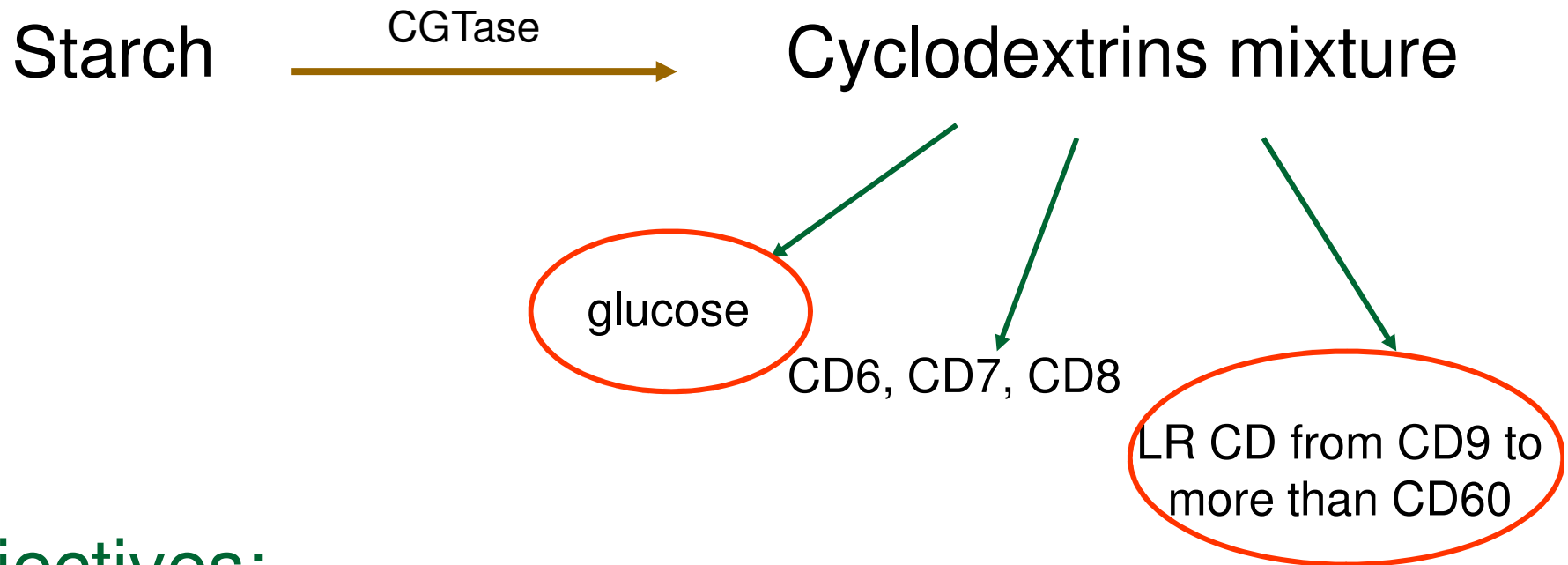

Membranes fractionation of Cyclodextrins mixture

F.Ellouze, N. Ben amar, A. Deratani,
W. Zimmermann.

Problematic

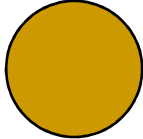


Objectives:

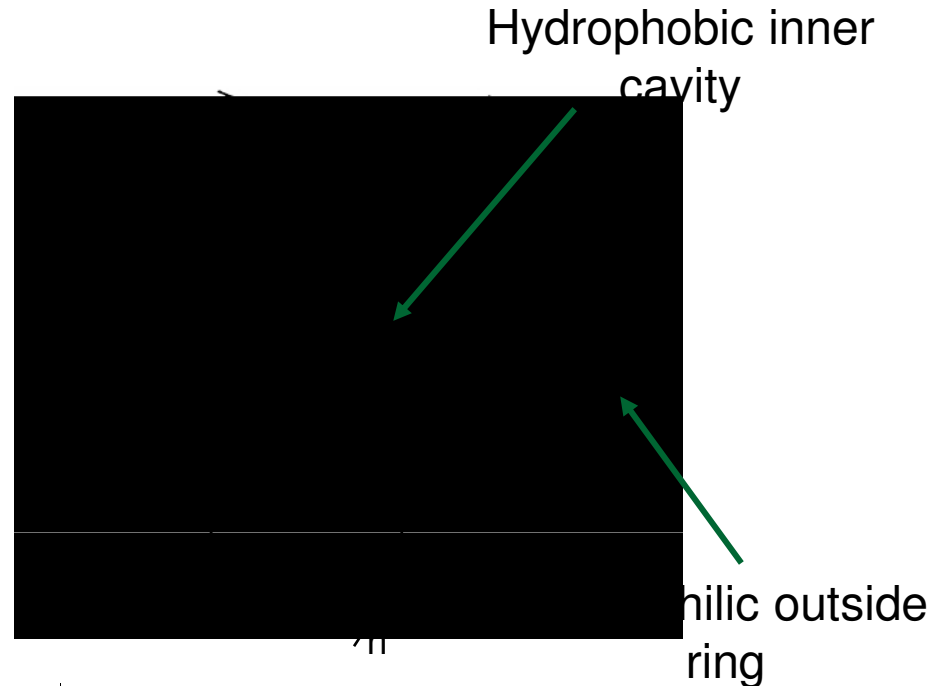
- Eliminate glucose
 - Isolate Large Ring Cyclodextrins from the mixture
- } By membrane filtration

Introduction

Cyclodextrins CD are cyclic oligosaccharides consisting in (1→4)-linked α -D-glucose.


