Design of a Simplified Hemodialysis Simulation

Onesmo Ogore, Kushal Sherpa, Caleb Baron,
Mansour Zenouzi, Ph.D., P.E., and Shankar Krishnan, Ph.D.
Electronics and Mechanical Department
Wentworth Institute of Technology
Boston, MA 02115

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ABSTRACT

The objective of the present study is to create a representation of a hollow fiber dialyzer which is a critical component of any hemodialysis system. This is done to facilitate the understanding of the mass transport and fluid dynamics processes that occur within the dialyzer, which affect the dynamic homeostasis of end stage renal disease (ESRD) patients. The proposed solution utilizes a computer generated model via COMSOL to represent the dialyzer unit and these processes. Co-current and counter-current flow inside the dialyzer are simulated. The simulated flow data is then used to determine the concentration gradients that occur within the fluids and the membrane. In conclusion, the design of the simplified interactive hemodialysis model shows promise to facilitate a simple and clear understanding of these processes by engineering students. Increasing awareness of hemodialysis function by the patients and the family members can have a positive impact on the overall care of the patient. This is an ongoing project for a Thermal Design course in the Electromechanical Engineering program at Wentworth Institute of Technology.

***Index Terms* – Hemodialysis, Dialyzer, COMSOL, Simulation**

I. INTRODUCTION

Dialysis is a procedure that is performed routinely on patients who suffer from acute, chronic renal failure, or who have ESRD. The process involves removing waste substances and fluid from the blood that are normally eliminated by the kidneys.

The main function of the kidneys is to remove waste products, generated from normal metabolic processes, and excess water from the blood. They play also a major role in regulating blood levels of various minerals such as calcium, sodium, and potassium. Other important functions are the production of hormones such as erythropoietin (EPO), which stimulates the production of red blood cells, renin, which controls blood volume and pressure, and the active form of vitamin D, involved in the intestinal absorption of calcium and phosphorus.

Many pathological events can cause the loss of renal function leading to kidney failure, which can be acute if it develops rapidly, or chronic if it occurs gradually, usually in months to years. ESRD is when the kidneys permanently fail to work. Over the past decades, technological improvements have lead to several treatment options that include peritoneal dialysis, hemodialysis, and continuous renal replacement therapies (CRRT). Furthermore, the progress in vascular catheters, semipermeable membranes and machinery has resulted in a variety of dialysis therapeutical options [1]. The choice of renal replacement therapy (RRT) often depends on several conditions that include clinical indication, and types of dialysis machinery.

The subsequent paper focuses on a computer generated model via COMSOL to represent the dialyzer unit and the processes that occur within. The primary goal is to facilitate a better understanding of the hemodialysis process and the biophysics involved in its design.

II. HEMODIALYSIS PROCESS

Hemodialysis units can be broken up into three basic subsystems: the blood delivery system **(I & IV)**, dialyzer or exchanger **(II & III)**, and the dialysate delivery & waste system **(IV & V),** (Figure 1). The blood delivery system is constituted by vascular access, catheres that carry the unfiltered blood to the dialyzer and filtered blood back to the body, heparin and blood pump.

The dialyzer consists of two chambers or paths **(II & III**) separated by a semi-permeable membrane **(F & E)** typically composed of cellulose, depending on the therapy employed [2]. The membrane is permeable to water and small molecules such as urea and impermeable to blood components like red blood cells, platelets and large proteins.

Within the chamber one path carries the unfiltered blood from the patient and the other is filled with the dialysate a special mixture that is carefully engineered to resemble the composition of the plasma and can be individualized based on the needs of the patient. The dialysate is usually delivered via a dialysate delivery system **(V)** composed of a proportioning unit, pumps, tubes, degasser and a temperature management unit **(D)**. This system also monitors concentration levels and blood temperature and acts as a bypass if these values are off. Inside the exchanger most of the uremic toxins and excess fluids found are extracted from the blood path into the dialysate.

