Membrane and Filter-Related Problems

William R. Clark, M.D.

Davidson School of Chemical Engineering

Purdue University

West Lafayette, Indiana USA

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Conflict of Interest Disclosure: William R. Clark, M.D.

- Consultant (last two years): Fresenius Medical Care; Medtronic; Nikkiso; Astute Medical
- Stock ownership: Baxter

Components of Filter Pressure Drop (ΔP)*

$$Q_B = \Delta P / (8\mu L / \pi r^4)$$

$$R = 8\mu L / \pi r^4$$

*: also called “end to end” pressure

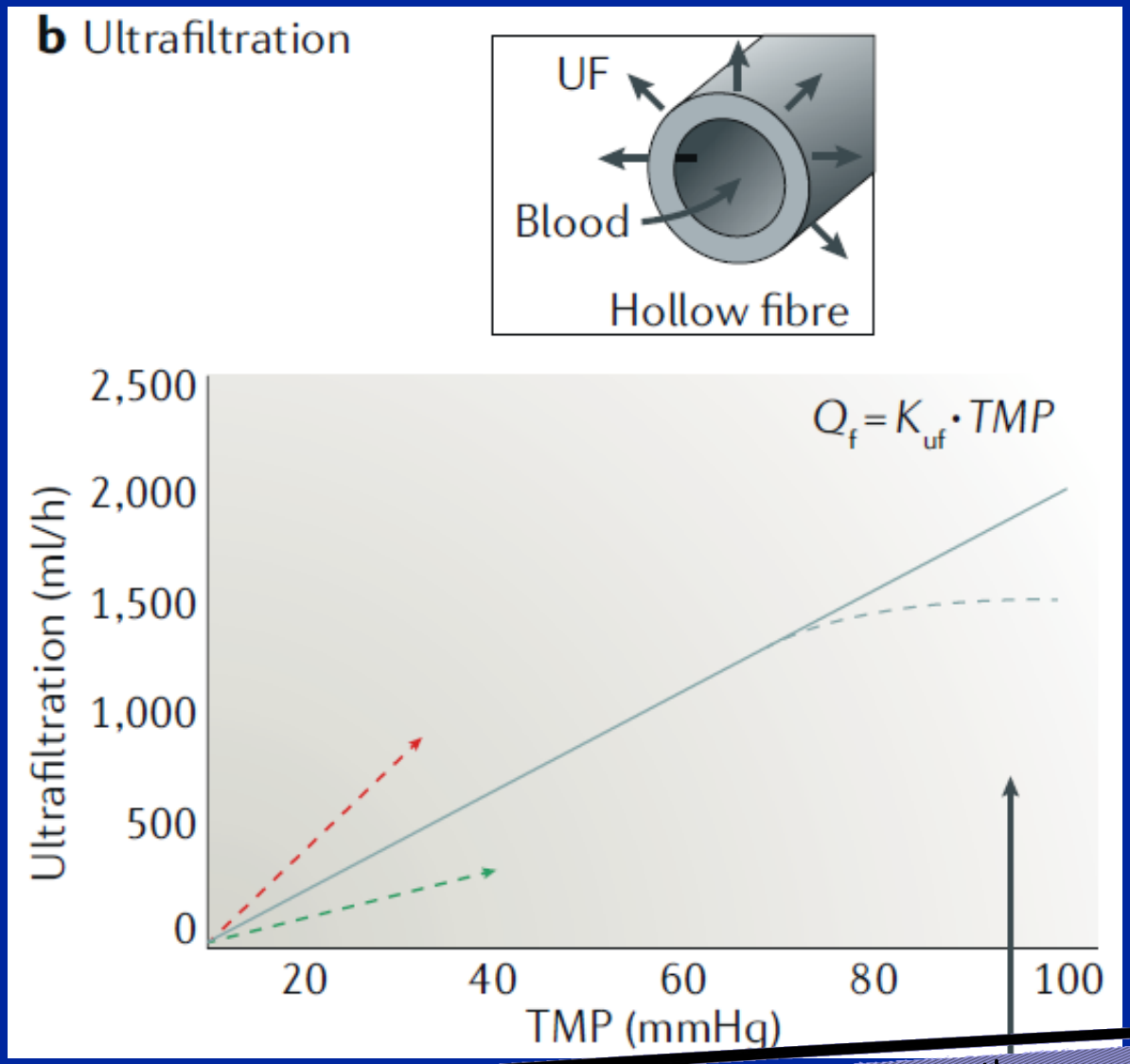
Components of TMP

Dungen et al, Int J Artif Organs 2001

$$TMP = \frac{(\text{pressure before filter} + \text{venous pressure})}{2} - \text{filtrate pressure}$$