Guest : Hydrophobic molecule

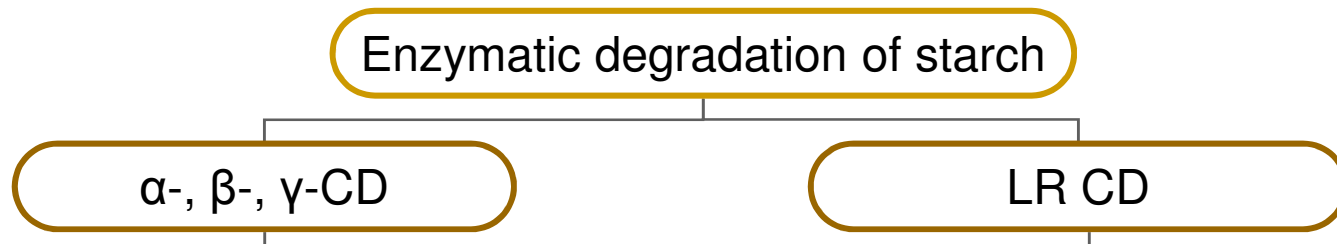

Host-guest complex



Change the guest molecule properties:

- aqueous solubility increase
- stability increase

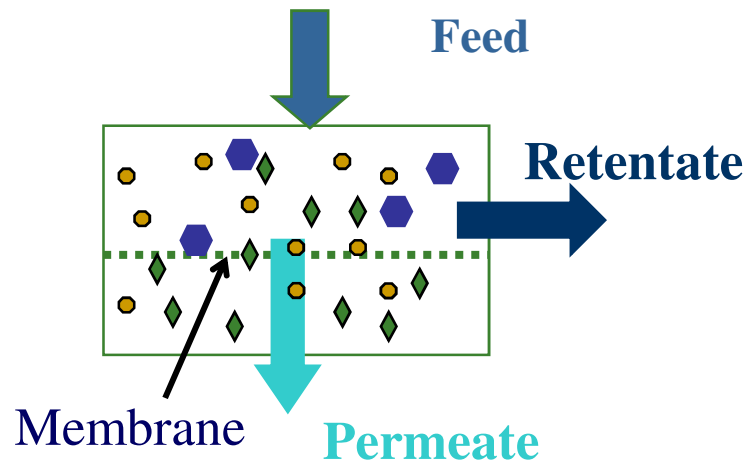
Introduction



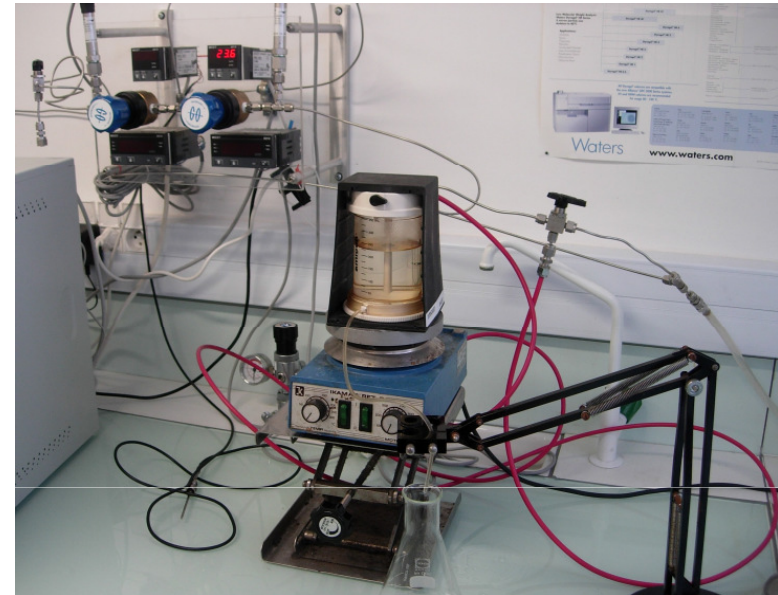
Methodology

CD mixture contains:

- ✓ glucose (MW = 180 Da)
- ✓ α -, β -, γ -CD (MW from 973 to 1297 Da)
- ✓ LR CD (MW from 1459 to 9721 Da)



Separation of LR CD from CD mixture will be based on steric hindrance effect



Dead end filtration cell

- ❖ Operating pressure: 1 to 4 bar
- ❖ Membrane area: 38.5 cm²
- ❖ Temperature: ambient
- ❖ Solute concentration: 1g/L

Methodology

Membranes

membranes	Class	L_p^0 (L/m ² .h.bar)	Experimental MWCO (Da)	MWCO _{manufacturer} (Da)
GK	UF	12.5	4900	3000
GH	UF	2.75	2700	2000
HL	NF	13.3	600	150-300

