

Industrial process intensification through biomimetic approaches : the ultimate based-life model proposed by membrane engineering

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1. Learning from nature...

Biological and artificial membranes => Motivation

2. Membranes and enzymes

Towards the EMR concept => 1st lesson

3. From heterogeneous to homogeneous reaction

How to open a new way thanks to membranes => 2nd lesson

4. You've said "membrane engineering" ?

The holy triptych : material, process, fluids => 3rd lesson

5. Tomorrow expectations



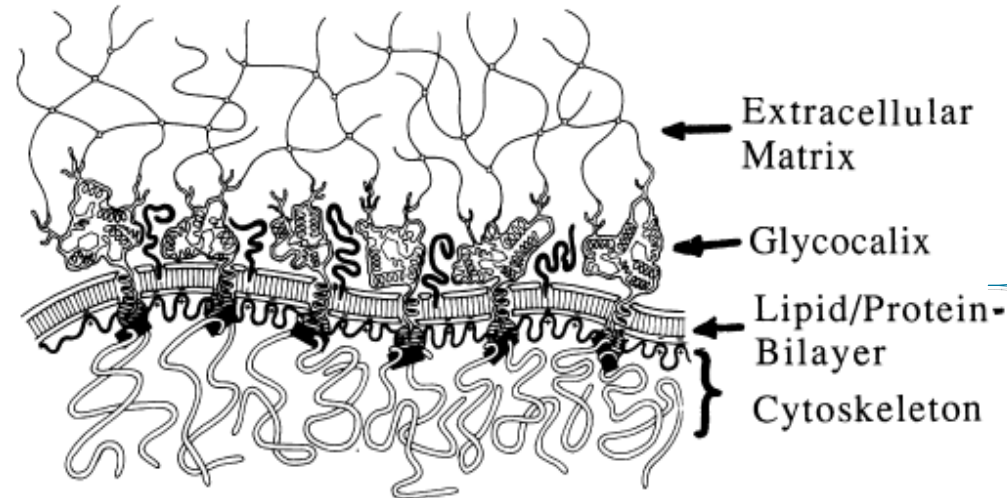
Biological membranes represent the ultimate achievement to ensure sustainable development and preservation of life systems

“Life in all its diversity became possible after nature had found the trick with the membrane. It enabled the separation of living entities from the lifeless and hostile environment under preservation of selective material exchange between the two worlds. It led to the evolution of cells the function of which depends on the well-controlled interplay and material exchange between compartments performing different functions. The reduction to two dimensions increased the efficiency drastically and opened the possibility for irreversible charge separation and transient storage of energy in the form of electrochemical potential gradients”

E. Sackmann in Handbook of biological physics

“Biological membranes . Architecture and function” - Elsevier 1995

One example of biological membrane : the plasma membrane of animal cells



On the schema the two top layers are enlarged in thickness by a factor of about 300 compared to cytoskeleton

Architecture : a three layered system

- Cytoskeleton : a quasi-two dimensional macromolecular network
- Lipid/protein bilayer
- Glycocalix : a macromolecular film formed by oligosaccharides
(from glycolipid and glycoprotein head groups)



Functions : The cytoskeleton : the resistance and stability of the system

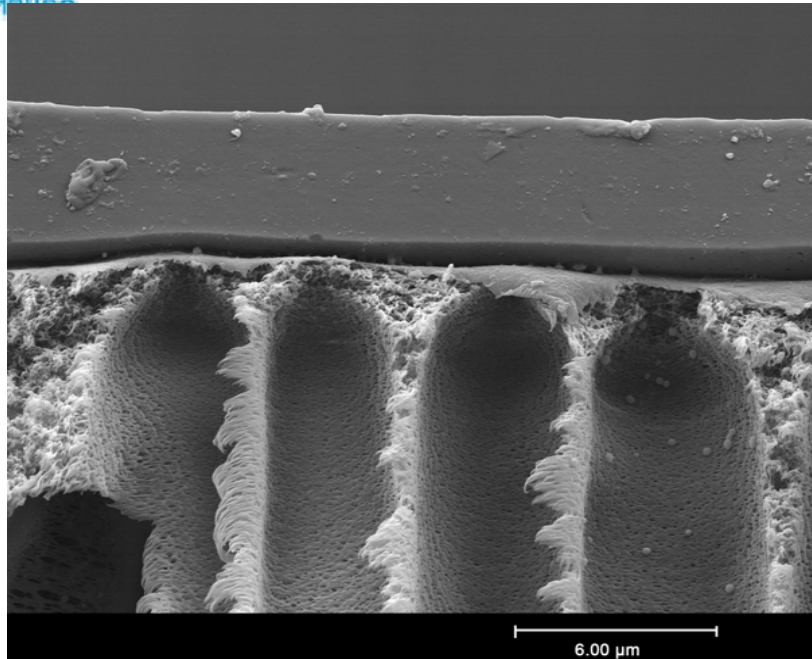
The two top layers form a selective filter which control the transfer of ions, molecules, molecular aggregates and even large particles (viruses , bacteria or even other cells)

The bilayer is a multifunctional system which can simultaneously be the site for energy producing processes (such as glycolysis) and for some signal transduction/amplification (hormones)

The glycocalix acts as receptor for extracellular signals and mediates the communication between the cell interior and its environment