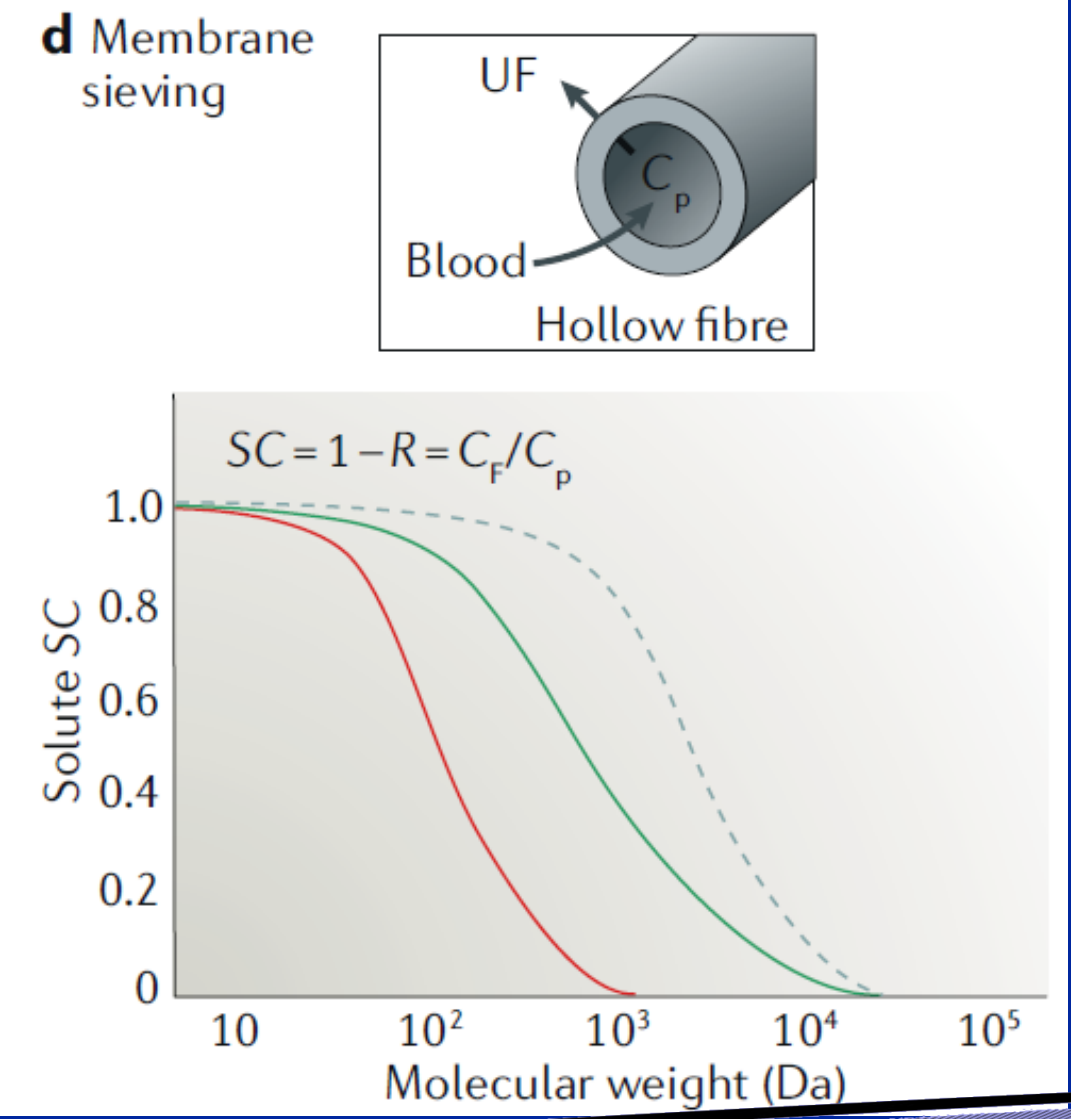
Membrane/Filter: Ultrafiltration

Ronco and Clark, Nature Revs Nephrol 2018



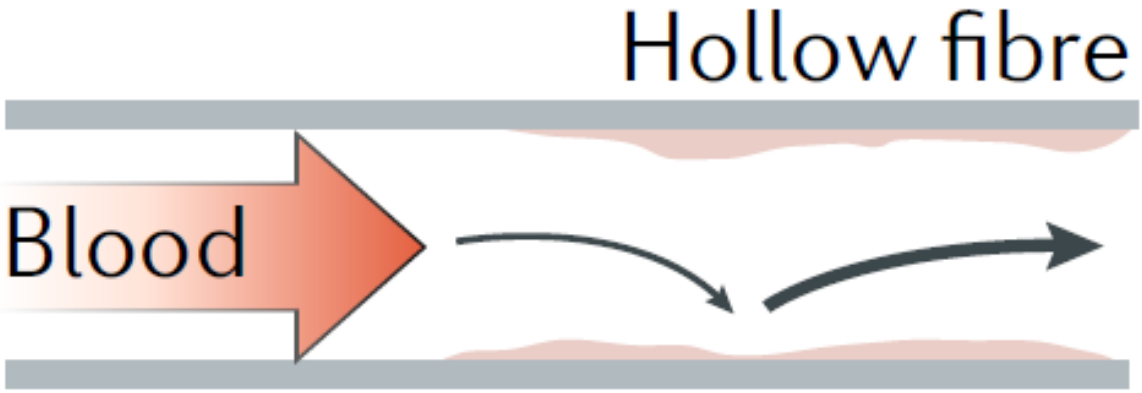
Membrane Sieving Characteristics

Ronco and Clark, Nature Revs Nephrol 2018



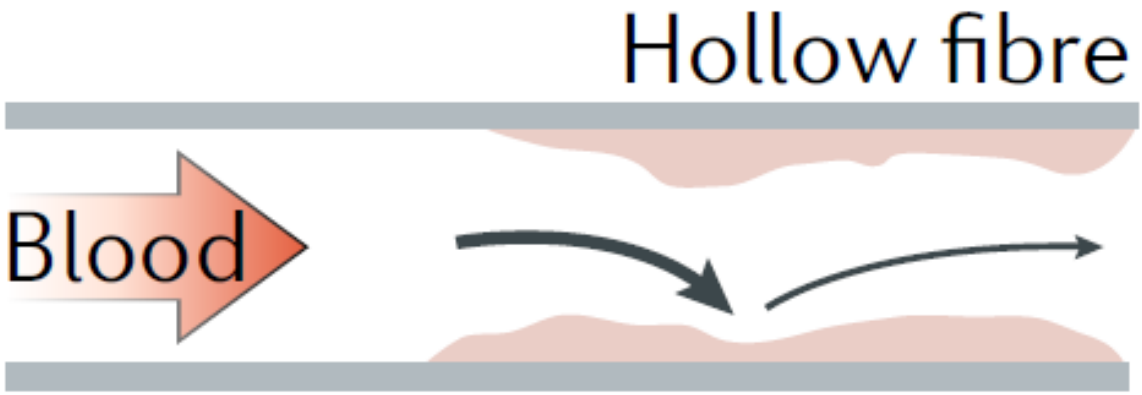
