Life Inside a Single Hollow Fiber

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Thursday, March 22nd, 2018 (4:00 pm – 5:30 pm)

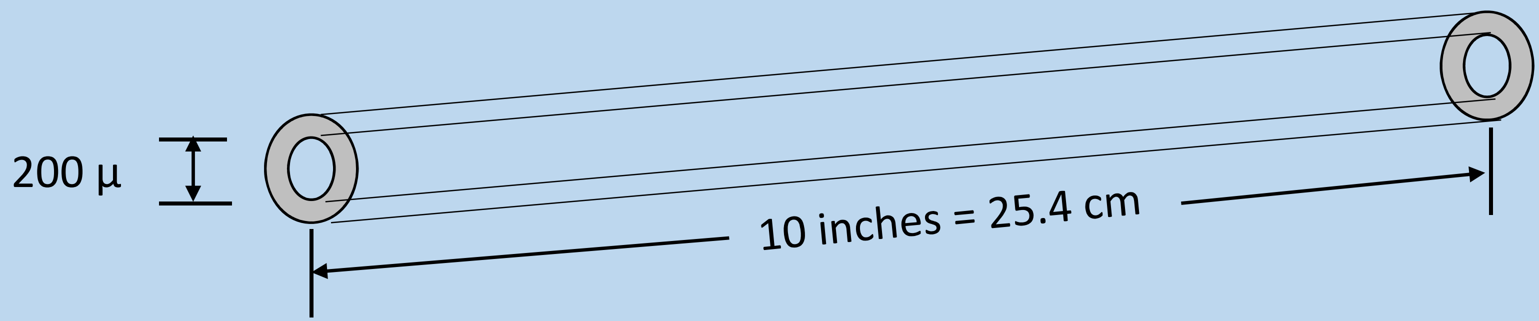
“Seeing” The Dialysis Process

As human beings, we are limited in our ability to observe the processes occurring inside a dialyzer

We can still understand what is happening in the dialyzer thanks to scientific experimentation, modeling, and application of these processes for benefit of the ESRD patient

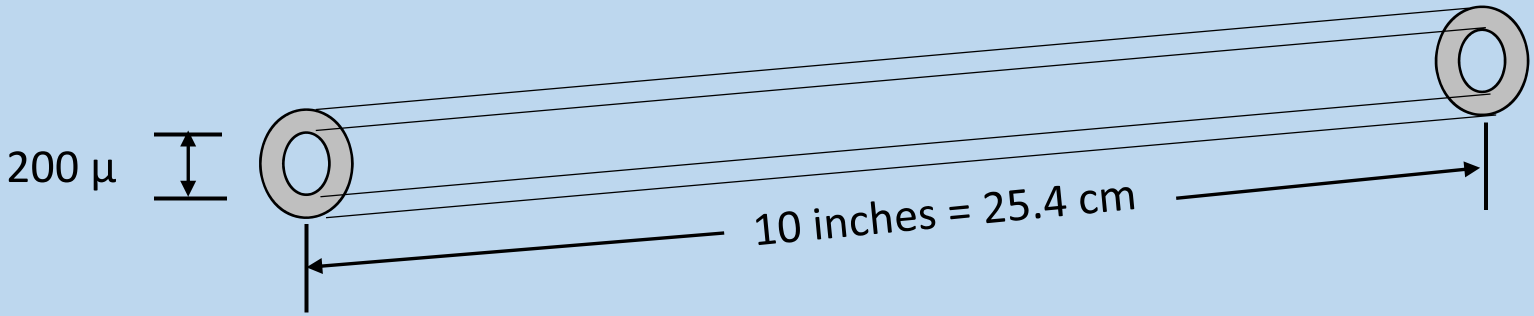
How well do you “picture” the dialysis process?   Follow along and find out

Introducing our hollow fiber



- Length (L) = 0.254 m, Radius = 100 µ = 100×10^{-6} m
- Its volume would be = $L \times \pi R^2 = 7.98 \times 10^{-9}$ m^3 = 7.98×10^{-6} liter = 7.98×10^{-3} mL
- 10,000 of these fibers will have a volume of 79.8 mL
- How long would our fiber have to be to hold a liter of fluid?

Introducing our hollow fiber



- Its internal surface area = L x 2πR = 1.60 x 10^{-4} m^2
- 10,000 of these fibers will have a total surface area of 1.60 m^2
- 12,500 fibers = 2.0 m^2

Hollow Fiber vs. a Red Cell

- Picture a hollow fiber with a red cell inside. If a beach ball represents the inside diameter of the hollow fiber what size would a red cell be?
- A) The size of a volleyball
- B) The size of a Baseball
- C) The size of a Ping Pong Ball
- D) The size of a Marble

Hollow Fiber vs. a Red Cell

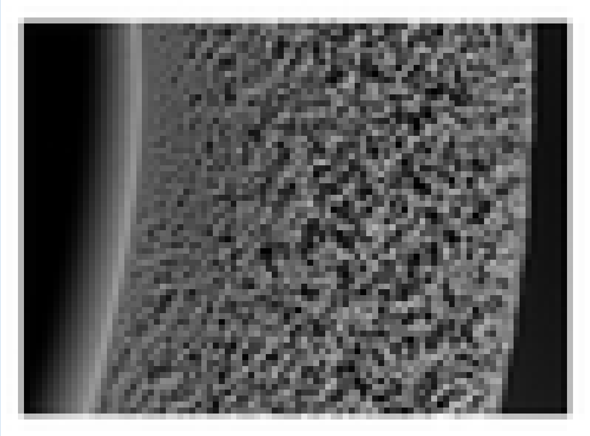
- The diameter of the average beach ball is about 16 inches = 41 cm
- The diameter of a hollow fiber is 200 microns
- The diameter of a red cell is 7 microns which means a red cell's diameter is about 28x smaller than a hollow fiber's diameter
- 41cm/28 = 1.46 cm = 14.6 mm
- Answer: D) A marble who's standard size is 15 mm

Note: A ping pong ball is 40 mm in diameter

Membrane Thickness vs. Pore Size

- Picture a piece of membrane. Which of these items best represents what you are picturing?
- A) A slice of Swiss Cheese
- B) A fine Sponge
- C) A Window screen
- D) A slice of bread

Membrane Thickness vs. pore size



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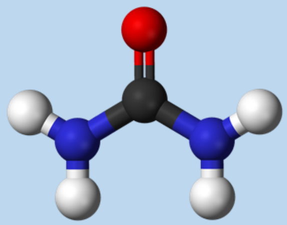
- The average membrane thickness is between 10 and 50 microns (1 to 5 x 10^{-5} m)
- The average pore size is about 100 angstroms (1 x 10^{-8} m)
- The membrane is about 3,000x thicker than the average pore diameter
- The answer is: b) A fine sponge

Note: The diameter of a urea molecule is 2.6 Angstroms so it can easily pass through the pores in a membrane.