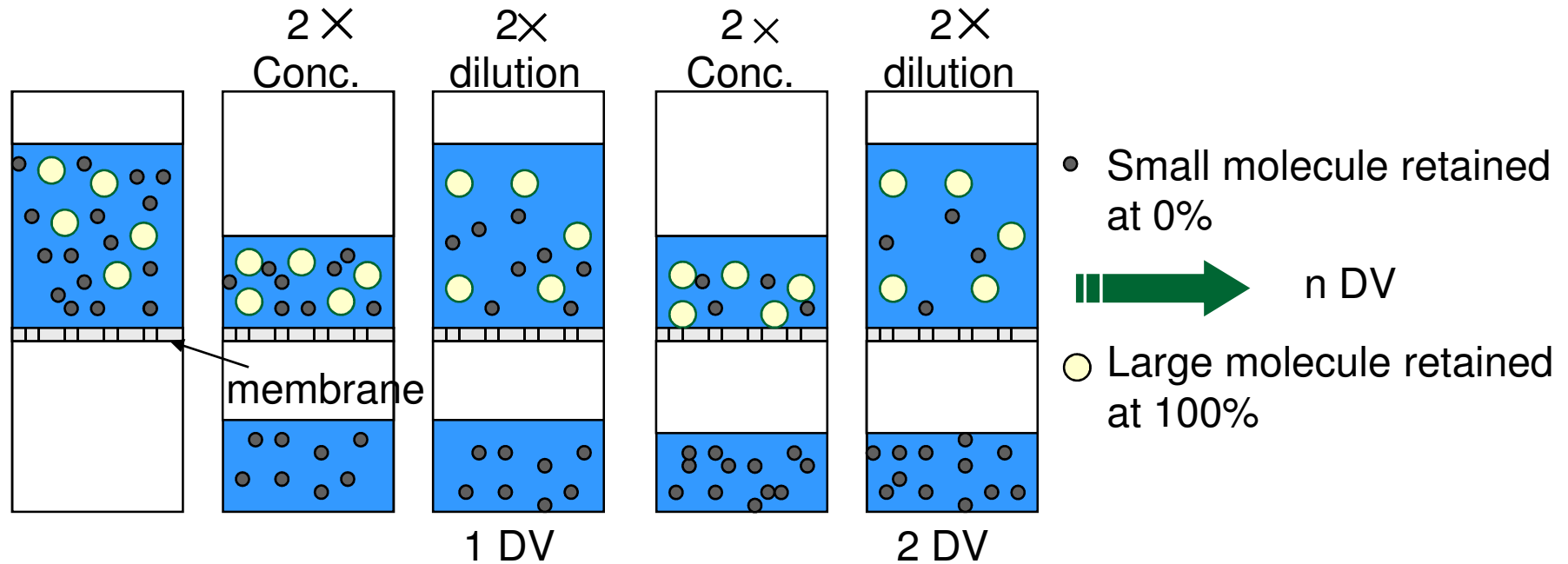
Solutes

- ❖ PEG with different MW to determine the MWCO of the membranes
- ❖ Glucose and β -CD to characterize the membranes performances for the CD mixture fractionation
- ❖ CD mixture

