Selective use of membranes in on-line HDF

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Selective use of membranes in on-line HDF

1. *Introduction*
2. **Modifications of HDF**
3. **Membrane Materials**
4. **Ultrafiltration and Adsorption**
5. **Conclusions**

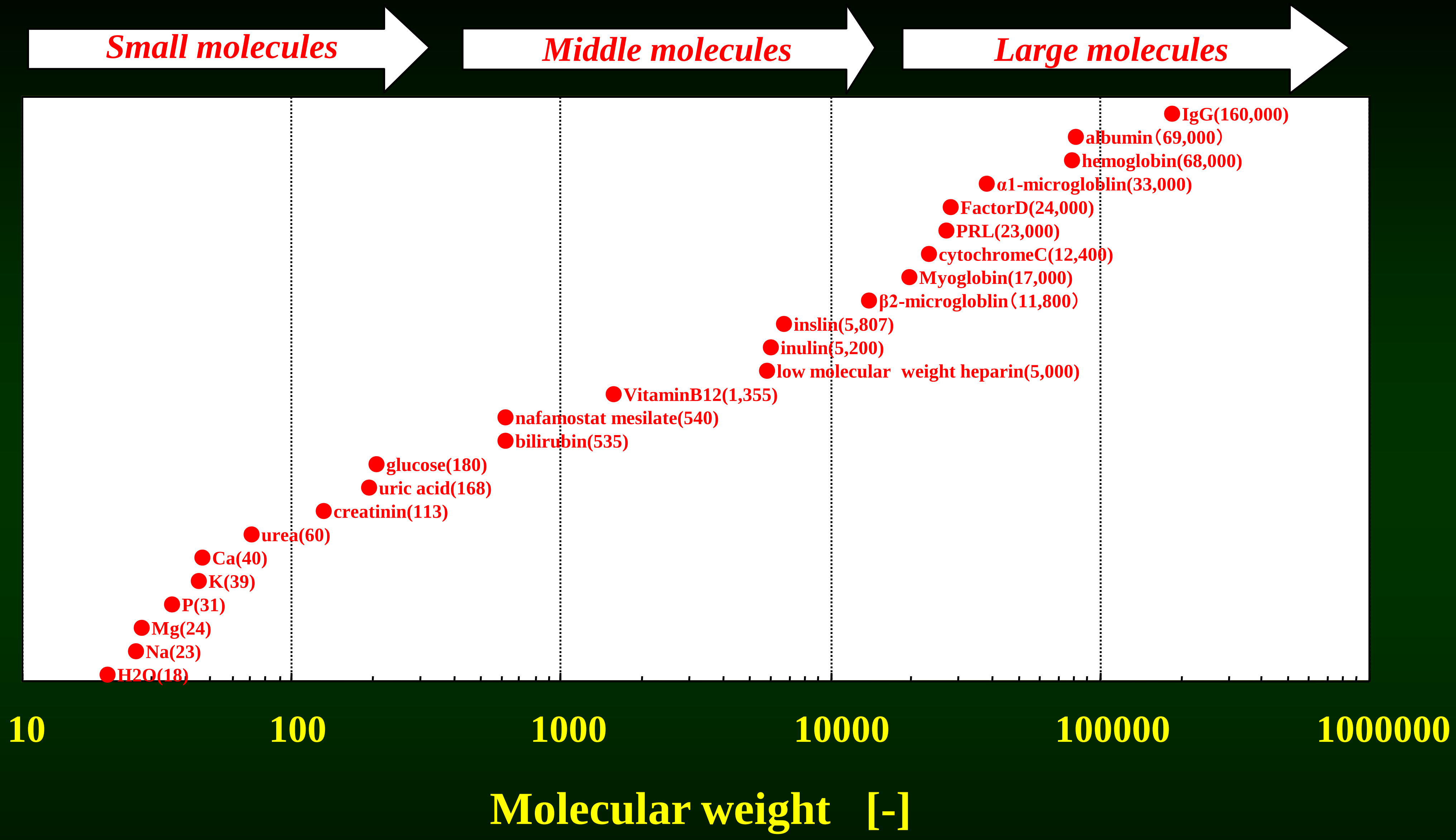

Fig.1 Molecular weight of target substances in renal replacement therapy

Table 1 Uremic toxin of middle molecule（22 types）

(molecular weight)

Adrenomedullin	(5,729)	Hyaluronic acid	(25,000)
Atrial natriuretic peptide	(3,980)	Interleukin-1b	(32,000)
β2-microglobulin	(11,800)	Interleukin-6	(24,500)
β-endorphin	(3,465)	κ-lg light chain	(25,000)
Cholesystolinin	(3,866)	λ-lg light chain	(25,000)
Clara cell protein	(15,800)	Leptin	(16,000)
Complement factor D	(23,750)	Methionine-enkephalin	(555)
Cystain C	(13,300)	Neuropeptide Y	(4,272)
DIP-I	(14,100)	PTH	(9,225)
Delta-sleep inducing peptide	(848)	Retinol-binding protein	(21,200)
Endothelin	(4,283)	TNF-α	(26,000)

Vanholder R, et al. Review on uremic toxins: Classification, concentration, and interindividual variability, KI, 63(2003), pp.1934-1943

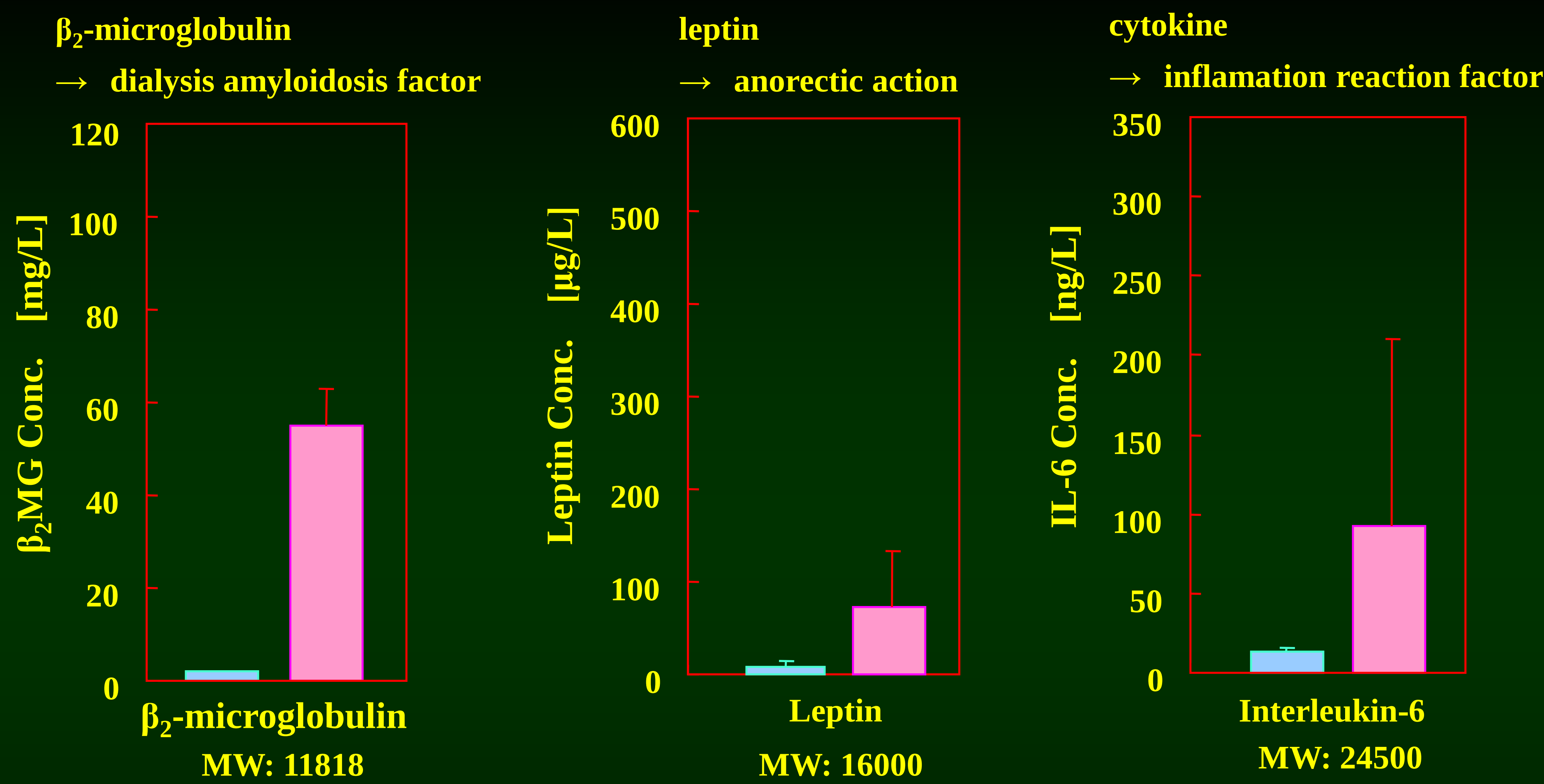

Fig.2 Middle molecules -- *uremic toxins*

Vanholder R, et al. Review on uremic toxins: Classification, concentration, and interindividual variability, KI, 63(2003), pp.1934-1943

Table 2 Uremic toxin of protein-bound solute（25 types）

(molecular weight)

2-methioxyresorcinol	(140)	Melatonin	(126)
3-deoxyglucosone	(162)	Methylglyoxal	(72)
CMPF	(240)	N-(carboxymethyl)lysine	(204)
Fructoselysine	(308)	P-cresol	(108)
Glyoxal	(58)	Pentosidine	(342)
Hippuric acid	(179)	Phenol	(94)
Homocysteine	(135)	P-OH hippuric acid	(195)
Hydroquinone	(110)	Putrecine	(88)
Indole-3-acetic acid	(175)	Quinolinic acid	(167)
Indoxyl sulfate	(251)	Retinol-binding plotein	(21,200)
Kinurenine	(189)	Sperimidine	(145)
Leptin	(16,000)	Spermine	(202)

Vanholder R, et al. Review on uremic toxins: Classification, concentration, and interindividual variability, KI, 63(2003), pp.1934-1943

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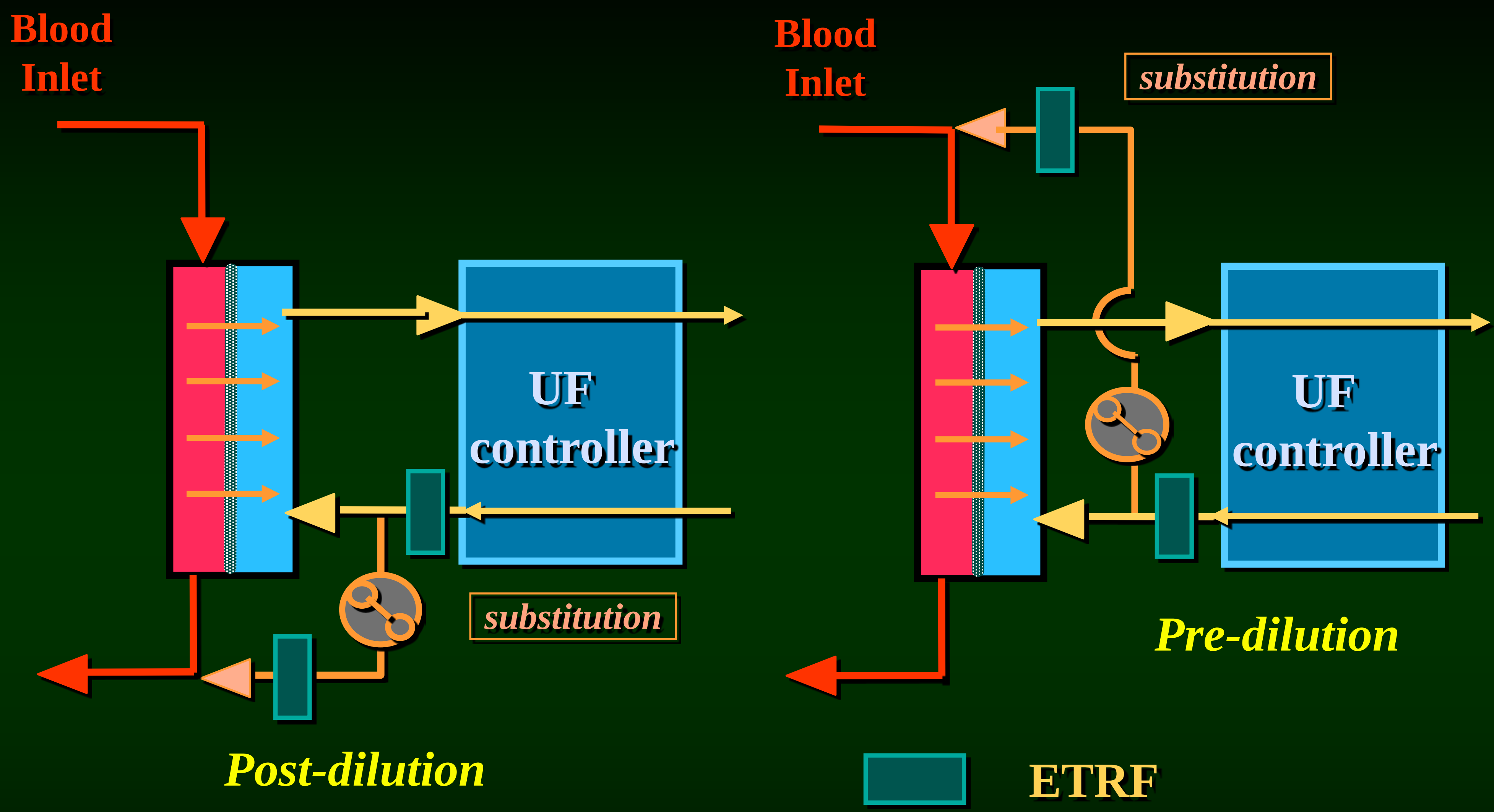

Fig.3 On-line HDF

Rindi P, *et al.*: Trans ASAIO, 34, 765, 1988.

