MA50176 **Yang Zhou**
Instructor: Carlos Galeano Rios Due Date: 11/05/2018

Case Study 2: Industrial Study on Mathematical Modelling: the Diffusion of Toxic Particles during Dialysis Treatment

1 Problem Background

In Case Study (I), we have discussed the heat conduction process in heat-sinks devices under simplified one-dimensional conditions, as well as some resultant results simulated numerically. Even though the model was basic, it produced many interesting results and gave some relatively accurate approximation of the real life problem. In this case study (II), we will examine the diffusion processes of pollutant particles in fluids, which is similar to heat conduction but slightly complicated. Both of the studies can be categorized as *Transfer Processes* which is essential for proper industry production and scientific studies. The pollutant diffusion modeling can be deduced as a two-dimensional version of the heat transfer process. (More details and explanations on the heat and mass transporting please refer to Appendix B on page 27). [7] With this modeling study we want to gain understanding in two-dimensional modeling and numerical simulation skills. The specific industry modeling topic is based on renal dialysis-a medical treatment commonly used for treating End-Stage Renal Disease (ESRD)[3] patients.

Kidneys are important organs to human body and when the kidneys' function falls under around 10 or 15 percent, a patient needs kidney/renal dialysis treatments. The fundamental governing laws of dialysis is based on the diffusion process in solutions where particles of higher concentration are transported through a semi-membrane to an environment of lower concentration.

The object of this case study is aiming to:

(i) formulate a simple two-dimension transport model of diffusion of wasted materials from blood to dialysis

(ii) gain understanding in maths modeling methodology and some important approaches to model a real life phenomenon;

(iii) gain some insight in how a extremely simple model can give useful insights to real life complex situations

1.1 Importance of Dialysis

Dialysis is an important process because it functions as artificial kidneys to patients whose own kidneys have serious conditions to function properly, especially those who are diagnosed to be End-stage renal disease (ESRD). ESRD is the irreversible failing of kidney functions to the stage that without renal replacement treatment or renal replacement therapy(RRT) life will not possible. [15] (Details about ESRD and RRT can be found in Appendix I on page 25)

Kidneys are organs of essential regulatory functions. One function of kidneys is to clean blood by excreting metabolic wastes from blood to urine. Meanwhile kidneys keep the body water balance, electrolyte balance, and acid-base balance. Another aspect of kidneys' function is producing or activating hormones which are important in erythrogenesis (producing blood cells, definition see page (25), calcium metabolism and blood flow regulation. [11] Considering that our body cells need a relatively stable fluid environment to conduct normal life process, the unbalanced fluid environment caused by extremely low kidney-functions can therefore threaten the life of a person.

Kidney failure can cause problems for the fluid environment balance control. When the failure happens, water and ion balance in the body cannot be regulated and controlled. Therefore levels of toxic fluid or urea will build up in one's body. Without treatment this will be fatal.

Additionally, even though diagnosing ESRD cannot still not be accurately defined, studies in countries have shown that the disease is common and strongly associated with aging in population. Based on clinical records, acceptance rates of being ESRD have increased over five times compared to the amount twenty years ago. And even in UK alone, most of the treatment requirement for medical instruments and budges are till not being met. [15]

Dialysis is an important renal replacement therapy to treat kidney failure patients.[20] For End-Stage Renal patients, there are two ways of medical treatments: kidney transplant and dialysis.[12] However due to the limited resource of living kidneys and the chances of proper DNA matching between the available donated organs and the DNA of a patient, the availability of successful transplant surgery can only reach a small amount of end-stage renal disease patients. Even for the patients who can receive the transplant surgery, there is still a preparing or waiting time which can sometimes last up to 10 years. Human body needs the regular renal cleaning process, therefore dialysis is an essential and commonly-studied medical treatment methods for renal diseases. [12]

1.2 Illustrations

There are two types of dialysis methods: hemodialysis and peritoneal dialysis. The former is a leading force for RRT[15], so this case study will focused on the hemodialysis process. (Explanations about hemodialysis and peritoneal dialysis can be found on page(25.)

The process of the Dialysis machine During the dialysis treatment, patients' blood (containing high concentration of waste particles) is connected to a dialysis machine, the artificial kidney, to remove the urea and keep the water and ion balance of the blood by allowing the two fluids to exchange relevant substances through semi-permeable membrane tubes[12]. As shown in the graph (1.1), before entering the exchange process, the blood is mixed with blood thinners to prevent clotting, and pumped into the exchanging machine. Inside the machine the semi-permeable membrane separates the two fluids and allow the fluids flow in the opposite direction.[22] After the exchanging process, clean and balanced blood is directed back to human body.

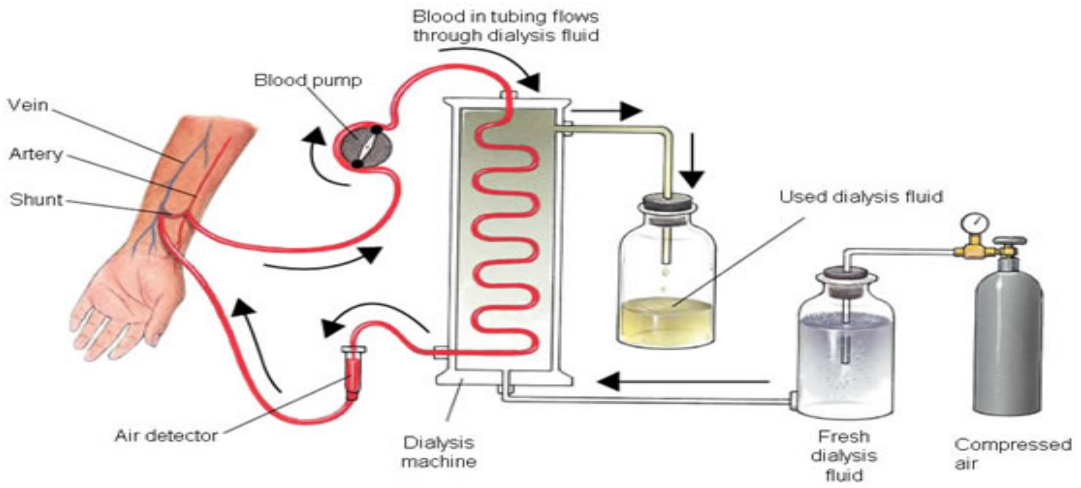


Figure 1.1: The hemodialysis therapy process.[14]

The semi-permeable membrane and diffusion The diffusion process is happening due to the concentration differences of substances in the two fluids and there is a special membrane separating the two fluids. The semi-permeable property of the membrane allows waste products, extra water to move from the blood through the membrane into the dialysate, but blocking normal protein molecules and blood cells to flow through.

The fresh dialysate contains no waste products and it contains a balanced water ion ratio and a normal blood sugar level compared to the blood. The lower concentration of waste products and higher concentration of water in dialysate pulls the wastes and extra water from blood to move to dialysate. And the lower concentration of glucose and certain ion particles in blood pulls those particles to diffuse from dialysate into blood. This process allows the artificial kidney to working resembling some function of a human kidney. [22]

Additionally, there are adjustment mechanisms in the machine to allow a medical control over the amount of removal of excess fluid removed from blood. Also the speed of both fluids flowing and temperature of dialysate can be adjusted to create a relatively suitable treatment based on individual requirement. However the process is time-consuming, an average treatment lasts 4 hours each time and the patients need to be in the hospital for around 3 or 4 times per week. [22]

2 Problem formulation

2.1 Physical Model

One important method used for scientific studies is to simplify the phenomenon such that it can be translated to a systemically structured maths problem. Based on the simpler problem, an easy model can be built to test some most general and common characteristics of the object being studied. Following this philosophy, we consider the one-side exchanging membrane system for blood dialysis in a three-dimensional model scheme as shown in figure (2.1). We simplified the whole dialysis process to a simple system of two boxes (This is a system set in the 2D Cartesian Coordinate.) which are separated

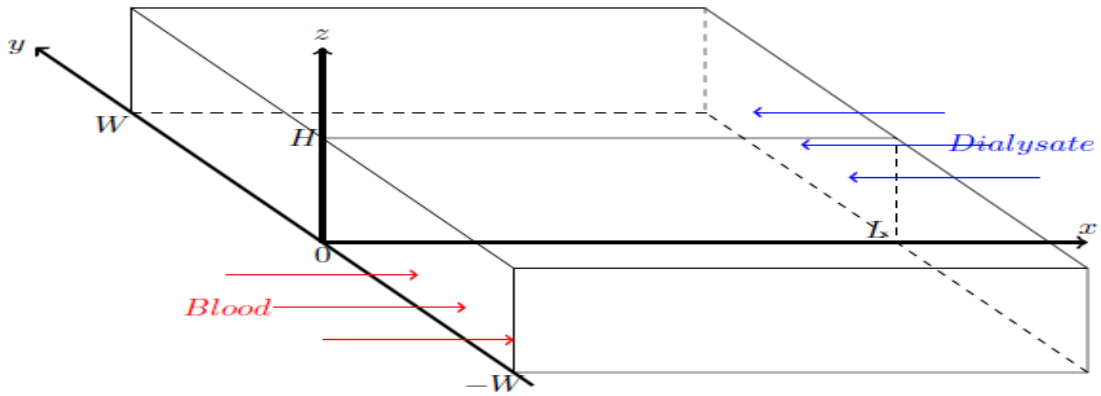


Figure 2.1: 3-D model of dialysis process under Cartesian coordinates

by one semi-membrane in between. Blood is flowing in the direction from left to right through the box located at the negative side of the y-axis. Dialysate is flowing through the box at the positive side of y-axis from right to left. In the middle of the boxes, there is the semi-membrane allowing the diffusion to happen. Even though there should be several substances diffusing into the other fluid system, we here only start by considering one type of small waste particles in the blood and these tracked particles scattering into dialysate during the exchange process. Here we take the length of each box to be L, wide of each to be W, and the height of each to be H.

Due to the fact that chemical potential energy difference resulted from the higher concentration of waste particles in the blood and the lower concentration of them in the dialysate, there is a overall transportation process of waste particles from blood to dialysate, which is perpendicular to the membrane and the velocity of flow of both the blood and the dialysate. So in the macro-scale scope, we observe that the concentration of waste substance in blood has the change: $\Theta_{x_0} > \Theta_{x_L}$; whereas the waste particles' concentration in dialysate follows: $\eta_{x_L} < \eta_{x_0}$.

We neglect the influence of gravity since the tube is supposed to have a relative short height. Additionally, we neglect the friction along the tube walls when the fluid flows by and assume that the flowing velocity remains constants for both liquids.

2.2 2-D Model

To make the problem even simpler, we reduced the three-dimensional model to a two-dimensional one as illustrated in Figure 2.2. The simplification is kept at 2D due to the consderation of influences on diffusion caused by the bulk flow of blood and dialysate fluids. We can consier this model was take from a perpendicular cut to the z-x plane and parallel to the x-y plane from Figure (2.1).

This model should not be simplified to a one-dimensional system, because we have movement of substances in two different directions. The velocity of flowing fluids and gradient of diffusion are perpendicular to each other. Thus this system which needs to be spanned by these two vectors is 2-D in space.