Plasma fluid volume vs. Total volume

- Total volume = 7.98×10^{-3} mL
- Assume 33% hematocrit then:
  - Hollow fiber plasma volume = 7.978×10^{-3} mL x 2/3 = 5.31×10^{-3} mL
- 6% of plasma is protein, therefore:
  - Hollow fiber fluid volume = $0.94 \times 5.31 \times 10^{-3}$ mL = 4.99×10^{-3} mL ≈ 5/1000 mL = 5 µL



Urea in Blood

- When a patient is put on dialysis at the start of a treatment their BUN will be about 80 mg/dL. How many urea molecules would be inside a single hollow fiber?
- A) millions (1,000,000) = 10^6
- B) Billions (1,000,000,000) = 10^9
- C) Trillions (1,000,000,000,000) = 10^{12}
- D) Quadrillions (1,000,000,000,000,000) = 10^{15}
- E) Quintillions (I,000,000,000,000,000,000) = 10^{18}

Urea in a hollow fiber

- Amount of BUN = 80 mg/dL = 800 mg/L = 0.8 g/L
- Urea G. M. W. is 60. BUN is 28
- Urea's weight in patient plasma is (60/28) x 0.8 g/L = 1.714 g/L = 0.0285 moles = 1.71 x 10^{22} atoms per liter
- 1.71 x 10^{22} atoms per liter x 5.00 x 10^{-6} L = 8.58 x 10^{16} molecules
- As the blood passes through the hollow fiber, the urea will be dialyzed out so the actual amount will be about half of the above number or 4.29 x 10^{16} molecules
- That's = 42.9 quadrillion molecules or 42.9 million billion molecules. Answer D.

Water and Sodium ions in a Hollow Fiber

- Water molecules = 1.67 hundred billion billion molecules = 167 quintillion molecules.
- Patient Sodium ion concentration = 140 mEq/L = 140 mmol/L
- Sodium ion number = 420 million billion ions = 420 quadrillion ions
- The ratios to water are:
  - Water/Sodium = 400/1
  - Water/ Urea = 4000/1
  - Sodium/Urea = 10/1

How fast does a urea molecule move in plasma at body temperature?

- A) Slower than a herd of turtles in a jar of peanut butter
- B) As fast as a sports car (100 miles/hr = 45 m/s)
- C) A thousand miles per hour = 450 m/s
- D) As fast as the Space Station (17,500 mph = 8,000 m/s)

The velocity of urea is directly proportional to its energy

- Energy (E) relates to speed by the following equation:

$$E = \frac{mv^2}{2} = \frac{3KBK}{2} \rightarrow \quad v = \sqrt{\frac{3KBK}{m}}$$

- Where:
  - m = mass of urea molecule = 9.963 x 10^{-26} kg
  - K_B = Boltzmann's constant = 1.3805 x 10^{-23} J/K
  - K = Degrees Kelvin (273^o K = 0^o C)
  - V = velocity in m/s
- The Urea velocity is: 359 m/s (Water Molecules = 655 m/s because they are lighter)
- The answer is: c) a thousand miles per hour = 450 m/s

Urea gets knocked around by the water molecules. About how many collisions are there per second?

- A) hundreds
- B) Thousands
- C) millions
- D) Billions
- E) Trillions
- F) Quadrillions

Urea collisions

- The distance a particle travels without colliding with another particle is called a "Mean free path".
- For water at room temperature, this distance is only 10^{-11} meter! For air it's 6,800x longer.
- The number of mean free paths covered by urea in one second would be:
  - 359.3 meters/10^{-11} meter = 3.593×10^{13} = 36 trillion mean free paths
- Since each mean free path ends with a collision, then the number of collisions will also be 36 trillion/second (Answer E)

Mean Free path (MFP) and Diffusion

- The average distance a particle will have moved from its starting point is the square root of the number of mean free paths taken times the length of the mean free path
- For 100 mean free path steps, the average distance traveled will be 10 x MFP
- If the rate of MFP steps is known per second as well as the MFP distance, then the time it takes to go a certain distance can be determined

How long will it take a urea molecule to move from the center of a hollow fiber to the membrane wall?

- MFP = 10^{-11} m, 3.6×10^{13} MFP/second, Hollow fiber diameter = 200 µm
- A) 3 milliseconds
- B) 3 seconds
- C) 3 minutes
- D) 0.05 hours