Flow Phenomena: Hemofiltration Mode

Ronco and Clark, Nature Revs Nephrol 2018



High shear rate

$SC_1 = 1 - R_1$

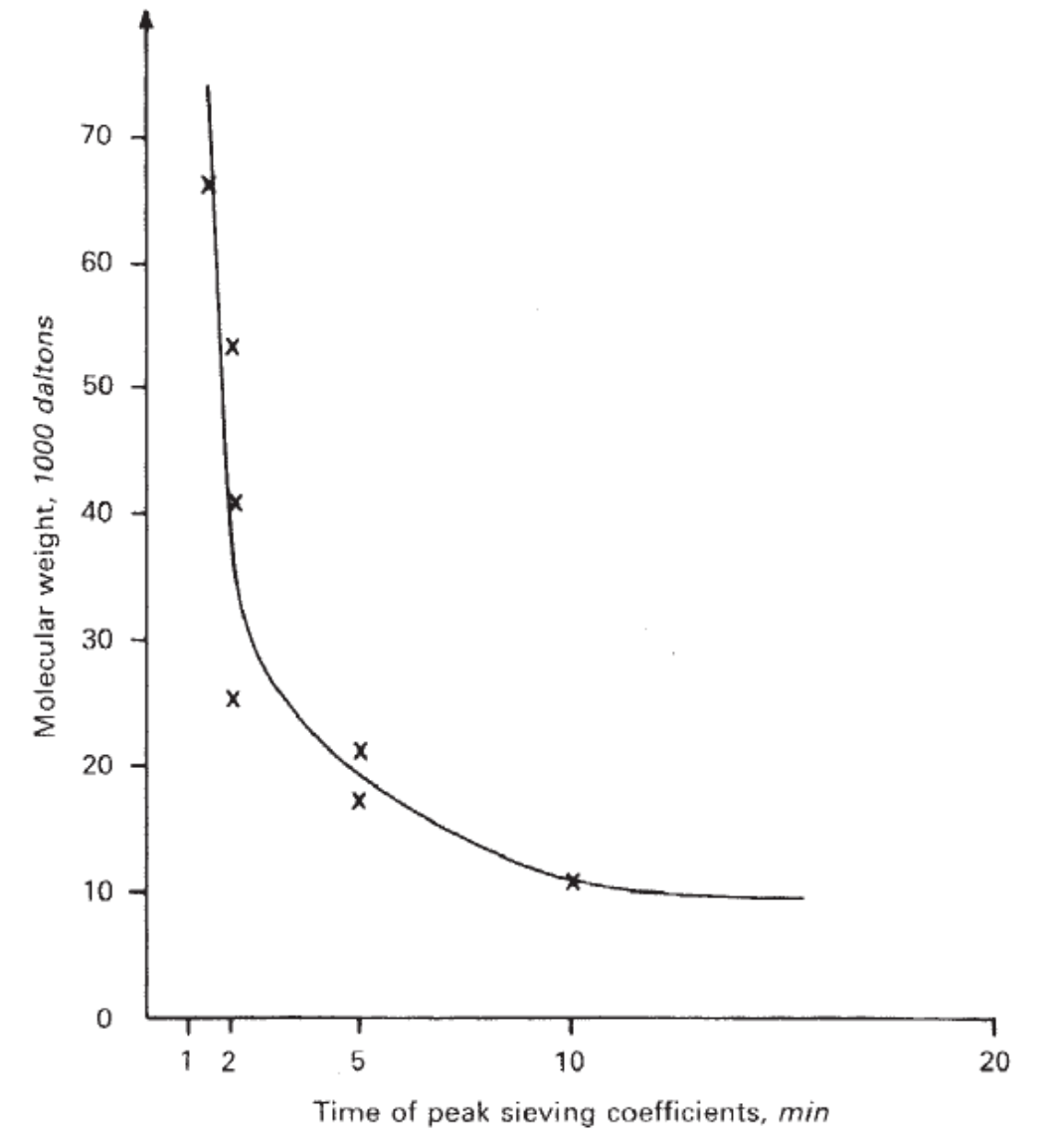


Low shear rate

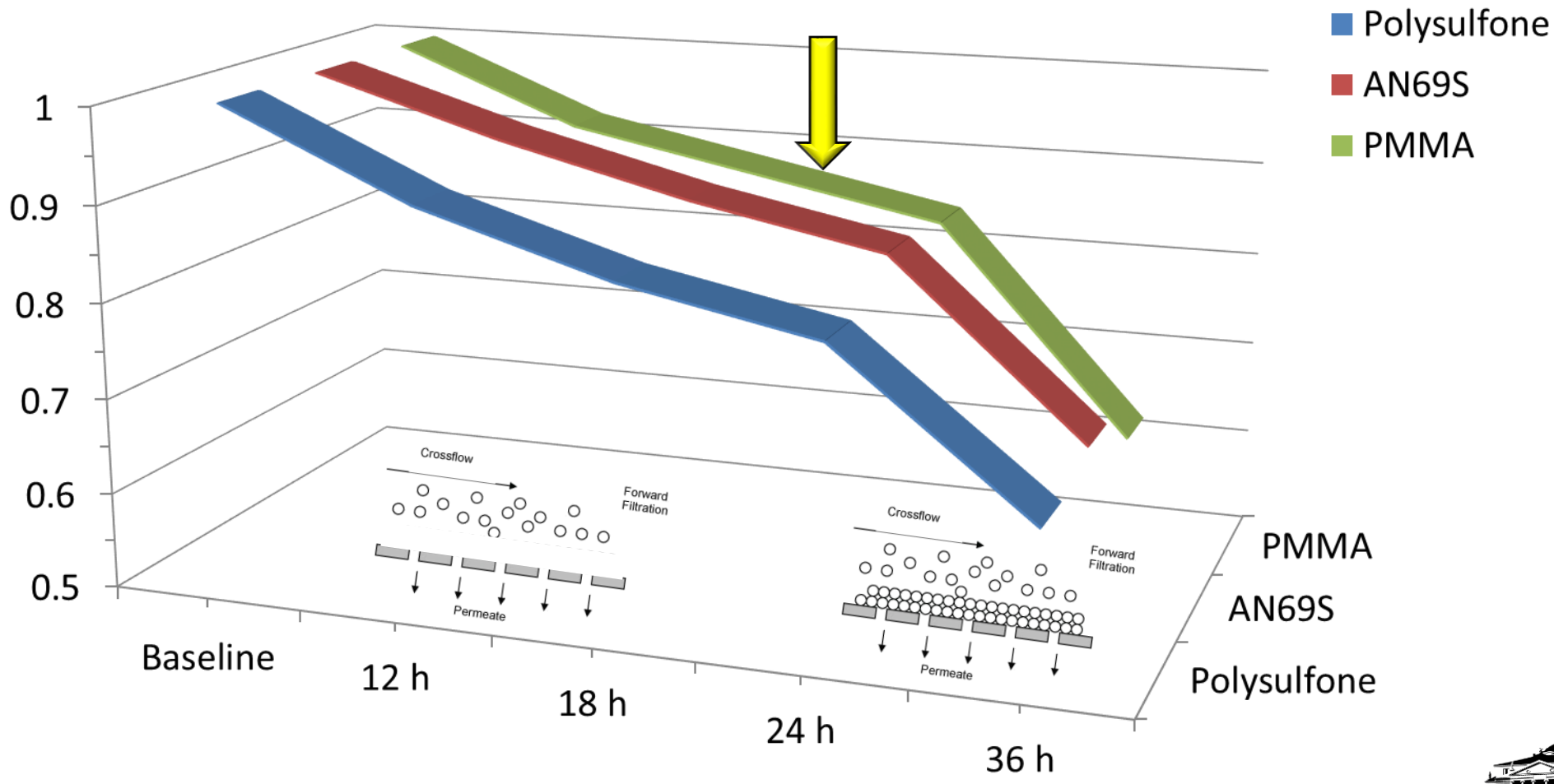
$SC_2 = 1 - R_2$