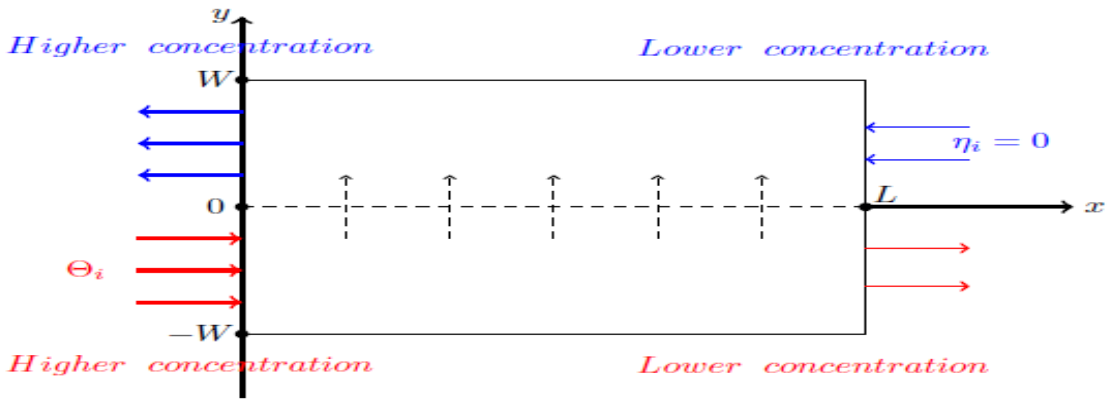


Figure 2.2: A 2-D model of dialysis process in Cartesian coordinates

In the graph, the blood entering the system with high concentration Θ_i of waste particles and flowing through the system with a constant velocity U_b. The diffusion process starts through the mebmrane and by the left hand side edge of the system, the blood left with lest amount of waste particles. The reduced amount of particles in the blood should be the change of increased concentration of this substance in the dialysate. So when dialysate enters the system, it contains $\eta_i = 0$ waste particles and by the edge that it leaves the system, it picks up those amount from the blood by diffusion process. In the way area where $y = W$ and $y = -W$ there is no exchanging process happening. This change of concentration phenomena in blood can be described by the following model (2.1)-(2.7):

$$\partial_t \Theta + \nabla(\Theta \mathbf{U}_b) = \nabla D_b \nabla \Theta, \quad \begin{array}{l} 0 < x < L, \ -W < y < 0 \\ 0 < Z < H, \ 0 < t < T_f \end{array} \tag{2.1}$$

$$\mathbf{Fn} = 0, \quad z = H, \tag{2.1}$$
$$\mathbf{Fn} = 0, \quad z = 0, \tag{2.2}$$
$$\mathbf{Fn} = 0, \quad y = -W, \tag{2.3}$$
$$\Theta(x = 0, y, z, t) = \Theta_i(t) \tag{2.4}$$
$$\mathbf{Fn} = \mathbf{F}_2\mathbf{n}, \quad x = L, \tag{2.5}$$

equation (2.5) means no diffusion flow at L back from outside of the box back to the box.

$$\mathbf{Fn} = \mathbf{F}_1\mathbf{n}, \quad y = 0, \tag{2.6}$$

equation (2.6) represents diffusion flux around the membrane at $y = 0$.

$$\Theta(x, y, z, t = 0) = 0, \quad \text{initial condition} \tag{2.7}$$

models are expressed under arbitrary coordinates with the help of expression of vectors. Rearrange the above models to a 2D Cartesian system we have the following model (2.8)-(2.13):

$$\partial_t\Theta + U_b^1\partial_x\Theta = D_b\Delta\Theta,\ (0 < x < L,\ -W < y < 0,\ 0 < t < T_f), \tag{2.8}$$
$$\partial_y\Theta(x, -W, t) = 0, \tag{2.9}$$
$$\Theta(0, y, t) = \Theta_1(t)\ = \Theta_M(1 - e^{-t/T}), \tag{2.10}$$
$$\partial_x\Theta(L, y, t) = -\frac{\partial_t\Theta(L, y, t)}{U_b^1}, \tag{2.11}$$
$$\partial_y\Theta(x, 0, t) = -\frac{h}{D_b}(\Theta(x, 0, t) - \eta(x, 0, t)), \tag{2.12}$$
$$\Theta(x, y, 0) = 0. \tag{2.13}$$

Similarly, the change of concentration in the dialysate can be described by the following 2D model(2.14)-(2.19):

$$\partial_t\eta + U_d^1\partial_x\eta = D_d\Delta\eta,\ (0 < x < L,\ 0 < y < W,\ 0 < t < T_f), \tag{2.14}$$
$$\partial_y\eta(x, W, t) = 0, \tag{2.15}$$
$$\eta(L, y, t) = 0, \tag{2.16}$$
$$\partial_x\eta(0, y, t) = -\frac{\partial_t\eta(0, y, t)}{U_d^1}, \tag{2.17}$$
$$\partial_y\eta(x, 0, t) = -\frac{h}{D_d}(\Theta(x, 0, t) - \eta(x, 0, t)), \tag{2.18}$$
$$\eta(x, y, 0) = 0. \tag{2.19}$$

Details of the meaning of the above equations will be explained in the next section. All the deriving steps and relevant proofs will be involved in appendix sections. Notations and meanings can be found in the Appendix: Nomenclature table on page 39.

2.3 Governing principles

Building mathematical models using physical laws means establishing relations or equations that have physical meanings at a point in space and at an instant in time.[21, p12] Therefore the instant states of physical points in a system is the starting point to formulate maths equations.

We can apply physical laws to a physical point in space and an instant in time to derive the equations. Since those laws are generally applied in a material system and a process, therefore the physical point is defined to be located within a extremely small and special region. Likewise we define the time instance as a extremely short and temporal time period.[21]

For example, in our 2D model: the equation 2.11 was obtained by considering a small region containing the membrane. The diffusion flux $\mathbf{F} \cdot \mathbf{n}$ is assumed to be influenced directly by the concentration difference of the two liquids $h(\Theta - \eta)$. That is we have taken the rectangle (x, y) to $(x + \Delta x, y + \Delta y)$. When $\Delta y \to 0$, we assume that the transporting by diffusion is linear. In the x-axis direction, since we have assumed that the flowing velocity of fluids is constant, the mass movement due to bulk flow of fluids is

assumed to be $v\Delta t$. Additionally, in the later numerical modeling, we will use the small time intervals of finite difference method- $\Delta t \to 0$ to approximate the changing process with respect to time.

Under such reasoning, our modeling process needs the clarification of the following important physical laws: the conservation of mass, concentration of atomic species in a solution, mass transfer process that follows the empirical Fick's law of diffusion flux, and the mass transportation due to mechanical movement of fluids. Those concepts are explained in the following subsections.

2.3.1 Conservation of mass and chemical species

The Conservation of Mass or Energy is the essential property supporting the study of science in different discipline:

> "A law stating that the total magnitude of a certain physical property of a system, such as its mass, energy, or charge, remain unchanged even though there may be exchanges of that property between components of the system."[6]

Concentration of certain solute in solution can be expressed by the ratio of number of the solute over the volume of the solution(equation (2.20)). Within one system, if the solute mass do not change, so does the number of solute species and the volume of the solution. The concentration of this solute will therefore remain the same. If we can remove ΔM amount of solute away from the original solution and assume that the volume was not reduced, the change of concentration will be proportional to the change in moles(equation (2.21)).

The above is the definition of density. Similarly, we have the solution concentration of number of molecules:

$$concentration = \frac{\text{number of moles}}{\text{volume of fluid}}, \tag{2.20}$$

$$\Delta C = \frac{\Delta M}{V}. \tag{2.21}$$

More definition details regarding concentrations please refer to appendix on page 28.

2.3.2 Diffusion and Fick's Law

Definition 2.3.1 (Diffusion) ***Diffusion*** *is the process of* ***mass transfer*** *when there exists a difference in the concentration of some chemical substances in a mixture. This mass transfer is when mass of some substance is in transit from higher concentration to lower concentration in a mixture. Similar to the temperature gradient in the heat transfer process, the difference in concentration is the called* ***concentration gradient****. (More details of mass transfer can be found on page 28.) [8]*

In the dialysis machine, the two fluids-blood and dialysate can be considered as two systems, where only the waste particles can be transported between the two systems by diffusion from blood to dialysate. So the whole mass or number of mole of the solute reduced in blood equals the quantity increased in dialysate. Therefore we can express

this relation of solute's number moles and its concentration in the solution as:

$$M(t) = \int_V C(x, y, z, t)dV, \tag{2.22}$$

where the common unit of C is mol/m^3, and the molar number is measured in unit: mol. Taking derivative on both sides of (2.22), we have:

$$d_t M(t) \ = \ d_t \int_V CdV \ = \ - \int_s \mathbf{F}\mathbf{n}ds, \tag{2.23}$$

where $\mathbf{F}$ is the overall diffusion flux out of the system.

Definition 2.3.2 (Diffusion Flux) *Diffusion flux is defined to be the diffusion amount that flows through a small area during a small time interval, unit: $mol/(m^{2s})$[23]*

For our modeling, we need the empirical Fick's Law - the first law. It is also know as the *Fick's law steady diffusion*. The second Fick's law is related to chemical reactions inside fluids which is not in the consideration of this case study modeling.

Definition 2.3.3 (Fick's Law) *The law states that there is a linear relation between the rate of diffusion and the local concentration gradient. [7, pp55]*

It is based on the the analogy between heat conduction and mass diffusion process. In Fouriers law of heat conduction(details of Fourier's law refer to Appendix on page 29), we have the same linear relation between flux and gradient.[7] To express the linear relation by maths:

$$\mathbf{J} \ = \ -\mathcal{D}\nabla C, \tag{2.24}$$

where:

$\mathbf{J}$, diffusion molar flux of the solute;
$\mathcal{D}$, the constant of proportionality, referred to as the binary diffusion coefficient or diffusivity;
C,molar concentration.

Praticles in a solution can be transported in two ways: diffusion and convection. We have discussed the former process of diffusion and its governing law(Fick's first law). The latter of convection means the bulk movement causes of movement of particles. (Details of classification of transfer process about diffusion and convection please refer to the discussion in Appendix on page 27.)

Therefore we have the total flux $\mathbf{F}$ is the combined effect of diffusion and fluid flow(conduction):

$$\mathbf{F} = \mathbf{J} + C\mathbf{v}, \tag{2.25}$$

where v is the velocity of the observed fluids.

Combining the diffusion flux (based on Fick's law), conservation of mass and total flux from combined diffusion and convection(equation (2.25)), we have the model equation (2.8).

2.4 Conditions for Determining the Solutions

Mathematical physical models describes the the global truth of physical laws, but the physical problem which is formed by a special phenomenon is located within a special region of space and time.[21] Therefore, even though the groups of solutions from the model are derived, we still need to special registrations to filter the relevant solutions for the spacial given event. In order to obtain the changing mass distribution over time and space, certain initial and boundary conditions need to be stated clearly before solving the equation systems.[9, p10]

2.4.1 Initial Conditions

Initial conditions of a diffusion is the concentration of one substance in a multi-component system at the beginning of time when the system is observed, t_0= 0 s. When blood is connected by the membrane with a flowing fresh dialysate, the diffusion will eventually be zeros due to the remove of all waste particles in the blood. Therefore the constant Θ_0, which is the mean value of concentration of waste particles in blood over a long time period, should be zero. This gives the equation in model (2.13).