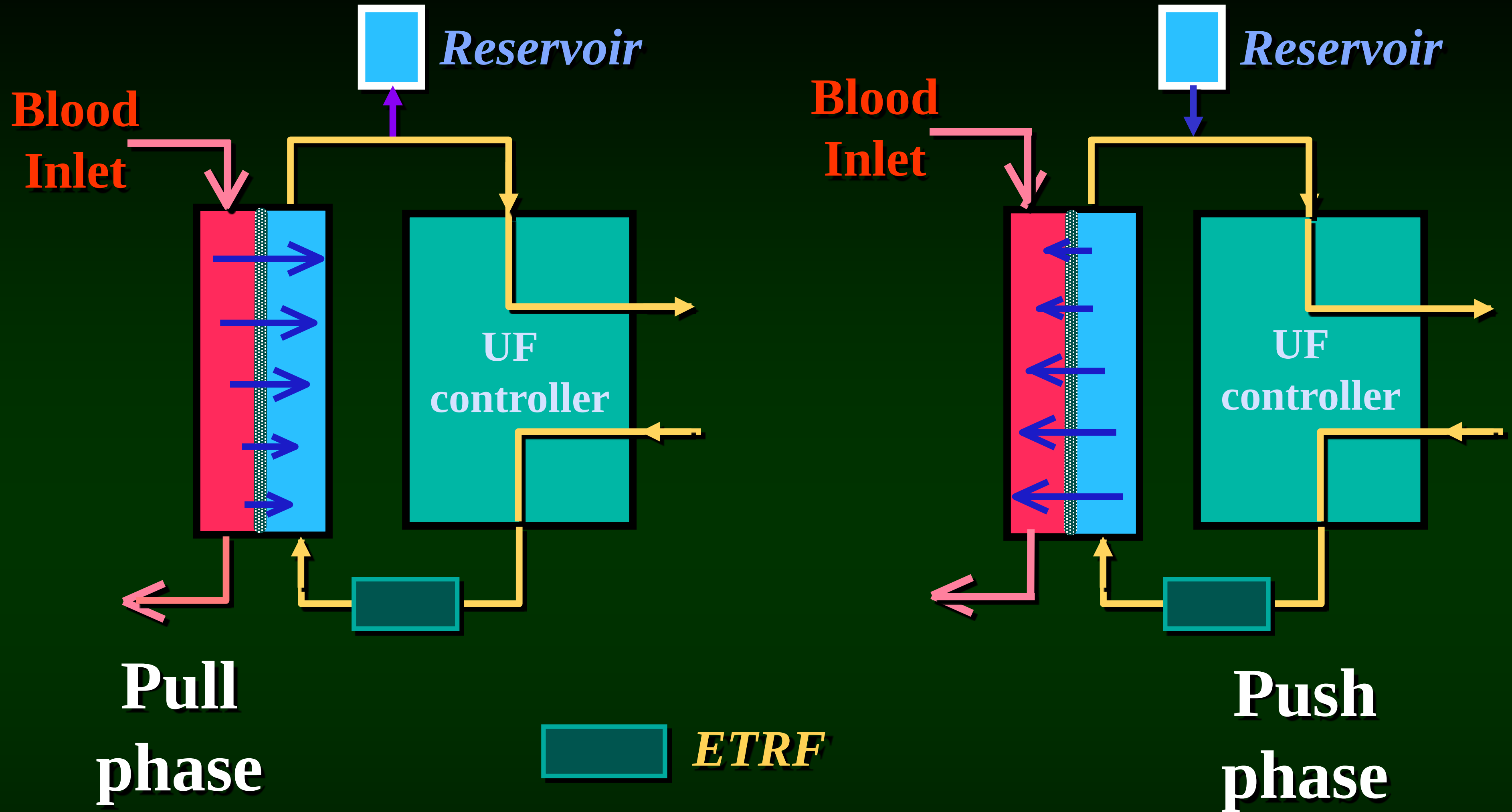

Fig.4 Push & pull HDF

Usuda M, *et al.*: Trans ASAIO, 28, 24, 1982.

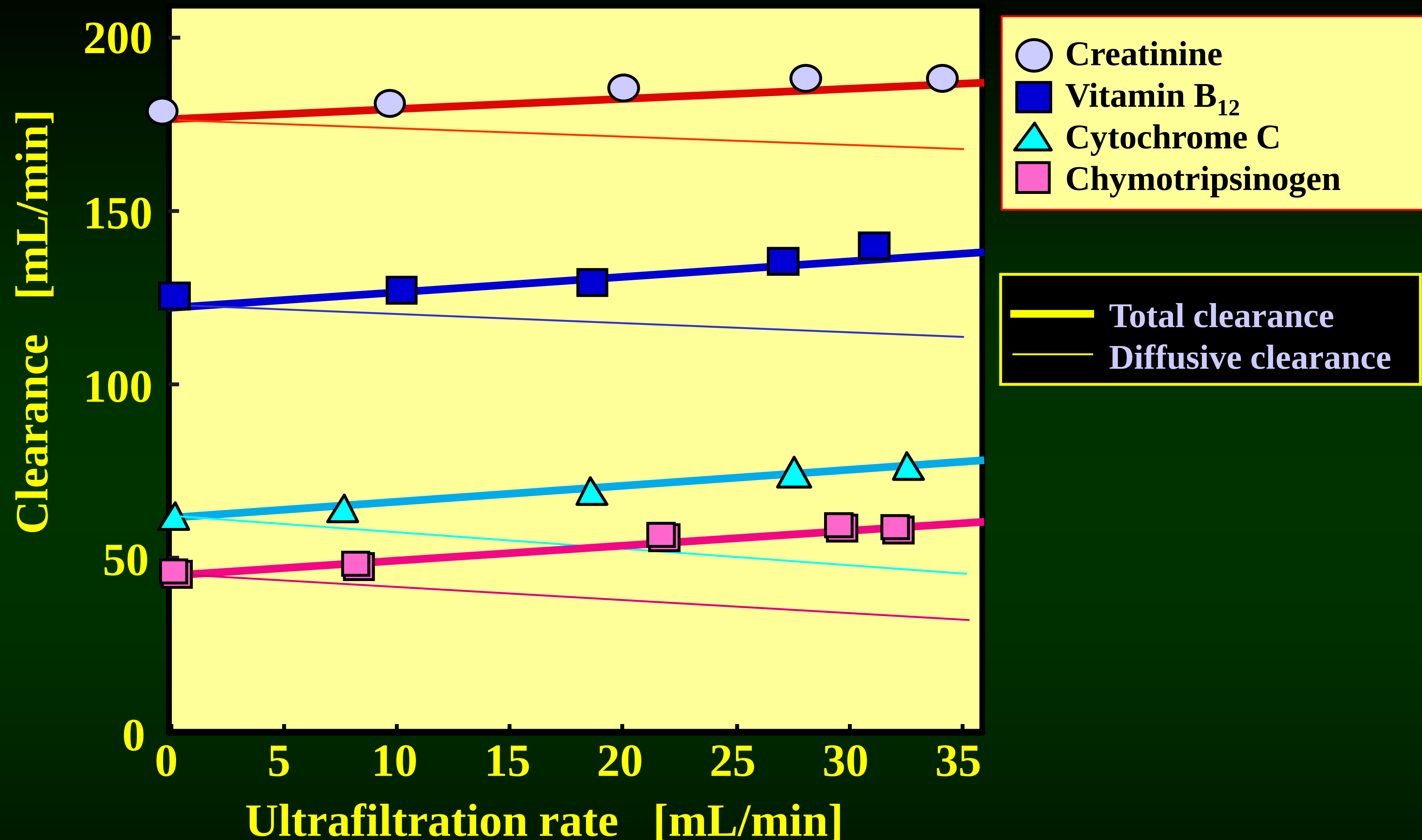

Fig.5 Relationship between clearances and ultrafiltration rate (aqueous *in vitro*; FB-150F dialyzer)