Sieving Coefficients in Chronic Hemofiltration

Rockel et al, Kidney Int 1986

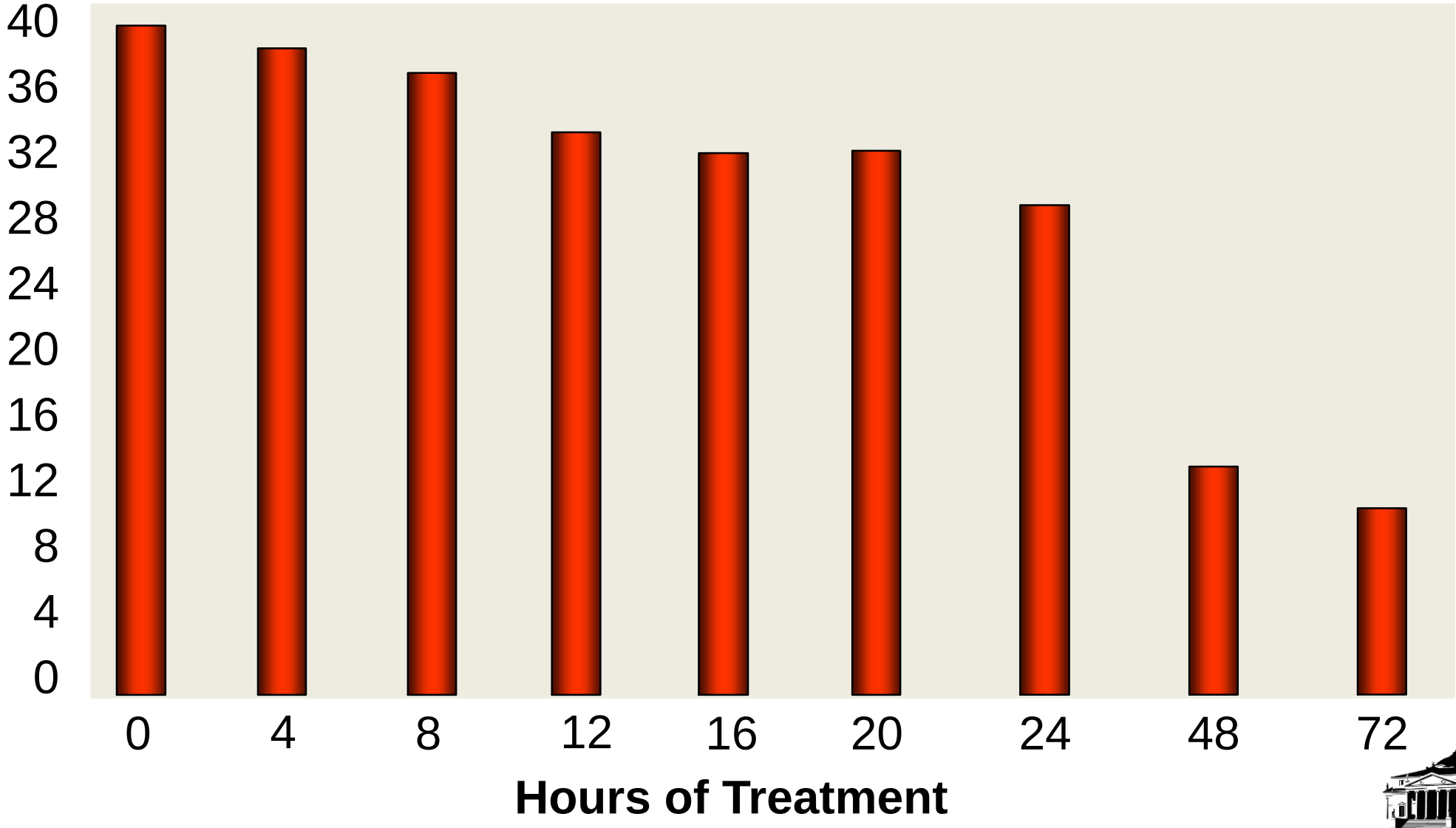


Creatinine Sieving Coefficient over Time



Slide courtesy of Prof Claudio Ronco

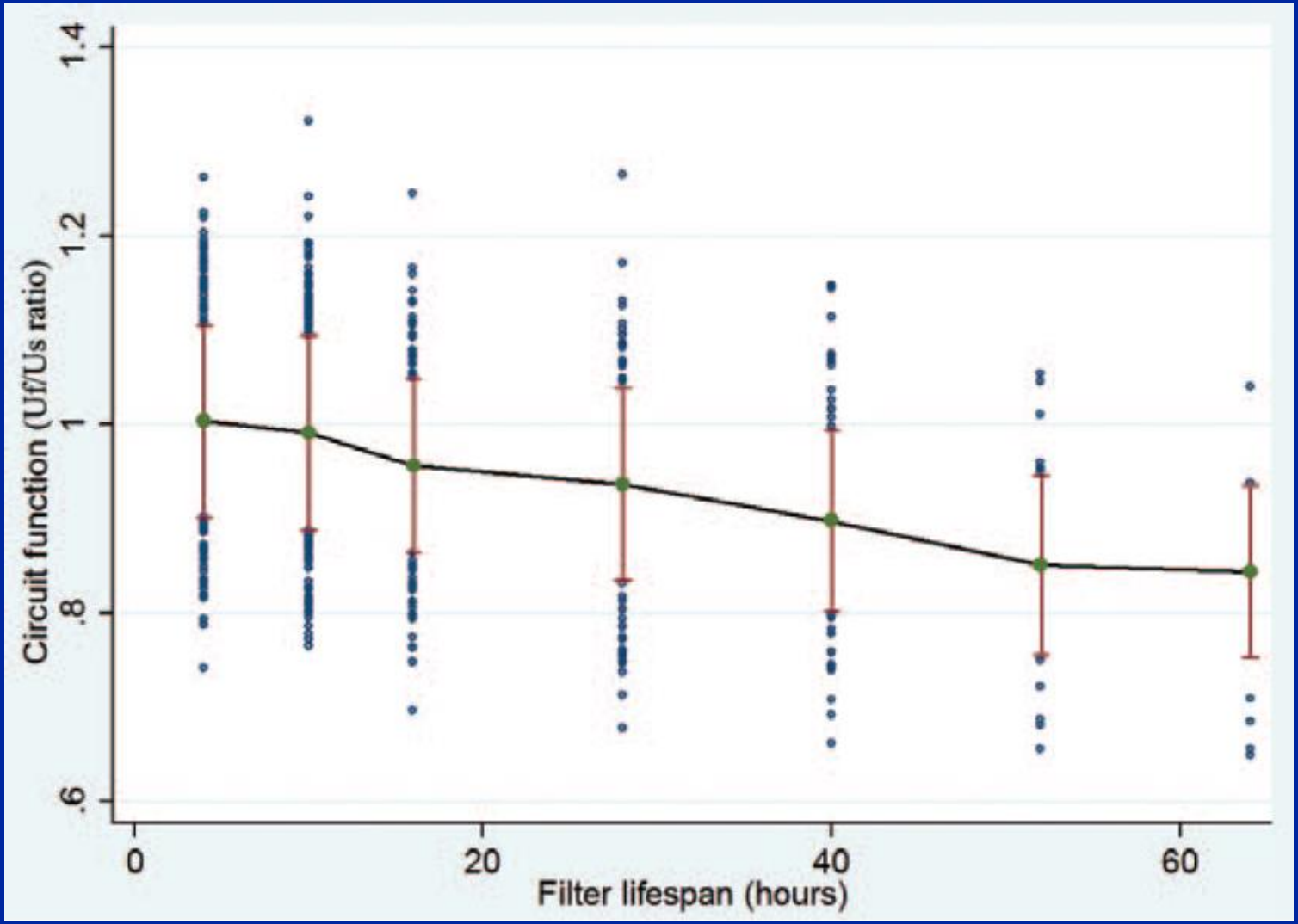
Ultrafiltration Behavior over Time (mL/min)