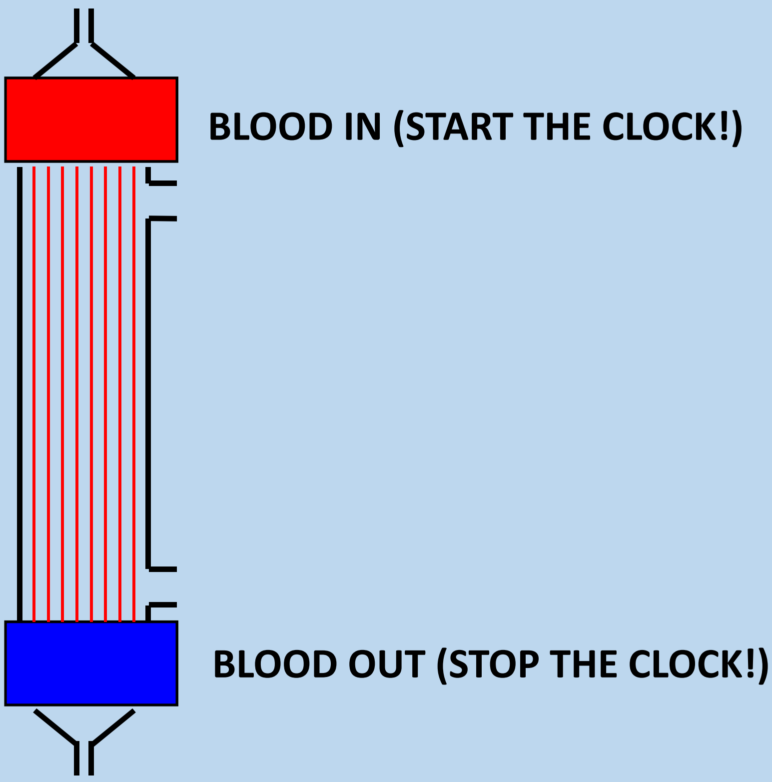
Urea Hollow Fiber Diffusion Time

- Distance to travel = 100 µm = 10^{-4} m
- Number of MFP = 10^{-4} m/10^{-11}m = 10^{7} MFP
- (Number of MFP)^{2} = 10^{14} = 100 TRILLION
- 100 TRILLION/ 36 TRILLION/SECOND = 2.77 Seconds
- The answer is : B) 3 Seconds

Urea Time and Distance

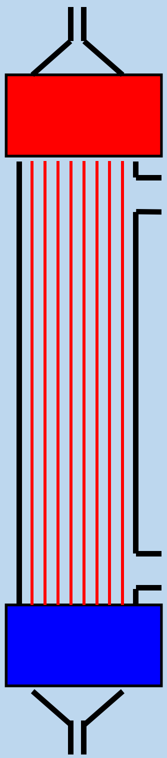
DISTANCE	TIME
1 µm	0.28 msec
10 µm	0.0277 sec
100 µm	2.77 sec
1 mm	4.6 min
1 cm	7.7 hr
10 cm	1 month
1 m	8.8 years

Hollow Fiber Dialysis Time



- Urea can only be removed from the blood while it's in the hollow fiber. If a dialyzer's blood volume is 100 mL, how long does it take for blood to pass through the fiber at the following flow rates?
  - 200 mL/min
  - 400 mL/min
  - 600 mL/min

Hollow Fiber Dialysis Time

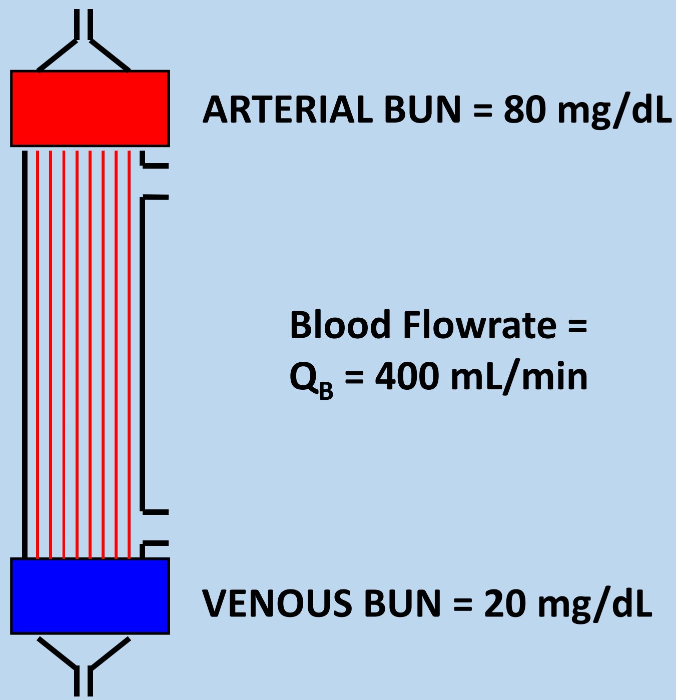


BLOOD IN (START THE CLOCK!)

BLOOD OUT (STOP THE CLOCK!)

- For Q_B = 200 mL/min The time is 30 seconds (with a blood volume of 100 mL, you could fill 2 dialyzers in a minute)
- For Q_B = 400 mL/min, The time is 15 seconds
- For Q_B = 600 mL/min, The time is 10 seconds
- (Dialyzer volume/Blood flowrate) x 60 = blood fiber time in seconds

The Concept of Extraction Ratio (ER)



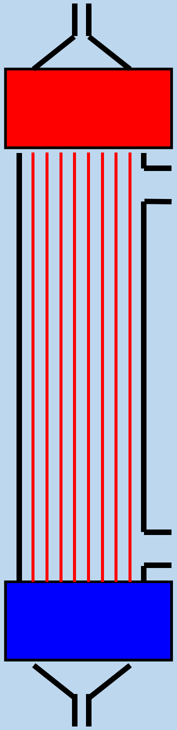
- Extraction Ratio is defined as the ratio of the BUN removed divided by the Total BUN entering the dialyzer
- ER = $(Art_{bun} – Ven_{bun})/Art_{bun}$
- ER = (80 – 20)/80 = 60/80 = 0.75
- 75% of the urea is removed in a single pass through the fiber

BUN of Venous Blood based on Dialyzer KoA

QB = 300 mL/min QD = 600 mL/min

KoA (mL/min)	Clearance (mL/min)	Arterial Blood BUN Values (mg/dL) 70	80	90	100	110
500	217	19.4	22.1	24.9	27.7	30.4
600	232	15.9	18.1	20.4	22.7	24.9
700	245	12.8	14.7	16.5	18.3	20.2
800	254	10.7	12.3	13.8	15.3	16.9
900	262	8.9	10.1	11.4	12.7	13.9
1000	269	7.2	8.3	9.3	10.3	11.4
1100	274	6.1	6.9	7.8	8.7	9.5
1200	278	5.1	5.9	6.6	7.3	8.1