Two examples of artificial membranes

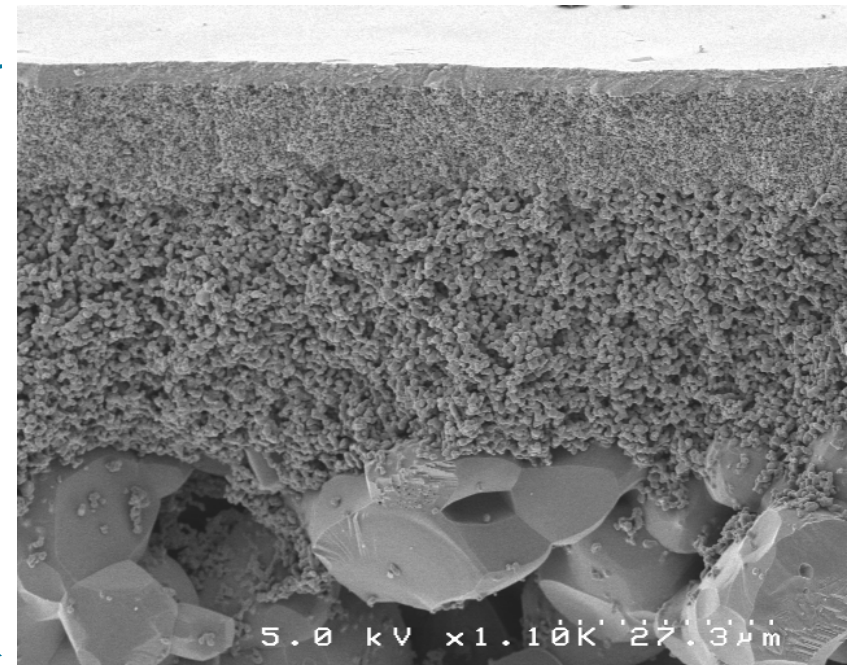


Alumina / Pall-Exekia
Support (10 μm) + 2 intermediate
layers (0.8 & 0.2 μm) +
separative layer (5 nm)

Function :
Gaz or liquid separation by
pressure effect

Architecture :

PVDF support
and polymeric top layer





A strong motivation : to exploit the tricks of nature with new systems/processes using artificial membranes

=> Strong advantages :

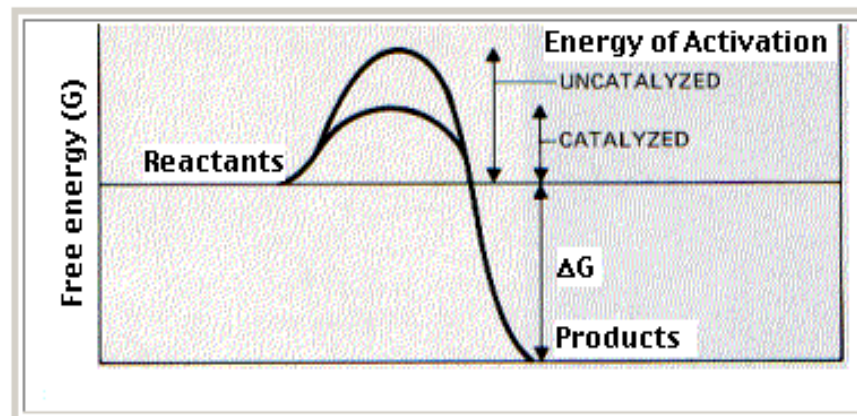
- "...the reduction to two dimensions increased the efficiency drastically..."
- easy-to-control driving forces (pressure, electrical...gradients)
- a-thermal and free-of-solvent (may be with the exception of cleaning steps...) working conditions
- modular, continuous, easy to combine and mainly quite simple device as regards other "intensification systems" !

=> The long-term vision :

replacing old-fashioned processes having a bad efficiency and poor outcomes (product quality, environmental footprint...) by new systems mimicking living systems !

Enzyme catalysis, a privileged tool for living systems

- Enzymes are catalysts (most of the time proteins) present inside the cell or anchored in the membrane cell
- Enzymes bind temporarily to one or more of the reactants => lowering the amount of activation energy needed => speeding up the reaction (up to several thousands and even more...)

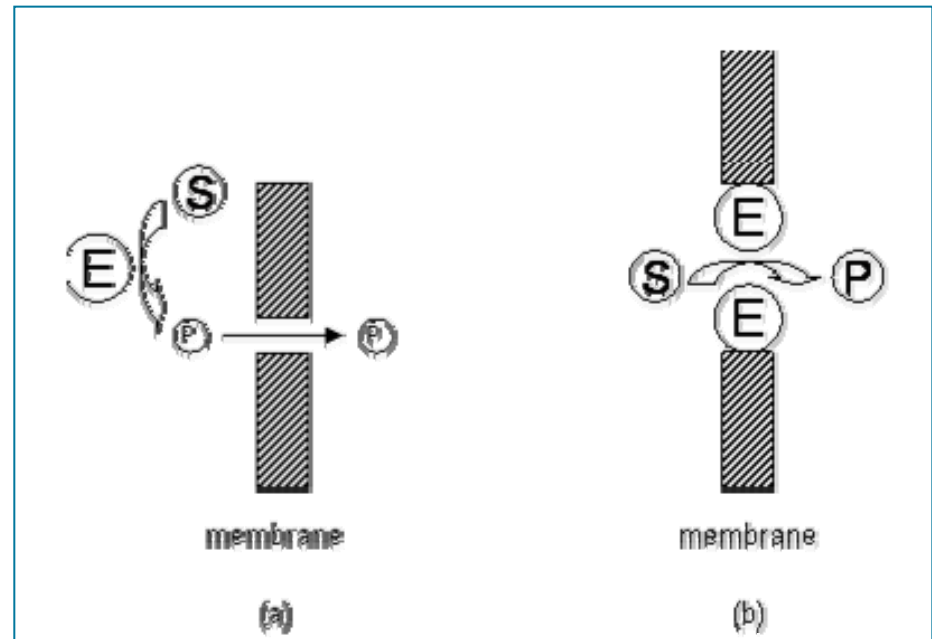


- Several mechanisms work to make enzyme activity efficient and well-coordinated => enzyme are locked into spatial relationships that enable them to interact efficiently.