A second situation suitable for being an initial condition is at the moment when blood is about to flowing through the machine. Before the start of the process, we can have clean dialysate filling both the boxes. (This will happen even if there originally is dialysate in only one box, the membrane will then allow the fluid to travel through and occupy the other box.) The starting state can be considered that when a patient's blood is starting to mix with the clean dialysate in the blood tube side and flowing through the machine tube steadily. A third initial state can be when the dirty blood from patient's body is cycled back to the machine which contains only clean blood at that time instant.

This initial state is a state of caution. We should not consider the process when the tubes are simply empty of vacuumed. And letting fluids flowing into a tub simply like the process of opening a water tap. This part need to neglected since it is not consistent in motion therefore cannot be modeled by our model. Otherwise it will violate the globally truth property of maths equations in either space or time. When there is nothing in the tub, this part contains no mass or no media for particles to move continuously and therefore should not be included as a part of the system. Additionally, when fluid flows into a vacuum area, the vacuum alone contains no mass and we cannot clearly guarantee that the conservation of mass hold.

Following the same reasoning, the initial state of the dialysate should have the $\eta_0 = 0$. This is because that when the clean dialysate flow passing the clean blood should not be able to pick up any waste particles. Physically the meaning of initial conditions depends on physics and nature of the variable C. In this mass transfer case, the concentration distribution should be constant without any external pollutant invasion. After a sufficiently long time, the two fluids should be in a diffusion static state, which means the concentration is zero. [21] Additionally, due to the need of consistency as discussed in previous paragraph, we also neglect the process when dialysate first flows into the tube.

2.4.2 Boundary Conditions

Our model is 2 dimensional, so we have length parameters x and y. We allow fluids to flow along the axis of x which is in the domain $[0, L]$. In our model diagram (Figure 2.2), blood is flowing from $x = 0$ to $x = L$ whereas dialysate flows from $x = L$ to $x = 0$. The width of the tube that blood flows through is in the domain $[-W, 0]$ and that of the dialysate tube is in the domain $[0, W]$. So in this simple model, we call the radius of the tube allows blood to flow through r_b, and $r_b = W$. r_d is the radius of the tube for dialysate to flow through, and $r_d = W$. To make the simulation process easier to track, we choose to monitor one pollutant substance in blood CO_2. In our 2-D model diagram (Figure 2.2), we call the density of carbon dioxide in blood at $x = 0$ be Θ_i and the density of carbon dioxide in dialysate at $x = L$ be η_i. And the concentration of pollutant close to the membrane is $\Theta(x, 0, t)$ at the blood side and $\eta(x, 0, t)$ at the dialysate side.

To be more precise, boundary of a system is the end point(s), boundary curve(s) or boundary surface(s) of the body. Since our model is in two dimensional space, the boundary considered in our report is referring to the four edges in each box in Figure (2.2). Boundary conditions therefore specifies situations of, or constrains on those dependent variables in our model on the system boundary. [21] There are typically four types of boundary conditions: Dirichlet conditions, Neumann conditions, Robin condition and boundary conditions for meeting surfaces problem of two or more systems'. [18], In our report we include only the first three conditions due to the simplicity of those conditions.

Dirichlet boundary In a general three-dimensional system, the inner domain is denoted as Ω and the boundary surface is denoted as $\partial\Omega$. Assuming that the surface concentration can be expressed by some known function $\varphi(S, t)$, S *in* $\partial\Omega$ [21], this known boundary temperature distribution is the *Dirichlet boundary condition.* It is expressed by:

$$C(S, t)|_{\partial\Omega} = \varphi_{\partial\Omega}(S, t)$$

[18] In our fluids model, it is fairly easy to obtain pollutant concentration measurements so we can assume that at the beginning location $x = 0$ the concentration of pollutant in blood follows Dirichlet conditions. The same applies for pollutant in dialysate at $x = L$. Where on the edeges of $y = -W$ and $y = W$, there is no diffusion process happening, so these two locations have function 0. In two-dimensional case, the equations for the Θ_i:

$$\begin{aligned}
\Theta(x, y, t)|_{x=0} &= \Theta(0, y, t) \\
\Theta(x, y, t)|_{y=-W} &= \Theta(x, -W, t) = 0 \\
\eta(x, y, t)|_{x=L} &= \eta(L, y, t) = 0 \\
\eta(x, y, t)|_{y=W} &= \eta(x, W, t) = 0.
\end{aligned}$$

where both $\Theta(0, t)$ and $\eta(L, t)$ can be known from measurement.

Additionally, we assume that Dirichlet conditions mean that there is a upper or lower limit of the know concentration function. This means using this Dirichlet boundary condition to model the concentration at the beginning location for pollutant in blood and dialysate is reasonable,since human body can survive within a upper limit of body fluid pollutant concentration and the values can be measured. In our model, we express it in the model as equation (2.10) and equation (2.16) on page 6. And the 0 diffusions are expressed in the models by equations (2.9) and (2.15).

Neumann boundary conditions In many situations, it is not always possible to have mensurable temperature values on the boundaries. In some applications, boundary conditions are instead given by directional derivative along outward normal vectors on the the boundary.[21] In practice is when the diffusion flux from a body surface can be obtained from measurements[18]:

$$k\nabla C \cdot \mathbf{n}|_A = J(\mathbf{r}_A, t).$$

In Cartesian system, such situation can be expressed as:

$$\left(k_{xx}\frac{\partial F}{\partial x}n_x + k_{yy}\frac{\partial F}{\partial x}n_y + k_{zz}\frac{\partial F}{\partial x}n_z\right) = J(\mathbf{r}_A, t), \tag{2.26}$$

where $\mathbf{r}_A$ is a positional vector of a point located at the boundary surface. This boundary condition is commonly applied on the surface of radiate systems.[18] Here since it is the boundary located at the end of diffusion($x = L$ for blood and $x = 0$ for dialysate), we simply assure that the change of concentration is mainly caused by the bulk flow of fluids. This boundary condition is expressed in equations (2.11) and (2.17) on page 6)

The Dirichlet and Neumann boundaries are easy to solve but have certain restrictions when applying. In order to use these two conditions, we need to assume that the concentration is not changing with respect of the location in y and also the fluid velocity.

Diffusion boundary conditions This this the location around the membrane or in Cartesian system $y = 0$. The diffusion is influenced directly with respect to the difference of concentrations in two fluids. It is similar to the Robin Boundary we have seen in Case study I.

The *Robin boundary* is also know as the *Newton law of cooling* in heat convection.[18] This condition is applied when the outer system have a constant parameter of temperature or in our case should be the concentration. However one difference is clear here since the two systems are interacting the pollutant in dialysate cannot stay as a constant, for pollutant in blood vise verse. Even though the difference exit, we can have our conditions similar to the simpler Robin boundary due to the following discussion.
The Robin boundary was used to model a simplified situation where the heat transmission on a surface interacts with another fluid in Case Study 1. Or the heat convection progress. Referring to the discussion about classification of mass transfer processes on Appendix B on page (27). We know the two situations of heat convection boundary and mass diffusion is originated from the same law. From Fick's law(similar to the Fourier's law for heat transportation), we have the concentration flux equation determined by gradient of concentration. As explained in the governing law subsection, we can assume that the thin layer of fluid on membrane wall have both the mass diffusion (same classification as heat conduction) and convection law due to the non-slip friction hypothesis of fluids' bulk flow. Therefore by changing the constant part in Robin we have our boundary conditions expressed by equations (2.12) and (2.18).

2.5 Non-dimensionalisation

Since we are building mathematical physical models, all the variables are of physical meanings. This means all quantities have their special units. Especially when we apply

differentiation of physical variables with respect to time and space coordinates, the maths equations are describing the local region relationships among those physical variables in space and time. However the followed solutions represent the global relationships among variables in space and time.[21] Therefore, due to the need of expressing true facts, we need to take away the units for each physical variables to maintain the philosophy that those equations are true under different measurement or units. And we use solidus notation to keep those variables dimensionless.(Definition and meaning of solidus notation see page 28) Thus it is a common practice to non-dimensionlisation the equations by changing of variables to take away the units and turn the quantity-value to be pure numbers.

For our original models (2.8)- (2.13), define:

$$\bar{x} = x/L \tag{2.27}$$
$$\bar{y} = y/W \tag{2.28}$$
$$\bar{t} = tU_b^1/L \tag{2.29}$$
$$\bar{C} = C/\Theta_M \tag{2.30}$$
$$\tag{2.31}$$

substitute back to (2.8)- (2.13), with some algebra calculation and exchange all the $\bar{variables}$ to the original variables for simplicity gives the non-dimensionalised model for blood:

$$\partial_t\Theta + \frac{U_b^1}{L}T\partial_x\Theta = \frac{D_bT}{W^2}\Big(\frac{W^2}{L^2}\partial_{xx}\Theta + \partial_{yy}\Theta\Big) \tag{2.32}$$
$$\partial_y\Theta(x,-1,t) = 0 \tag{2.33}$$
$$\partial_y\Theta(x,0,t) = -\frac{hW}{D_b}[\Theta(x,0.t) - \eta(x,0,t)] \tag{2.34}$$
$$\Theta(0,y,t) = \Theta_i(t) = 1 - e^{t/(T/\mathcal{T})} \tag{2.35}$$
$$\partial_x\Theta(1,y,t) = -\frac{\partial_t\Theta L}{U_b^1T} \tag{2.36}$$
$$\Theta(x,y,0) = 0. \tag{2.37}$$

where $T = \frac{L}{U_b^1}$, $0 < x < 1$, $-1 < y < 0$, and $0 < t < T_f/L$.

Similarly, for model and model (2.14)- (2.19), define the following variables and substitute back.

$$\bar{x} = x/L \tag{2.38}$$
$$\bar{y} = y/W \tag{2.39}$$
$$\bar{t} = tU_b^1/L \tag{2.40}$$
$$\bar{\eta} = C/\Theta_M \tag{2.41}$$
$$\tag{2.42}$$

After similar calculation gives the non-dimensionalised model for dialysate:

$$\partial_t \eta + \frac{U_d^1}{L} T \partial_x \eta = \frac{D_d T}{W^2}\Big(\frac{W^2}{L^2}\partial_{xx}\eta + \partial_{yy}\eta\Big) \tag{2.43}$$

$$\partial_y \eta(x, 1, t) = 0 \tag{2.44}$$

$$\partial_y \eta(x, 0, t) = -\frac{hW}{D_d}[\Theta(x, 0.t) - \eta(x, 0, t)] \tag{2.45}$$

$$\eta(1, y, t) = 0 \tag{2.46}$$

$$\partial_x \eta(0, y, t) = -\frac{L\partial_t \eta}{U_d^1 T} \tag{2.47}$$

$$\eta(x, y, 0) = 0. \tag{2.48}$$

where $\mathcal{T} = \frac{L}{U_b^1}$, $0 < x < 1$, $0 < y < 1$, and $0 < t < T_f/L$.

