

# Downstream Without a Paddle

## Speakers:

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# Introduction to TFF

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Chapter

2



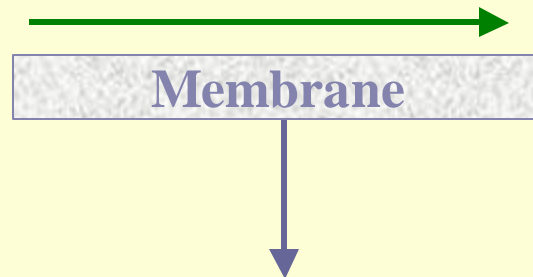
# Safety First

## Safety Concerns for TFF

- Typical cleaning regime for TFF membranes is hot sodium hydroxide. Contact with the solution can result in serious chemical burns. It is critical to therefore wear personnel protective equipment as directed by procedures.

# What is TFF?

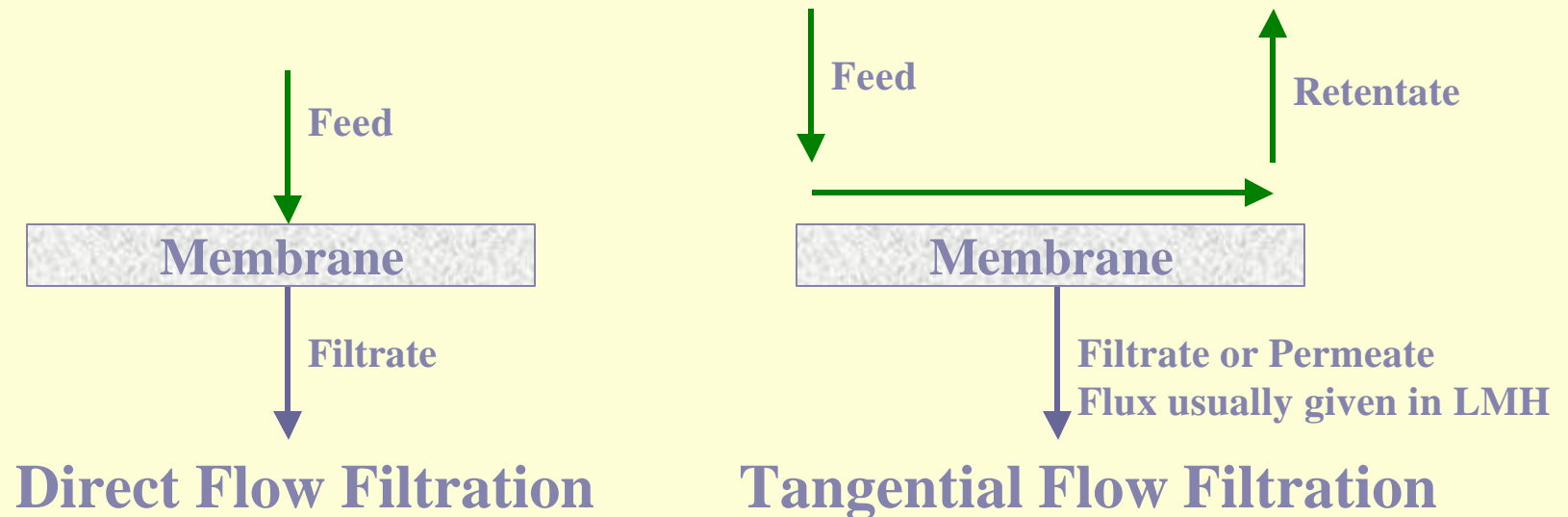
- Tangential Flow Filtration (TFF) may also be referred to as Crossflow Filtration
- Tangential Flow – Feed Flow Parallel to Membrane Surface
- Cross Flow – Feed Flow Perpendicular to Filtrate Flow
- TFF is performed such that there is a constant sweeping of the filtration membrane.
- TFF has continuous flow across the surface of the membrane.



**Tangential Flow Filtration**

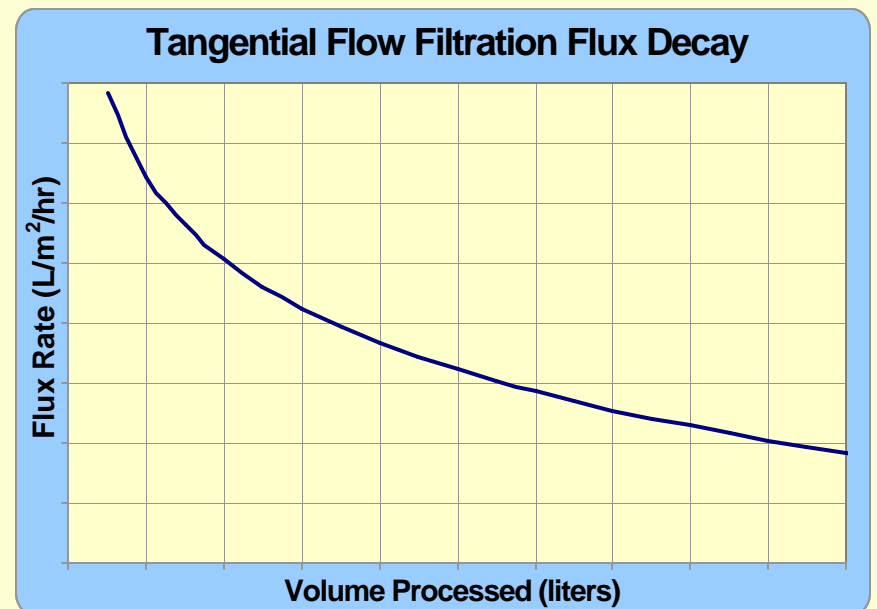
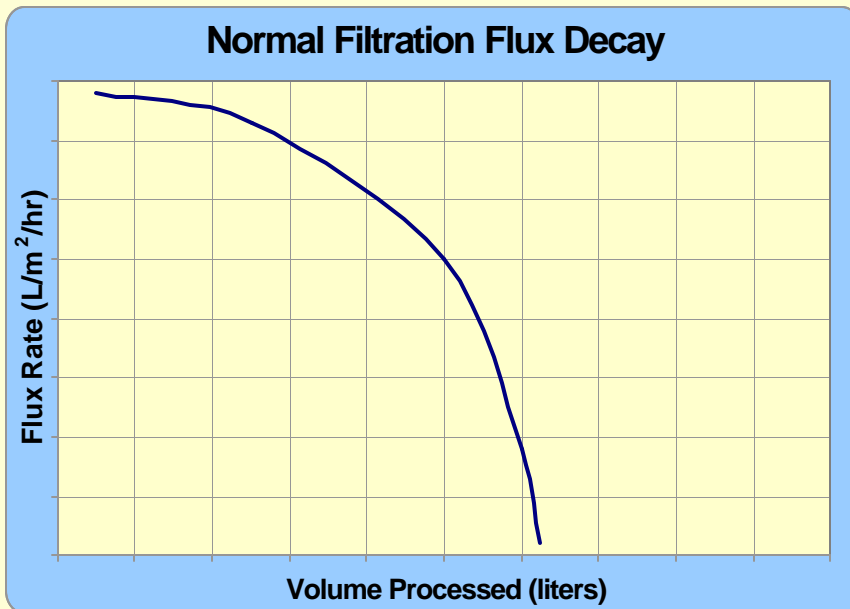
# TFF comparison to Direct Flow

