

People's Democratic Republic of Algeria

Ministry of Higher Education and Scientific Research

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Faculty of Technology

Department of Process Engineering and Petrochemical

Cours Reaction Engineering I: Non-Ideal Reactors and Bioreactors

Intended for students of a master's degree in chemical engineering

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2025-2026

Semester: 2

Course Unit: UEF 1.2.2

Subject 1: Reaction Engineering I: Non-ideal Reactors and Bioreactors

VHS: 45 hours (Lecture: 1.5 hours, Tutorial: 1.5 hours)

Credits: 4, Coefficient: 2

Summary

This course focuses on the analysis and design of non-ideal chemical reactors, where real flow behavior deviates from ideal models such as the Plug Flow Reactor (PFR) and the Continuous Stirred Tank Reactor (CSTR). To describe these deviations, the concept of Residence Time Distribution (RTD) is introduced as a key tool. RTD provides a statistical description of how long fluid elements remain inside the reactor, allowing engineers to detect flow irregularities such as dead zones, bypassing, and recirculation. It is experimentally determined using tracer techniques and mathematically described through functions like $E(t)$, $F(t)$, mean residence time, and variance. By combining RTD with reaction kinetics, it becomes possible to accurately predict reactor performance, including conversion and yield.

The course also covers hydrodynamic modeling of real reactors using models such as tanks-in-series and axial dispersion, as well as the role of dimensionless numbers like the Péclet and Damköhler numbers. In addition, it introduces bioreactors, which are used for enzymatic and microbial processes, emphasizing mass transfer, mixing, and reaction kinetics. Key models such as Michaelis–Menten and Monod equations describe enzymatic reactions and microbial growth. The course highlights the importance of coupling reaction kinetics, mass transfer, and fluid dynamics in reactor design, showing that real reactor behavior results from the interaction of these phenomena rather than ideal assumptions.

Keywords : Non-Ideal Reactors ; Residence Time Distribution (RTD) ; Reactor Modeling ; Reaction Kinetics ; Bioreactors

Nomenclature - List of Symbols

Symbol	Definition
t	Time
dt	Differential time element
t_s	Residence time
τ	Time of passage (V/Q)
α	Internal age of a molecule
λ	Remaining lifetime inside the reactor
$E(t)$	Residence Time Distribution (RTD) function
$F(t)$	Cumulative distribution function
$I(\alpha)$	Internal age distribution function
$f(x,y,z,\alpha,t)$	Local age distribution function
Q	Volumetric flow rate
$C(t)$	Tracer concentration at the outlet
C_0	Initial concentration
C_∞	Final (steady-state) concentration
n_0	Number of moles injected (tracer)

n	Number of moles leaving the reactor
$\bar{t}$	Mean residence time
σ^2	Variance of the distribution
σ	Standard deviation
V	Reactor volume
V_R	Total reactor volume
V_a	Active (accessible) volume
V_m	Dead (stagnant) volume
$G(s)$	Transfer function
$X(s), Y(s)$	Laplace transforms of input/output signals
r	Reaction rate
k	Reaction rate constant
C_A	Concentration of reactant A
S	Substrate concentration
X	Concentration (Impulse (Dirac) injection)
P	Product (metabolite)
r_{max}	Maximum reaction rate

K_m	Michaelis–Menten constant
$[S]$	Substrate concentration
J	Mass flux
D	Diffusion coefficient
D_{eff}	Effective diffusion coefficient
Da	Damköhler number
Re	Reynolds number
Fr	Froude number
N_p	Power number
We	Weber number
L	Reactor length
R	Radius
Ω	Cross-sectional area
μ	Specific growth rate
Y	Yield coefficient

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Introduction :

The actual behavior of flow reactors often deviates from ideal assumptions, particularly with regard to internal hydrodynamics. To better understand and characterize these deviations, it is essential to study the **residence time distribution (RTD)**, which describes the statistical distribution of the times that fluid elements spend inside the reactor.

Analyzing the RTD provides valuable insights into the reactor's hydrodynamic behavior, such as the presence of dead zones, bypass flows, or trailing effects. When these data are combined with the **chemical kinetics** of the reaction, it becomes possible to more accurately predict the **overall performance of the reactor**, in terms of conversion, yield, and thermal stability.

This chapter thus aims to introduce the theoretical foundations of RTD, explore the experimental methods used to determine it, and demonstrate how it serves as a powerful tool for diagnosis and modeling in the field of chemical reaction engineering

Liquid nitration is the process by which organic compounds are nitrated with a mixture of nitric and sulfuric acids to form materials such as nitroglycerin. The chlorination of liquid benzene and other hydrocarbons with chlorine gas is an example of a gas-liquid reaction.

In the study of homogeneous reactors, we have established a foundational understanding of how ideal reactor models are used to describe chemical transformations under steady-state conditions. Two canonical flow patterns are traditionally considered in this context:

The plug flow regime, in which all fluid elements spend exactly the same amount of time inside the reactor. This results in a uniform and predictable reaction progress along the reactor length.

The perfectly mixed regime, or continuous stirred tank reactor (CSTR), where molecules can exit at any time and are assumed to be instantaneously and uniformly mixed throughout the reactor volume.

These two idealizations are not just mathematical simplifications—they serve as reference models in design, performance evaluation, and kinetic interpretation. However, it has been consistently observed that real industrial reactors rarely exhibit ideal flow behavior. Instead, they lie somewhere between these two extremes, exhibiting partial mixing, channeling, stagnation zones, or even recirculation phenomena.

Such deviations, even when minor, can have substantial impacts on reactor performance. For instance, non-idealities may reduce the conversion of reactants, alter the product distribution, or introduce thermal instabilities that compromise safety or efficiency. This becomes especially critical when dealing with exothermic reactions, parallel reaction networks, or sensitive kinetic systems.

To better account for these deviations, the concept of residence time distribution (RTD) has been developed. RTD provides a statistical description of how long different fluid elements spend inside the reactor. It captures the macroscopic consequences of hydrodynamic imperfections and serves as a bridge between the physical flow patterns and chemical performance.

The objective of this chapter is thus threefold:

- 1- To introduce the theoretical basis and mathematical description of residence time distributions;
- 2- To explore how RTD can be experimentally determined, often using tracer techniques;
- 3- To demonstrate how RTD, when coupled with reaction kinetics, can be used to predict reactor conversion, yield, and selectivity more accurately.

Ultimately, this macroscopic approach—referred to as macromixing analysis—forms a cornerstone of reactor diagnosis and design. It is complemented, at a finer scale, by micromixing studies, which focus on how reactants come into molecular contact. The micromixing aspect will be the focus of the next chapter.

The topics addressed in this course cannot be confined to a fixed list of reactor types or standard situations. Each industrial or experimental case raises specific questions: What data are essential for analysis? What laboratory experiments or pilot-scale tests should be conducted?

Conversely, researchers or engineers aiming to gain a deep understanding of a reaction mechanism must reflect carefully on the choice of reactor and the operating conditions best suited to their objective. For example: how can one accurately measure an intrinsic reaction rate without interference from mass or heat transfer phenomena? These are precisely the kinds of questions that chemical reaction engineering seeks to answer, by relying on rigorous mathematical models supported by targeted experimental observations.

This educational resource has been designed to accompany Master's students through this analytical journey. It provides a clear methodological framework, grounded in the theoretical foundations of reaction engineering, while integrating tools for hydrodynamic diagnosis, modeling, and performance prediction.

As such, this manuscript serves both as:

A reference treatise, due to the depth and breadth of concepts covered (non-ideal flows, residence time distribution, micromixing, etc.);

In addition, a practical guide, structured for direct use in calculations, reactor design, and process operation.

Its primary goal is to support the scientific and technical training of students in process engineering, by offering a reliable, well-structured, and coherent tool that bridges theory, experimentation, and industrial application.

Chapter I

Residence Time Distribution (RTD)

I.1. Residence Time Distribution (RTD):

I.1.1. Definition and Principle:

The concept of residence time distribution (RTD) was introduced by Danckwerts in 1953 as a means of providing a quantitative description of flow system behavior. It allows for the identification of geometric imperfections in reactors and the modeling of non-ideal flow patterns that frequently occur in real processes.

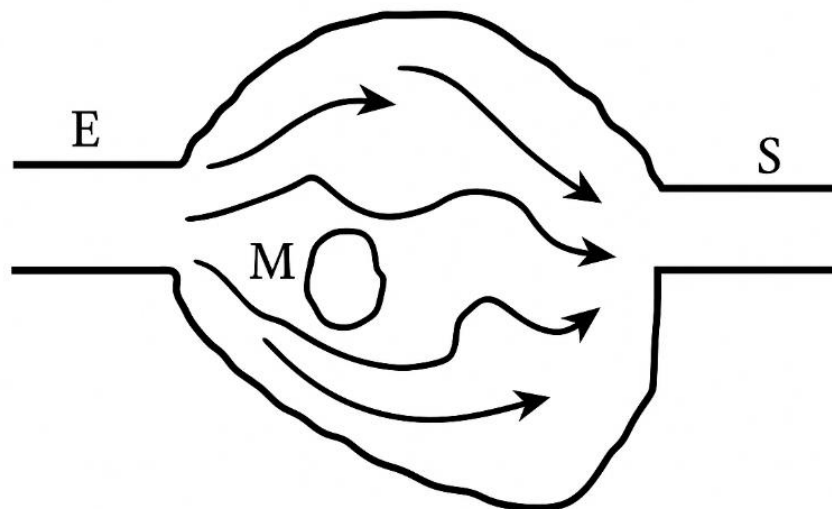
The purpose of RTD analysis is to characterize the hydrodynamic behavior of a system by tracking the complete—or partial—trajectory of a material stream passing through the reactor. As such, RTD serves as a fundamental tool to:

- Identify deviations from ideal reactor models (plug flow or perfectly mixed);
 - Detect anomalies such as dead zones, recirculation loops, or preferential pathways;
 - Provide an experimental basis for developing realistic models in chemical reaction engineering
 - Identify its flow irregularities.
-
- **Internal age α of the molecule:** the time that has elapsed since the molecule entered the reactor (i.e., since it crossed the inlet surface).
 - **Remaining life λ :** the time the molecule still has to spend inside the reactor before crossing the outlet surface.
 - **Residence time t_s :** the total time the molecule will have spent inside the reactor from entry to exit.

Note:

- The residence time is simply the **internal age** of the molecule **at the moment of exiting** the reactor.
- In general, we have the relation:

$$t_s = \alpha + \lambda$$



Open reactor

with complex internal flow

Since the number of molecules in the reactor is sufficiently large, this population can be described statistically using **distribution functions**.

I.1.2. Residence Time Distribution Function $E(t)$:

The **residence time distribution function $E(t)$** is defined such that "*the fraction of fluid (or molecules) that remains in the system (the reactor) for a time between t and $t + dt$ is equal to the product $E(t) \cdot dt$* ", as illustrated in the following figure.

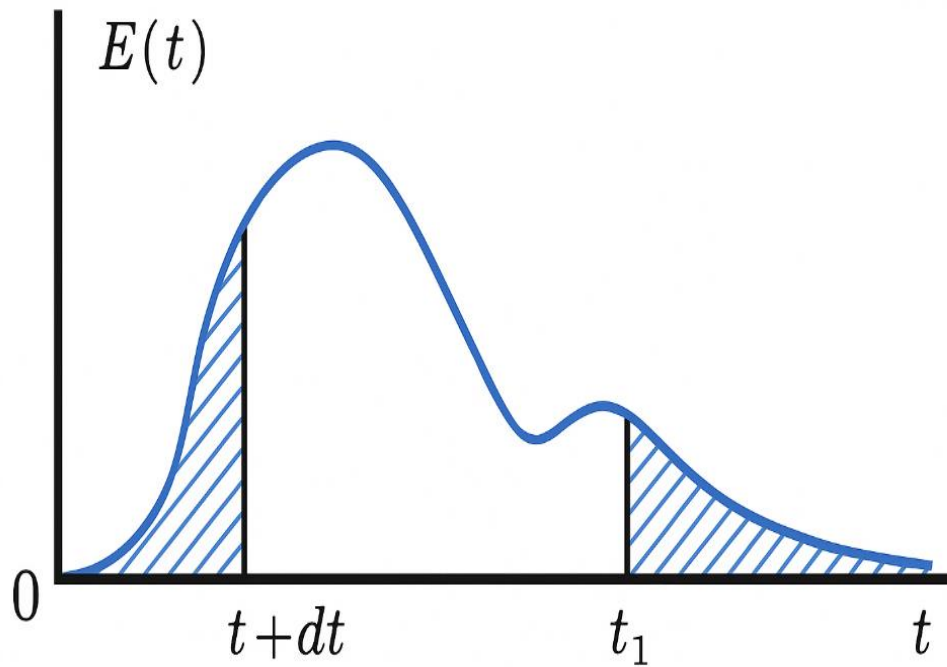


Figure.1: Residence Time Distribution $E(t)$

Based on this definition, it becomes evident that if we sum all the fractions corresponding to residence times ranging from zero to infinity, the result equals one. This indicates that $E(t)$ is a **normalized function**.

$$\int_0^{\infty} E(t) dt = 1$$

$\int_{t_1}^{t_2} E(t) dt$: Fraction of the flow that remained in the reactor between times t_1 and t_2 in the reactor.

I.1.3. Local Internal Age Distribution Function f :

We define the function $f(x, y, z, \alpha, t)$ such that $f(x, y, z, \alpha, t) \cdot d\alpha$ represents the fraction of the total number of circulating elements (molecules) at time t within the volume $dV_R = dx \cdot dy \cdot dz$, whose age lies between α and $\alpha + d\alpha$.

I.1.4 Global Internal Age Distribution Function $I(\alpha)$:

The global internal age distribution $I(\alpha)$ is defined such that $I(\alpha)d\alpha$ represents the fraction of the internal volume containing molecules whose age lies between α and $\alpha + d\alpha$.

Its expression as a function of f is:

$$I(\alpha) = \frac{1}{V_R} \int_{V_R} f dV_R = \overline{(f)}$$

Equation means that $I(\alpha)$ is the volumetric average of the local distribution function f .

$\int_0^{t_1} I(\alpha) d\alpha$ Represents the fraction of molecules 'younger' than t_1 within the reactor.

I.2. Experimental Determination of the Residence Time Distribution (RTD):

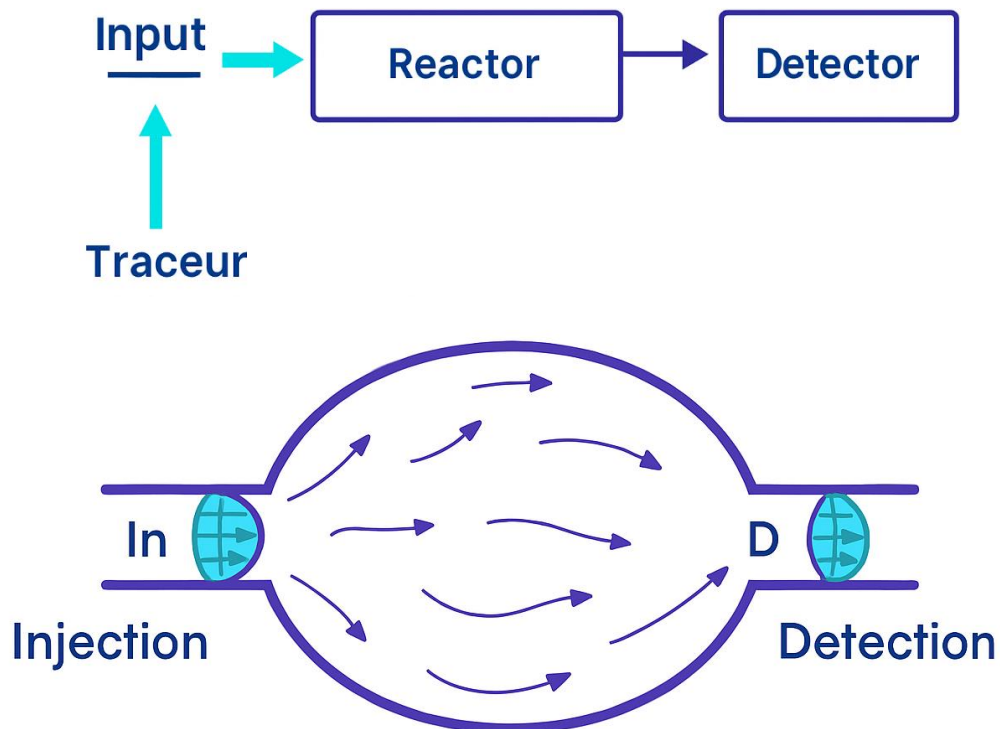


Figure.2: Determination of the Residence Time Distribution (RTD) via Tracer Injection at the Reactor Inlet

The Residence Time Distribution can be experimentally determined by injecting a tracer at the reactor inlet and monitoring its concentration at the outlet. This method allows the characterization of the flow pattern within the reactor.

Several types of tracers and detection techniques can be employed. The most common options are summarized in the following table.

Table.1 : Common Tracer Types and Detection Methods Used in RTD Experiments

Main Fluid	Tracer	Detection Method
Inert gas, air	Gaseous hydrocarbon	Flame ionization, catharometry, or mass spectrometry
Gaseous hydrocarbon	Inert gas	Catharometry or mass spectrometry
Aqueous phase	Electrolyte (e.g., salt) or dye	Conductivity, colorimetry, or spectrometry
Non-aromatic liquid hydrocarbon	Aromatic hydrocarbon	UV spectrometry
Solid	Particles similar in shape and density, but with a detectable property and no flow impact (e.g., magnetic particles)	Appropriate detector, magnetic detector

I.2.1. Tracer:

The tracer is used to label the fluid without disturbing its flow. It must meet the following criteria:

- Have the **same physical properties** as the fluid.
- Be **chemically inert** (no reaction with the fluid or the reactor).
- Be **continuously measurable**.
- Be **injected and detected** uniformly across the **entire cross-section** of the flow

➤ Pulse Injection (or Dirac Injection)

This method involves injecting a number of moles n_0 over a **very short period of time** at the reactor inlet.