To increase the efficiency of this process the exchange within the membrane is done under countercurrent flow conditions. Once the unwanted toxins and fluids are extracted, the dialysate is delivered out **(III)** via the use of small plastic tubes **(G)** and disposed off appropriately **(IV).** Then the filtered blood within the dialyzer chamber is pumped out of the dialyzer **(II)** and delivered to the patient's venous system via the use of tubes **(VI & S)** after being monitored for air bubbles,

it is also at this stage that venous pressure is monitored. During this process the blood has to be kept at body temperature using a thermo management system. This cycle usually takes 2 to 4 hours and is done about 3 times a week. The frequency depends upon the severity of CKD. [3]

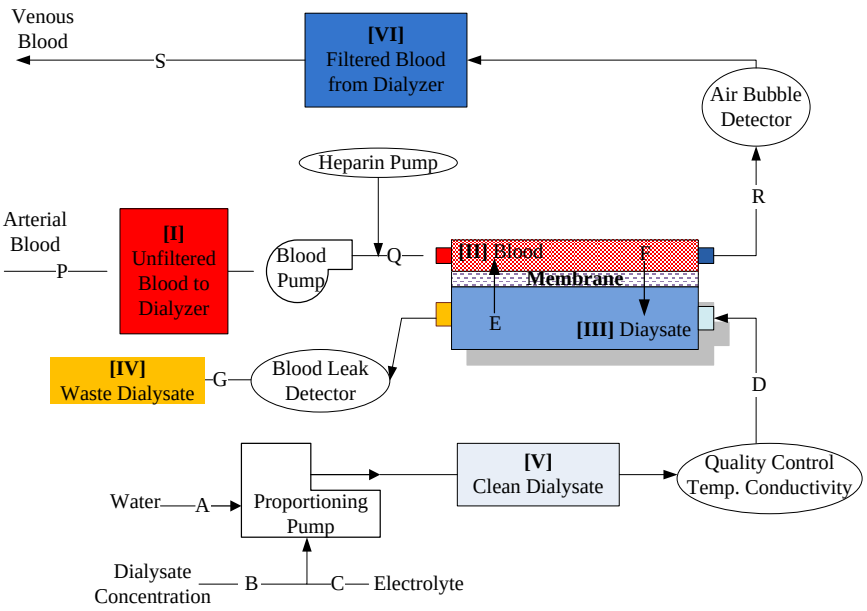


Figure 1: Simplified model of hemodialysis process

This analysis attempts to simulate the dialytic process using biophysical equations to demonstrate the effect of changing dialyzer parameters on the treatment process. For example how adjusting system flow rate affects the extraction of toxins and the duration of dialysis. (See Appendix A for diagram nomenclature)

III. MODELING HEMODIALYSIS

Closer inspection of the dialyzer (**II & III**), its chambers and its semi-permeable membranes (**F & E**), reveals that it is imperative for dialyzer designers to understand the mechanisms that govern the bidirectional flow and restriction of the solvent and solutes found within the solution. Solvent being the excess fluid found in the blood and the fluid found in the dialysate. Solvents being the toxins, blood components, and particles found within the dialysate.

The physical processes that regulate the transport rate of the solutes and solvents across the dialyzer membrane are: diffusion (toxins and electrolytes), convection (larger molecules > 1,000 Daltons or g/mol), ultra-filtration (plasma water removal), and osmosis (body fluid shift). This excludes adsorption, which is controlled by electrostatic and Van der Waals forces between solute and membrane, absorption-based removal can be beneficial or harmful depending on the compound involved. [4]

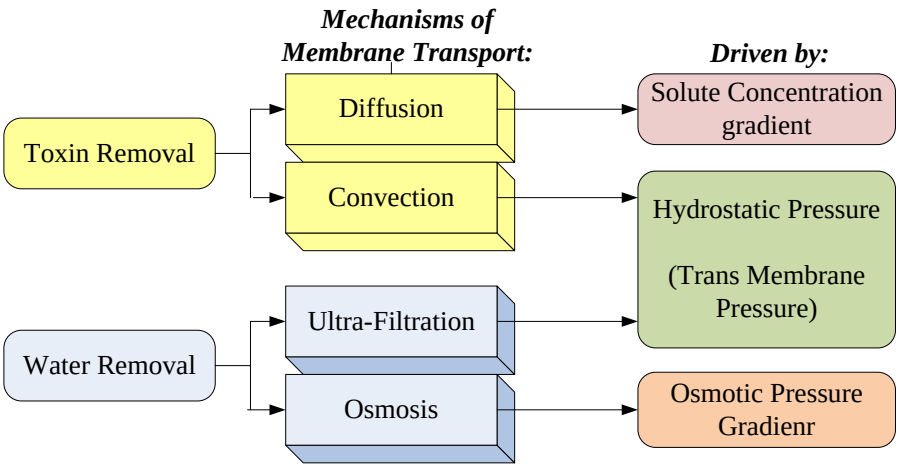


Figure 2: Mechanisms of membrane transport used in hemodialysis

Removal of uremic toxins from the blood is mainly governed by two mechanisms: diffusion which eliminates mostly toxins and electrolytes, and convection which is responsible for removing larger molecules greater than 1000 daltons, excluding adsorption with removes the largest molecules such as beta-2-microglobulin. Water removal across the membrane is primarily controlled by ultrafiltration and osmosis (Figure 2).