- In Direct Flow Filtration particulates are retained at the surface of the filter.
- In TFF particulates are retained in the retentate stream.

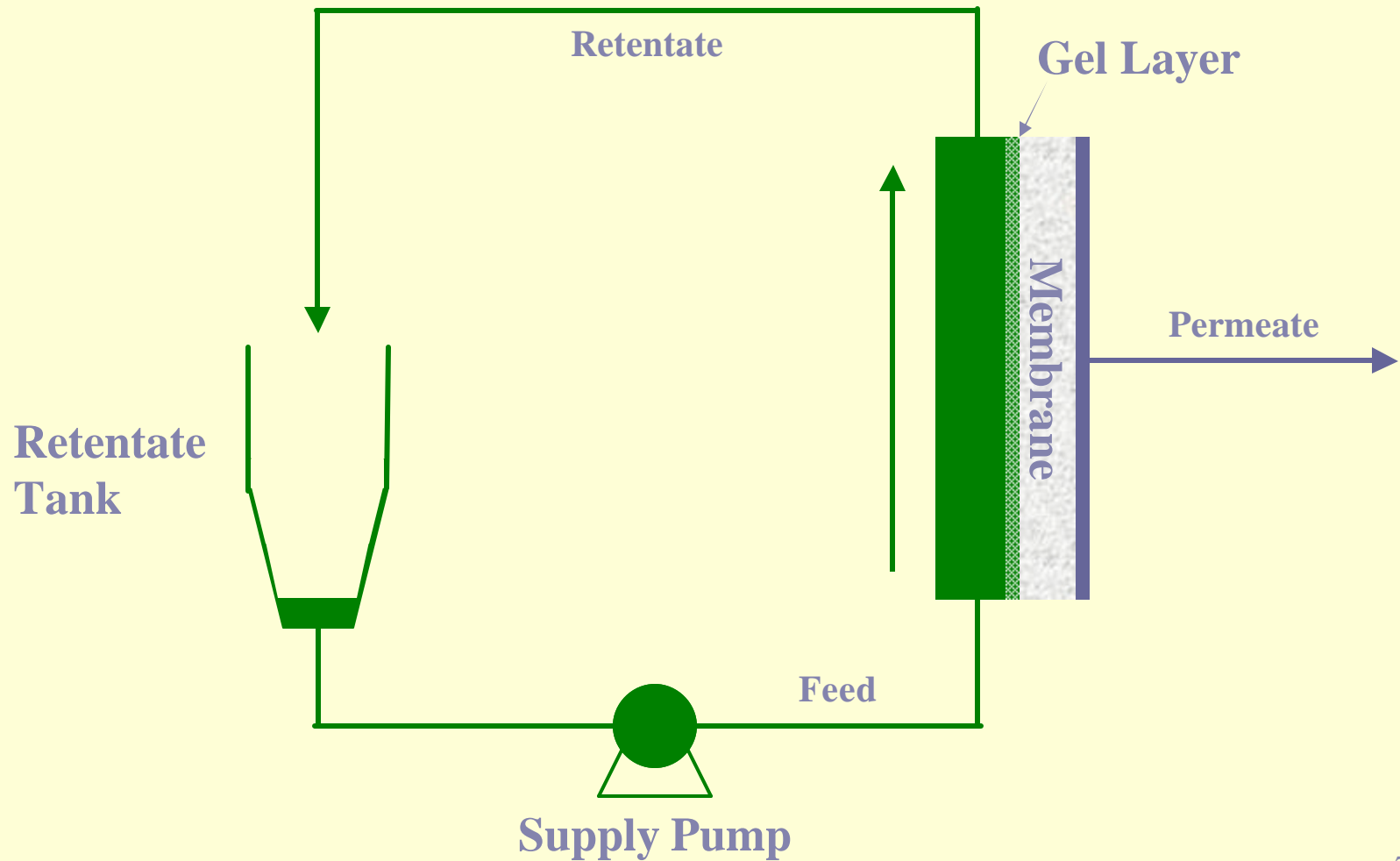


# Why TFF vs Normal Filtration?

## Comparison of Flux Decay



# TFF Diagram - Concentration

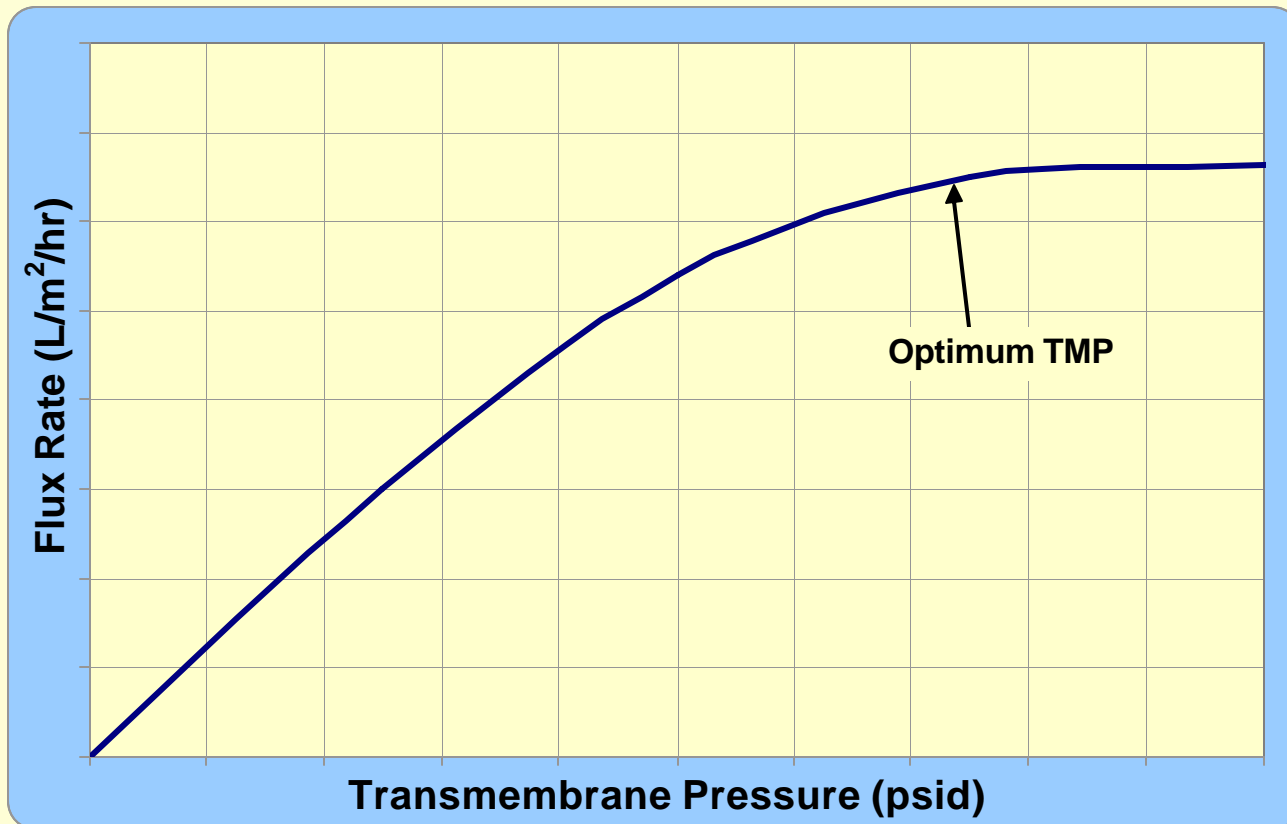


# Transmembrane Pressure (TMP)

## ● Transmembrane Pressure

Driving force for filtration. Defined as;

$$[\text{Inlet Pressure} + \text{Retentate Pressure}]/2 - \text{Permeate Pressure}$$