	glucose	α -, β -, γ -CD	LR CD
Composition (%)	8	17	74

Methodology

Discontinuous Diafiltration



$$VCR = \frac{V_0}{V_r} = 2 \quad Y_i = \frac{m_{r,i}}{m_0} = (VCR)^{n(R_i-1)}$$

$m_{r,i}$ = mass of the solute i in the retentate

m_0 = total mass of the solute in retentate

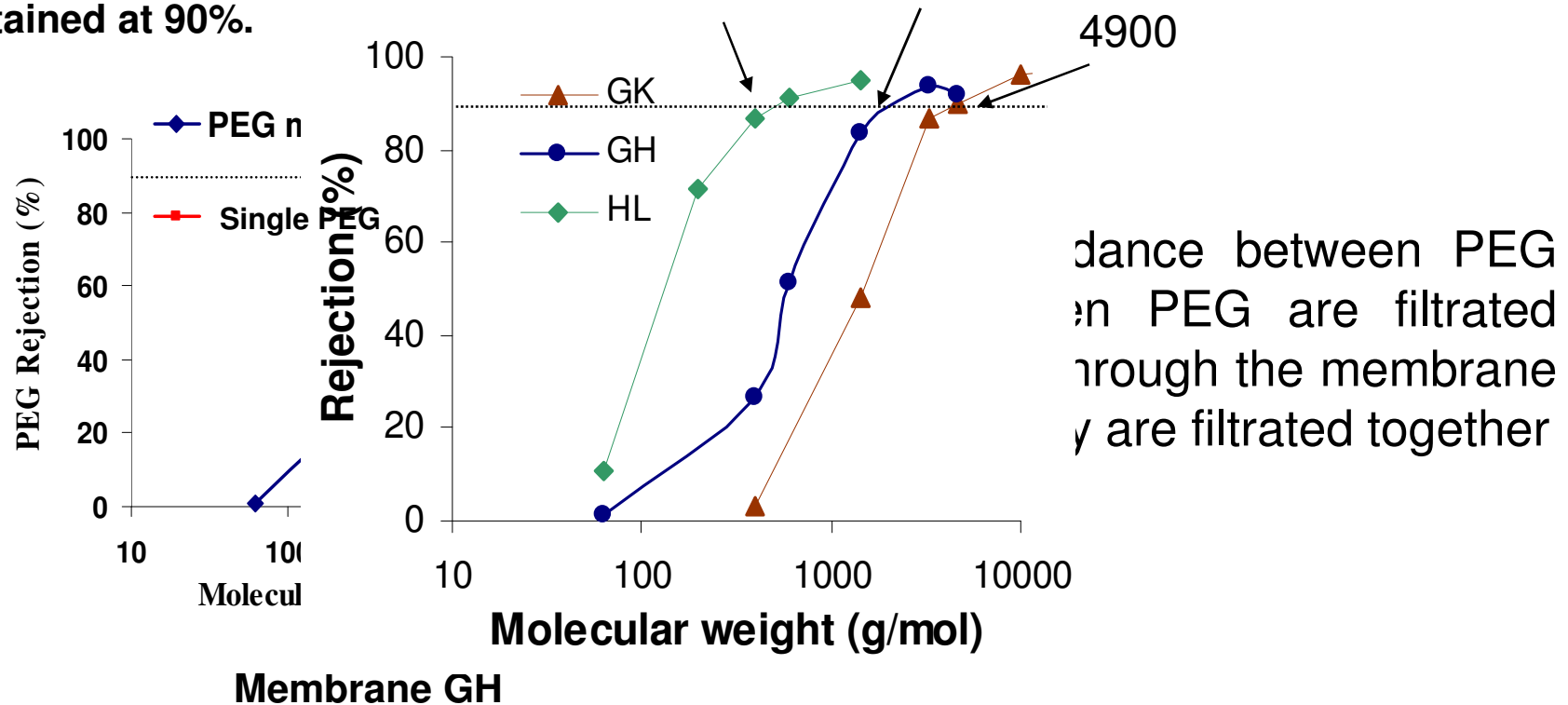
R_i = rejection of the solute i

Results and discussion

■ Membranes characterization

Membrane MWCO

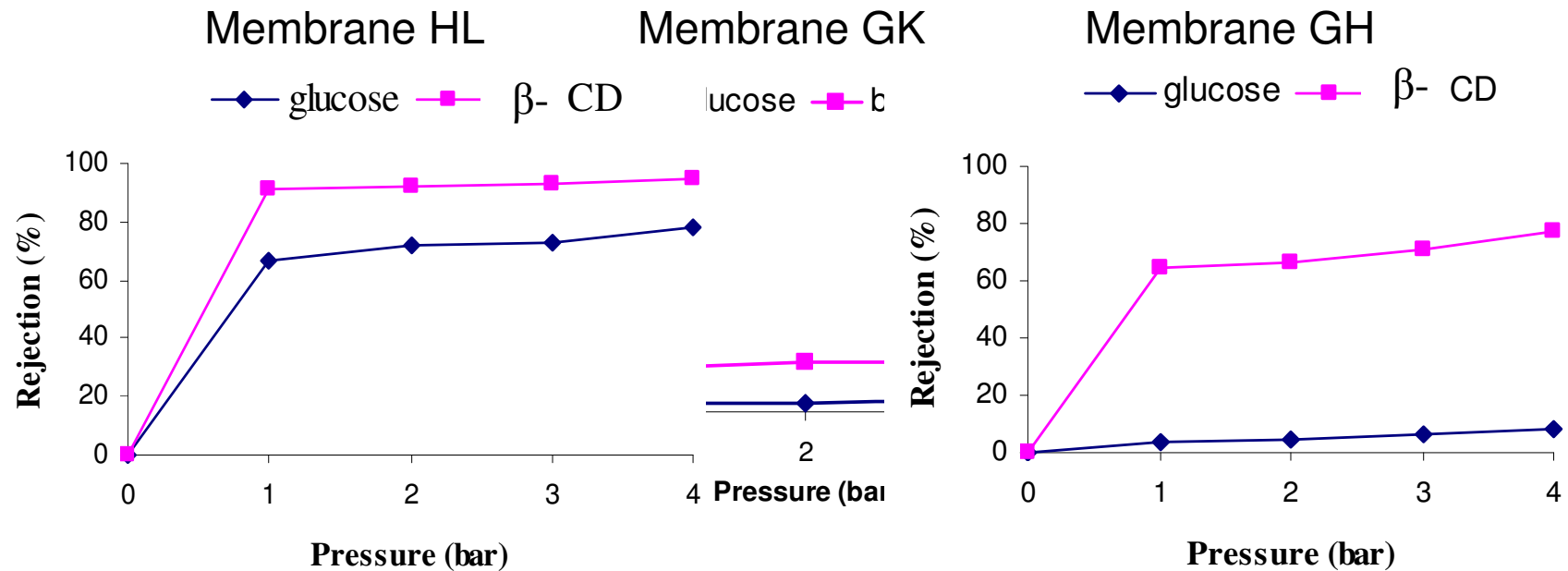
MWCO: Molecular Weight Cut Off: the molecular weight of the smallest molecule retained at 90%.



distance between PEG n and PEG are filtrated through the membrane y are filtrated together

Results and discussion

Glucose and β -CD rejection



Glucose and β -CD rejection at 2 bar

β -CD is totally retained by the membrane and glucose rejection is 66%

Membrane	glucose	β -CD
HL	3.4	19

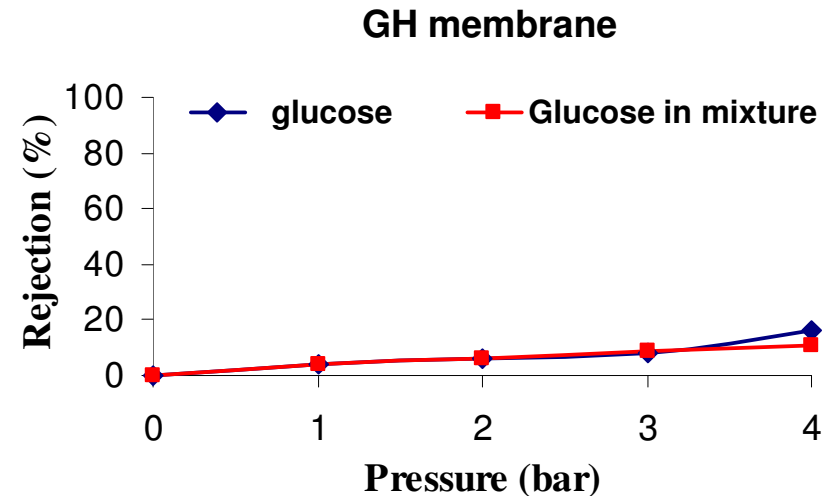
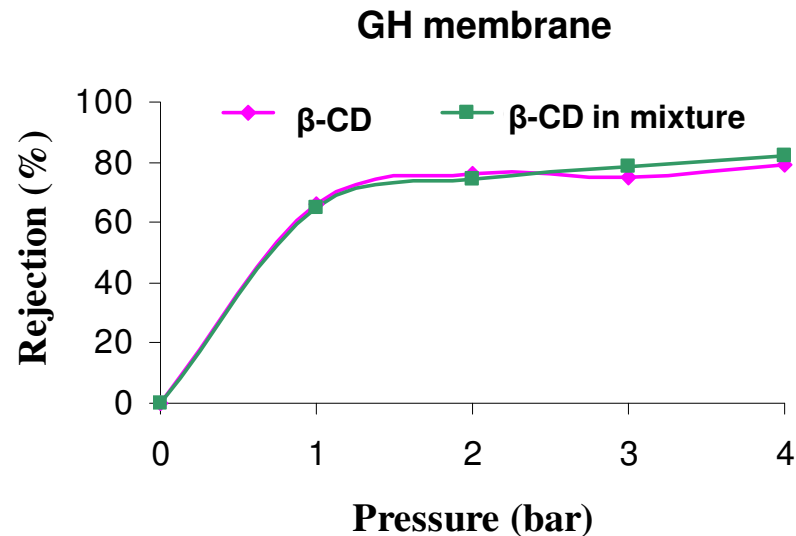
Glucose is not retained, however β -CD rejection is 80%