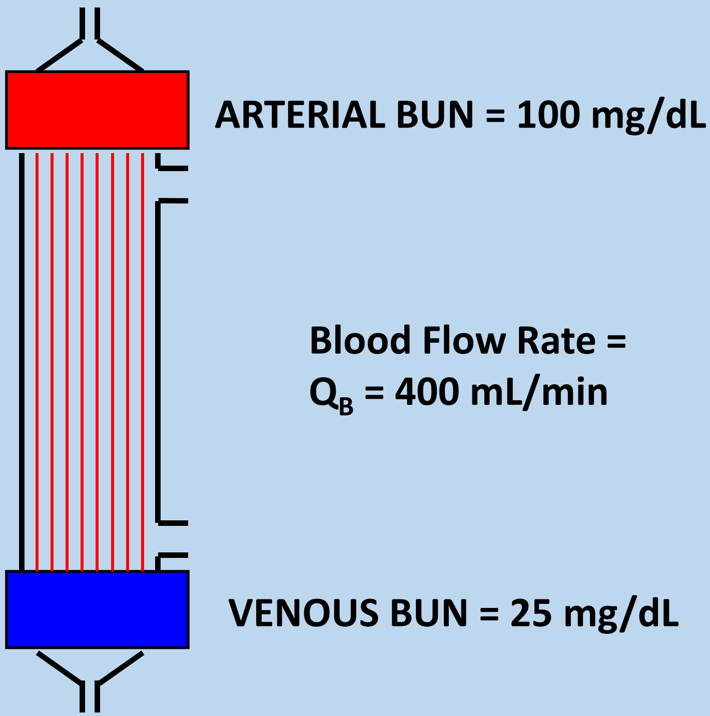
Extraction Ratio (ER)



- What happens to the extraction ratio if the BUN is increased at the Dialyzer inlet?

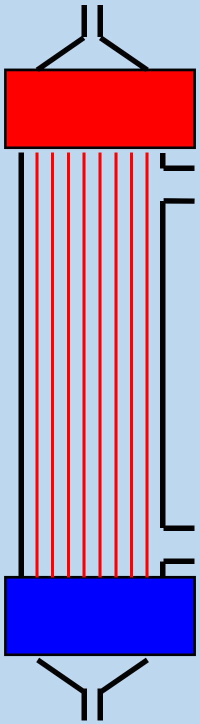
- A) it increases
- B) it decreases
- C) it remains the same

Extraction Ratio (ER)



- C) = it remains the same
- This means the concentration leaving the venous end of the dialyzer will be 25 mg/dL
- $ER = (Art_{bun} – Ven_{bun})/Art_{bun}$
- $VEN_{BUN} = ART_{BUN} (1 – ER)$
- $VEN_{BUN} = 100 (1 – 0.75) = 25$ mg/dL
- BUN 80 mg/dL ⇨ 60 mg/dL
- BUN 100 mg/dL ⇨ 75 mg/dL

Extraction Ratio (ER)



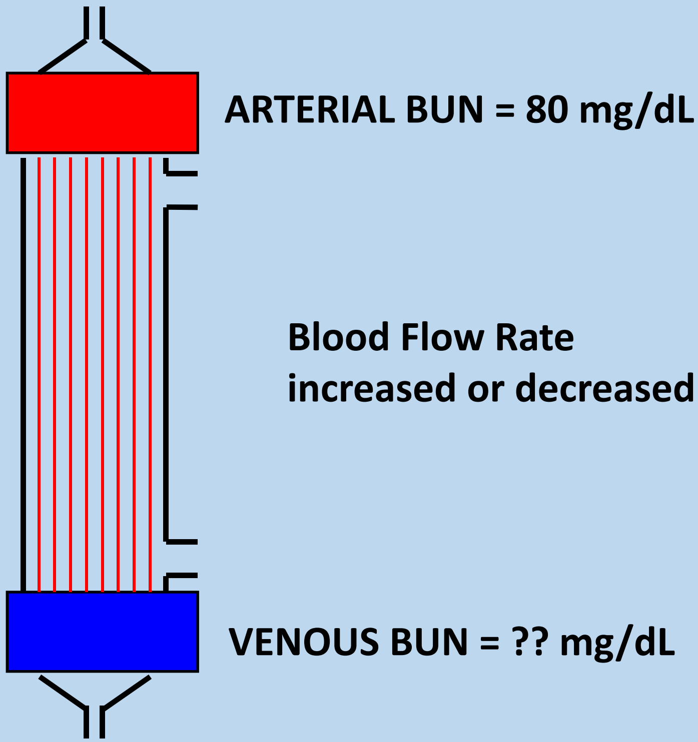
ARTERIAL BUN = 80 mg/dL

Blood Flow Rate increased or decreased

VENOUS BUN = ?? mg/dL

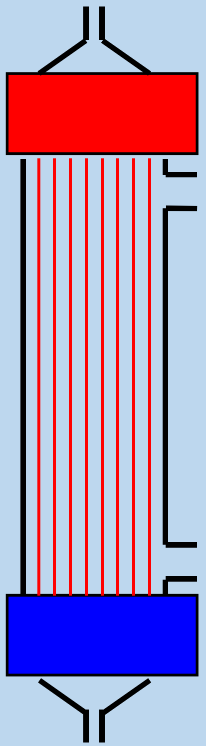
- What happens to the ER if the Blood Flow Rate is increased or decreased?
- A) As Q_b increases, ER increases
- B) As Q_b increases, ER decreases
- C) As Q_B decreases, ER increases
- D) As Q_B decreases, ER decreases
- E) ER remains the same

Extraction Ratio (ER)



