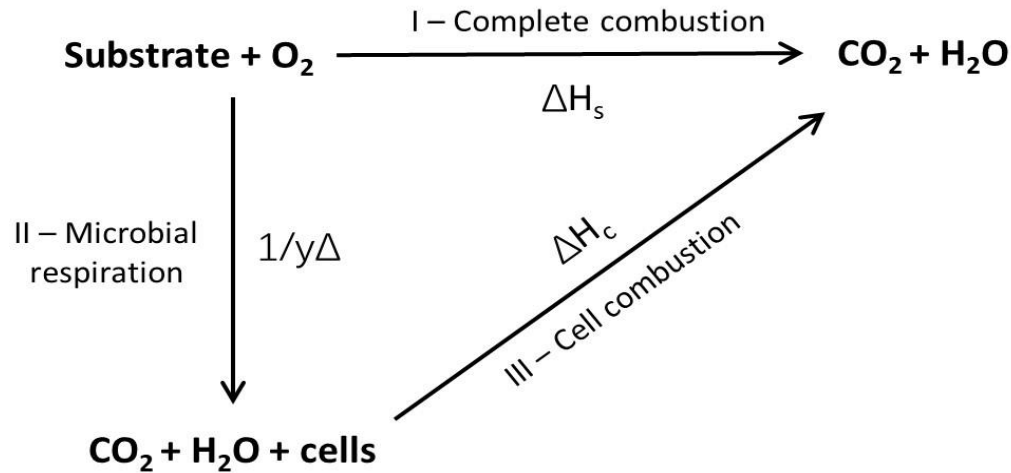
$$Q_{sen} = \ll Q_{ger}$$

$Q_{evap} \rightarrow$ very small (if saturated air at T is used = fermentation)

$Q_{agit} \rightarrow$ can be calculated experimentally

$Q_{acc} \rightarrow$ can be measured in transient state in isolated reactor

Calculation of heat generated by microorganisms (Q_{ger}):



Substrate combustion heat = metabolism heat + cell combustion heat

$$\frac{\Delta H_s}{Y_{x/s}} = \frac{1}{Y_{\Delta}} + \Delta H_c$$

ΔH_s – heat of substrate combustion (kJ/g sub)

$y_{x/s}$ – yield coeficiente (g cel/g sub)

ΔH_c – heat of cell combustion (kJ/g cel)

$1/Y_{\Delta}$ = specific metabolic heat (kJ/g cel)

Calculation of heat generated by microorganisms (Q_{ger}):

$$\frac{\Delta H_s}{Y_{x/s}} = \frac{1}{Y_\Delta} + \Delta H_c \Leftrightarrow Y_\Delta = \frac{Y_{x/s}}{\Delta H_s - Y_{x/s} \Delta H_c}$$

Where $Y_{x/s}$ is:

$$\frac{1}{Y_{x/s}} = \frac{1}{Y'_{x/s}} + \frac{m}{\mu}$$

m – maintenance coefficient (g sub/g cel h)

$Y'_{x/s}$ – true growth yield (g cel/g sub)

$Y_{x/s}$ - apparent growth yield (g cel/g sub)

and ΔH_c e ΔH_s are calculated by combustion reactions

III.3 - Heat balance (1st approach)

Calculation of heat generated by microorganisms (Q_{ger}):

Y_{Δ} depends on: type of microorganism (ΔH_c and m)

type of substrate (ΔH_s)

$$Q_{\text{Ger Hydroc}} > Q_{\text{Ger Carbohyd}}$$

Table 8.7. Comparison of yield coefficients for bacteria grown on various carbon sources†

Substrate	Y_s , g cell/ g substrate	Y_o , g cell/ g O_2 consumed	Y_{Δ} , g cell/ kcal
Maleate	0.34	1.02	0.30
Acetate	0.36	0.70	0.21
Glucose equivalents (molasses, starch, cellulose)	<u>0.51</u>	1.47	<u>0.42</u>
Methanol	0.40	0.44	0.12
Ethanol	0.68	0.61	0.18
Isopropanol	0.43	0.23	0.074
<i>n</i> -Paraffins	1.03	0.50	0.16
Methane	0.62	0.20	0.061

- **Calculation of heat generated in batch reactor**

$$Q_{Ger} = V \mu X \frac{1}{y_{\Delta}}$$

V = reactor volume(l)

μ = specific growth rate(h⁻¹)

x = cell concentration (g cel/l)

y_{Δ} = (g cel/KJ)

Q_{Ger} = heat generated (KJ/h)

- **Calculation of heat generated in continuous reactor (CSTR)**

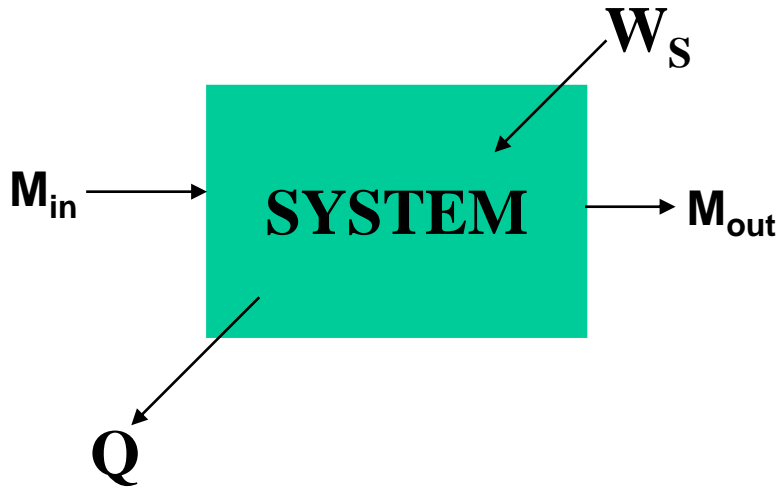
$$\frac{Q_{Ger}}{V} = \left[(S_0 - S) Y_{x/s} D - \frac{X K_e}{V} \right] / Y_{\Delta}$$

