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Group 7

Modelling Species Transport through Membrane in Haemodialysis

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Abstract. The purpose of this project is to study the blood flow in a haemodialyzer device, specifically model the velocity profile of the fluid and the evolution of the concentration of wastes (urea, creatine, etc.) contained in the patient's blood, and present how these variables depend on each other, considering various cases fluid type (e.g. Newtonian & Casson fluid). Furthermore, the optimal positioning of the tubes in the haemodialyzer unit is also investigated.

7.1 Introduction

Haemodialysis is a medical procedure employed in order to reduce the concentration of wastes such as creatine and urea in blood, usually applied to patients suffering from kidney failure.

A haemodialysis unit (haemodialyzer) consists of many tubes through which the blood flows. Outside these tubes, a fluid called the *dialysate* flows in the opposite direction, so that the solutes from the blood are diffused through a semipermeable membrane.

Depending on the patient, this process takes place several times per week, with sessions lasting from two to four hours. It is thus a painful and time consuming operation, so there is a crucial need to improve its efficiency and reduce the time required.

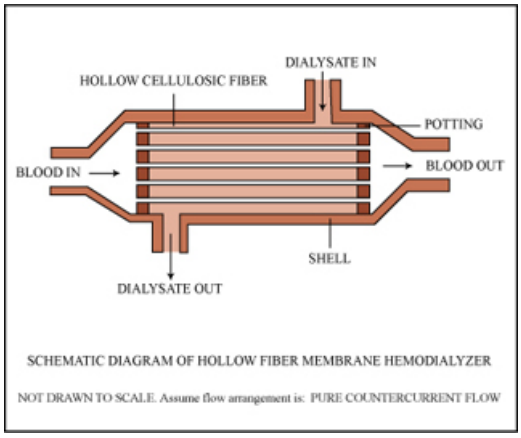

Figure 7.1: A haemodialysis unit, demonstrating the parts it consists of and the flows of the blood and the dialysate.

7.2 Modelling the Problem

Initially, in dimensions of the length and the radius of the tube, the system is described in the $(x, y)-$plane (the generalization to the 3D case of a tube is easy due to axial symmetry):

$$P = (0, 1) \times (-1, 1)$$

by the Navier-Stokes equations for the blood flow and the species transport equation for the concentration of wastes:

$$\begin{cases} u\frac{\partial u}{\partial x} + v\frac{\partial u}{\partial y} = -\frac{\partial p}{\partial x} + \frac{\partial}{\partial y}(\tau) \\ \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0 \\ \frac{\partial c}{\partial t} + u\frac{\partial c}{\partial x} + v\frac{\partial c}{\partial y} = D\frac{\partial^2 c}{\partial y^2} \end{cases} \tag{7.1}$$

where u and v are the velocity components for the blood in the x and y axes respectively, p is the pressure, μ is blood's dynamic viscosity, c is the concentration of the species, D is the diffusion coefficient and τ is the shear stress tensor, on which the morphology of the velocity profile and the flow type (Newtonian or Casson) depend.

It is remarkable that the above system is characterized by *one-way coupling*, in the sense that the concentration is not included in the Navier-Stokes equation whilst the velocity is contained in the species transport equation, thus the latter's evolution can be treated seperately, after the velocity profile haw been obtained.

Furthermore, in this project, only cases where:

$$v = 0$$

known as *Laminar Flows* are considered, i.e. cases where the blood flows only in the x direction, which implies that no blood is transferred through the membrane, and thus the boundary condition:

$$u(x, -1) = u(x, 1) = 0,$$

which indicates the trivial fact that the velocity on the walls should be zero.

Apart than the velocity profile and the evolution of the concentration, what plays an important role for the whole procedure is the volumetric flux per time unit, as it affects the time requirement of the process. That flux then would be:

$$Q = u_m \cdot A,$$

where u_m is the mean value of the velocity profile and A is the sum of the cross-sections of the fibres in the unit, and depends on the pressure drop and the viscosity coefficient of the blood, thus the patients condition (e.g. fever, hematocrit, PVC, high/low blood pressure etc.).

7.2.1 Constant Velocity Profile

The simplest case to consider is the one for which the velocity u of the blood is constant both in the x and y direction, when for the shear stress it is considered that:

$$\tau = 0$$

In this case, the blood is not treated as a Newtonian fluid and the problem reduces to solving the concentration PDE:

$$\frac{\partial c}{\partial t} + u_c \frac{\partial c}{\partial x} = D \frac{\partial^2 c}{\partial y^2} \tag{7.2}$$

where u_c and D are constants. Of course, in order for the boundary conditions of the velocity to hold, there has to be a thin layer near each wall, where the velocity increases from 0 to u_c in a continuous manner. Although mathematically convenient, the above approach is not very realistic, when reffering to blood.