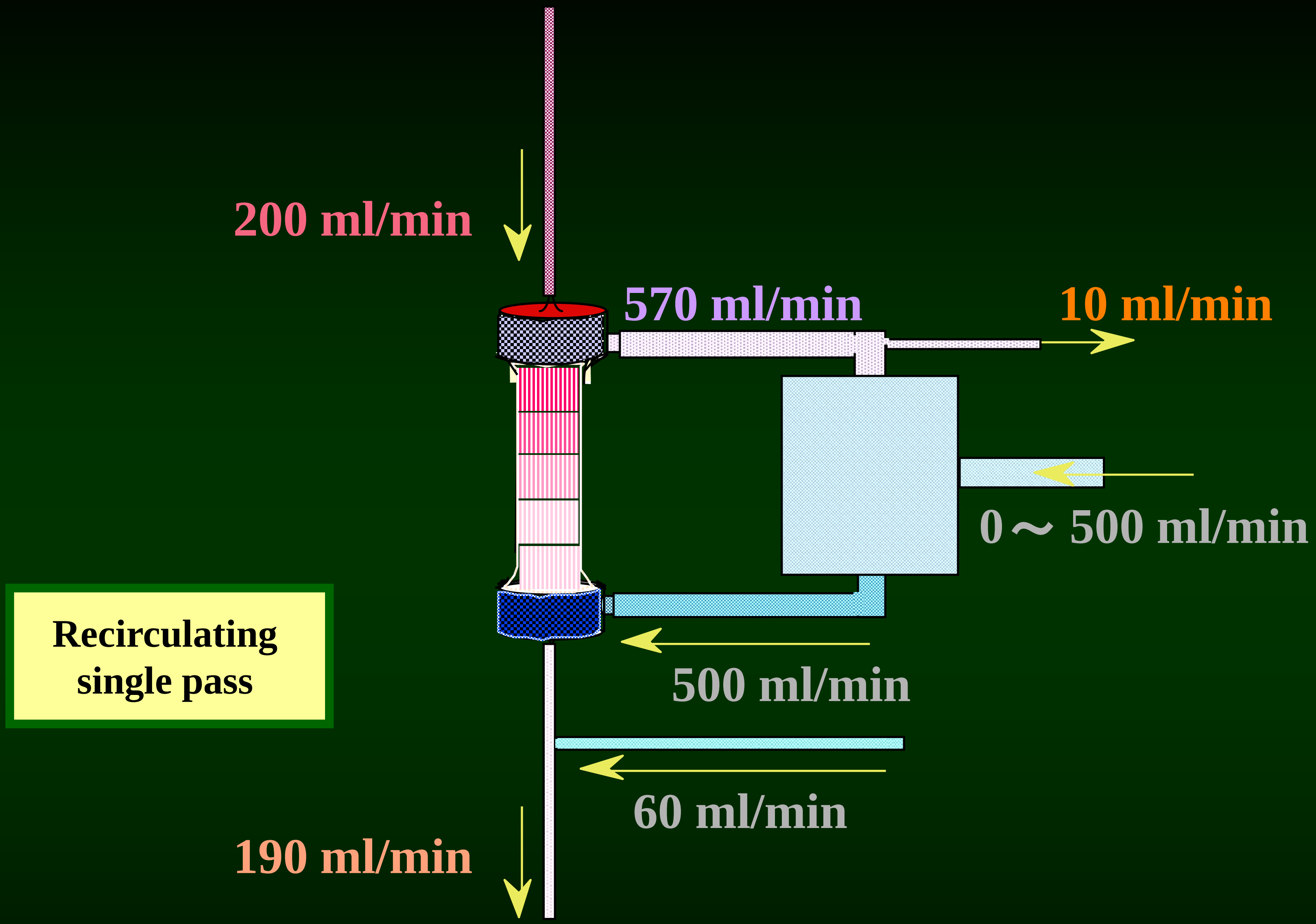

Fig.6 Recirculating Single Pass HDF
Post-dilution method

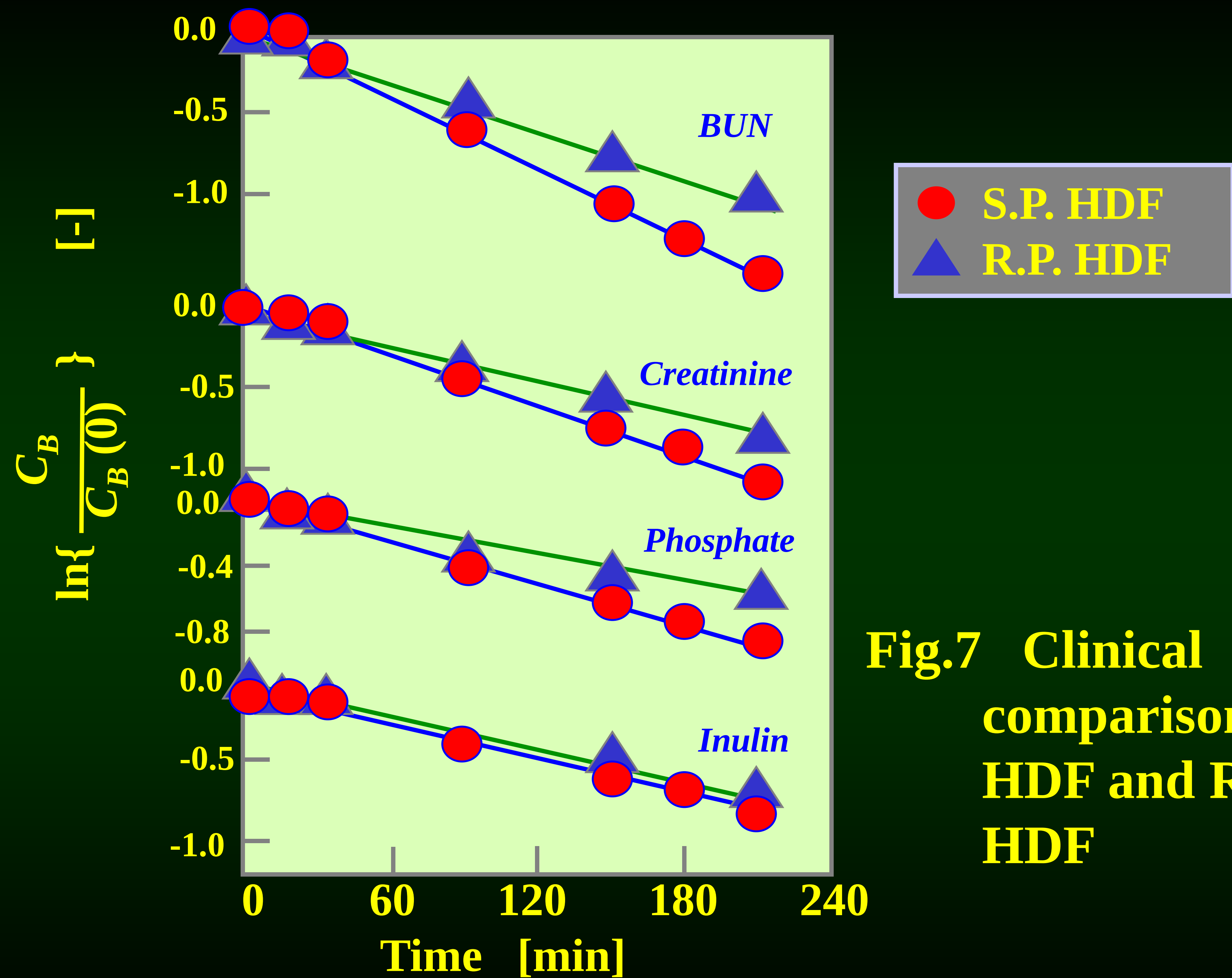

Fig.7 Clinical comparison of S.P. HDF and R.P. HDF

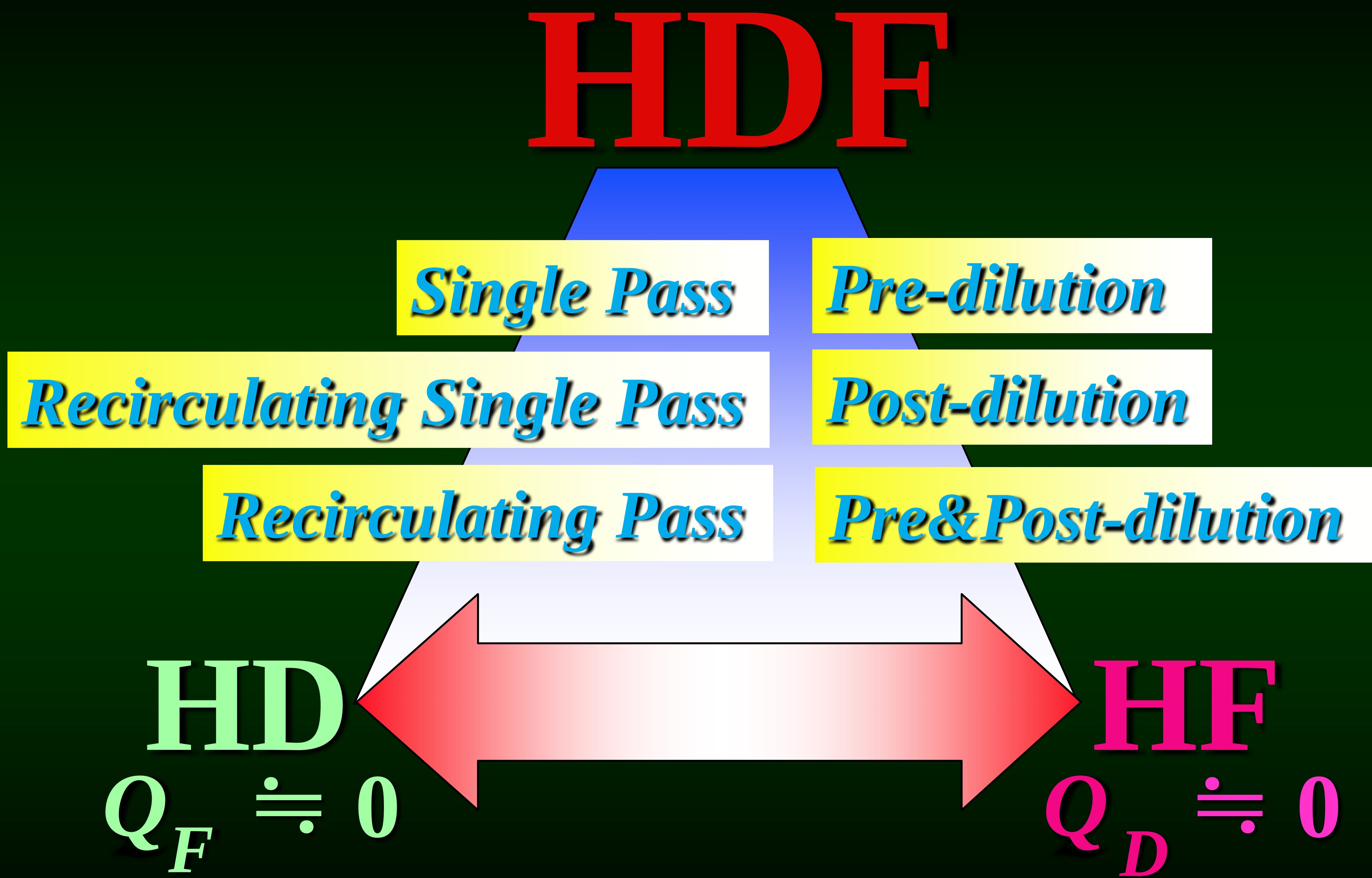
HDF
Single Pass
Recirculating Single Pass
Recirculating Pass
Pre-dilution
Post-dilution
Pre&Post-dilution
HD
$Q_F \fallingdotseq 0$
HF
$Q_D \fallingdotseq 0$

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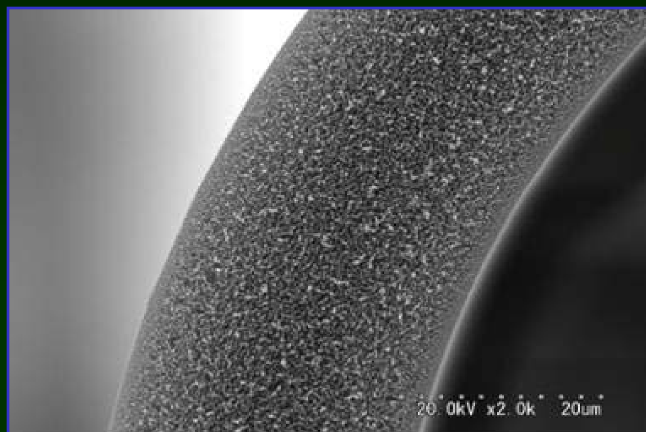
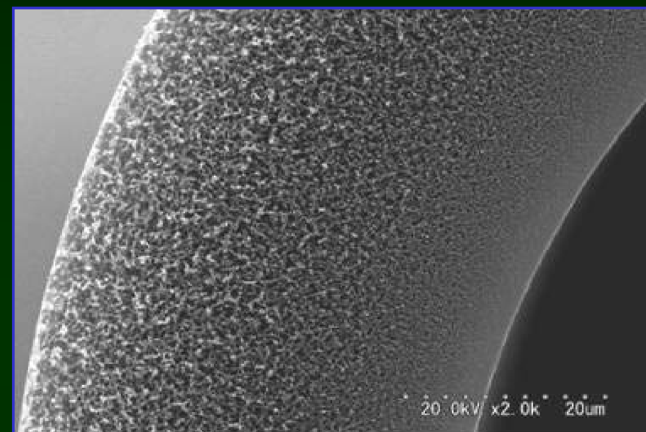
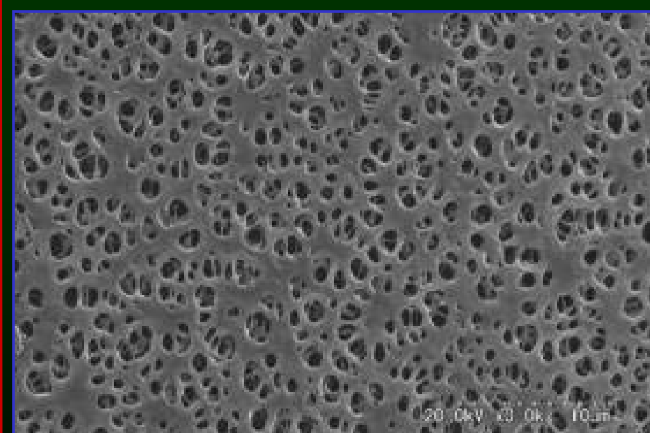
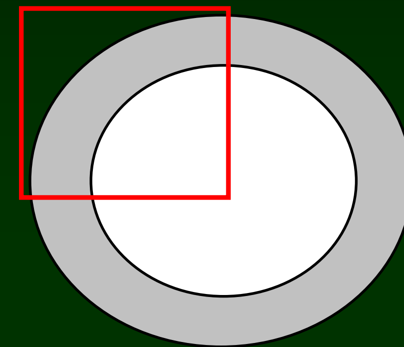
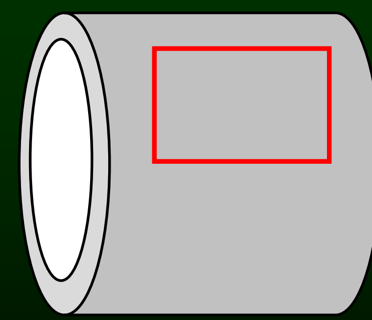
Table 3 Comparison of physical structures – PEPA vs. PS –

	PEPA	PS
section (×2,000)		
outer surface (×3,000)		