F – feed flow rate

K_e – maintenance rate

V – reactor volume

D – dilution rate



Q – heat released from the system (kJ)

Q is positive

W_s - heat due to mechanical agitation (kJ)

M_{in} – mass entering the system (kg)

M_{out} – mass leaving the system (kg)

Incoming Energy - Outgoing Energy = Accumulated Energy

$$\sum (M_i h) - \sum (M_o h) - Q + W_s = \Delta E$$

ΔE = Energy accumulated in the system
 h = Specific enthalpy of formation (kJ/kg)

In steady state:

$$\sum (M_i h) - \sum (M_o h) - Q + W_s = 0$$

$$\Delta H_{rxn} = \underbrace{\sum (Mh)}_{\text{Products}} - \underbrace{\sum (Mh)}_{\text{Reagents}}$$

ΔH_{rxn} = Reaction energy (kJ)

$$\sum (M_i h) - \sum (M_o h) - Q + W_s = 0$$

$$- \Delta H_{rxn} - Q + W_s = 0$$

If evaporation in the system is significant :

$$- \Delta H_{rxn} - Q + W_s - M \Delta h_v = 0$$

M – mass of liquid evaporated (kg)

Δh_v – latent heat from evaporation (kJ)

$$Q = - \Delta H_{rxn} + W_s - M \Delta h_v$$

$\Delta H_{rxn} > 0$ endothermic reaction

$\Delta H_{rxn} < 0$ exothermic reaction

CALCULATION OF PARAMETERS

$W_s \rightarrow$ calculated from agitator power

$\Delta h_v \rightarrow$ tabulated for water at a certain temperature

$\Delta H_{rxn} \rightarrow ?$

$$\Delta H^0_{rxn} = \underbrace{\sum M \Delta h^0_c}_{\text{reagentes}} - \underbrace{\sum M \Delta h^0_c}_{\text{produtos}}$$

ΔH^0_{rxn} - Reaction heat

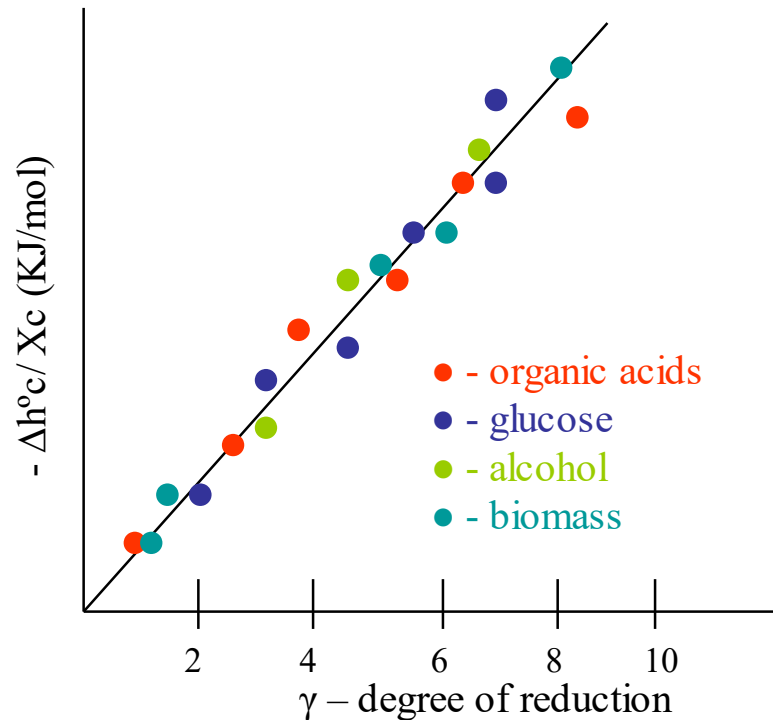
Δh^0_c - Heat of combustion
(tabulated values)

Table 5.1 Heats of combustion for bacteria and yeast

(From J.-L. Cordier, B.M. Butsch, B. Birou and U. von Stockar, 1987, *The relationship between elemental composition and heat of combustion of microbial biomass*. Appl. Microbiol. Biotechnol. 25, 305-312)

Organism	Substrate	Δh_c (kJ g ⁻¹)
Bacteria		
<i>Escherichia coli</i>	glucose	-23.04 ± 0.06
	glycerol	-22.83 ± 0.07
<i>Enterobacter cloacae</i>	glucose	-23.22 ± 0.14
	glycerol	-23.39 ± 0.12
<i>Methylophilus methylotrophus</i>	methanol	-23.82 ± 0.06
<i>Bacillus thuringiensis</i>	glucose	-22.08 ± 0.03
Yeast:		
<i>Candida lipolytica</i>	glucose	-21.34 ± 0.16
<i>Candida boidinii</i>	glucose	-20.14 ± 0.18
	ethanol	-20.40 ± 0.14
	methanol	-21.52 ± 0.09
	lactose	-21.54 ± 0.07
<i>Kluyveromyces fragilis</i>	galactose	-21.78 ± 0.10
	glucose	-21.66 ± 0.19
	glucose	-21.07 ± 0.07
		-21.30 ± 0.10
		-20.66 ± 0.26
		-21.22 ± 0.14