The calculation process to derive this dimensionless model from the original model can be found in Appendix B on page 31. Referring to the explanation of the non-dimensionalisation process in the Appendix B. We have the final form of our models: For pollutant in blood:

$$\begin{cases} \partial_t \Theta + \partial_x \Theta & = Pe(\alpha^2 \partial_{xx}\Theta + \partial_{yy}\Theta) \\ \partial_y \Theta(x, -1, t) & = 0 \\ \partial_y \Theta(x, 0, t) & = -He(\Theta(x, 0, t) - \eta(x, 0, t)) \\ \Theta(0, y, t) & = (1 - e^{-t/C}) \\ \partial_x \Theta(1, y, t) & = -\Theta_t(1, y, t) \\ \Theta(x, y, 0) & = 0. \end{cases} \tag{2.49}$$

For pollutant diffused into dialysate:

$$\begin{cases} \partial_t \eta + Ve\partial_x \eta & = DePe(\alpha^2 \partial_{xx}\eta + \partial_{yy}\eta) \\ \partial_y \eta(x, 1, t) & = 0 \\ \partial_y \eta(x, 0, t) & = -\frac{He}{De}(\Theta(x, 0, t) - \eta(x, 0, t)) \\ \eta(1, y, t) & = 0 \\ \partial_x \eta(0, y, t) & = -\frac{\partial_t \eta(0, y, t)}{Ve} \\ \eta(x, y, 0) & = 0. \end{cases} \tag{2.50}$$

The relevant definition and equations of those constants in the two groups of equations 2.49 and 2.50 can be found in equations (10.7), (10.8) and (10.9) on the same Appendix on page 32.

3 Solution of the Model Problem

In practice, most of the differential equations for physical models may not have exact analytically solutions. Or the solutions could be difficult to comprehend. Under such situations, numerical approaches offer a easier and clearer way to obtain further interpretation from the model. [19] To approach a problem numerically, we first need to reduce the infinitely continuous domain space to a discrete space. In this case study, we will use

the same Crank Nicolson finite difference method as we did in Case study I. This method can produce valid approximation and do not require a really small grid length. More details about Crank-Nicolson implicit method can be found in the book by Smith[17]: the scheme driving process on page 19 to 24; derivative boundaries on page 29 and page 30; The convergence and stability of solutions simulated by finite difference methods on page 43 to 49.

3.1 Numerical Approach-the Crank-Nicolson Finite Difference Method

To approach the problem using numerical methods, we need to put the non-dimentionalized models into the *finite difference* scheme. Therefore computers can simulate the infinite event in a discrete system. To do this we need to place the domain in a discrete grid. For simplicity, we choose the uniform grid in space and time. In our two-dimension model, we take finitely many equally distanced points along each direction of x and y in our box diagram (e.g take distance spacing $\Delta x = 0.2cm$ and $\Delta y = 0.1cm$) and measure the concentration on each points and their concentration changes with certain time intervals say take the time spacing $\Delta t = 0.1s$. [19] To illustrate this method, see Figure 3.1 bellow: The Figure 3.1 shows the two-dimension box with length L and width W set to grids with

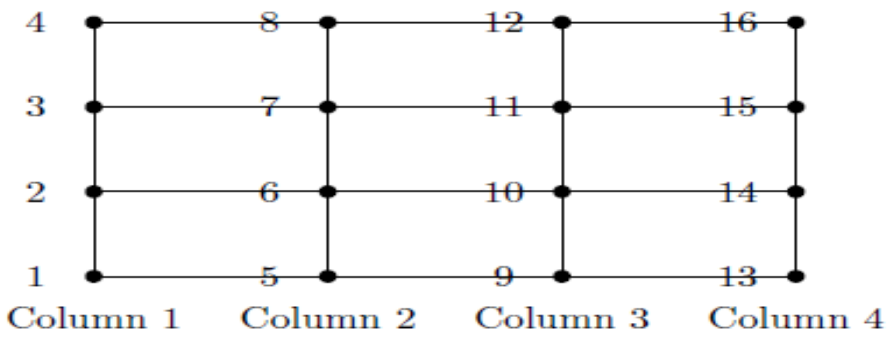


Figure 3.1: Finite different method: grid graphs of pollutant concentration $\Theta(i)$ on discrete grids with labeled nodes

3 intervals in x direction of equal length Δx and 3 intervals in y axis of interval length Δy. The change with respect to time can be considered as the same box only the data on each node are changing. Therefore many layers of same shape as in graph (3.1) expand the grid to the space-time domain, with equal time increment Δt. We label the nodes on the lattices from bottom to top and from left to right (n_i, $i = 1, ..., 16$) as in Figure 3.1.

Before looking at the new column graph (3.2), We need to understand how data are being approximated by using such grids. The box domain can be approached by approximating the solution of our model at the nodes on the lattice. Therefore, define the function on black node n_i to be $\Theta(x, y, t)$. For example, we have concentration measured at nodes n_2, n_5, n_{10} and n_7. With those values we can approximate the modeled concentration at node n_6. Using the same logic, we need to consider the influence of time. This will be a 3D 3 layers of our grids box folding on top of the each other. And the order of arranging those 3 layers is to follow the time.

Using the above idea, we can make the previous continuous models to be discrete on

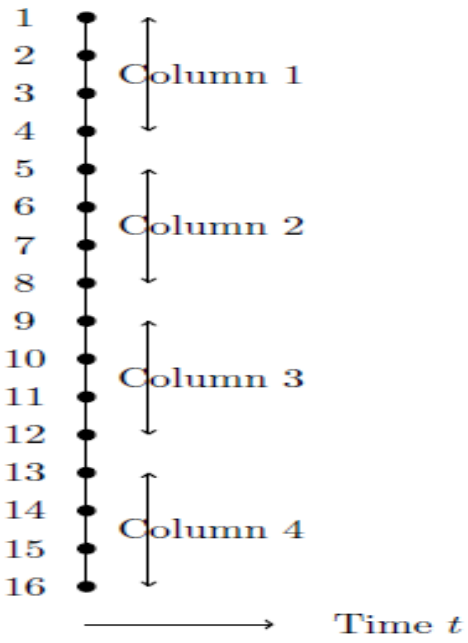


Figure 3.2: Finite different method: grid graphs of pollutant concentration $\Theta(i)$ on discrete grids with labeled nodes

interior nodes:

$$\begin{aligned}\frac{\Theta_i^{k+1}-\Theta_i^k}{\Delta t}+O(\Delta t^2) = &-\frac{1/2}{2\Delta x}(\Theta^k_{i+(ny+1)}-\Theta^k_{i-(ny+1)}+\Theta^{k+1}_{i+(ny+1)}-\Theta^{k+1}_{i-(ny+1)})\\ &+O(\Delta x^2)+\frac{Pe\alpha^2}{2\Delta x^2}(\Theta^k_{i+(ny+1)}-2\Theta^k_i+\Theta^k_{i-(ny+1)}\\ &+\Theta^{k+1}_{i+(ny+1)}-2\Theta^{k+1}_i+\Theta^{k+1}_{i-(ny+1)})\\ &+\frac{Pe}{2\Delta y^2}(\Theta^k_{i+1}-2\Theta^k_i+\Theta^k_{i-1}\\ &+\Theta^{k+1}_{i+1}-2\Theta^{k+1}_i+\Theta^{k+1}_{i-1})+O(\Delta y^2)\end{aligned}$$

In order to continue to use computers for simulation, the 2D matrix cannot work. We need to transform it to a vector to be stored in computers. This process is shown in Figure (3.2). This figure (3.2) shows how we arranged the data for each nodes in figure(3.1) to a column for computer to do simulations. With the change of time, each step of simulation will update new data to the next column on the right hand side of the first column.

By doing the transforming, we can turn the above discrete model for interio nodes into systems of linear equations. Therefore we need to form the matrices and vectors and add certain boundary nodes to the different location insides those matrices. Due to the length of all those matrices, plots are omitted here. Those systems should take the general forms of:

$$\Theta^{k+1} = A\Theta^k$$

And eventually turning the expanded systems of linear equations to MatLab codes for simulations. Calculation details can be found on book by Thomas[19, p6-14]. All used Matlab codes can be found in Appendix C on page 33.

3.2 Validating the Numerical Method

In Case Study 1, we have derived the analytical solution of a simple heat equation to show that the numerical approach works as expected according to that analytical solution. Here we will skip this step due to the length of calculation. And especially that diffusion process is originated from heat conduction and convection process.

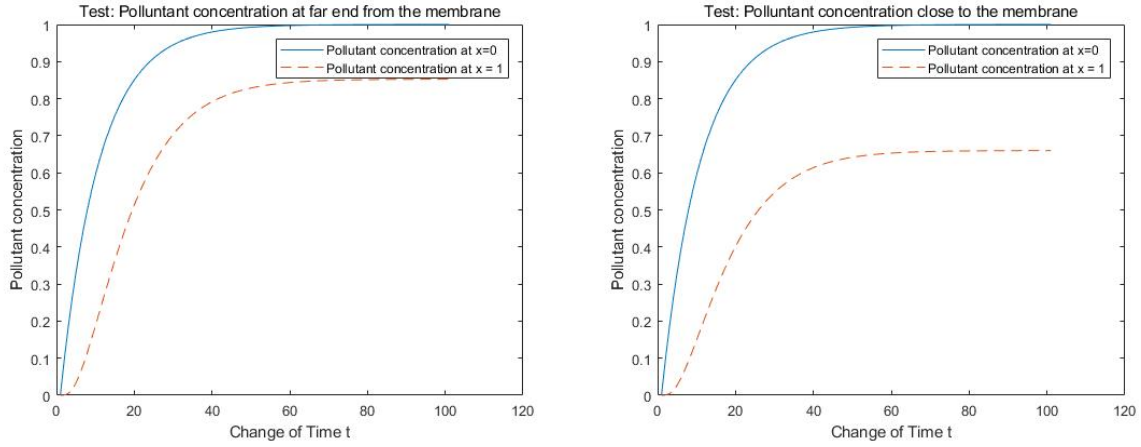
Existence and Uniqueness of the solution The Crank-Nicolson scheme methods can converge nicely to our desired results. This can be easily proved by applying von Neumann analysis on our models written in discrete scheme. More details about von Neumann analysis can be found in the book by Thomas[19, pp125]. Additionally, the existence and uniqueness of the exact solution has been a well studied problem, so details of proof will not be involved in this report. Relevant proofs can be found in the book by Wang[21, p122-125].

3.3 Validity of the Numerical Approach

3.3.1 Model performance of simple uniform parameters

We run the numerical MatLab Code to with all uniform parameters. Therefore we do not have special meaning for the choice only for the simplicity. And we can test the results by this simple simulation.

By tracking the concentration changes located 1/8 of radius close to the tube wall and the 1/8 of radius close to the membrane. Then the numerical simulation give the following graphs:



(a) Pollutant concentration changes at a location far from the membrane

(b) Pollutant concentration changes at a location close to the membrane

Figure 3.3: Testing of our model: Performance of our model with uniform parameters.

Even though the current data does not represent any real-life situation, we can see this one sided model of pollutant in blood is producing what we are anticipating. In figures (3.3a) and (3.3b) for the point close to membrane and the point far from the membrane, the inflow was for both locations continuously increasing at $x = 0$ until reached the maximum possible value of 1. This process represents the process that dirty blood is flowing in and eventually replaced all the previous clean fluid. Even though it is for the point that

is close to membrane, since it is merely the beginning of dialysis, we are not expecting to observe any reduce in pollutant concentration.

When we observe the two curves representing the exit point (where $x = 1$) in figures (3.3a) and (3.3b), we clearly see there is a reduction of concentration. Additionally, we observe that the pollutant concentration reduced more where blood is close to the membrane and reduced less e=where it is far from the membrane. Considering our governing laws for building this model and assumptions, such results matches our model. This can also show that our numerical model produces reliable results.