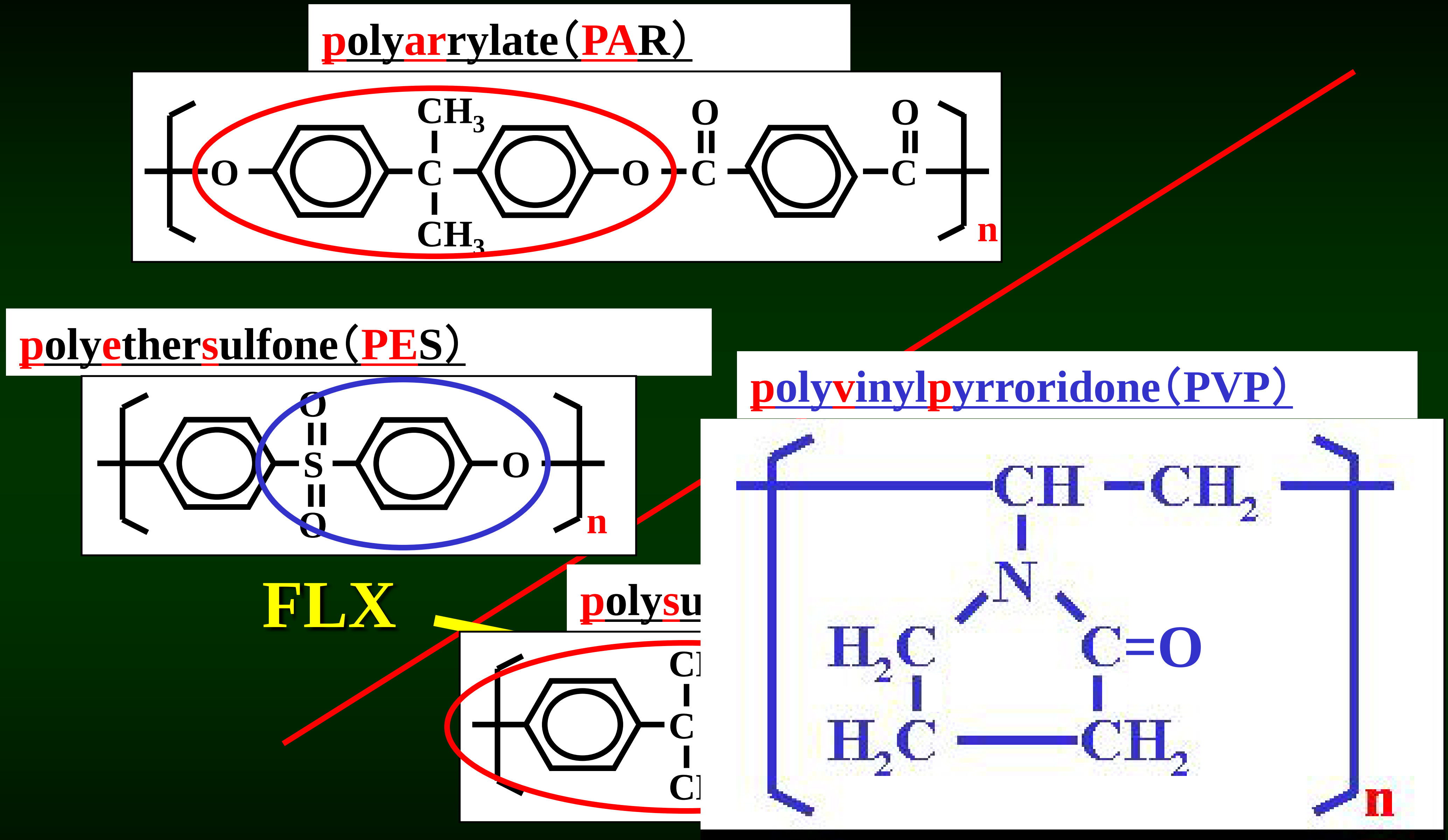


Fig.8 Chemical structures of PEPA

Blood Compatibility

WBC, Platelet

CH50, *C3a* C5a

TNF-α, IL-6

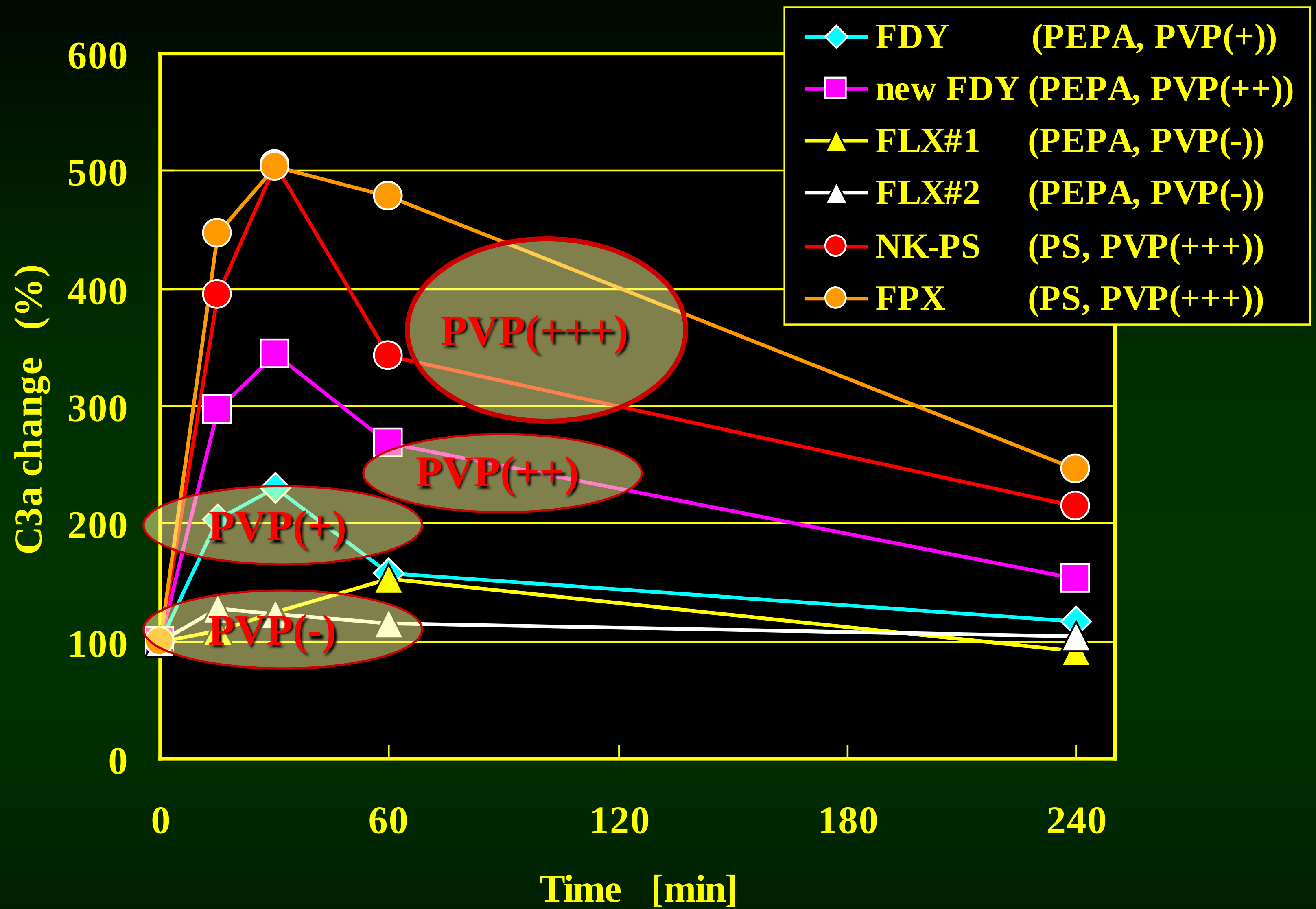


Fig.9 Time course of C3a conc. during HD treatment
C3a conc. were measured every Monday.

Separation Characteristics of albumin

Sieving coefficient

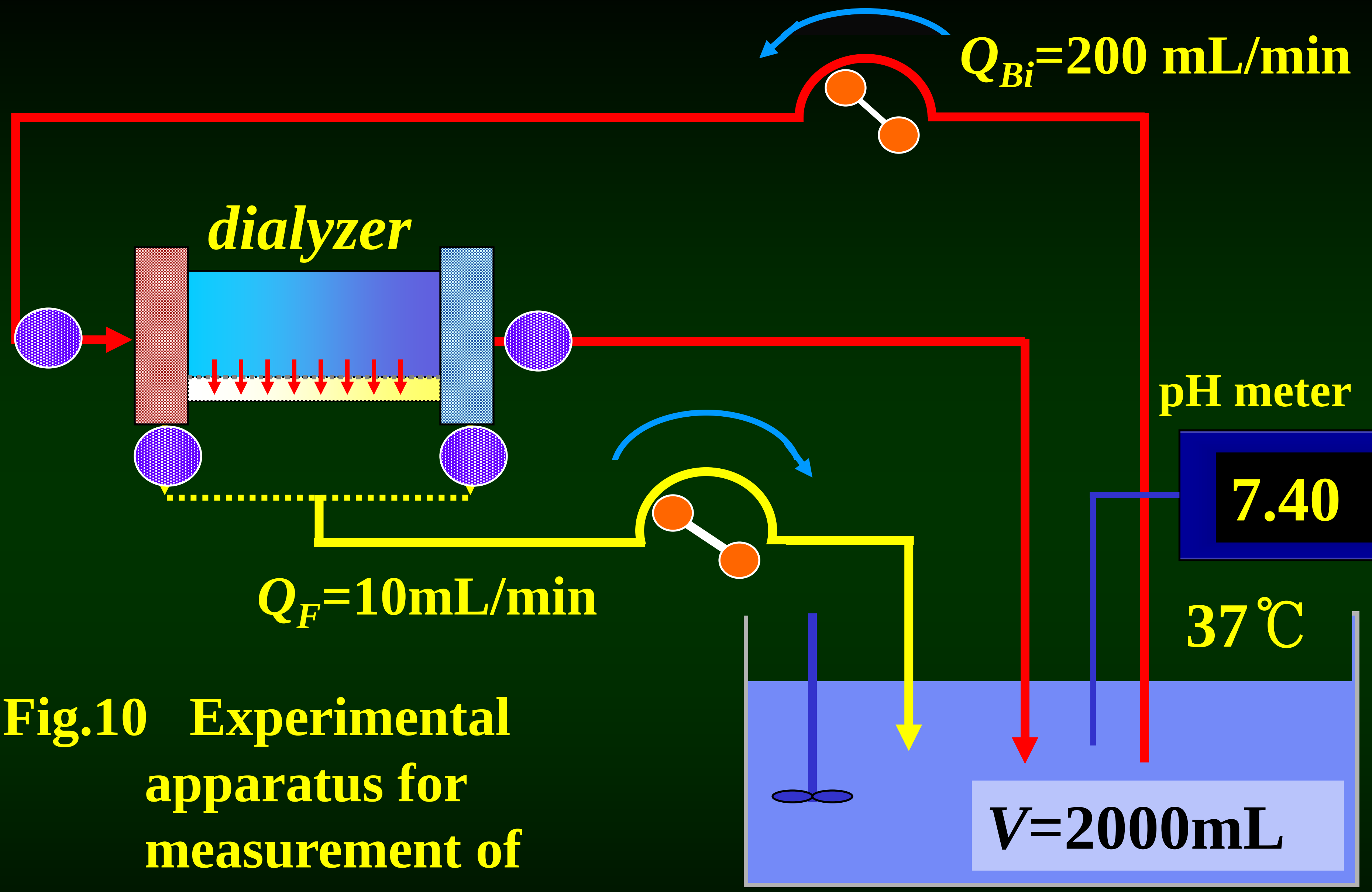


Fig.10 Experimental apparatus for measurement of sieving coefficient

Table 4 Technical specifications of investigated dialyzers

#	Brand name	Abbrebiated name	Area [m^2]	Main materials	PVP	Pore size	Make
1	PS-1.6UW	PS	1.6	PS	PVP(+++)	(Not available)	Fresenius Medical Care, Germany
2	FLX-15GW	FLX	1.5	PEPA	PVP(-)	standard	Nikkiso Co., Tokyo
3	FDX-15GW	FDX	1.5	PEPA	PVP(+)	standard	Nikkiso Co., Tokyo
4	FDY-15GW	FDY	1.5	PEPA	PVP(+)	larger	Nikkiso Co., Tokyo
5	FDX-150GW	newFDX	1.5	PEPA	PVP(++)	standard	Nikkiso Co., Tokyo
6	FDY-150GW	newFDY	1.5	PEPA	PVP(++)	larger	Nikkiso Co., Tokyo