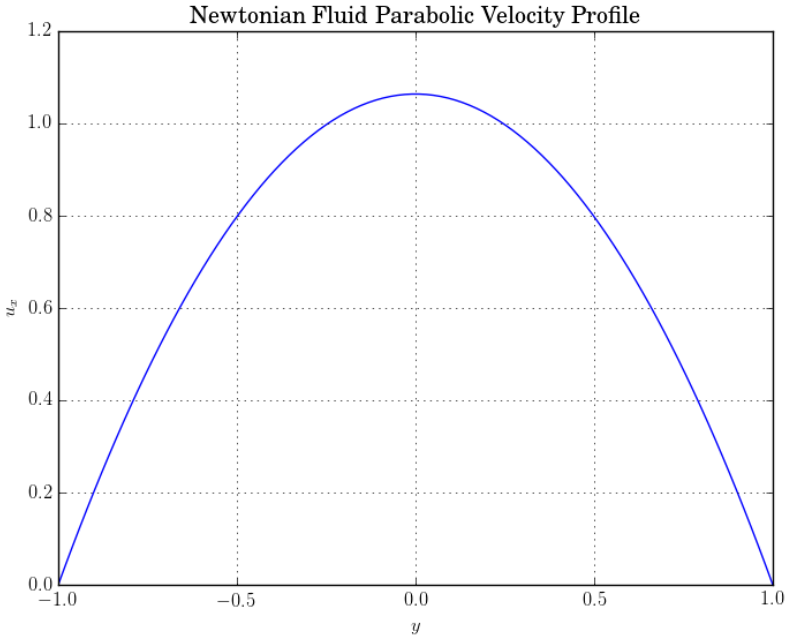

Figure 7.2: Parabolic velocity profile, for the case of Newtonian Fluid.

7.2.2 Newtonian Fluid and Parabolic Velocity Profile

Assuming that the horizontal velocity u depends only on the y variable and the fluid is Newtonian:

$$\tau = \mu \frac{\partial u}{\partial y},$$

the Navier-Stokes equations of system (7.1) read as:

$$\begin{cases} \mu \frac{\partial^2 u}{\partial y^2} = \frac{\partial p}{\partial x} \\ \frac{\partial p}{\partial y} = 0 \\ \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0, \end{cases} \tag{7.3}$$

where the first equation is solved via the separation of variables method as:

$$\mu \frac{\partial^2 u}{\partial y^2} = \frac{\partial p}{\partial x} = -A$$

thus the expressions of the velocity and the pressure are respectively:

$$u(y) = -A\frac{y^2}{2\mu} + B_1 y + C$$
$$p(x) = -Ax + B_2$$

and using the boundary condition $u(-1) = u(1)$:

$$u(y) = \frac{\Delta p}{2\mu}(1 - y^2)$$
$$p(x) = p_0 - \Delta p \cdot x,$$

where p_0 the pressure at $x = 0$ and Δp the pressure drop between the edges of the tube.

Thus, the velocity profile is analytically obtained, and substitution in the concentration PDE results to the equation:

$$\frac{\partial c}{\partial t} + \frac{\Delta p}{2\mu}(1 - y^2)\frac{\partial c}{\partial x} = D\frac{\partial^2 c}{\partial y^2}.$$

In the following figure, the relation between the volumetric flux per time unit as a function of the pressure drop between the edges of the haemodialyzer is demonstrated.