3.3.2 Relative Error Analysis

Another to check the validity of our model is to check the convergence of errors. Even though we do not have an exact solution here, we can still apply the relative error analysis by comparing our coarser grid results to much finer grid results. In the code I compared the results from $ny = 2^2$ to $ny = 2^5$ against the result from $ny = 2^6$. (It would be more accurate if we compare to the results from $ny = 2^7$. However due to my computer's computing limit and the comparation based on $ny = 2^6$ was satisfying, I did not run the simulation for the most finer grids.)

The compared errors are plotted in the figure (3.4). From this graph we can see that the errors are converging close to the 10^{-6}. This is an acceptable results.

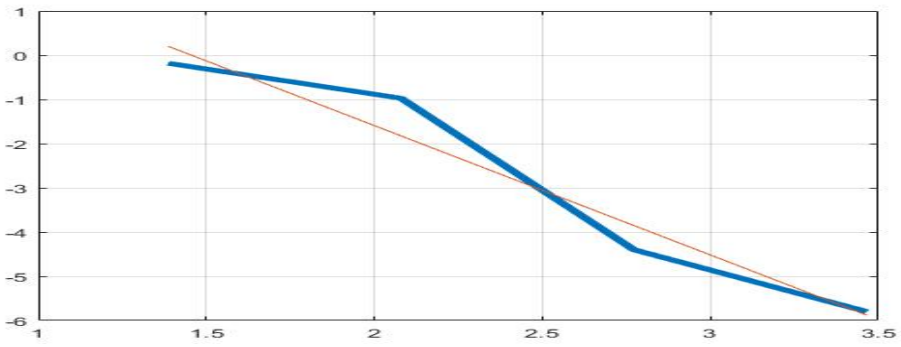


Figure 3.4: Finite different method: grid graphs of pollutant concentration $\Theta(i)$ on discrete grids with labeled nodes

Therefore we have checked that this numerical method gives accurate approximation of our simple example. (This MatLab code is in Appendix E: Validity Checking on page 33 and Relative Error Analysis on page 34)

4 Results and Interpretation

We have checked the validity of our numerical methods, therefore we can proceed to run another simpler simulation of our model using some empirical data from literature reports to test the performance of our model and see if there is any improvement we can make.

4.1 Simulation of One-side Model

Before running simulation, we need to specify a few constants which will be used in our model. The pollutant we have chosen is carbon dioxide and we assume that there is no chemical reactions with water. We only consider the situation under the same temperature conditions, as shown in Table 1:

Table 1: Empirical data for simulation[3]

symbols	meaning	value
$D_{CO_2,b}$	diffusion coefficient $(m^2 s^{-1})$	3.4 E -10
$D_{CO_2,d}$	diffusion coefficient $(m^2 s^{-1})$	1.59 E -10
h_{CO_2}	Membrane permeability of CO_2 $(m^2 s^{-1})$	1.72 E -9
r_b	radius of blood channel (m)	2 E -4
r_d	radius of dialysate channel (m)	1.25 E -4
u_b	velocity at blood inlet (ms^{-1})	1.73 E -2
u_d	velocity at dialysate inlet (ms^{-1})	1.21 E -2

Based on the literature data from table (1) gives the following constants:

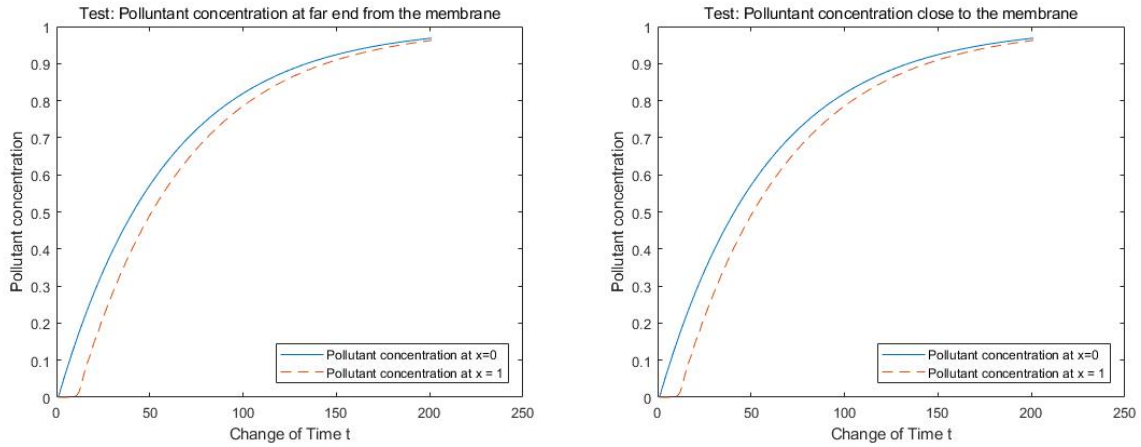
$$Pe^b = 0.0049 \qquad \mathcal{T} = 0.578 \qquad He = 0.001 \tag{4.1}$$

However, when we check the length of tubes L need to be set t 0.001 meters to avoid the memory limit of MatLab. And Lab date radius and the length L gives a α value in the range of 10^{-6}. This also causes problem to the numerical calculation. We need to adjust the data slightly to make the simulation meaningful since the length of dialysis tubes cannot be 0.001 meters in real life. By setting $L = 0.1$ we have increased the radius to 0.02 meters. Thus we have the new set of constants:

Table 2: Empirical data for simulation[3]

symbols	value	symbols	value
Pe	4.9133e-06	He	0.1012
$\mathcal{T}$	5.7803	α^2	0.0400

Using those data, our one sided model produced the two graphs in Figure 4.1.



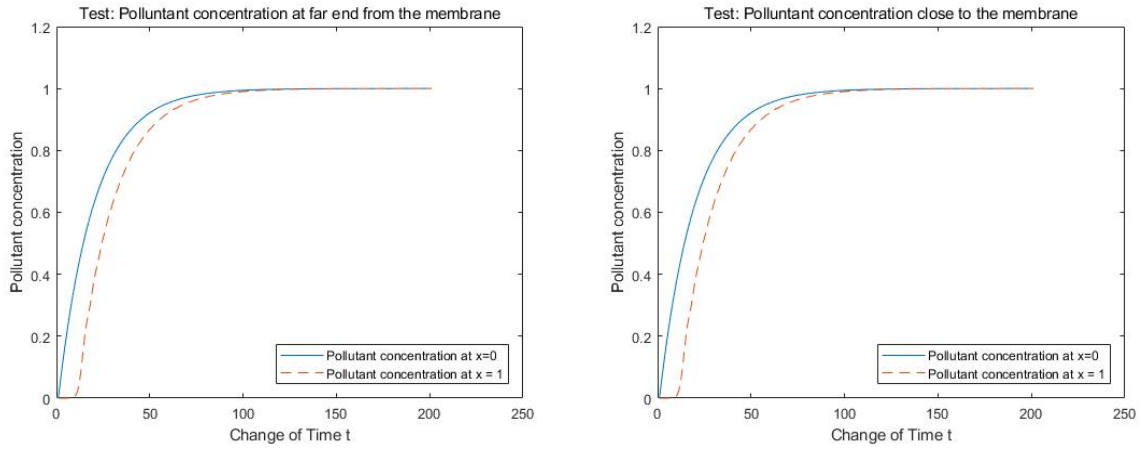
(a) Simulation: concentrations at far end from the membrane

(b) Simulation: concentrations at close end from the membrane

Figure 4.1: Simulation graphs double fluid speed

We see from the above figures (4.2a) and (4.2b) the reduction is not really effective. This result is logical due to the fact that diffusion process is not a extremely fast process. And we are only examining a tube of 10 cm. This could explain in a sense that why kidney cannot be replaced by the man-made renal machine. Inside human body, kidney uses proteins to actively help to transport the unwanted materials away rather than only relaying on diffusion process.

Due to the limit of calculation for this numerical model, we cannot increase the length of L without keep increasing the width of the tube radius. If we try to increase the fluid speed to its triple value, we have the following results:



(a) Simulation for triple fluid flow: concentrations at far end from the membrane

(b) Simulation for triple fluid flow: concentrations at close end from the membrane

Figure 4.2: Simulation graphs double fluid speed

This change only increases the speed for dirty blood to take over the original clean blood. The diffusion does not seem to have improved under our current short space scale.

4.2 Discussion regarding the results

I have run many different simulations by adjusting the data reasonable, however all could not produce any obviously improved results. Therefore the results data and figures are not presented here. This cannot produce any support to our initial guess.

However such a situation does not mean our modeling cannot give us any insight regarding the problem. One understanding is that simply increasing the dimension can produce many problems to our model. These can be caused by the quadratic relations between many parameters. Especially the grids size. Therefore, we do not have the linear relationship between parameters and solutions. We need to understand more of the problem from other angles to have a better insight regarding how to improve the performance.

The complexity of this two dimensional model gives us another warning. Simulations based on mainly maths knowledge may not be able to give us a clear result. This indicates our original maths model possibly has ignored some important aspects to cause the numerical process less productive. This indicates the importance of referring to empirical

data and real life problem observations.

Another way of understanding our result is that the nearly 0 clean effect observed in our model was actually in the length of 10 cm. This is not realistic in medical treatment nor for biological truth. Consider our body contains long tubes for blood to spread nitration, oxygen and collect waste product. Considering the fact that nature should have chosen the most efficient way of staying alive, our man-made machine could only be less efficient. The dialysis results should be modeled in a tube length of meters and radius of 1e-4 meters. This ratio difference is in the range of machine error. Therefore the programming needs update to solve the problem.

5 Further Modelling

In this section, we try to apply our model by combining two sided models together and hopefully can obtain some useful conclusions. In the second part, we will discuss briefly some further study possibilities based on all the simulation results.

5.1 Double-Sided Model Simulation

Based on the relation we have obtained in the maths models we adjusted boundary conditions along the membrane to allow the two systems to interact with each other.

To avoid the same complexity we have seen in the previous section. We set all parameters to be 1. Run the simulation and recorded the video. I listed the following four screen-shots in Figure (5.1) from the simulation.

In the groups of screen-shots, we can see that the right hand side blood is diffusing its pollutant to the left hand side dialysate. Figure (5.1a) was taken at the beginning of the simulation. Dialysate was clean and dirty blood started to flow into the original clean blood.

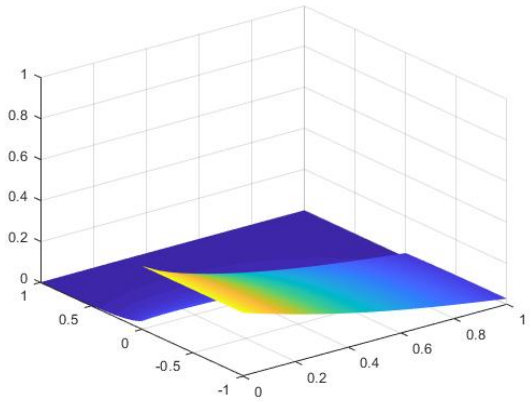
After a few seconds, the Figure (5.1b) was taken. It shows that under our assumed environment (uniform parameters) the dialysate is gradually absorbing the pollutant from the blood. And Figure (5.1c) was taken a few seconds after Figure (5.1b), the pollutant concentration in dialysate is clearly increasing. At the end of simulation, Figure (5.1d) shows that this process is not efficient as most of the pollutant are still inside blood and the dialysate absorbed merely a small amount of the pollutant.