Membrane	glucose	β -CD
GK	4.5	66
GH*	66	93

*: Rejection at 1 bar

Results and discussion

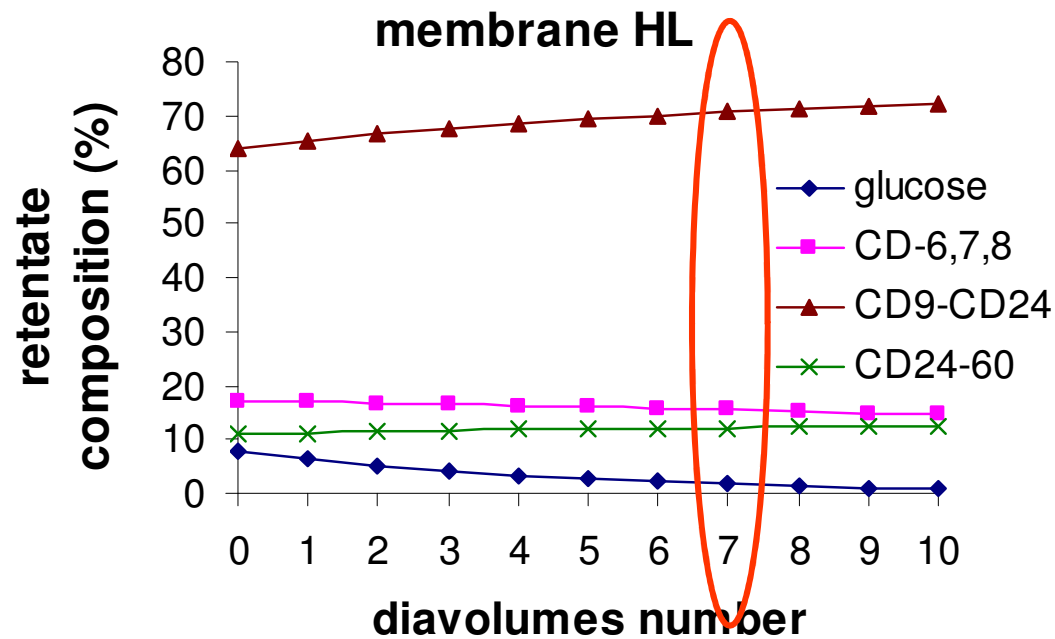
Glucose and β -CD rejection



Experiments done with glucose and β -CD separately and with a mixture of glucose and β -CD (50/50) show similar rejection  no interaction between glucose and β -CD when mixed together.

Results and discussion

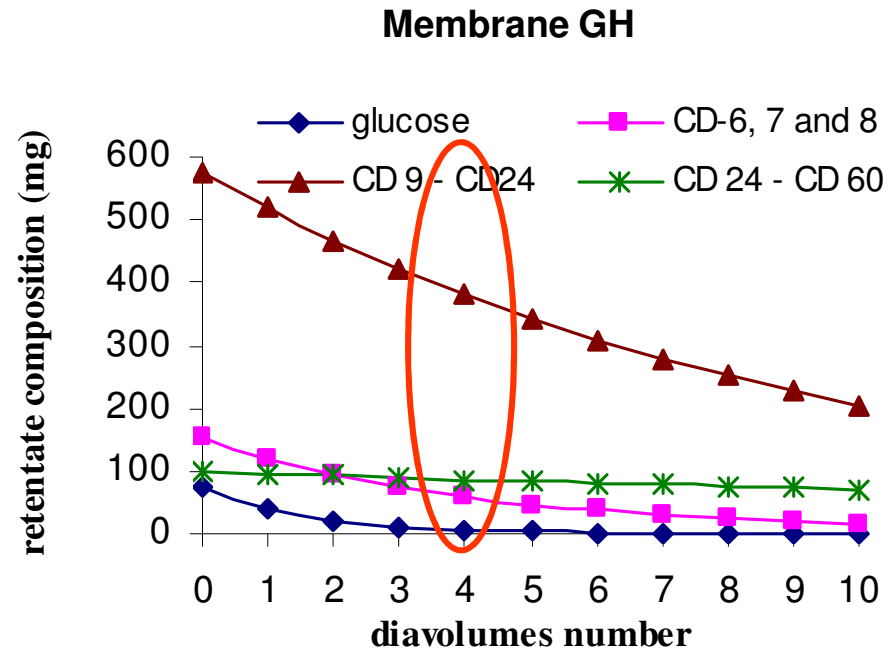
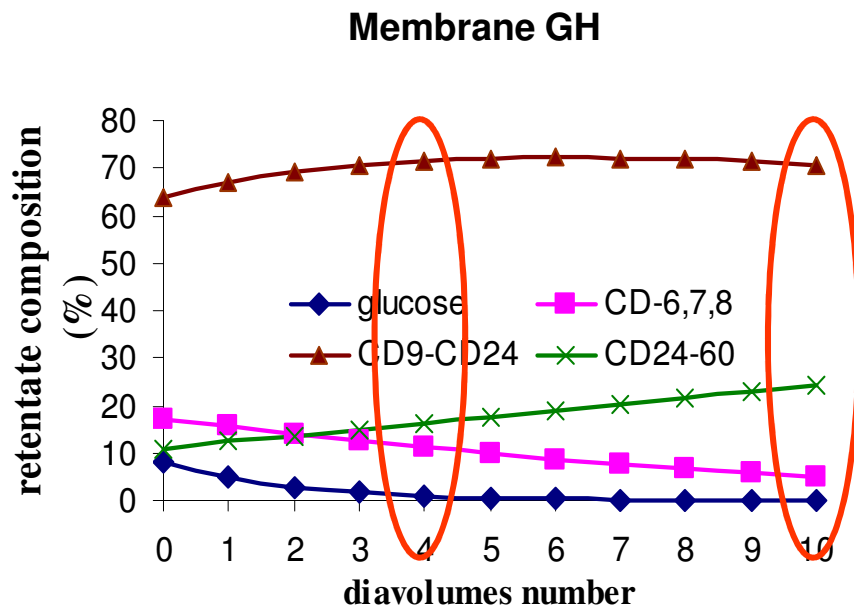
- Simulation of Diafiltration process