Renal replacement therapy (RRT) uses all these processes in combination, but diffusion and convection are the most relevant. In dialysis, diffusion is the prominent mechanism which clears small molecules more effectively. While ultrafiltration uses convection, and is very effective in the removal of very large amount of extracellular fluids and middle-size molecules. Therefore the choice of the methodology will be based on the needs of the patient.

IV. COMSOL DIALYSIS SIMULATION

This simulation mainly focuses on modeling the steady state diffusive flux of toxins across the dialyzers semi-permeable membrane due to the concentration gradients created across it. More specifically it will simulate the diffusion of small molecules across the hollow fibers in the dialyzer shell, in order to demonstrate how the diffusive process within a fiber of the dialyzer lowers the concentration of toxins in the blood stream into the dialysate.

The configuration of a modern hollow fiber hemodialysis assembly can be seen in the (Figure 3). It is usually composed of an outer shell consisting of a bundle of many capillaries made out of semi-permeable membrane material, usually cellulose. The blood flows through these artificial capillary channels while the dialysate flows across the shell over the capillaries in a counter-current manner similar to a shell and tube heat exchanger. In this application the flow is laminar.

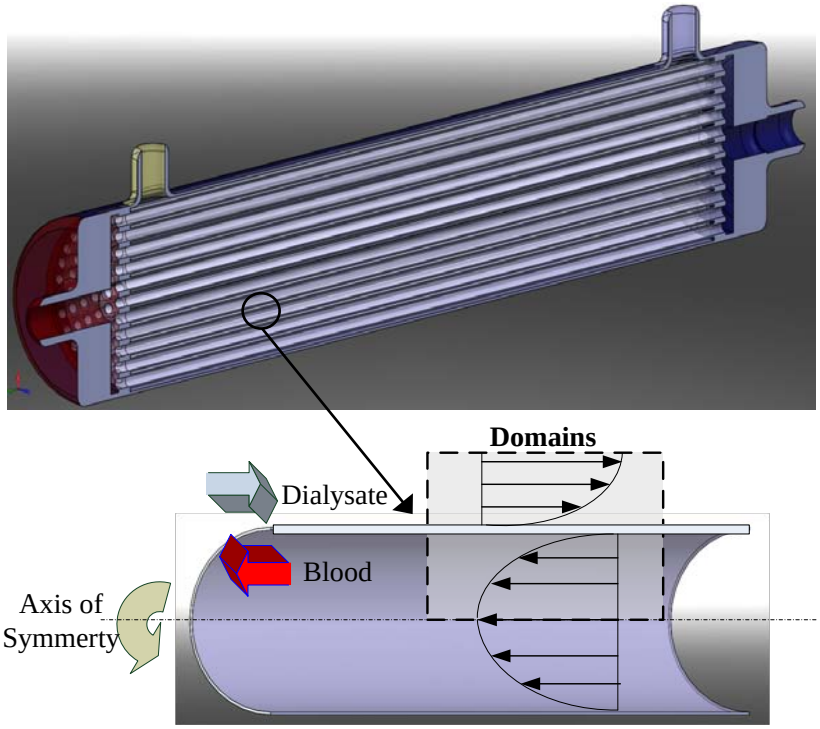


Figure 3: Diagram of hemodialysis hollow-fiber dialyzer.

For the COMSOL simulation the flow fields, and diffusive and convective concentration gradients, within a single capillary in the dialyzer, are simulated. Since there are no angular concentration gradients at a cross section of the hollow fiber an axisymmetrical estimate can be used to determine a solution (Figure 3). Figure 4 shows the three sections of the axisymmetrical domain: the domain on the right models the blood flow in the capillary, the small domain in the middle models the membrane, and the domain on the left represents the outer dialysate flow in the shell.