5.2 Further Discussions

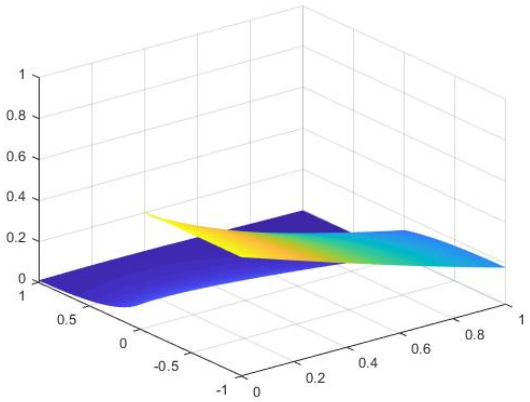
There are many directions to expand the model. Due to the length limit and purpose of this report, here only list a few brief description about possible further explorations.

5.2.1 Models of Efficiency under Different Width of Boxes

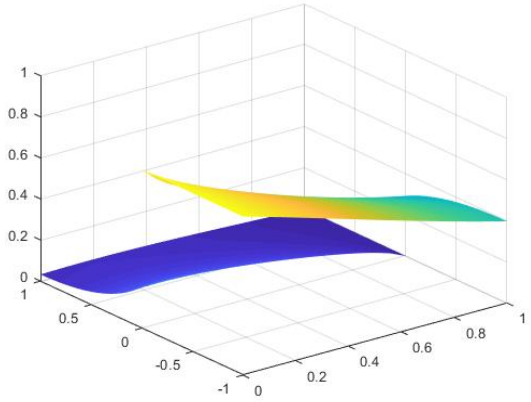
At the beginning we have chosen uniform length for L and W . A natural question to ask is whether other ratio can be used to produce a better performance. We can notice that in Figures (5.1) the pollutant concentration on the far side from the membrane was not reduced as efficient as on the region close to the membrane. Therefore it is natural to assume that if we reduce the width or radius of the box, the diffusion effect could be



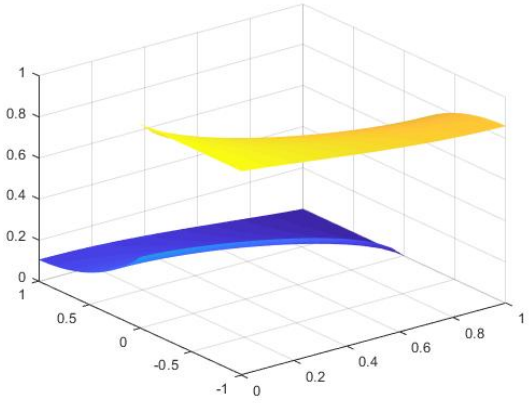
(a) Simulation for coupled models-beginning



(b) Simulation for coupled models-a few seconds after



(c) Simulation for coupled models-around the middle of total time



(d) Simulation for coupled models-finished

Figure 5.1: Simulation graphs double fluid speed

improved. But we have seen in discussion section, our numerical model cannot produced a proper micro scaled simulation. We need to adjust the numerical program to see the possibility of simulating this aspects.

5.2.2 The Constant Velocity Presumption

In this diagram 2.2, we assumed that each point along the y axis have the same constant speed. This is a huge violation against our assumptions for have the proper diffusion process. Since the liquid on the membrane should have a nearly 0 velocity. Therefore we should change the constant speed of fluids inside our model to a parabola shaped function. This could improve the performance of our model.

Additionally, it should make more sense if we consider that the velocity is changing with respect to the location point x. Especially when the fluids are flowing through a quite narrow and really long tube.

5.2.3 A Different Coordinate System

We only examined our model in two-dimension Cartesian system in space. In reality, the blood should flow through a tube instead of a box. One way of a further study could go to a three-dimension model in Cartesian coordinates or a cylinder coordinate. However the philosophy would be that simpler is better. We can try to replace the Cartesian system to a polar system. Allowing blood flows inside the inner tube and it is located inside the dialysate tube.

And once inside the polar system we can consider problems such as finding a proper radius value to optimize the model performance.

5.2.4 Approaching the Model using Probability Theory-Urns of Balls

As described in the Problem Formulation Section on page 4, the diffusion process is the macro-observation of the the transportation of particles from one region to another region due to the concentration difference. Under such observation, we have the continuous function modeling the change of concentration with respect to fluid speed and the concentration flux. However, we know that in micro scale, the process is the moving of particles, molecules, which is discrete than continuous. Therefore, it is natural to consider the problem from the micro discrete scheme and a question is whether a discrete scheme could give a much accurate assumption. As know from scientific experiments, small particles all make continuous random Brownian movements. Since the movement is random, it is natural to consider a different approach using concepts and models from Probability Theory. One approaches can be the famous models "urns of balls". For example, those most simple and famous models are drawing coloured balls from an urn either with replacement or without replacement. Many serious questions have their answer by simulating simple games like these urns of balls. [4]

The Ehrenfest's Urn Model For our diffusion process, we can start with the simple Ehrenfest's urn model[4, pp140]. In this model, we have two urns(U_1 and U_2) containing n balls together. At discrete time point $t = 1, 2, ...$ one ball is drawn at random and moved from the urn it was taken to the other urn. E_k denotes the state k balls are in urn U_2, where $k = 0, 1, ..., n$. Allow all the balls are in U_1 at the starting time, 0 balls in U_2 as the beginning state E_0. This system is a one-dimension model which can be used to find the expected time μ_n for reaching a certain state E_k [4, pp141]:

$$\mu_n = e_0 + e_1 + ... + e_{n-1}, \text{ leads to:}$$
$$e_k = \frac{m + ke_{k-1}}{m - k}, \text{ replacing with an integration:}$$
$$e_k = m \int_0^1 x^{m-k-1}(2 - x)^k dx,$$

where e_k is the mean time changing from state E_k to E_{k+1}. Replacing $x = 1 - y$ gives the result:

$$\mu_n = \frac{n}{2} \int_0^1 (1 - y)^{m-n}[(1 + y)^n - (1 - y)^n]\frac{1}{y} dy. \tag{5.1}$$

This is the simplified diffusion movement model of molecules between two systems which is commenly used by theoretical physicists. [4, pp140-141]

Markove Chain-the Ehrenfest's II model An extension can use Markov chains for urns of balls model, which is the Ehrenfest's II model [4, pp162-163].

An expansion to 2-D Another concern of modeling the original 2-D space, I had asked our lecturer for some advice(Jarai. (pers.comm.) 20 August 2018). A 2-D model can be viewed as having a number of urns (B_0, B_1,B_2,...,B_n) lined up together from left to right. Balls started in urn B_0 and move from left to right. In the opposite side to the family B urns, there are empty family of D urns (D_0, D_1,D_2,...,D_n) arranged from left to right.

(More details can be found in the book by Blom[4, pp133-pp146] and more application of urn of balls models can be found in the book by Johnson see the reference [10]. Another relevant paper by Balaji models gas diffusion process can be found in reference [5].) Since such model requires many advanced probability knowledge, I cannot continue in theory models nor numerical approaches further due to the knowledge gaps and page limit for this case study. However, it is an fascinating idea, I kept it here in case of further possible study in this combined area.

6 Conclusion

Mathematically saying, we have examined the process of model building and explored the governing law and showed the diffusion is caused by the same reason as heat conduction and convection in a micro particles' scale. The numerical model has used relative error comparison and von neumann analysis. This allows us to understand how to approach a problem when there is no exact solution to refer to.

Not surprisingly our models demonstrated its complexity when we do simulations. This suggests that in order to understand a complex problem, only theoretical analysis cannot satisfy our need to solve the problem. We also need to combine empirical and practical data and therefore we need our model to be more compatible. However due to the time limit for this case study, we could not update the program to obtain a better results.

Even thought the real data based simulation was not satisfying. Our model with uniform parameters produced some interesting results. The model works properly when the parameters are less correlated. Also it shows our current assumptions did not use the dialysate well. Most liquid will be wasted and the blood was not cleaned.

However, combining literature reports and practical tips from using dialysis machine, we can assume that we can relatively increase the temperature to increase the diffusion process (This need to be kept within the safe range for human body temperature and also patient physical feeling needs to be considered, because increasing temperature can create side effect for certain patients[12].). The effect of different materials for making the membrane should be compared.

References

[1] Adkins, C.J., 1987.*An introduction to thermal physics.* Cambridge : Cambridge University Press.

[2] Alkan-Sungur, A. and Özdural, A.R., (2009). *Prediction of overall mass transfer coefficients in continuous dialyzers: comparison of pseudo steady state approximation and unsteady state solution.* Desalination, 240(1), pp. 64-70.

[3] Annan, K., 2011. *Mathematical modeling of the dynamic exchange of solutes during bicarbonate dialysis.* Mathematical and Computer Modelling.

[4] Blom, G., 1994. *Problems and Snapshots from the World of Probability.* New York, NY : Springer New York.

[5] Balaji, S., Mahmoud, H. and Tong, Z., 2010. *Phases in the diffusion of gases via the ehrenfest urn model.* Journal of Applied Probability, 47(3), pp. 841-855. Available online: (https://pdfs.semanticscholar.org/9107/d48948f11d81ac998d7a7fd46f90b6f31841.pdf)

[6] Daintith, J., 2008. *law of conservation of mass.* A Dictionary of Chemistry 6th edition, Oxford University Press.

[7] Edwards, D.K., 1976. *Transfer processes : an introduction to diffusion, convection and radiation.* Washington [D.C.] ; London

[8] Incropera, F.P., 1996. *Fundamentals of heat and mass transfer. 4th ed.*Chichester: New York ; Chichester : Wiley.

[9] Jiji, L.M., 2009. *Heat conduction. 3rd ed* Heidelberg: Berlin, Springer-Verlag.

[10] Johnson, N.L., 1977. *Urn models and their application : an approach to modern discrete probability theory.* New York ; London: New York ; London : Wiley.

[11] Layton, A.T., 2014. *Mathematical Modeling in Renal Physiology.* Berlin, Heidelberg : Springer Berlin Heidelberg : Imprint: Springer.

[12] The National Kidney Foundation (NKF)(2018). *Hemodialysis Health Guide.*[online]. [Accessed 04 April 2018]Available at: (https://www.kidney.org/atoz/content/hemodialysis)

[13] 2010. erythrogenesis *Concise Medical Dictionary*,8 ed.: Oxford University Press.

[14] Custom Clinic HQ (2018). *The Truth Behind the Expensive Cost of Dialysis in the U.S.*[online]. [Accessed 01 April 2018]Available at: (https://customclinichq.com/truth-behind-expensive-cost-dialysis-u-s/)

[15] Roderick, P., 2002. *Epidemiology of end- stage renal disease.* Clinical medicine, London, England, 2(3), p. 200.

[16] Simmons G.F., 1996 *Calculus with Analytic Geometry 2nd Edition.* Colorado: The McGraw-Hill Companies.

[17] Smith, G. 1985 *Numerical Solution of Partial Differential Equations: Finite Difference Methods, third edition.* Clarendon Press, Oxford.

[18] Taler, J. and Duda, P., 2006. *Solving Direct and Inverse Heat Conduction Problems*. Berlin, Heidelberg: Springer Berlin.

[19] Thomas, J.W., 1995. *Numerical Partial Differential Equations: Finite Difference Methods*. New York, NY : Springer New York.

[20] Waniewski, J., 2006. *Mathematical modeling of fluid and solute transport in hemodialysis and peritoneal dialysis.* Journal of Membrane Science, 274(1), pp. 24-37.

[21] Wang, L., 2008. *Heat conduction : mathematical models and analytical solutions*. Berlin: Springer.