After 7 diafiltration, glucose will be eliminated from the CD mixture

Results and discussion

■ Simulation of Diafiltration process



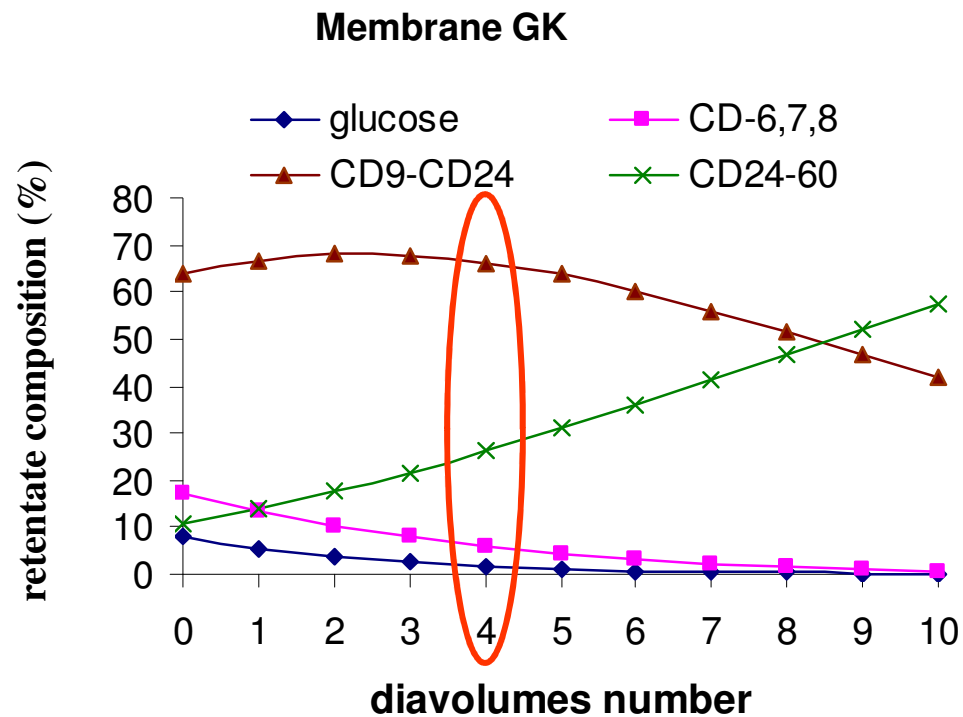
After 10 diafiltration, small ring cyclodextrins are eliminated from the CD mixture.

The best compromise between mass and purification degree is obtained after 4 diafiltration

The problem is that purification is accompanied by a loss in mass of fraction CD9-CD24.

Results and discussion

- Simulation of Diafiltration process



After 4 diafiltration, the fraction CD24 – CD60 will be enriched. The mass of this fraction pass from 11% to 26%.