Then, the **outlet concentration** $c_{I(t)}$ is measured as a function of time

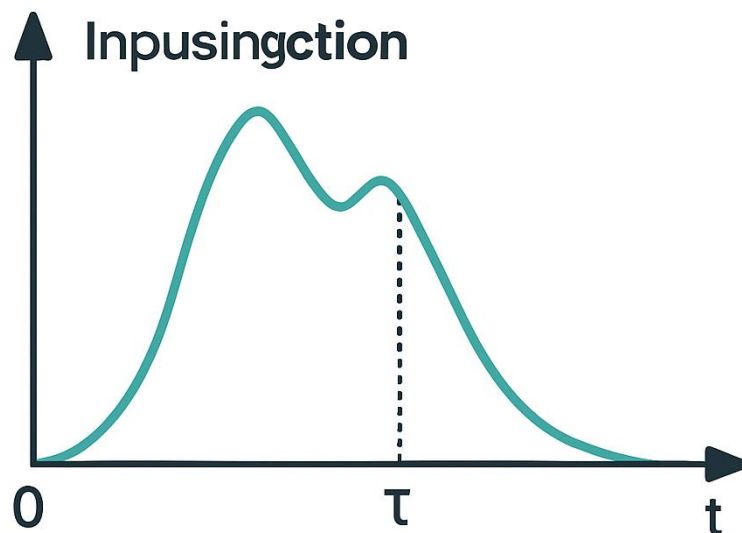


Figure.3: Pulse Injection.

➤ Tracer Balances:

➤ Pulse injection (or Dirac):

- At the outlet, during a time interval dt :

$$\frac{Q \cdot c_I(t) dt}{n_0} = E(t) dt$$

Fraction of the tracer having resided in the reactor between time t and $t + dt$

- Inlet and outlet of the reactor

$$n_0 = \int_0^{+\infty} Q \cdot c_I(t) dt$$

$$E(t) = \frac{c_I(t)}{\int_0^{+\infty} c_I(t) dt}$$

If the flow rate is uniform

The RTD function $E(t)$ is therefore the normalized response of the reactor to a pulse injection.

➤ **Response to a pulse injection:**

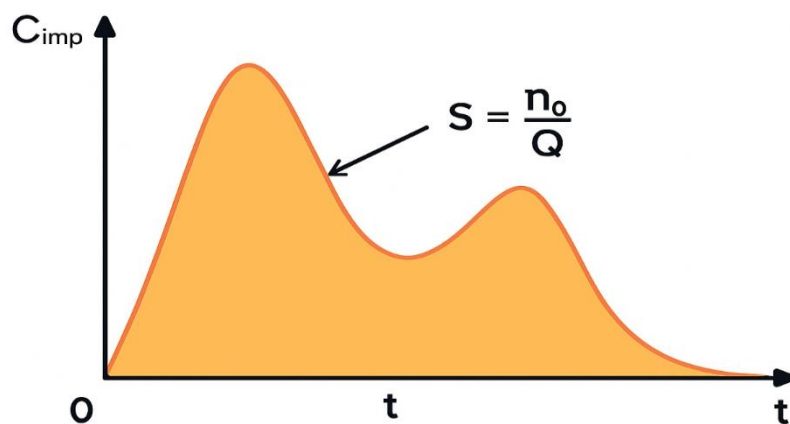


Figure.4: Response to a pulse injection.

$$n = Q C(t)dt$$

Where:

n is the number of moles exiting during the time interval dt ,

Q is the volumetric flow rate of the fluid (in m^3/s or L/s),

$C(t)$ is the concentration of the tracer at the reactor outlet at time t ,

This equation represents the material balance on the tracer, allowing the determination of the residence time distribution function $E(t)$ through normalization of the measured outlet concentration.

The total number of moles (n_0) introduced into the reactor is expressed by the following relation:

$$n_0 = \int_0^{\infty} Q C(t)dt$$

$$E(t) = \frac{C(t)}{\int_0^{\infty} C(t)dt}$$

This function can also be written from the previous equation:

$$E(t) = \frac{1}{\tau} * \frac{C(t)}{C_0}$$

At time t , the amount of tracer that has exited the reactor since the beginning of the experiment corresponds to that with a residence time less than t :

$$\int_0^t Q c dt = n \int_0^t E(t_s)dt_s$$

$$Q c(t) = n E(t)$$

Let us define $C_0 = \frac{n}{V_R}$: the concentration that the tracer would have if it were uniformly distributed throughout the entire volume.

In discretized form ($\Delta t = \text{constant}$):

$$\int_0^{\infty} C(t) dt = \sum_{i=1}^N c_i \Delta t_i$$

I.2.2.Characteristic of a Mean Distribution: it represents the **mean residence time**.

$$\bar{t}_s = \int_0^{\infty} t E(t) dt = \frac{\int_0^{\infty} t C(t) dt}{\int_0^{\infty} C(t) dt}$$

In discretized form:

$$\bar{t}_s = \frac{\sum_{i=1}^N t_i c_i \Delta t_i}{\sum_{i=1}^N c_i \Delta t_i}$$

This discretized form is generally used when we have n experimental data points (C_i measured at t_i), where Δt_i represents the interval between two measurements.

I.2.3. Characteristic of a distribution - Variance (σ^2): It characterizes the spread of the distribution around the mean.

$$\sigma^2 = \frac{\int_0^{\infty} t^2 C(t) dt}{\int_0^{\infty} C(t) dt} - (\bar{t}_s)^2$$

$$\theta = \frac{t}{\overline{(t_s)}} \quad quad \quad d\theta = \frac{dt}{\overline{(t_s)}}$$

The relationship between $E(t)$ and $E(\theta)$ is determined based on the fact that both functions physically represent, at the reactor outlet, the same fraction of fluid corresponding to a residence time t , that is:

$$E(\theta)d\theta = E(t)dt$$

$$E(\theta) = \overline{(t_s)}E(t)$$

- **Reduced variance :**

$$\sigma^2(\theta) = \frac{\sigma^2(t)}{\overline{(t_s)}^2} = \int_0^\infty (\theta - 1)^2 E(\theta) d\theta$$

➤ **Step injection**

Positive step: the inlet suddenly switches from zero concentration to concentration c_0 . The outlet concentration is measured as: $c_E(t)$

$$\frac{c_E(t)}{c_0} = \int_0^t E(t) dt = F(t)$$

Fraction of fluid that entered after $t = 0$ (younger than t)

The function $F(t)$ appears as the dimensionless response of the reactor to a positive step input of tracer.

$$E(t) = \frac{dF}{dt}$$

Therefore, we can calculate $E(t)$ from $F(t)$.

Negative step (or purge-step): the inlet concentration abruptly shifts from concentration c_0 to zero concentration. The outlet concentration is measured: $c_{PE}(t)$

$$\frac{c_{(PE)}(t)}{c^0} = \int_t^{+\infty} E(t') dt' = 1 - F(t)$$

Fraction of fluid older than t .

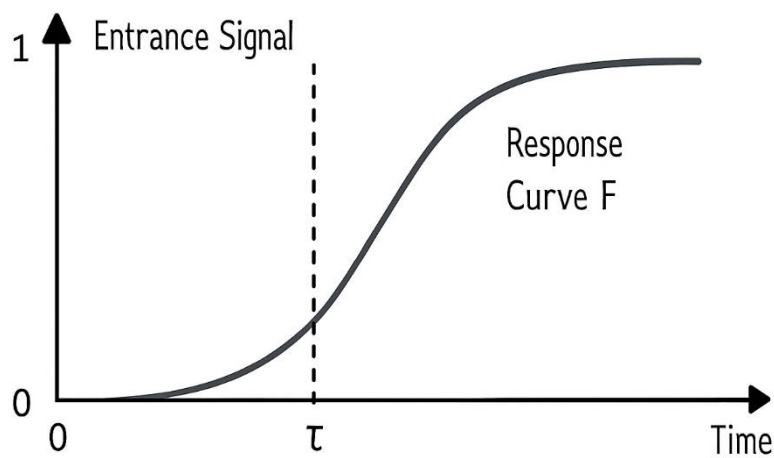


Figure.5: Fraction of fluid older than t .

I.3. Arbitrary Input, Two-Point Measurement Method

A system is said to be **linear** when the input and output variables are related by a set of differential or partial differential **linear** equations. In this case, the usual superposition principle can be applied: the response to a sum of disturbances is equal to the sum of the responses to each disturbance acting alone.

The tracer concentration signal at the outlet of the reactor following an arbitrary input injection can thus be considered as the response of a linear system to a disturbance in the input signal. Let $x(t)$ be the input concentration signal and $y(t)$ the corresponding output response. We consider the normalized signals with: $S=n/Q$

In order to eliminate the constraints of injection and detection methods, two concentration measurements can be taken at two different levels in the reactor: $x(t)$ and $y(t)$.

$$\int_0^{\infty} x(t)dt = \int_0^{\infty} y(t)dt = 1$$

$$y(t_2) = \int_0^{t_2} x(t_1)E(t_2 - t_1)dt_1$$

Signal Superposition Principle

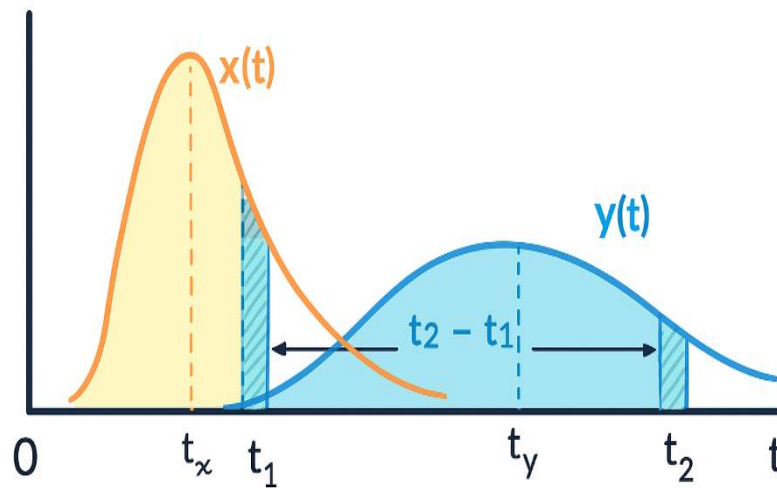


Figure.6: signal superposition principal.

If the system is linear, the Laplace transform $L(f)$ can be applied to $x(t)$ and $y(t)$ to obtain $X(s)$ and $Y(s)$.

$$L(f) = \int_0^{+\infty} \exp(-s t) f(t)dt$$

$$Y(s) = X(s)G(s)$$

$G(s)$, transfer function of the system, $G = L(E)$

I.4. Moments:

Definition of the moment μ_n and the centered moment μ'_n of order n of the distribution $E(t)$:

$$\mu_n = \int_0^{+\infty} t^n E(t) dt \quad ; \quad \mu'_n = \int_0^{+\infty} (t - \overline{ts})^n E(t) dt$$

➤ **First-order moment:**

$$\overline{(t)} = \mu_1 = \int_0^{+\infty} t E(t) dt$$

Mean residence time.

$$\overline{(t)} = \tau = \frac{V}{Q}$$

(if there is no dispersion at the reactor inlet/outlet)

➤ **Second-order central moment:**

$$\sigma^2 = \mu'_2 = \int_0^{+\infty} (t - \overline{ts})^2 E(t) dt = \mu_2 - \overline{(ts)^2}$$

σ^2 : variance of the distribution; **σ : standard deviation**.
Characterizes the spread of the distribution $E(t)$, and therefore the mixing in the reactor.

Linear systems:

$$\mu_n = (-1)^n \lim_{s \rightarrow 0} \left(\frac{\partial^n G}{\partial s^n} \right)$$

Van der Laan's theorem.

The moments of the system located between the two measurement points $x(t)$ and $y(t)$ are expressed as:

$$\overline{(t_s)} = \overline{(t_y)} - \overline{(t_x)} \quad , \quad \sigma_s^2 = \sigma_y^2 - \sigma_x^2$$

I.5 Residence Time Distribution in Ideal Reactors (*Incompressible Fluid*)

I.5.1 Plug Flow Reactor (PFR)

A **plug flow reactor** behaves like a pure delay system. All molecules have the same residence time $(t_s) = \tau = \frac{V_R}{Q}$ The **Residence Time Distribution (RTD)** is a very narrow peak located at time τ , given by:

$$E(t_s) = \delta(t_s - \tau)$$

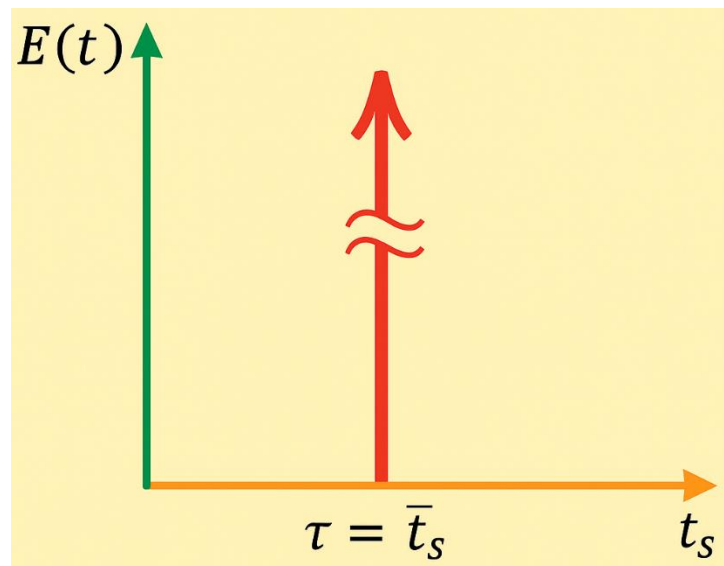


Figure.7: The Residence Time Distribution (RTD) is a very narrow peak located at time τ

In the case of a step injection, the tracer concentration abruptly changes at $t=t_0$, from a value of 0 to a value of C_0 in the feed. This signal is described by the mathematical function $H(t-t_0)$, where H is the unit step function of Heaviside.

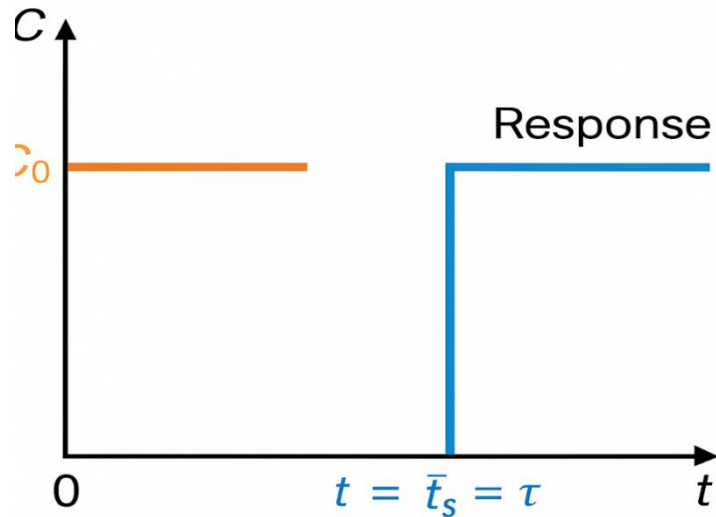


Figure.8: the tracer concentration abruptly changes at $t=t_0$, from a value of C_0

- **Response to a Step Injection**

Distributions E and F:

$$E(t) = \delta(t - \bar{t}) \qquad F(t) = H(t - \bar{t})$$

Moments:

$$\bar{t} = \tau \qquad \sigma^2 = 0$$

1.5.2. Continuously Stirred Tank Reactor (CSTR)

To establish the expression for $E(t)$, let us consider the response to an impulse injection. We introduce a quantity of tracer (n moles) into the reactor. The concentration instantly rises $C_0 = \frac{n}{V_R}$, to then evolves according to the equation:

$$0 = Q C + \frac{V_R(d C)}{d t}$$

It can be easily deduced that:

$$C(t) = \frac{C_0}{\tau} \exp\left(-\frac{t}{\tau}\right)$$

Thus, the RTD is derived based on equation:

$$E(t_s) = \frac{1}{\tau} \exp\left(-\frac{t_s}{\tau}\right)$$

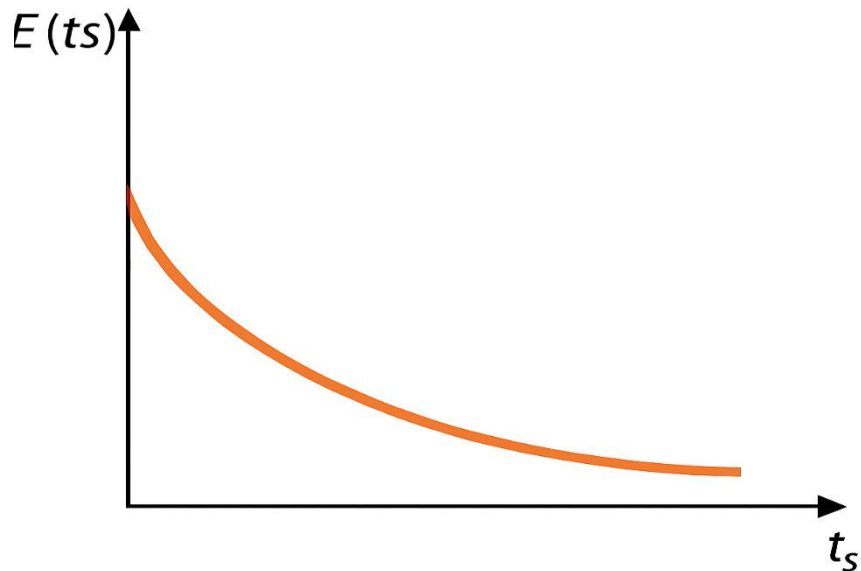


Figure.9: the RTD is derived based on equation $E(t)$

In addition, the function F (the integral function):

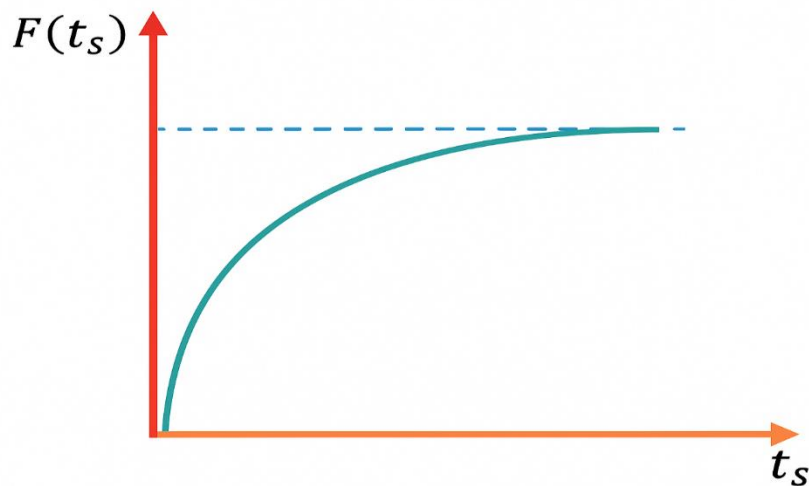


Figure.10: the RTD is derived based on equation F

$$F(t_s) = \int_0^{t_s} E(t) dt$$

$$F = 1 - \exp\left(-\frac{t_s}{\tau}\right)$$

Impulse response:

$$c_{I(t)} = c^0 \exp\left(-\frac{t}{\tau}\right) \quad \text{and} \quad E(t) = \frac{1}{\tau} \exp\left(-\frac{t}{\tau}\right)$$

Step response:

$$c_{E(t)} = c_0 \left(1 - \exp\left(-\frac{t}{\tau}\right)\right) \quad F(t) = 1 - \exp\left(-\frac{t}{\tau}\right)$$

Moments:

$$t = \tau \quad \sigma^2 = \tau^2$$

I.5.3 Arbitrary Reactor

In a real reactor where the flow is of arbitrary type, intermediate curves are generally observed between the two limiting behaviors (PFR and CSTR).