It was empirically determined that the energy contained in organic compounds is related to their degree of reduction:



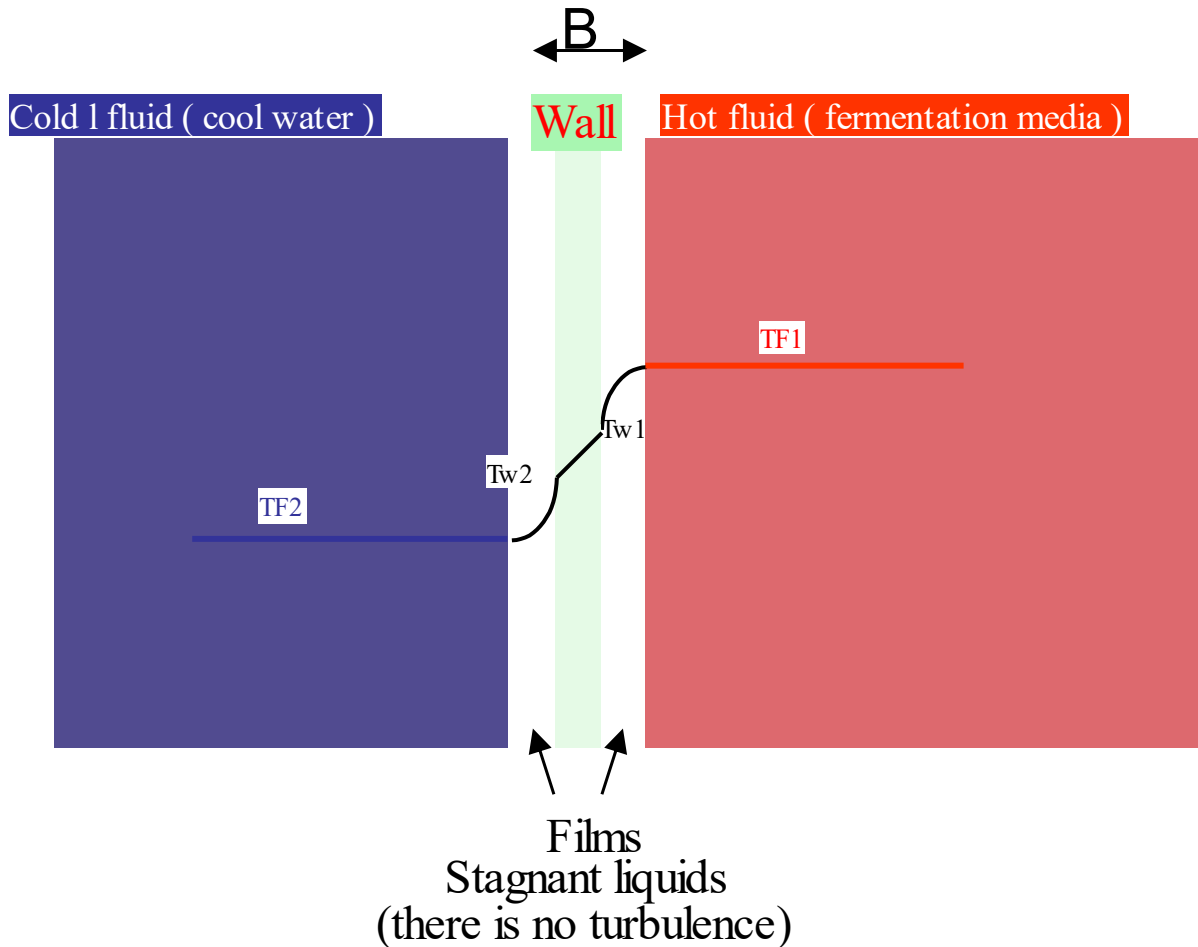
$$\Delta h_c^\circ = -q \gamma x_c$$

Δh_c° – heat of molar combustion in standard conditions
 q – heat released by moles of electrons transferred to O_2
 γ – degree of reduction of the compounds relative to the N_2
 X_c – number of carbon atoms in the formula

In aerobic systems, for **each mole of transferred electrons, 115 KJ of energy is released**: as O_2 accepts 4 electrons, **460 kJ** are released.

The amount of heat released can be determined from the amount of oxygen consumed (in aerobic systems)

III.5 - Calculation of Heat Transfer Area



$TF1$ – temperature of fluid 1

$Tw1$ – temperature of wall 1

$Tw2$ – temperature of wall 2

$TF2$ – temperature of fluid 2

B - Wall thickness

$$Q = \bar{h} A \Delta T$$

Q = Heat transfer rate (Js^{-1})

h = Global heat transfer coefficient ($\text{J s}^{-1}\text{m}^{-2} \text{ } ^\circ\text{C}^{-1}$)

A = Heat transfer area (m^2)

ΔT = temperature difference between fluids, or
logarithmic mean ($^\circ\text{C}$) = driving force of the process