[22] Warady, B.A., 1999. *Dialysis therapy for patients with chronic kidney failure.* Exceptional Parent, 29(8), pp. 34-38. [Accessed 12 April 2018] Available at: (http://web.a.ebscohost.com/ehost/detail/detail?vid=0&sid=72b11cf4-bbb6-4b65-875c-ab676dd957da%40sessionmgr4006&bdata=JnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#AN=507

[23] Vadim Lvovich 2018, *Fick's Laws* [Accessed 14 April 2018] Knovel Corporation, Available at:(https://app.knovel.com/ie/#equation/CHEMA0049E)

7 Appendix A: Relevant Medical Terms

Definition 7.0.1 (Erythrogenesis) *n. "the process of red blood cell (erythrocyte) production, which normally occurs in the blood-forming tissue of the bone marrow. The ultimate precursor of the red cell is the haemopoietic stem cell, but the earliest precursor that can be identified microscopically is the proerythroblast. This divides and passes through a series of stages of maturation termed respectively early, intermediate, and late normoblasts, the latter finally losing its nucleus to become a mature red cell. See also haemopoiesis." [13]*

Definition 7.0.2 (End-stage renal disease) *In the above table 3, syndromes that can be classified as ESRD are listed. Any patients who received matched diagnose from a doctor can be considered as have the ESRD.*

Table 3: UK Registry definition of ESRD[15, page200]

	A new patient with ESRD is defined as:
·	one who is accepted for treatment and transplanted or dialysed for more than 90 days or
·	one who is diagnosed as ESRD(ie accepted for dialysis in the anticipation that they will need RRT indefinitely), dialysed, and who dies within 90 days or
·	one who is dialysed initially for ARF but who is subsequently diagnosed as having ESRD
·	This excludes patients who were thought to have ESRD and started RRT in the expectation that this would continue indefinitely, but who subsequently recovered within 90 days and were therefore classified in retrospect as having had ARF

Definition 7.0.3 (Hemodialysis (HD)) *Hemodialysis (HD) is performed with a special machine called a dialysis machine. The machine contains a pump that moves blood through a dialysis circuit." Blood is pumped first from the "access"*

*through tubing into the dialysis machine. There it passes through a special filter, called the artificial kidney or dialyzer. In the dialyzer, a membrane allows the blood to come into contact with dialysate, a fluid that removes waste products and excess water. Once cleansed, the blood completes the dialysis circuit by passing through tubing back into the body through the access. Throughout this process, the dialysis machine monitors blood flow and alerts the patient and caregivers if the settings need adjustment. The access is a crucial component for successful HD. There are three types of accesses that can be used: * fistula - an artery and a vein in the patient's arm are surgically connected (see Figure 1); * graft - as above, but a soft tube is used to connect the artery and vein; and * catheter - a soft tube is inserted into a large vein in the neck. The fistula is the preferred method of access for adults because it lasts the longest and has the fewest potential complications. By contrast, most children who receive HD have a catheter access since their blood vessels are so small that it is difficult to create a fistula or place a graft. Needles are placed into the access to allow the blood to flow from the body through the dialysis circuit. The catheter has the advantage of being pain-free in this regard, but it carries with it the greatest risk of complications, particularly infection.*
[22]

Definition 7.0.4 (Peritoneal dialysis (PD)) *Peritoneal dialysis (PD) takes place entirely within the body. The dialysate is infused into the peritoneal (abdominal) cavity by way of a catheter. This catheter, made of a soft, flexible material, is surgically placed just below the waistline and can remain in place for many years. Catheters come in various sizes to meet the needs of people of all sizes, from infants to adults. Peritoneal dialysis is provided almost universa11y as a home therapy. There are two types of PD: continuous ambulatory PD (CAPD) and automated PD (APD). In CAPD, the dialysis is self-administered, machine-free, and takes place 24 hours a day. In APD, the person connects the catheter to an automated dialysis machine that does its work while he or she sleeps. Many people who receive APD also have dialysate in their abdominal cavity during their waking hours. Although pediatric dialysis programs in North America currently favor the use of PD by 2 to 1 over HD, neither has been shown to be superior for pediatric patients. Selection of the type of dialysis must be made based on the child and family's individual needs. In practice, virtually all infants receive PD, but the type of dialysis chosen–HD or PD–is nearly evenly split in adolescents. [22]*

Table 4: Relevant Medical Terms: Abstraction and meanings list

Abstractions	Meanings
ESRD	End-stage renal disease
ARF	Acute renal failure
RRT	Renal replacement therapy
HD	Hemodialysis
PD	Peritoneal dialysis

8 Appendix B: Physical Terms and Physical laws

8.1 Heat and Particle diffusion

Transfer processes The transmit of thermal energy, momentum and mass of species of matter exists in all conditions except in an equilibrium dynamic system. The rate of transfers are influencing many fundamental aspects of our industry products, engineering designing and scientific studies. For example, in the design of nuclear power stations, the transferring rates in heat and mass of the reactors needs to be clearly understood for designing heat shields and separators and other such devices.The exchange rates is also essential for scientists to understand those transfer processes for planning experiment and understanding lab data. [7]

The physics mechanics behind those processes are always combined and can be generally classified to the following three categories: diffusion, convection, and radiation. [7]

Diffusion This category includes processes of heat conduction, viscous transfer of momentum, and mass diffusion. *Diffusion* process exits in dense materials. When particles are moving, they always collides into other particles on their way. [7, pp1-2] In micro scale, diffusion represents a "short mean free path process". [7, pp2]

Convection This refers to the process of transporting heat, mass or momentum by the flowing of fluids. To be clear, the transferring process is happening due to bulk motion of flowing media. The transferring of fluids' momentum causes the movement of thermal energy and mass, which in a broader view, can be considered as a process combining both diffusion and radiation in flowing fluids. [7, pp2]

Radiation This category contains process like heat radiation, neutron transport, and free molecule flow. The process happens in low dense medium or vacuum, where particles can move with high speed without colliding into others. Therefore the radiation process is a "long mean free path process". [7, pp2]

Definition 8.1.1 (The Mean Free Path) ***The mean free path*** *measures the average distance that a molecule can move freely without a collision happens: [7, pp198]*

$$l = vt_c = \frac{1}{\sqrt{2}\pi d^2 \mathcal{N}},$$

where l is the average molecule free moving distance, t_c is the average time between collisions, d is the assumed diameter of a molecule, $\mathcal{N}$ is the average number of molecules per unit volume.

Note: This formulation of *mean free path* has neglected the existence of weak forces between molecules for simplicity.

Here only includes a brief discussion about the relations among different physical transfer processes to obtain a relatively deep understanding of the two models in the Case Study I and Case Study II. More details can be found in the book by Edwards in reference [7]. The microscopic process and analysis of the cause of concentration difference for diffusion flux can be found in Chapter 7 in the book[7].

8.2 Physical Terms

Mass Transfer and Diffusion The term **mass transfer** is specially used to referee to the diffusion process. It is not referring to the mass movement along a fluid's movement. Such situations are movement due to mechanical work. The term **mass transfer** is used to describe the relative motion of substances in a mixture due to the presence of concentration gradients or under the work of chemical potential energy. For example: the motion of air caused by a fan or flow of water forced into a pipe. These two are due to mechanical works therefore the particle movement cannot be described by the term mass transfer. However the spread of oxides of sulfur from a smoke into the environment is diffusion or the mass transfer process.[8, pp785-787]

The physics behind concentration and diffusion In a multi-component system or a mixture, the local concentration of one substance can be expressed by the number of molecules(number density), the mass of molecules(macroscopic definition of mass concentration), or number of moles (the molar basis) present over the considered volume size. Thus we can express the concentration in three measurements species number of molecules, mass concentration and molar concentration:

$$Number\ density\ of\ species = \frac{\text{number of molecules}}{\text{volume of fluid}},\ \ or \tag{8.1}$$

$$\mathcal{N} = \frac{N}{V}. \tag{8.2}$$

$$Mass\ concentration = \frac{\text{mass of solute}}{\text{volume of fluid}},\ \ or \tag{8.3}$$

$$\rho = \frac{M}{V}. \tag{8.4}$$

$$Molar\ concentration = \frac{\text{number of moles}}{\text{volume of fluid}},\ \ or \tag{8.5}$$

$$C = \frac{Moles}{V}. \tag{8.6}$$

The standpoint of diffusion modeling is molecular activity which is also the reason behind heat conduction. The **Fick's law** is about the analogy between the two phenomenon. [7, pp52-55]

Solidus Notation A physical quantity contains a value and a unit. For example, the mass m_e of the electron is given by:

$$m_e = 9.11 \times 10^{-31}\ \ kg \tag{8.7}$$

Definition 8.2.1 *An equivalent notation of the above equation is:*

$$m_e/kg = 9.11 \times 10^{-31} \tag{8.8}$$

This is the solidus notation. It now using the division of a physical quantity by it's unit giving a pure number. Complex equations involving physical quantities should often be written in this concise and unambiguous solidus notation to keep involved quantities dimensionless. This is due to the reason that equations are representing a true physical fact that is true regardless of how a quantities being measured or in which unit is being measured. Therefore those quantities need to be dimensionless in mathematical equations.

[1, p viii]

8.3 Fourier's Law

Definition 8.3.1 *A material is said to be isotropic when it behaves all the same in all different directions[1]. A homogeneous and isotropic solid is defined as a type of material that its thermal conductivity is independent of direction within the solid.*

For such a solid, the heat flow and the temperature gradient have the follow relation[21]:

$$q(M,t) = -k\nabla T(M,t), \tag{8.9}$$

where the *temperature gradient* ∇T is a vector normal to the iso-thermal surface; the *heat flux* $\mathbf{q}(M,t)$ is the flow of heat per unit time, per unit area of the iso-thermal surface of the direction of the decreasing temperature; k is the *thermal conductivity* of the material.[21] The thermal conductivity depend on the in location in space, but for isotropic system it is a positive scalar. The above relationship is the Fourier's law of conduction or the *constitutive relation of heat flux*. In a Cartesian system, this constitutive relation can be re-written as:

$$\mathbf{q}(x,y,z,t) = -k(\partial_x T \cdot \mathbf{i} + \partial_y T \cdot \mathbf{j} + \partial_z T \cdot \mathbf{k}), \tag{8.10}$$

where $\mathbf{i}$, $\mathbf{j}$ and $\mathbf{k}$ are the unit direction vectors along the x, y and z directions respectively.[21]

8.4 Relevant Maths Theorems

Theorem 8.4.1 (Divergence Theorem) *The Divergence theorem or the Gauss's Theorem states that the flux of a vector field $\boldsymbol{F}$ out through a closed surface S equals the integral of the divergence of $\boldsymbol{F}$ over the region R bounded by S:*

$$\iint_S \boldsymbol{F} \cdot \boldsymbol{n}\, dA = \iiint_R \nabla \boldsymbol{F}\, dV, \tag{8.11}$$

where

$$\nabla = \boldsymbol{i}\frac{\partial}{\partial x} + \boldsymbol{j}\frac{\partial}{\partial y} + \boldsymbol{k}\frac{\partial}{\partial z}.$$