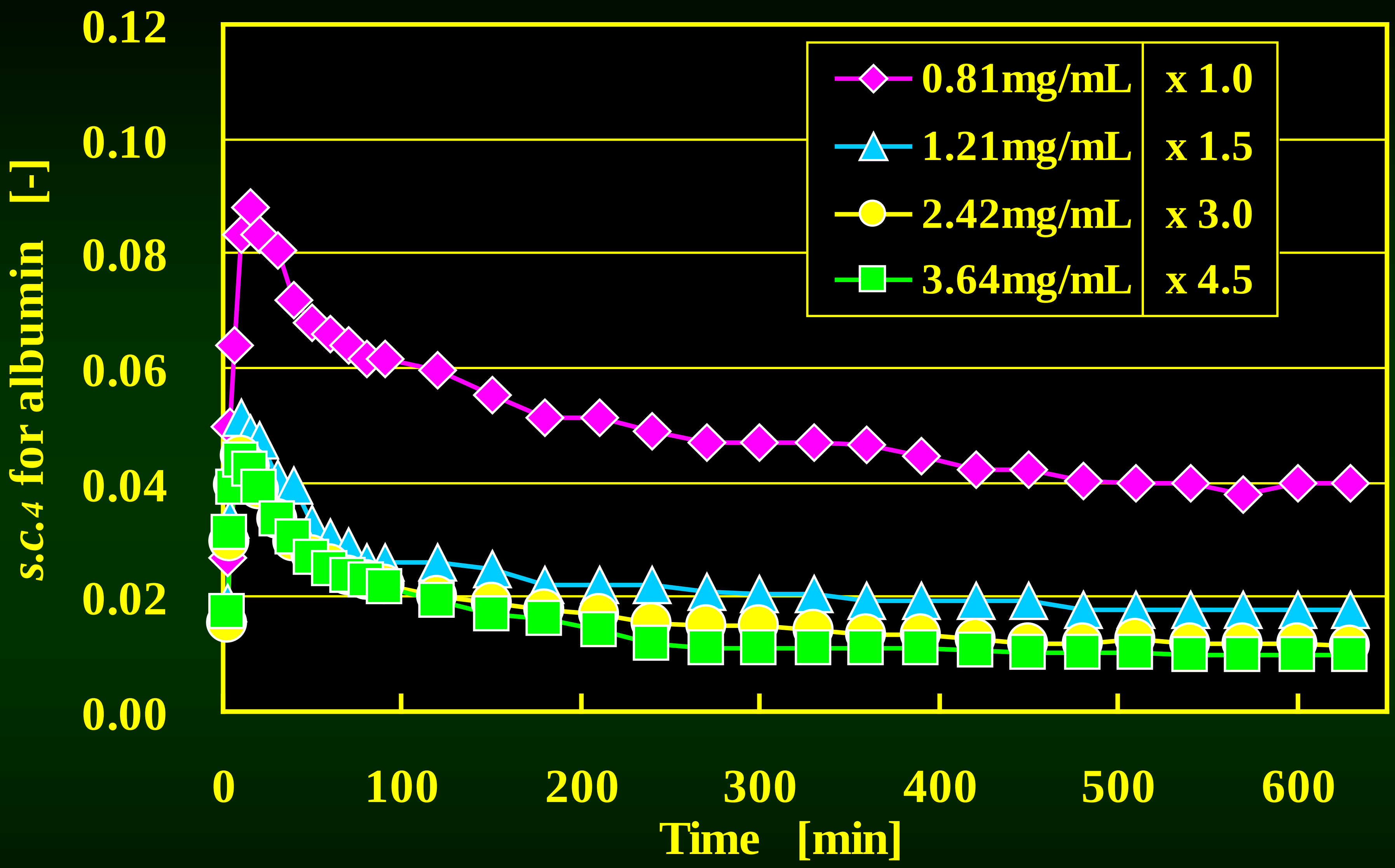


Fig.11 Time course of $s.c._4$ for albumin in PS-1.6UW under various albumin concentrations

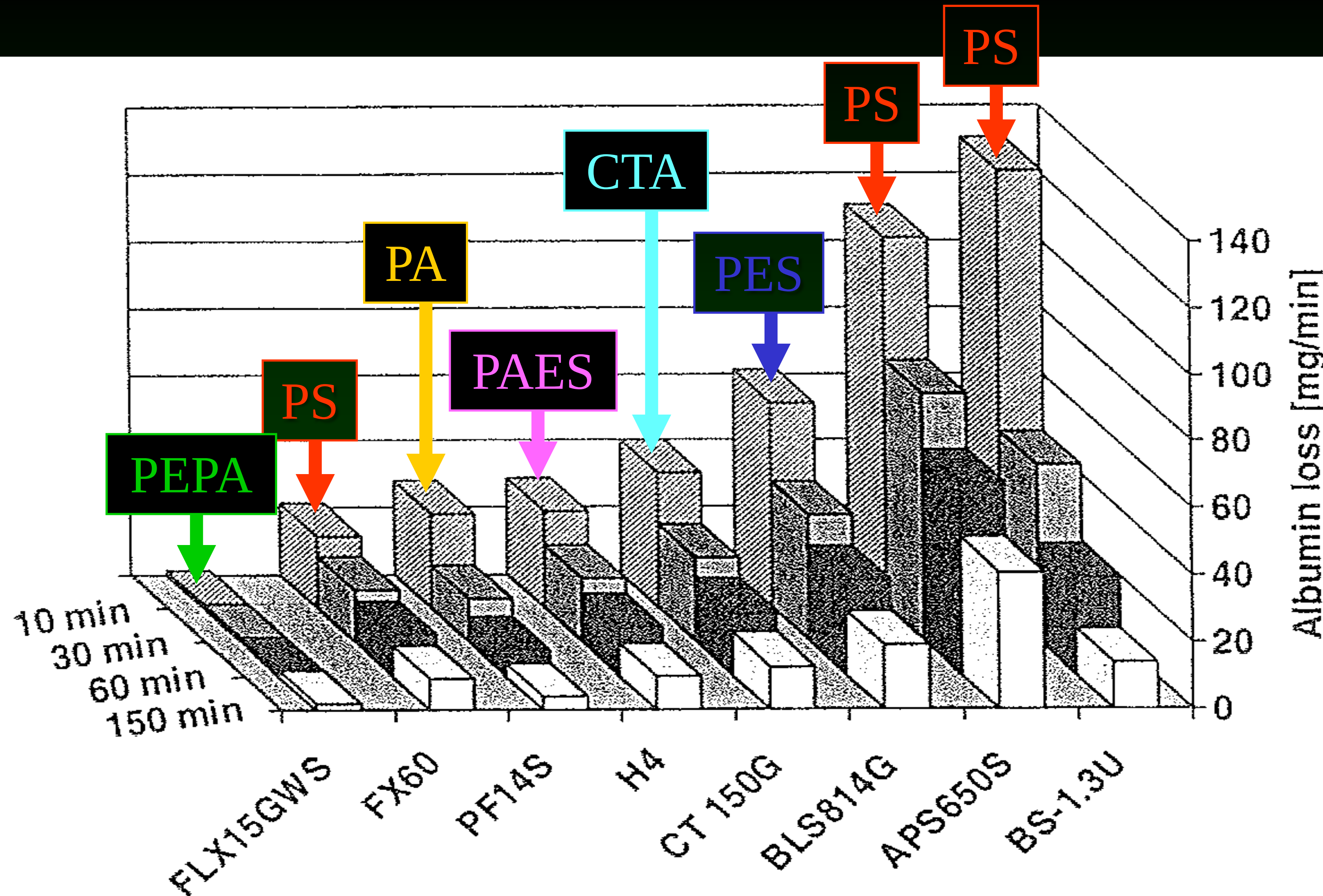


Fig.12 Time course of albumin loss (mg/min) into the diafiltrate for each of the dialyzers evaluated in the study after 10, 30, 60 and 150 min of treatment. Values were derived from the 32 treatment sessions of a single patient (total UFR = 73 – 102 ml/min).

Ahrenholz PG *et al.*: *Clin Nephrol* 62(1), 2004:21-28.