Assuming that the blood is a binary mixture of a solvent B (blood) and a solute U (urea), which is transported across the membrane to the solvent D (dialysate), we can use Fick's law in the COMSOL Chemical Engineering Module [12] to describe the diffusive and convective transport of U in the blood and dialysate and the diffusive transport across the membrane. The details of the general partial differential equations (PDE) that are used by the module can be found in the COMSOL manual [5]. The following simplified PDE's that described the convective and diffusion processes in the blood and the dialysate (1 & 2) and the purely diffusive transport in the membrane (3) are used by the module:

$$\nabla \cdot (D_{CB} c_1 + u_B c_1) = 0 \qquad \text{Blood domain (1)}$$
$$\nabla \cdot (D_{CM} c_2) = 0 \qquad \text{Membrane domain (2)}$$
$$\nabla \cdot (D_{CD} c_3 + u_D c_3) = 0 \qquad \text{Dialysate domain (3)}$$

(See Appendix A for nomenclature)

In the 5cm dialyzer shell diameter, they are typical 10^4 capillaries, which have an inner diameter of only 200-250µm and a length of 15cm. The radius of these fibers is therefore about 600 times smaller than the length. Using this exact geometry in COMSOL would cause it to generate a large number of mesh elements. We introduced a scaling factor to reduce the amount of mesh elements in the computational domains. As a result this increases simulation speed, decreases the amount of memory needed by the computer to obtain a solution, and makes the analysis of the solution less troublesome to observer.

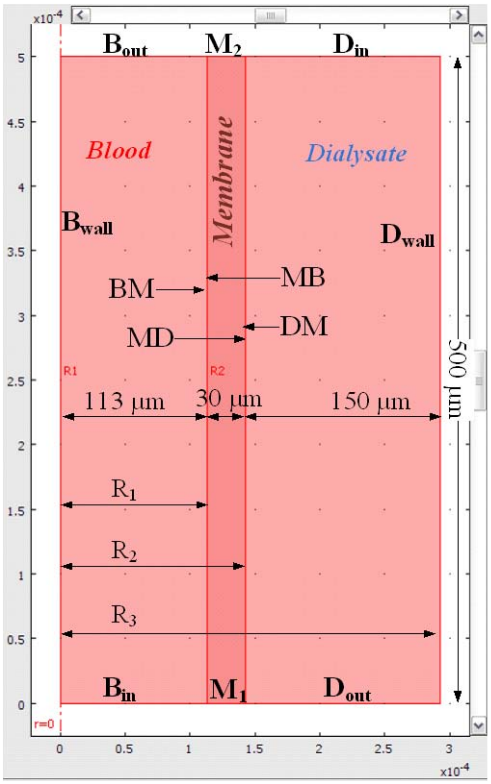


Figure 4: Model geometry

For the simulation the scaling factor is used to model the entire length of a hollow fiber using geometry of a smaller length in the COMSOL interface. This scaling in length has a direct effect on the velocity fields and the diffusive and convective transportations along this scaled length. Such that the subdomains flow velocity and diffusivity used in the simulation are no long viewed as isotropic but as nonisotropic with respect to the fact that the actual radial dimension is kept the same while the length is scaled. (See Appendix B for Dimensions & Properties)