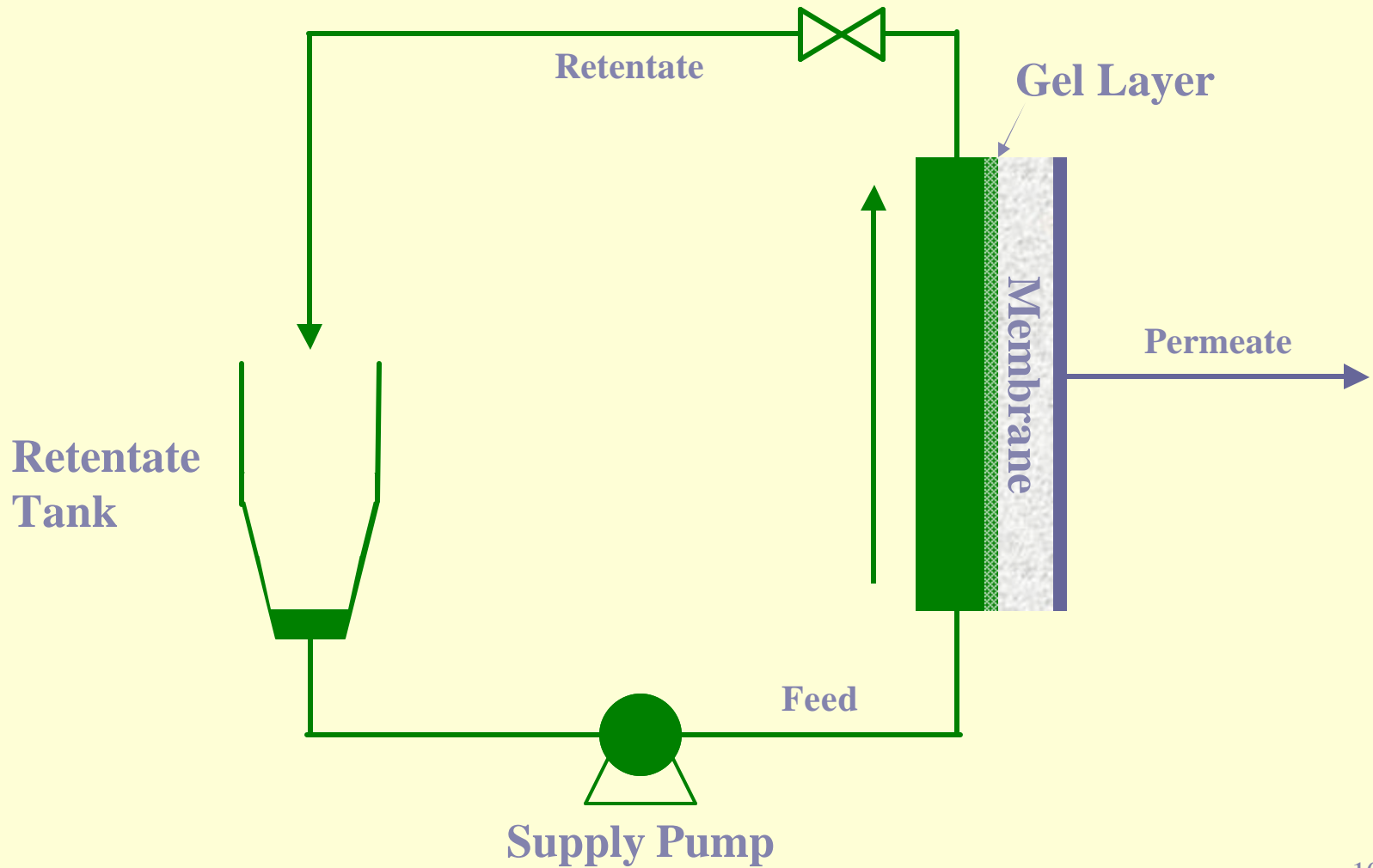




# Transmembrane Pressure

- The filtrate flux or flux rate is defined as follows;
- $J$  (Flux) =  $A * TMP$ 
  - $A$  = Mass Transfer Coefficient
  - $A = 1/[R_g + R_m]$
  - $R_g$  = hydraulic resistance of gel layer
  - $R_m$  = hydraulic resistance of membrane
- $R_m$  is constant for the installed membranes. May vary slightly from one lot to another.
- $R_g$  changes as the gel layer changes. Thus the asymptotic nature of the previous graph.