\bar{h} depends on

- Fluid properties
- flow conditions
- system geometry

In steady state:

heat transfer rate through the film on the hot fluid side = rate of the heat transfer
through the wall = the heat transfer rate through the film on the cold fluid side

$$Q_1 = Q_w = Q_2 = Q$$

III.5 - Calculation of Heat Transfer Area

$$Q = h A \Delta T$$

$$Q_1 = h_i A_i (T_{F1} - T_{w1})$$

III.5 - Calculation of Heat Transfer Area

$$Q_1 = h_i A_i (T_{F1} - T_{w1}) \Rightarrow T_{F1} - T_{w1} = \frac{Q}{h_i A_i}$$

$$Q = h A \Delta T$$

III.5 - Calculation of Heat Transfer Area

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$$Q_w = \frac{K_w}{B} A_w (T_{w1} - T_{w2})$$

III.5 - Calculation of Heat Transfer Area

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K_w = wall thermal
conductivity ($\text{J m}^{-1} \text{s}^{-1} \text{ } ^\circ\text{C}^{-1}$)
 B - wall thickness (m)

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conductivity ($\text{J m}^{-1} \text{s}^{-1} \text{ } ^\circ\text{C}^{-1}$)
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$$Q_2 = h_e A_e (T_{w2} - T_{F2})$$

III.5 - Calculation of Heat Transfer Area

$$Q = h A \Delta T$$

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$$Q_2 = h_e A_e (T_{w2} - T_{F2}) \Rightarrow T_{w2} - T_{F2} = \frac{Q}{h_e A_e}$$

$$Q_1 + Q_w + Q_2 =$$

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$$Q_1 + Q_w + Q_2 =$$

$$T_{F1} - T_{w1} + T_{w1} - T_{w2} + T_{w2} - T_{F2} = Q \left(\frac{1}{h_i A_i} + \frac{B}{K_w} \frac{1}{A_w} + \frac{1}{h_e} \frac{1}{A_e} \right)$$

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$$T_{F1} - \cancel{T_{w1}} + \cancel{T_{w1}} - \cancel{T_{w2}} + \cancel{T_{w2}} - T_{F2} = Q \left(\frac{1}{h_i A_i} + \frac{B}{K_w} \frac{1}{A_w} + \frac{1}{h_e} \frac{1}{A_e} \right)$$

$$\underbrace{T_{F1} - T_{F2}}_{\Delta T} = Q \left(\frac{1}{h_i} \frac{1}{A_i} + \frac{B}{K_w} \frac{1}{A_w} + \frac{1}{h_e} \frac{1}{A_e} \right)$$

III.5 - Calculation of Heat Transfer Area

$$Q = h A \Delta T \quad \Leftrightarrow \Delta T = \frac{Q}{h A}$$

$$\underbrace{T_{F1} - T_{F2}}_{\Delta T} = Q \left(\frac{1}{h_i} \frac{1}{A_i} + \frac{B}{K_w} \frac{1}{A_w} + \frac{1}{h_e} \frac{1}{A_e} \right)$$

$$\frac{Q}{h A} = Q \left(\frac{1}{h_i} \frac{1}{A_i} + \frac{B}{K_w} \frac{1}{A_w} + \frac{1}{h_e} \frac{1}{A_e} \right)$$

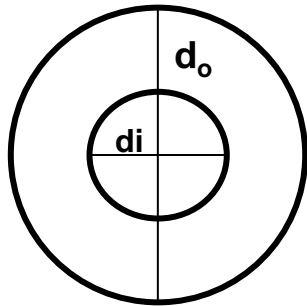
$$\Rightarrow \underbrace{\frac{1}{h A}}_{\text{Resistência global à T.C.}} = \underbrace{\frac{1}{h_i} \frac{1}{A_i}}_{\text{Resistência do filme interior à T.C.}} + \underbrace{\frac{B}{K_w} \frac{1}{A_w}}_{\text{Resistência da parede à T.C.}} + \underbrace{\frac{1}{h_e} \frac{1}{A_e}}_{\text{Resistência do filme exterior à T.C.}}$$

III.5 - Calculation of Heat Transfer Area

→ Flat surfaces: $A = A_i = A_w = A_e$

$$\frac{1}{h} = \frac{1}{h_i} + \frac{B}{K_w} + \frac{1}{h_e}$$

→ Cilindric surfaces:



d_o - external diameter

d_i - internal diameter

$$\frac{1}{h_o d_o} = \frac{1}{h_i d_i} + \frac{\ln \frac{d_o}{d_i}}{2 K_w} + \frac{1}{h_o d_o}$$

DEFINITION:

Sterilization is a form of pre-treatment to remove or destroy organisms that may adversely affect the process (fermentation, bioconversion, storage) or the product.

Sizing and Problem Solving:

- Efficiency in removal or destruction
- Reliability
- Validation
- Effect on product and medium quality
- Operating and investment costs

Killing cells and spores

- Incineration
- Chemical agents
- Ionization radiation
- Ultrasounds
- Thermal
- Saturated steam $>121\text{ }^{\circ}\text{C}$
- Dry heat at $160\text{-}170\text{ }^{\circ}\text{C}$