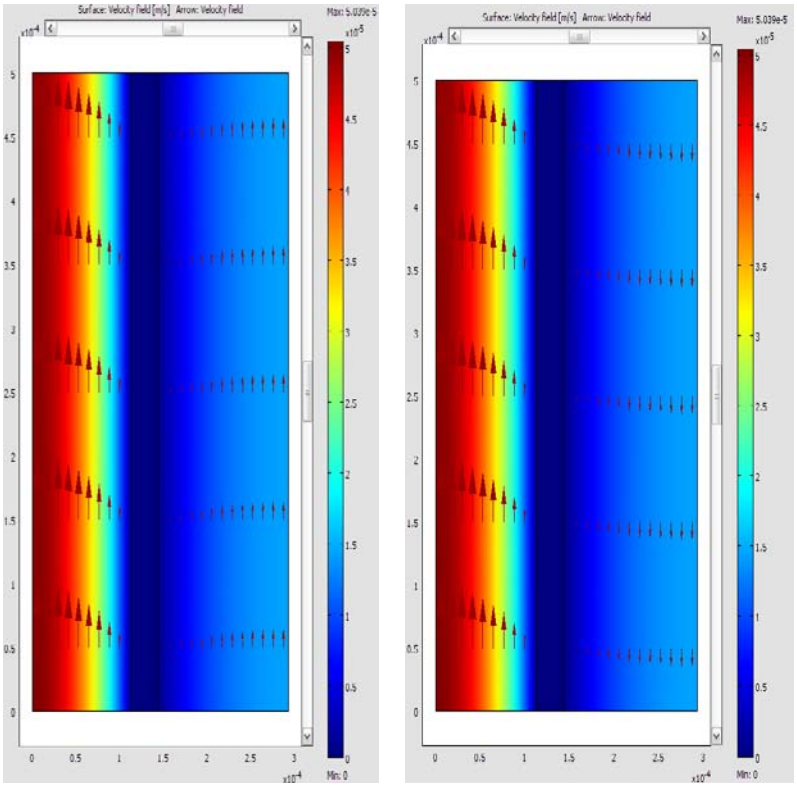
For the convective component of the dialysate and the blood the Reynolds number for these flows were calculated to be 0.386 and 2.141 respectively. Therefore these flows can be considered fully developer laminar flow. Under these conditions the flow fields on both sides of the membrane could be simulated using COMSOL's Chemical Engineering Module Incompressible Navier-Stokes application mode. First the fluid subdomain property's of viscosity and density where defined by the values shown below.

The boundary layers where then defined as follows: B_{wall} and D_{wall} has slip condition since their where modeling the center of the laminar flow through the tube. B_{out} and D_{out} where model with pressured drop condition that were set to zero. B_{in} was model having an inlet velocity condition in the y-direction described by the equation show below:

$$v_B = \frac{\left(\frac{2 \cdot Q_B}{\pi \cdot R_1^2 \cdot n}\right)\left[1-\left(\frac{y}{R_1}\right)^2\right]}{\text{scale}} \qquad (4)$$

D_{in} was model have an inlet velocity condition in the y-direction described by the equation show below:

$$v_D = \frac{8 \cdot Q_D}{4 \cdot \pi (R_3^4 - R_2^4) \cdot n \cdot scale} \left[r^2 - R_2^2 - 2 \cdot R_3^2 \cdot \ln\left(\frac{y}{R_2}\right)^2 \right] \quad (5)$$



(a) (b)

Figure 5: Co-current (a) and counter-current (b) velocity profiles.

Usually during hemodialysis the toxin in the blood stream has to dissolve into the membrane before it can be transported out by the dialysate. For this reason a dimensionless partition coefficient K is used to describe this interaction between the membrane and the fluids:

$$K = \frac{c_{MB}}{c_{BM}} = \frac{c_{MD}}{c_{DM}} \qquad (6)$$

For this simulation this coefficient was assumed to be 1 by neglecting toxin flux delays cross the membrane due to toxin absorption in the membrane material. The concentration simulation boundary layers where then defined as follows: B_{wall} and D_{wall} had insulation symmetry condition. B_{out} and D_{out} where modeled as convection flux regions having a great contribution to conversion than diffusion. B_{in} was model as having a set inlet concentration c_0. D_{in} was model as have a set inlet concentration of 0. The membrane boundary conditions and more details of the mathematical modeling can be found in the COMSOL manual [5].

