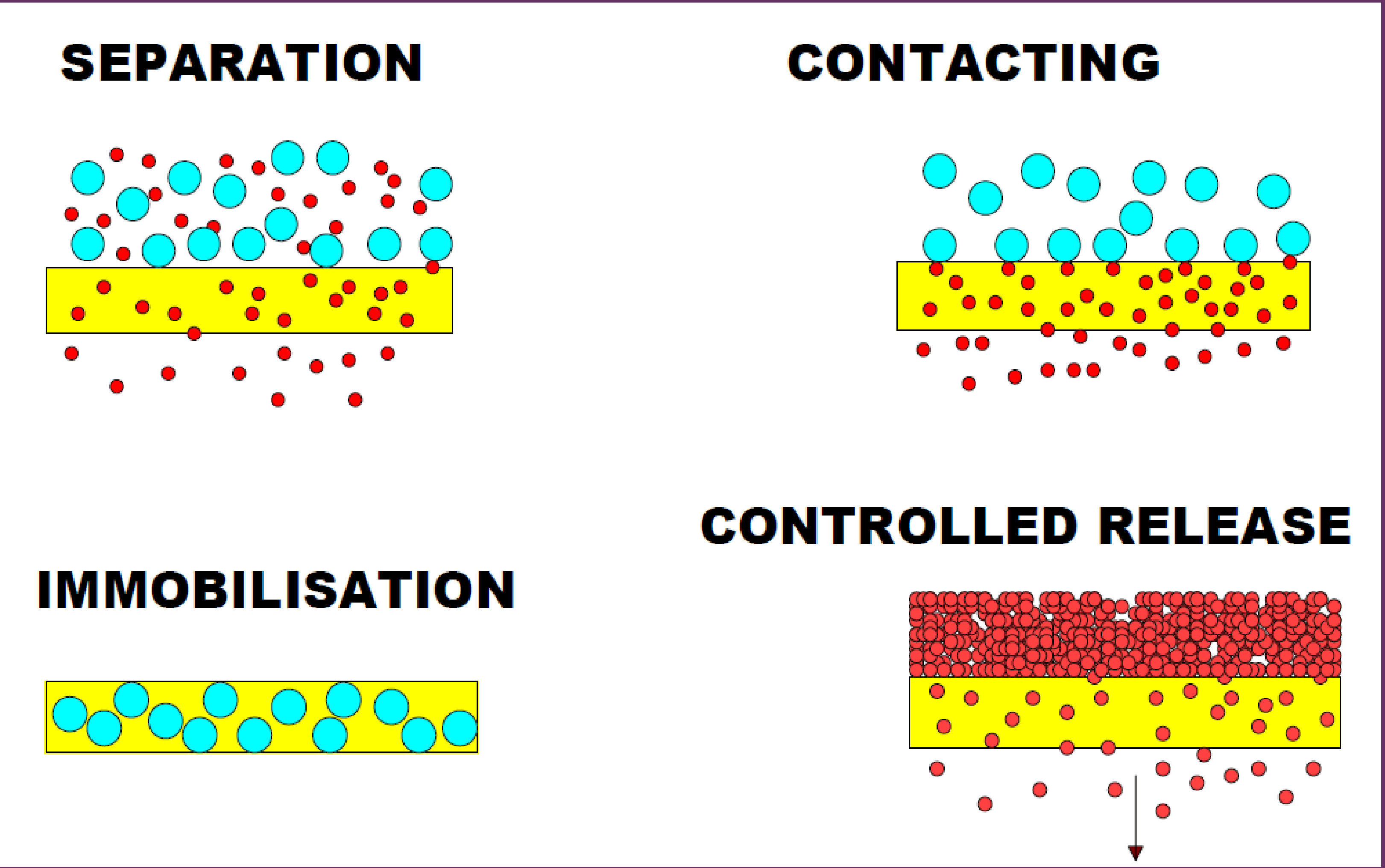
Dialyser membranes

What matters most?

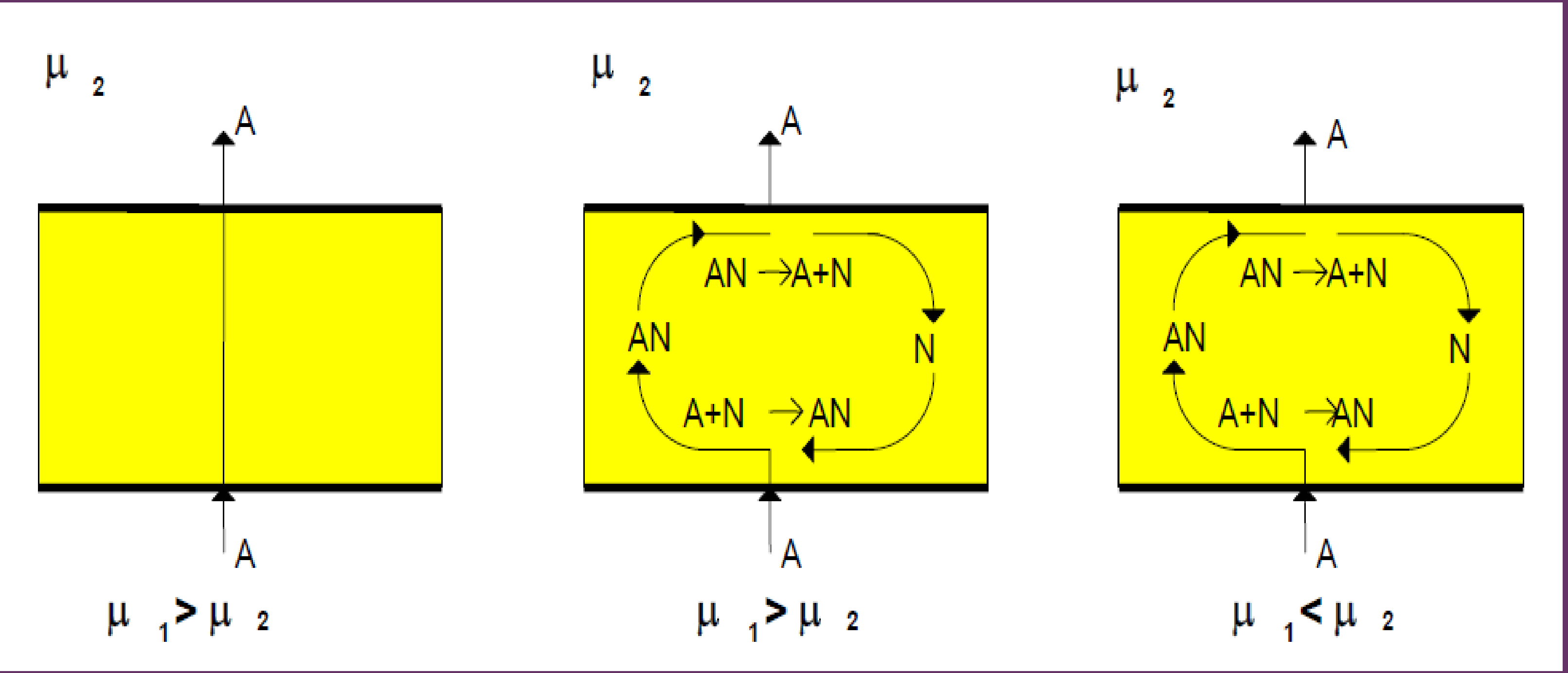
Dr Rajesh B Kumar
Director
Apex Kidney Care

Functions of the membrane



Mass transport through membrane Separation

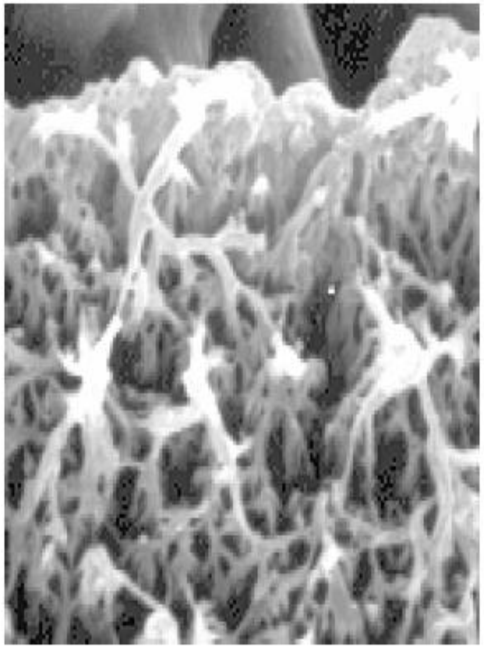
Passive diffusion | facilitative diffusion | Active transport



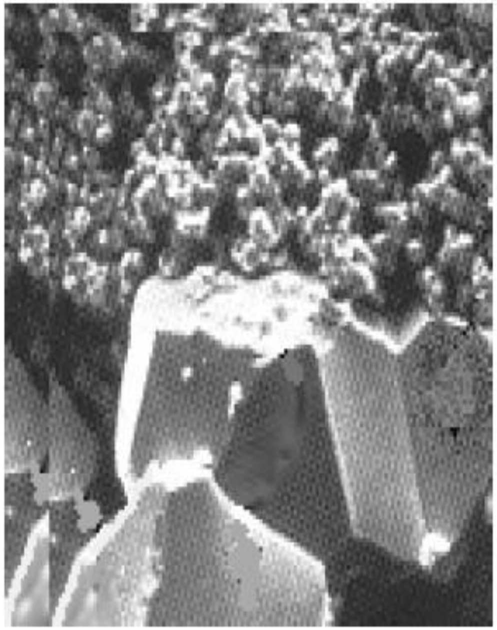
Engineering in Membrane

Structure: assymetric
Material: Polysulphone
Method: casting

Structure: symetric
Material: Polysulphone
Method: casting

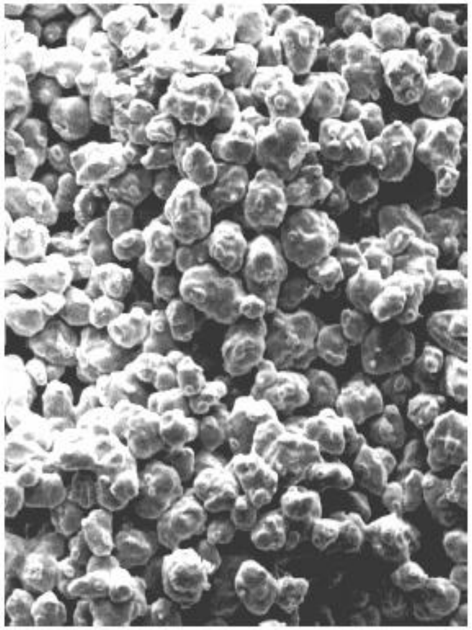


Structure: assymetric
Material: α-Al2O3/ZrO
Method: sintering

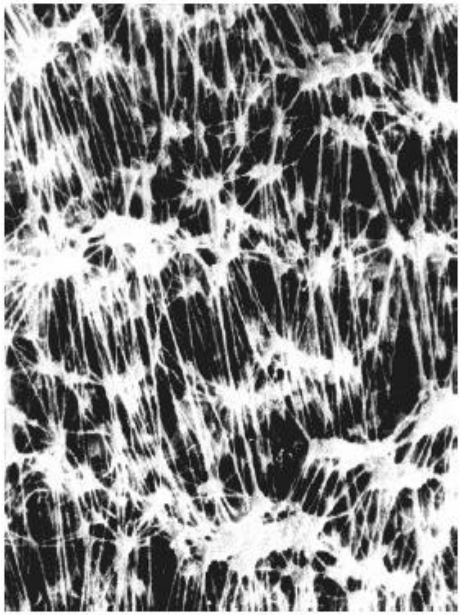


Membrane structure

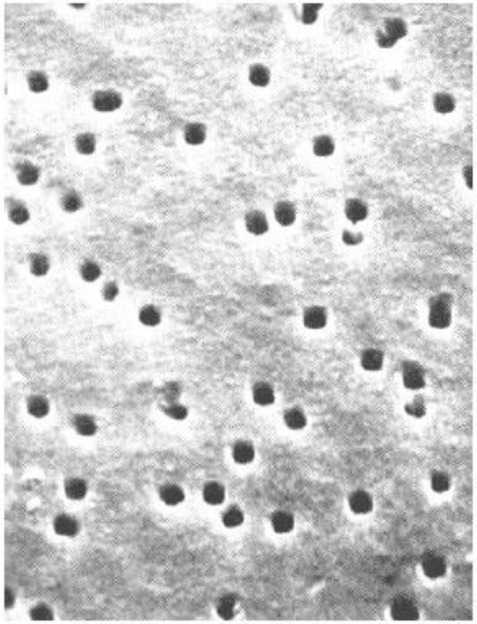
Structure: symetric
Material: glass
Method: sintering