# TMP





# TFF Design

## ● Rejection Coefficient ( $\sigma$ )

- A rejection coefficient of 1 is complete retention of a particle.
- A rejection coefficient of 0 is complete passage of a particle.

## ● Volumetric Concentration Ratio (VCR)

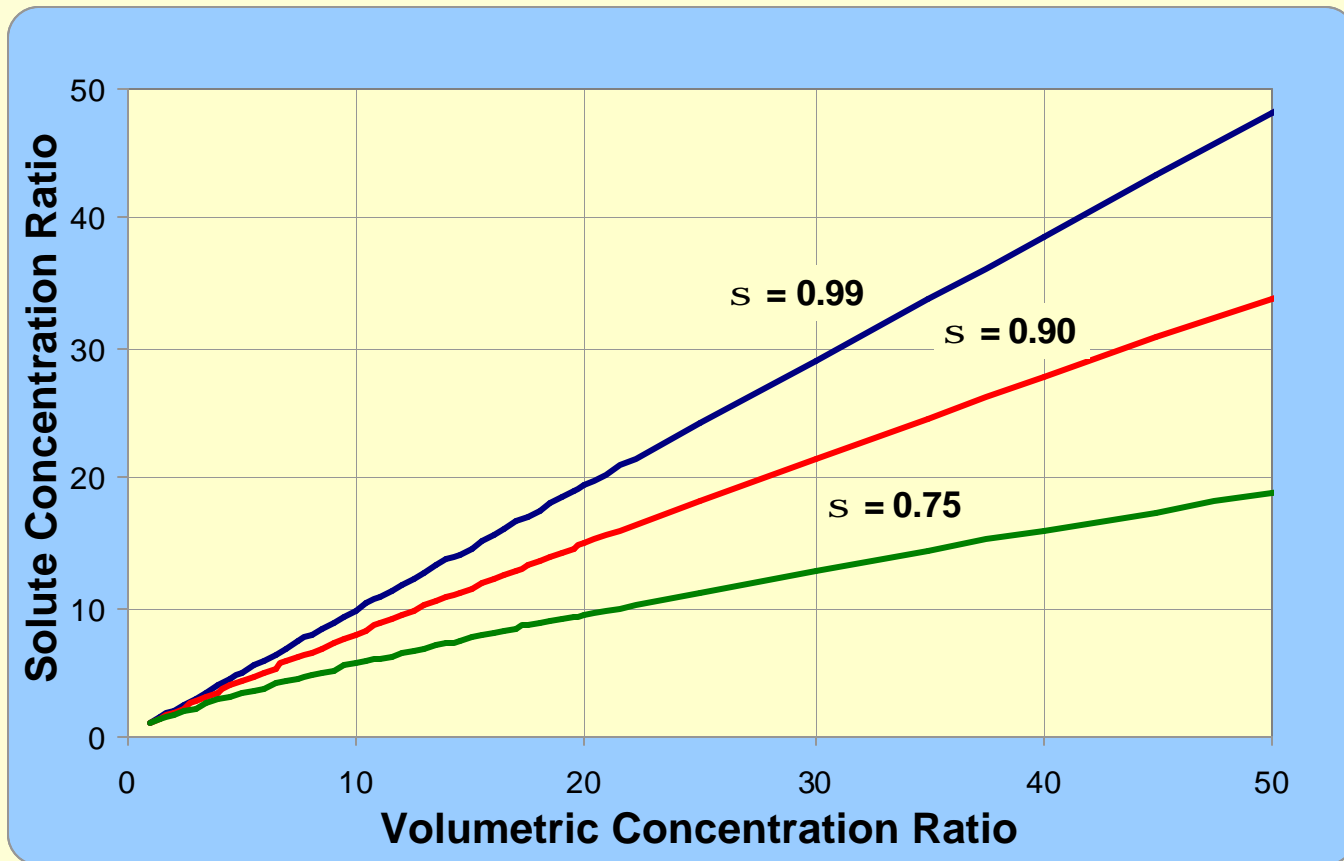
- $VCR = \text{Initial Volume (V}_0) \div \text{Retentate Final Volume (V}_R)$

## ● Solute Concentration Ratio (SCR)

- $SCR = \text{Final Concentration (C}_R) \div \text{Initial Concentration (C}_{R0})$