I.5.4 Example: Tubular Reactor with Steady Laminar Flow

It is assumed that the flow is purely convective in the absence of any diffusion. The velocity profile across the reactor section is parabolic.

$$u = u_0(1 - y^2)$$

Where $y = \frac{r}{R}$ is the radial distance to the axis of the tube, of radius R.

u_0 is the maximum velocity at the center of the tube.

The average velocity of the fluid is $\overline{u} = \frac{u_0}{2}$.

Let L be the length of the tube. The residence time in the tube is

$$\tau = \frac{V}{Q} = \frac{\Omega L}{\Omega \overline{(u)}}$$

With Ω the cross-sectional area of the tube

$$\tau = \frac{L}{\overline{(u)}}$$

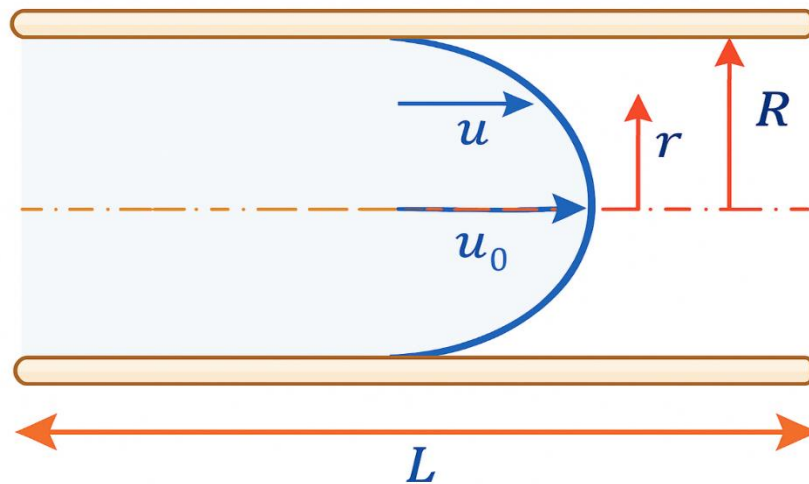


Figure.11: Tubular Reactor with Steady Laminar Flow

The residence time of the fluid stream located at the relative distance 'y' from the axis of the tube is:

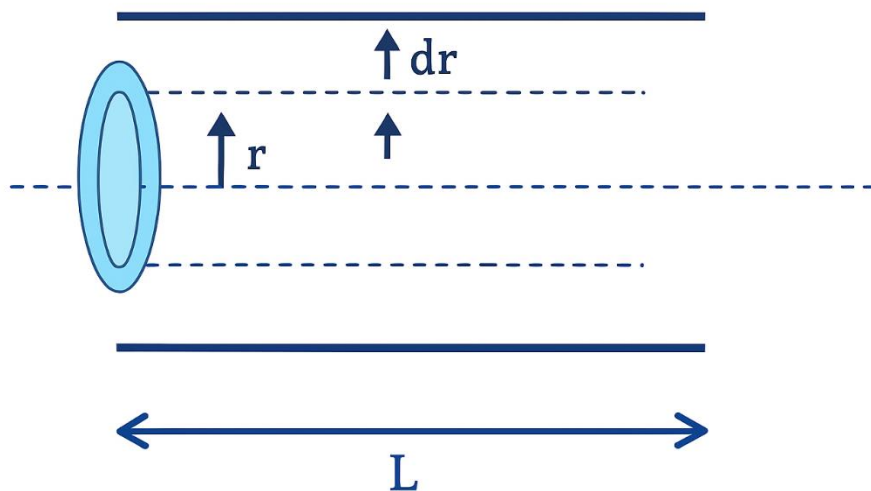


Figure.12: the relative distance 'y' from the axis of the tube

$$t_s = \frac{d V_R}{d Q} = \frac{2 \pi r . dr . L}{u . 2 \pi r . dr}$$

$$t_s = \frac{L}{u} = \frac{L}{u_0(1 - y^2)} = \frac{L}{2 \overline{(u)}(1 - y^2)}$$

$$t_s = \frac{\tau}{2(1 - y^2)}$$

By definition of the RTD (Residence Time Distribution).

$$\begin{aligned} E(t_s).dt_s &= \frac{dQ}{Q} = \frac{u . 2 \pi r . dr}{\overline{(u)}. \pi R^2} = \frac{u_0(1 - y^2). 2 r . dr}{\overline{(u)}R^2} \\ &= 4 y (1 - y^2). dy \end{aligned}$$

On the other hand, from the expression of t_s , we obtain:

$$(1 - y^2) = \frac{\tau}{2 t_s} \quad ; \quad y = \left(1 - \frac{\tau}{2 t_s}\right)^{\left\{\frac{1}{2}\right\}}$$

$$dy = \left(\frac{1}{2}\right) \left(1 - \frac{\tau}{2 t_s}\right)^{\left\{-\frac{1}{2}\right\}} \left(\frac{\tau}{2 t_s^2}\right) dt$$

By referring back to relation, we obtain:

$$E(t_s).dt_s = 4 \left(1 - \frac{\tau}{2 t_s}\right)^{\left\{\frac{1}{2}\right\}} \left(\frac{\tau}{2 t_s}\right) \times \left(\frac{1}{2}\right) \left(1 - \frac{\tau}{2 t_s}\right)^{\left\{-\frac{1}{2}\right\}} \left(\frac{\tau}{2 t_s^2}\right) dt$$

We finally obtain:

$$E(t_s) = \frac{\tau^2}{2 t_s^3}$$

However, it must be noted that the smallest possible residence time is $t_s = \frac{\tau}{2}$ corresponding to the central streamline; thus, we obtain:

$$E(t_s) = \frac{\tau^2}{2 t_s^3} H\left(t_s - \frac{\tau}{2}\right)$$

$$H(t_s - \tau/2) \begin{cases} = 0 & t < \tau/2 \\ = 1 & t_s \geq \tau/2 \end{cases}$$

We can also obtain F(t):

$$F(t) = \int_{\frac{\tau}{2}}^t E(t) dt = 1 - \left(\frac{1}{4}\right) \left(\frac{t}{\tau}\right)^{-2}$$

I.6. Diagnostics of Reactor Operation Modes :

The measurement of the RTD using the tracer method can provide valuable insights into reactor malfunctions.

a. 1st case: the existence of a dead volume $(V_m) \overline{(t_s)} < \tau$

This indicates that the volume available for fluid flow is smaller than the total volume of the reactor. It follows that there are regions in the reactor where the fluid does not circulate properly, which are referred to as *dead zones*.

$$V_R = V_m + V_a$$

Where:

V_R : Reactor volume

V_m : Dead (stagnant) volume

V_a : Accessible volume

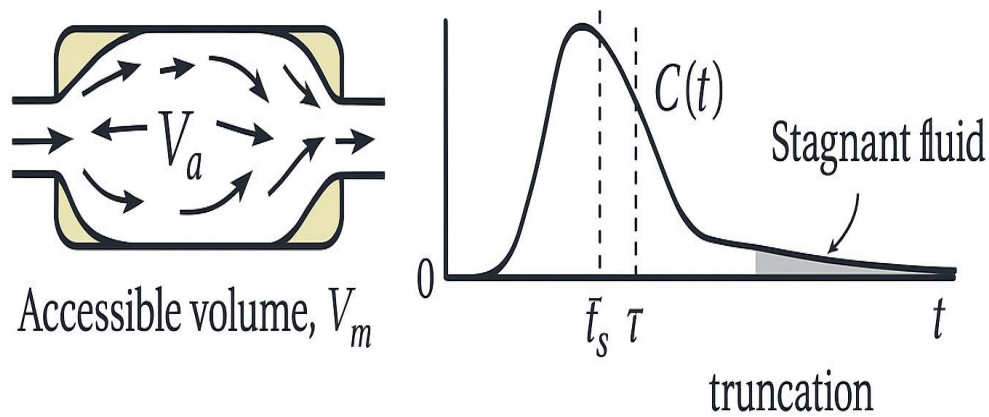


Figure.13: the existence of a dead volume (V_m) $(\bar{t}_s) < \tau$

b. Second case: the existence of a short circuit $(\bar{t}_s) > \tau$

In such a situation, the volumetric flow rate of fluid passing through the total volume of the reactor is smaller than the total volumetric flow rate. The fraction of flow that passes through the reactor as a short-circuit can be determined as follows:

$$Q = Q_a + Q_c$$

$$\frac{Q_c}{Q} = 1 - \frac{\tau}{(\bar{t}_s)}$$

However, if a sharp peak appears just after injecting the tracer at the inlet, this indicates the presence of a tracer short-circuit flow. A short-circuit is a flow of fluid that passes very quickly through the vessel without mixing with the rest of the fluid.

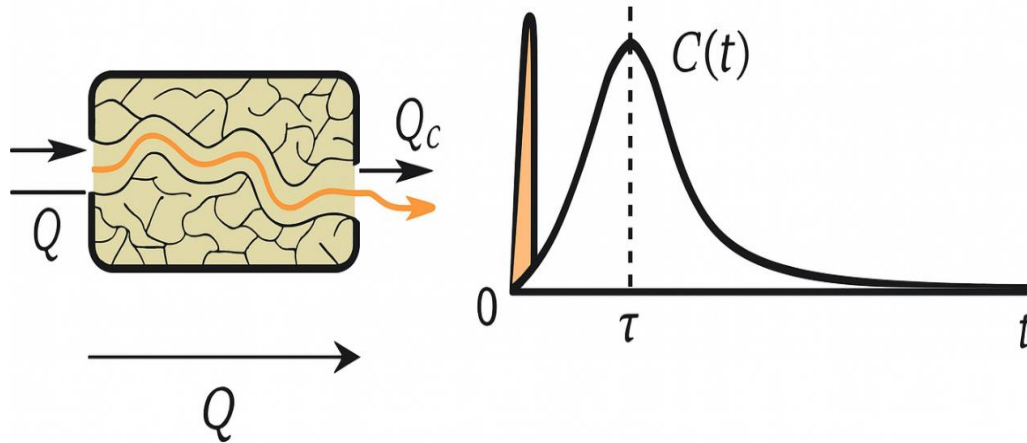


Figure.14: the existence of a short circuit $\overline{t_s} > \tau$

I.7. Determination of Conversion in Non-Ideal Reactors:

For reactant A in the outlet stream, the average concentration of reactant at the outlet C_{AS} is given by the sum of the products of C_A remaining in a time interval between t and $t + \Delta t$, multiplied by the fraction of the outlet stream during that time.

The average outlet concentration of the reactant (C_{AS}) is given by :

$$\overline{\{C\}_{\{AS\}}} = \int_0^{\infty} C_A E(t) dt$$

$$\frac{\overline{\{C\}_{\{AS\}}}}{C_{\{A0\}}} = 1 - X_A = \int_0^{\infty} \left(\frac{C_A}{C_{\{A0\}}} \right) E(t) dt$$

a. Zero-order reaction: ($r = k$)

$$-\frac{dC_A}{dt} = r = k$$

$$\frac{\overline{\{C\}_{\{AS\}}}}{C_{\{A0\}}} = 1 - X_A = \left(\frac{1}{\tau} \right) \int_0^{\infty} \left(1 - \frac{k t}{C_{\{A0\}}} \right) e^{-\frac{t}{\tau}} dt$$

b. First-order reaction: ($r = k \cdot C_a$)

$$-\frac{dC_A}{dt} = k C_A \Rightarrow \frac{C_A}{C_{A0}} = e^{\{-kt\}}$$

$$1 - \overline{\{X\}_{AS}} = \left(\frac{1}{\tau}\right) \int_0^\infty e^{\{-(k + \frac{1}{\tau})t\}} dt$$

c. Second-order reaction: ($r = k C_a^2$)

$$-\frac{dC_A}{dt} = k C_A^2 \Rightarrow \frac{1}{C_A} - \frac{1}{C_{A0}} = k t$$

$$\frac{\overline{\{C_{AS}\}}}{C_{A0}} = 1 - X_A = \int_0^\infty \left(\frac{1}{1 + k C_{A0} t} \right) * \left(\frac{1}{\tau} \right) * e^{\{-\frac{t}{\tau}\}} dt$$

Chapter II

Macroscopic modeling of flow in a real reactor

II.1 Methodology (steps to follow)

1st step *(in green italic)*:

Determine the experimental RTD curve of the real reactor to be modeled (*tracer method*)

$$\rightarrow E_{ex}(t_s)$$

2nd step *(requires a good understanding of the reactor's operation)*:

Propose a **hydrodynamic model** (*flow model*) with its **circulation diagram**

II.2 Parallel filaments model

The fluid flow in the free volume V_R with a flow rate Q is modeled as many parallel plug flow filaments, each having a residence time t_s . By arranging these filaments in order of increasing residence time, the fluid enters all of them at the same moment and leaves the reactor progressively from the shortest to the longest times.

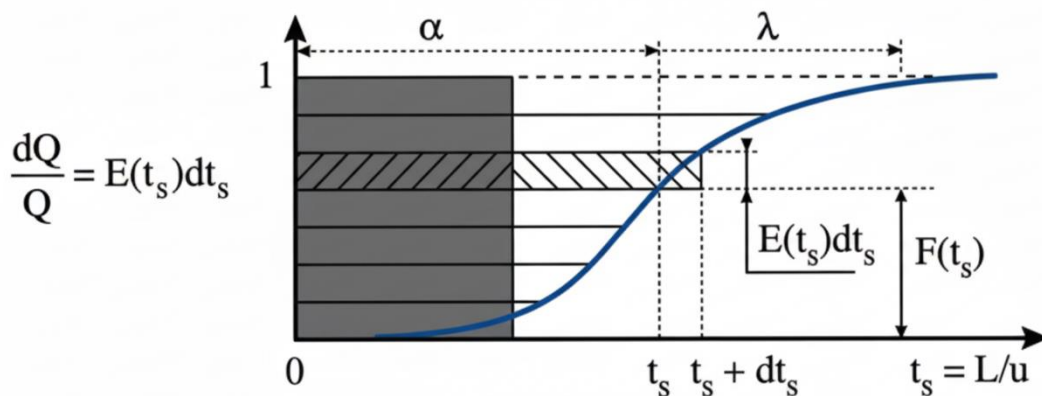


Figure.1: Parallel filaments model.

By definition of the RTD, the stream with residence time between t_s and $t_s + dt_s$ receives a fraction of the total flow rate Q given by:

$$E(t_s)dt_s = \frac{dQ}{Q}$$

Hence, the stream with residence time t_s is located at the normalized “height

$$\frac{\Delta Q}{Q} = \int_0^{t_s} E(t) dt$$

- The curve $F(t)$ is the envelope of the ends of the flow filaments and represents the evolution of the fluid inside the reactor.
- Using this model, the internal age of the molecules, α , and their mean lifetime, λ , can be defined such that $\alpha + \lambda = t_s$.
- The fraction of volume occupied by fluid with an age less than α is equal to the ratio of the shaded area to the total area between the curve F and its horizontal asymptote.
- The internal age distribution $I(t)$ is defined so that $I(t) dt$ represents the fraction of volume occupied by fluid whose age lies between t and $t + dt$.

$$\frac{\int_0^\alpha (1 - F) dt}{\int_0^\infty (1 - F) dt} = \frac{\int_0^\alpha (1 - F) dt}{\bar{t}_s} = \int_0^\alpha I(t) dt \quad \text{ou} \quad I(\alpha) = \frac{1 - F(\alpha)}{\bar{t}_s}$$
$$= \left(\frac{1}{\bar{t}_s} \right) \int_0^\infty E(t_s) dt_s$$

II.3 Modeling of a Real Continuous Stirred Tank Reactor Using Ideal Reactor Networks

To account for key flow characteristics, the real reactor is modeled by combining ideal reactors that represent:

- Well-mixed zones, approximated by an ideal mixer;

- Recycles or short-circuiting flows, represented by ideal connections between units;
- Partially inactive (dead) zones that exchange material with more actively flowing regions.