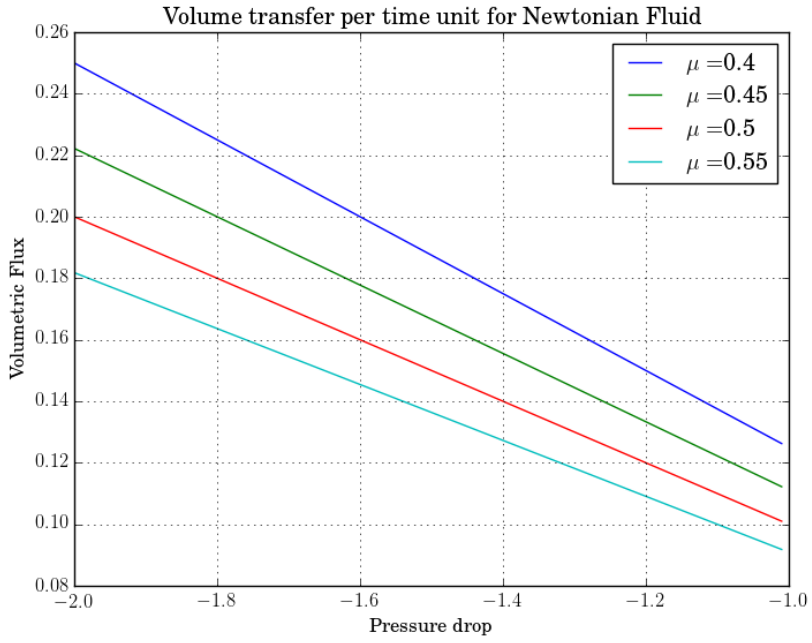

Figure 7.3: Volumetric flux, depending linearly on the pressure drop.

7.2.3 Casson Fluid

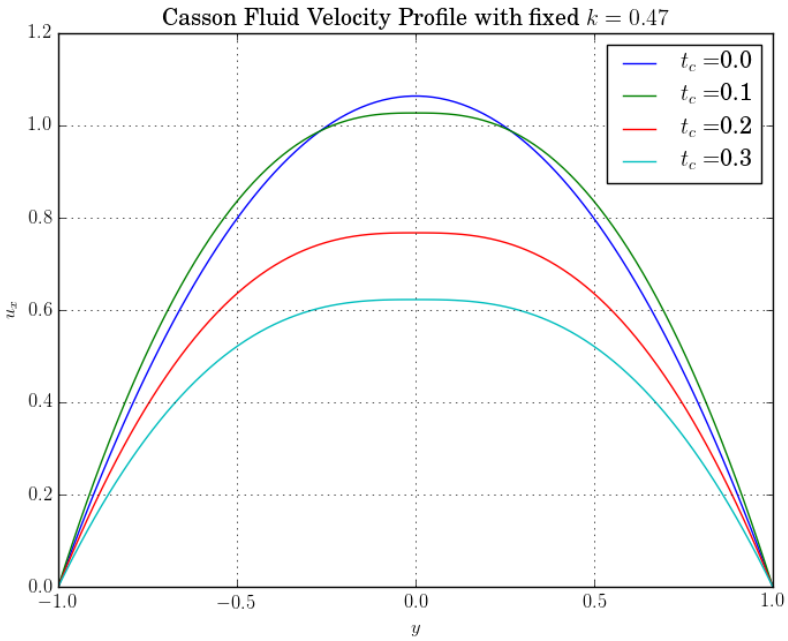

Figure 7.4: Velocity profile of a casson fluid, for various values of the yield stress τ_c. For $\tau_c = 0$, the fluid is Newtonian.

In general, for a casson fluid, the relationship between the shear stress and the strain rate is given by:

$$\frac{du}{dy} = \begin{cases} \frac{1}{k}(\sqrt{\tau} - \sqrt{\tau_c})^2, & \tau \geq \tau_c \\ 0, & \tau \leq \tau_c \end{cases} \tag{7.4}$$

where τ_c is the yield stress and k is the viscosity coefficient. The Navier-Stokes equation thus for this case read as:

$$\begin{cases} \frac{\partial^2 u}{\partial y^2}\left(k + \sqrt{\frac{k\tau_c}{u_y}}\right) = \frac{\partial p}{\partial x} \\ \frac{\partial p}{\partial y} = 0 \\ \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0, \end{cases} \tag{7.5}$$

which are again solved using the separation of variables technique. The above velocity differential equation is a non linear boundary value problem which cannot be solved analytically, thus the "Shooting" numerical method is employed, in order to obtain the velocity profile. In the following figures, the velocity profiles for various values of the yield stress τ_c and viscosity coefficient k. Finally, the relation between the volumetric flux and the pressure drop is slightly non linear.