Slide courtesy of Prof Claudio Ronco

Urea Sieving Coefficient vs Time in Pre/Post CVVH*

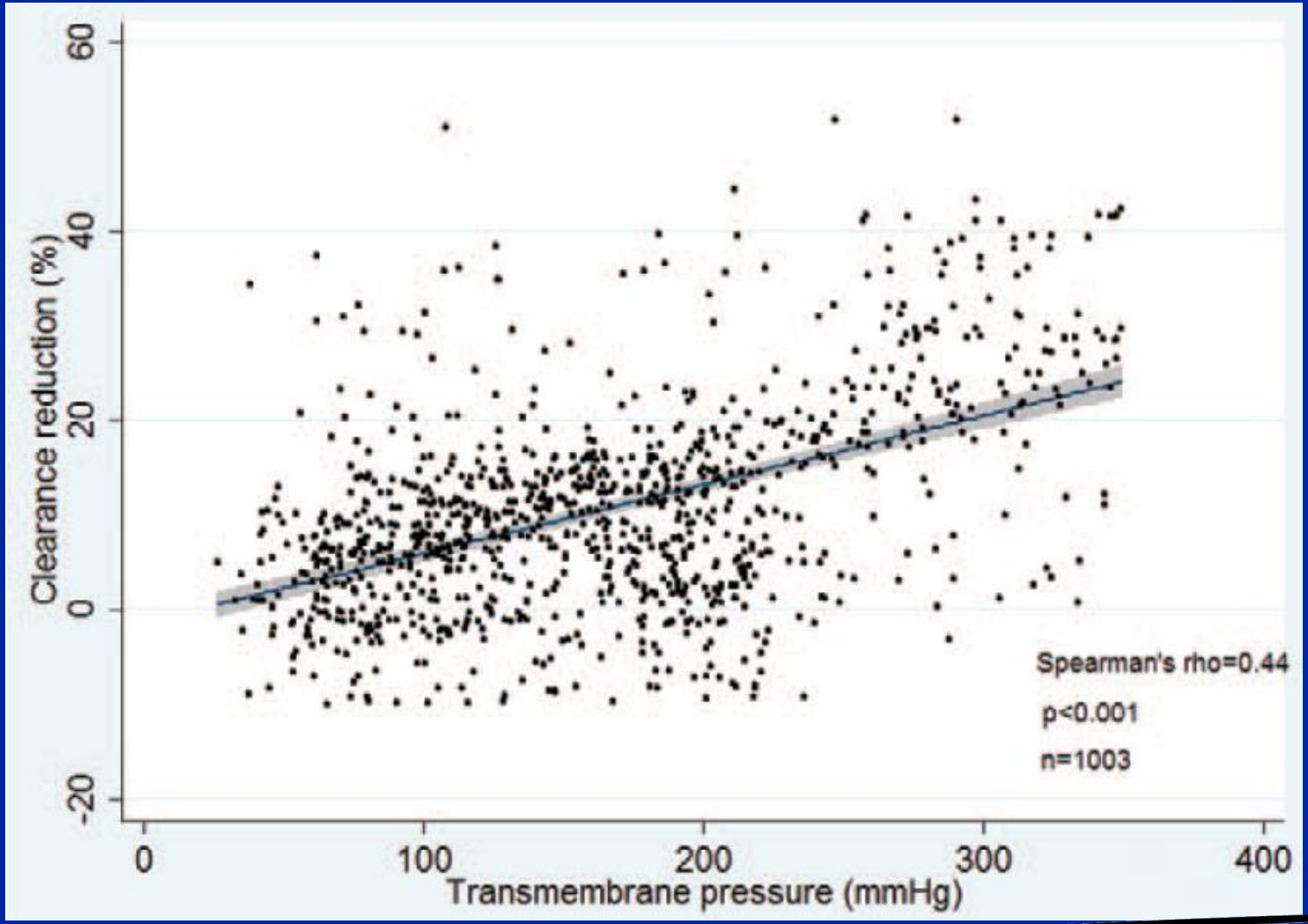
Zhang et al, ASAIO J 2013



*: heparin anticoagulation; prescribed dose 25-30 mL/kg/hr

Clearance Reduction vs TMP in Pre/Post CVVH*

Zhang et al, ASAIO J 2013



*: heparin anticoagulation

Filter-Related Pressure Changes During CRRT

- Transmembrane pressure (TMP): effect at the pore level
  - Reflects effective hydraulic permeability and sieving capabilities of filter
  - Primarily determined by secondary membrane - albumin (40 g/L), immunoglobulin G (15-20 g/L), and fibrinogen (3 g/L) are main components
  - Pore narrowing or occlusion sometimes called “clogging”
- Filter (end-to-end) pressure: effect at the fiber level
  - Fiber occlusion or narrowing due to clotting results in increased resistance to flow (due to decrease in effective pore radius) and decreased effective surface area
  - Result: decreased clearance; increased pressure required to achieve desired blood flow rate

Causes of CRRT Downtime in CVVHDF*

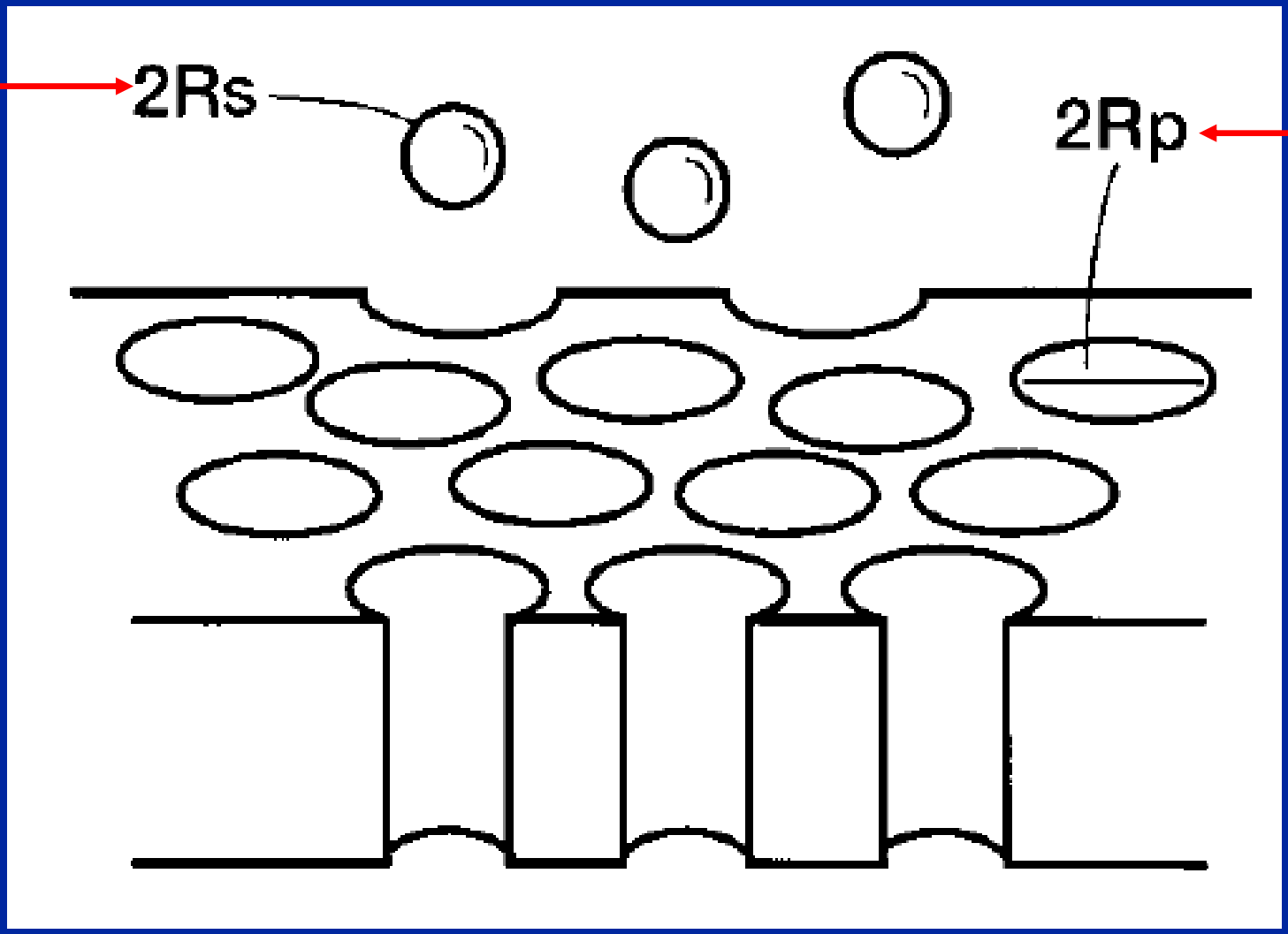
Claure et al, Clin J Am Soc Nephrol 2011