Representation of Non-Ideal Continuous Stirred Tank Reactors

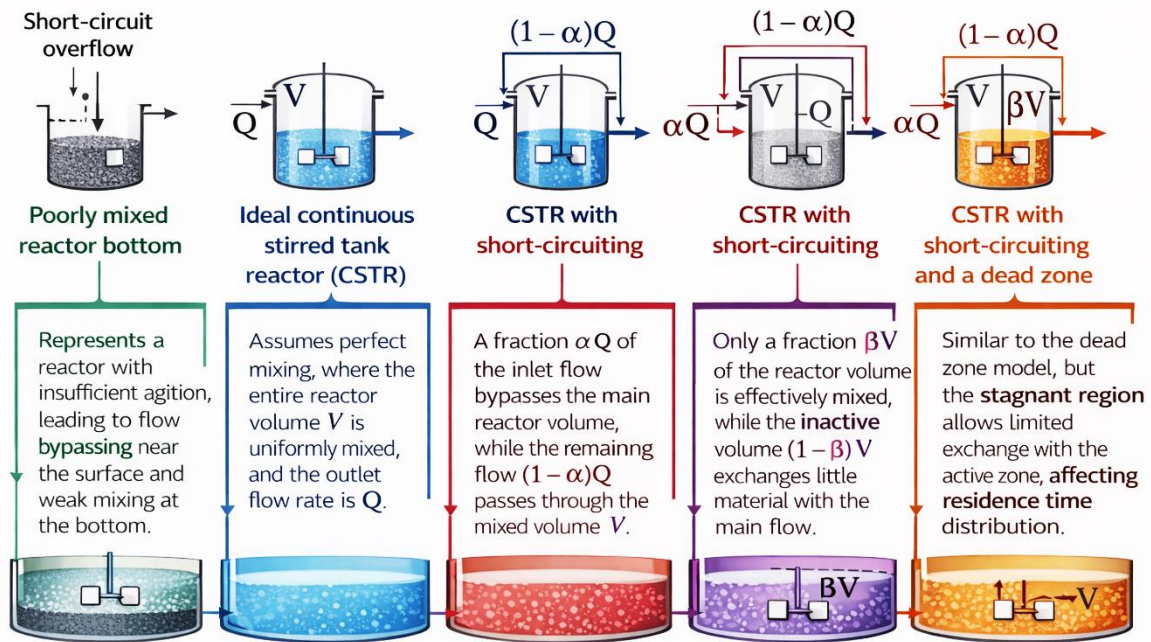


Figure.2: Real continuous stirred tank reactor (left) and four associated hydrodynamic models.

The simplest model consists in assimilating the real reactor to an ideal continuously stirred tank reactor (CSTR).

There is only one unknown parameter, V/q , which can be easily obtained through a DTS (Residence Time Distribution) measurement.

However, it is a rough model, unable to account for short-circuiting and stagnant fluid at the bottom of the tank.

The second model considers short-circuiting but ignores stagnant fluid. It has two unknowns: α (active flow rate fraction) and residence time $V/(\alpha Q)$.

The third model adds an inaccessible fluid volume $(1 - \beta)V$ with unknowns α and $(\beta V)/(\alpha Q)$. It's a variation of the second model.

The fourth model is the most detailed. It includes exchange between ideal and stagnant zones with four unknowns: α , $V/(\alpha Q)$, β , and γQ (recycle flow).

Using transient and nodal mass balances, the Laplace transform of $E(t)$ can be obtained. The moments are then derived using Van der Laan's theorem:

$$\mu_n = (-1)^n \lim_{s \rightarrow 0} \partial^n G / \partial s^n$$

The table shows expressions for $G(s)$, $\bar{t}$, σ^2 , and optionally $E(t)$ as functions of: $\tau = V/Q$, α , β , and γ .

II.4 Tubular Reactor Modeling

Tubular reactors operate close to ideal plug flow, with deviations mainly due to axial mixing and pressure drop. Their RTD is typically bell-shaped and narrows as flow approaches ideal behavior. Common models include **plug flow with dispersion** and **tanks-in-series**.

II.4.1 Axial Dispersion Model (1 parameter)

The tubular reactor deviates from ideal plug flow due to axial dispersion, assumed to follow **Fick's law**. Reactor properties are uniform across any cross-section.

$$\frac{D_A \partial^2 C}{\partial z^2} - \bar{u} \frac{\partial C}{\partial z} = \frac{\partial C}{\partial t}$$

$$X = z/L$$

$$C^* = C/C_0$$

$$\theta = t/\tau$$

$$\frac{\partial^2 C^*}{\partial X^2} - P \frac{\partial C^*}{\partial X} = P \frac{\partial C^*}{\partial \theta}$$

$$P = \frac{\bar{u}L}{D_A}$$

II.4.2 Peclet Criterion (Peclet Number)

The **Peclet number (P)** quantifies the relative importance of **convection** compared to **axial dispersion** in a tubular reactor.

Physical Interpretation (very short)

P $\gg$ **1**: Convection dominates $\rightarrow$ near **ideal plug flow**

P $\ll$ **1**: Dispersion dominates $\rightarrow$ strong **axial mixing**

P $\rightarrow \infty$: Ideal plug flow

P $\rightarrow 0$: Perfectly mixed behavior

The solution depends on the applied boundary conditions (three types).

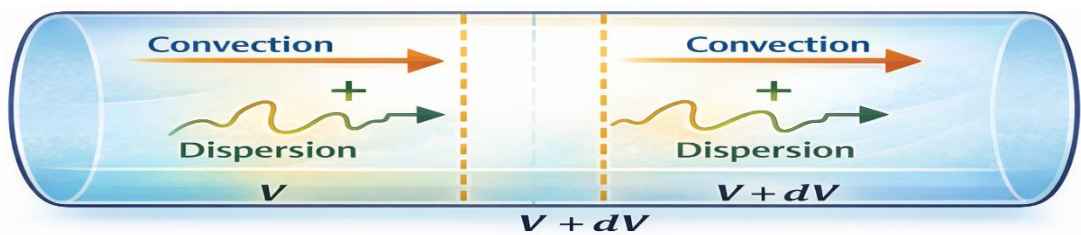


Figure.3: convection compared to axial dispersion in a tubular reactor

The table below summarizes the expressions of μ_1 and σ^2 of $E(\theta)=C^*(1,\theta)$, obtained from integration.

II.4.3 Types of boundary conditions applied to the model:

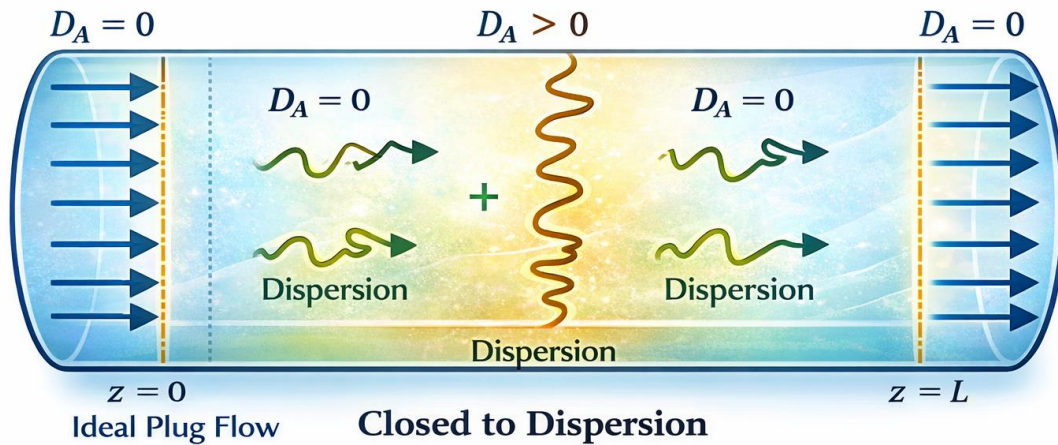


Figure.4: Types of boundary conditions applied to the model

$$\sigma^2 = \tau^2 * \left(\frac{2}{P} - \left(\frac{2}{P^2} \right) * (1 - e^{-P}) \right)$$

$$\bar{t}_s = \tau$$

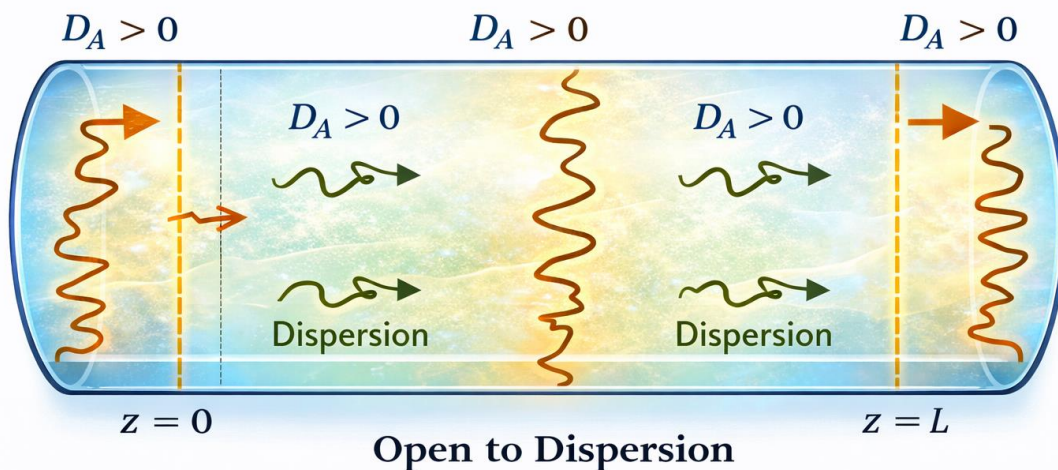


Figure.5: Types of boundary conditions open to dispersion

$$\bar{t}_s = \left(1 + \frac{2}{P} \right) \tau$$

$$\sigma^2 = \tau^2 * \left(\frac{2}{P} + \frac{8}{P^2} \right)$$

Semi-open to dispersion (upstream) / Semi-open to dispersion (downstream)

Semi-open to dispersion

$$\bar{t}_s = \left(1 + \frac{1}{P} \right) \tau$$

$$\tau^2 * \left(\frac{2}{P} + \frac{3}{P^2} \right)$$

When the deviation from ideal plug flow is negligible ($P > 100$).

$$E(t_s, P) = \left(\frac{1}{2\tau} \right) * \sqrt{\left(\frac{P}{\pi} \right)} * \exp \left(- \frac{P * (\tau - t_s)^2}{4\tau^2} \right)$$

RTD for the weak axial dispersion model, characterized by the Péclet number P .

$$E(\theta, P) = \frac{1}{2} * \sqrt{\left(\frac{P}{\pi} \right)} * \exp \left(- \frac{P * (1 - \theta)^2}{4} \right)$$

$$E(\theta) = \tau E(t_s)$$

When the Péclet number is well below 100 ($P \sim 10$).

Deviations become significant, requiring exact expressions; however, the dispersion model may not be physically valid at very low P .

II.5. Cascade of Perfectly Mixed Reactors Model (One-Parameter Model)

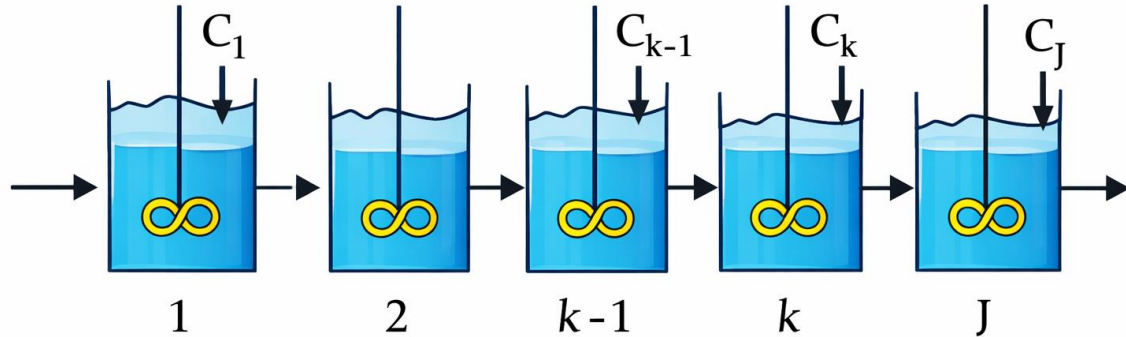


Figure.6: Cascade of Perfectly Mixed Reactors Model

- **Method of Moments**

The transient tracer balance in the mixer of rank k in the cascade is written as:

$$Q C_{k-1} = Q C_k + \left(\frac{V_R}{J} \right) * \frac{dC_k}{dt}$$

By successive steps, over the entire cascade.

$$G(s, J) = \left(1 + \left(\frac{\tau}{J} \right) s \right)^{-J}$$

Transfer function of the tanks-in-series model.

The model parameter is J (the number of tanks in the cascade).

The first moment μ_1 and the variance σ^2 are derived using Van der Laan's relation.

$$mu_1 = \bar{t}_s = (-1) * \lim_{s \rightarrow 0} \left(\frac{\partial G}{\partial s} \right)$$

$$mu_2 = (-1)^2 * \lim_{s \rightarrow 0} \left(\frac{\partial^2 G}{\partial s^2} \right)$$

$$\sigma^2 = mu_2 - mu_1^2$$

$$\bar{t}_s = \tau$$

The inverse of $G(s)$ (the original function in the time domain) corresponds to the RTD.

It is a **Gamma (or Poisson) distribution**.

- **RTD of the tanks-in-series model:**

The model parameter is J (the number of tanks in the cascade).

$$E(t_s, J) = \left(\frac{J}{\tau}\right)^J * \frac{t_s^{J-1}}{(J-1)!} * \exp\left(-\left(\frac{J}{\tau}\right) * t_s\right)$$

Chapter III

Bioreactors

Bioreactors are generally designed based on the same principles as chemical reactors. They are vessels made of glass (for laboratory-scale systems) or stainless steel. They are used to carry out **enzymatic reactions** (enzymatic reactors) or **cell-based reactions** (fermenters or cell culture reactors). Biological reactors are also referred to as **bioreactors**.

A bioreactor allows precise control of culture conditions such as **temperature, pH, aeration**, and others, which ensures the collection of reliable experimental data. Industrial bioreactors are widely used to produce products such as **beer, yogurt, vaccines, antibiotics, antibodies, vitamins, and organic acids**.

A fermenter is generally a bioreactor equipped with an aeration system. Although the terms *fermenter* and *bioreactor* are sometimes used interchangeably, they often distinguish the type of culture: **bacteria and yeast** for fermenters, and **animal cells** for bioreactors.

Bioreactors are designed to ensure **four main functions**:

- Efficient **mass transfer**
- Effective **heat transfer**
- Maintenance of **sterility**
- Monitoring **and control** of operating parameters

III. Classification and Characteristics of Bioreactors:

III.1 Definition:

A bioreactor is a vessel in which a biochemical reaction takes place. It includes fermenters and cell culture reactors. Two main types are distinguished: **enzyme bioreactors** and **cell-based bioreactors**.

Governing equation inside the bioreactor:



- **Substrate:**
The raw material transformed by cells or enzymes (e.g., sugars, amino acids, lipids), depending on the biological process.
- **Biomass:**
The amount of cells (or enzymes) present in the bioreactor, acting as the biological agent responsible for substrate conversion.
- **Increased Biomass ("Biomassn):**
- The initial biomass multiplies during the process, leading to cell growth, particularly relevant for cell-based bioreactors.
- **Metabolites:**
Desired products of the biological process, such as proteins, organic acids, antibiotics, biofuels, depending on the reactor objective.
- **Residual Substrate:**
- The fraction of substrate not converted into metabolites, due to incomplete conversion or non-metabolizable components.

III.2 Industrial Applications

Industrial bioreactors are used to produce beer, yogurt, vaccines, antibiotics, antibodies, vitamins, and organic acids. Fermenters are bioreactors typically equipped with aeration systems and are mainly used for bacterial or yeast cultures.

Types of Bioreactors

Two main types are distinguished:

- **Single-use bioreactors**
- **Multi-use bioreactors**
- **Single-use bioreactor:**
A disposable bioreactor that eliminates maintenance operations.

➤ **Multi-use bioreactors:**

- **Membrane bioreactor:**

A bioreactor coupled with a membrane, mainly used for soil and water treatment (carbon, nitrogen, and phosphorus removal).

- **Photo-bioreactor:**

A bioreactor that uses light and is designed for the cultivation of microorganisms, particularly microalgae.

III.3 Mechanism and Kinetics of Homogeneous and Heterogeneous Enzymatic Reactions

Most biochemical reactions in living systems require specific catalysts called **enzymes**. These protein molecules accelerate reactions by lowering the activation energy, significantly increasing reaction rates.

In an enzymatic reaction, the reactant is called the **substrate (S)**. The enzyme binds to the substrate to form an **enzyme-substrate complex (ES)**, which facilitates the conversion of the substrate into **product(s) (P)**. After the reaction, the enzyme is released unchanged and can catalyze further reactions.

III.3 .1 Enzymatic Reactions

Most biological reactions are catalyzed by specific substances called **enzymes**. These are biological catalysts belonging to the class of **proteins**, which are polypeptide polymers formed by the polycondensation of α -amino acids of the type $\text{NH}_2\text{-CHR-COOH}$.

In enzymatic reactions, the reactant is called the **substrate (S)**.

- **Mode of Action**

Lewis generalized the concepts of acids and bases as follows:

- A substance that can **accept an electron pair** (electrophile) is an **acid**.