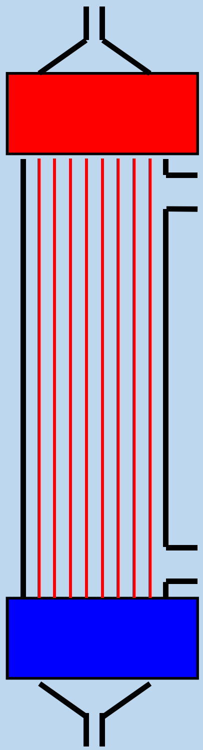
- B) As Q_b increases, ER decreases
- C) as Q_B decreases, ER increases
- The way to think of this is that at higher flow rates the BUN spends less time in the dialyzer and hence has less time to diffuse over to and then through the membrane
- It's just the opposite for lower blood flow rates

Extraction Ratio (ER)



- If the ER goes down with increasing Q_B, why do MD's prescribe high Q_B's for their patients?
- A) MD's don't understand dialyzer dynamics
- B) Faster is always better
- C) The Q_B increase is larger than the ER decrease
- D) ER has nothing to do with clearance

Extraction Ratio and Clearance (C_X)



- C) The Q_B increase is larger than the ER decrease
- ER is directly related to clearance
- Clearance = ER x Q_b
- Remember this Formula?

$$C_X = \left(\frac{A_X - V_X}{A_X} \right) Q_B$$

Clearance vs. Blood Flow

Arterial BUN = 80 mg/dL Q_D = 500 mL/min

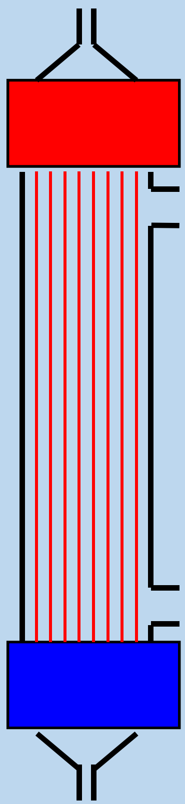
BLOOD FLOW (400 mL/min)	EXT. RATIO %	CLEARANCE (mL/min)	VENOUS BUN (mg/dL)
20,000	2	422	78
2,000	20	403	64
1,000	38	379	50
500	65	327	28
200	96	193	3
100	100	100	0

Thinking Clearance

- Clearance as blood volume
- Let Q_B = 400 mL/min and C_X = 300 mL/min
  - 300 mL of blood will be completely cleared of BUN and 100 ml will be unchanged
  - In actuality, all 400 mL will have a reduction of 75%
  - The clearance rate remains constant during the treatment.

- Clearance as BUN removed
- Let ART_{BUN} = 80 mg/dL and VEN_{BUN} = 20 mg/dL
  - 60 mg/dL is removed
  - QB = 400 mL/min = 4 dL/min
  - 60 mg/dL x 4 dL/min = 240 mg/min is removed
- The amount of BUN removed per minute will drop during the treatment as the ART_{BUn} and VEN_{BUN} decrease.

Clearance vs. Dialysate Flow



BLOOD FLOW = 400 mL/min

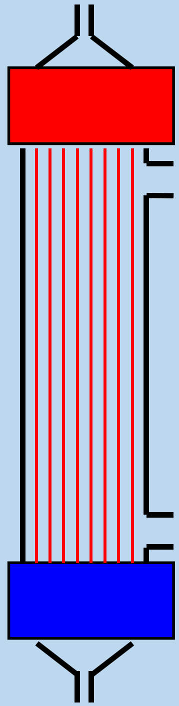
DIALYSATE FLOW = 500 mL/min

DIALYZER KoA = 945

CLEARANCE = 300 mL/min

- How much will the clearance change if the dialysate flow rate is increased to 800 mL/min?
  - A) 10%
  - B) 6%
  - C) 4%
  - D) 0%
  - E) -4%

Clearance vs. Dialysate flow



BLOOD FLOW = 400 mL/min

DIALYSATE FLOW = 500 mL/min

DIALYZER KoA = 945

CLEARANCE = 300 mL/min

- THE ANSWER IS: B) 10%
- INCREASING DIALYSATE FLOW WILL INCREASE CLEARANCE
- THE CLEARANCE FORMULA IS:

$$C_X = \frac{Q_B\left(e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-1\right)}{e^{KoA\left(\frac{1}{Q_B}-\frac{1}{Q_D}\right)}-\frac{Q_B}{Q_D}}$$