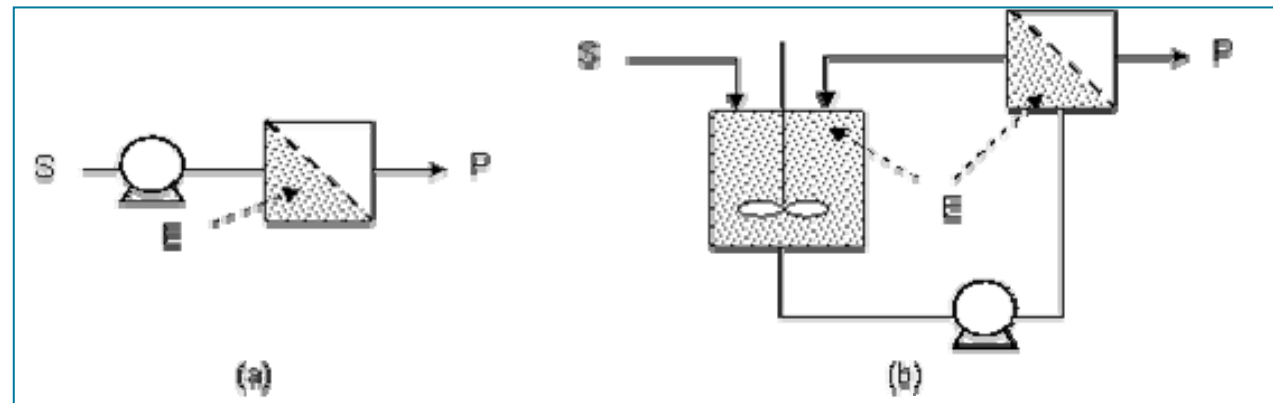
Enzymatic membrane reactors : the concept

- ❑ The main objective of the EMR configuration : maintaining the full activity inside the reacting volume by a full rejection of enzyme molecules
- ❑ Case a : the function of the membrane is to reject free enzymes => FEMR
- ❑ Case b : the membrane is the catalyst media and reaction occurs during membrane crossing => New function => IEMR



FEMRs

- ❑ Attractive when substrate and enzyme both present a size quite higher than those of the products: rejection of catalyst and non-transformed substrates
- ❑ Two types of reactors :



a) dead-end cell reactor (DECR) (b) continuous recycled membrane reactor (CRMR)

- ❑ For a lot of enzymes : $10 \text{ kDa} < M_w < 80 \text{ kDa} \Rightarrow$ UF membranes $< 100 \text{ kDa}$
- ❑ Effect on performance of electrostatic or hydrophobic interactions between the biological molecules and the membrane material