- A substance that can **donate an electron pair** (nucleophile) is a **base**.

The presence of these donor-acceptor sites within a substance leads to the formation of **active sites**, which are fundamental to many chemical and biochemical reactions.

The specificity of enzymatic action is based on structural complementarity between the substrate and the enzyme's active site. The substrate must have an appropriate spatial conformation to fit precisely into the active site, forming an enzyme-substrate complex. This interaction is essential for catalysis.

Recognition between the substrate and the active site occurs through non-covalent interactions of varying strength. Active sites are often composed of specific functional groups, such as hydroxyl (OH) or imine (C=N) groups, which participate in substrate binding and catalytic activity.

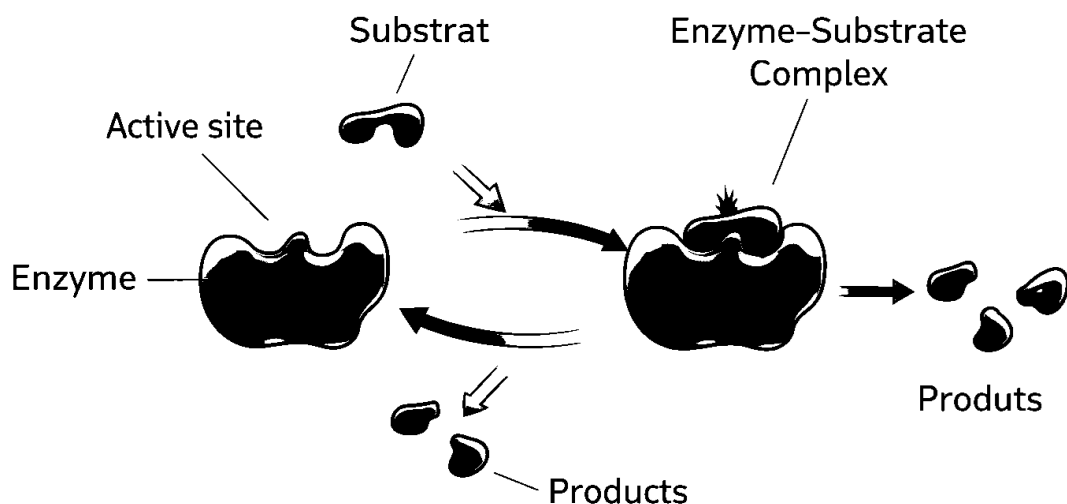


Figure 1: The active site of an enzyme is the location of the enzymatic reaction.

III.3.2 Use of Enzymes

Enzymes can be used in two main ways: either as **soluble enzymes**, where the reaction medium is homogeneous, or as **insoluble enzymes immobilized on a solid support**, resulting in a heterogeneous reaction medium. Accordingly, two types of enzymatic kinetics can be studied:

- **Homogeneous enzymatic kinetics**, governed by the laws of homogeneous catalysis.
- **Heterogeneous enzymatic kinetics**, governed by the laws of heterogeneous catalysis.

III.4 Homogeneous and Heterogeneous Reactions

III.4.1 Homogeneous Enzymatic Kinetics

The catalytic activity of an enzyme depends on **pH** (optimal pH). This activity increases with **temperature** according to the **Arrhenius law**; however, above a critical temperature, the protein structure becomes denatured and catalytic activity decreases.

An enzymatic solution contains a **fixed number of active catalytic sites** to which the substrate can bind. Beyond a certain substrate concentration, all active sites are occupied, and the **reaction rate becomes independent of substrate concentration**.

The **Michaelis–Menten rate law** is one of the earliest and simplest models proposed to describe **enzymatic reaction kinetics**.

$$r = \frac{r_{\max}[S]}{K_m + [S]}$$

Where:

- **r** ($\text{mol}\cdot\text{m}^{-3}\cdot\text{s}^{-1}$): reaction rate
- **r_{max}** ($\text{mol}\cdot\text{m}^{-3}\cdot\text{s}^{-1}$): maximum reaction rate

- K_m ($\text{mol}\cdot\text{m}^{-3}$): Michaelis–Menten constant
- $[S]$ ($\text{mol}\cdot\text{m}^{-3}$): substrate concentration

The maximum reaction rate $r_{\max}$ is proportional to the **initial enzyme concentration** in the solution (S_0). This relationship can be explained by a **two-step mechanism**:

- The first step is the rapid and equilibrium formation of an **activated enzyme–substrate complex** (ES^*).
- The second step is the decomposition of this activated complex into **product (P)** and **regenerated enzyme (E)**.

The **Michaelis–Menten constant** K_m measures the **affinity of the enzyme for the substrate**; the affinity increases as the value of K_m decreases.

The Michaelis–Menten equation does not describe the kinetic behavior of all enzyme-catalyzed reactions. More complex models have been developed to account for **inhibition phenomena**, where molecules other than the substrate can reversibly bind to the enzyme's active sites. This aspect will not be addressed in this course.



Using the equilibrium assumption

$$k_1 [E][S] = k_{-1} [ES]$$

The dissociation constant of the enzyme–substrate complex $[ES]$ is given by K_s :

$$\frac{[E][S]}{[ES]} = \frac{k_{-1}}{k_1} = K_s$$

The total enzyme concentration $[E_0]$ is equal to the sum of the concentrations of **free enzyme** $[E]$ and **bound enzyme** $[ES]$:

$$[E] = [E_0] - [ES]$$

$$\frac{([E_0] - [ES])[S]}{[ES]} = K_s$$

$$K_s[ES] = [E_0][S] - [ES][S]$$

$$[ES]([S] + K_s) = [E_0][S]$$

$$[ES] = \frac{[E_0][S]}{[S] + K_s}$$

The concentration of the enzyme-substrate complex [ES] governs the rate of product formation:

$$R_0 = k_2[ES]$$

By substituting the expression of [ES] into the above equation, we obtain:

$$R_0 = \frac{(k_2[E_0][S])}{([S] + K_s)}$$

The **maximum initial rate** $r_{\max}$ is reached when the substrate concentration is very high and all enzymes are present as enzyme-substrate complexes:

$$r_{\max} = k_2[E_0]$$

$$R_0 = \frac{r_{\max}[S]}{([S] + K_s)}$$

Where:

- R_0 ($\text{mol} \cdot \text{m}^{-3} \cdot \text{s}^{-1}$): reaction rate
- $r_{\max}$ ($\text{mol} \cdot \text{m}^{-3} \cdot \text{s}^{-1}$): maximum reaction rate

- **K_s** ($\text{mol}\cdot\text{m}^{-3}$): dissociation constant
- **$[S]$** ($\text{mol}\cdot\text{m}^{-3}$): substrate concentration

If the initial substrate concentration $[S_0]$ is much greater than the initial enzyme concentration $[E_0]$, the formation of the enzyme–substrate complex causes a negligible change in the free substrate concentration. Therefore, the initial reaction rate R_0 can be expressed as:

$$R_0 = \frac{r_{\max}[S_0]}{([S_0] + K_s)}$$

III.5. Monod Kinetics

Monod proposed an equation to describe the relationship between the growth rate of a microbial culture and the concentration of the limiting substrate. This equation became widely known as the *Monod equation* and is generally expressed as follows:

$$\mu = \frac{\mu_m * S}{K_s + S}$$

In this equation, μ represents the specific growth rate, S denotes the substrate (or nutrient) concentration, μ_m is a constant often referred to as the maximum specific growth rate, and K_s is a constant known as the Monod constant.

It is important to note that a microorganism may require several substrates for growth; however, it is generally assumed that all substrates except one are present in excess relative to the organism's needs. The substrate represented by S is therefore considered the limiting component. The value of K_s the value of μ_m may also vary. In practice, μ_m and K_s are typically reported for the primary carbon (and energy) source supporting microbial growth.

Graphically, the constants in the Monod equation have the same interpretation as the corresponding constants in the *Michaelis–Menten* model for enzyme kinetics. The specific growth rate initially increases with increasing substrate concentration

and approaches the limiting value μ_m at high substrate concentrations. When $S \gg K_S$:

$$u = \frac{u_m * S}{K_S + S} \Rightarrow \frac{u_m * S}{S}$$

Where:

$$\mu_m = \mu$$

Furthermore, when $\mu = \mu_m/2$, substituting into Equation gives:

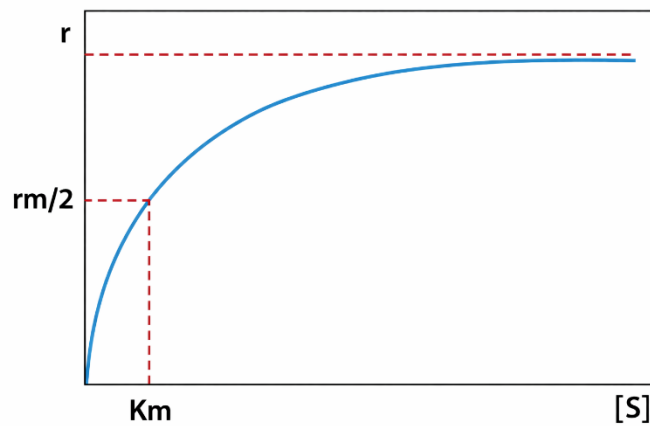
$$\frac{u_m}{2} = \frac{u_m * S}{K_S + S}$$

After dividing by μ_m and rearranging, we obtain:

$$K_S = S$$

This means that when the specific growth rate equals half of its maximum value, the limiting substrate concentration is numerically equal to K_S .

Figure 2. Variation of enzymatic reaction rate as a function of substrate concentration.



If the feed contains no microorganisms (i.e., it is sterile), then $X_0 = 0$, and at steady state the expression becomes:

$$D = \mu$$

Where D is the dilution rate.

If the dependence of the specific growth rate on substrate concentration is described by the Monod equation, then substituting into Equation gives, under steady-state conditions:

$$D = \frac{u_m * S}{K_S + S}$$

By rearranging this expression, the substrate concentration at steady state is obtained in the following form:

$$S = \frac{D * K_S}{u_m - D}$$

The biomass concentration under this condition depends on the value of S_0 . The biomass behavior can be determined from Equation:

$$X = X_0 + Y(S_0 - S)$$

Then, by substituting S from Equation, for a perfectly mixed continuous reactor at steady state, the biomass concentration becomes:

$$X = Y \left(S_0 - \frac{D * K_S}{u_m - D} \right)$$

Y: yield coefficient

X: biomass concentration

III.6. Main Types of Bioreactors:

III.6.1 Mechanically Stirred Tank

The mechanically stirred tank is the preferred reactor when all components involved in the bioreaction (substrates, enzymes, microorganisms) are present in a single liquid phase, provided that sufficient agitation ensures complete mixing of the liquid phase.

The stirred tank is commonly used to carry out enzymatic reactions with enzymes in solution, as well as anaerobic fermentations.

Under aerobic conditions, the reactor used is a mechanically stirred and aerated tank. In this case, oxygen acts as the limiting substrate. The overall rate of microorganism formation results from the coupling between the intrinsic microbial growth rate and the oxygen transfer rate from the dispersed gas phase into the fermentation medium.

The mechanical power supplied serves both to mix the liquid phase and to generate a large interfacial area between gas bubbles and the fermentation medium.

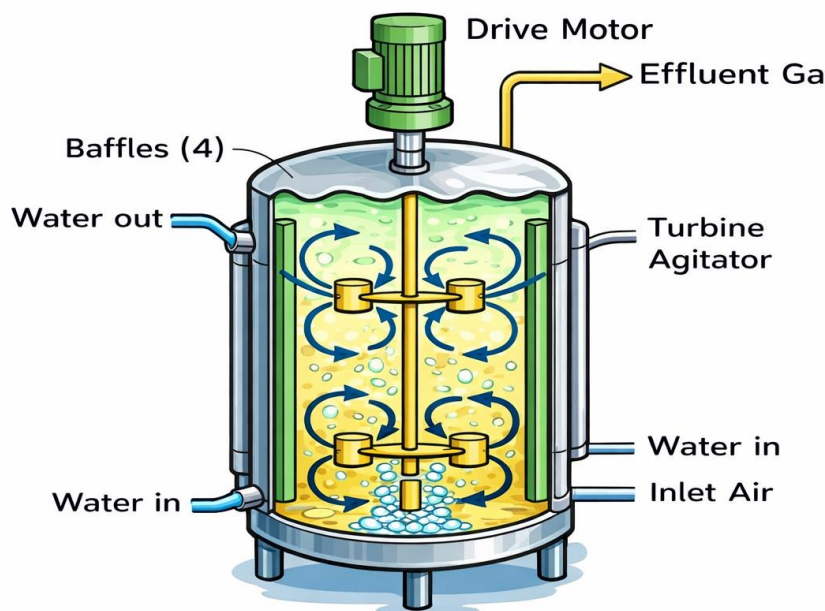


Figure 3. Schematic diagram of a mechanically stirred bioreactor.

III.6.2 Fixed-Bed and Fluidized-Bed Reactors:

The use of enzymes in solution leads to their loss after the reaction, since it is difficult to recover them from the reaction medium. Immobilizing enzymes on the surface or within a solid support is a technique that allows their easy separation from the liquid reaction medium and thus enables their reuse.

Reactors using immobilized enzymes are typically columns through which the liquid flows, containing either a fixed bed or a fluidized bed of solid particles. In this case, the overall rate of the enzymatic reaction results from the coupling between the substrate transfer rate from the bulk liquid phase to the surface of the solid particles, the diffusion rate of the substrate within the particles, and the intrinsic rate of the bio-reaction.

The choice between a fixed bed and a fluidized bed depends on the fouling characteristics of the solutions to be treated and on the size of the solid particles. Fluidization helps reduce the risk of clogging; however, liquid–solid mass transfer performance in a fluidized bed is generally more limited than in a fixed bed.

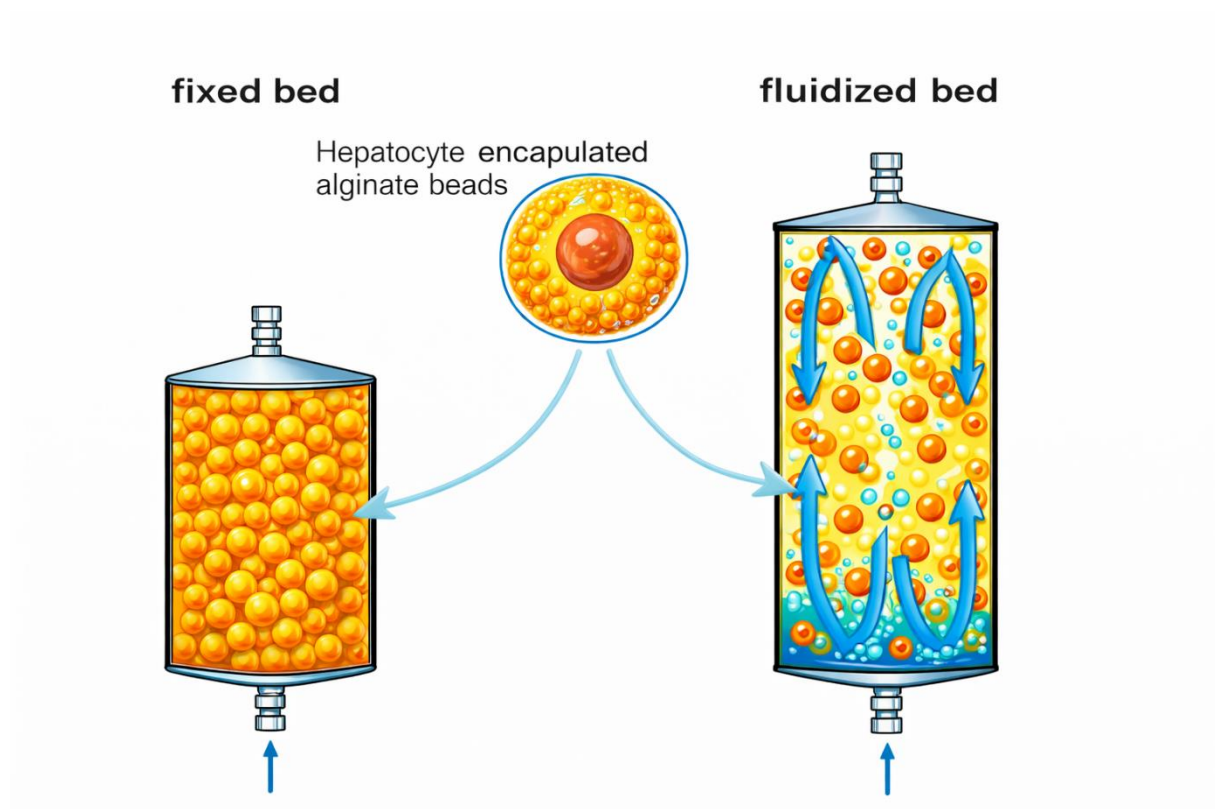


Figure 4. Comparison between fixed-bed and fluidized-bed reactors.

III.6.3 Bubble Column and Airlift Reactor:

The bubble column is a reactor also used for the production of microorganisms under aerobic conditions. Air bubbles injected at the base of the column supply oxygen to the microorganisms and mix the liquid phase as they rise.

The bubble column is also employed in anaerobic fermentations, where pneumatic agitation is provided by carbon dioxide bubbles generated in situ during fermentation; winemaking tanks are a typical example.

The airlift reactor is a device derived from the bubble column and is used exclusively for aerobic cultures.