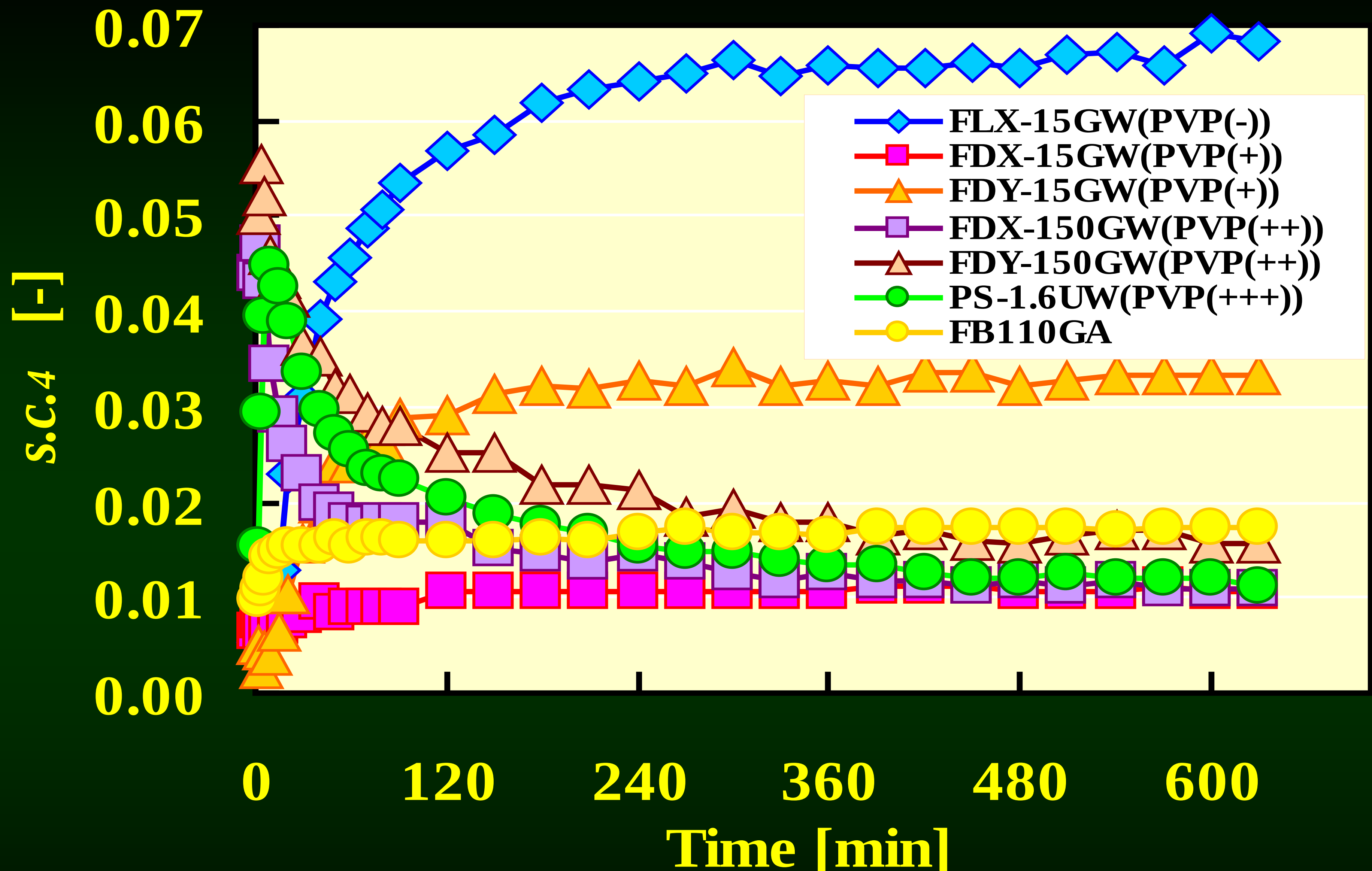


Fig.13 Time course of $s.c._4$ for albumin
Initial Conc.= 2.42 mg/mL

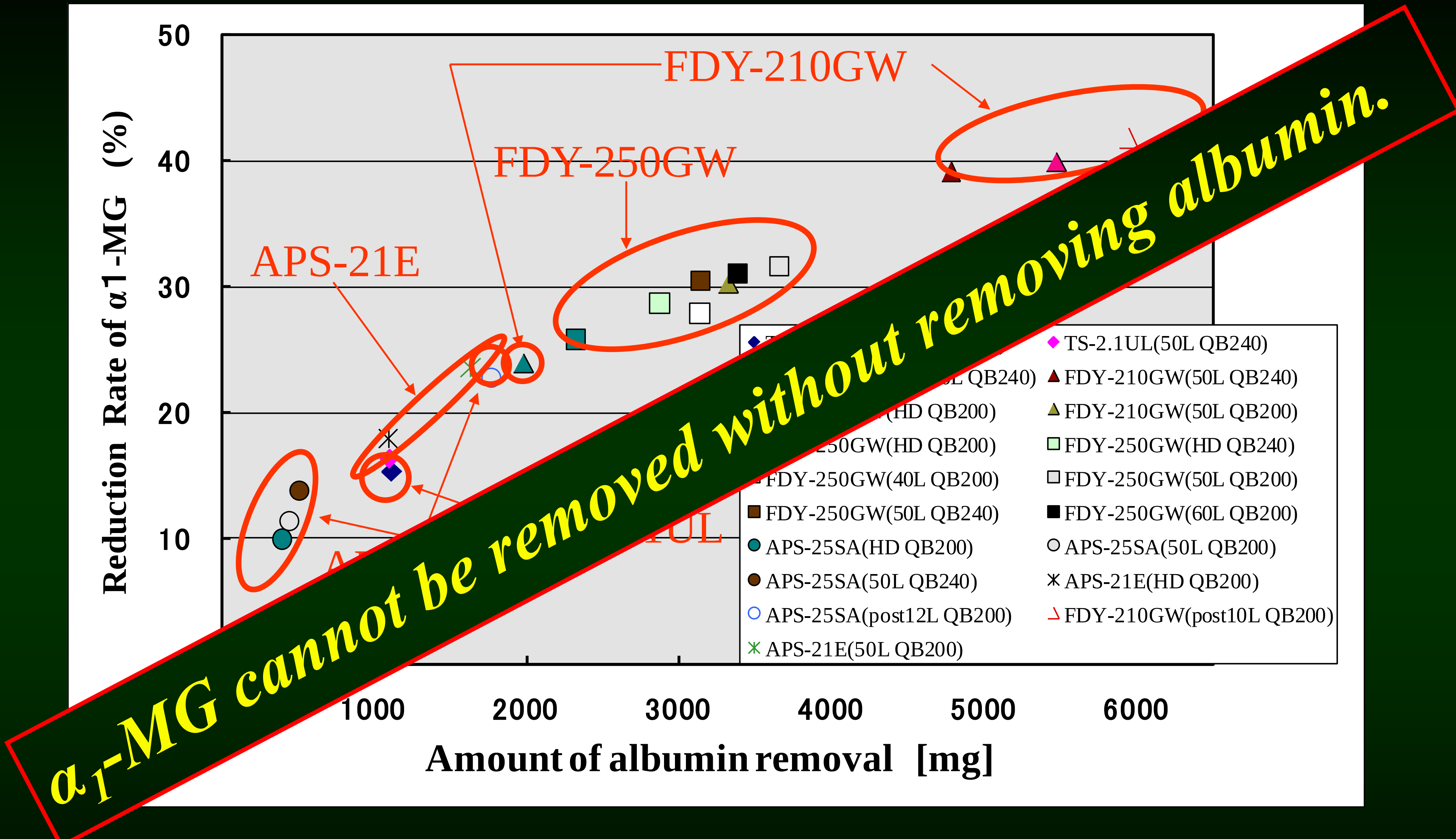


Fig.14 Relationship between reduction rate of α_1-MG and amount of albumin removal

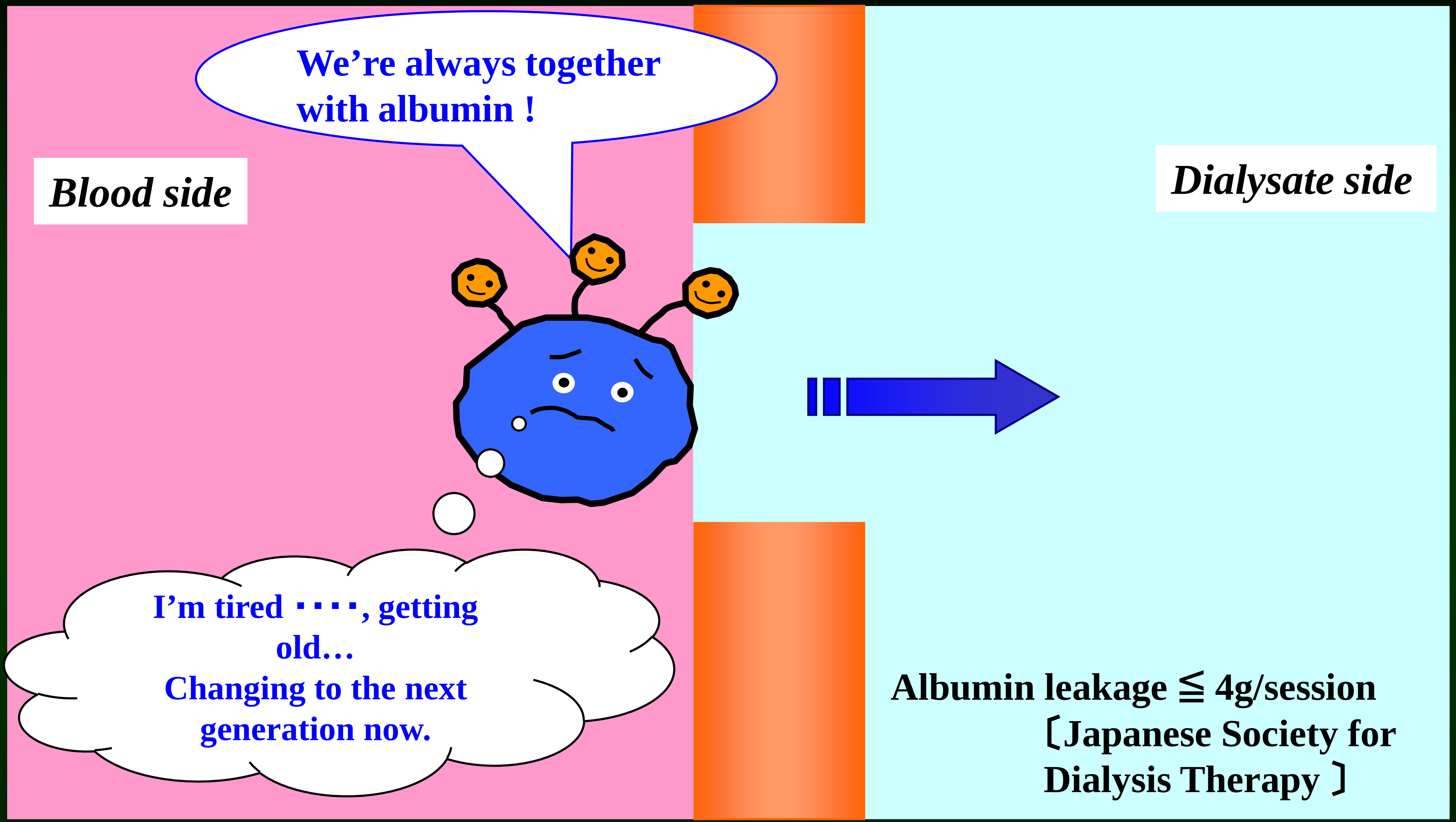


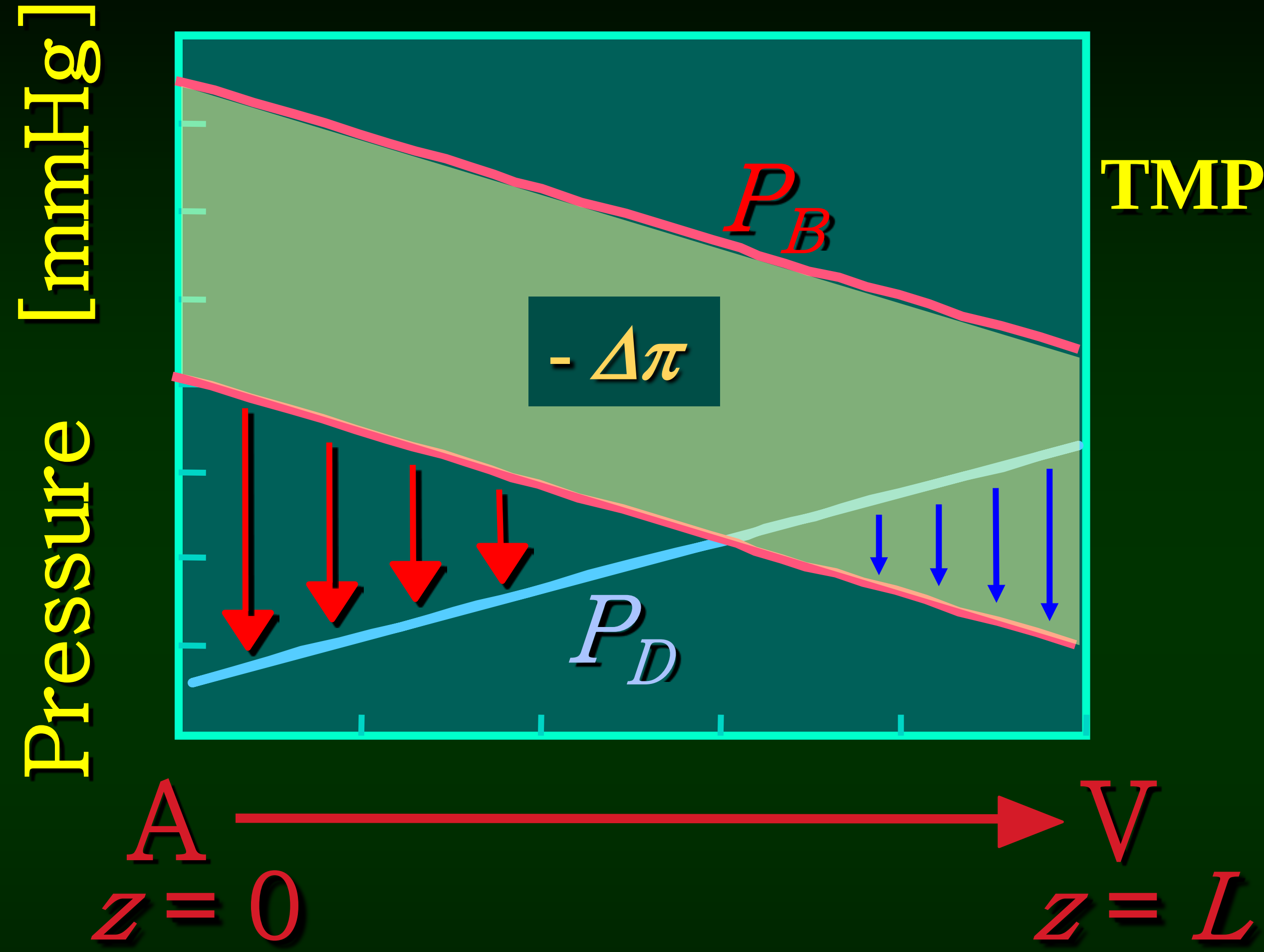
Fig.15 Removal of protein-bound substances

Toxic substances may be removed together with albumin!

※ Toseki care vol.9 no.7 631 (2003)

HD with Internal Filtration

New category of HDF



$$\mathrm{TMP} = \Delta P - \Delta\pi = (P_B - P_D) - (\pi_B - \pi_D)$$

$(P_B - P_D)$: static presusre

$-(\pi_B - \pi_D)$: osmotic pressure

Fig.16 Pressure distribution in a dialyzer

Dellanna F, *et al.*: Nephrol Dial Transplant, 11(Supple 2), 83-86, 1996.