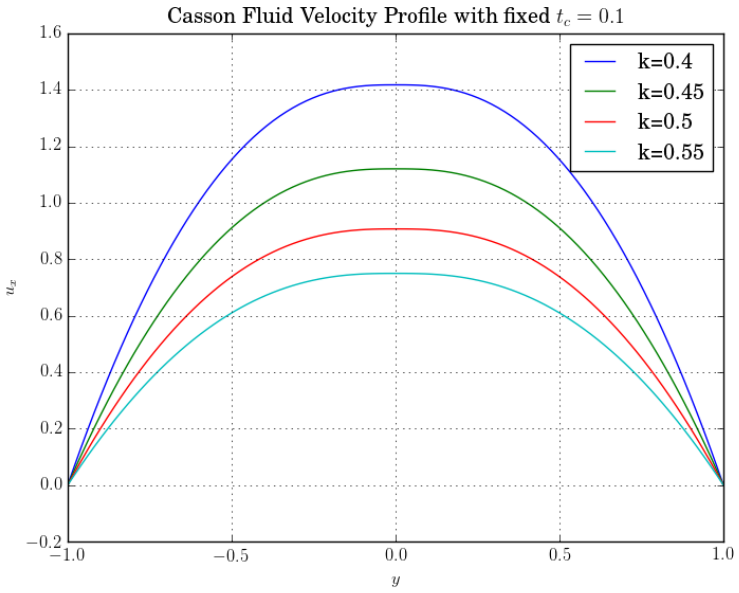

Figure 7.5: Velocity profile of a casson fluid, for various values of the viscosity coefficient k.

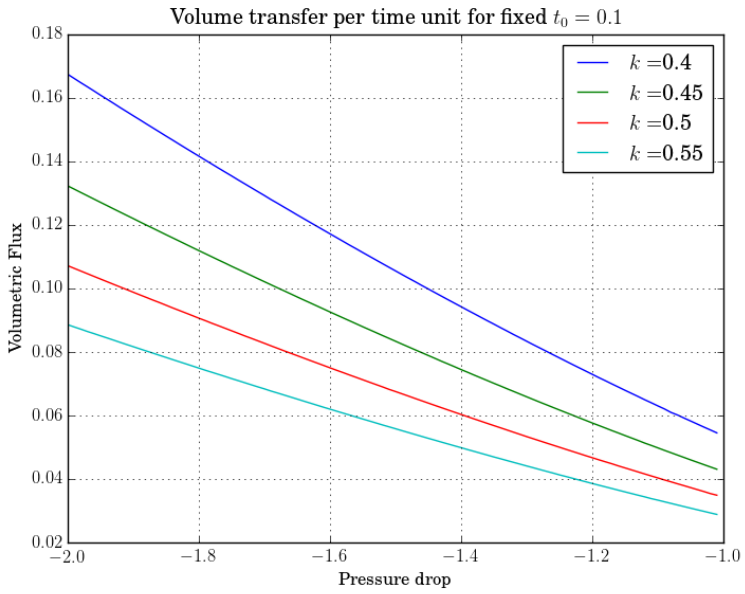

Figure 7.6: Slightly non-linear relation between the volumetric fluc and the pressure drop.

7.3 Optimal positioning of the tubes in the haemodialyser

We consider the problem for optimising the position of the blood vessels inside the haemodialyser and also to optimize the form of the cross section of the haemodyaliser so that it works better (For example in artificial kidney).

7.3.1 Voronoi diagram and heamodialysis

Let us consider the cross section of the haemodialyser. Let the centers of the little circles (which are the tubes in which the blood flows) be P_1, P_2, ..., P_n. A Voronoi cell is a region for which

$$R_k = \{x | d(x, P_k) < d(x, P_i) \ \forall i \neq k\}$$

Hence we make the Voronoi diagram of the cross section with sites (the points from which the Voronoi diagram is constructed) P_1, P_2, ..., P_n.

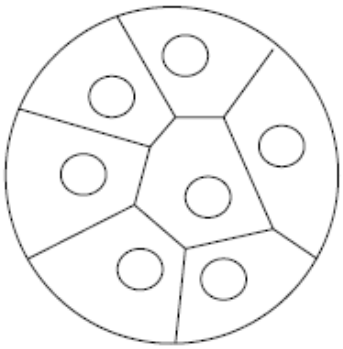

Figure 7.7: Voronoi diagram.

Now let us consider the dual graph of the diagram which is called the Delaunay triangulation of the centers of the circles. If we consider a single triangle from the upper picture

We realise that the sum of the arcs of the circles that are inside the triangle is always constant for every position of the circles (since the sum of the angles in a triangle is π). That means that the volume of the diffused particles from the blood is always a constant in every triangle of the triangulation no matter the position of its vertices. Then since the velocity of the dialyse is constant it is better to have the blood vessels as close as possible:

Then the assumption is that if we have the vessels in the upper composition then the haemodialyser will work better. It is natural to deduce that if the cross section of the dialyser is an equilateral triangle or a regular hexagon then we will have an optimal situation.