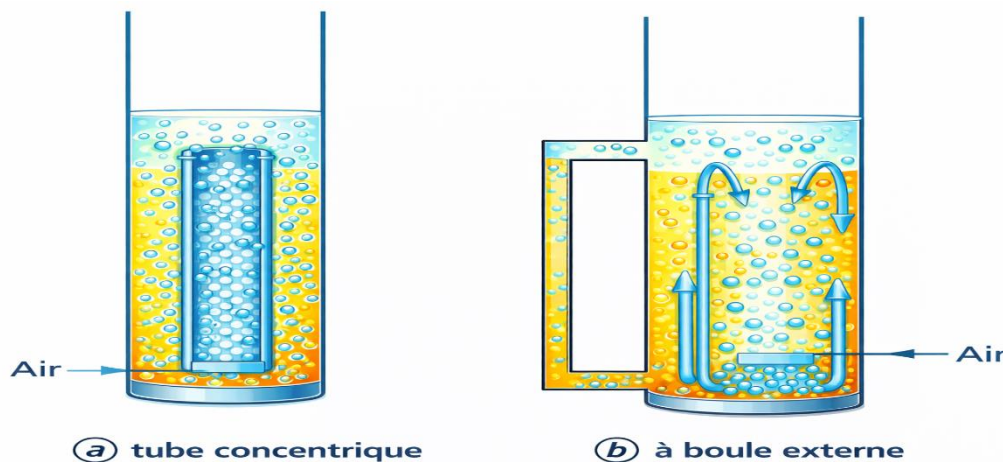


Figure.5: the bubble column and is used exclusively for aerobic cultures.

III.7 Operating Mode:

III.7.1 Batch Operation:

In bioprocesses, reactions are generally carried out in closed reactors where the catalyst is brought into contact with the substrates in a stirred, closed vessel for a defined period, during which pH and temperature are controlled.

Product recovery after each biotransformation cycle is typically performed by filtration, centrifugation, or precipitation.

Despite its simplicity, this type of reactor presents several drawbacks inherent to closed systems, such as variability in product quality, labor costs associated with frequent start-ups and shutdowns, the use of large volumes, and the need for an additional separation step to recover products from the reaction medium.

III.7.2 Continuous Operation:

There are several types of bioreactors that operate under continuous conditions. Among the different continuous reactors, we distinguish:

- ✓ Continuously stirred tank reactors (CSTR)
- ✓ Fixed-bed and fluidized-bed reactors

It should be noted that the latter types are generally considered plug-flow reactors.

III.7.3 Kinetics of Enzymatic Reactions:

All living organisms possess a metabolism, meaning that chemical reactions occur within them to ensure their survival. The duration of these reactions can vary: some take only a few seconds, while others may extend over several days.

However, there exists a type of protein capable of accelerating these chemical reactions: enzymes. These proteins catalyze reactions and therefore act as biological catalysts (or biocatalysts). In biochemical reactions, the reactant is referred to as the substrate (S).

The following table provides examples of enzymes used in the food industry.

The substrate binds temporarily to the active site of the enzyme, which is located on its surface. When the substrate is bound (forming the enzyme–substrate complex), the enzyme undergoes a conformational change, adopting an induced form that enhances its ability to catalyze the reaction. Once the reaction occurs, the product leaves the active site, and the enzyme emerges from the reaction unchanged.

III.8 Heterogeneous Enzymatic Kinetics

To facilitate enzyme recovery after a reaction, enzymes can be immobilized either on the surface of non-porous particles or within porous particles. Immobilization improves enzyme stability by providing a favorable microenvironment (e.g., temperature and pH) and strong interactions with the support.

Three main immobilization methods are commonly used:

- Adsorption
- Covalent bonding
- Entrapment (inclusion)

Although the rate laws remain similar to those of free enzymes, the expression of reaction rates changes. For surface immobilization, rates r and $r_{\max}$ are expressed per unit surface area ($\text{mol}\cdot\text{m}^{-2}\cdot\text{s}^{-1}$) or per unit mass of support ($\text{mol}\cdot\text{kg}^{-1}\cdot\text{s}^{-1}$). For enzymes entrapped in porous particles, rates are expressed per unit solid volume ($\text{mol}\cdot\text{m}^{-3}\cdot\text{s}^{-1}$) or per unit mass of support.

For spherical or cylindrical particles, unit conversion can be easily performed using particle size and density.

In kinetic equations, the relevant substrate and product concentrations are those at the liquid–solid interface for surface immobilization, or within the liquid phase inside the pores for entrapment.

In both cases, diffusion at the interface (liquid–solid or gas–solid) must be considered. The substrate is in the fluid phase, while the enzyme is immobilized in the solid phase (as particles, membranes, films, or beads).

Mass transfer to the enzyme can become the rate-limiting step and is governed by Fick's law of diffusion.

III.8.1 Mass Diffusion:

The mass flux J is defined as the amount of substance (moles) passing through a unit surface area (cm^2) per unit time (s).

According to Fick's first law:

$$J = -D * \text{grad}[S]$$

Where:

D : diffusion coefficient ($\text{cm}^2 \cdot \text{s}^{-1}$)

$\text{grad}[S]$: concentration gradient at the location where the flux is evaluated

The concentration gradient is given by:

$$\text{grad}[S] = \frac{d[S]}{dx}$$

Here, x represents the direction of diffusion.

A more concentrated medium creates a diffusion gradient toward a less concentrated medium.

The solute diffuses from the region of higher concentration to the region of lower concentration.

If the enzyme is immobilized inside a solid support (such as a membrane), the diffusivity of the substrate within the support may differ from its diffusivity in solution due to interactions with the support. This is referred to as the effective diffusivity, denoted D_{eff} .

$$J = -D_{eff} * \left(\frac{d[S]}{dx} \right)$$

III.9 Enzymatic Reactors:

Enzymatic reactions are carried out in reactors designed according to factors such as reaction type, target molecule, production scale, enzyme form (free or immobilized), and cost.

Homogeneous catalysis (free enzymes) is used when the catalyst is inexpensive and disposable. Heterogeneous catalysis (immobilized enzymes) is preferred when the enzyme is costly, allowing its recovery and reuse.

III.9.1 Batch reactors:

Reactions occur in closed stirred vessels with controlled pH and temperature. Products are recovered after each cycle. However, this mode may involve quality variability, high labor costs, large volumes, and enzyme loss.

III.9.2 Continuous reactors:

Types include:

- Continuously stirred tank reactors (CSTR)
- Fixed-bed reactors
- Fluidized-bed reactors
- Membrane reactors (REM)

The last three generally operate as plug-flow reactors.

III.9.3 Diffusion-Limited Reactors :

III.9.3.1 Liquid–Solid Mass Transfer for a Non-Porous Film

When an enzyme is immobilized on the surface of a solid support, the reaction when an enzyme is immobilized on a solid surface, the overall rate results from the coupling between enzymatic reaction and liquid–solid mass transfer. The substrate diffuses from the bulk liquid to the liquid–solid interface, where it is consumed by the reaction.

At quasi-steady state, the mass transfer rate equals the reaction rate. For a reaction following Michaelis–Menten kinetics, this balance can be written as:

$$k_l * a * ([S] - [S_i]) = \frac{r_{max} * [S_i]}{K_m + [S_i]}$$

Where:

k_l : liquid–solid mass transfer coefficient

a : specific surface area of the solid

r_{max} : maximum reaction rate per unit mass of support

$[S]$: substrate concentration in the bulk liquid

$[S_i]$: substrate concentration at the interface

K_m : Michaelis constant

In dimensionless form, the relation introduces the Damköhler number (Da), which compares reaction rate to mass transfer rate and indicates whether the process is reaction-controlled or diffusion-limited.

$$\left(\left(\frac{K_m}{[S]} \right) + \left(\frac{[S_i]}{[S]} \right) \right) * \left(1 - \left(\frac{[S_i]}{[S]} \right) \right) = Da * \left(\frac{[S_i]}{[S]} \right)$$

Where the Damköhler number (Da) is defined as:

$$Da = \frac{r_{max}}{k_l * a * [S]}$$

The Damköhler number represents the ratio between the maximum reaction rate and the maximum mass transfer rate.

Since mass transfer and reaction occur in series, the slower step controls the overall process.

- If Da is large, the system is diffusion-limited.

- If Da is small, the system is reaction-controlled.

When the Damköhler number is much greater than 1 ($Da \gg 1$), the reaction rate is much higher than the mass transfer rate. Therefore, mass transfer becomes the limiting step. In this case, $[S_i] \ll [S]$, and the overall rate is:

$$r = k_l * a * [S]$$

When the Damköhler number is much less than 1 ($Da \ll 1$), the biochemical reaction is the limiting step. In this case, $[S_i] \approx [S]$, and the overall rate becomes:

$$r = \frac{r_{max} * [S]}{K_m + [S]}$$

Thus:

$Da \gg 1 \rightarrow$ Diffusion-limited regime

$Da \ll 1 \rightarrow$ Reaction-controlled regime

When the Damköhler number is neither very large nor very small compared to 1, the previous second-order equation in $[S_i]$ can be solved to determine the ratio $[S_i]/[S]$:

$$\left(\frac{[S_i]}{[S]}\right) = \frac{1}{2} * \left(Da + \frac{K_m}{[S]} - 1\right) \pm \frac{1}{2} * \text{sqrt} \left(\left(Da + \frac{K_m}{[S]} - 1\right)^2 + 4 * \frac{K_m}{[S]} \right)$$

The appropriate sign is chosen so that the ratio remains positive.

The interfacial concentration $[S_i]$ allows the calculation of the effectiveness factor η_e , defined as the ratio between the observed reaction rate under diffusion limitation and the maximum reaction rate without diffusion limitation:

$$\eta_e = \frac{\left(\frac{[S_i]}{[S]}\right) * \left(1 + \frac{K_m}{[S]}\right)}{\left(\frac{[S_i]}{[S]}\right) + \frac{K_m}{[S]}}$$

For optimal performance, it is desirable to operate with an effectiveness factor close to 1, meaning that mass transfer is much faster than the reaction rate ($Da \ll 1$).

III.9.3.2 Liquid-Solid Mass Transfer in a Porous Support :

This case occurs when enzymes or microorganisms are entrapped within porous particles or gels, and also in microbial films (biofilms).

Here, intraparticle mass transfer and substrate consumption by reaction occur **simultaneously**, rather than sequentially.

Inside a porous particle, substrate diffusion and reaction occur simultaneously, creating an internal concentration gradient.

Under quasi-steady state, the substrate mass balance gives:

- Spherical particle (radius R)

$$D_{\text{eff}} * \left(\frac{d^2[S]}{dz^2} + \frac{2}{z} * \frac{d[S]}{dz} \right) = r$$

$$D_{\text{eff}} * \left(\frac{d^2[S]}{dx^2} \right) = r$$

- At the external surface ($x = L$ or $z = R$), substrate concentration is continuous:

$$[S] = [S_i]$$

- At the center of the particle ($z = 0$) or at the base of the film ($x = 0$), there is no flux (symmetry condition):

$$\frac{d[S]}{dz} = 0$$

Or

$$\frac{d[S]}{dx} = 0$$

Where:

- L = film thickness
- R = particle radius
- $[S]$ = substrate concentration inside the porous medium
- $[S_i]$ = substrate concentration at the particle surface
- r = specific reaction rate per unit solid volume
- D_{eff} = effective diffusivity (depends on substrate diffusivity, porosity, and tortuosity).

Solving the diffusion–reaction equations gives the effectiveness factor (η_e), defined as the ratio between the observed reaction rate (with internal diffusion limitation) and the intrinsic reaction rate without internal concentration gradients.

For a bioreaction following Michaelis–Menten kinetics, the effectiveness factor η_e depends on the ratio $K_m/[S_i]$ and on the Thiele modulus (Θ) defined as:

- Spherical particle:

$$\Theta = \frac{R}{3} * \text{sqrt} \left(\frac{r_m}{D_{eff} * K_m} \right)$$

- Planar film:

$$\Theta = L * \text{sqrt} \left(\frac{r_m}{D_{eff} * K_m} \right)$$

Intrinsic kinetic parameters such as r_m and K_m are difficult to determine experimentally because diffusion and reaction phenomena cannot be completely separated. Numerical analysis is therefore required to extract them from observed reaction rate data as a function of substrate concentration.

III.10 Bioreactor Design:

The first step in implementing a bioreaction is sizing and designing the bioreactor components to optimize the process. In chemical and biochemical engineering, mixing is a key parameter, as it controls mass transfer within the reactor.

III.10.1 Mechanical Agitation and Shear:

Agitation devices, whose role is to mix the liquid phase, are classified into two categories:

- Shear (radial-flow) impellers
- Non-shear (axial-flow) impellers

III.10.2 Radial-Flow Impeller (Shear Type):

This turbine generates radial flow, increasing turbulence and mixing. However, it creates high shear forces that may damage cells. It improves oxygen transfer and is suitable for bacteria and yeast.

Examples: flat-blade turbine, curved-blade turbine, Rushton turbine.

III.10.3 Axial-Flow Impeller (Non-Shear Type):

This impeller produces axial flow with lower shear stress, making it suitable for fragile cells. It creates a circulation loop inside the reactor but provides lower oxygen transfer efficiency.

Example: marine-type propeller.

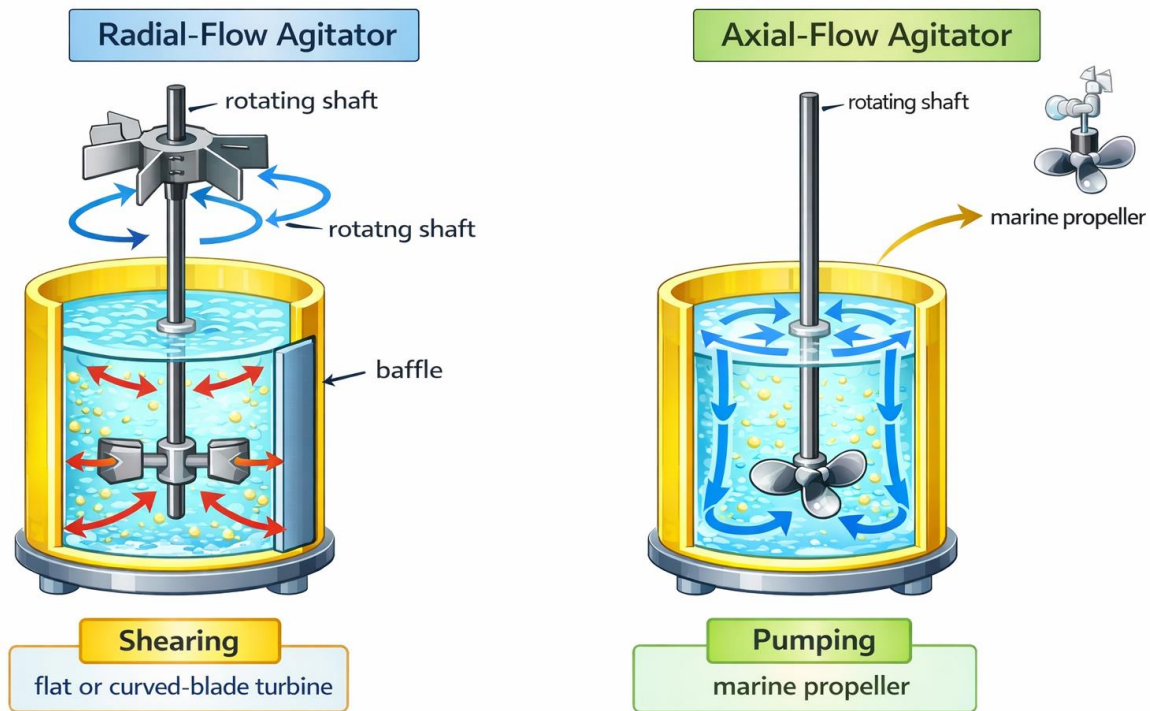


Figure.6: marine-type propeller.

III.10.4 Mixing Time :

The mixing time t_M is the time required to make the liquid phase homogeneous in concentration after a disturbance.

In turbulent regime, the mixing time is given by:

- For a marine propeller (axial impeller):

$$t_M = 6 * \frac{\left(\frac{d_c}{d_a}\right)^2}{N}$$

- For a turbine (radial impeller):

$$t_M = 4 * \frac{\left(\frac{d_c}{d_a}\right)^2}{N}$$

Where:

d_c = tank diameter

d_a = impeller diameter

N = rotational speed (s^{-1})

A reactor is considered perfectly mixed when the mixing time is shorter than the reaction half-time.

Under standard conditions, the mixing time t_M is achieved at:

- 55 rpm with a propeller
- 35 rpm with a turbine

III.11 Reactor Hydrodynamics :

III.11.1 Dimensionless Characteristic Numbers:

Using the Buckingham theorem, reactor power relationships can be expressed in terms of key dimensionless numbers.

1) Reynolds Number (Re):

The Reynolds number represents the ratio between inertial forces and viscous forces and predicts the flow regime:

- Laminar flow: $Re < 10$
- Turbulent flow: $Re > 10^4$

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

Where:

- d_a = impeller diameter
- N = rotational speed
- ρ = liquid density
- μ = viscosity

In laminar flow, $N_p * Re$ is constant.

In turbulent flow, the power number (N_p) is constant:

$N_p = 6$ (turbine)

$N_p = 0.4$ (marine propeller)

The marine propeller consumes less power than the turbine.

2) Froude Number (Fr) :

The Froude number represents the ratio between inertial forces and gravitational forces and predicts vortex formation:

$Fr \leq 1 \rightarrow$ no vortex

$Fr \geq 3 \rightarrow$ vortex forms

$$Fr = \frac{N^2 * d_a}{g}$$

Where:

$g = 9.81 \text{ m/s}^2$ (gravitational acceleration)

To prevent vortex formation, tanks are equipped with baffles

3) Power Number (Np):

The Power number represents the drag coefficient of the impeller and expresses the consumed power.

$$N_p = \frac{P}{p * N^3 * d^5}$$

Where P is the mechanical power (W).

4) Weber Number (We):

The Weber number characterizes the effect of **surface tension forces**.

$$We = \frac{p * N^2 * d^3}{\gamma}$$

Where γ is the surface tension.

5) Relationship Between Numbers:

These dimensionless numbers are related by:

$$Np = K * (Re^x) * (Fr^y) * (We^z)$$

Where K, x, y, z depend on impeller geometry and are determined experimentally.