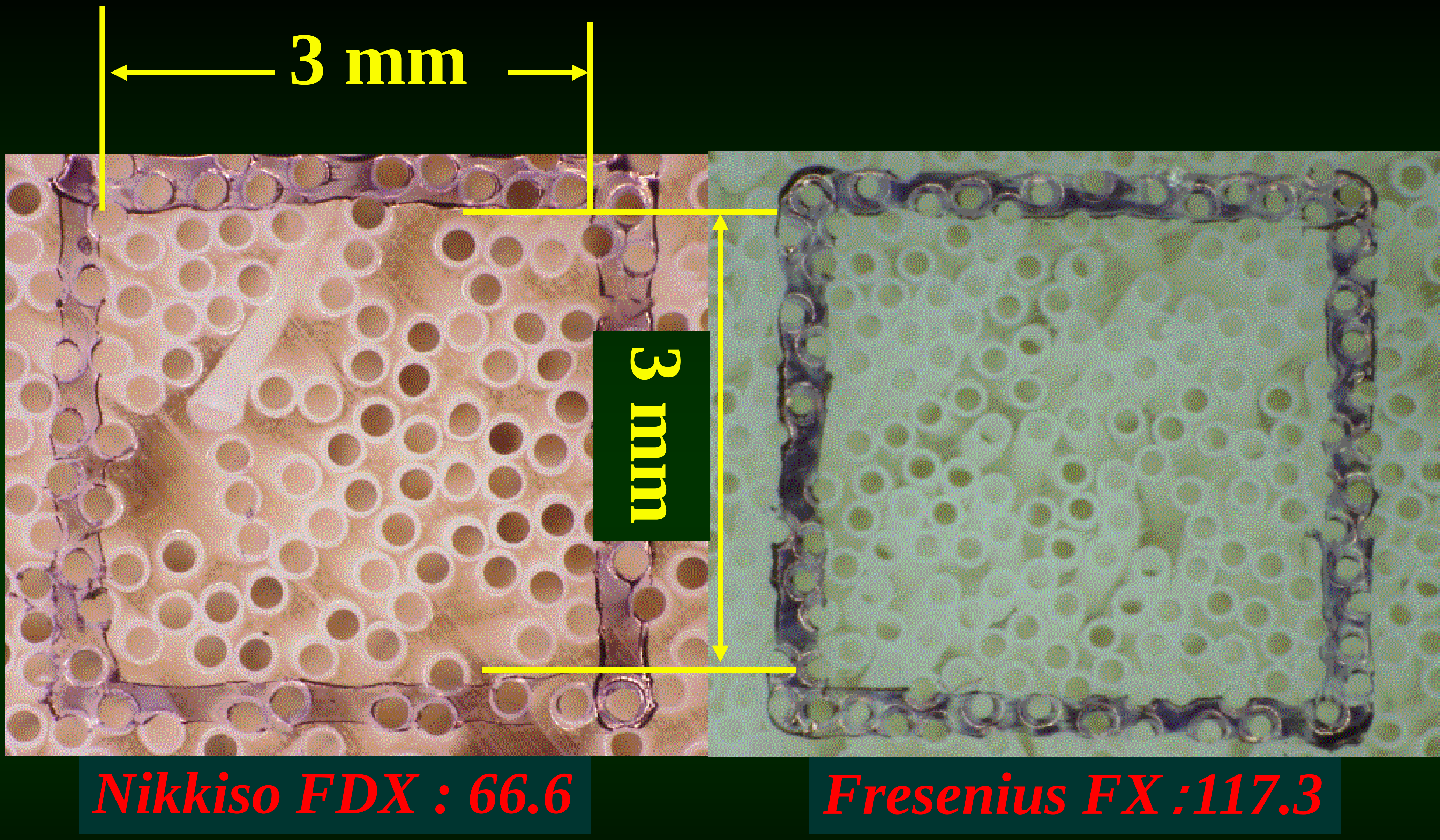


Fig.17 Number of hollow fibers in 3mm x 3mm

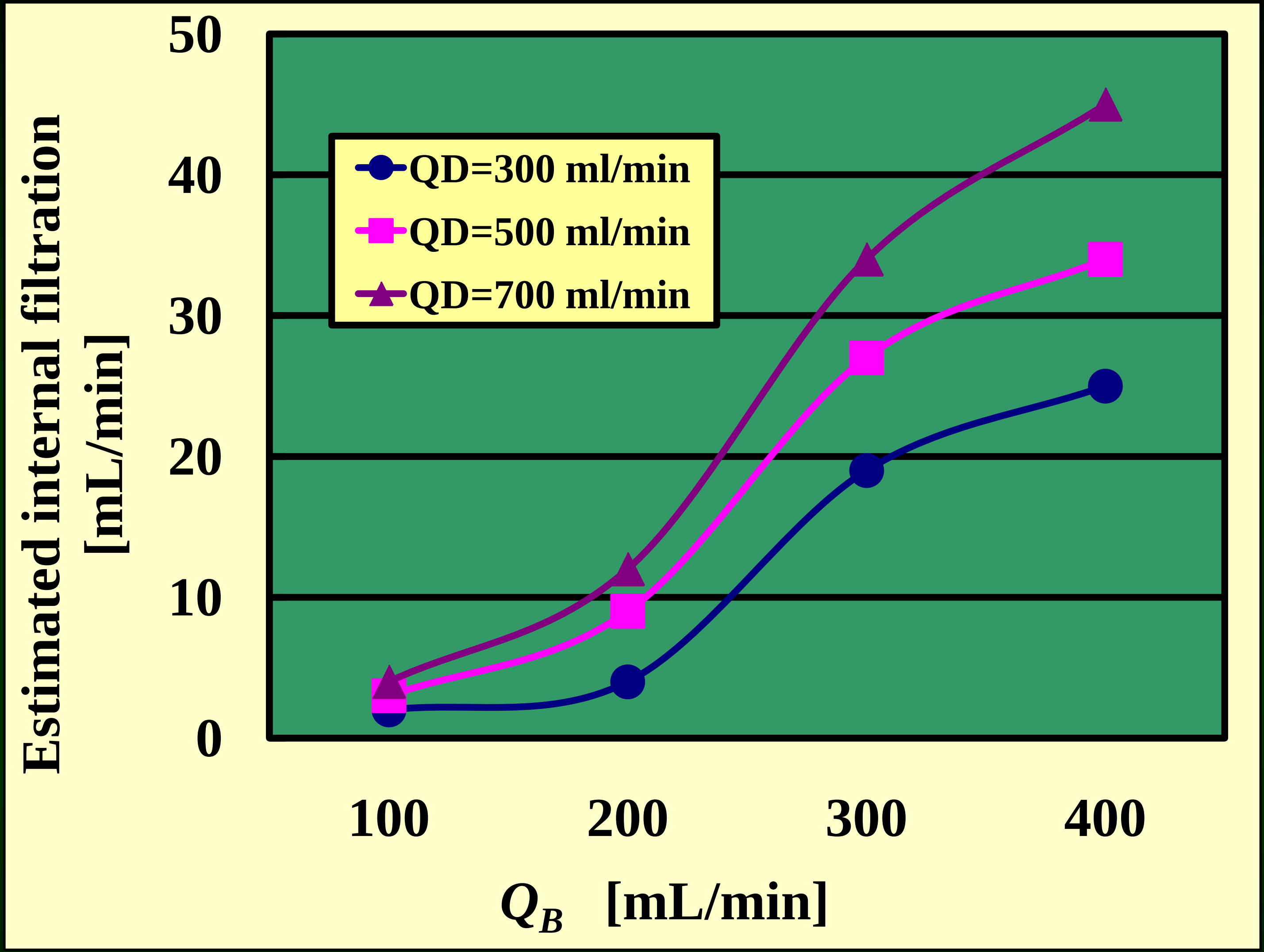


Fig.18 Relationship between estimated amount of internal filtration and Q_B

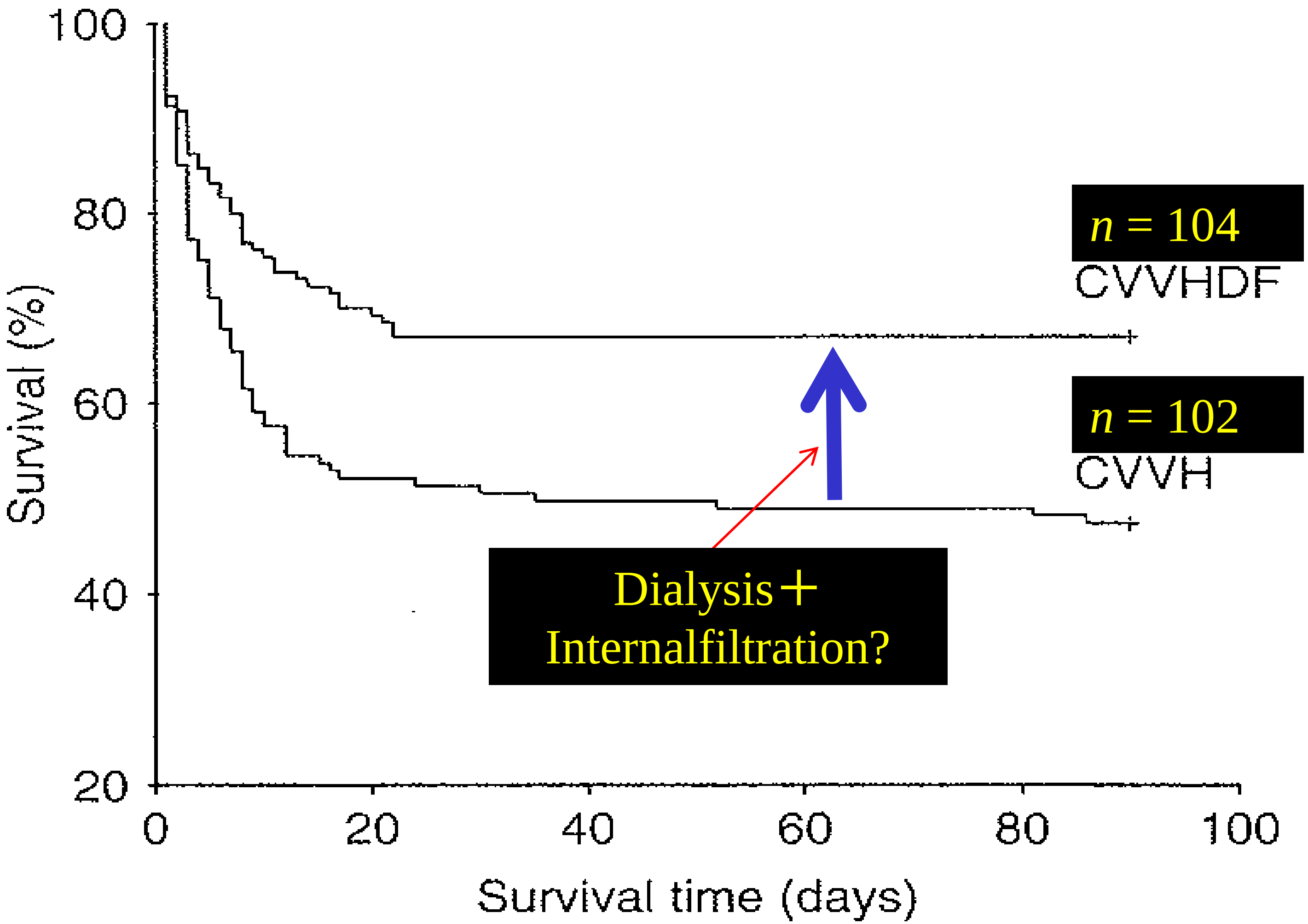


Fig.19 **Kaplan–Meier analysis of survival rates in the two groups.**

Saudan P, *et al.*: Adding a dialysis dose to continuous hemofiltration increases survival in patients with acute renal failure, *Kidney Int* 2006, 70, 1312-1317