Reasons	Number of Filters	Percentage (%)	FUN/BUN Ratio
Factors affecting treatment time without affecting filter function			
D/C for surgical procedures	10	6.3	0.93 (0.92 to 0.99)
D/C for medical procedures	9	5.7	1.0 (0.95 to 1)
routine filter changes	16	10.1	0.95 (0.84 to 1.0)
machine problems	8	5.0	0.97 (0.85 to 1.0)
transition to IHD	17	10.7	0.96 (0.82 to 0.97)
venous access clot	6	3.8	0.97 (0.96 to 0.98)
physician decision	10	6.3	0.98 (0.94 to 1)
patient or family decision	11	6.9	0.96 (0.94 to 1)
patient recovery	6	3.8	0.95 (0.92 to 0.99)
death	3	1.9	0.98 (0.87 to 1.0)
access change	9	5.7	0.9 (0.87 to 0.95)
Factors affecting filter function			
filter clotted	41	25.8	0.89 (0.83 to 0.94)
filter leak	1	0.63	0.745
low-sieving concentration	12	7.5	0.86 (0.79 to 1.0)
polarization			

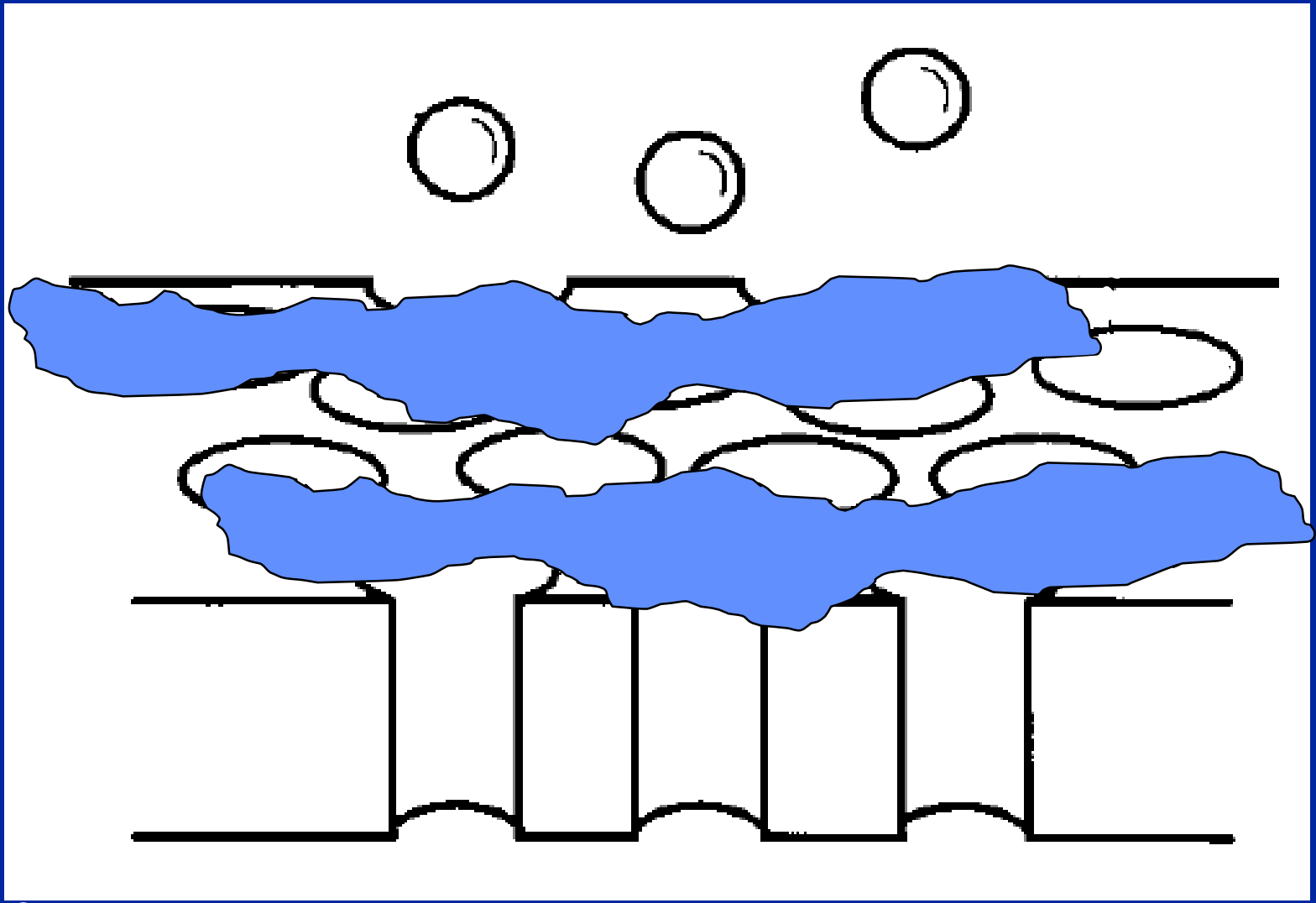
*: citrate anticoagulation

Idealized Membrane

Takeyama and Sakai, Contrib Nephrol 1998



Filter “Clogging”



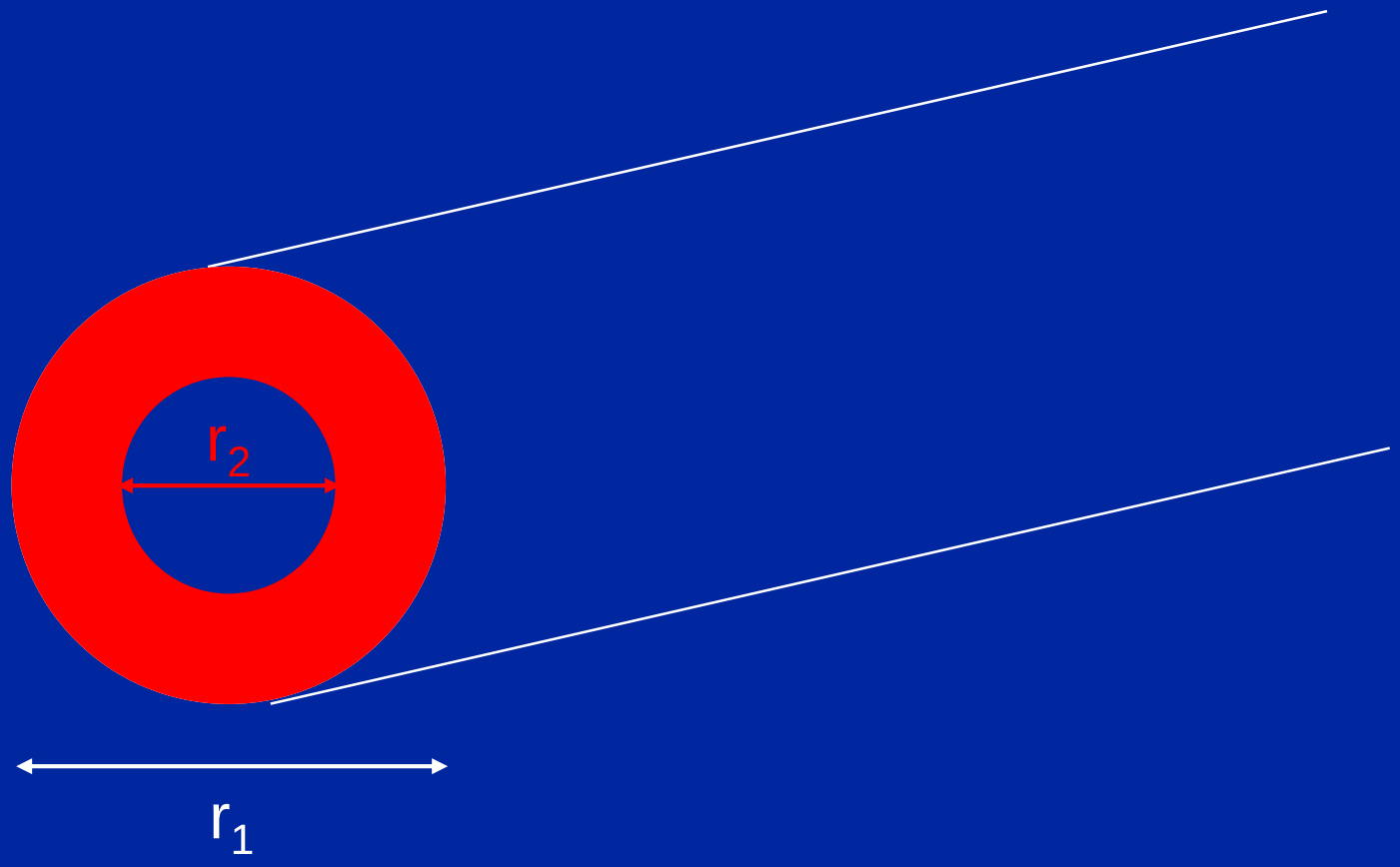
Fibrinogen:
- MW: 340 kDa
- Length: 45 nm
- Conc: 3 **g/L**