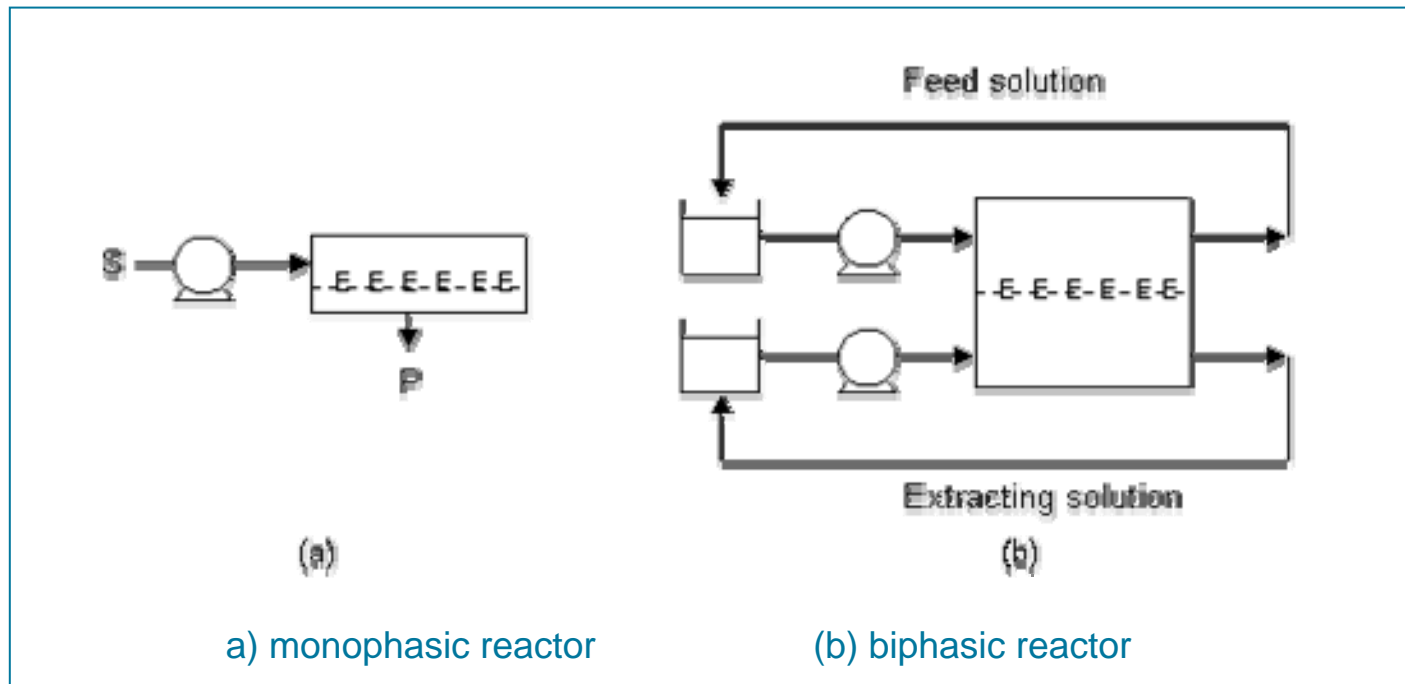
Main advantages and drawbacks

Advantages	Drawbacks
Continuous mode (substrate feeding)	Decrease of enzyme activity versus time (Loss of catalyst, effect of shear stress...)
Free enzyme	
Retention /reuse of catalyst	Heterogeneity of reaction conditions between the core of solution and membrane wall
Reduced substrate/product inhibitions	
Free enzyme end-product	Polarization layer & induced limitation
Control of product properties by enzyme and/or membrane choice	Membrane fouling
Integrated process (single step reaction/separation)	



IEMRs

- ❑ Enzyme immobilized on/in a porous material => “active membranes” at the heart of the immobilized enzyme membrane reactors (IEMR)
- ❑ Two types of reactors :





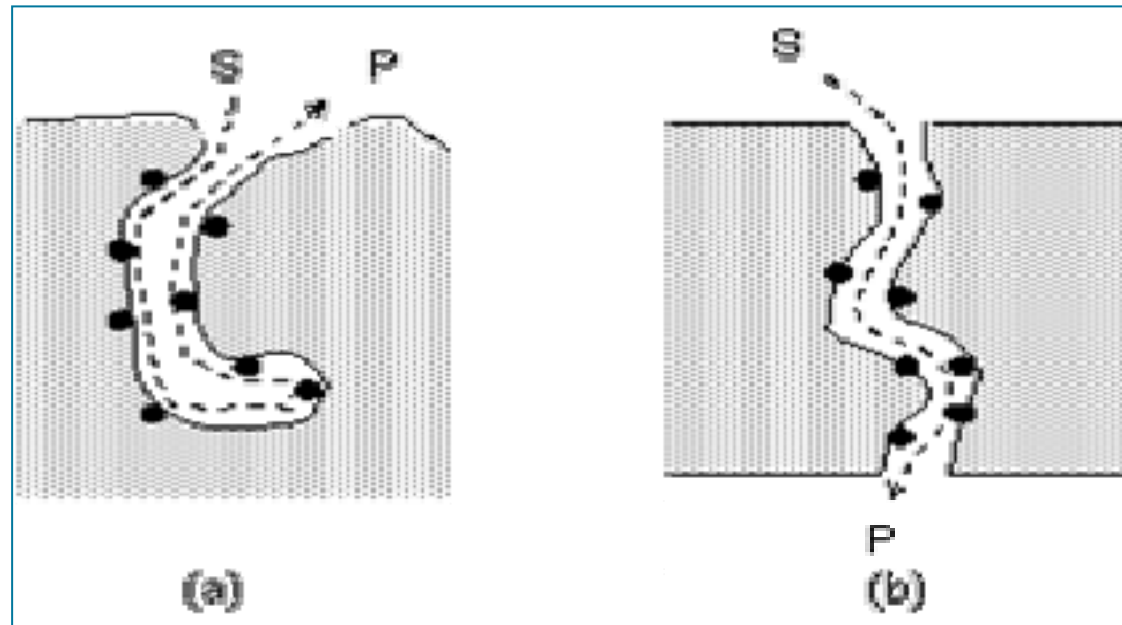
Monophasic system

□ Substrate flushed through the microporous medium by applying a transmembrane pressure. Low pore size => high probability of capture of substrate molecules by catalyst as well as an improved contact time!

The thin layer = a specific macrosystem resulting from the assembly of swarms of microsystems: each pore represents a particular microreactor!

=> a precise control of the reaction with minimized substrate and catalyst losses, faster reactions and higher yields, cleaner products and lower operating costs!

- Compared to fixed or fluidized bed reactors, 3 main advantages:
 - ✓ *Extraction of products => good if product inhibition*
 - ✓ *A small thickness => dramatic pressure reduction*
 - ✓ *A convective control => mass transfer increase*