Power characteristics (N_p vs Re) depend on the type of impeller and are obtained from characteristic curves.

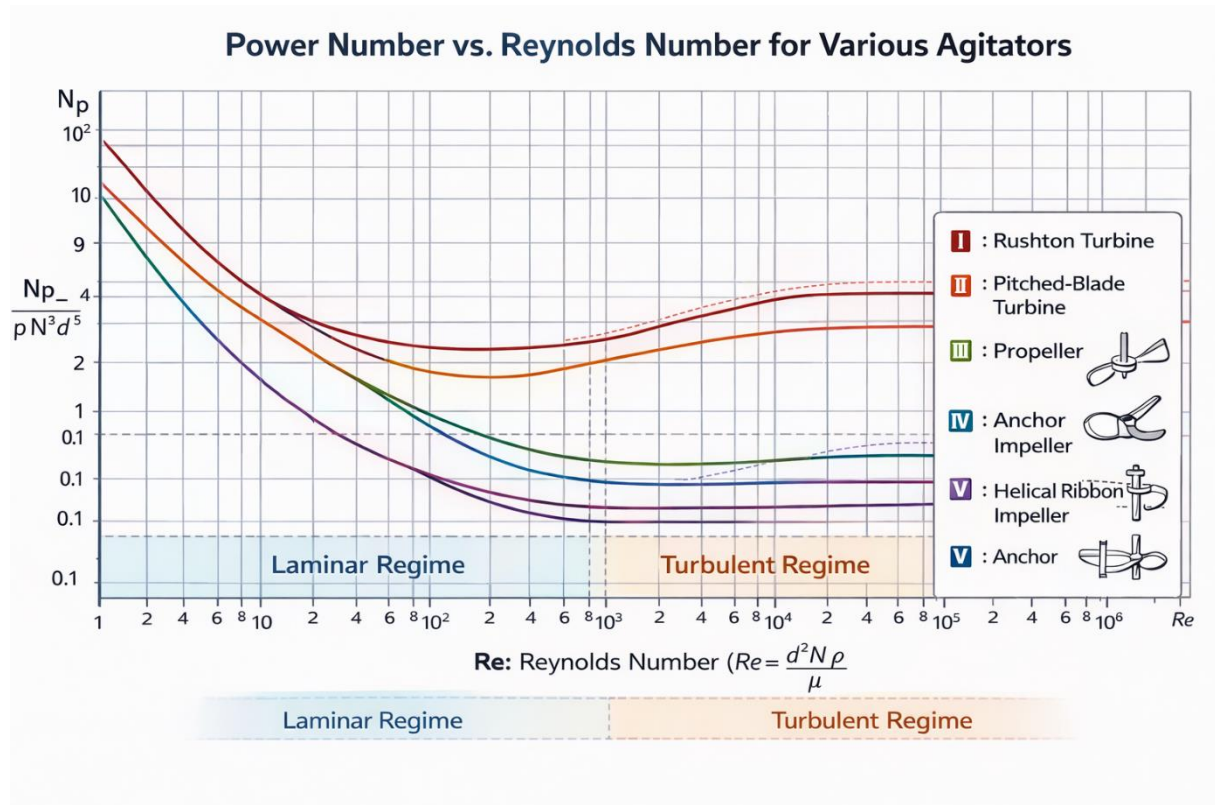


Figure.7: Power characteristics (N_p vs Re) depend on the type of impeller.

In the laminar regime, the product $N_p \times Re$ remains constant.

In the turbulent regime, the power number (N_p) becomes constant:

$N_p = 6$ for a turbine

$N_p = 0.4$ for a marine propeller

Therefore, the marine propeller consumes less power than the turbine.

III.12 Standard Mechanically Agitated Tank :

Tank (Vessel)

Cylindrical tank with a flat bottom.

Liquid height H equals tank diameter D.

The ratio H/D may be 2 to 3 in aerated bioreactors or when multiple impellers are used.

- **Baffles**

Number of baffles: $n_b = 4$

Baffle width: $b = D/12$ to $D/10$

Baffle height: $h_b = H$

Clearance from tank wall: $e_b = 0$ to $0.2D$

- **Impeller**

Impeller diameter: $d = D/3$

Distance from tank bottom: $Y = D/3$

Number of blades and blade dimensions depend on the impeller type.

Example (Rushton turbine – TD6):

$n_b = 6$ blades

Blade proportions: $d / l / w = 20 / 5 / 4$

Colored Explanation of the Diagram

To understand the geometry clearly:

Blue → Tank Dimensions

D = tank diameter

H = liquid height

Standard design: $H = D$

- **Green → Baffles**

4 vertical plates fixed to the wall

Prevent vortex formation

Improve mixing efficiency

- **Red → Impeller**

Diameter equals one third of tank diameter

Positioned at one third of tank diameter from the bottom

Responsible for fluid circulation and mixing

- Important Design Ratios (Standard Configuration)

$$H = D$$

$$d = D/3$$

$$Y = D/3$$

$$b \approx D/10$$

$$n_b = 4 \text{ baffles}$$

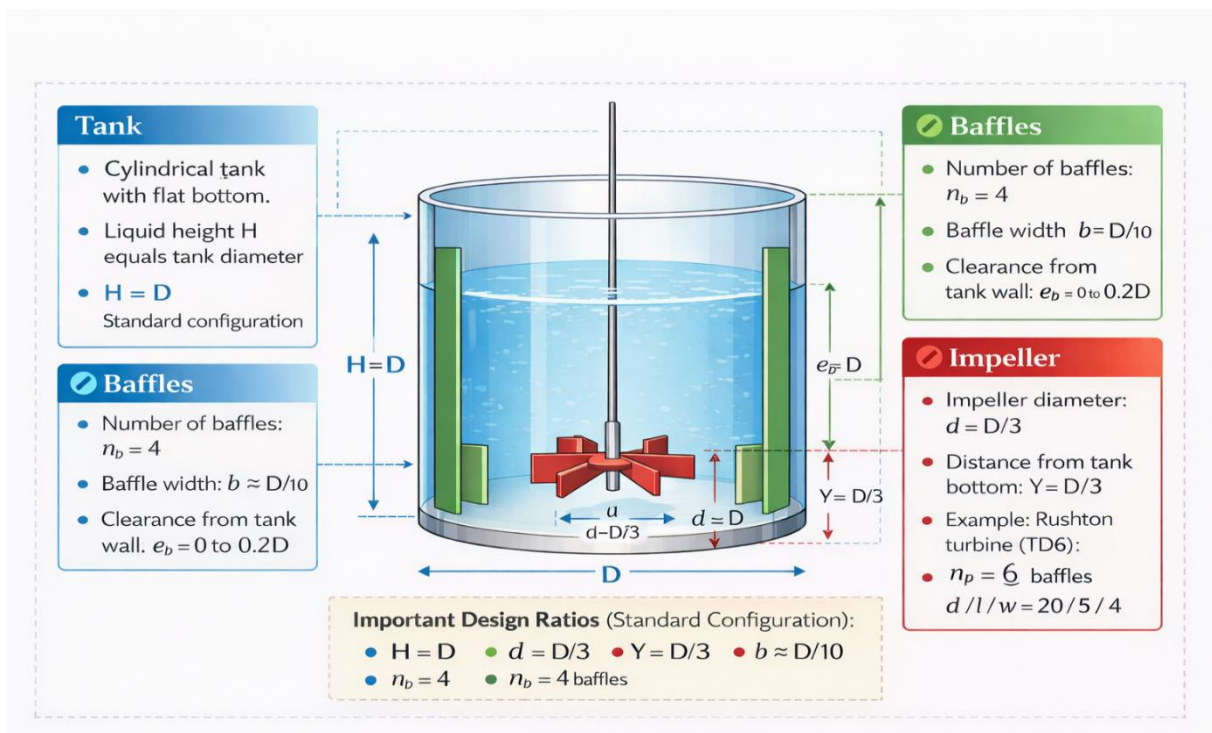


Figure.8: Standard Mechanically Agitated Tank.

In industrial practice, bioreactors are built in various tank designs and with different types of agitators. The configuration known as the standard stirred tank ensures good liquid-phase homogeneity.

Baffles (vertical strips inside the tank) are used to prevent vortex formation around the impeller shaft.

III.13 Fixed-Bed Reactors :

A fixed-bed reactor increases bacterial concentration or enzyme activity by immobilizing cells or enzymes on solid supports (particles or beads) packed inside a column. The liquid flows through the bed while the solid phase remains stationary.

This configuration provides high productivity and enzyme-free products, since the biocatalyst remains confined inside the reactor. However, it may cause high pressure drop, clogging, and diffusion limitations, reducing performance.

For spherical particles:

Solid phase fraction ≈ 0.6

Liquid phase fraction (void fraction ε) ≈ 0.4

The pressure drop across the packed bed is estimated by the Ergun equation:

$$\frac{\Delta P}{H} = \left(150 * u_l * \frac{U_l}{d_p^2} \right) * \left(\frac{(1 - \varepsilon_l)^2}{\varepsilon_l^3} \right) + (1.75 * \rho_l * U_l^2 / dp) * \left(\frac{1 - \varepsilon_l}{\varepsilon_l^3} \right)$$

Where:

ΔP = pressure drop (Pa)

H = bed height (m)

d_p = particle diameter (m)

U_l = superficial liquid velocity (m/s)

ε_l = bed void fraction

u_l = liquid viscosity (Pa·s)

ρ_l = liquid density (kg/m³)

III.8 Fluidized-Bed Reactor

III.14 Fluidized-Bed Reactor :

In a fluidized-bed reactor, solid particles carrying immobilized cells or enzymes are kept in motion by an upward fluid flow.

The reactor consists of a vertical column filled with active solid particles. When the liquid velocity exceeds the minimum fluidization velocity, the bed expands and the particles move freely within the liquid–solid suspension.

This configuration improves mixing and enhances mass and heat transfer while reducing clogging and gas entrapment compared to fixed-bed reactors.

TD Series No. 1

Exercise 1

Three moles of dye are rapidly injected into a real reactor. The concentration is measured as shown in the table below.

A tracer test is performed on a reactor with:

Volume: $V = 150 \text{ L}$

Flow rate: $Q_0 = 80 \text{ L/min}$

t(min)	5	10	15	20	25	30	35	43	45	50	55	60
c(g/l)	0.36	0.45	0.53	0.60	0.64	0.71	0.75	0.78	0.82	0.84	0.865	0.865

-Determine the residence time distribution.

-Determine the mean residence time.

- Determine the residence time distribution

Exercise 2

Three moles of dye are rapidly injected into a real reactor. The concentration is measured as shown in the table below. A tracer test is carried out on a reactor with a volume $V=150 \text{ L}$, fed with a flow rate $Q_0=80 \text{ L/min}$.

t (min)	0	1	2	3	4	5	6	7	8	9	11	12	13	14
C_t (g/l)	0	0.15	0.55	0.84	0.89	0.78	0.61	0.43	0.29	0.19	0.07	0.04	0.02	0

Questions:

-Determine the residence time distribution.

-Determine the mean residence time.

-Injection–Impulse: Determine the residence time distribution

Exercise 3

We aim to model the hydrodynamic behavior of a reactor with:

Volume: 280 liters

Liquid flow rate: $Q_0 = 11.4 \text{ m}^3/\text{h}$

A tracer method is used. Water flows under the given conditions, and at time $t=0$, 0.27 moles of tracer are injected over a very short time at the reactor inlet.

The tracer concentration is measured at the reactor outlet. The results are given below:

t(s)	10	20	30	40	50	60	70	80	90	100
c(mol/m ³)	0.02	0.1	0.26	0.48	0.65	0.82	0.89	0.88	0.84	0.7
t(s)	110	120	130	140	150	160	170	180	190	200
c(mol/m ³)	0.64	0.53	0.43	0.34	0.27	0.2	0.13	0.075	0.03	0

Questions:

Diagnosis:

Is there abnormal operation (presence of short-circuiting or dead volume)?

Justify your answer and verify the validity of the tracer experiment.

The reactor is modeled using the tanks-in-series model.

- Determine the model parameter.
- Does this model adequately represent the experiment?

A first-order reaction is studied in this reactor with $k=0.01 \text{ s}^{-1}$.

Calculate the conversion achieved in the real reactor and compare it with that obtained using the model.

Solutions**Exercise 1**

Given:

$$V = 12 \text{ m}^3$$

$$Q = 0.2 \text{ m}^3/\text{min}$$

$$\tau = V/Q = 60 \text{ min}$$

$$C_\infty \approx 0.865 \text{ g/L}$$

$$F(t) = C(t)/C_\infty$$

a) Residence Time Distribution:

$$E(t) \approx 0.0626 \exp(-0.0626 t)$$

b) Mean residence time:

$$\bar{t} \approx 16 \text{ min}$$

$$I(t) \approx (1/15.98) \exp(-t/15.98)$$

Exercise 2

$$V = 150 \text{ L}$$

$$Q = 80 \text{ L/min}$$

$$E(t) = C(t) / 4.99$$

Mean residence time:

$$\bar{t} \approx 4.95 \text{ min}$$

Exercise 3

$$V = 0.280 \text{ m}^3$$

$$Q = 0.003167 \text{ m}^3/\text{s}$$

$$\tau \approx 88.42 \text{ s}$$

$$\bar{t} \approx 89.47 \text{ s}$$

Tracer recovery $\approx 97\%$

Conclusion:

No abnormal behavior.

Model:

$N \approx 6$ CSTRs in series

First-order reaction ($k = 0.01 \text{ s}^{-1}$):

Real conversion:

$X \approx 56.5\%$

Model conversion:

$X \approx 56.6\%$

Conclusion:

Excellent agreement between model and experiment.

TD Series No. 2

Exercise 1

We consider a non-ideal stirred reactor with:

Volume: 8 m^3

Flow rate: $0.1 \text{ m}^3/\text{min}$

A step tracer injection experiment is performed. The results

t(min)	3	8	12	18	23	38	33	38	43	48	53	58	5
c(g/l)	0.31	0.40	0.48	0.55	0.59	0.66	0.70	0.73	0.77	0.79	0.81	0.82	0.84

Questions:

- a) Determine the residence time distribution $E(t)$.
- b) Calculate the model parameters.

The Cholette–Cloutier model represents:

- Perfect mixing zone
- Stagnant zone
- Short-circuit zone

Exercise 2

The following data are obtained at the outlet of a real continuous reactor after a pulse tracer injection:

t(min)	0	5	10	15	20	25	30	35
c(mol/l)	0	3	5	5	4	2	1	0

Questions:

- Determine and plot $E(t)$ Determine:
- Mean residence time
- Variance
- Dimensionless functions $E(\theta)$ and σ_{θ}^2
- Represent the reactor by a tanks-in-series model and determine N

Exercise 3

Data obtained downstream of a pyrex tube:

- Diameter: 2.85 cm
- Length: 2.75 m
- Flow velocity: 20 cm/s
- Pulse injection

t(s)	0	2	4	6	8	10	12	14	16	18	20
C(mg/l)	0	11	53	64	58	48	39	29	22	16	11
t(s)	22	24	26	28	30	32	34	36	38	40	42
C(mg/l)	9	7	5	4	2	2	2	1	1	1	1

Questions:

- Determine:
- Mean residence time
- Variance
- $E(t)$ and $E(\theta)$

Solution

Exercise 1

Given:

Volume $V = 8 \text{ m}^3$

Flow rate $Q = 0.1 \text{ m}^3/\text{min}$

Step tracer experiment results are provided.

Solution:

Residence time: $\tau = V/Q = 80 \text{ min}$

Final concentration $\approx 0.82 \text{ g/L}$

$$F(t) = C(t)/C_{\infty}$$

Cholette–Cloutier model:

$$E(t) \approx (1/(m\tau)) \exp(-t/(m\tau))$$

With:

$$m \approx 0.30 \rightarrow m\tau \approx 24 \text{ min}$$

Result:

$$E(t) \approx (1/24) \exp(-t/24)$$

Mean residence time $\approx 24 \text{ min}$

Exercise 2

Given pulse injection data.

Solution:

Integral of concentration ≈ 105

$$E(t) = C(t)/105$$

Mean residence time:

$$\bar{t} \approx 15 \text{ min}$$

Variance:

$$\sigma^2 \approx 50$$

Tanks-in-series model:

$$N = \bar{t}^2 / \sigma^2 \approx 4.5 \rightarrow N \approx 4-5 \text{ reactors}$$

Exercise 3

Given tracer data in a tubular reactor.

Solution:

Mean residence time:

$$\bar{t} \approx 12 \text{ s}$$

Theoretical time:

$$t \approx 13.75 \text{ s}$$

Variance:

$$\sigma^2 \approx 25$$

$$E(t) = C(t) / \int C(t) dt$$

Dimensionless:

$$E(\theta) = \bar{t} \cdot E(t)$$

Conclusion:

Flow close to plug flow with dispersion.

TD Series No. 3

Exercise 1

We want to study the hydrodynamics of a real reactor using the RTD (Residence Time Distribution). The response to an impulse injection of tracer is given in the following table:

t(min)	0	2	4	6	8	10	12	14	16
c(g/l)	0	0.6	1	1	0.8	0.4	0.15	0.05	0

The reactor volume is:

$$V_R = 1000 \text{ liters}$$

And the feed flow rate is:

$$Q_0 = 200 \text{ L/min}$$

Questions:

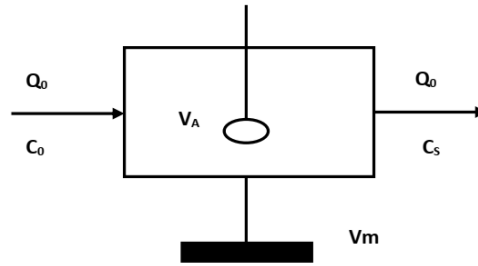
1. Calculate the mean residence time and determine the experimental $E(t)$.
2. A first-order liquid-phase reaction is to be carried out in this real reactor:

with: $k = 0.7 \text{ min}^{-1}$

- Calculate the conversion rate obtained in this reactor.