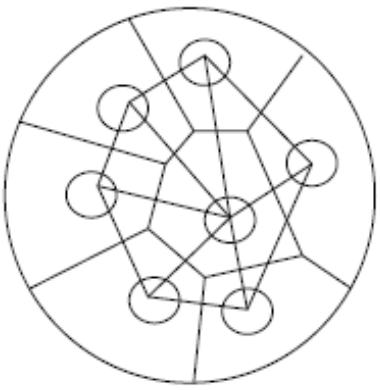

Figure 7.8: Delaunay triangulation.

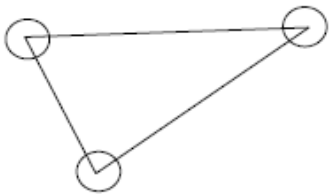

Figure 7.9: A single triangle.

7.3.2 Analytical model

We considered a simplified system constrained by several assumptions:

- The velocity of the blood is constant across the channel (plug flow).
- Diffusive transport of solutes in the direction of flow is negligible compared to convective transport.
- The concentration of any blood solute of interest in the region beyond the membrane is always zero (a perfect sink).

The first two of these assumptions taken together mean that diffusion occurs in only one dimension (towards or away from the membrane) and over an interval of time given by the ratio of the membrane length in the direction of flow to the flow velocity (overall dimensions of time), which is the total residence time for a fluid element in the active region of the channel. The third assumption is founded on the fact that fresh dialysate is constantly washing away the solute beyond the membrane. This will find important application as a boundary condition shortly.

These assumptions allow us to describe the concentration of the solute within the dialyzer as a function of only two independent variables: the distance between the wall and the membrane x, and the local residence time of a fluid element

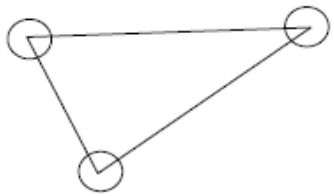

Figure 7.10: A single triangle.

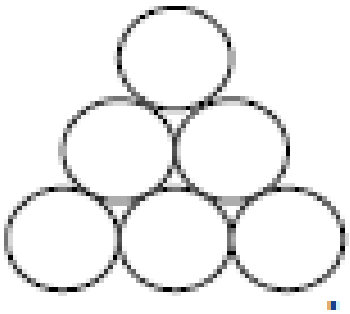

Figure 7.11: Vessels as close as possible.

in the channel, t. Our model is then constructed mathematically from Fick's second law in one dimension,

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \tag{7.6}$$

where x is the location along the axis of diffusion and c represents the concentration of the solute of interest at a given x and t. Since the solute is bounded within the channel on one side by the membrane and on the other by an impermeable wall, this equation can be rewritten non-dimensionally as:

$$\frac{\partial \bar{c}}{\partial \bar{t}} = D\frac{\partial^2 \bar{c}}{\partial \bar{x}^2} \tag{7.7}$$

for $0 \leq \bar{x} \leq 1$ and $\bar{t} \leq 0$, and where:

$$\bar{x} = \frac{x}{a}; \bar{c} = \frac{c}{c_0}; \bar{t} = \frac{tD_0}{a^2} \tag{7.8}$$

where a is the distance between the membrane and the wall, c_0 is the initial concentration of the solute, and D_0 is the free diffusion coefficient of the solute within the solvent. Assuming that the membrane poses no resistance to diffusion of the solute, we can apply three boundary conditions to Equation(7.2):