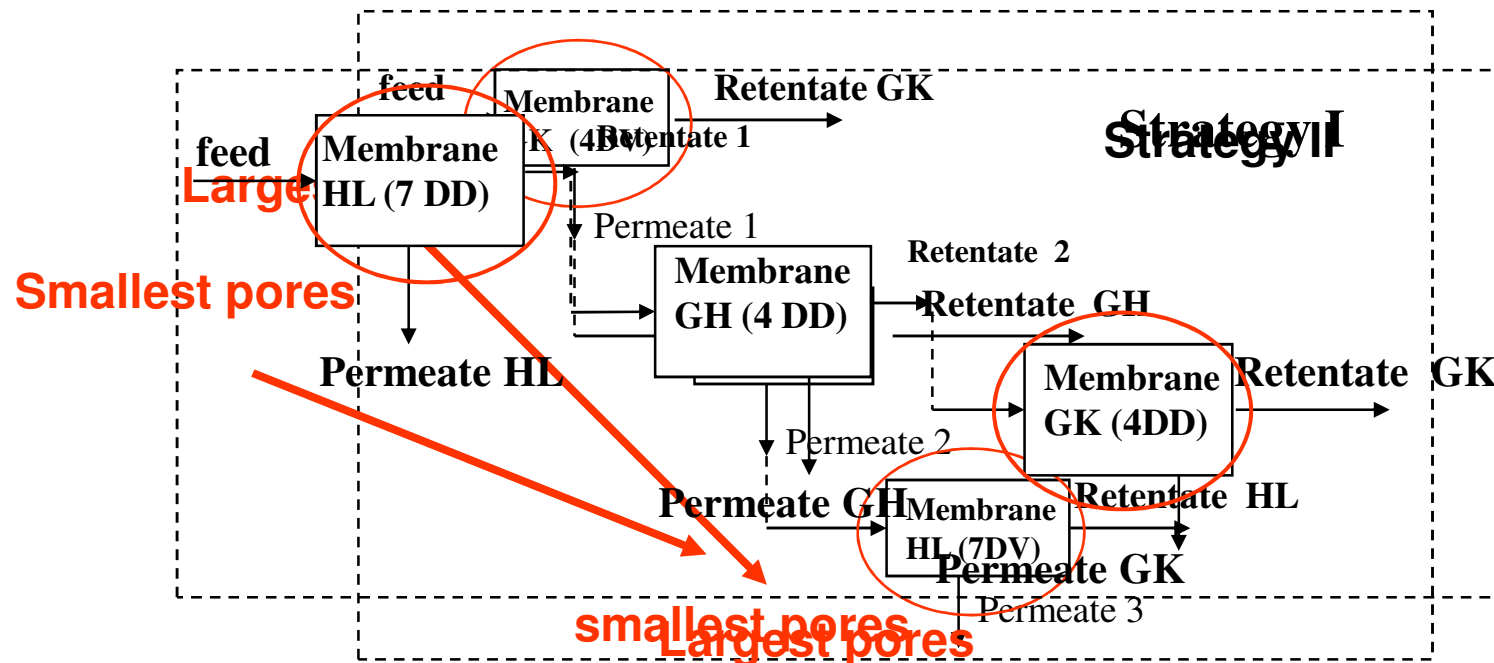
Results and discussion

Simulation Results

- The Three membranes HL, GH and GK are interesting for the CD fractionation.
- The best compromise between mass and purification degree is to use a cascade of the three membranes with 7 diafiltrations for HL membrane, and 4 diafiltrations for GH and GK membranes.

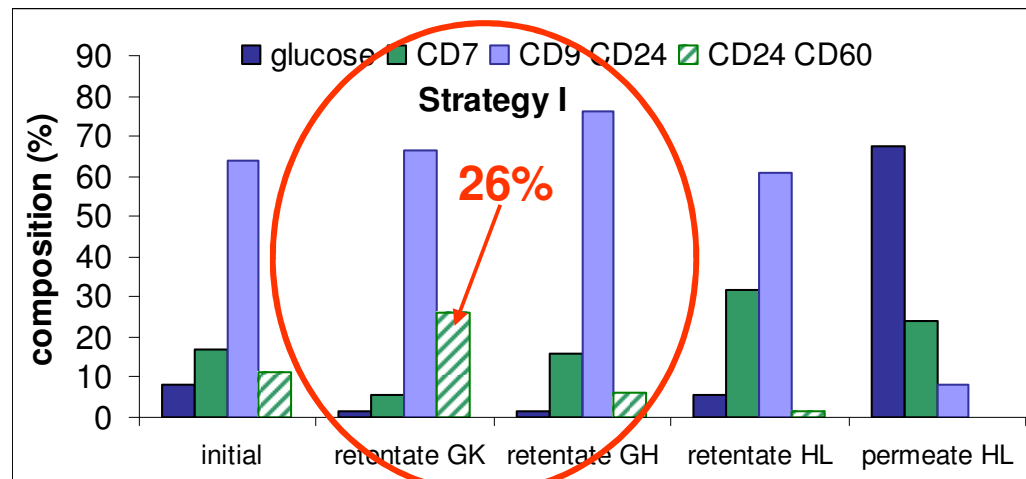
Results and discussion

The question that arises is in which order the fractionation process will be done?



Results and discussion

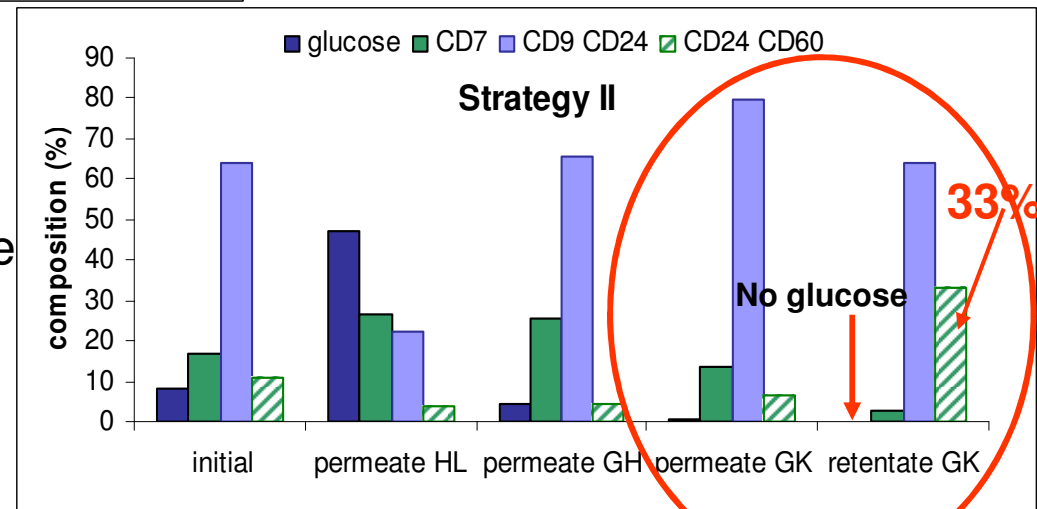
Theoretical result



The aim of this study is to purify and enrich LR CD in the CD mixture.