Structure: symetric
Material: Polypropylene
Method: stretching

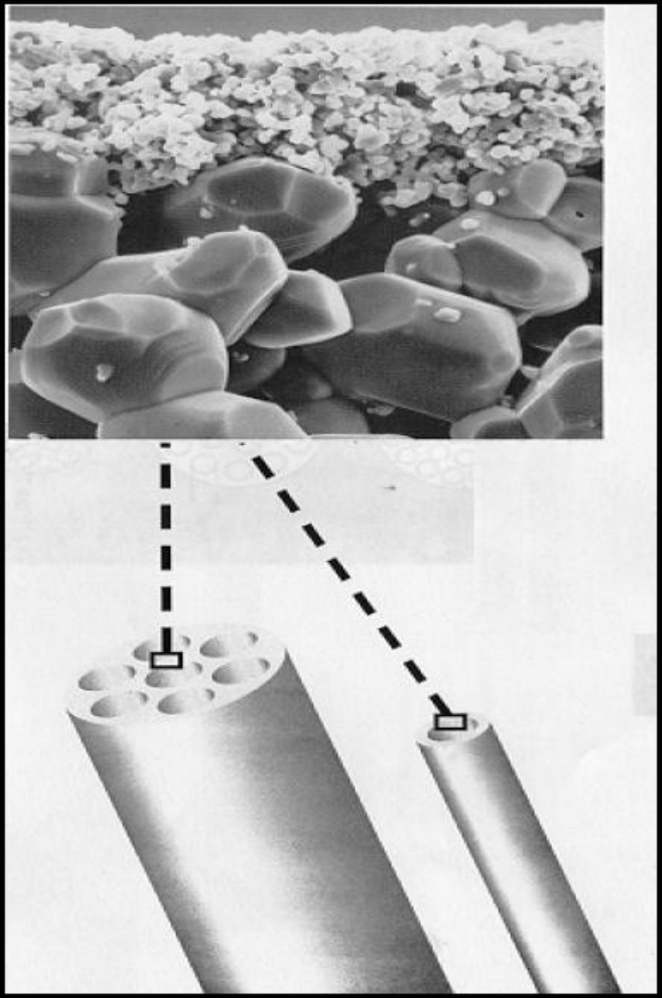


Structure: assymetric
Material: polycarbonate
Method: track-etching

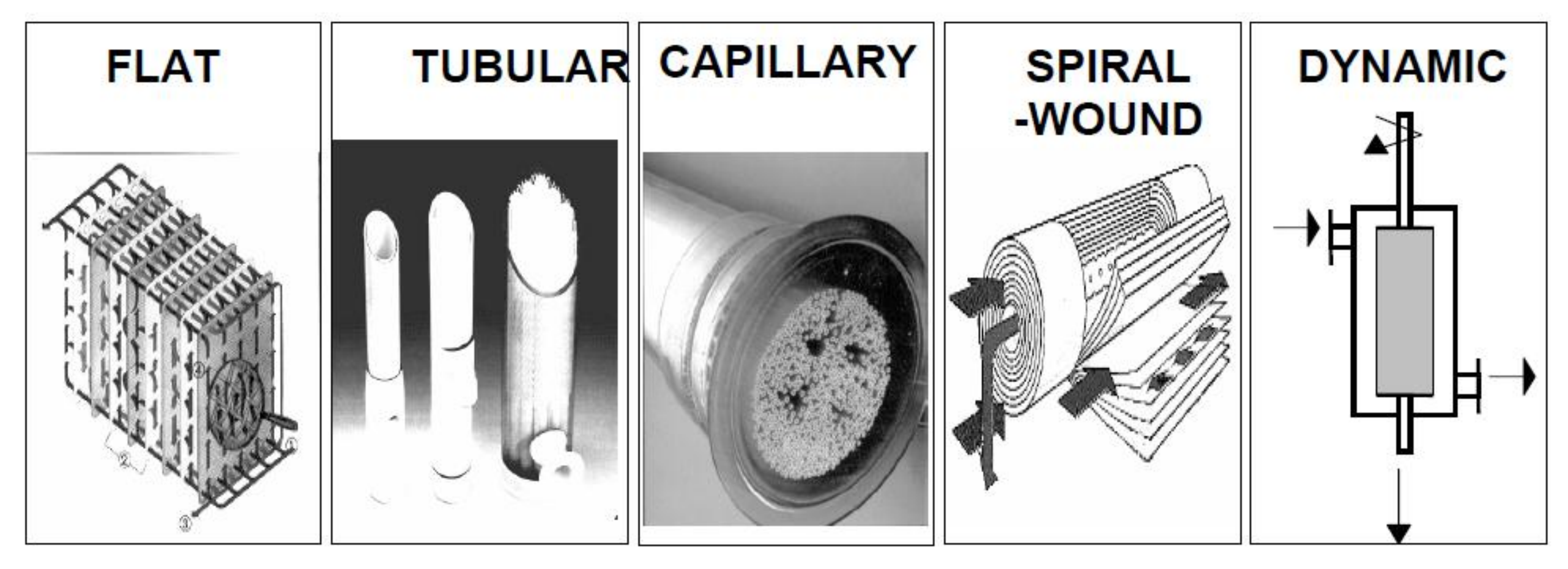


Hollow fiber membrane

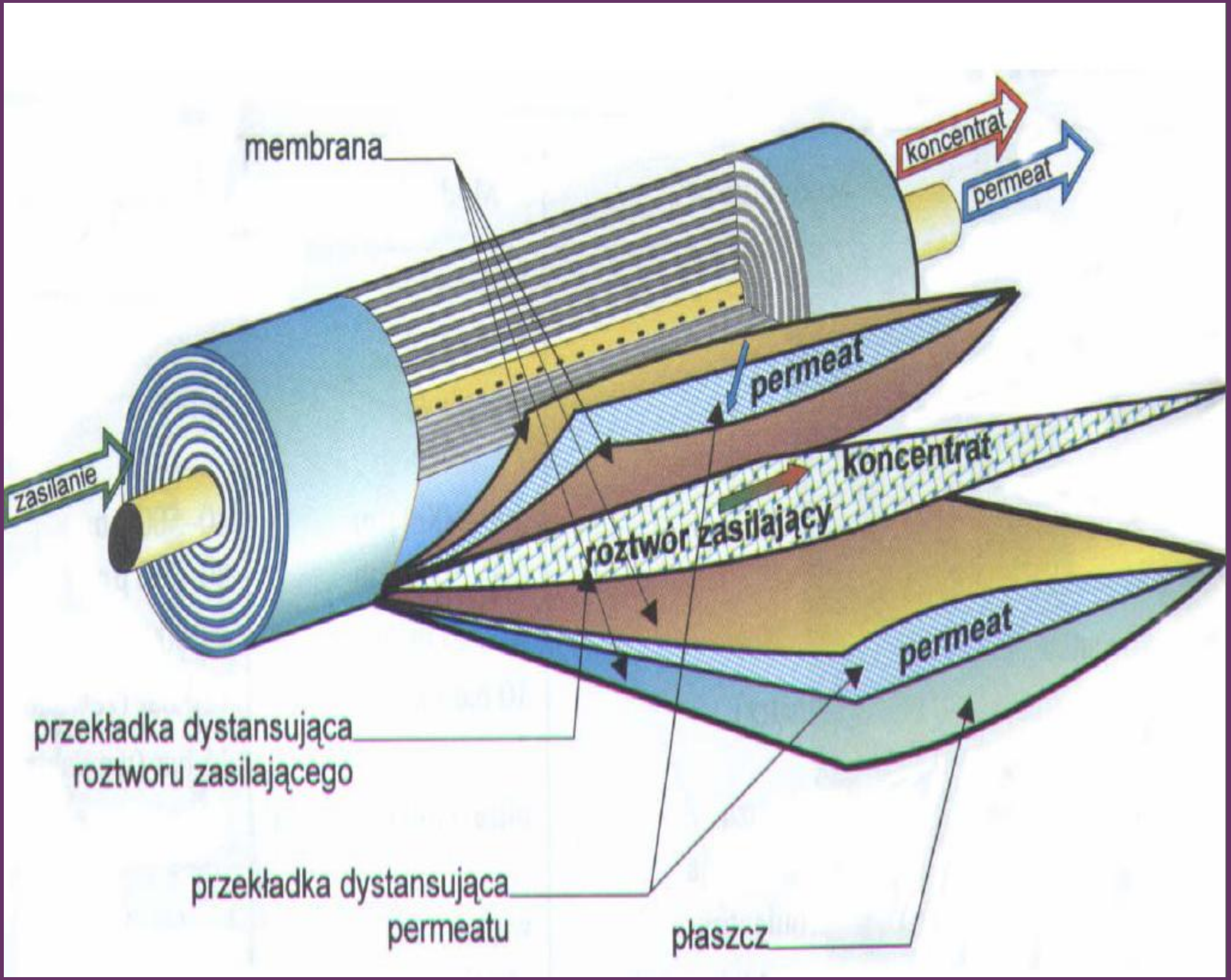
Ceramic membrane



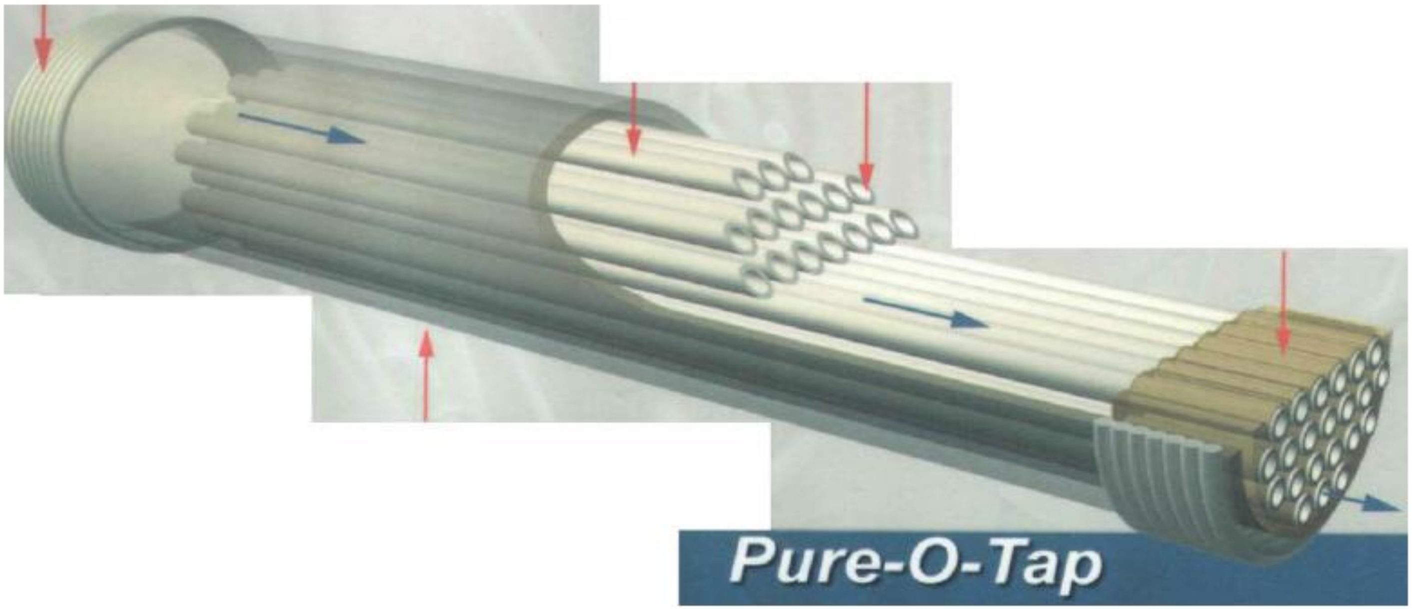
Membrane modules



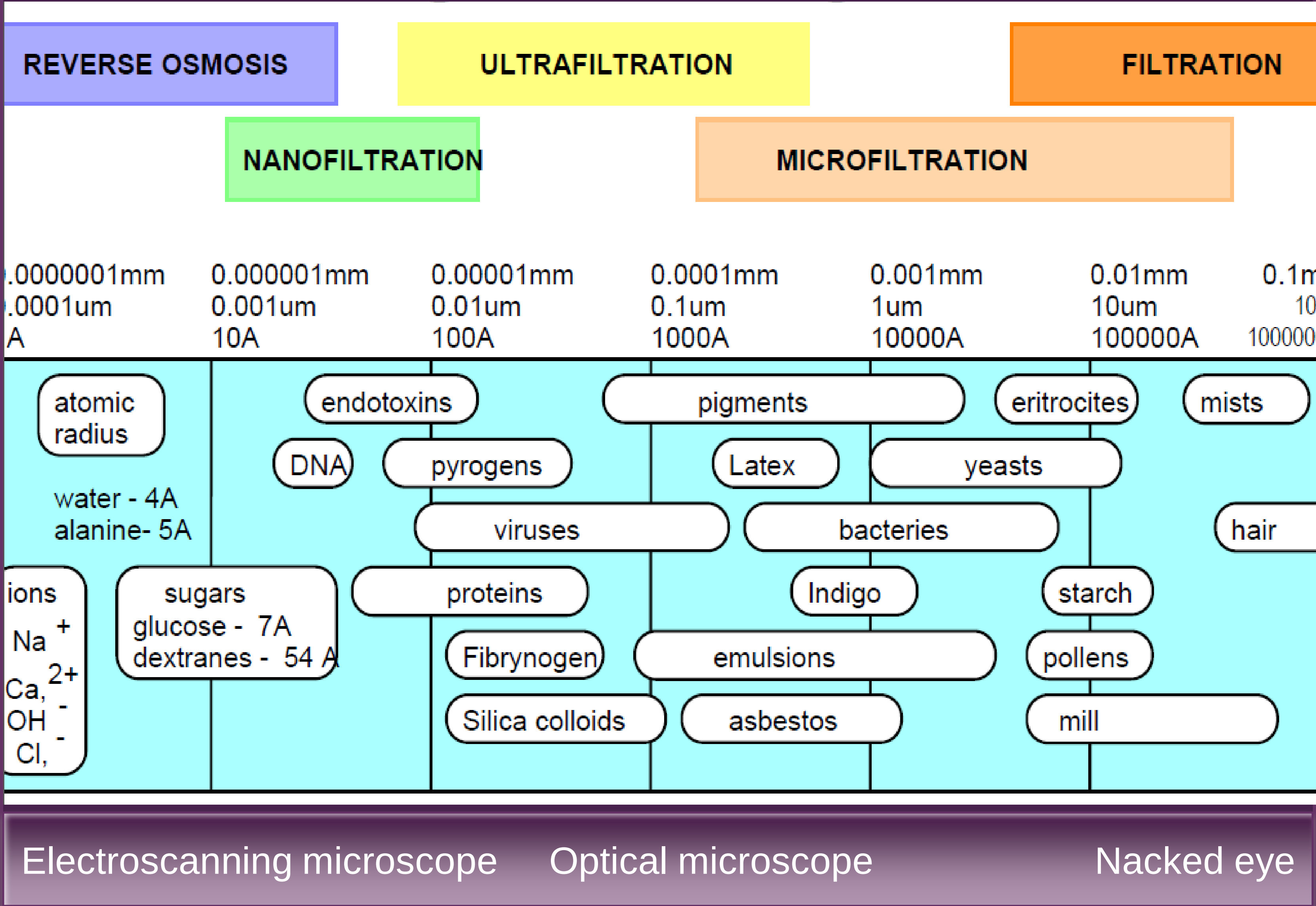
Spiral wound module



Tubular module



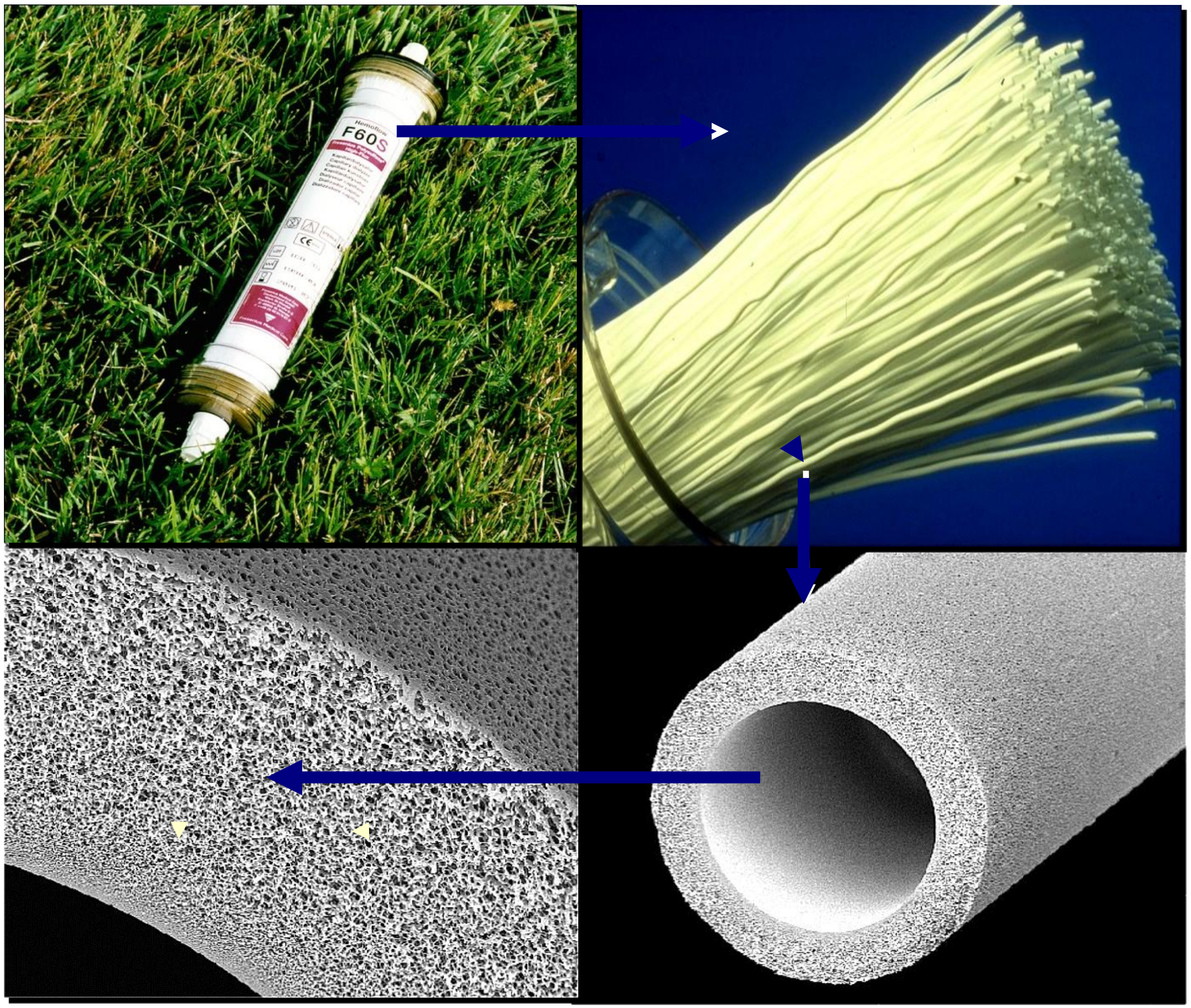
Range of membrane separation



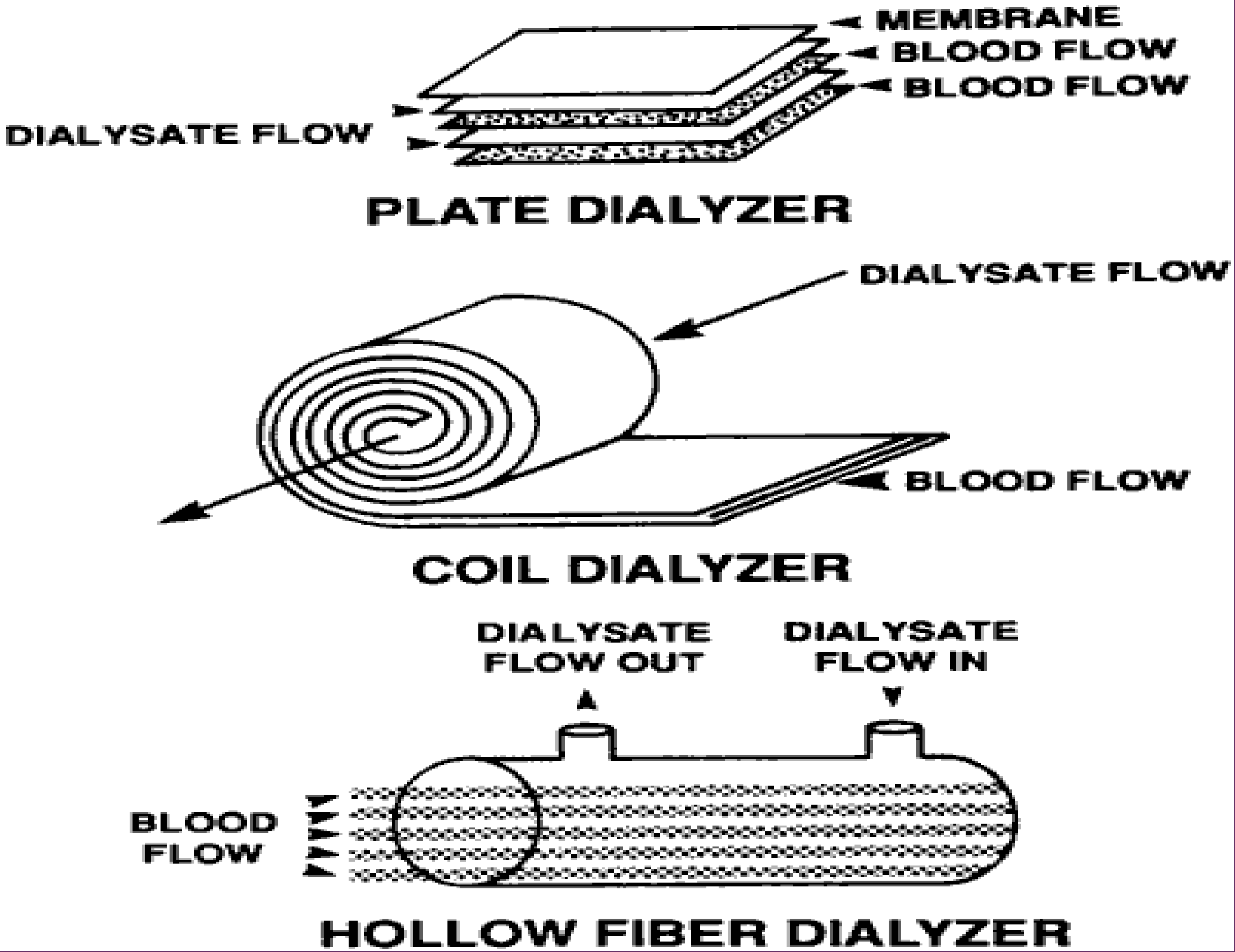
Learning objectives

- Classification of membranes used in dialysis
- Basic polymers
- Cellulosic membranes
- Membrane Manufacturing Process.
- Some physicochemical properties of membranes
- Common dialysis membrane polymers
- Functional characteristics of membranes
  - solute transport
  - water transport
  - Biocompatibility

The Dialyser & Membrane



Type of dialyzer



Parallel Plate Dialyzer

Sheets of membrane are mounted on plastic support screens, and then stacked in multiple layers ranging from 2 to 20 or more.

This design allows multiple parallel blood and dialysate flow channels with a lower resistance to flow.

There have been major improvements which provide

(1)thinner blood and dialysate channels with uniform dimensions,

(2) minimal masking or blocking of membranes on the support, and

(3) minimal stretching or deformation of membranes across the supports.