β_2-microglobulin
- MW: 11 kDa
- Length: 4.5 nm
- Conc: 1-50 **mg/L**

Pore size: ~5 nm

Adapted from Takeyama and Sakai, Contrib Nephrol 1998

Filter Clotting

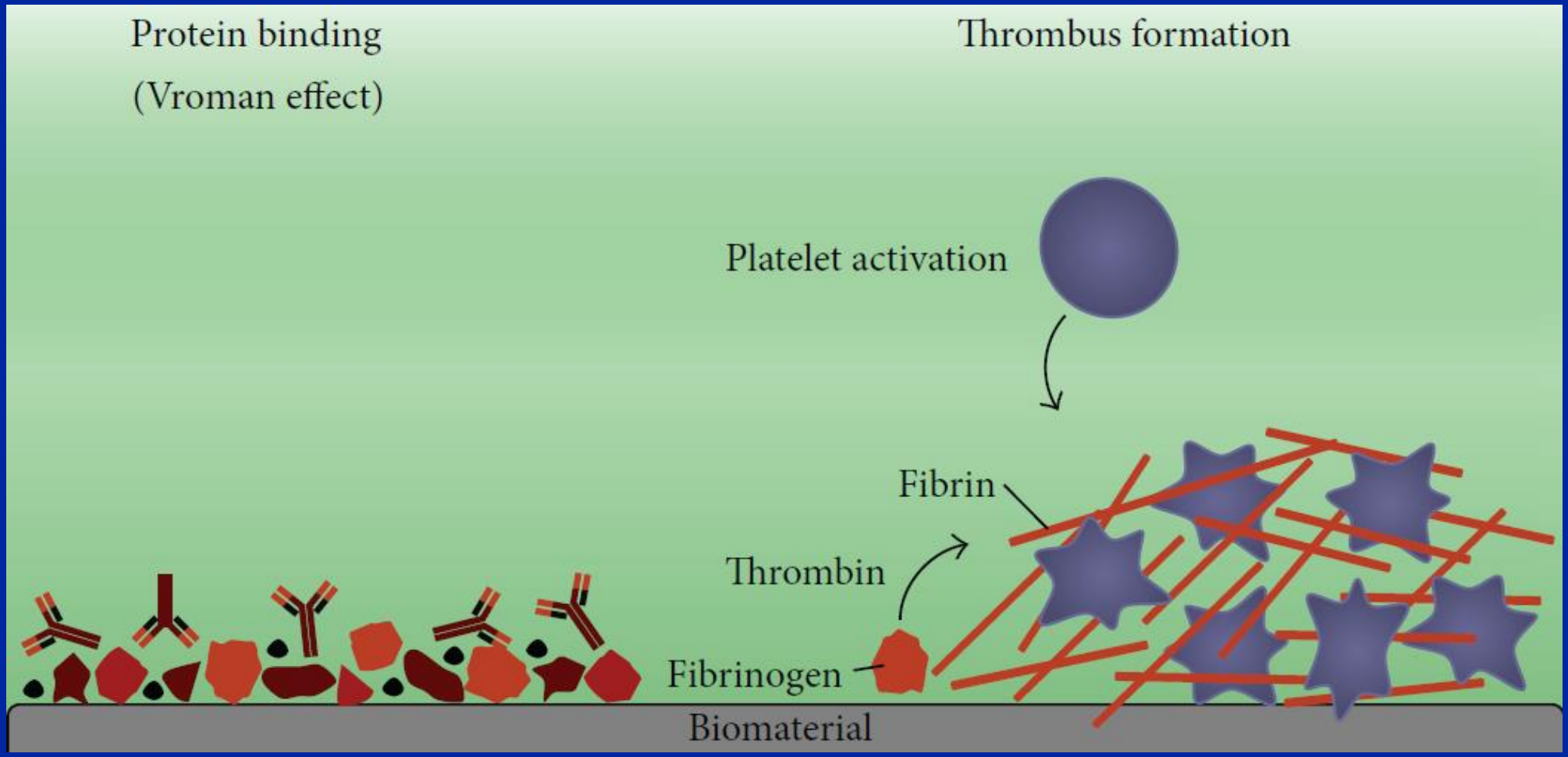


$$Q_B = \Delta P / (8\mu L / \pi r^4)$$

$$R = 8\mu L / \pi r^4$$

Biomaterial-Induced Thrombus Formation

Christo et al, Biomed Res Int 2015



Mitigation Steps

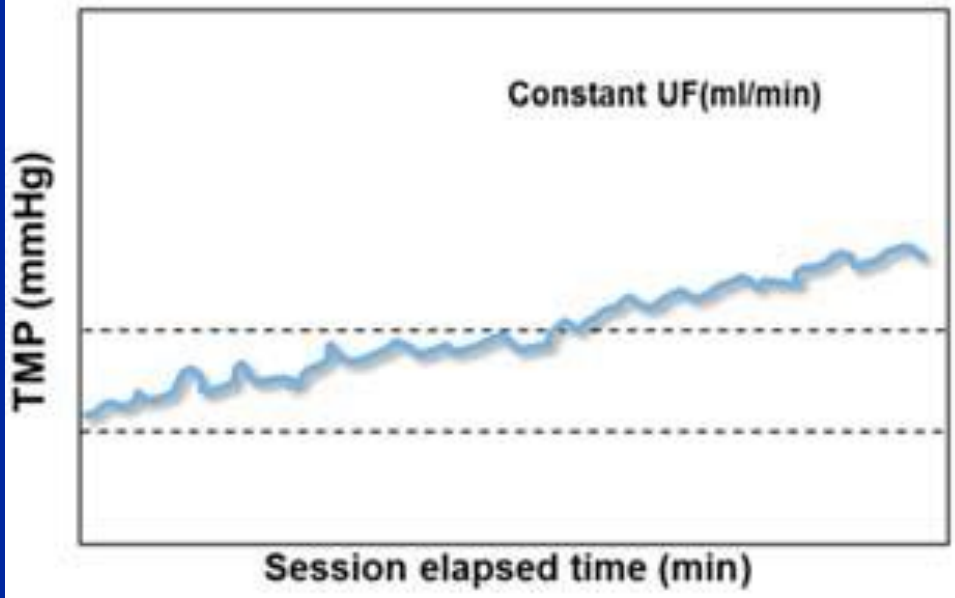
- Filter clotting
  - Adequate anticoagulation (RCA)
  - Pre-dilution techniques
  - Maintaining filtration fraction in target range
  - Influence of modality?
- Filter clogging
  - Adequate blood flow (based on surface area of filter) – access is critical
  - Pre-dilution techniques
  - Maintaining filtration fraction in target range
  - Influence of modality