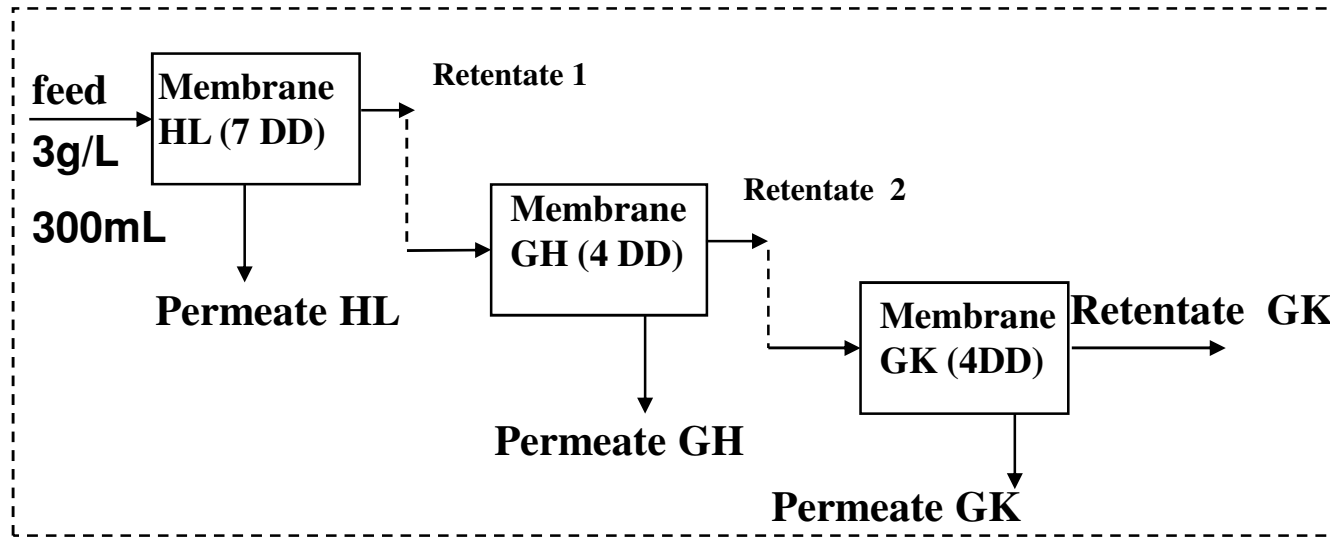
With strategy II

- CD24 –CD60 are more enriched in retentate GK.
- Glucose are eliminated in retentate GK
- CD9 – CD24 are more enriched in permeate GK comparing to retentate GH



Results and discussion

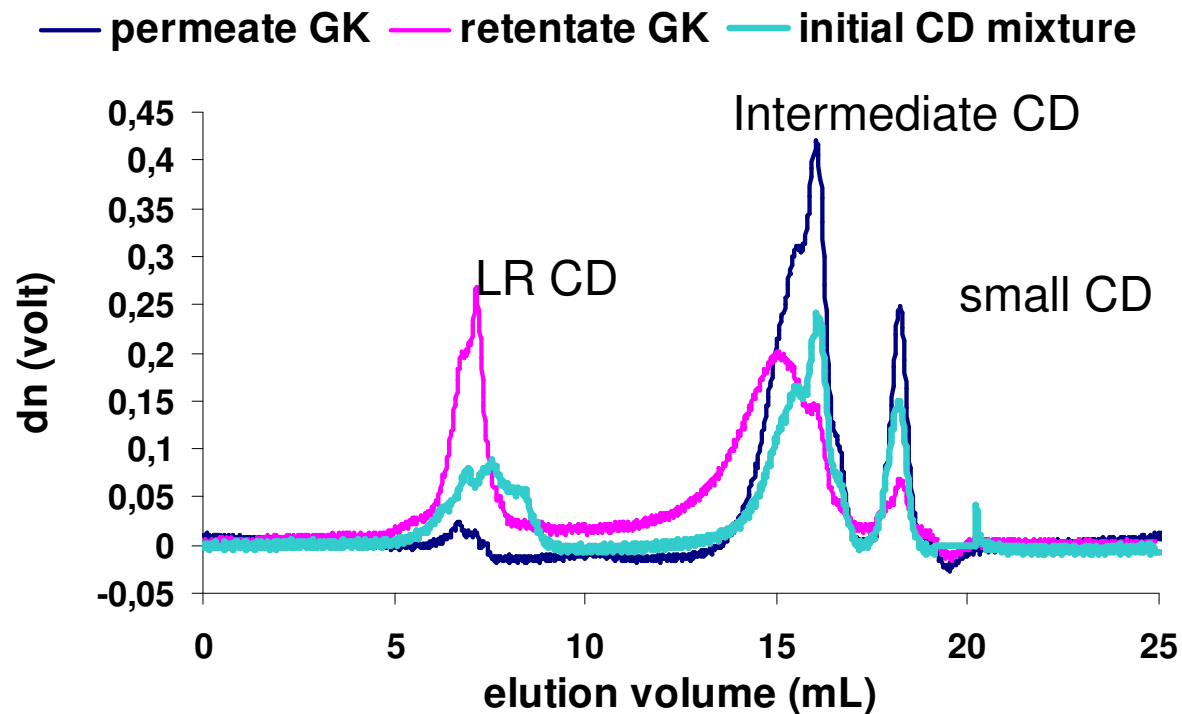
■ Application



	Permeate HL	Permeate GH	Permeate GK	Retentate GK	Total mass
Calculated mass by simulation (mg)	123	285	305	187	900
Real mass (mg)	150	120	386	196.4	852.4

Results and discussion

■ Experimental result



CD mixture analysis by Steric Exclusion
Chromatography

As expected:

In retentate GK, LRCD are enriched to 250% and small CD are impoverished

In permeate GK, Intermediate CD are enriched to 120% and LRCD are impoverished

Conclusion

- UF and NF can be applied to fractionate the CD mixture.
- Good concordance between experimental and theoretical results.
- In retentate GK, LRCD are enriched 2.5 times and small ring CD are eliminated.
- In permeate GK, Intermediate CD are enriched to 120%