Coil dialyzer

An early design in which the blood compartment consisted of one or two long membrane tubes placed between support screens and then tightly wound around a plastic core.

This design had serious performance limitations, which gradually restricted its use as better designs evolved.

The coil design did not produce uniform dialysate flow distribution across the membrane. More efficient devices have replaced the coil design.

Hollow Fiber Dialyzer:

This is the most effective design for providing low-volume high efficiency devices with low resistance to flow.

The fibers in the device are termed the fiber bundle.

The fibers are potted in polyurethane at each end of the fiber bundle in the tube sheet, which serves as the membrane support.

Hemodialyser

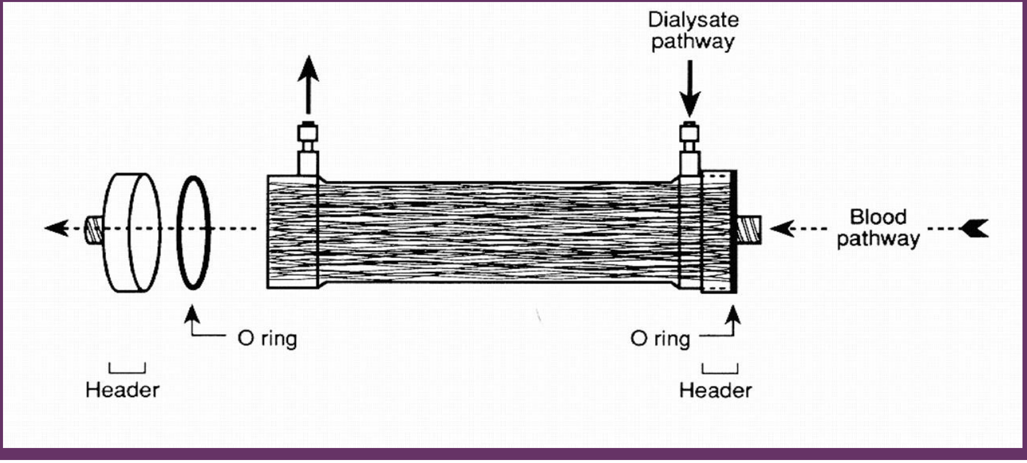
Hollow fiber dialyzers are chemically complex, having several compounds incorporated in their structural components:

Housing material,

End cap compartments,

Potting material and

Transport surface (membrane)



Dialyzer membranes

Categorize on the basis of

- Surface area
- Pore size
- Type of membrane

Physical property of membrane

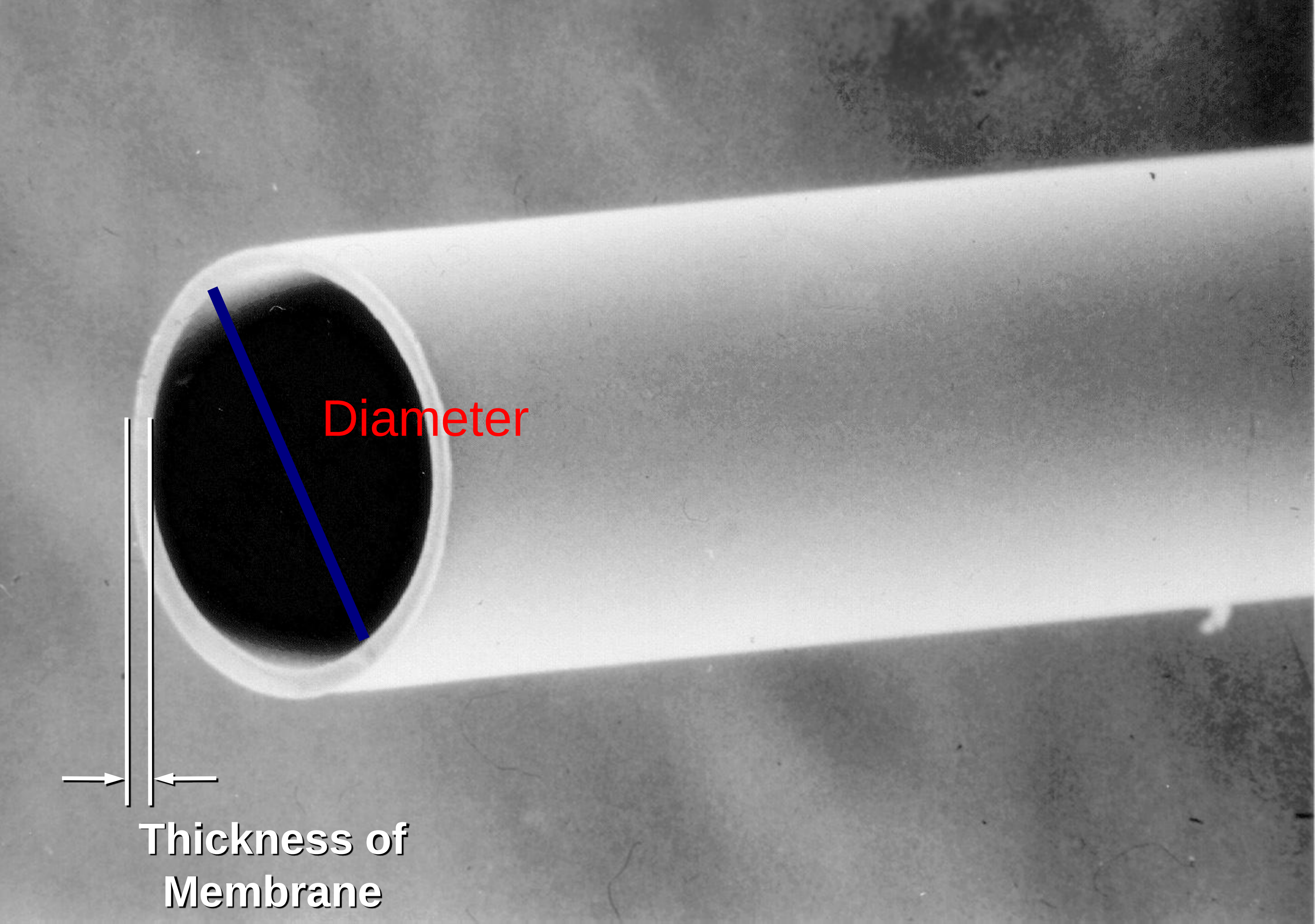
The geometric characteristics of a hollow fiber determine the membrane surface area.

1. Number of fibers,

2. Length of Fibres

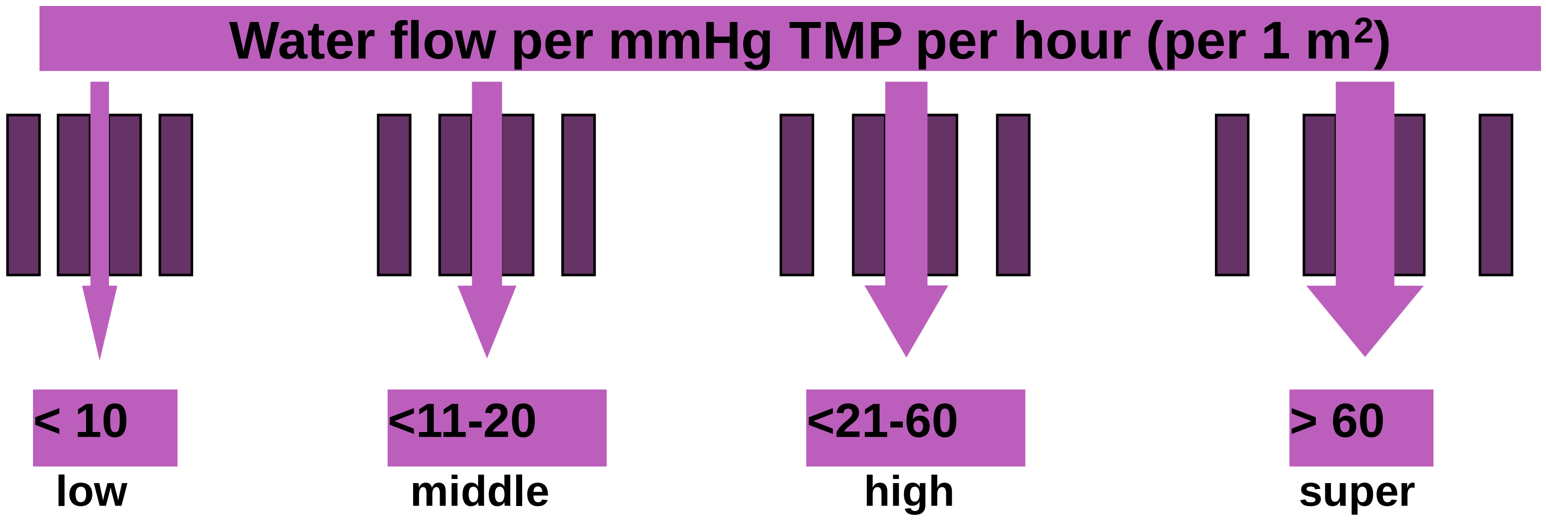
3. Internal diameter of fiber.