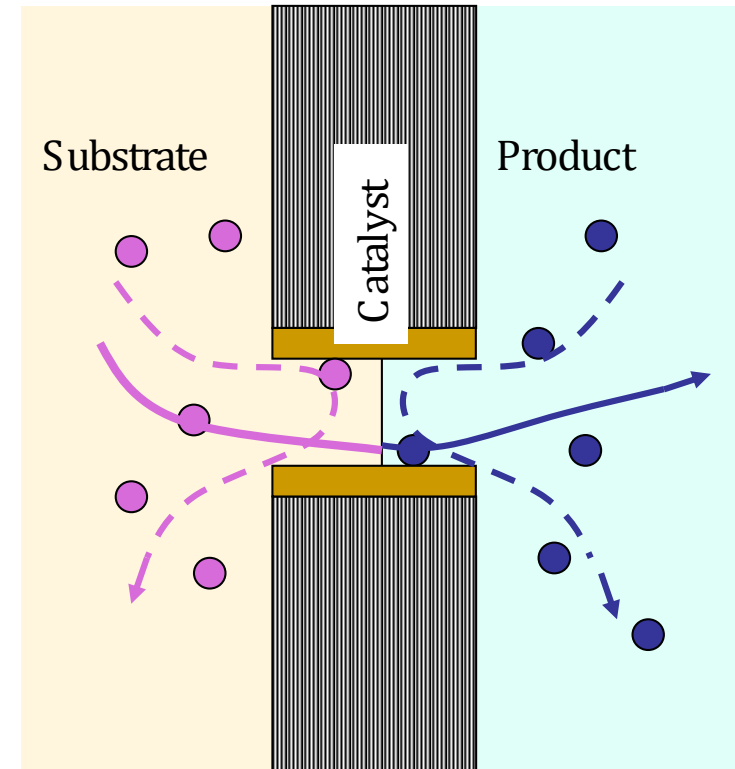


a) Diffusion

(b) convection

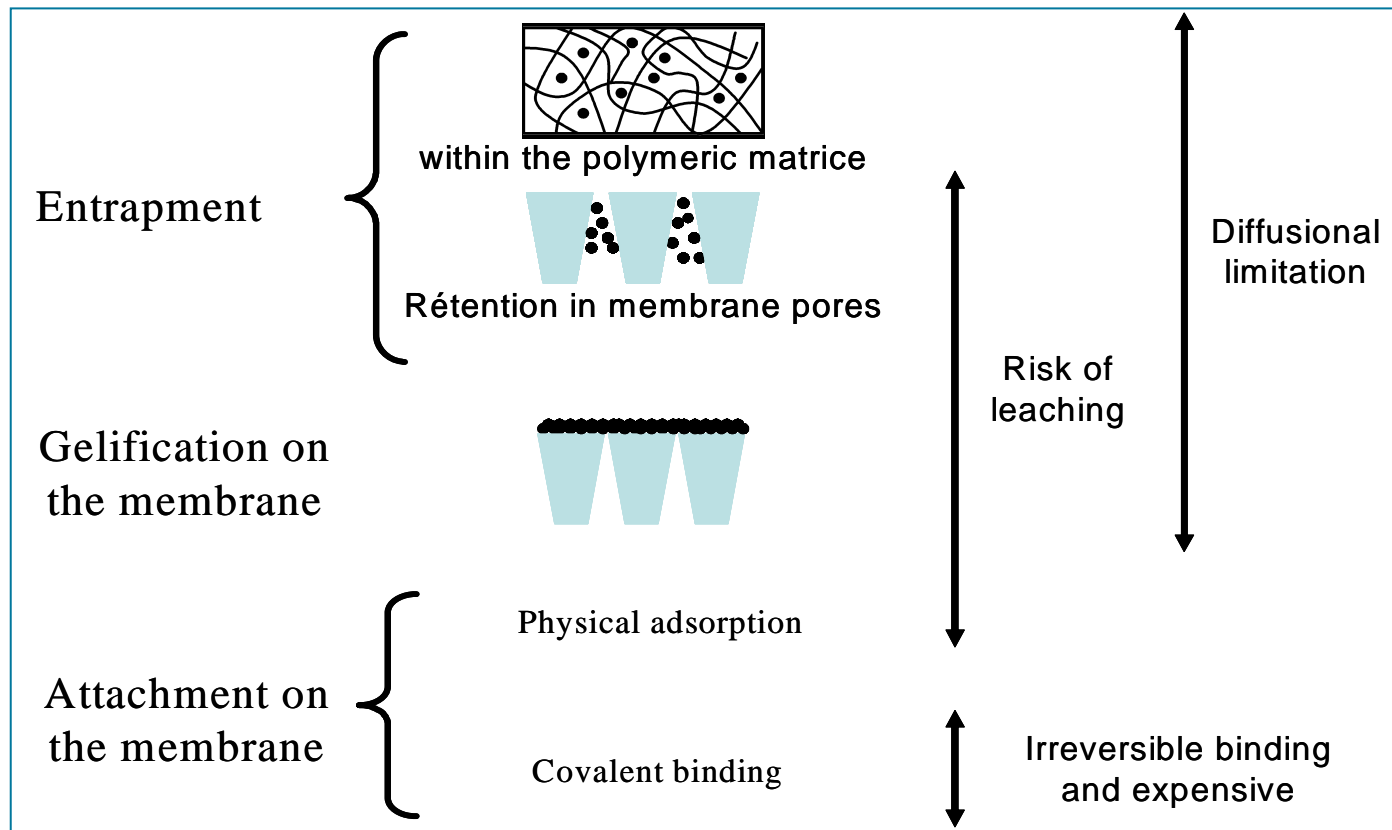
Biphasic system

- ❑ A membrane contactor quite useful when working with low soluble products into aqueous or organic solutions, or when the extraction of an undesirable by-product is needed...
- ❑ Two non miscible solutions separated by an enzymatic membrane. The substrate diffuses from the feed solution, reacts with the biocatalyst and the product diffuses toward the extracting solution with which it presents a very high affinity.
- ❑ Performance limited by mass transfer resistance... but no emulsion formed and product recovery in a single phase.



Enzymatic thin layer preparation

- Mainly three different ways for the preparation of active membranes





1st lesson...

- ❑ **Biomimetism, the inspiring way** : positioning of biocatalyst (inside or on the material), configuration (imbedded in gel layer to take advantage of the environment : lipases for esterification...)
- ❑ **A royal pathway for green chemistry** : waste treatment (phenols..), lower temperature gas treatments (catalytic conversion of light alkanes), very selective synthesis for fine chemistry and pharmaceuticals...
- ❑ **A lot of new tools ... but no “ideal route”** : the need for a case-by-case approach accounting for the membrane material, the fluid properties (from molecular to macroscopic level) and the working conditions : the need for a holistic approach !