V. RESULTS & DISCUSSION

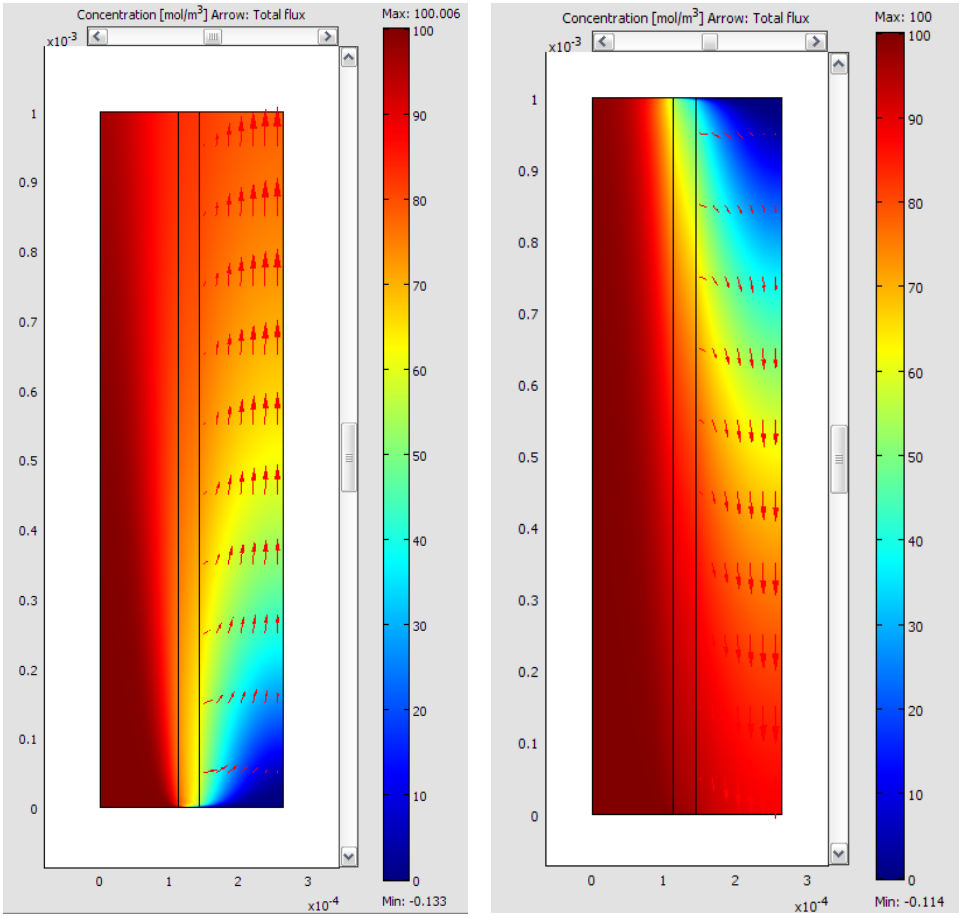
COMSOL simulations of the dialysate and blood in a counter-current and co-current flow setup within a dialyzer were analyzed and their capacities for effecting mass transfer were compared. These simulations yielded the following results:

Co-current flow:

Initial inlet urea concentrations in blood stream set at 100 mol/m^3
Inlet dialysate stream urea concentration set to 0 mol/m^3
Outlet steady state values in blood of urea is 91 mol/m^3
Outlet steady state values and dialysate of urea is 75 mol/m^3

Counter-current flow:

Initial inlet urea concentrations in blood stream set at 100mol/3
Inlet dialysate stream urea concentration set to 0 mol/m^3
Outlet steady state values in blood of urea is 92 mol/m^3
Outlet steady state values and dialysate of urea is 90 mol/m^3



(a) (b)

Figure 6: Co-current (a) and counter-current (b) concentration gradients

Simulations were executed and analyzed with dialysate flowing in a co-current and a counter-current manner. These two characteristically different simulations resulted in fairly similar concentrations in both the blood outlet urea streams of 91 mol/m^3 and 92 mol/m^3 for co-current flow and counter current flow respectively. Discrepancies arose however in the dialysate outlet stream urea concentrations. As mentioned; the co-current simulations this outlet urea concentration was $15mol/m^3$ higher than in the counter-current flow simulation. This implies that changes in flow method have a direct affect on the urea concentration that is removed from the blood flow. The results of this simulation show that the change from a co-current to counter-current flow causes an increase in the diffusive flux across the membrane therefore increasing the concentration of urea in the dialysate fluid.

VI. CONCLUSIONS

For our purposes, analysis of a complete hemodialysis system was unnecessary and proved too cumbersome. It was for this reason that we chose to focus on the dialyzer, the core component of the hemodialysis system. Furthermore, our findings indicate that manipulation of various subsystems have only negligible effects on the efficiency of the system as a whole, whereas manipulation of physical and functional aspects of the dialyzer itself have a significant effect on the outcome of the filtration process. Simulations were executed and analyzed with dialysate flowing in a co-current and a counter-current manner. These two characteristically different simulations resulted in fairly similar concentrations in both the blood outlet urea streams of 91 mol/m^3 and 92 mol/m^3 for co-current flow and counter current flow respectively**.** Discrepancies arose however in the dialysate outlet stream urea concentrations. As mentioned; the co-current simulations this outlet urea concentration was $15mol/m^3$ higher than in the counter-current flow simulation. This implies that changes in flow method have a direct affect on the urea concentration that is removed from the blood flow. The results of this simulation show that the change from a co-current to counter-current flow causes an increase in the diffusive flux across the membrane therefore increasing the concentration of urea in the dialysate fluid.