Thermal destruction with heat

- death kinetics
- Temperature Effect
- Cells vs. spores
- Sizing Criteria

Death kinetics

$$\frac{dN}{dt} = -kN$$

$$\frac{dN}{N} = -k dt$$

$$\int_{N_0}^N \frac{dN}{N} = - \int_0^t k dt$$

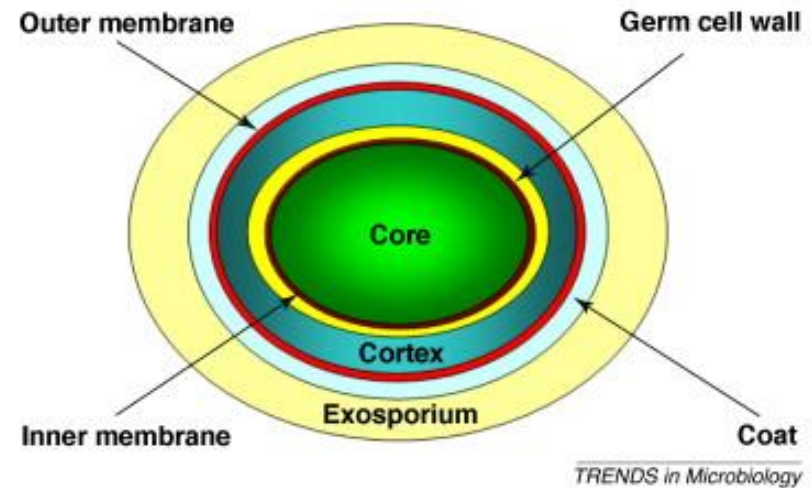
$$\ln \frac{N_0}{N} = \int k dt$$

$$\ln \frac{N}{N_0} = - \int k dt$$

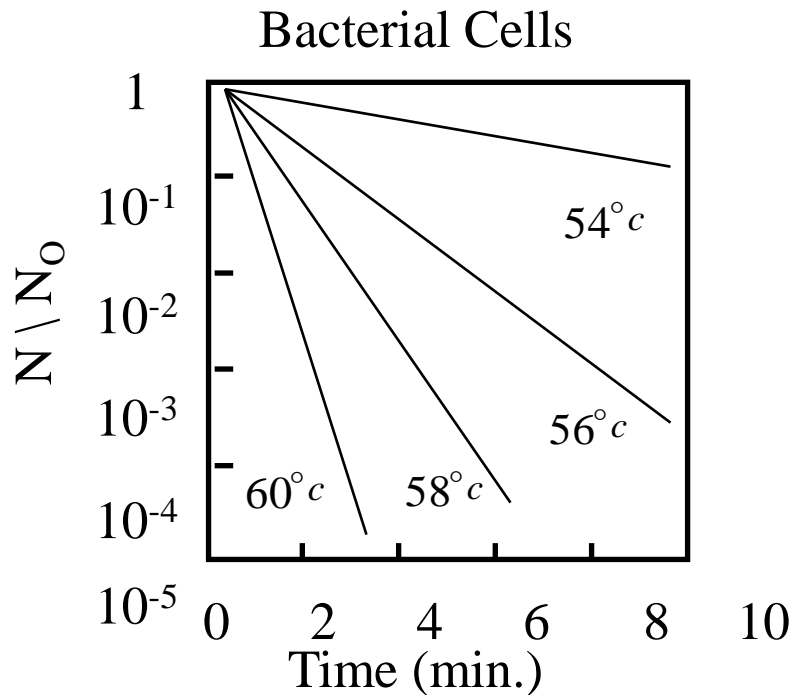
Bacterial and Fungal Spores



Image courtesy of Steve Gschmeissner/
Science Photo Library.