Rationale

Heterogeneous catalysts generally preferred for industrial processes :

- easier removal after reaction
- continuous operation mode facilitated

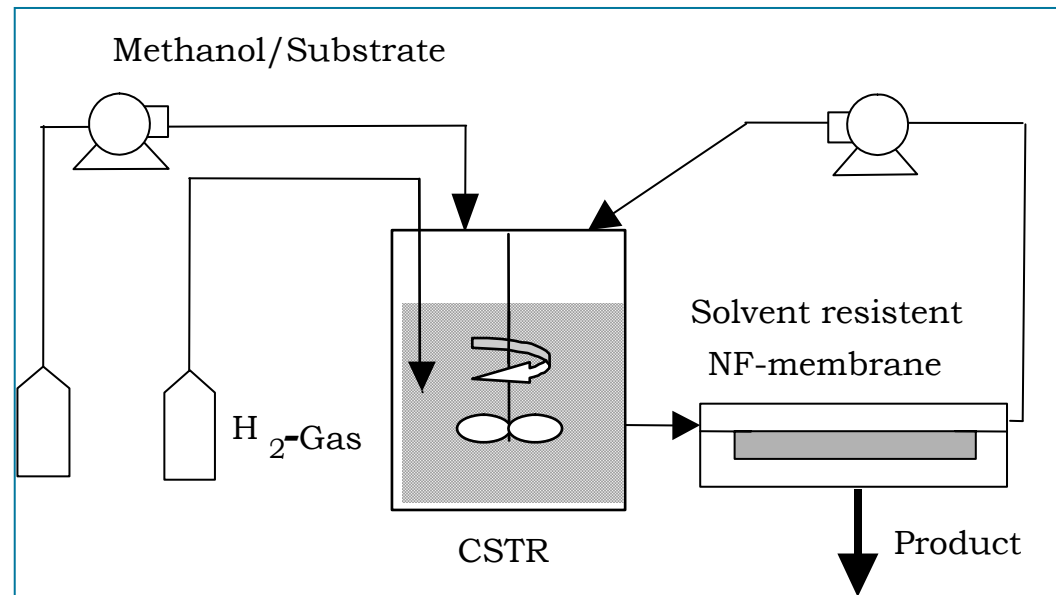
Heterogeneous catalysts preparation :

- sometimes tedious with a high preparative effort
- in certain cases, mass or heat transfer limitations and decreased activities

Homogeneous reactions : generally higher chemo- and enantio-selectivity.

→ Trying to integrate as well as possible all these constraints

A new concept : NF + homogeneous catalysis



- Use of a nanofiltration (NF) - membrane : products permeate and dissolved catalyst is rejected .
- Thanks to the recent development of solvent resistant NF-membranes with a molecular weight cut-off (MWCO) in the range of 200 to 700 Dalton and working conditions below 40 °C and 35 bar



Applications

- Chiral catalysts : among the preferred systems for this hybrid process
 - extremely high cost of catalysts
 - sensitivity towards traditional heterogenisation methods
 - transition metal complexes with a MW above 500 D
 - high activity and selectivity at moderate reaction conditions.

- The case of continuous enantioselective hydrogenation with a high industrial relevance:
 - dimethyl itaconate (DMI)
with Ru-BINAP (MW = 929 D)
 - methyl 2-acetamidoacrylate (MAA)
with Rh-EtDUPHOS (MW= 723 D)



2nd lesson...

- ❑ By mimicking nature, and thanks to the development of new materials the possibility to develop new systems and processes.
- ❑ Not for the moment the idea to reproduce *per se* living mechanisms ... because we are yet too far from our ultimate biological model, but to push new breakthrough tools to carry out more properly operations in the framework of our traditional flowsheet : new materials with a very low cut-off able to resist to traditional solvent (a great opportunity today : recycling of solvents without phase-change!); in the future new mesoporous thin layers for heat transfer (heating or cooling)...
- ❑ The need also to develop new visions integrating correctly all the necessary ingredients to be successful and a new frontier for education : membrane engineering !

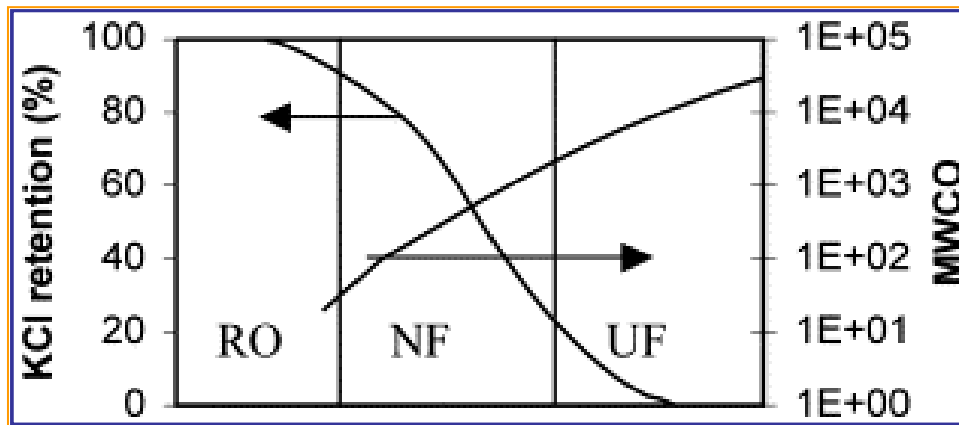


A new global and holistic approach directly inspired from nature !