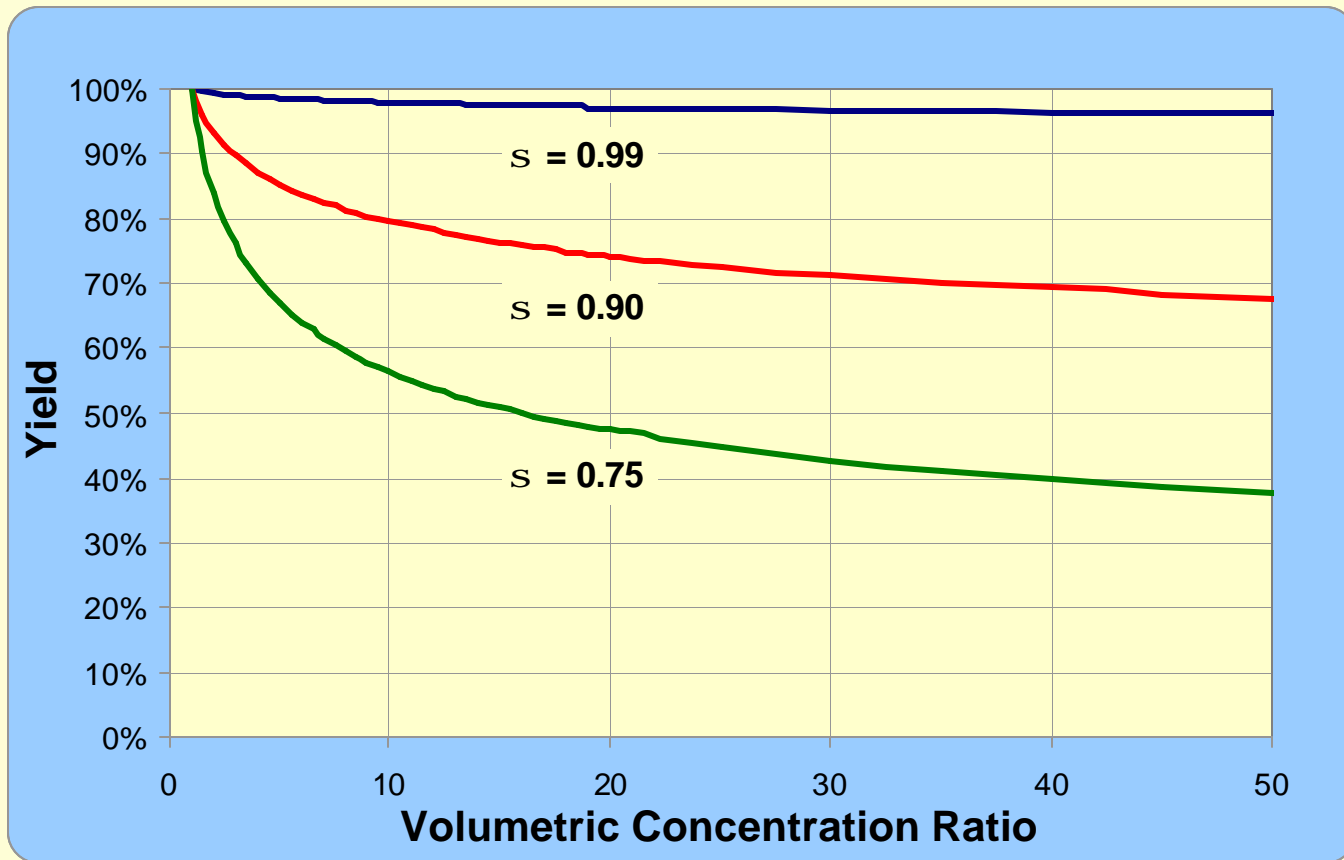
# TFF Design

● Design Formula:  $SCR = (VCR)^\sigma$



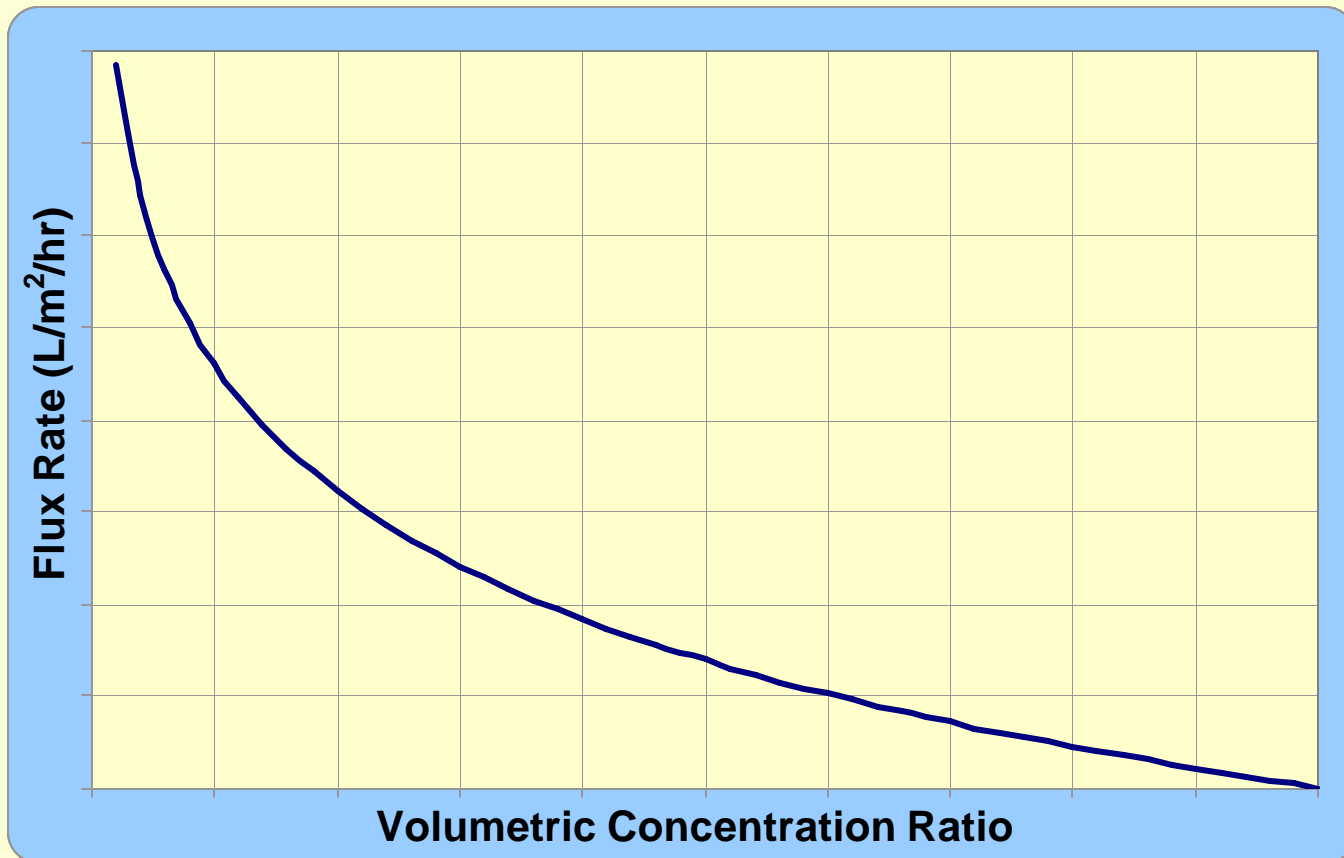
# Theoretical Yield

● Yield:  $\text{Yield} = (\text{VCR})^{\sigma-1} \times 100\%$



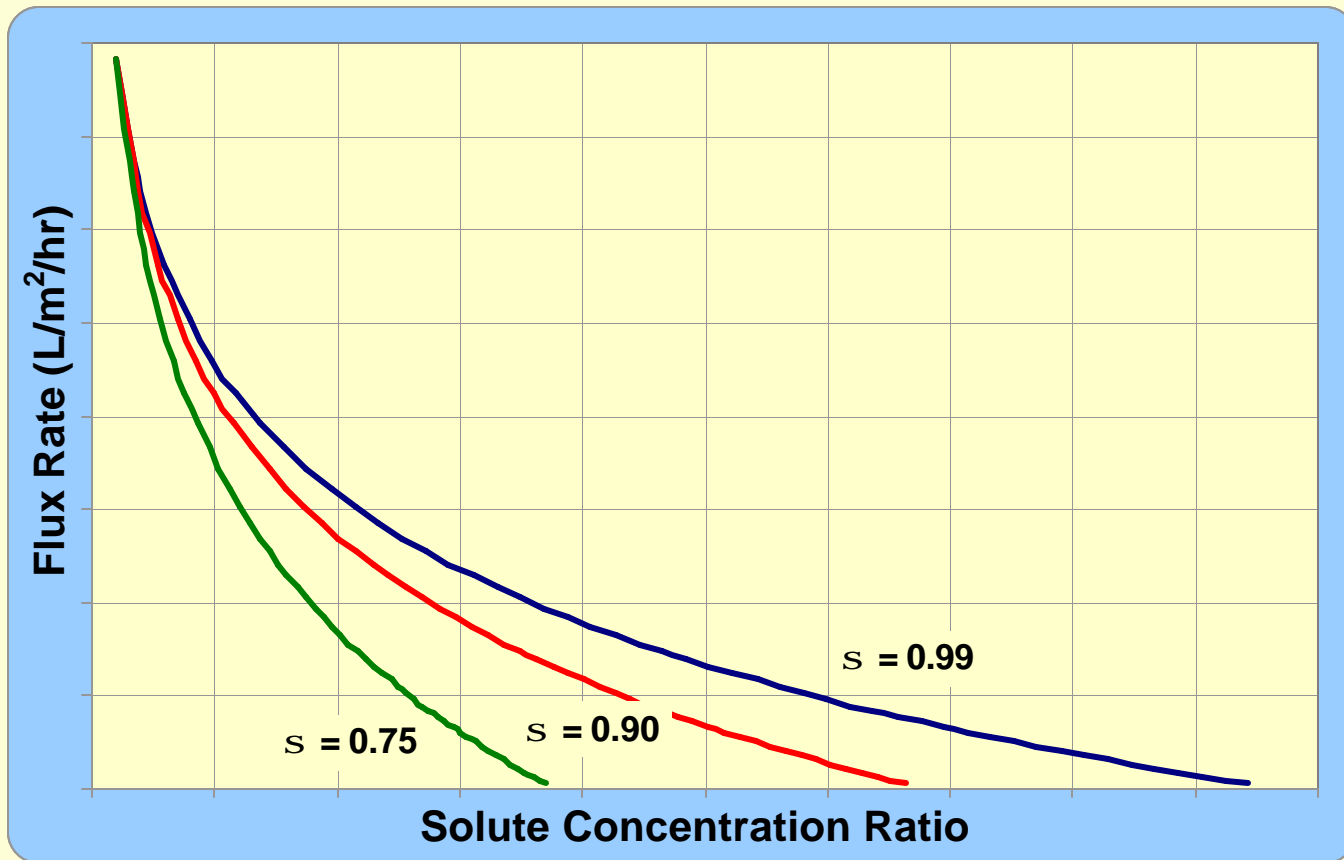
# Flux Characteristics

- Filtrate Flux as a function of VCR



