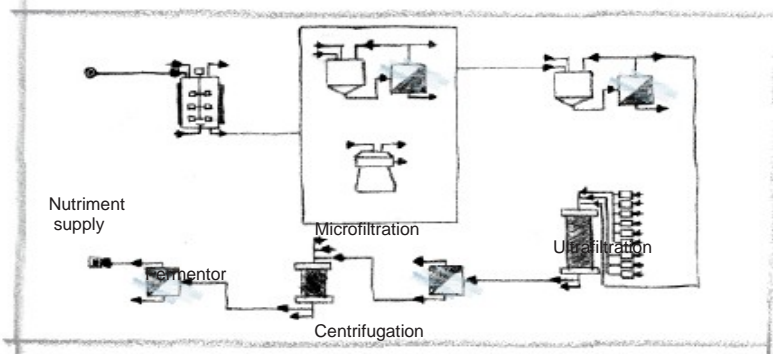


Cell Culture Processing



Final Concentration Chromatography Concentration Chromatography

Flow Diagram

Fermentation is the most important process in the production of modern biopharmaceutical products. Within this process, membrane technology has proved its performance which substitutes conventional techniques in many areas, e.g. in the preparation of the sterile feed, the removal of cell fragments or the concentration and isolation of the target products.

The major advantage of the PP capillaries is the stability against steam sterilization.

The hollow fiber can also be used as a hydrophobic dead end cartridge to vent gases produced during fermentation such as carbon dioxide.

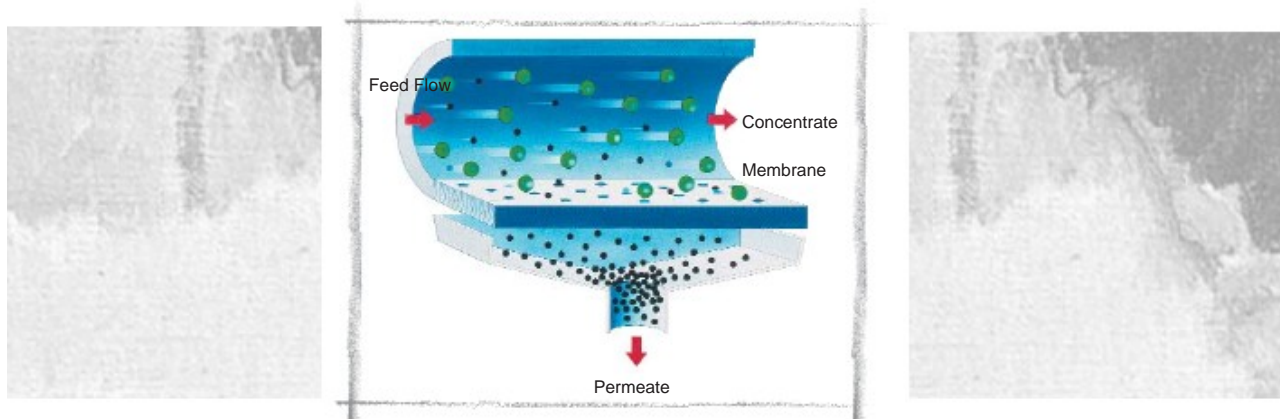
Already in the nutrient supply for the fermentation, a pre-filtration using capillary membranes with an absolute rated pore size of 0,2 µm will achieve a sterile feed solution. In the upstream process MICRODYN® capillary membranes are applied to work up the fermentation broth in a clarification step. In this filtration step the cells are retained while the target product can pass for further downstream processing.

One typical application of the microfiltration with Polypropylene hollow fiber membranes is the harvesting of cells in viral vaccine applications.

The use of polyethersulfone membranes in the concentration step during the production of therapeutic proteins is a typical example for ultrafiltration. MICRODYN-NADIR offers a variety of these membranes in the form of die-cuts, spirals and modules. They offer an improved permeate flux while at the same time they show a sharp MWCO separation performance.

In the production of enzymes after removing the biomass solution can be purified by using the UF membranes.

Features of our new and enhanced cross flow technology



The hollow fiber and tubular membrane products are the easiest modules for the operator to set up and install. In addition the cleaning process can be enhanced by back flushing or reversing the flow.

In cross flow filtration the fluid stream is fed across the membrane. This concept supports the turbulent mixing of the fluid stream during the filtration process and prevents the deposition of particles on the membrane surface. Of all products, flat sheet membranes converted to spiral modules offer the best economical approach to store the maximum filtration area in a given volume.

In the biopharmaceutical industry cassettes are being used more and more. We offer cassettes with an advanced design which show improved performance over existing products. By using an innovative design of the cassettes a much higher flux rate can be achieved. The improved fluid dynamics guarantees a uniform flow in all parts of the cassettes leaving no dead areas for debris or impurities. Additionally the improved fluid dynamics enhances the cleaning efficiency of the entire module.

The cassettes are available with the widest range of membrane selection in the industry. Sizes range from cassettes suitable for laboratory evaluation, pilot plant optimizations and manufacturing environments. Installed plants in the market range up to a processing capacity of 2 million liters per day with a membrane area of 1280 m.



A new Generation of Membrane Products

Our new generation of membranes and filtration elements for the micro-, ultra- and nanofiltration provides better performance and stability and is compliant with FDA-specifications.

Modules are available in sanitary and industrial versions for high temperature and high pH conditions.

Our membranes are available in roll stock, flat sheet, die-cuts, spirals, cassettes, hollow fibers cartridges and tubular configuration and a wide range of standardized or customized modules depending on the required membrane material and molecular weight cut-off (MWCO).

Our production processes meet the FDA standards, and we require all our suppliers to do so as well. We assist our customers in process development with our laboratory and pilot service. Our capabilities for field service and short delivery times, also for custom products, are more essential qualities of the MICRODYN-NADIR organization.



Application	Process	Advantage
Fermentation for the production of biopharmaceuticals such as: Therapeutic proteins Monoclonal antibodies Vaccines, animal and humane Enzymes Antibiotics Vitamins Flavors High purity water Pharma water	Inlet air sterile filtration Pre-filtration of nutrients Vent filtration	MICRODYN-NADIR PP capillary membranes with absolute rated 0,2 µm pore size afford complete contamination and bacterial retention. The modules are several times sterilizable and autoclavable.
	Clarification of fermentation broth	Target product is secreted into the fermentation broth, remove cells and cell debris are removed by microfiltration or ultrafiltration, using NADIR® UF-membranes, available in a wide range of MWCO.
	Cell harvest, lysate clarification	Target product is retained in the cells, after lysing, cells and debris are removed by MICRODYN microfiltration for further processing.
	Buffer depyrogenation Endotoxin removal	Micro- or ultrafiltration membranes available from NADIR® or MOLSEP® hollow fiber range.
	Diafiltration and concentration	Membrane selection depends on retained protein size. A wide range of MWCO and base polymers is available for UF and NF filtration in the form of flat membranes, die-cuts, spirals, hollow fibers.
	Virus removal	NADIR® ultrafiltration or nanofiltration membranes are used depending on the required MWCO.
	Dialysis	Diaperm hollow fibres on basis of regenerated cellulose, autoclavable.
	Product separation, -concentration	The Optisep® novel cassette design together with NADIR® membranes offer a much higher flux rate and can be cleaned efficiently without leaving debris in the cassettes and easier scale up.
	Product isolation	The innovative new chromatography system combines advantages of cross flow filtration and chromatography for much sharper product separation and better yields.