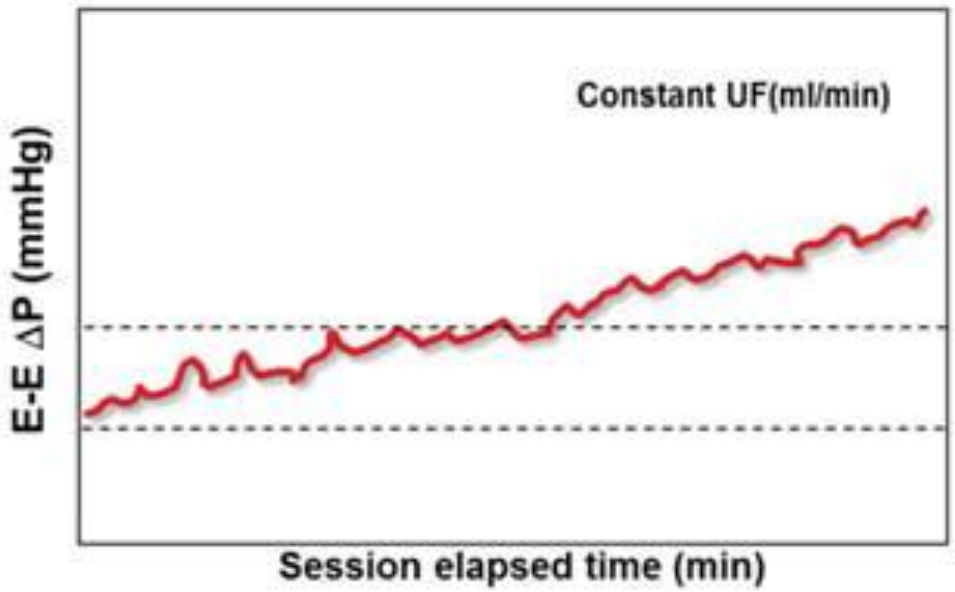
Changes During Course of OLHDF Treatment

Ronco, Blood Purif 2015

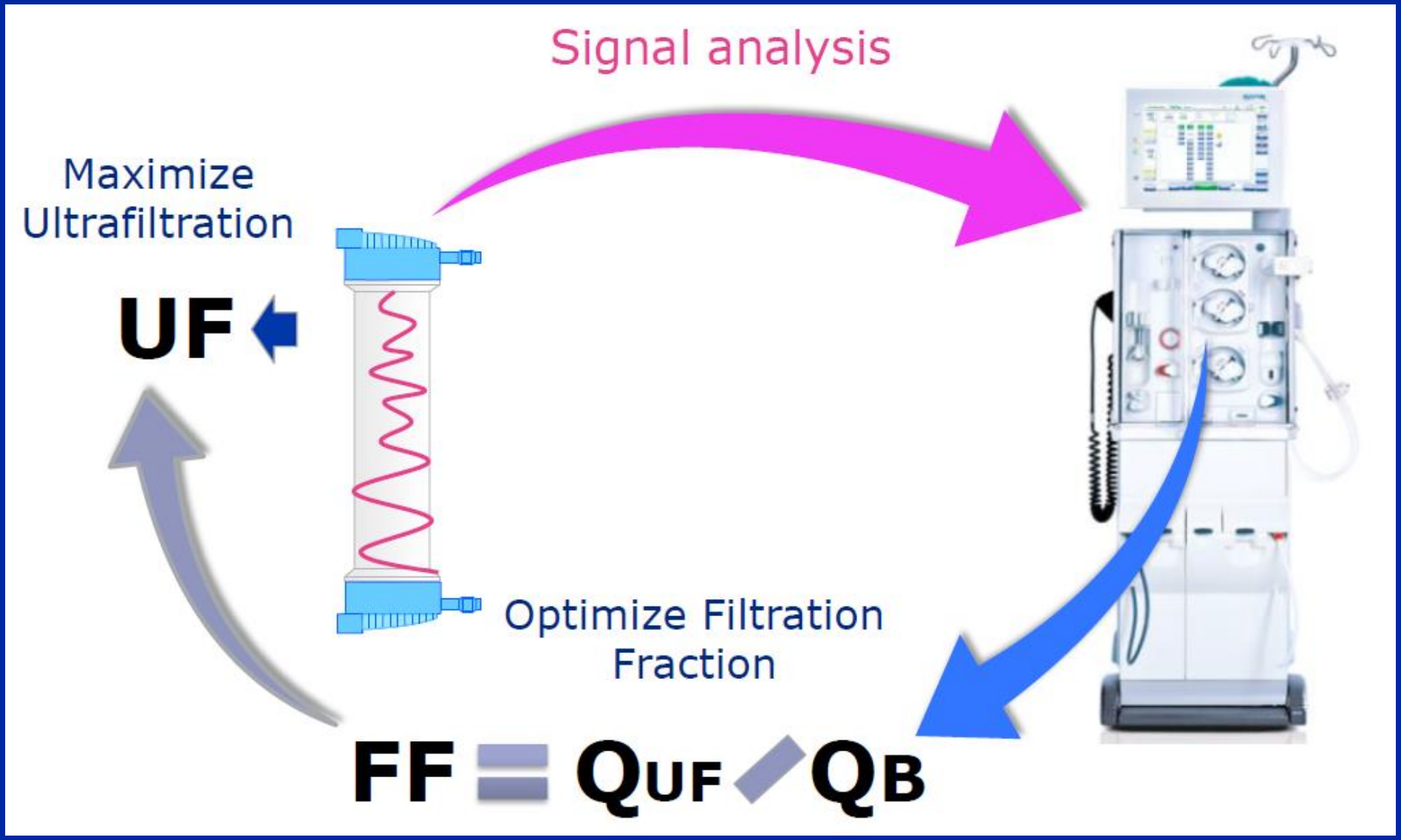
High Filtration Fraction
Membrane fouling
Fibers clotting
Hemoconcentration

High flow resistance
Increase in TMP
Reduced CS Area
High blood Viscosity





Automated Administration of Substitution Fluid



Slide courtesy of Dr. Bernard Canaud

Summary

- Both membrane clotting and clogging are important phenomena which have a detrimental impact on CRRT delivery
  - The surrogates for these phenomena are filter pressure drop and TMP, respectively
- Although regional citrate anticoagulation (RCA) prolongs CRRT filter life, very little is known about longitudinal filter performance
- In addition to RCA, interventions that potentially mitigate clotting and clogging include pre-dilution mode, higher blood flow rates, and careful control of filtration fraction
- In the future, chronic dialysis techniques used to preserve filter function may be adapted as a way to maintain CRRT filter performance over time