# Flux Characteristics

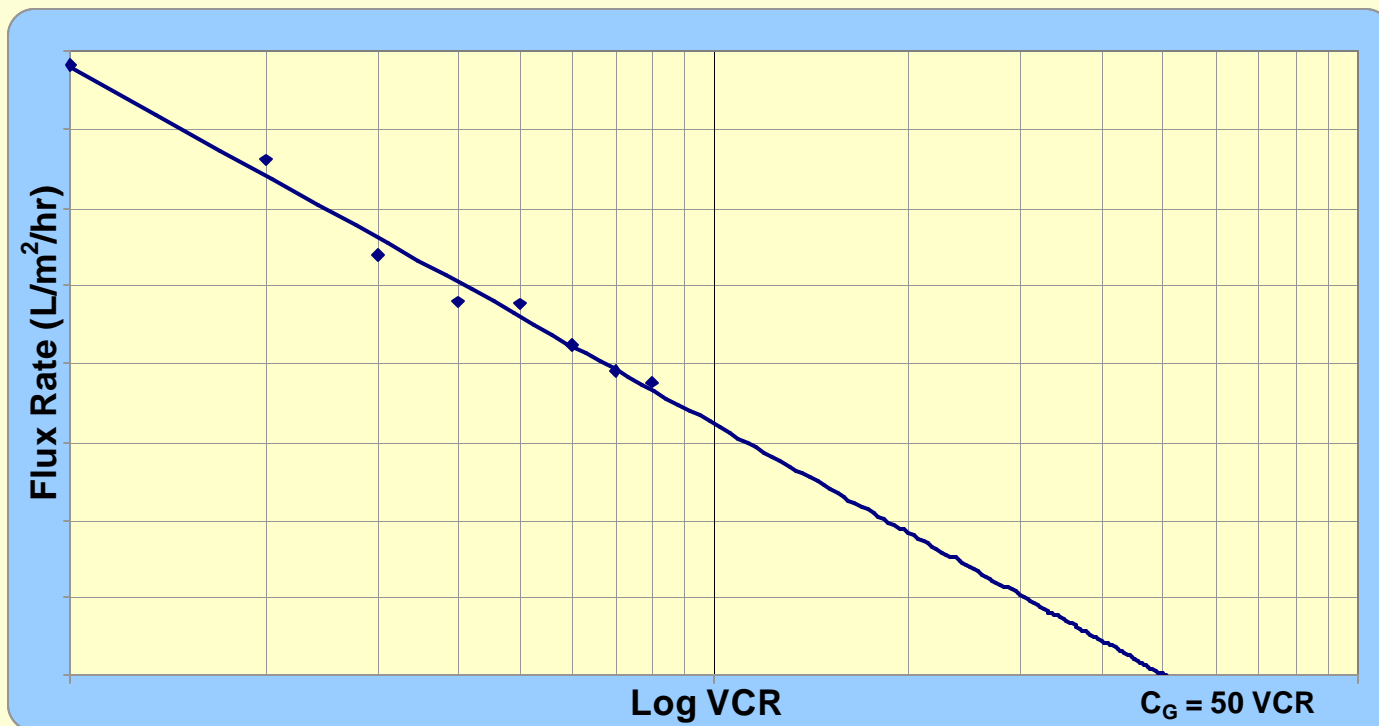
## ● Filtrate Flux as a function of SCR



# Flux Characteristics

## ● Filtrate Flux

- Flux is affected by the concentration of the gel layer. Gel layer concentration is determined by plotting Flux versus Log of VCR. Gel layer concentration is where flux = 0.