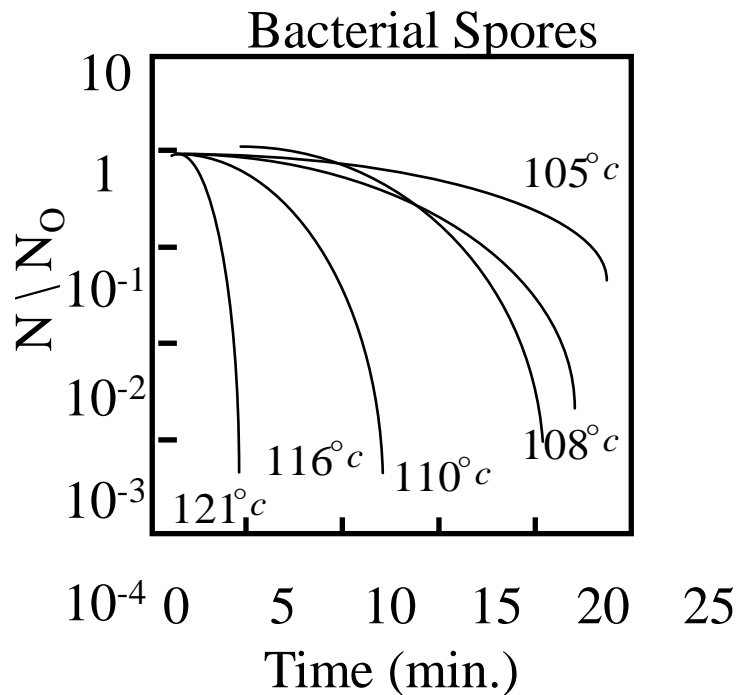
Thermal Death Kinetics



N = number of viable cells as a function of time

N_0 = number of viable initial cells

Thermal Death Kinetics



N = number of viable spores as a function of time

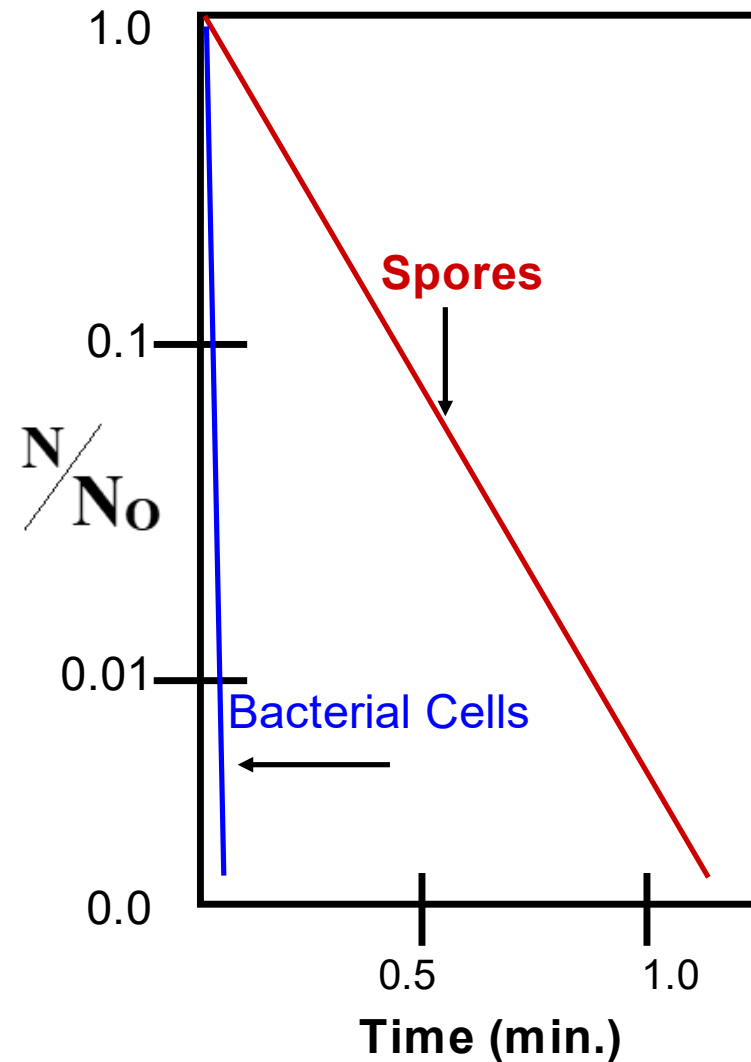
N_0 = number of viable initial spores

Cell and spore death rate

Comparison of thermal death rate of bacterial cells and spores to 121°C

$$k_{\text{cell}} \approx (10^6) k_{\text{spores}}$$

$$\ln \frac{N}{N_0} = -kt$$



Relative heat resistance of microorganisms

Type of Microorganism	Relative Resistance
Bacteria and Yeast	1.0
Bacterial Spores (<i>Bacillus and Clostridium</i> sp's.)	3×10^6
Mold Spores	2 - 10
Virus and Bacteriophage	1 - 5

(Source: Kan, U., Bact. Rev. 91, 1-47)

Effect of temperature on death kinetics

The death rate dependence (K) is described by the Arrhenius equation

$$k = Ae^{-E/RT}$$

A - Arrhenius constant

R - Perfect gas constant

E - Activation Energy

Thermal inactivation of *B. stearothermophilus**

T°C	Thermal death constant (min ⁻¹)
100	0.019
110	0.212
120	2.037
130	17.52
140	135.9
150	956.1

Activation Energies Bacterial Spores (Kcal/mol)

<i>Bacillus stearothermophilus</i>	67.7
<i>Bacillus subtilis</i>	76.0
<i>Clostridium botulinum</i>	82.0

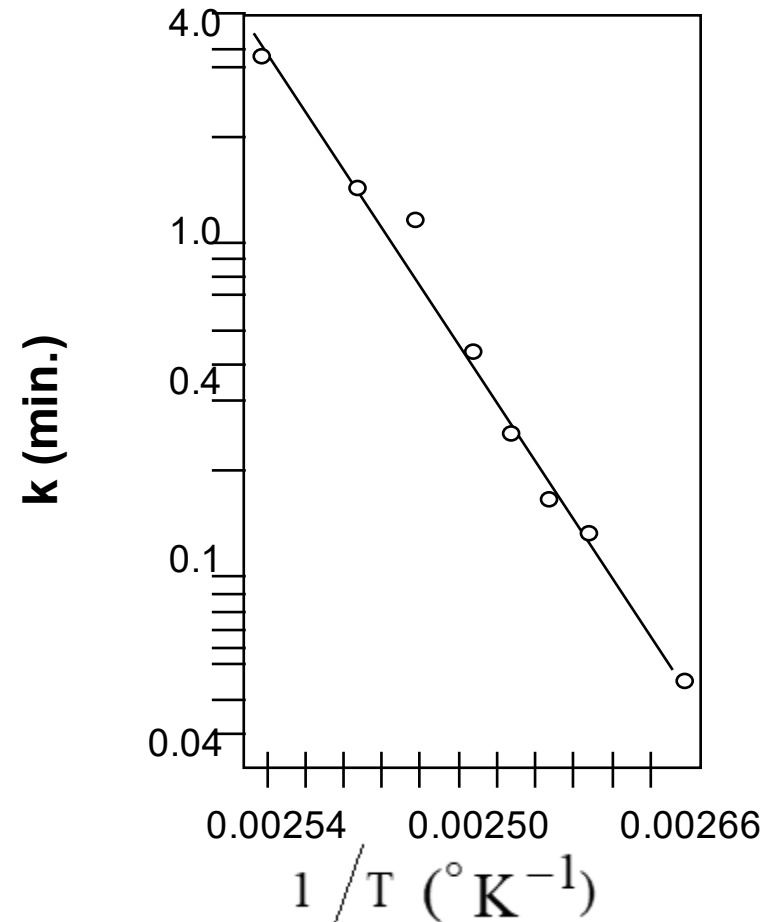
Effect of temperature on death kinetics

Arrhenius model

$$k = Ae^{-E/RT}$$

$$\ln k = \ln A - \frac{E}{R} \frac{1}{T}$$

intercept slope



Sizing a batch sterilization cycle

Death rate is described by first-order kinetics.