DIALYZER FIBER



Membrane hydraulic permeability

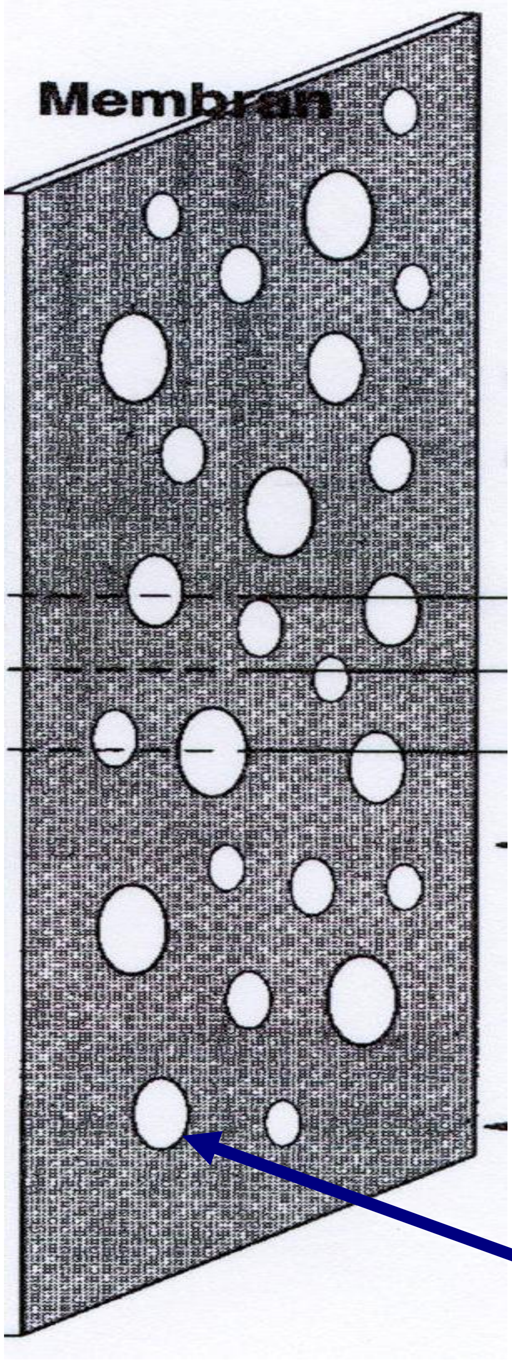
- Low Flux
- Middle Flux
- High Flux
- Super Flux