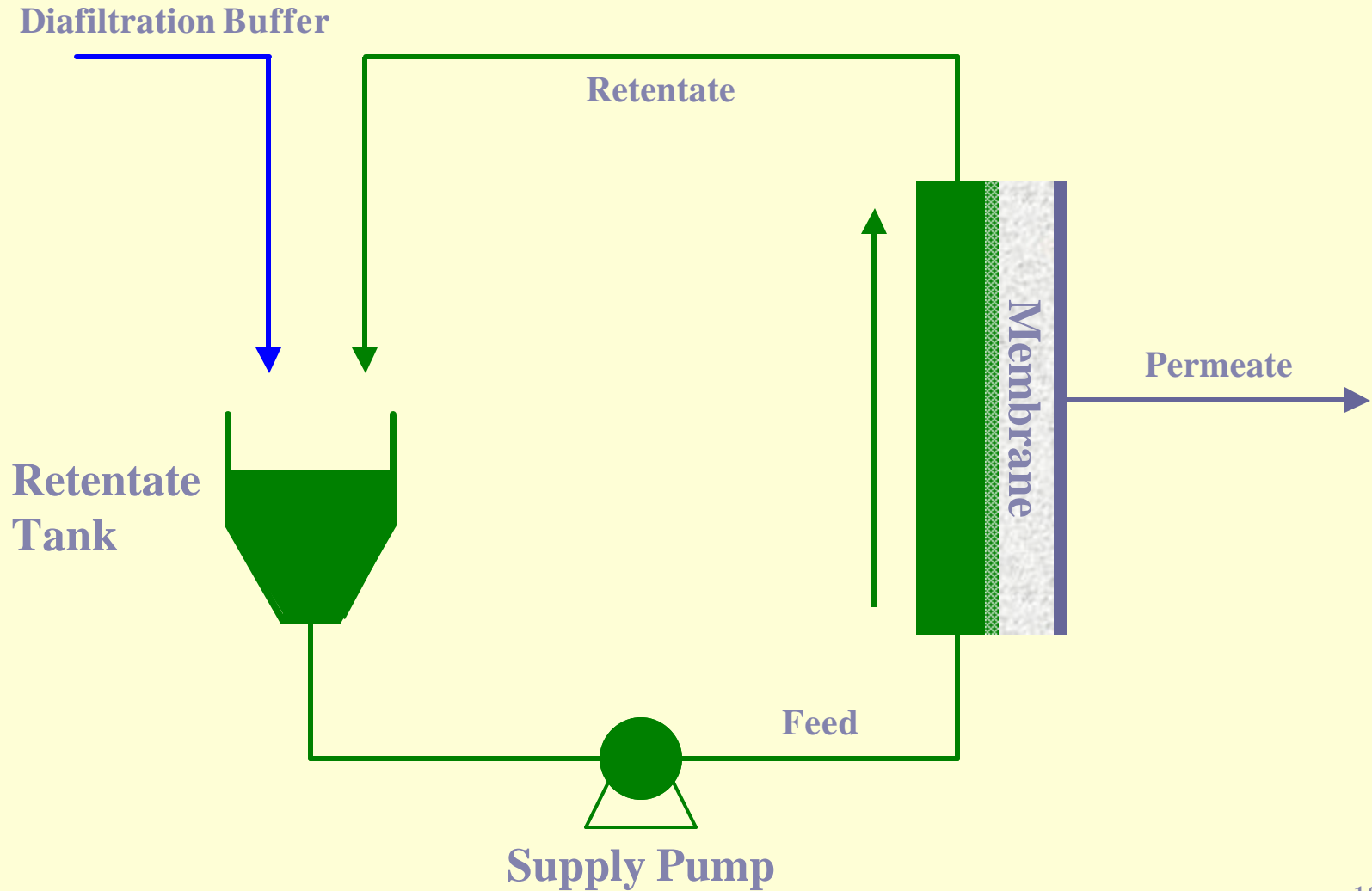


# Flux Characteristics

## Filtrate Flux

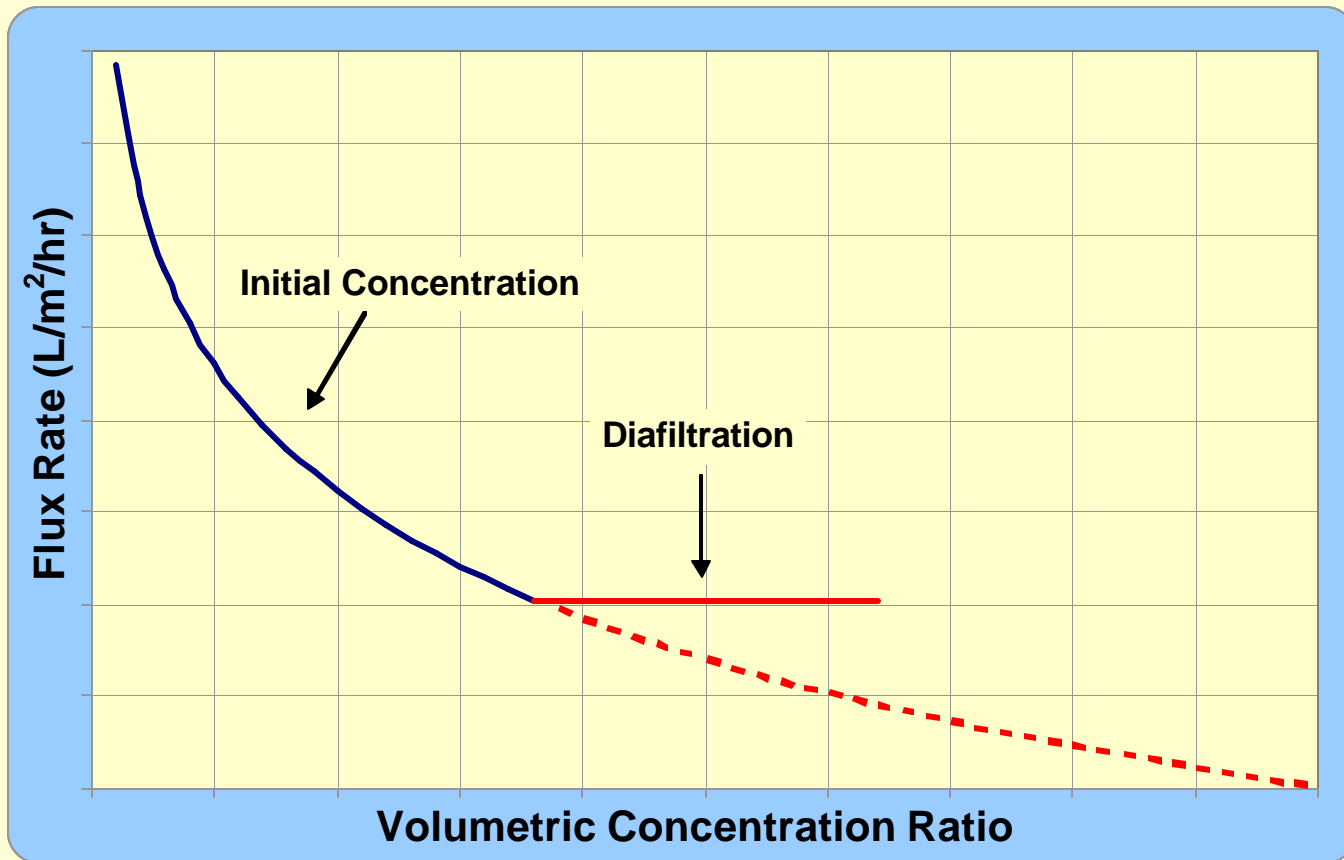
- The ideal maximum bulk concentration is determined by the following equation,
  - $C_B = C_G / e$
  - In this example,
    - $C_B = 50 / 2.718$
    - $= 18.4 \text{ VCR}$
  - What does 18.4 VCR mean,
    - If Initial Volume = 1000 liters, 18.4 VCR results in a final volume of 54 liters.
- This results in the minimum processing time.