Material properties : improving the local function ...

- Flitting from basic properties- sieving (MF, UF) or charge (ED) effects- ... to much more advanced properties

→ NF with an improved resistance...



dp <1-2 nm (IUPAC) / Electric charges on the material

Sieving effect : MWCO between 200 and 1500 daltons

Donnan effect : separation of ions and charged molecules

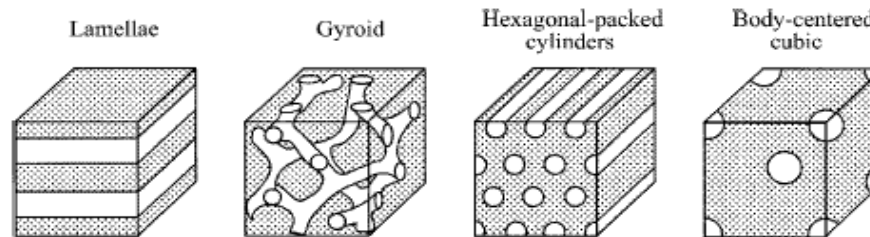
→ Active membranes : enzymatic or chromatographic effect ...



- By new ways of elaboration :

- molecular self-assembly

Self organization : an important building principle of biological membranes. Efforts to imitate nature with other kind of molecules (block copolymers) to fabricate ordered nanometer-scale structures



- => anti-fouling surface , pores functionalized,....

- supramolecular chemistry

- => making real channels with an attractive transport of neutral molecules or ions, mimic reaction sites

- A very clear trend :

Trying to exploit the most recent advances of nanotechnology to develop biomimetic materials !



Working conditions : making the best ...

- Using “porous membranes materials” for contacting purposes :

The new concept of “membrane contactor”

The membrane material = The “chip” of chemical engineering

=> Osmotic evaporation

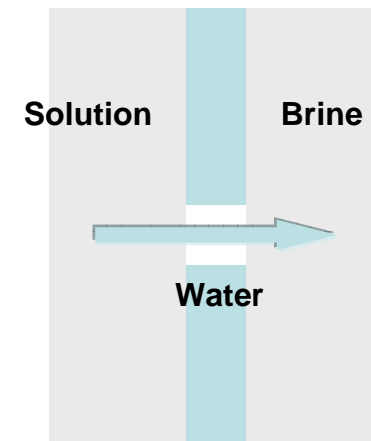
=> Liquid-Liquid extraction

=> Emulsification

=> Crystallization

=> Fluid distribution

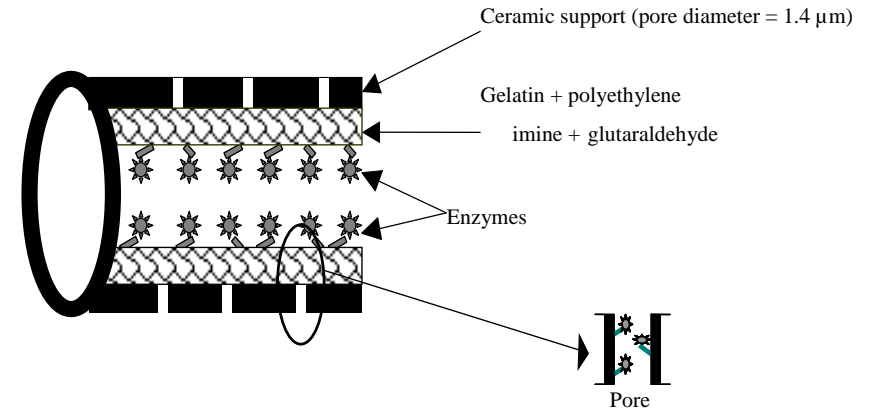
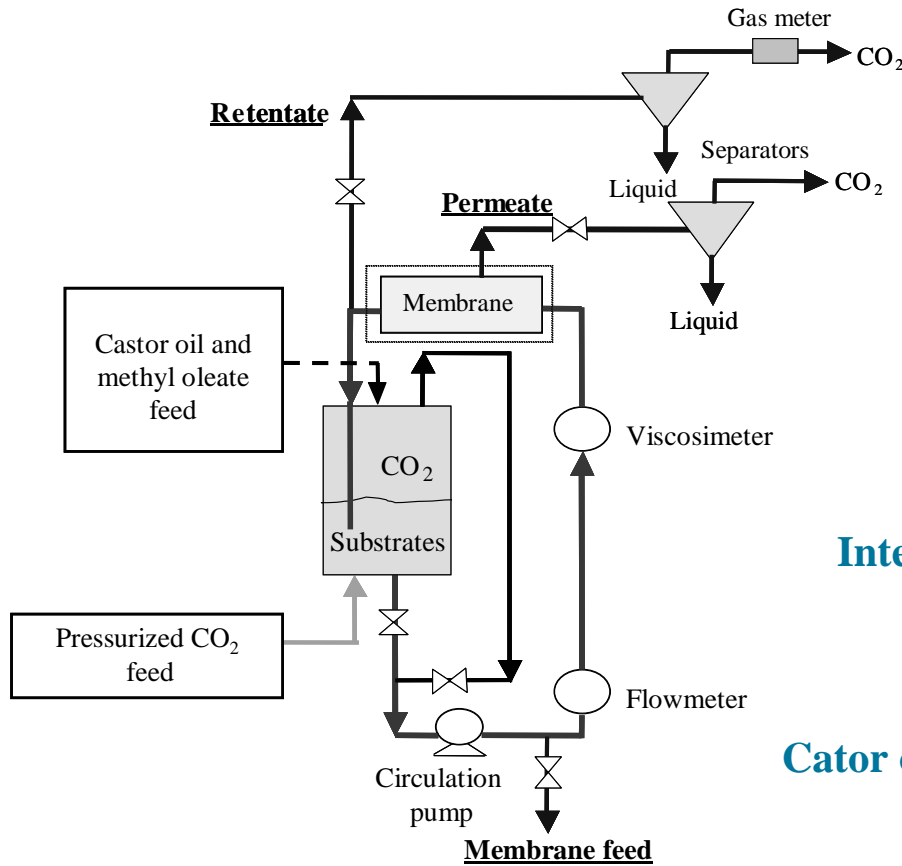
=> Reaction : a swarm of microreactors !