Where: C_X = Clearance of solute, X

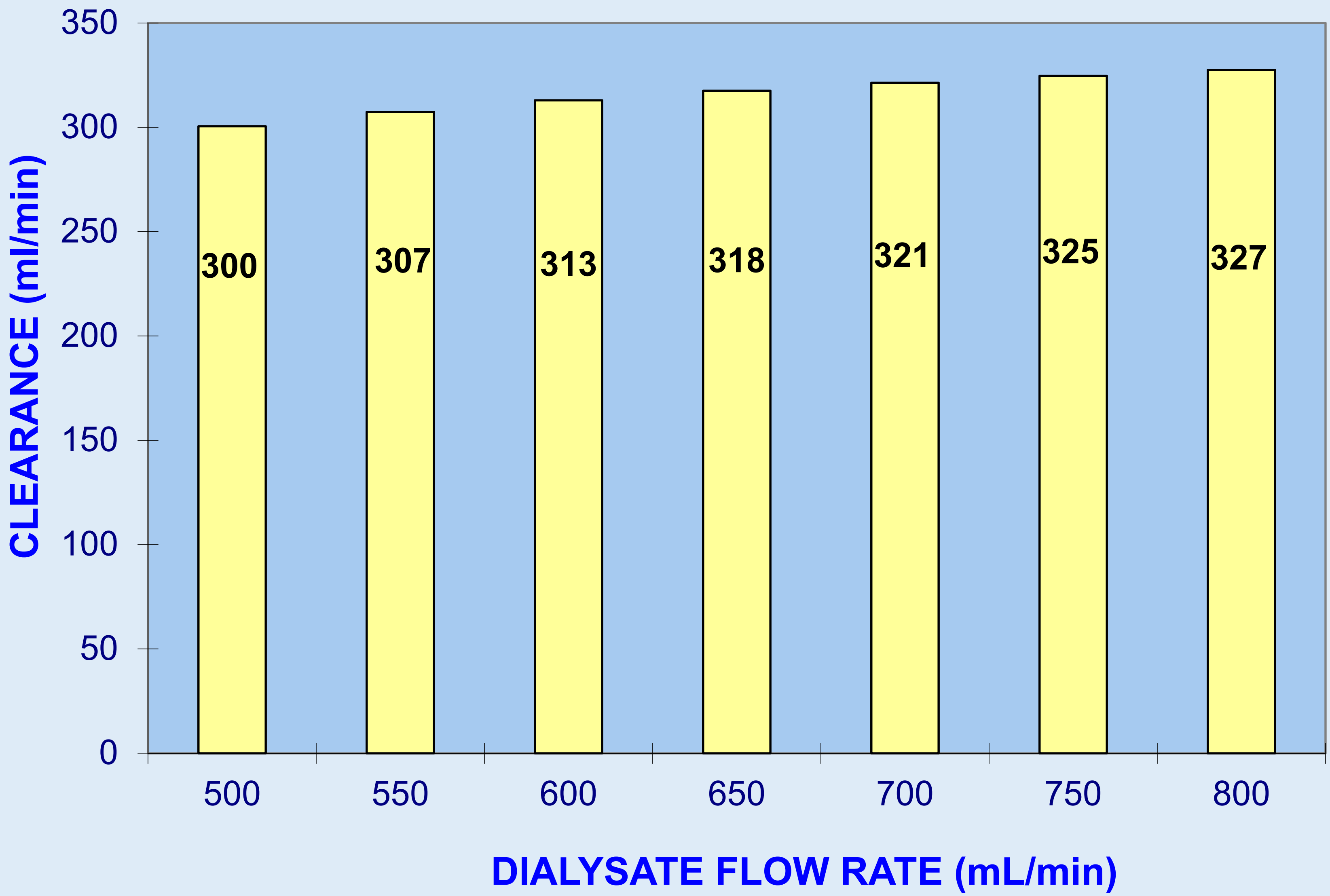
Q_B = Blood flowrate

Q_D = Dialysate flowrate

ln = Natural logarithm = e

e = 2.718281828..

CLEARANCE for KoA = 945, Q_B = 400 mL/min



NEWS Break: Increasing Q_D may have zero benefit !

- RENAL WEEK 2010 abstract (Ward RA, et al: TH-FC038)
  - 28 patients, crossover study
  - Q_D = 600 mL/min alternating with 800 mL/min BABA ABAB
  - Q_B averaged 435 mL/min
  - Revaclear or Revaclear MAX dialyzers were used
- RESULTS:
  - 600 mL/min had Kt/V of 1.67 ± 0.04
  - 800 mL/min yielded KT/V of 1.65 ± 0.04
- Benefits of higher dialysate flow may not be true anymore, especially with today's newer dialyzers.

Pressure/Flow Relationship Equation

- The relationship of Pressure to Flow in a hollow fiber is given by the Hagen-Poisseuile Equation:

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

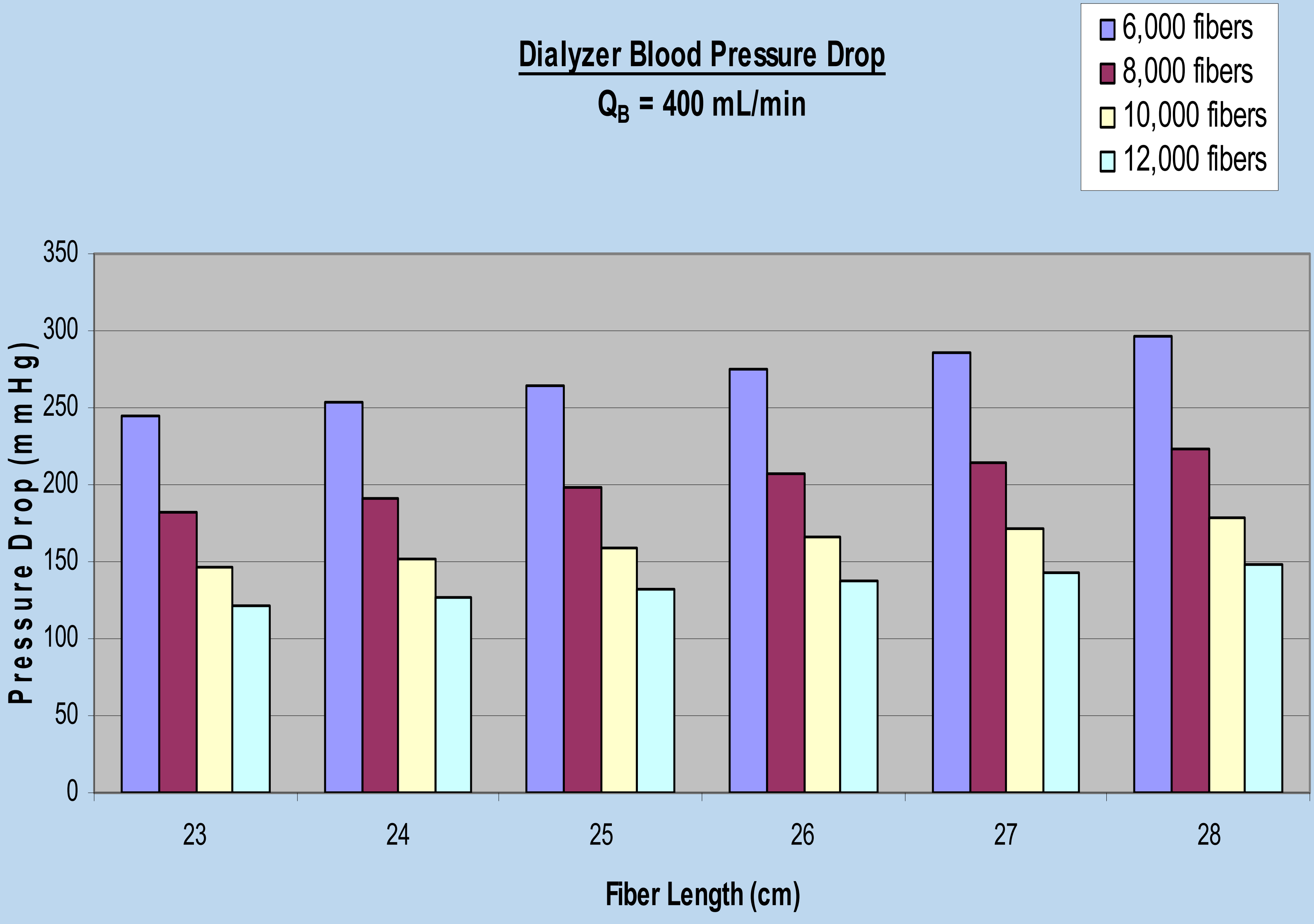
Where: Q_B = Blood Flowrate

ΔP = Blood Pressure drop through the fiber.