# TFF Diagram - Diafiltration



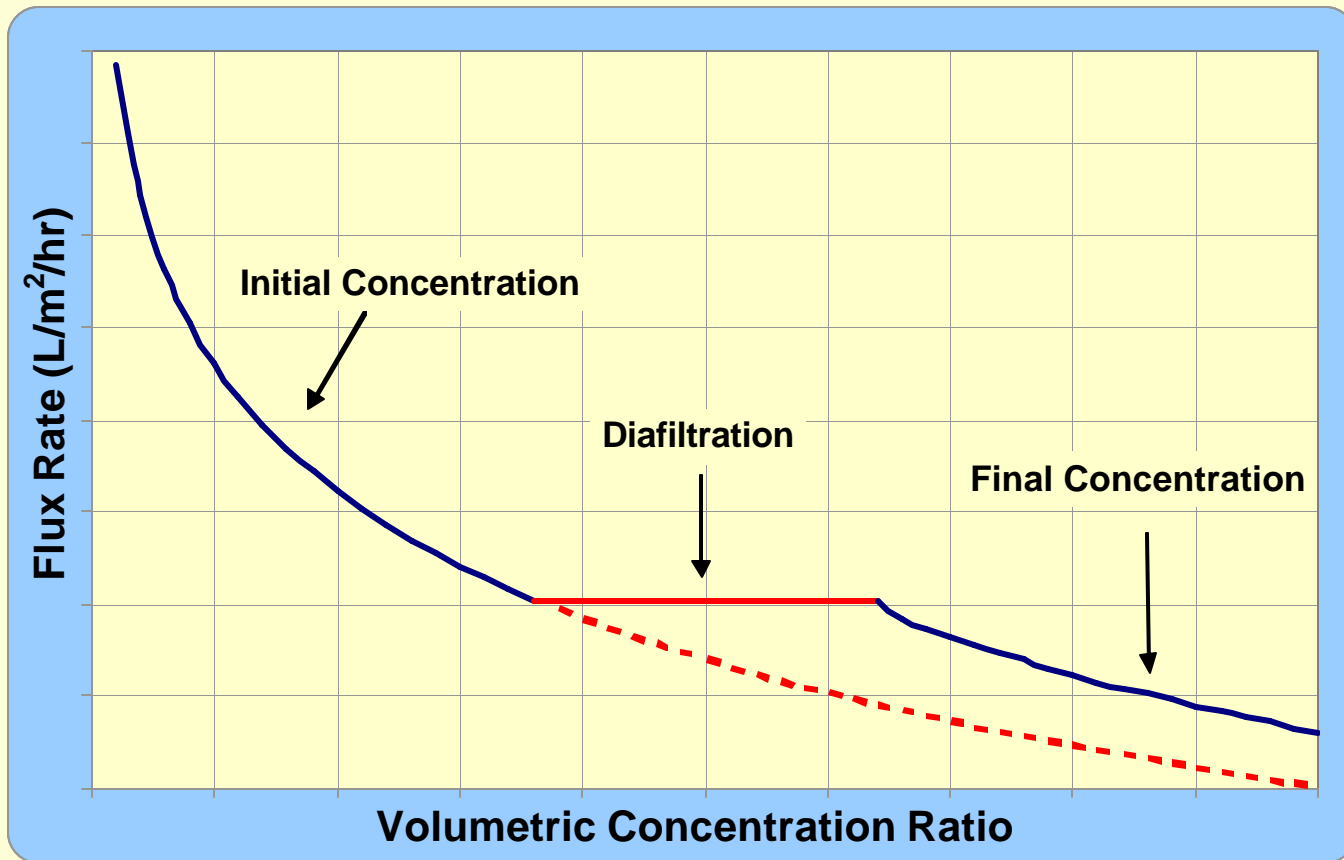
# Diafiltration Flux

## ● Filtrate Flux as a function of VCR



# Final Concentration

## ● Filtrate Flux as a function of VCR





# TFF Scale-Up

- What is needed from Development
  - Flux Rate vs Volumetric Concentration Ratio
  - Rejection Coefficient
- Scale up is typically based on desired processing time (perform in 1 shift).
  - Depending on facility shift schedule this could be 8 or 12 hours.
  - With setup and cleaning, total process time may be less than 4 hours.



# TFF Scale-Up, Input Data

## ● Input Data

- Minimum Process Time
- Initial Product Mass
- Initial Product Volume
- Final Concentration
- Crossflow Rate

## ● Development Data

- Rejection Coefficient
- Flux vs VCR



# Equipment Considerations

## ● Pump Selection

- Chosen to minimize shear
- Shear can lead to protein degradation and cell disruption

## ● Pipe Diameter

- Selection must be made to ensure turbulent flow for cleaning purposes