$$\frac{d(NV)}{dt} = -kNV$$

N_o = Initial concentration of spores

N_f = Final concentration of spores

$$\frac{d(NV)}{NV} = -kdt$$

k = Death rate constant

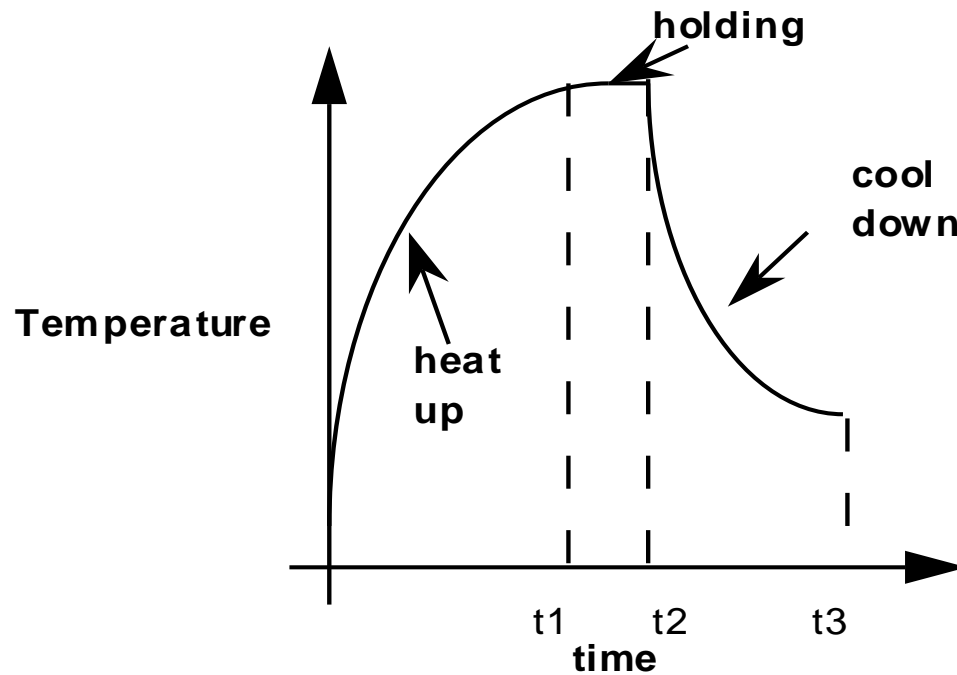
V_o = Initial liquid volume

$$\ln \frac{(NV)_o}{(NV)_f} = \int kdt$$

V_f = Final liquid volume

Criteria for batch sterilization

Temperature profile as a function of time



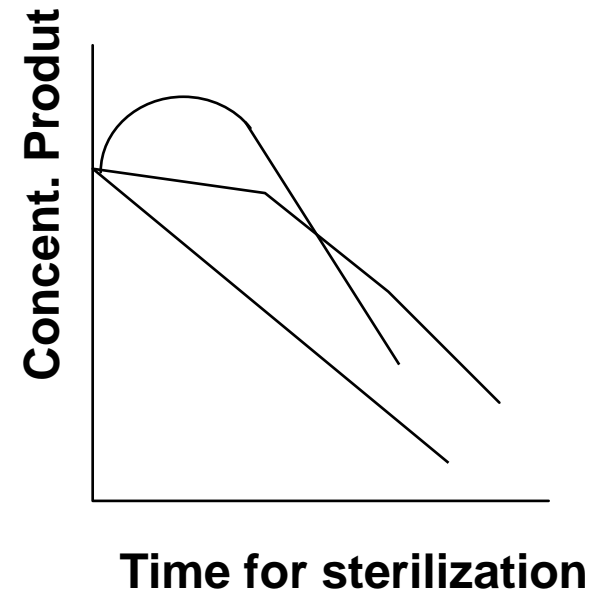
Effect of sterilization on product quality

Nutrient Inactivation – In addition to causing cell death, sterilization can cause nutrient destruction which can have a negative effect on the efficiency of the fermentation process.