We decide to represent this real reactor by the model of a CSTR of volume V_A and a stagnant zone of volume V_m (see figure below).

- Determine the function $E(t)$ of the model.



Given:

$$1 - \bar{X} = \sum e^{-kt} E(t) \Delta t$$

Exercise 2

To study the residence time distribution (RTD) of a laboratory tubular reactor of volume: 863.5 cm³ the KCl tracer method is used.

The injected mass in the form of an impulse is: 8 g

Tests are carried out for three different flow rates: $Q_0=1$ L/min, 3 L/min, 5 L/min

The obtained results are reported in the table below.

Questions:

- Calculate, for each test, the residence time distribution $E(t)$.
- Perform a mass balance to check the conservation of tracer mass.

What can be concluded?

- Plot the corresponding RTD graphs $E(t)$.
- Deduce, for each case, the mean residence time.

Time (s)	$C_1(t)$ at 1 L/min	$C_2(t)$ at 3 L/min	$C_3(t)$ at 5 L/min
3	0.0447	0.0325	0.10415
6	0.0455	0.0406	0.10415
9	0.074	0.0406	0.479251
12	0.0769	7.453214	3.433686
15	0.441416	13.5476	8.315704
18	1.775834	19.1744345	1.74939
21	8.85272	6.250163	0.589097
24	16.286	3.280952	0.211554
27	18.087876	1.399912	0.163548

30	26.590724	0.829983	0.111473
33	16.013019	0.585942	0.1131
36	13.062083	0.197908	0.107404
39	11.407648	0.135001	0.10415
42	8.5052	0.0886	
45	6.525631	0.114972	
48	5.711961	0.0764	
51	3.433686	0.0813	
54	3.270952	0.000065	
57	2.673718		
60	2.3214		
63	1.887714		
66	1.589097		
69	1.046379		

Solutions

Exercise 1

1) Experimental RTD $E(t)$ and mean residence time

For an impulse injection, the residence-time distribution is obtained from the measured concentration by:

$$E(t) = c(t) / \int c(t) dt$$

Using the trapezoidal rule with a time step $\Delta t = 2$ min, the area under the concentration curve is:

$$\int c(t) dt \approx 8.0 \text{ g}\cdot\text{min}/\text{L}$$

Therefore:

$$E(t) = c(t) / 8$$

t (min)	c(t) (g/L)	E(t) (min ⁻¹)
0	0	0
2	0.6	0.075
4	1.0	0.125
6	1.0	0.125
8	0.8	0.100
10	0.4	0.050
12	0.15	0.01875
14	0.05	0.00625

16	0	0
----	---	---

The mean residence time is computed from:

$$\bar{t} = \int tE(t)dt =$$

Numerical evaluation gives: $\bar{t} \approx 6.03$ min.

The nominal hydraulic residence time is $\tau = V_R / Q_0 = 1000/200 = 5$ min.

Since $\bar{t} > \tau$, the reactor is non-ideal and exhibits delayed exit/retention effects.

2) Conversion for a first-order reaction

Reaction: $A \rightarrow B$, with $k = 0.7 \text{ min}^{-1}$.

For a real reactor characterized by $E(t)$, the outlet fraction of reactant is:

$$1 - \bar{X} = \int \exp(-kt) E(t) dt$$

Using the discrete data: $1 - \bar{X} \approx \sum \exp(-kt) E(t) \Delta t$

Substituting the values of $E(t)$ above gives: $1 - \bar{X} \approx 0.0568$

Hence: $\bar{X} = 1 - 0.0568 = 0.9432$

Final result: $\bar{X} \approx 94.3\%$

3) CSTR + stagnant-zone model

If the real reactor is represented by one perfectly mixed active zone of volume V_A and one stagnant zone of volume V_m , only the active zone is crossed by the flow.

Therefore:

$$\tau_A = V_A / Q_0$$

For an impulse input, the RTD of a single CSTR is:

$$E(t) = (1/\tau_A) \exp(-t/\tau_A) = (Q_0 / V_A) \exp[-(Q_0/V_A)t]$$

The total reactor volume is $V_R = V_A + V_m$.

If one forces the model to match the experimental mean residence time, then $V_A = Q_0 \bar{t} \approx 200 \times 6.03 = 1206 \text{ L}$, which would imply $V_m = 1000 - 1206 = -206 \text{ L}$.

Because a negative stagnant volume is physically impossible, this simple model does not adequately represent the experimental data.

Exercise 2

Given: tubular laboratory reactor volume $V = 863.5 \text{ cm}^3 = 0.8635 \text{ L}$; injected tracer mass $m_0 = 8 \text{ g}$. The pulse tests were performed at $Q_0 = 1, 3$, and 5 L/min .

For a pulse input, the RTD is determined in each case from:

$$E_i(t) = C_i(t) / \int C_i(t) dt$$

1) RTD and mean residence time for each flow rate

Using numerical integration of each concentration curve gives the following areas:

$$\text{For } Q = 1 \text{ L/min: } \int C_1(t) dt \approx 447.54 \text{ g}\cdot\text{s/L}$$

$$\text{For } Q = 3 \text{ L/min: } \int C_2(t) dt \approx 159.94 \text{ g}\cdot\text{s/L}$$

$$\text{For } Q = 5 \text{ L/min: } \int C_3(t) dt \approx 46.45 \text{ g}\cdot\text{s/L}$$

Hence the residence-time distributions are:

$$E_1(t) = C_1(t) / 447.54$$

$$E_2(t) = C_2(t) / 159.94$$

$$E_3(t) = C_3(t) / 46.45$$

The mean residence time is computed from: $\bar{t} = [\int tC(t)dt] / [\int C(t)dt]$

$$\text{For } Q = 1 \text{ L/min: } \bar{t}_1 \approx 34.7 \text{ s}$$

$$\text{For } Q = 3 \text{ L/min: } \bar{t}_2 \approx 18.0 \text{ s}$$

$$\text{For } Q = 5 \text{ L/min: } \bar{t}_3 \approx 15.3 \text{ s}$$

2) Tracer mass conservation

The recovered tracer mass is obtained from: $m_{\text{rec}} = Q \int C(t) dt$, with Q expressed in L/s.

At 1 L/min: $Q = 1/60$ L/s, so $m_{\text{rec},1} \approx (1/60) \times 447.54 = 7.46$ g, i.e. 93.2% recovery.

At 3 L/min: $Q = 3/60$ L/s, so $m_{\text{rec},2} \approx (3/60) \times 159.94 = 8.00$ g, i.e. about 100% recovery.

At 5 L/min: $Q = 5/60$ L/s, so $m_{\text{rec},3} \approx (5/60) \times 46.45 = 3.87$ g, i.e. 48.4% recovery.

3) Interpretation and conclusions

The nominal residence time of the tubular reactor is $\tau = V/Q$.

For $Q = 1$ L/min: $\tau_1 = (0.8635/1) \times 60 = 51.81$ s

For $Q = 3$ L/min: $\tau_2 = (0.8635/3) \times 60 = 17.27$ s

For $Q = 5$ L/min: $\tau_3 = (0.8635/5) \times 60 = 10.36$ s

Comparison with the experimental mean residence times leads to:

At 1 L/min, $\bar{t}_1 < \tau_1$, which suggests non-ideal hydrodynamics and possible dead volume or bypassing.

At 3 L/min, $\bar{t}_2 \approx \tau_2$, so this experiment is the most reliable and consistent with the reactor volume.

At 5 L/min, $\bar{t}_3 > \tau_3$ while only 48.4% of the tracer mass is recovered; therefore the measurements are incomplete and the tail of the RTD was probably not fully recorded.

Overall conclusion: the 3 L/min experiment is the best data set; the 1 L/min run indicates hydrodynamic non-idealities; and the 5 L/min run is experimentally incomplete.

TD Series No. 4

Exercise 1:

Glucoamylase

hydrolyzes maltose into glucose according to:



At 40°C, the kinetic parameters of glucoamylase are:

- $V_{\max}=10 \text{ } \mu\text{mol of maltose min}^{-1} \text{ (mg enzyme)}$
- $K_M=35 \text{ mmol/L}$

Glucose, the reaction product, behaves as a competitive inhibitor of maltose with:

- $K_i=10 \text{ mmol/L}$

The reaction is carried out in a 1000 L batch reactor. The initial maltose concentration is $[S]_0=1 \text{ mol/L}$, and the enzyme concentration is 1 g/L.

1. Neglecting inhibition by glucose, determine the time required to hydrolyze 99% of the maltose.
2. Taking into account the competitive inhibition by glucose, determine the time required to hydrolyze 99% of the maltose. Conclude.

Solution

- Without inhibition: $t=115.118 \text{ min}$
- With competitive inhibition by glucose: $t=2643.7 \text{ min}=44.09 \text{ h}$
- Conclusion: product inhibition increases the reaction time by about 23 times.

Exercise 2:

The conversion of glucose into another substance by an enzyme in a batch reactor gives the following results:

$[S] \times 10^4$ (mol/L): 0.1, 0.2, 1.0, 3.0, 5.0

V/C_{E0} (min⁻¹): 150, 256, 600, 770, 818

Assume the following reaction mechanism:



where C_{E0} is the initial enzyme concentration and V is the reaction rate.

1. Using the kinetic data, calculate k_2 and K_M .
2. Determine the time required in batch operation to reach **95% conversion**, starting from $S_0 = 0.2 \times 10^{-4}$ mol/L and $V_{\max} = 1.82 \times 10^{-5}$ mol/L·min.
3. What is the reaction rate at this conversion?
4. For industrial continuous production with the same 95% conversion and the same inlet concentration, choose the most suitable open reactor and justify your choice.
5. Determine the reactor volume required to treat a flow rate of $Q = 5$ m³/h.

Solution

From the worked solution in the PDF:

- $k_2 = 909.09$ min⁻¹
- $K_M = 5.45 \times 10^{-5}$ mol/L
- Time for 95% conversion in batch: $t_{95\%} = 10.14$ min
- Residence time in a mixed reactor: $\tau = 57.94$ min
- Residence time in a plug-flow reactor: $\tau = 10.02$ min

Therefore, the plug-flow reactor is selected as the best reactor.

For $Q = 5$ m³/h, the required reactor volume is:

- $V_R = 853$ L

Exercise 3:

A sugar fermentation is studied in a batch fermenter over a reaction time of 3 hours. The bacterial growth rate is:

$$\mu = 0.2 \text{ h}^{-1}$$

The initial bacterial concentration is:

$$X_0 = 2 \text{ g/L}$$

Determine the final biomass concentration at the end of the experiment.

Deduce the final substrate concentration if the initial substrate concentration was 4.5 g/L, given that $Y_{X/S} = 0.5$.

Calculate the final product concentration, given that the product/biomass yield is 2.2.

Solution

The final values given in the solution are:

Final biomass concentration: $X_f = 3.644 \text{ g/L}$

Final substrate concentration: $S_f = 1.211 \text{ g/L}$

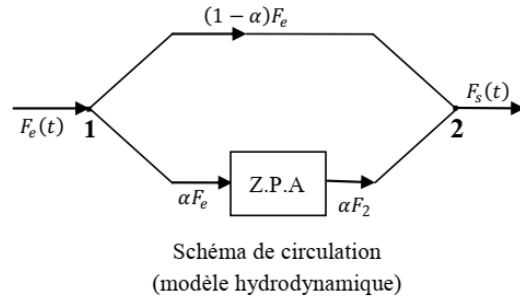
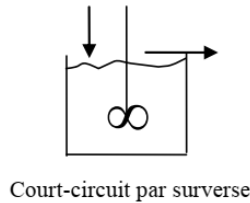
Final product concentration: $P = 3.617 \text{ g/L}$

Appendix

A. 1 Modélisation du réacteur agité continu réel

1. Modèle à un paramètre

Exemple : Réacteur agité avec court-circuit



Méthode des moments

$G(s)$ du modèle hydrodynamique ?

$$G(s) = \frac{\bar{F}_s}{\bar{F}_e} \quad \bar{F}_s : \text{la T.L de } F_s, \quad \bar{F}_e : \text{la T.L de } F_e$$

$$F_s(t) = ? \quad \text{bilan au nœud 2 : } (1 - \alpha)F_e + \alpha F_2 = F_s \quad \text{sa T.L est : } (1 - \alpha)\bar{F}_e + \alpha \bar{F}_2 = \bar{F}_s$$

$$G(s) = \frac{(1-\alpha)\bar{F}_e + \alpha \bar{F}_2}{\bar{F}_e} \quad , \quad G(s) = (1 - \alpha) + \alpha \frac{\bar{F}_2}{\bar{F}_e}$$

avec $\frac{\bar{F}_2}{\bar{F}_e} = G_1(s)$? la fonction de transfert de la Z.P.A

bilan de matière dans la Z.P.A :

$$\alpha F_e = \alpha F_2 + \frac{d}{dt}(C_2 V) \quad , \quad \alpha F_e = \alpha F_2 + V \frac{d}{dt} \left(\frac{\alpha F_2}{\alpha Q} \right) \quad , \quad \alpha F_e = \alpha F_2 + \alpha \frac{V}{\alpha Q} \frac{dF_2}{dt}$$

sa T.L est :

$$\alpha \bar{F}_e = \alpha \bar{F}_2 + \alpha \frac{\tau}{\alpha} [s \bar{F}_2 + \underbrace{F_2(t=0)}_0] \quad , \quad \alpha \bar{F}_e = \alpha \bar{F}_2 \left(1 + \frac{\tau s}{\alpha} \right) \quad , \quad \frac{\alpha \bar{F}_2}{\alpha \bar{F}_e} = \frac{1}{1 + \frac{\tau s}{\alpha}} = G_1(s)$$

Enfin :

$$G(s, \alpha) = (1 - \alpha) + \frac{\alpha}{1 + \frac{\tau}{\alpha} s}$$

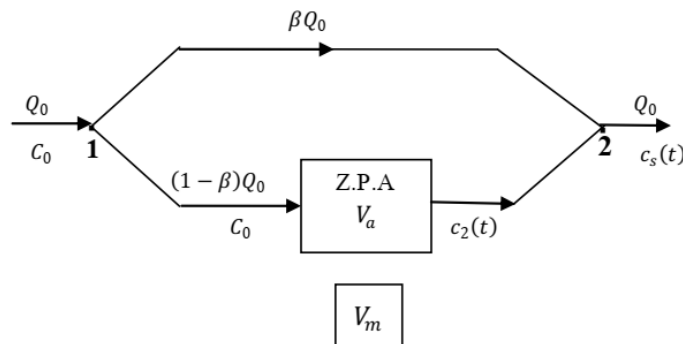
Fonction de transfert du R.A avec court-circuit.
Le paramètre du modèle est α , la fraction du débit dans la Z.P.A.

$$\mu_1 = (-1) \lim_{s \rightarrow 0} \frac{\partial G}{\partial s} \quad , \quad \mu_2 = (-1)^2 \lim_{s \rightarrow 0} \frac{\partial^2 G}{\partial s^2}$$

$$\bar{t}_s = \tau \quad , \quad \sigma^2 = \tau^2 \left(\frac{2}{\alpha} - 1 \right)$$

2. Modèle à 2 paramètres

Exemple : Réacteur agité avec court-circuit et volume mort



Le bilan de traceur dans la Z.P.A, à un instant t après l'injection donne :

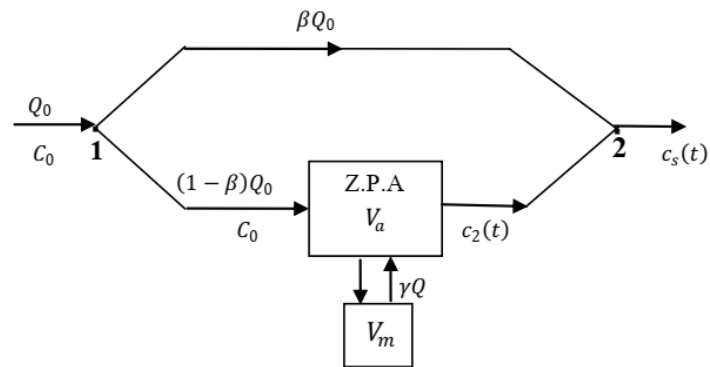
$$C_0 = c_2 + \frac{\alpha}{1-\beta} \tau \frac{dc_2}{dt} \quad \text{après intégration : } \frac{c_2}{C_0} = 1 - \exp \left[-\frac{1-\beta}{\alpha} \left(\frac{t}{\tau} \right) \right] \quad (1)$$

$c_2 = f(c_s)$? le bilan au nœud 2 : $c_2 = \frac{c_s}{1-\beta} - \frac{\beta}{1-\beta} C_0$, dans (1) : $\frac{C_0 - c_s}{C_0} = (1-\beta) \exp \left[-\frac{1-\beta}{\alpha} \left(\frac{t}{\tau} \right) \right]$ ou encore $\frac{C_0}{C_0 - c_s} = \frac{1}{(1-\beta)} \exp \left[\frac{1-\beta}{\alpha} \left(\frac{t}{\tau} \right) \right]$ les deux paramètres du modèle sont β et α (à déterminer)

Reste à calculer les valeurs de α et β qui sont celles du modèle, à condition que celui-ci représente convenablement le réacteur réel. Pour vérifier ceci, il faut confronter les résultats expérimentaux aux résultats du modèle et déterminer par la même les paramètres α et β ; graphiquement on trace $\ln \left[\frac{C_0}{C_0 - c_s} \right]_{exp} = f(t)$, si le modèle représente bien le réacteur réel, on doit obtenir une droite. La pente et l'ordonnée à l'origine permettent la détermination de α et β .

3. Modèle à 3 paramètres

Exemple : Réacteur agité avec court-circuit et volume stagnant échangeant de la matière avec la Z.P.A



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