Hydrophobic membrane
*Isothermal concentration
of highly thermal sensitive
solutions (VE, DO, CR)*



Looking for new synergy by integrating properly operations :



Inter esterification between castor oil triglycerides (TG) and methyl oleate with SC CO₂ :

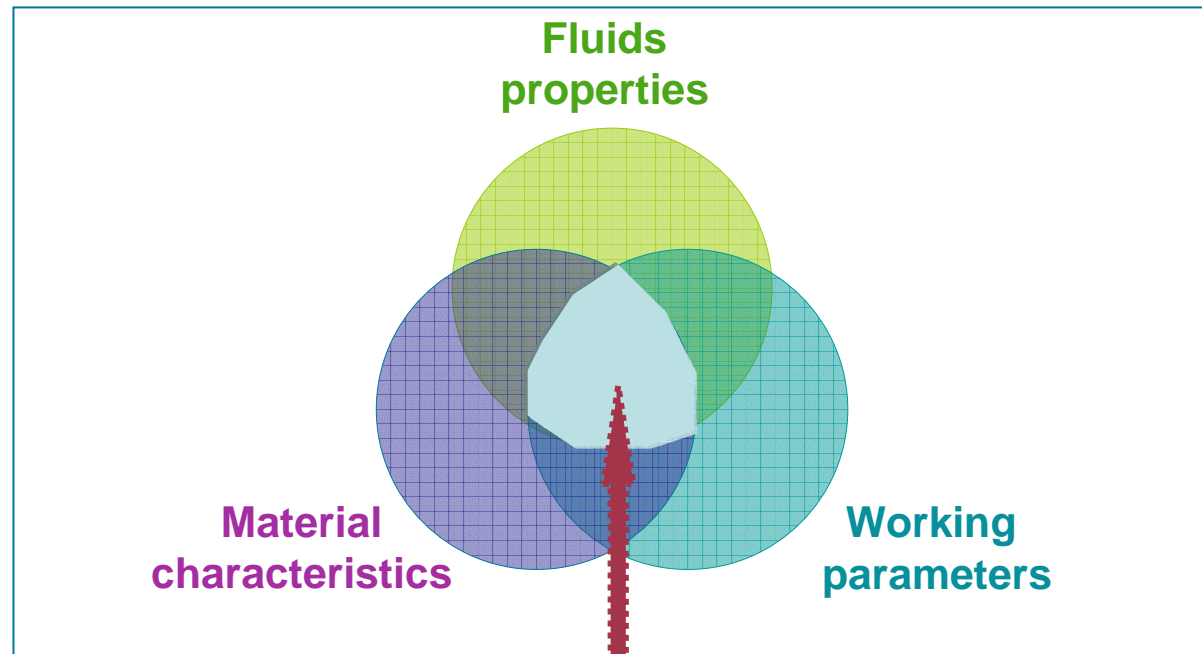


Accounting for fluid characteristics ... !



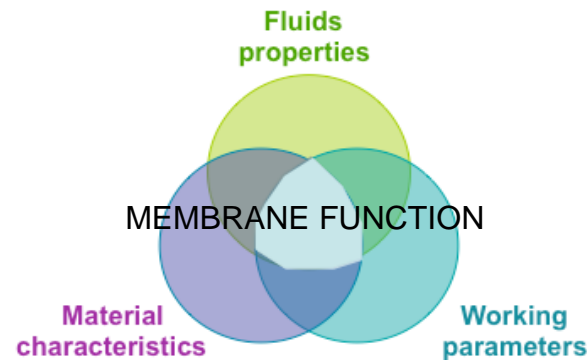
3rd lesson...

A new think-tank organized around the “holy triptych” :



→ Trying to integrate the data at all the scales in order to get an optimized “membrane function”

→ The need to make the most of modeling to reach this objective through simulation



By always keeping in mind the need to carry out an approach as holistic as possible, and to perform an optimization as wide as needed for intensification purposes , three levels to consider :

- Design of new nanomaterials in order to reproduce more and more accurately biological mechanisms : mimicking reaction site function by building appropriate spatial distribution of functional groups, getting improved transport of species, tuning phenomena with new driving forces such as electric potential , oxidation state or specific radiation...



- Building new integrated systems to simplify and/or to intensify existing processes : combination of membranes with electronic and optoelectronic devices to design new sensors or “more intelligent” modules...; coupling membranes and micro-reactors...; conception of new heat exchange systems; spreading membrane contactor technologies...
- And in the long term : trying to imagine new production plants that would mimic the “cell plants” by working in a sustainable way at low temperature, without no solvent..!

As a whole trying to do in a lot of applications fields (and not only biotechnology) what nature is doing so successfully with living systems since so many time ...