$$\frac{\partial \bar{c}}{\partial \bar{x}}(0,\bar{t}) = 0 \tag{7.9}$$

$$\bar{c}(\bar{x},0) = 1 \tag{7.10}$$

$$\bar{c}(1,\bar{t}) = 1 \tag{7.11}$$

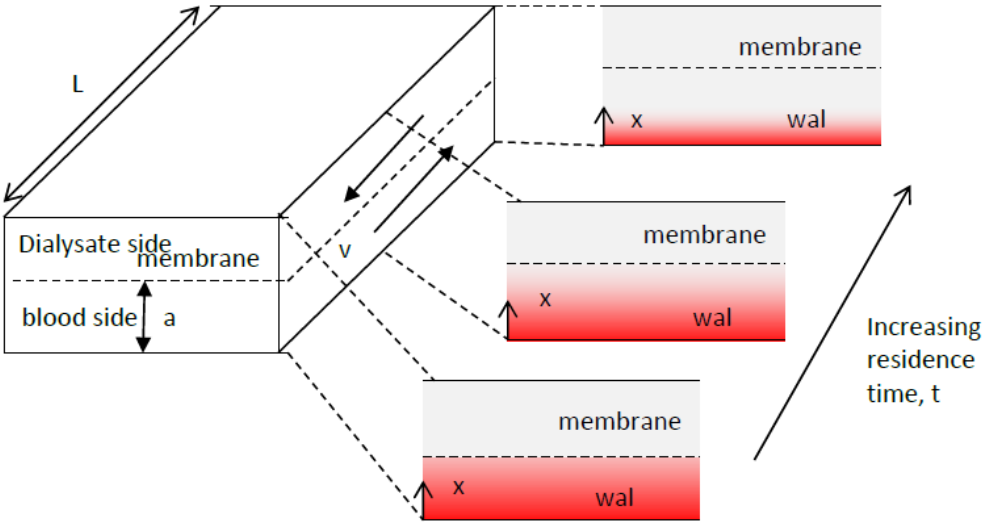

Figure 7.12: Diagram of system considered by the analytical models. The system is initially at some constant concentration (depicted as red shading) and becomes less concentrated in a gradient over time. Mathematically, the system is one-dimensional; however, it is shown here with a second dimension to illustrate the relationship between the temporal and spatial evolution of the concentration profile.

Conceptually, this means that solute that reaches the membrane is swept away by the flow of the dialysate (third assumption from earlier) and that transport across the membrane is unrestricted and instantaneous. Both of these assumptions will be revisited. The solution to this problem is:

$$\bar{c}(\bar{x},\bar{t}) = \frac{2}{\pi}\sum_{n=1}^{\infty}\frac{(-1)^{n+1}}{n-\frac{1}{2}}cos(\lambda_n \bar{x})e^{-\lambda_n^2 \bar{t}} \tag{7.12}$$

where

$$\lambda_n = \pi\left(n-\frac{1}{2}\right) \tag{7.13}$$

Alternatively, if we consider that the membrane does resist diffusion across it, we can quantify the contribution of the membrane to the overall diffusive resistance:

$$\beta = \frac{\frac{d}{D_m}}{\frac{a}{D_0}} \tag{7.14}$$

where d is the thickness of the membrane and D_m is the effective diffusion coefficient of the molecule within the membrane space, as calculated by the pore hindrance model in Snyder. Due to the extreme thinness of nanomembranes β will be very small when considering the transport of small molecules (e.g., urea or creatinine) but may become significant for larger protein solutes. We can incorporate this into the analytical model by redefining Boundary Condition as:

$$\bar{c}(1,\bar{t}) + \beta \frac{d\bar{c}}{d\bar{x}}(1,\bar{t}) = 0 \tag{7.15}$$

This expression simplifies to Equation (7.6) in the case that $\beta \to 0$, and in such a case the solution in Equation (7.12) is valid. Otherwise, the concentration profile is given by

$$\bar{c}(\bar{x},\bar{t}) = \sum_{n=1}^{\infty} cos(z_n \bar{x}) e^{-\lambda_n \bar{t}} \tag{7.16}$$

where $\lambda_n = z_n^2$, and

$$C_n = \frac{2sin(z_n)}{1 + sin(z_n)cos(z_n)} \tag{7.17}$$

The values of z_n are the solutions to the eigenfunction,

$$tan(z_n) = \frac{1}{\beta z_n} \tag{7.18}$$

where z_1 is the smallest absolute value of z that is a solution to Equation (7.18), z_2 is the next smallest, and so on.

Whether Equation (7.12) or Equation (7.16) is appropriate, the fraction of solute remaining in the blood channel at the outlet for a given time, channel height, and diffusion coefficient can be obtained by averaging the value of $\bar{c}$ over x. Fractional clearance can be obtained by subtracting this value from one. In this work, Equation (7.12) is used unless otherwise stated.

Conclusion

In this report, blood flow profiles were investigated assuming various types of fluid behaviour. Apart than that, the blood transfer with respect to the patient's condition was studied and finally an optimal positioning for the fibres inside the haemodialyzer was recommended.

In general, although it is easy to obtain the velocity profile of the fluid, the whole solution of the one-way coupled system including the concentration requires further computational treatment, and along with some simulation is a challenge for future work on the problem.

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