$$\frac{dC}{dt} = -k_c C$$

$$\int_{c_1}^{c_2} \frac{dC}{C} = - \int_0^t k_c dt$$

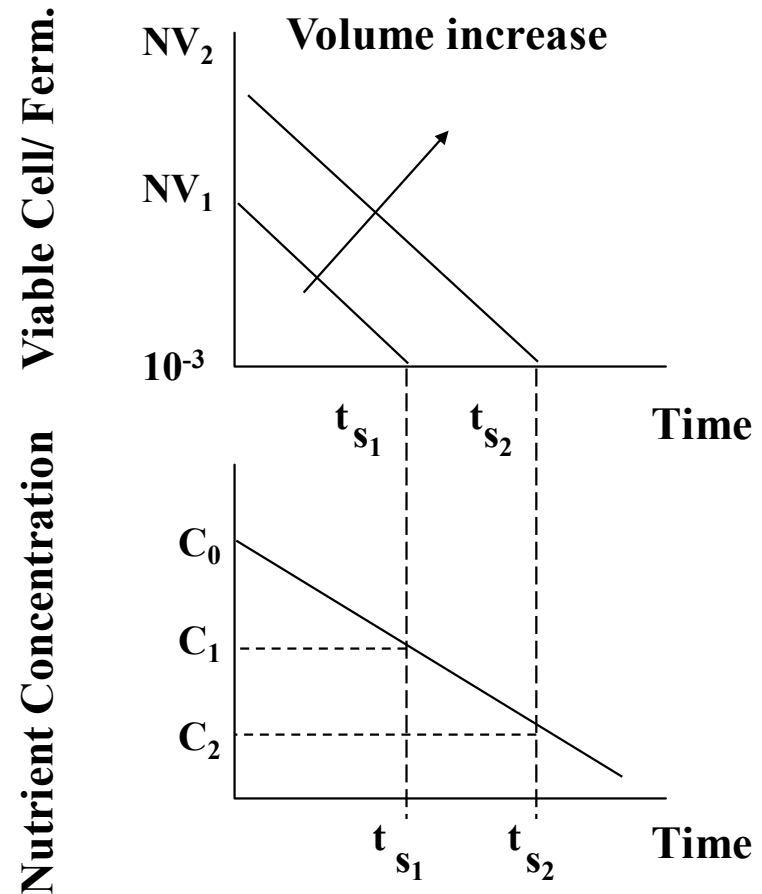
$$\ln \frac{C_2}{C_1} = - \int_0^t k_c dt$$



Effect of scaling up on sterilization

- When the volume increases from V_1 to V_2 the time necessary to obtain the same degree of sterilization increases from t_{s1} to t_{s2} .

- One consequence of the increase in time is the breakdown of nutrients (C). If this nutrient is important in product synthesis, it may reduce the concentration of product in scale up.



Continuous Sterilization

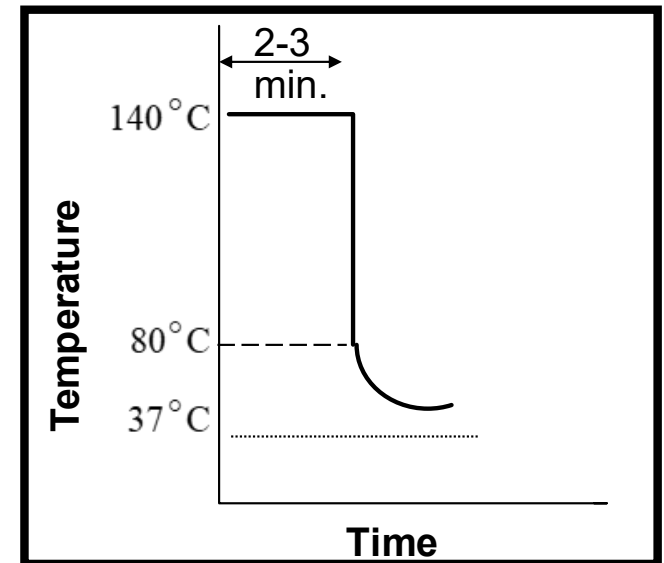
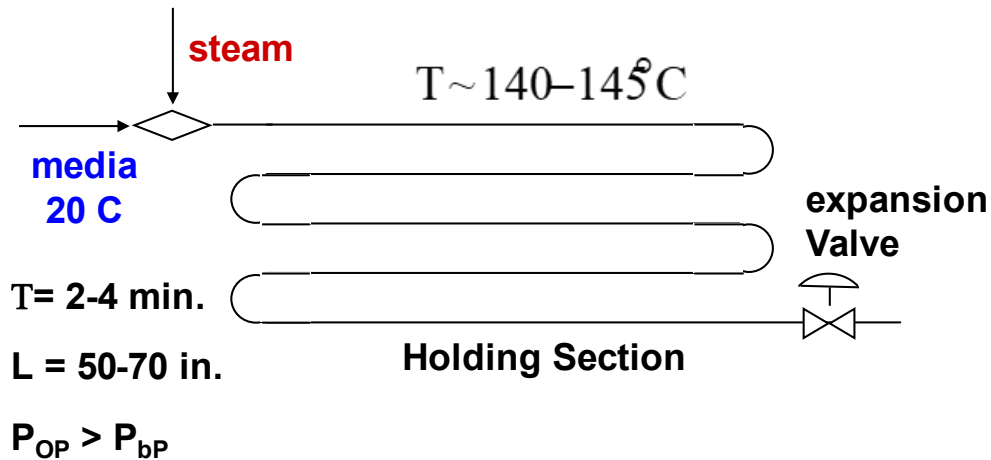
High temperature short time (HTST)

Rationale for using Continuous Sterilization vs Batch Sterilization:

- Continuous processes require continuous sterilization
- Steam saving
- Heating water reduction
- In heat-sensitive media, overheating is minimized
- Increased production capacity
- Easy to scale up

The advantages of HTST depend on the relationship between temperature and time.

Continuous sterilization with steam injection



III.6 – Media sterilization

Sizing of a continuous sterilizer

$$P_e B = \frac{VL}{E_z} \quad Da = k \frac{L}{V}$$

Pe = Peclet number

Da = Damkohler number

K = death constant

N_0 = initial number of
viable microorganisms

N = Final number of
viable microorganisms

E_z = dispersion coefficient

L = Sterilizer length

V = velocity of the fluid