L = Length of fiber.

r = Inside radius of the fiber.

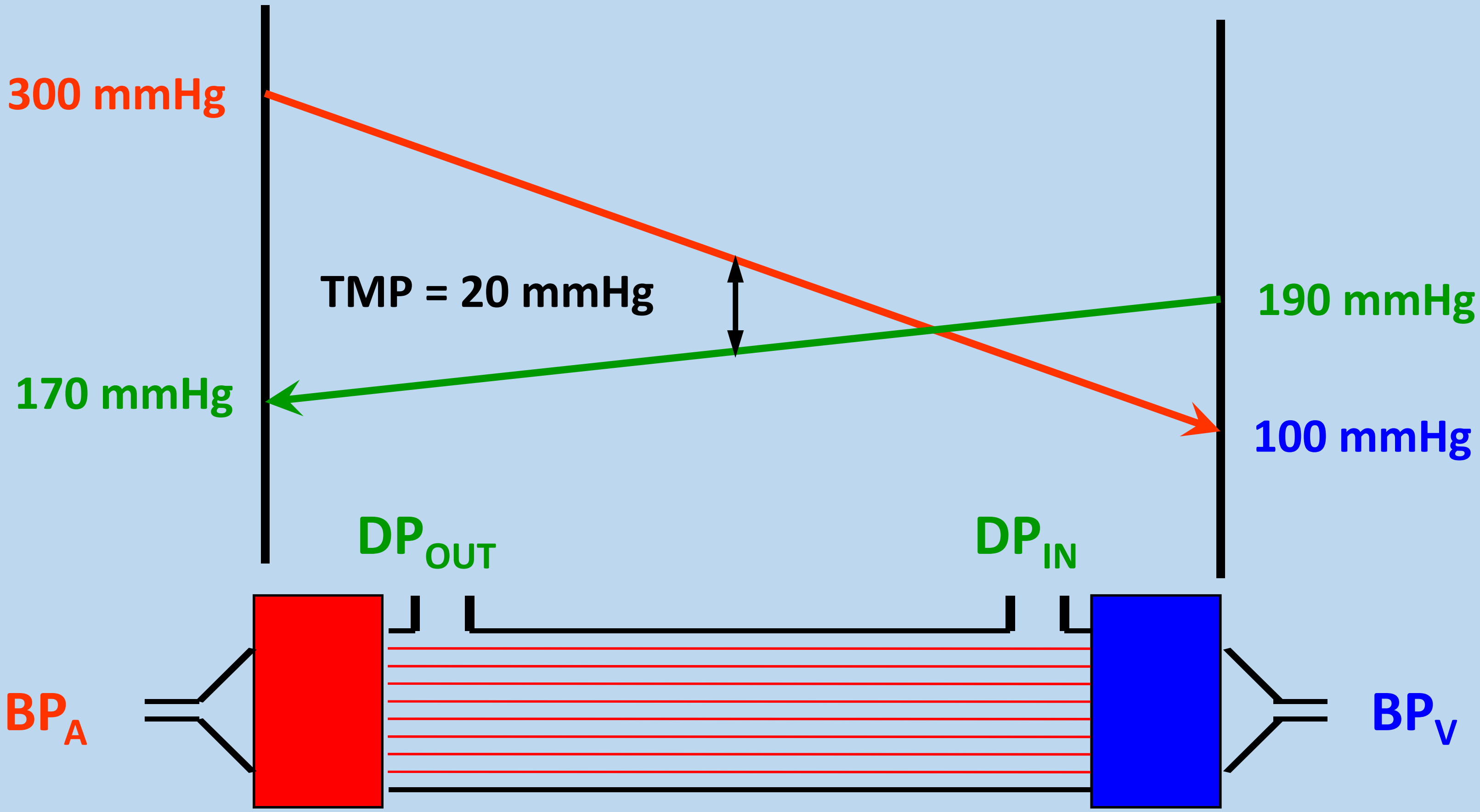
μ = Blood viscosity



Dialyzer Blood Pressure Drop
Q_B = 400 mL/min
6,000 fibers
8,000 fibers
10,000 fibers
12,000 fibers
Pressure Drop (mmHg)
350
300
250
200
150
100
50
0
23
24
25
26
27
28
Fiber Length (cm)