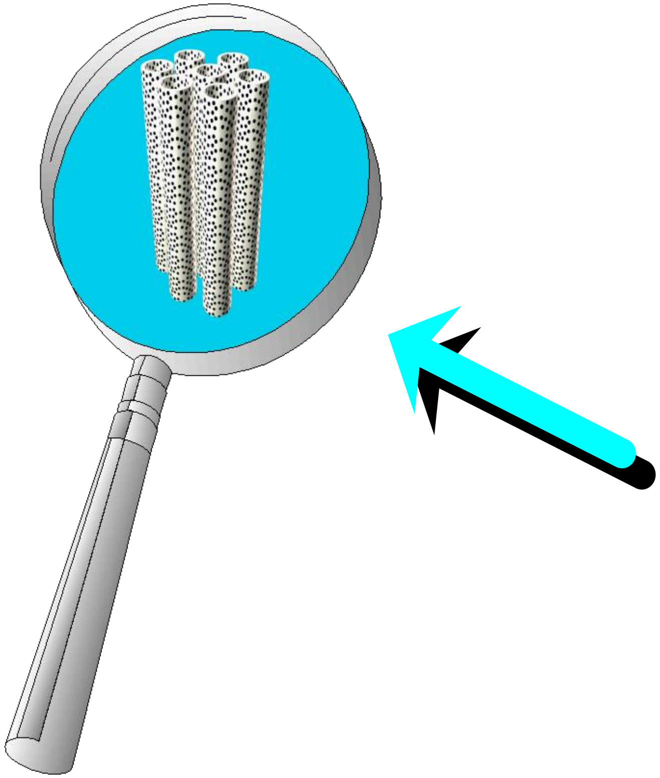


PORE SIZE

Low Flux or High Flux

HOLLOW FIBRE DIALYSER





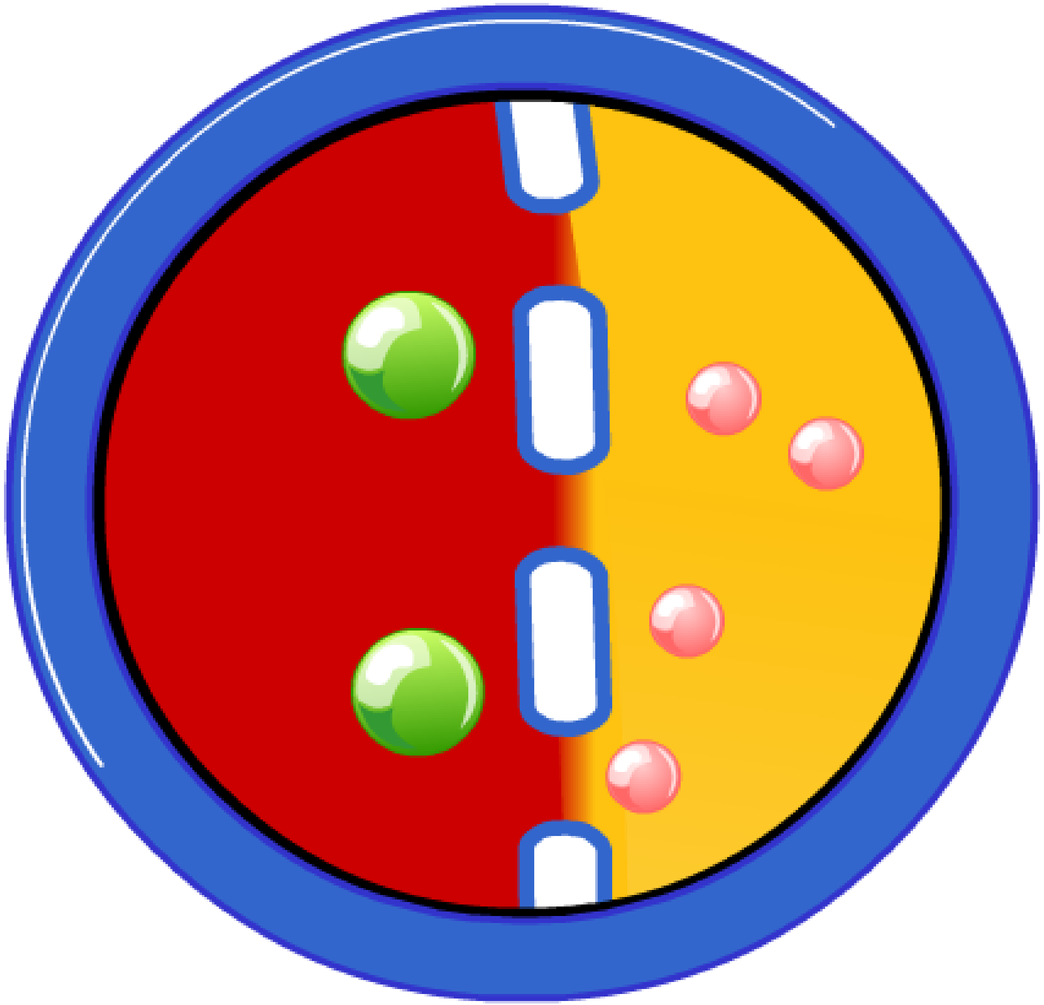
PORE SIZE

Low flux dialyser: Average Pore size ~ 1.0 nm

High flux dialyser:
average Pore size ~ 3.0 nm

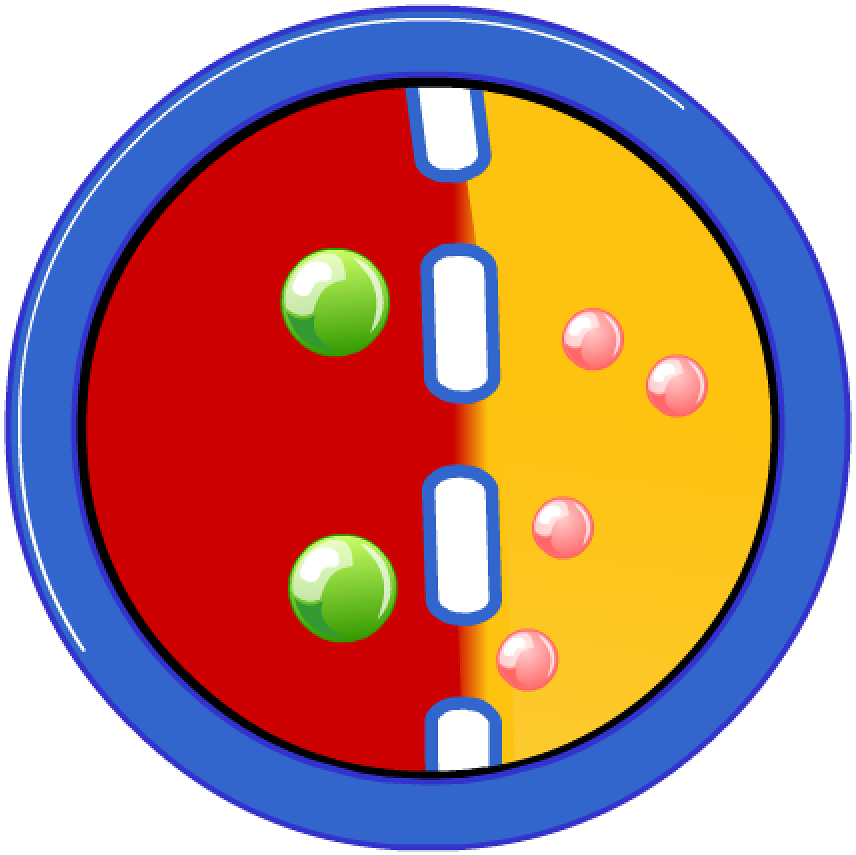
Pore Size

MOLECULES SIZES

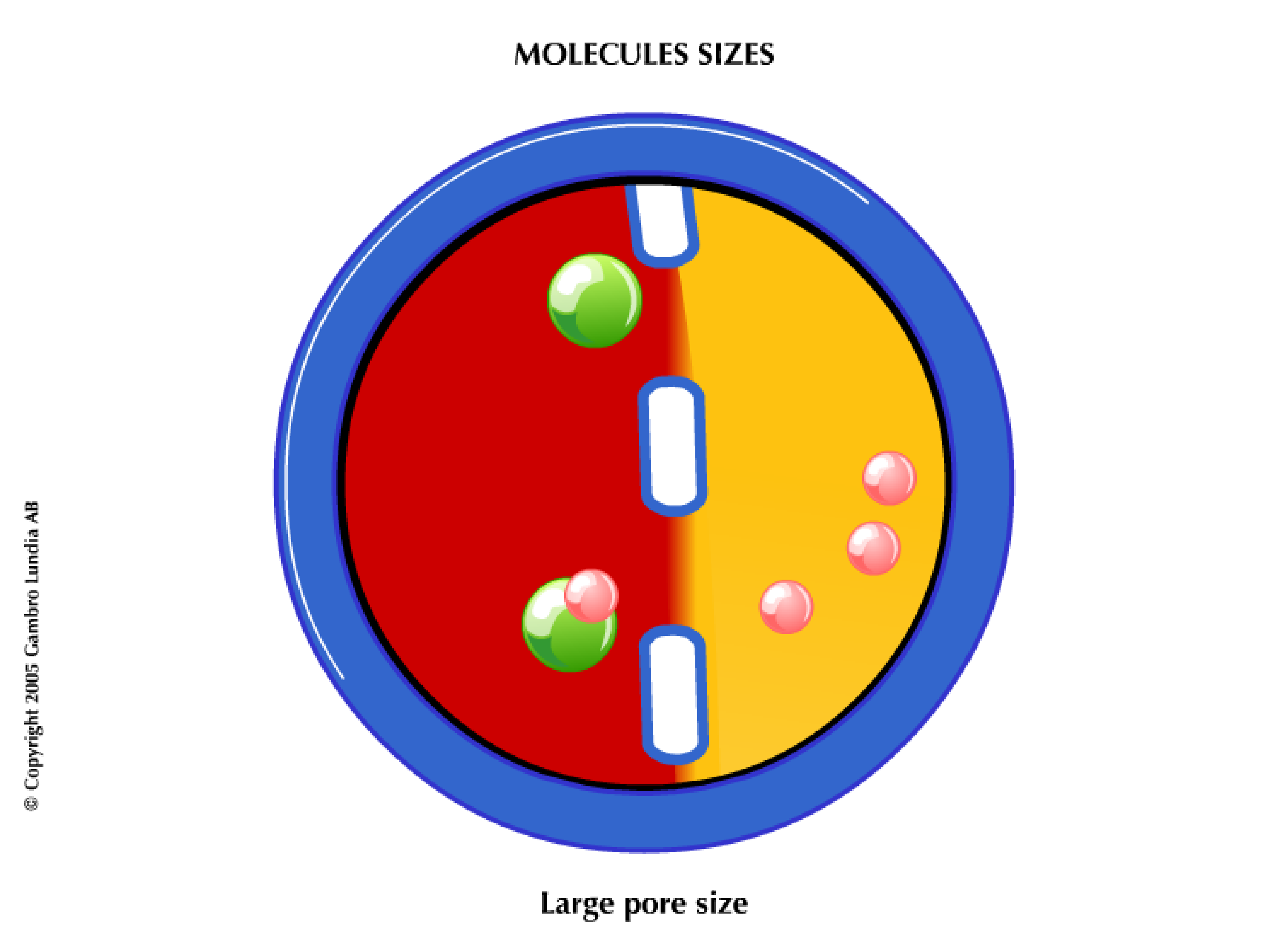


Small pore size

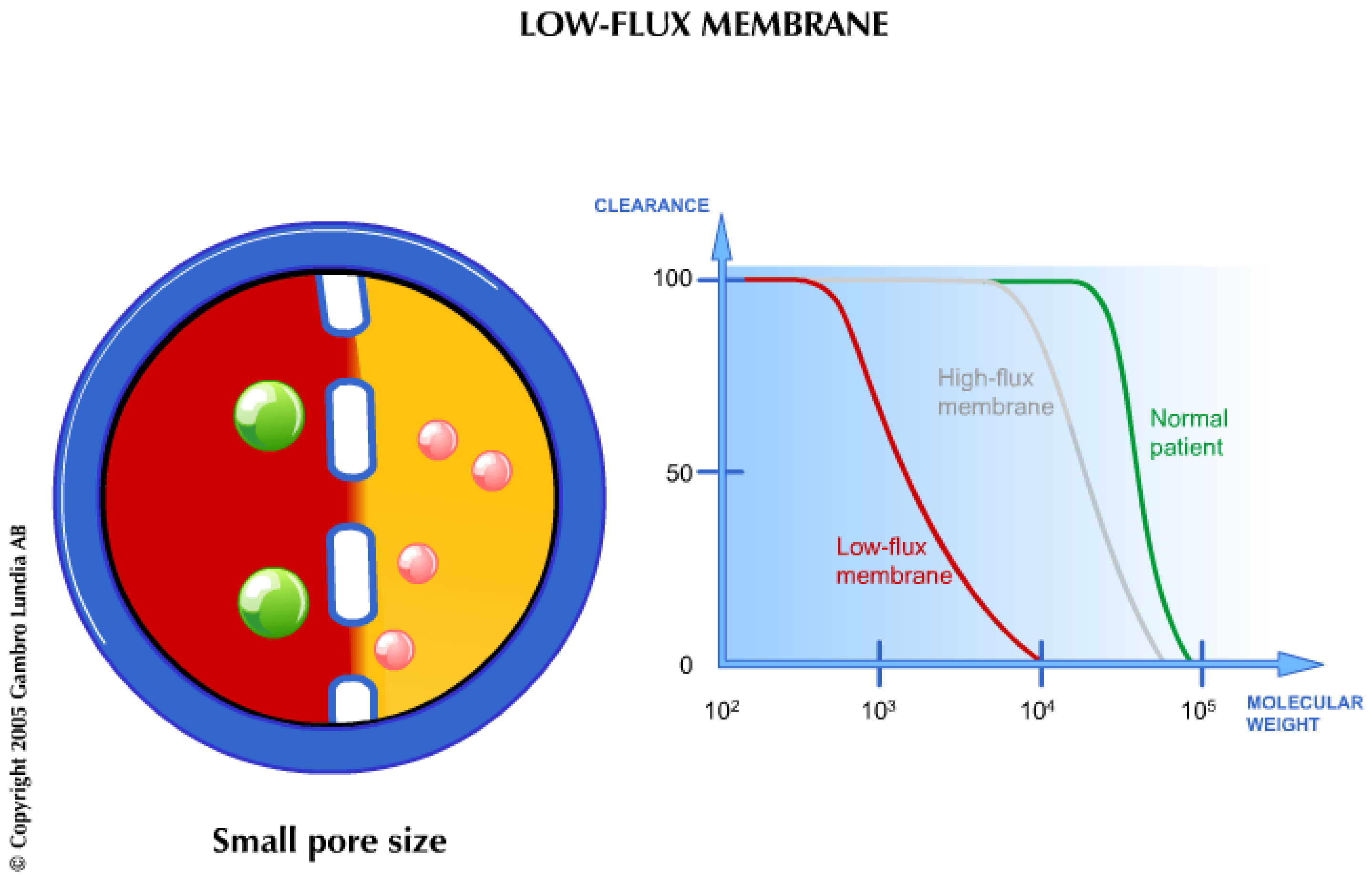
Small pores removes small molecules



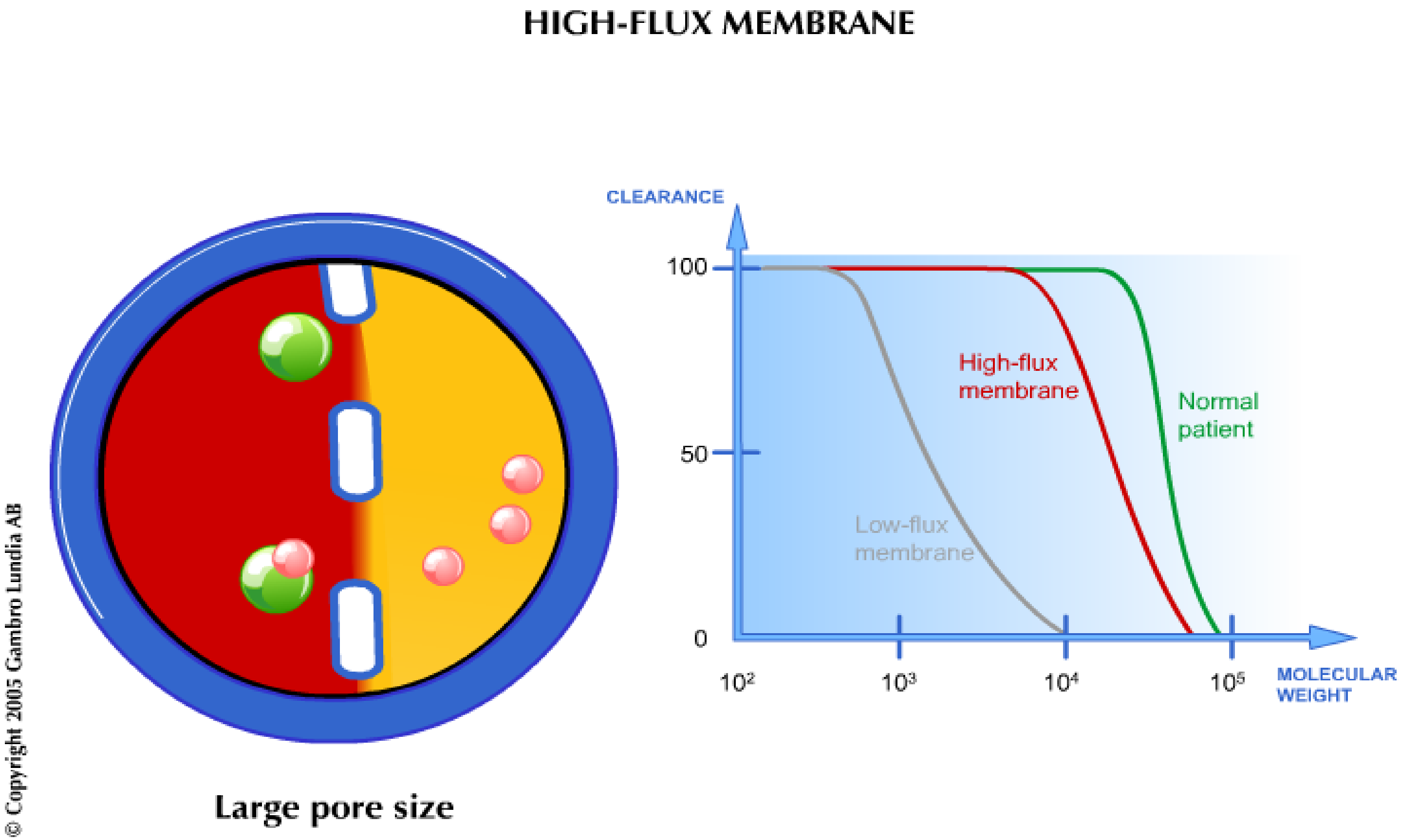
Large pores removes large molecule



Low-Flux Membrane



High Flux Membrane



Haemodialysis Membranes

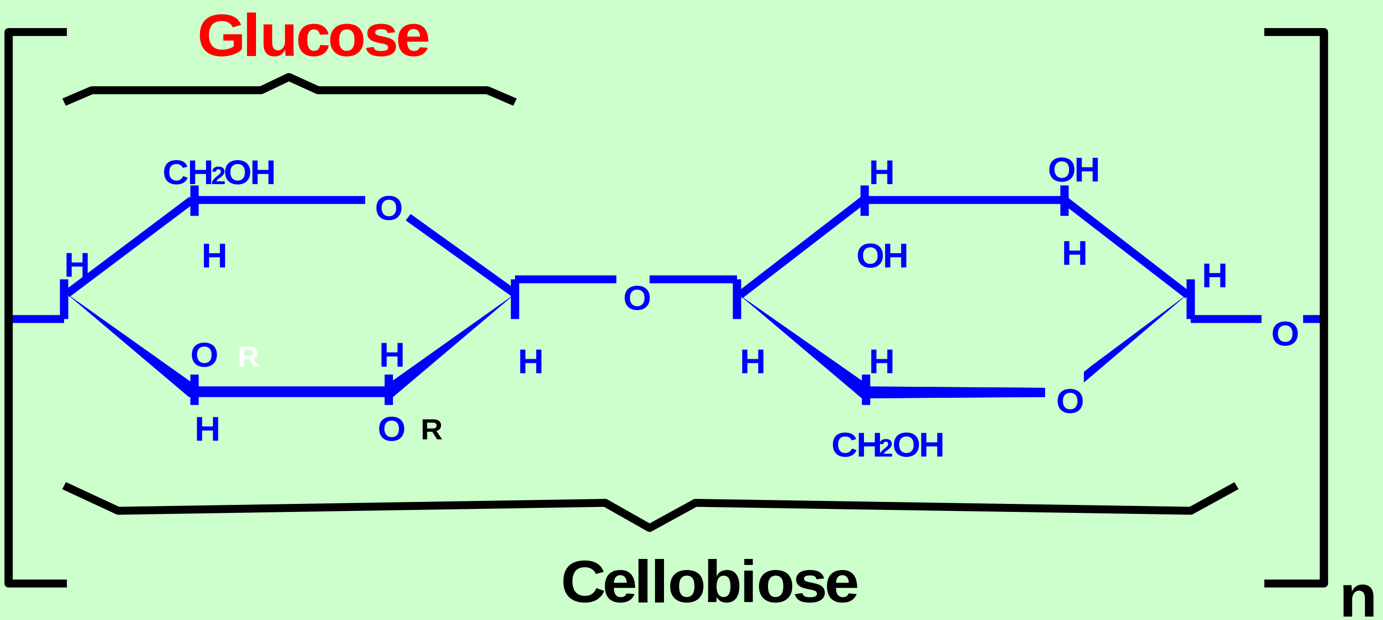
Dialysis membrane is composed of four different materials:

- Cellulose,
- Substituted cellulose,
- Cellulosynthetic, and
- Synthetic

Cellulosic Membranes

Synthetic Membranes

Glucose - The Basic Unit of Cellulosic Membranes



Cuprophan® R = -OH

Hemophan® R = DEAE (di-ethyl-amino-ethyl)

Cell. Acetate: R = Acetyl-

E.g. Cuprophan - hydroxyl groups have implications for blood interactions

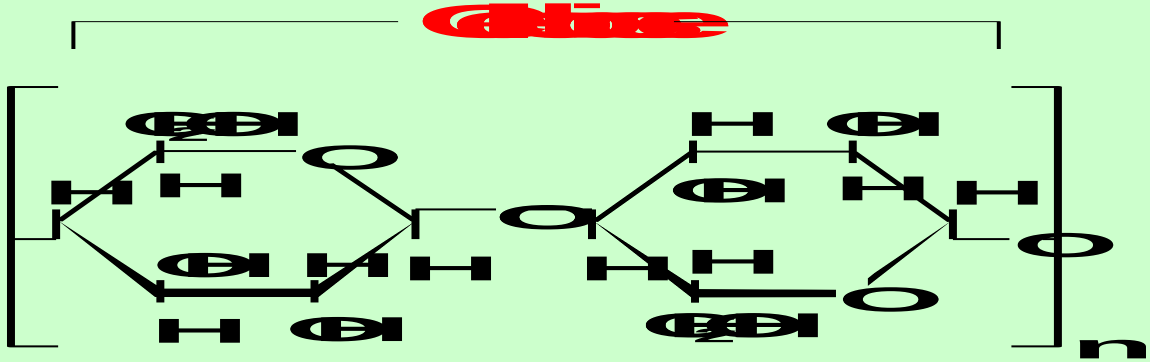
Regenerated cellulose

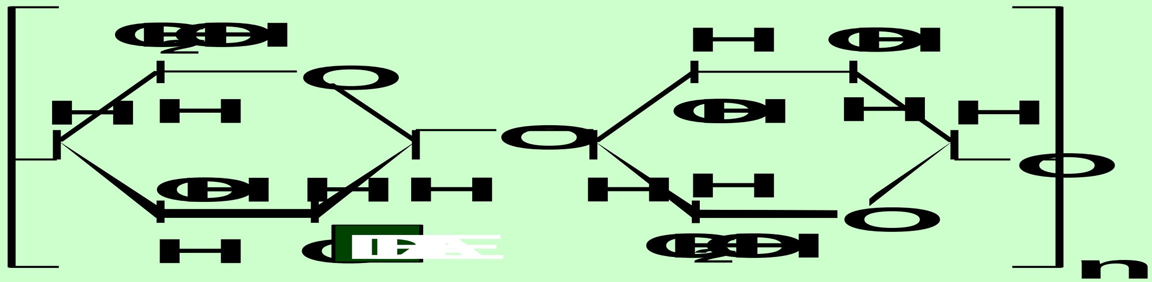
- Realization of -OH related problems

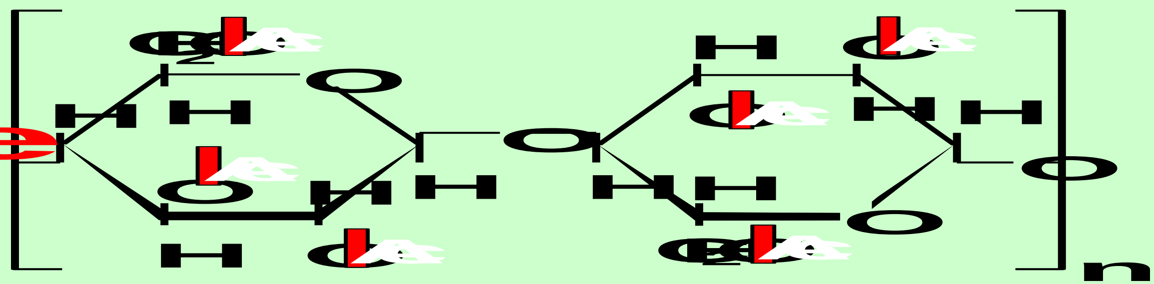
- Replacement of -OH with alternative radicals:-

  e.g. Hemophan - DEAE (di-ethyl-amino-ethyl)