APPENDIX A: NOMENCLATURE

A: Water supply
B: Dialysate concentration
B_{IN} : Boundary inlet condition from blood
BM : Boundary condition from blood to membrane
B_{OUT} : Boundary outlet condition from blood
B_{WALL}: Boundary condition for wall on blood side
C: Electrolyte
c_1: Concentration of urea in the blood entering the membrane (mol/m^3)
c_2: Concentration of urea in the membrane entering the dialysate
c_3: Concentration of urea in the dialysate leaving the membrane
C_{BM}: Conc. in blood entering membrane
C_{BM}: Conc. absorbed from blood entering membrane
C_{BM}: Conc. in membrane entering dialysate
C_{BM}: Conc. in dialysate taken form membrane
D: Dialysate inlet tubing
D_{IN} : Boundary inlet condition from dialysate
DM : Boundary condition from dialysate to membrane
D_{OUT} : Boundary outlet condition from dialysate
D_{WALL}: Boundary condition for wall on dialysate side
D_{CB}: Diffusion coefficient of urea in blood (mol/(m^3·s))
D_{CM}: Diffusion coefficient of urea in membrane
D_{CD}: Diffusion coefficient of urea in dialysate
E & F: Transport across membrane
G: Waste dialysate outlet tubing
MB: Boundary condition from membrane to blood
MD: Boundary condition from membrane to dialysate
M_1: Membrane inlet
M_2: Membrane outlet
n: Number of fibers
P: Arterial blood access
Q: Blood entering dialyzer
Q_B: Blood flow rate
Q_D: Dialysate flow rate
R: Filtered blood leaving dialyzer
r: Radial direction
R_1: Fiber inner radius
R_2: Fiber outer radius
R_3: Radius from the center to where the outer flow is observed
S: Venous blood access
y: y direction
u_B: Blood flow velocity vector (m/s)
u_D: Dialysate flow velocity vector
I: Unfiltered Blood to Dialyzer
II: Blood
III: Dialysate
IV: Waste Dialysate
V: Clean Dialysate
VI: Filtered Blood from Dialyzer

APPENDIX B: Dimensions and Properties:

Typical Hemodialysis Dialyzer Parameters			**Cordis-Dow Model**
Shell length	L	0.25 m	13.5 cm
Shell inner diameter	D_S	0.05 m	0.05 m
Number of fiber	n	6,000-10,000	11,000
Tube inner diameter	D_T	200-250 μm	0.0225 cm
Tube thickness	t	dry wall 10 μm	wet wall 30 μm
Membrane surface area	A	0.5-1.5 m^2	1.05 m^2
Blood side pressure	P	100-500 mmHg > dialysate pressure	100-500 mmHg > dialysate pressure
Blood flow rate	Q_B	200 to 250 ml/min	200 cm^3/min
Dialysate flow rate	Q_D	500 ml/min	500 cm^3/min

Table 1: Values used in simulation (Tissue Engineering and Artificial Organs)

Diffusivity of Urea (m^2/s)		
Blood Side	D_{UB}	3.017e-11
Membrane	D_{UM}	4.505e-11
Dialysate Side	D_{UD}	1.4953-11

Table 2: Diffusivity values used in simulation taken at 37 °C (Brenner & Rector. The Kidney, Second Edition. W.B. Saunders Company, 1981: 2433 pg.)

Range of Viscosity for Normal Blood		
Hematocrit	$\boldsymbol{\mu(poise)}$	$\boldsymbol{\mu(Pa\ s)}$
39	0.053	0.0053
20	0.026	0.0026

Table 3: Viscosity values used in simulation taken at 37 °C valid for $\boldsymbol{\gamma} > 100\ \frac{\mathbf{1}}{\boldsymbol{sec}}$ *(*Brenner & Rector. The Kidney, Second Edition. W.B. Saunders Company, 1981: 2433 pg.)

Solute	**Temp (°C)**	**Mass Density** ($\frac{kg}{m^3}$)
Whole Blood	37	1060
Dilaysate	37	1000

Table 4: Density values used in simulation taken at 37 °C (Cutnell, John & Johnson, Kenneth Physics, Fourth Edition. Wiley, 1998: 308)

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