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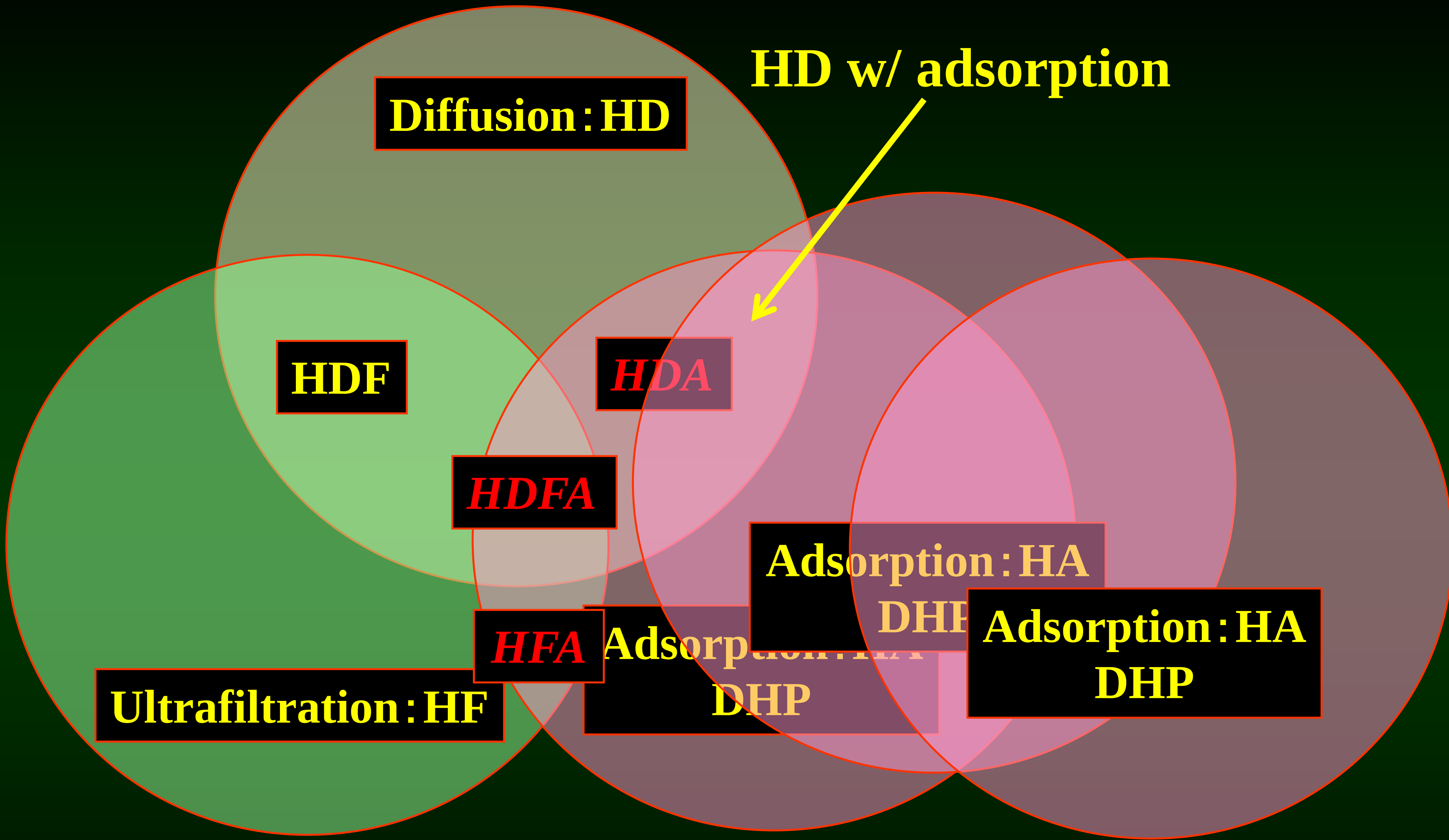
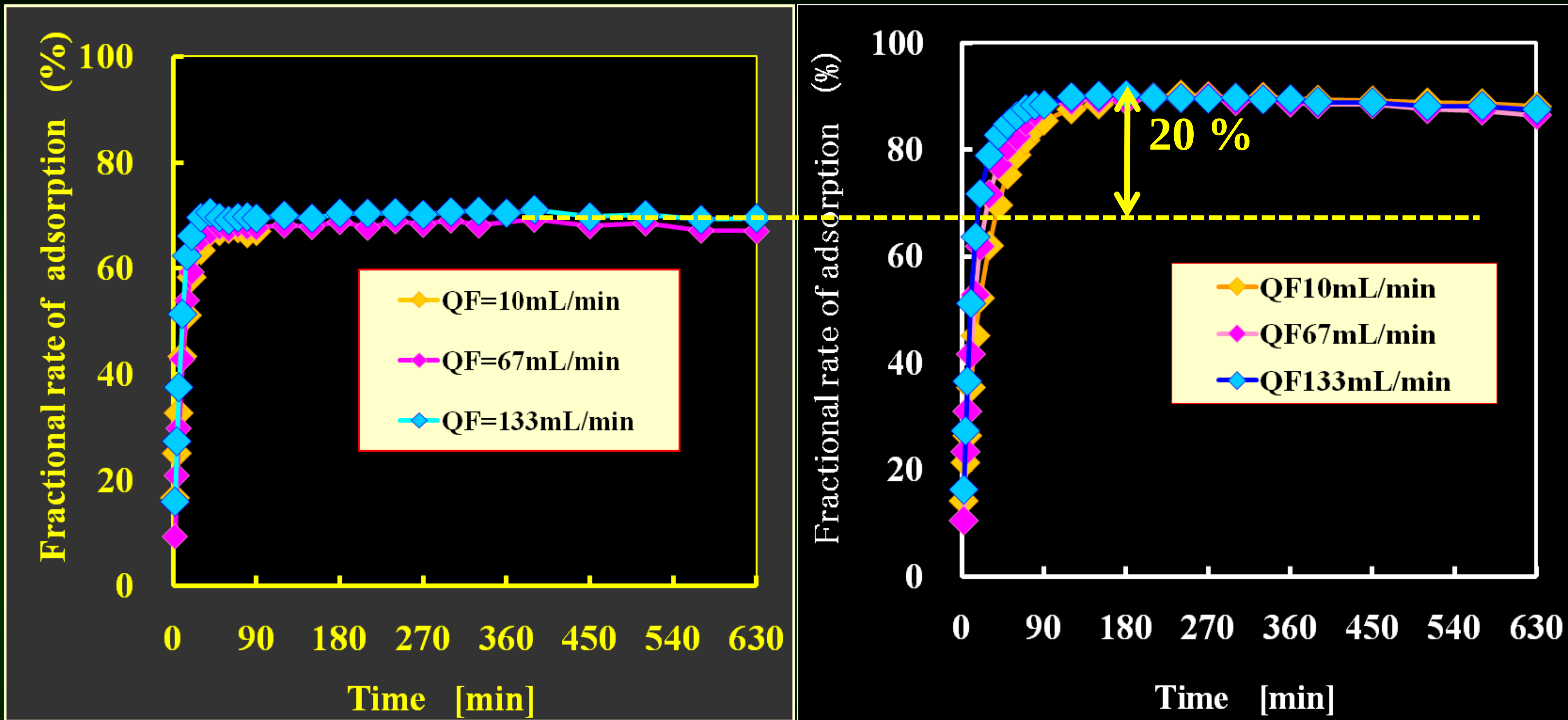


Fig.20 Modalities and Basic Principles



PEPA PMMA

Fig.21 Fractional rate of adsorption for chymotripsinogen in PEPA and PMMA dialyzers

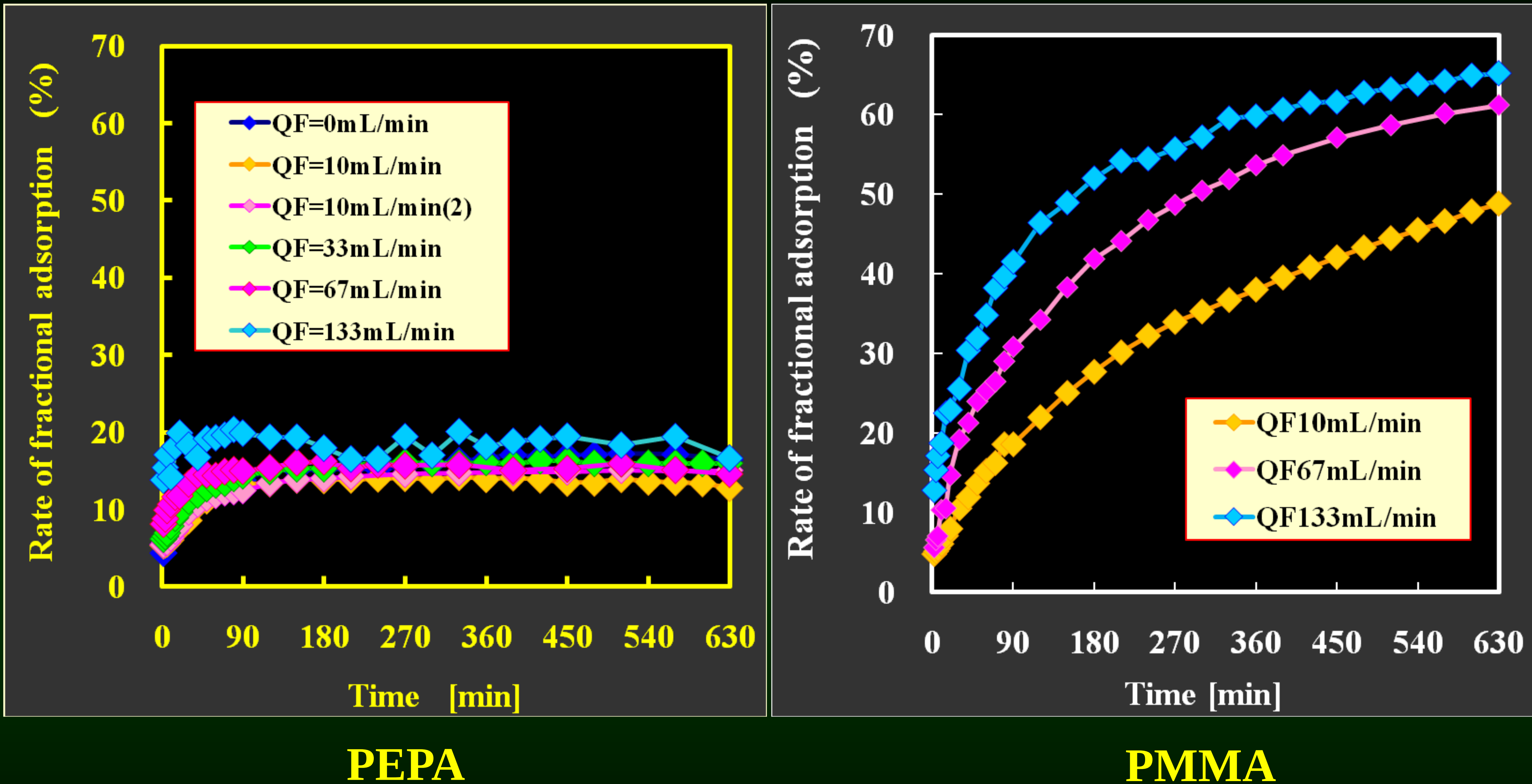


Fig.22 Fractional rate of adsorption for albumin in PEPA and PMMA dialyzers

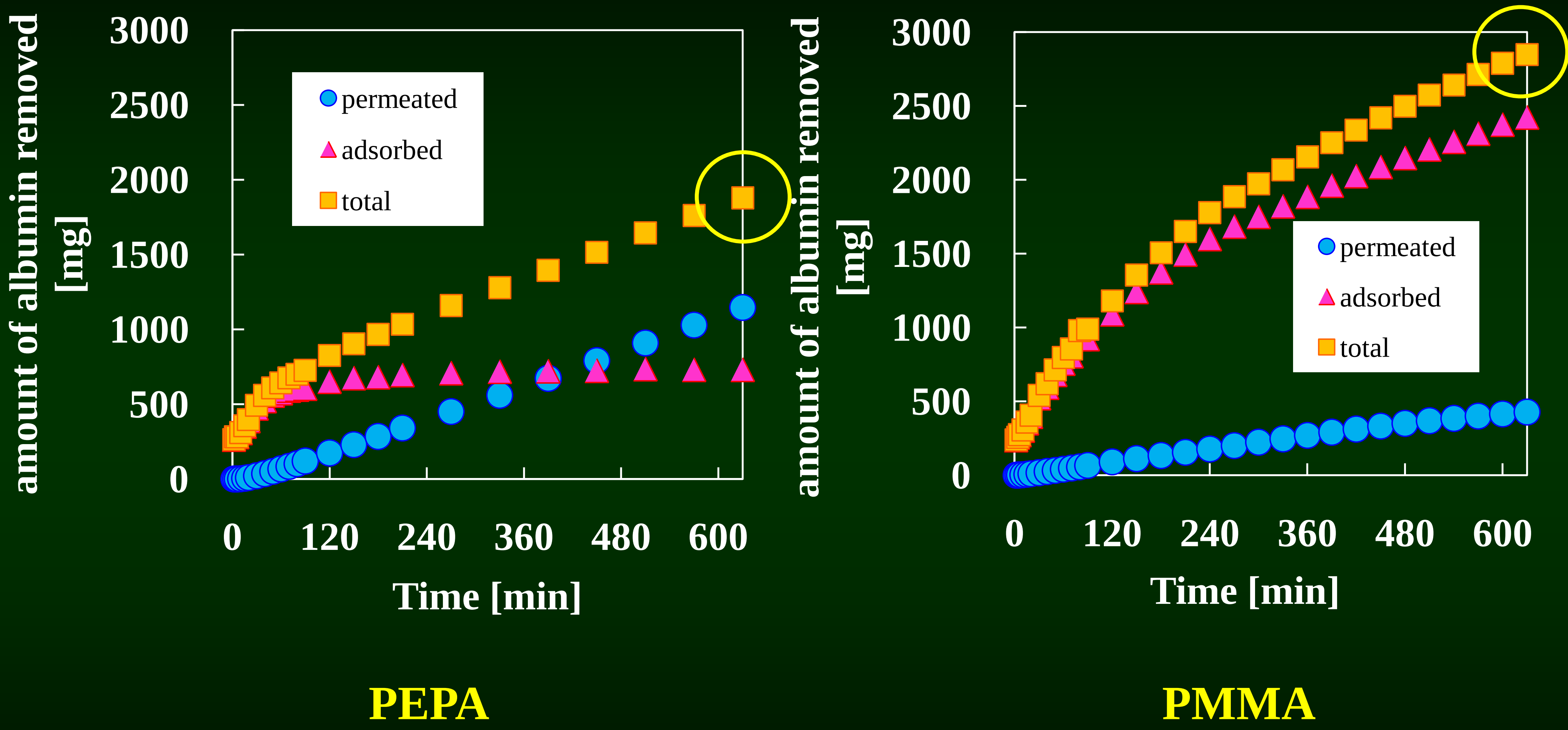


Fig.23 Time course of albumin removed by permeation or by adsorption (Q_B = 200 mL/min, Q_F = 10 mL/min)

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Conclusions

1. Many modifications of HDF are available, trending on-line mode, which requires perfectly purified dialysis fluid.
2. PVP is not only influences on the biocompatibility but also on the solute permeability of the membrane.
3. Internal filtration enhancing HD is a new category of limited scale HDF, requiring the super-high flux dialyzers.
4. Adsorption may serve as the third mechanism for removing toxic substances, following diffusion and ultrafiltration.
5. Comprehensive understanding of these facts may be necessary for selecting an appropriate dialyzer.