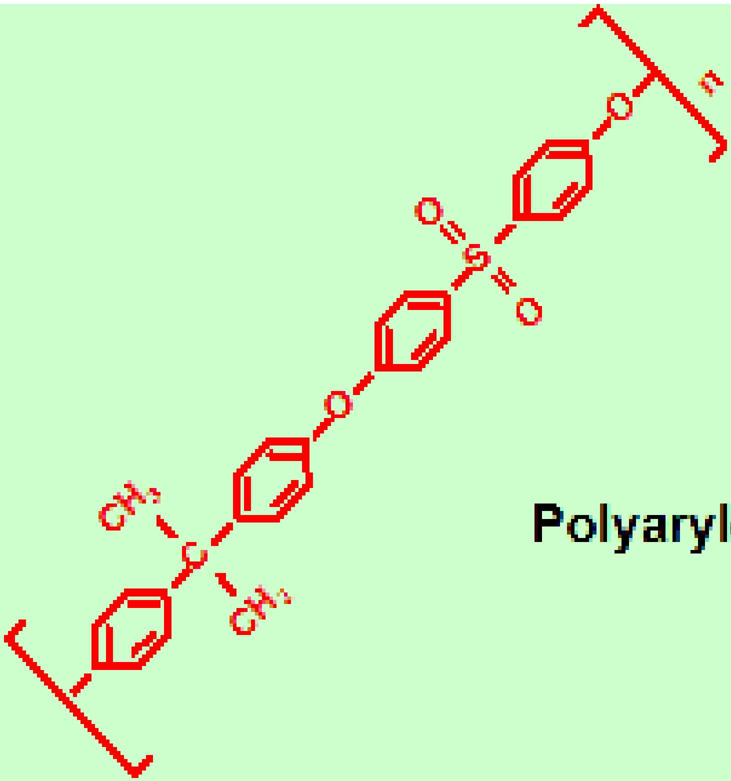
  e.g. Cellulose Acetate - Acetyl







Polysulfone Membrane – basic polymer



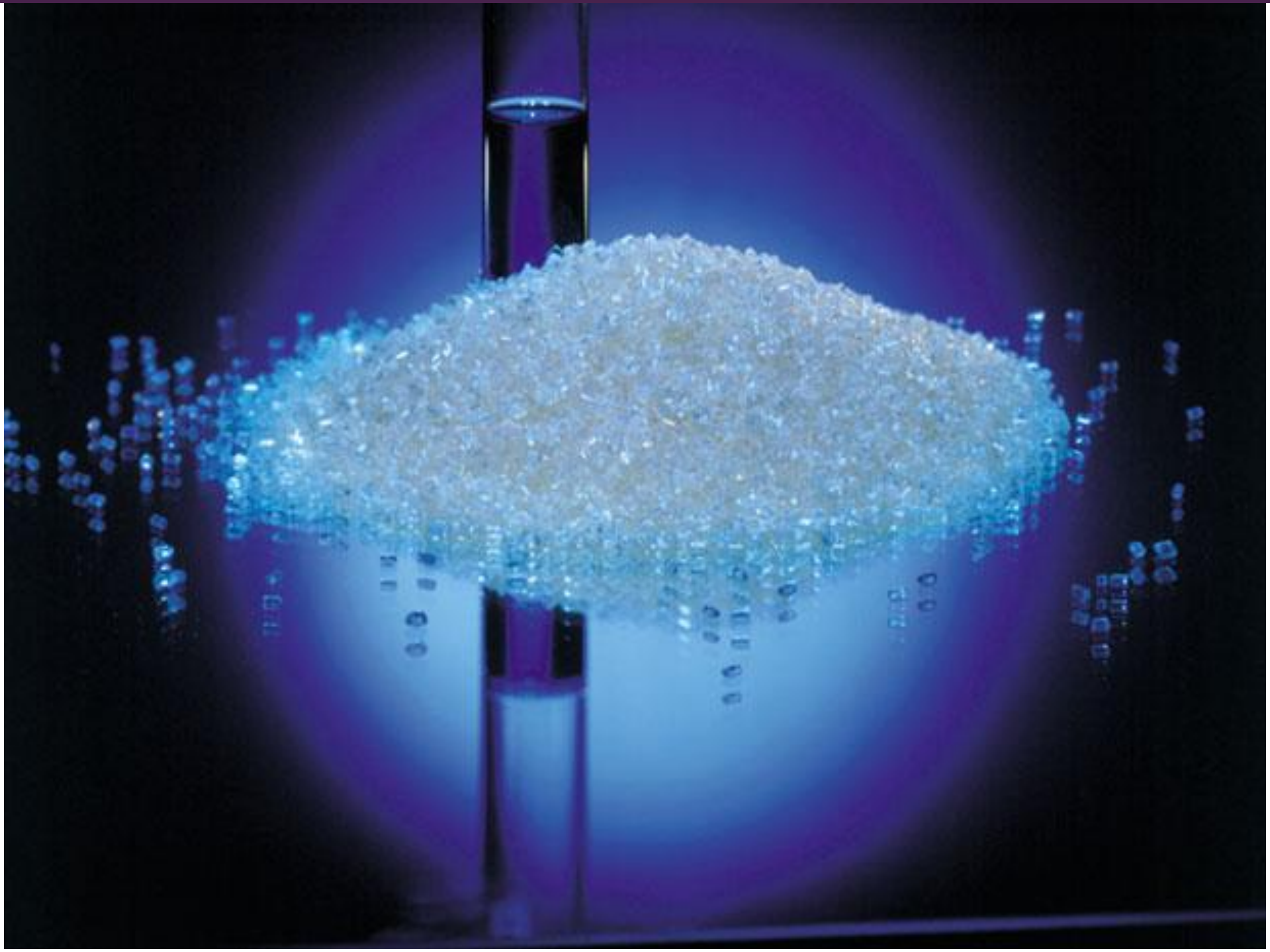
Polyarylethersulfone

+

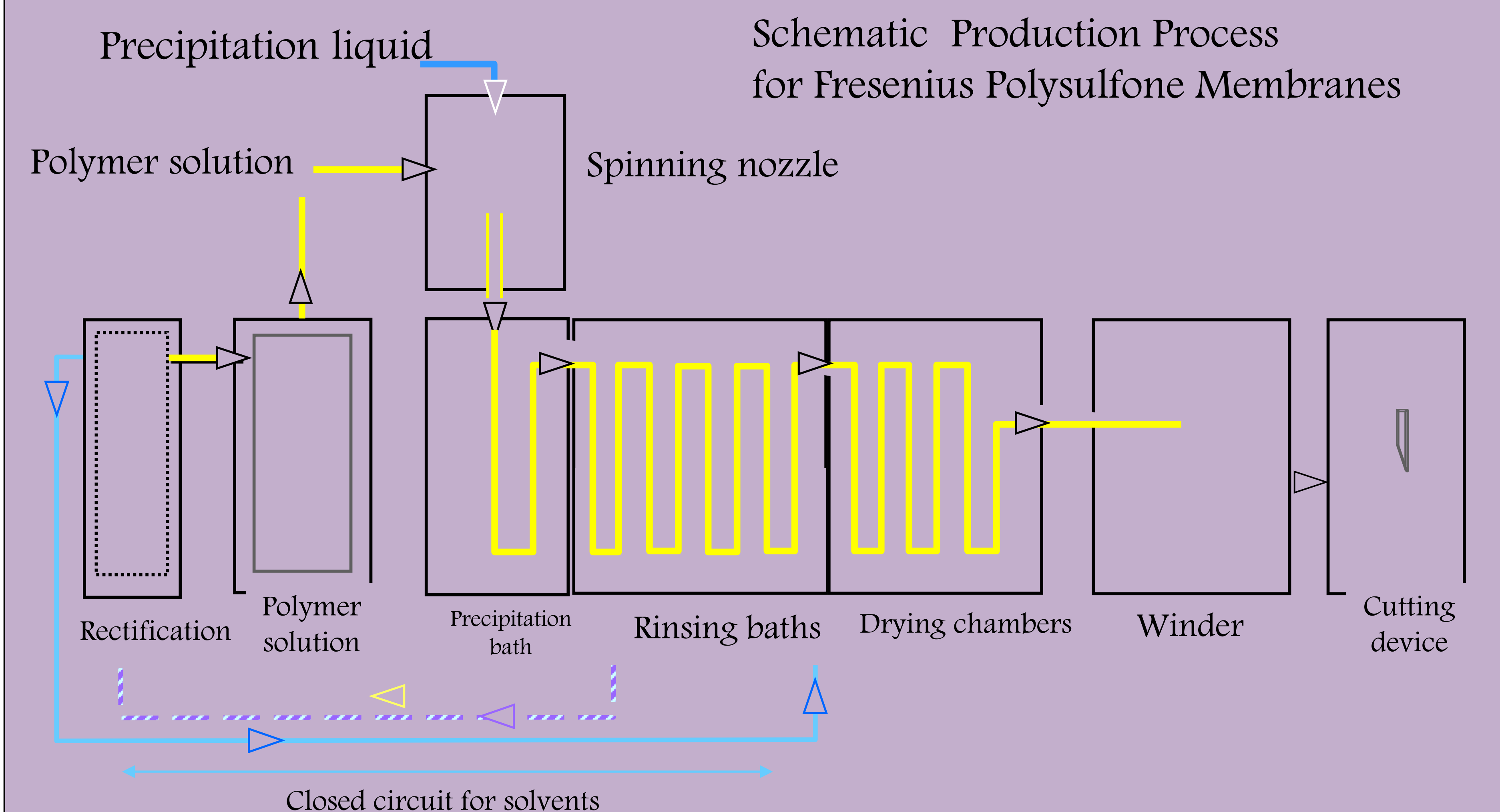
Polyvinylpyrrolidone (PVP)

0068

The Polymer → The Fibre → The Dialyser



Polysulfone Membrane Production



Comparison of Membranes

Cellulose	Modified Cellulose	Synthetic
Cotton Based material	Cotton based but removal of Hydroxyl groups and replaced by acetate/ AA / polymers.	Polymer like PVP, and other
Fibre Wall 8-15 microns	22-40 microns	30-55 microns
3,000 Daltons molecules	15,000 Daltons	15,000 Daltons
No endotoxin retention	No endotoxin Retention	Endotoxin Retention(Special Membrane like Fresenius)
Poor Biocompatibility	Good Biocompatibility	Excellent Biocompatibility
High complement activation	Moderate Complement activation	Low Complement activation
Poor Adsorption	High Adsorptive	Highly Adsorptive

Membranes Used in Hollow Fiber Dialyzers

Cellulose Based

- Regenerated Cellulose
- Cuprophan
- Saponified cellulose ester
- Several varieties of regenerated cellulose

Modified Cellulose

- Cellulose acetate
- Cellulose diacetate
- Cellulose triacetate

Synthetically modified cellulose

- Hemophan
- SMC
- PAN-Regenerated cellulose

Synthetic Based

Hydrophilic by nature

EVAL C

EVAL D

Hydrophilic by process

Polycarbonate

PMMA

PAN (AN69,PAN-DX,SPAN)

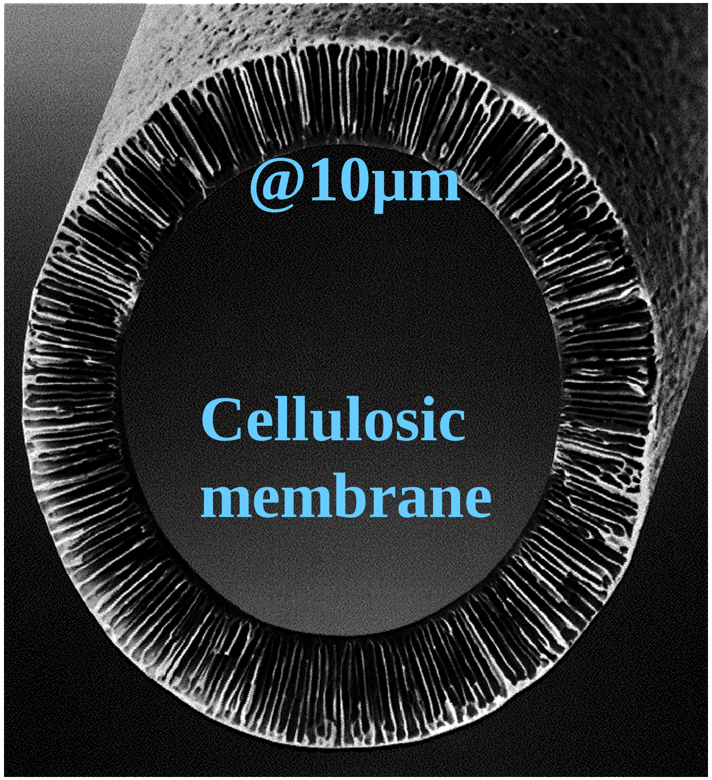
Hydrophilic by blending

Polyamide

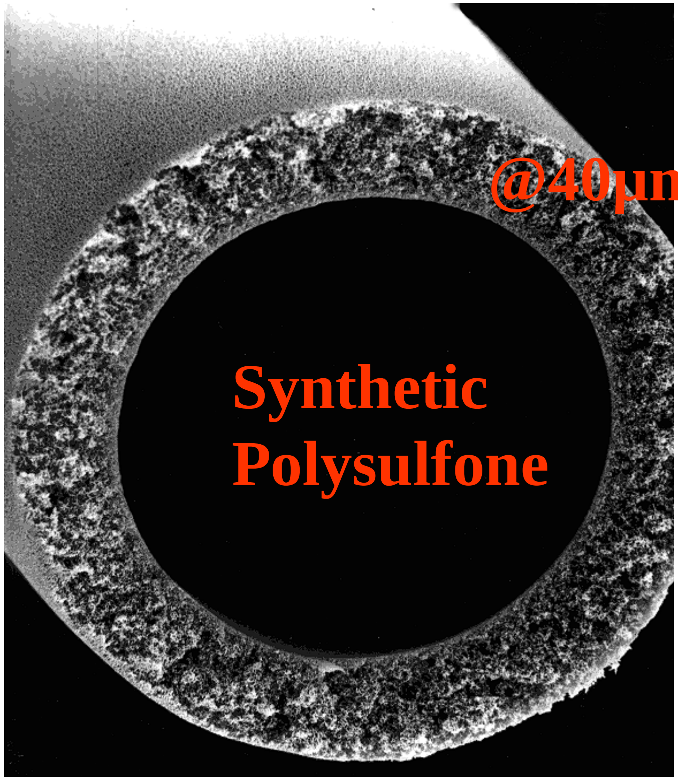
Polysulfone

Polyethersulfone/polyarylate (PEPA)