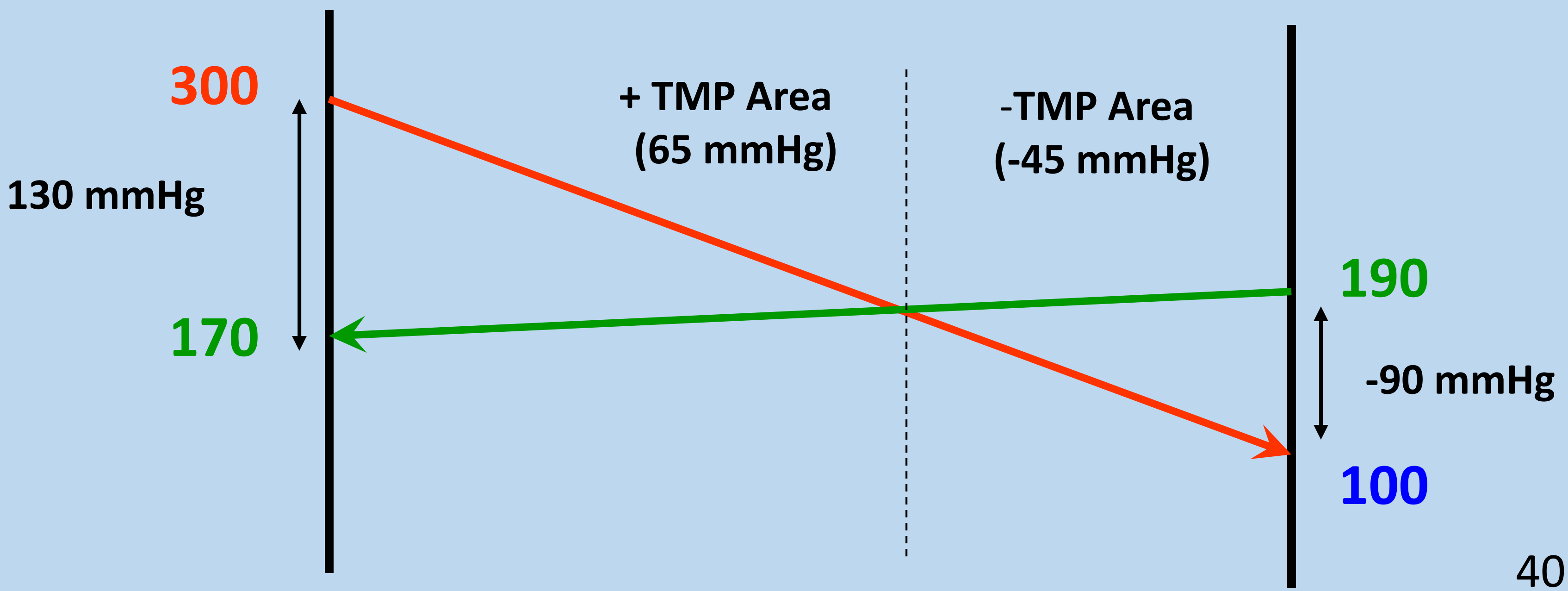
Pressures inside a Hollow Fiber

Kuf = 50 mL/hr/mmHg TMP. Desired UFR = 1000 mL/hr.



TMP along the hollow fiber

- **+TMP$_{AVG}$ = (TMP$_{PRE}$ + 0) / 2 = TMP$_{PRE}$ / 2**
  = (130 + 0) / 2 = 130 / 2 = 65 mmHg
- **-TMP$_{AVG-}$ = (TMP$_{POST}$ + 0) / 2 = TMP$_{POST}$ / 2**
  = (-90 + 0) / 2 = -90 / 2 = -45 mmHg



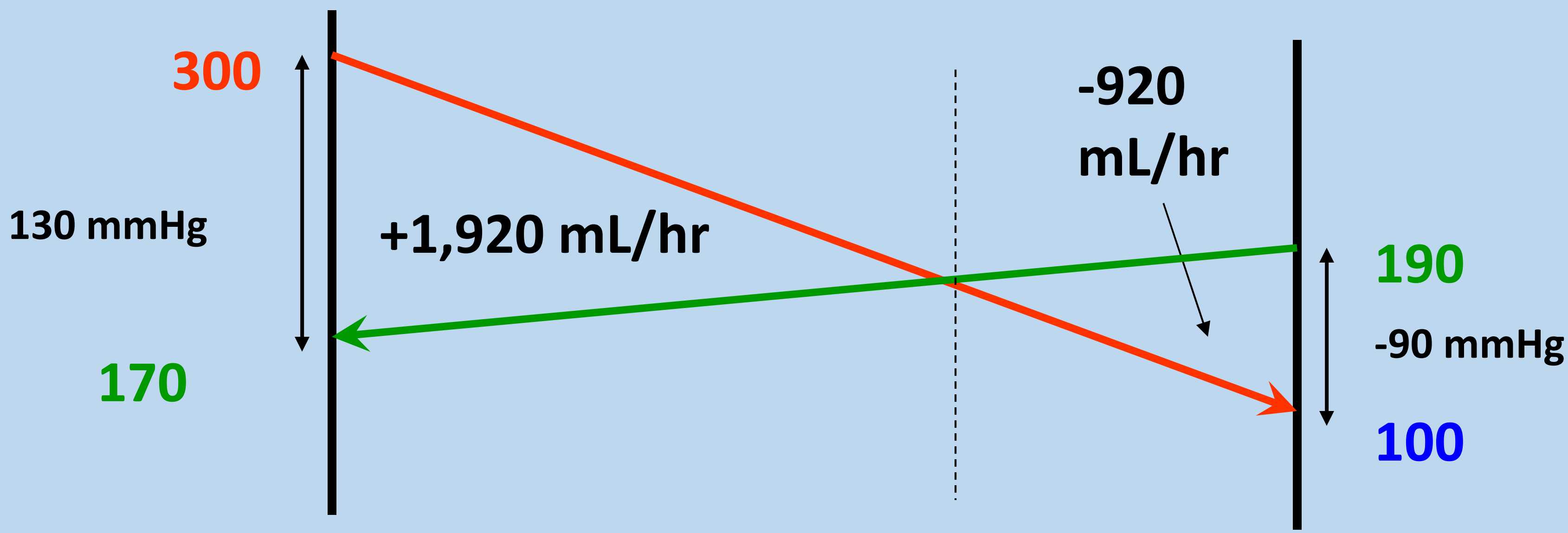
UFR along the hollow fiber

$+UFR = K_{UF} \times (+TMP_{AVG}) \times PRE/(PRE + POST)$

$= 50 \times 65 \times 130/(130 + 90) = 1{,}920$ mL/hr

$-UFR = K_{UF} \times (-TMP_{AVG}) \times POST/(PRE + POST)$

$= 50 \times -45 \times 90/(130 + 90) = -920$ mL/hr



The party in the hollow fiber is now officially over…
Thanks for coming!