Symmetrical vs. asymmetrical membranes

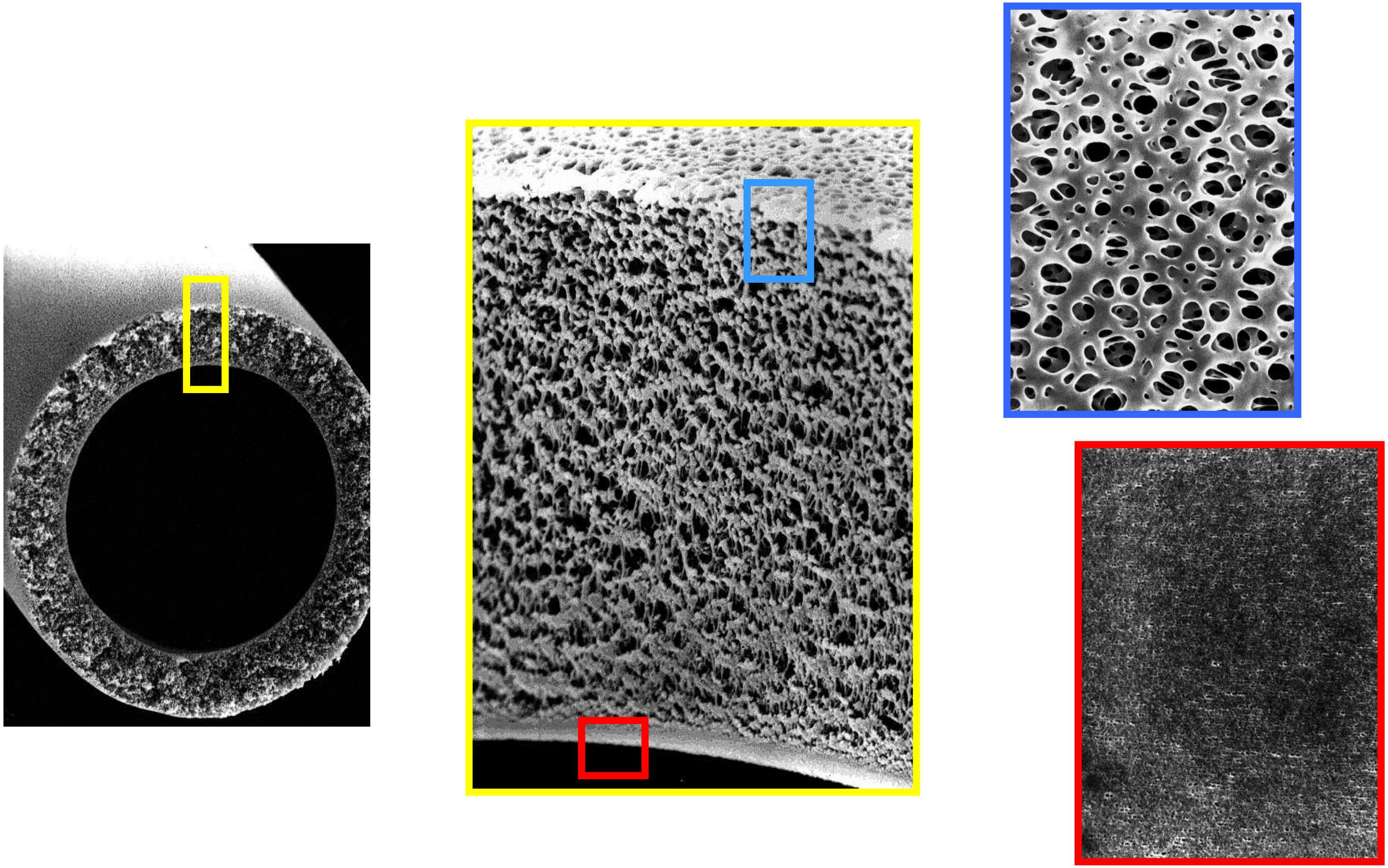


Diameter @ 150µm

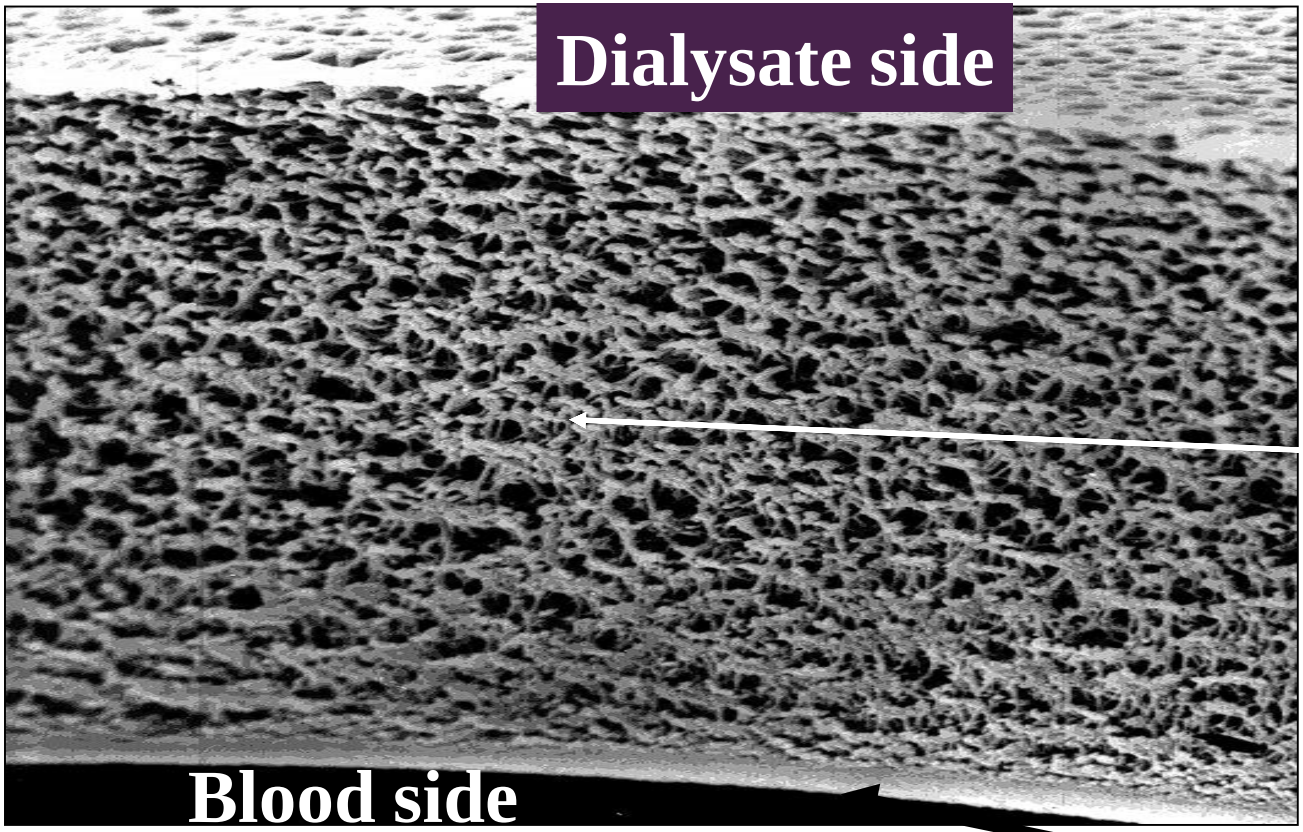


Diameter @ 200µm

Polysulfone: a sponge-like structure.

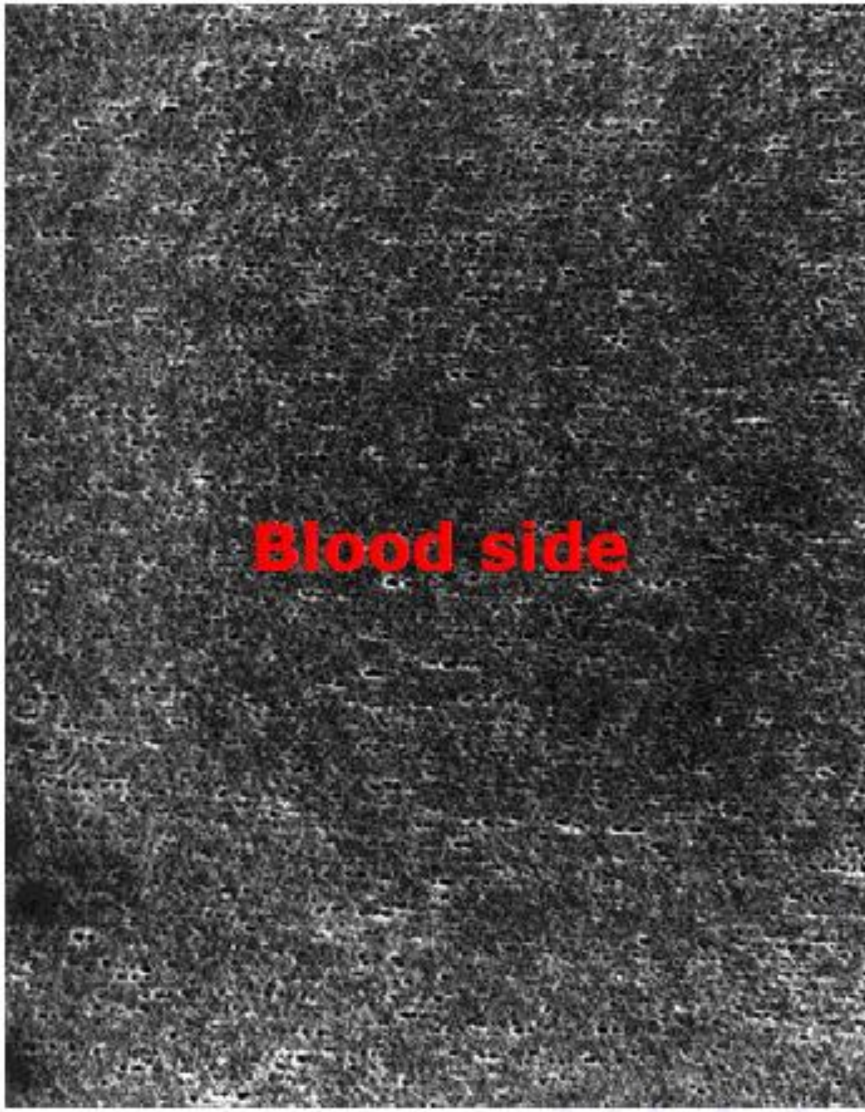


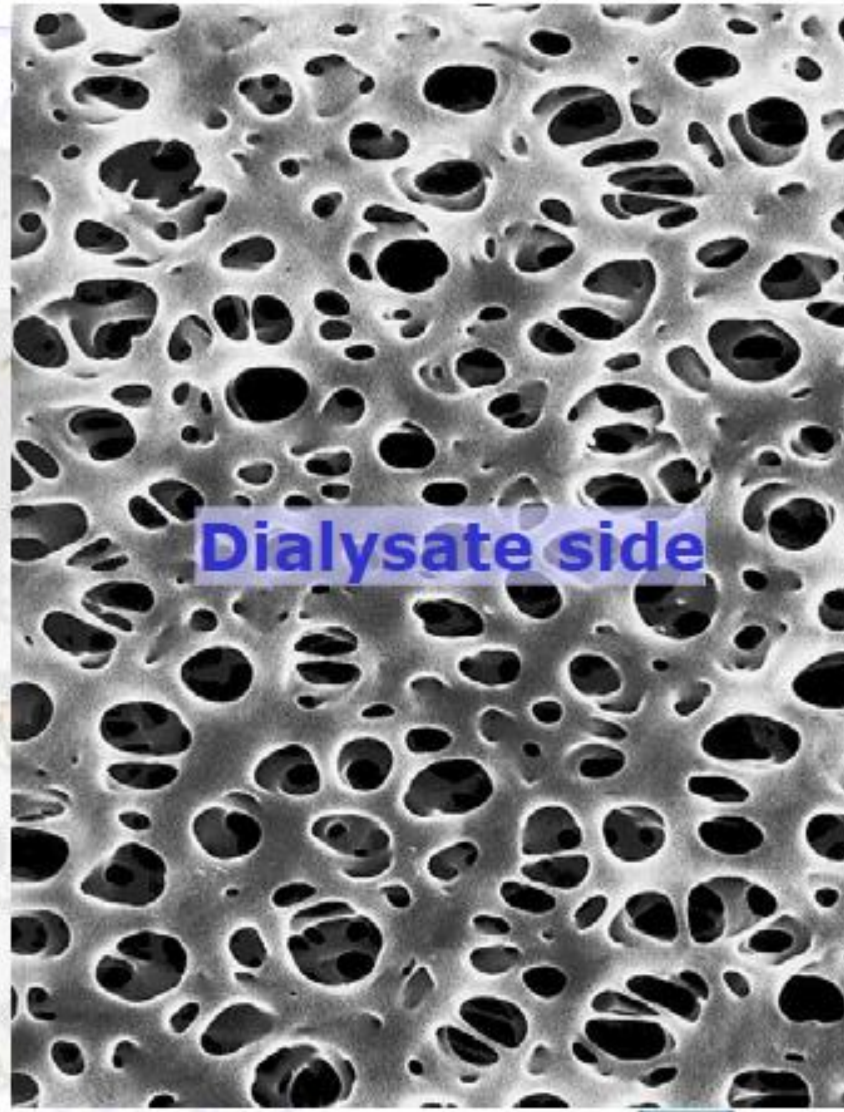
Asymmetrical synthetic membrane structure



Supporting structure (40µm)

Membrane asymmetry





Membrane physico-chemical properties

- Water repellence
  - hydrophilic: wettable: may swell: low protein adsorbance
  - hydrophobic: non-wettable: no swelling:

    protein adsorbance

- Mixed co-polymer
  - hydrophobic with hydrophilic domains,
  - e.g. PS mimics the endothelium - more biocompatible

- Electrical charge
  - negative, positive, neutral: various advantages, disadvantages and trade-offs (endotoxin retention)

Dialysis Membranes - classification by polymer type

- Cellulosic
  - **cuprophane**
- Modified Cellulosic
  - **Hemophan**
  - **Cellulose acetate**
  - **Cellulose triacetate**
  - **Saponified Cellulose esther**
  - **synthetically modified cellulose**
  - **Polysynthane**
- Synthetic
  - **Polyacrylonitrile**
  - **Polysulfone**
  - **Polycarbonate**
  - **Polyamide**
  - **Polymethylmeth-acrylate (PMMA)**
  - **Polyethylene vinyl alcohol**
  - **Polypropylene**
  - **Polyehosulfone.**

Membranes – functions of interest

1) Solute transport

2) Water transport

3) Biocompatibility

1. Solute transport

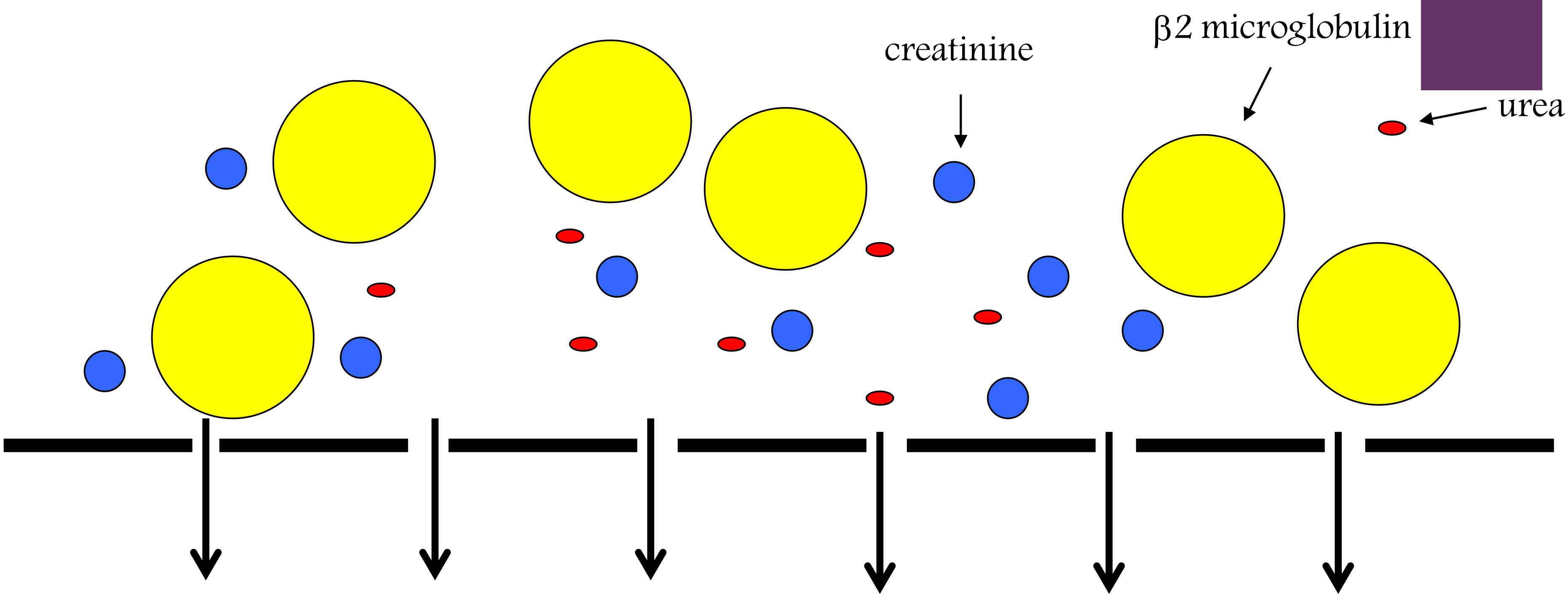
Diffusion most important for small solutes

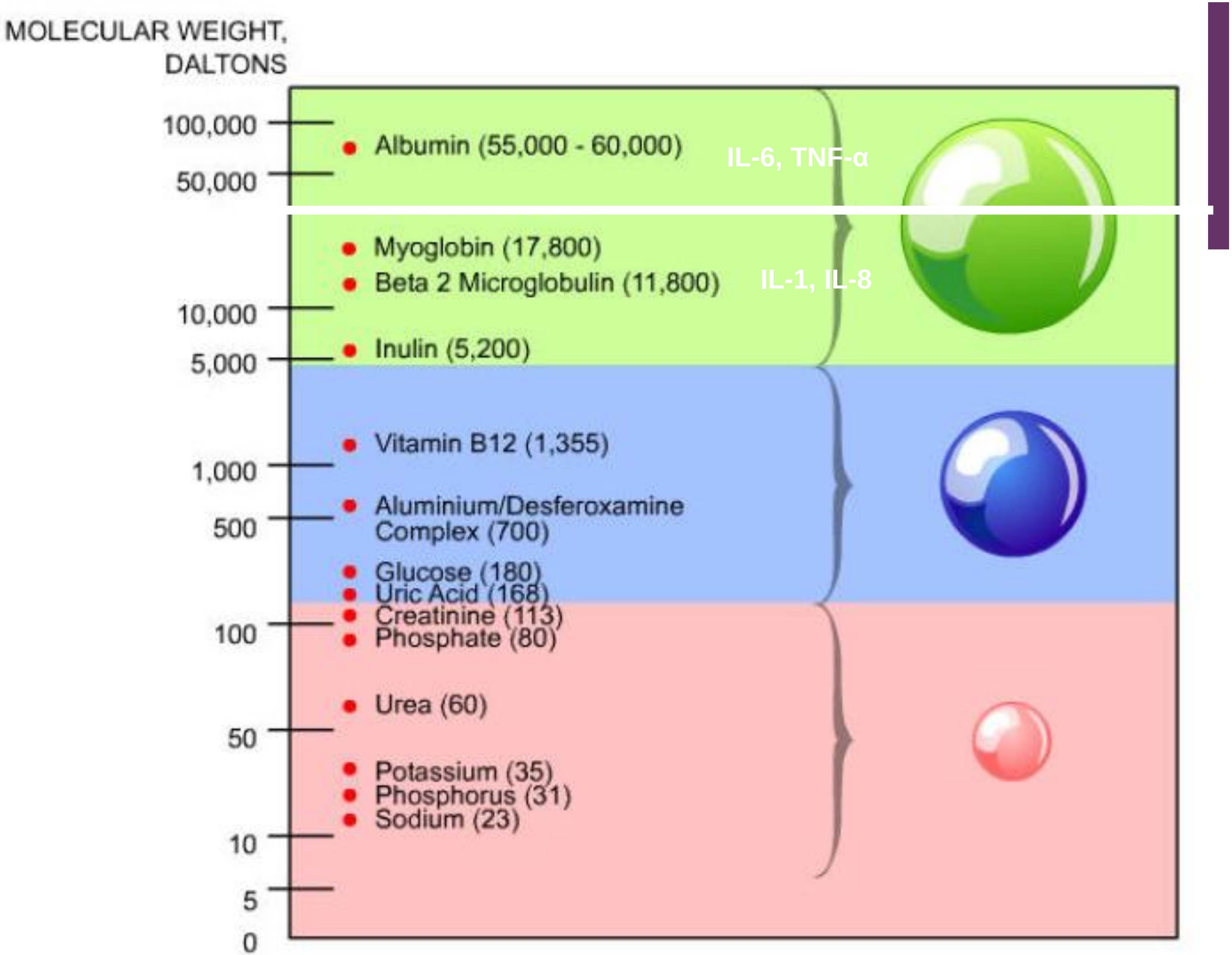
Membrane thickness limiting factor

Increased LF cellulosic clearances during last 20yrs due to reduced membrane thickness
(Hence, fragile, endotoxin transfer risk, etc.)

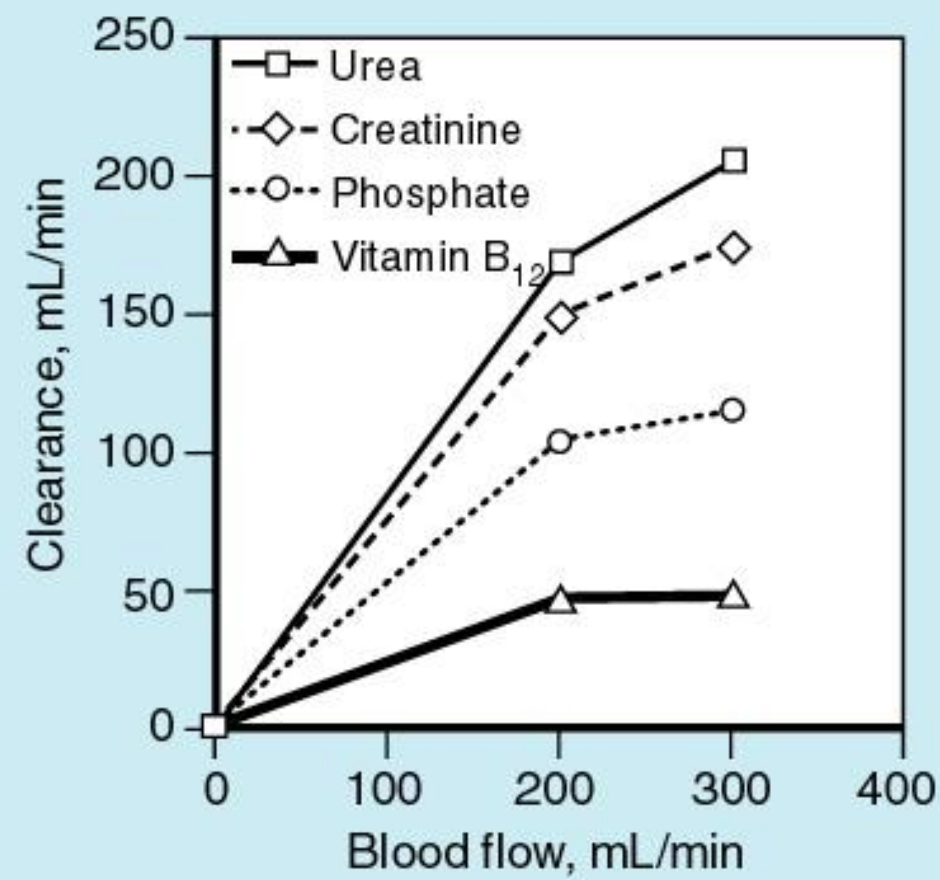
Hydrophobic membranes that adsorb a protein layer can have a reduced in-vivo clearance

Types of solutes and their clearance





MOLECULAR WEIGHT, DALTONS
100,000
50,000
10,000
5,000
1,000
500
100
50
10
5
0
Albumin (55,000 - 60,000)
IL-6, TNF-α
Myoglobin (17,800)
Beta 2 Microglobulin (11,800)
IL-1, IL-8
Inulin (5,200)
Vitamin B12 (1,355)
Aluminium/Desferoxamine Complex (700)
Glucose (180)
Uric Acid (168)
Creatinine (113)
Phosphate (80)
Urea (60)
Potassium (35)
Phosphorus (31)
Sodium (23)



Urea
Creatinine
Phosphate
Vitamin B_{12}
Clearance, mL/min
250
200
150
100
50
0
0
100
200
300
400
Blood flow, mL/min

2) Water transport

Ultra filtration:

All excess fluid must be removed from the bloodstream as the patient's blood flows through the dialyzer. The process of water removal from the bloodstream is called ultra filtration, and the amount of fluid removed is the ultra filtrate.

Hydraulic permeability is a function of pore size - dialysers classified according to their KUF

Rate of flow across membrane $\propto$ TMP

Low flux (KUF < 10ml/hr/mmHg/m2)

High flux (KUF > 20ml/hr/mmHg/m2)

Hydrophobic membranes that adsorb a protein layer can exhibit a reduction in permeability as the dialysis session progresses

3) Biocompatibility–
What does this mean?

- An ideal membrane would be inert in terms of blood activation (maximal biocompatibility)

+

- Body responses are very similar to the inflammatory & immune responses

Biocompatibility depends on...

Polymer structure

Hydrophobicity / hydrophilicity

Surface electrical charge

Protein adsorption

But not exclusively related to the membrane...

Long term responses to bioincompatibility in hemodialysis

- Dialysis related Amyloidosis (DRA)
- Accelerated loss of residual renal function
- Co morbidity
  - Anemia
  - Endothelial dysfunction and Cardiovascular disease
  - Infection
  - Malnutrition
- Impaired survival

3) Measures of bioincompatibility

Bioincompatibility is not quantifiable.
Depends on evidence of activation.

1) Thrombogenesis
2) Complement activation
3) Leukocyte activation
4) Cytokine induction
5) Oxidative stress

Measures of bioincompatibility

- Using the markers from the previous slide, a hierarchy of bioincompatibility can be constructed:
- Regenerated cellulose
- Modified cellulose
- Synthetic
- …but results can be varied

While Selecting Membrane……

- Low compliment activation, Leucopenia, Thrombogenity, and reduced morbidity.
- In-Line Steam Sterilization, Minimal Residues.
- Membrane integrity test after sterilization.
- High Capillary density.
- Membrane should be hydrophilic and hydrophobic character.
- Superior & Excellent biocompatibility, unaffected by sterilization.
- Effective Endotoxin retention - Better Patient Outcome.

Thank You

Structural differences

CELLULOSIC MEMBRANES

- Cellulosic membrane thickness: 8-12μm.
- Wettable membranes form a “gel” with hydrated channels of uneven size (pores) through which uremic solutes diffuse & convect.

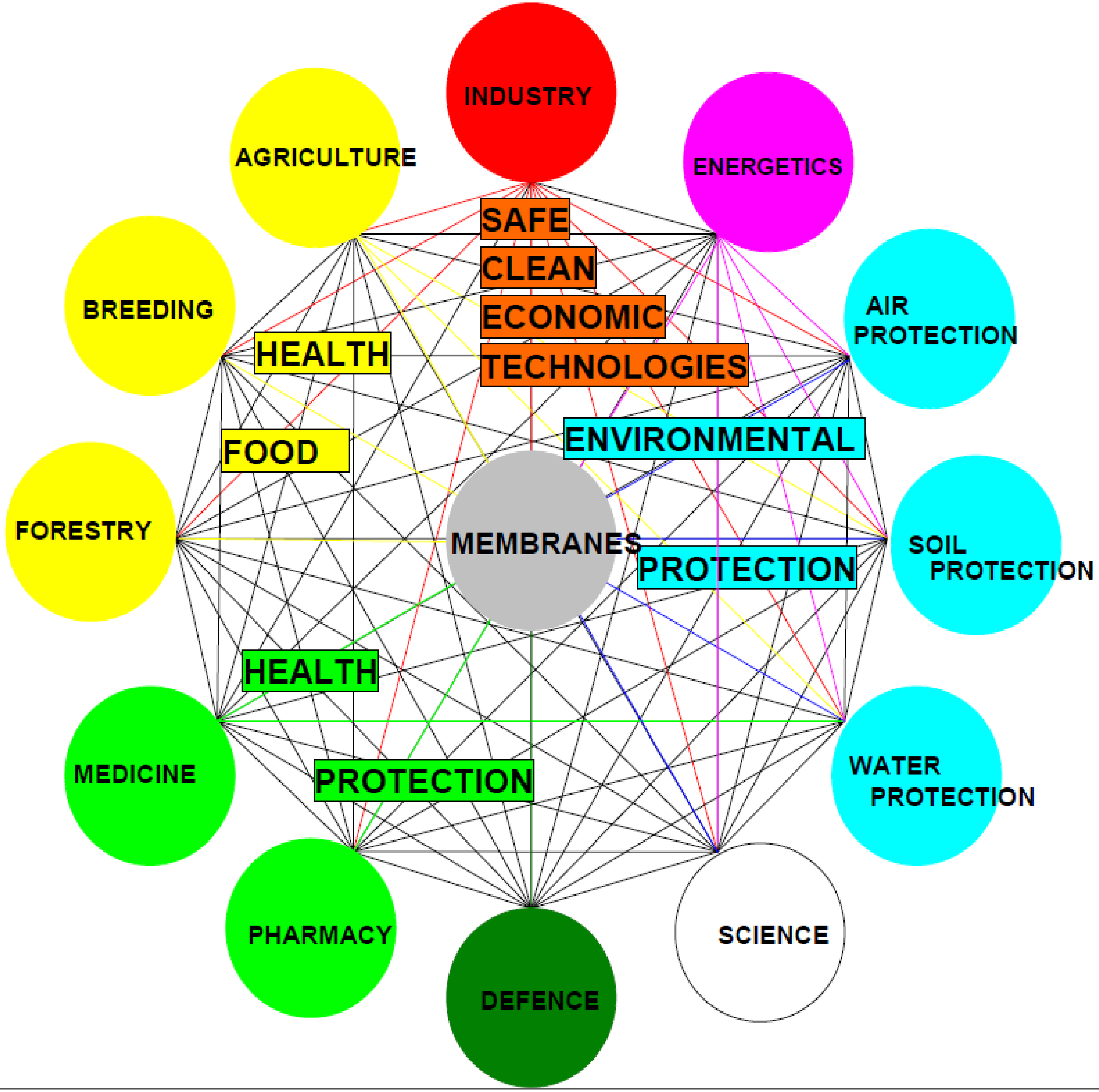
Structural differences

SYNTHETIC MEMBRANES

Skin thickness @1μm.

Supporting layer 40μm – does not reduce efficiency for solute & water transport.

Extra strength, adsorbance of dialysate contaminants, etc.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ENERGETICS
BREEDING
AIR PROTECTION
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CLEAN
ECONOMIC
TECHNOLOGIES
HEALTH
FOOD
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FORESTRY
MEMBRANES
SOIL PROTECTION
PROTECTION
HEALTH
MEDICINE
PROTECTION
WATER PROTECTION
PHARMACY
DEFENCE
SCIENCE