The vectors in $\mathbf{F}$ are perpendicular to the surface S. There this means the outward flux of $\mathbf{F}$ over the entire area A can be approximated by the sum of the divergence of $\mathbf{F}$ over the entire volume. [16, p775] **Gradient operator**: ΔC is applying the gradient operator ∇ twice on C. In Cartesian system, the gradient operator is:

$$\begin{aligned}\Delta C = \nabla(\nabla \cdot C) &= \nabla \begin{bmatrix} C_x \\ C_y \\ C_z \end{bmatrix} \\ &= \begin{bmatrix} C_{xx} \\ C_{yy} \\ C_{zz} \end{bmatrix}.\end{aligned}$$

9 Appendix C: Proofs of the Conservation Equations

9.1 Proof of Conservation of Mass in Arbitrary Coordinates

It is important to select a controlled volume system or the controlled part of a system. Let the volume be V. Let $\mathbf{n}$ denotes the outward directed unit normal vector to the

system surface. Then the change of volume with respect to time is caused by the change in density:

$$\frac{\partial}{\partial t}\int_V \rho dV = \int_V \frac{\partial \rho}{\partial t} dV$$

The change of density is due to the flow in and out of the system across the whole surface S. Let $\mathbf{v}$ be the velocity of fluid flow on surface:

$$\int_V \frac{\partial \rho}{\partial t} dV = -\int_S \rho \mathbf{v}\mathbf{n} dS$$

Applying the divergence theorem (refer to the theorem on page 29 for more information.):

$$\int_V \frac{\partial \rho}{\partial t} dV = -\int_V \nabla \cdot (\rho \mathbf{v}) dV$$

The arbitrary choice of volume V gives

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{v}) = 0)$$

[7]

9.2 Proof of Conservation of Chemical Species

We need a controlled fixed amount of volume V as before. For simplicity, we consider only one substance dissolved in water. Take the density of this species ρ, the change of density within time t is then equals to:

$$\frac{\partial}{\partial_t}\int_V \rho dV$$

This change over time is influenced by the combination effect of diffusion and bulk flow.

The change of density due to net flow into the system across the whole surface S. Combining the divergence theorem:

$$-\int_V \nabla \cdot (\rho \mathbf{v}) dV$$

The net flow of species into the system caused by diffusion is:

$$-\int_V \nabla \cdot (\mathbf{j}) dV$$

In our example, we neglect chemical reaction process, therefore the total system over an arbitrary choice of volume V gives:

$$\frac{\partial \rho}{\partial_t} = -(\nabla \cdot (\rho \mathbf{v}) + \nabla \cdot (\mathbf{J})) \tag{9.1}$$

10 Appendix D: Detailed process of the Non-Dimensionalisation of our Model

Here shows only a brief calculation details for the non-dimesionalisation process of equations in page 11. The calculation is based on simple algebra manipulation, and due to the simplicity of calculation and length of models, exact calculation will be skipped here. The logic and reasoning is similar to our simpler model derived in Case Study I. The whole calculation can be referred to the appendix in Case Study I.

The following are the original model for the pollutant concentration in blood:

$$\begin{aligned}\partial_t\Theta + \nabla(\Theta\mathbf{U}_b) = \nabla D_b\nabla\Theta, \;\; & 0 < x < L, \; -W < y < 0 \\ & 0 < Z < H, \; 0 < t < T_f\end{aligned}$$

$$\begin{aligned}\mathbf{Fn} &= 0, \;\; z = H, \\ \mathbf{Fn} &= 0, \;\; z = 0, \\ \mathbf{Fn} &= 0, \;\; y = -W, \\ \Theta(x = 0, y, z, t) &= \Theta_i(t) \\ \mathbf{Fn} &= \mathbf{F}_2\mathbf{n}, \;\; x = L, \\ \mathbf{Fn} &= \mathbf{F}_1\mathbf{n}, \;\; y = 0, \\ \Theta(x, y, z, t = 0) &= 0.\end{aligned}$$

First step To turn the model equations of 3D general system to 2D Cartesian systems:

$$\begin{aligned}\partial_t\Theta + U_b^1\partial_x\Theta = D_b(\partial_{xx}\Theta + \partial_{yy}\Theta), \; & 0 < x < L, \; -W < y < 0 \\ & 0 < Z < H, \; 0 < t < T_f.\end{aligned}$$

$$\begin{aligned}\partial_y\Theta(x, \, -W, \, t) \; &= \; 0 \\ \partial_y\Theta(x, \, 0, \, t) \; &= \; -\frac{h}{D_b}\left[\Theta(x, \, 0, \, t) \; - \; \eta(x, \, 0, \, t)\right] \\ \Theta(0, \, y, \, t) \; &= \; \Theta_i(t) \; = \; \Theta_M(1 - e^{-t/T}) \\ \partial_x\Theta(L, \, y, \, , t) \; &= \; -\frac{\partial_t\Theta}{U_b^1} \\ \Theta(x, \, y, \, 0) \; &= \; 0.\end{aligned}$$

Second step is to take the influence of tube lengths and width away from our function of Θ.Remove the influence of the maximum concentration constants Θ_M, the constant fluid speed U By defining:

$$\begin{aligned}\bar{x} &= x/L & \bar{y} &= y/W & \bar{\Theta} &= \Theta/\Theta_M \\ \bar{U} &= U/U_b^1 & T &= L/v & \bar{t} &= (tU_b^1)/L\end{aligned}$$

By substituting those changed variables back to the Cartisian 2D models, and change all the $\bar{variable}$ to original variables for simplicity, we have the following:

$$\begin{aligned}
&\partial_t\Theta + \frac{U_b^1}{L}T\partial_x\Theta = \frac{D_bT}{W^2}\Big(\frac{W^2}{L^2}\partial_{xx}\Theta + \partial_{yy}\Theta\Big)\\
&\partial_y\Theta(x,-1,t) = 0\\
&\partial_y\Theta(x,0,t) = -\frac{hW}{D_b}[\Theta(x,0.t) - \eta(x,0,t)]\\
&\Theta(0,y,t) = \Theta_i(t) = 1 - e^{t/(T/\mathcal{T})}\\
&\partial_x\Theta(1,y,t) = -\frac{\partial_t\Theta L}{U_b^1T}\\
&\Theta(x,y,0) = 0.
\end{aligned}$$

Step Three Following exactly the same processor as in Step One to Step two, we have the models for pollutant concentration in dialysate:

$$\partial_t\eta + \frac{U_d^1}{L}T\partial_x\eta = \frac{D_dT}{W^2}\Big(\frac{W^2}{L^2}\partial_{xx}\eta + \partial_{yy}\eta\Big) \tag{10.1}$$

$$\partial_y\eta(x,1,t) = 0 \tag{10.2}$$

$$\partial_y\eta(x,0,t) = -\frac{hW}{D_d}[\Theta(x,0.t) - \eta(x,0,t)] \tag{10.3}$$

$$\eta(1,y,t) = 0 \tag{10.4}$$

$$\partial_x\eta(0,y,t) = -\frac{L\partial_t\eta}{U_d^1T} \tag{10.5}$$

$$\eta(x,y,0) = 0. \tag{10.6}$$

Step Four To make the model readable, we give different groups of constants different symbols and names:

$$Pe^b = \frac{D_b\mathcal{T}}{W^2} \qquad \mathcal{T} = \frac{L}{U_b^1} \qquad \alpha^2 = \frac{W^2}{L^2} \tag{10.7}$$

$$He = \frac{hW}{D_b} \qquad C = \frac{T}{\mathcal{T}} \qquad Ve = \frac{U_d^1\mathcal{T}}{L} = \frac{U_d^1}{U_b^1} \tag{10.8}$$

$$Pe^d = \frac{D_d\mathcal{T}}{W^2} \qquad D_e = \frac{D_d}{D_b} \qquad \frac{He}{D_e} = \frac{hW}{D_d} \tag{10.9}$$

Therefore we have the final non-dimension coupled models in the following form final form: The final model for pollutant in blood:

$$\begin{cases}
\partial_t\Theta + \partial_x\Theta &= Pe(\alpha^2\partial_{xx}\Theta + \partial_{yy}\Theta)\\
\partial_y\Theta(x,-1,t) &= 0\\
\partial_y\Theta(x,0,t) &= -He(\Theta(x,0,t) - \eta(x,0,t))\\
\Theta(0,y,t) &= (1 - e^{-t/C})\\
\partial_x\Theta(1,y,t) &= -\Theta_t(1,y,t)\\
\Theta(x,y,0) &= 0.
\end{cases} \tag{10.10}$$

The final models for pollutant diffused into dialysate:

$$\begin{cases} \partial_t \eta + Ve\partial_x \eta &= DePe(\alpha^2 \partial_{xx}\eta + \partial_{yy}\eta) \\ \partial_y \eta(x,1,t) &= 0 \\ \partial_y \eta(x,0,t) &= -\frac{He}{De}(\Theta(x,0,t) - \eta(x,0,t)) \\ \eta(1,y,t) &= 0 \\ \partial_x \eta(0,y,t) &= -\frac{\partial_t \eta(0,y,t)}{Ve} \\ \eta(x,y,0) &= 0. \end{cases} \tag{10.11}$$

11 Appendix E: MatLab Scripts

This section involves MatLab scripts for the numeriacal approaches.

11.1 Code forValidity Checking

```
% Validation simulation: One sided model
close all
clear
clc
%Physical Parameters
Pe = 1; %Peclet number
He = 1;
Te = 1;
alpha2 = 1; %ratio of the squares of the length and width
%Length of simulation
Tend = 10;
%Numerical parameters
ny = 20; save('ny.mat','ny') %number of intervals in the y direction
nx = ceil(ny/sqrt(alpha2)); save('nx.mat','nx') %number of intervals in the x direction
ndelt = 10;
nt = Tend*ndelt;
%Resulting discretisation
dx = 1/nx;
dy = 1/ny;
dt = 1/ndelt;
beta2 = (dy/dx)^2;
%Variables to store results
Results = zeros((nx+1)*(ny+1),nt+1);
%System constants
delta = -dt/(4*dx);
gamma = Pe*dt/(2*dy^2);
%System Matrices
%D0 and D1
D0 = zeros(nx*(ny+1),nx*(ny+1));
D0(1:ny+1,ny+2:2*(ny+1)) = eye(ny+1);
for kk = 2:nx-1
    D0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = -eye(ny+1);
    D0((kk-1)*(ny+1)+1:kk*(ny+1), kk   *(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
end
D1 = D0;
D0(end-ny:end,end-ny:end) =  4*dx*eye(ny+1)/dt;
D1(end-ny:end,end-ny:end) = -4*dx*eye(ny+1)/dt;
%A
A = zeros(nx*(ny+1),nx*(ny+1));
Adiag = -2*eye(ny+1)+diag(ones(1,ny),-1)+diag(ones(1,ny),1);
Adiag(1,2) = 2;
Adiag(end,end-1) = 2;
Adiag(end,end) = Adiag(end,end)-2*dy*He;
for kk = 1:nx
    A((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:kk*(ny+1)) = Adiag;
end
% B0 and B1
B0 = zeros(nx*(ny+1),nx*(ny+1));
B0(1:ny+1,1:ny+1) = -2*eye(ny+1);
B0(1:ny+1,ny+2:2*(ny+1)) = eye(ny+1);
for kk = 2:nx-1
    B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = eye(ny+1);
```

```
    B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:(kk  )*(ny+1)) = -2*eye(ny+1);
    B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk  )*(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
end
B0(end-ny:end,end-(2*ny+2)+1:end-(ny+1)) = 2*eye(ny+1);
B1 = B0;
B0(end-ny:end,end-ny:end) = (-2+4*dx/dt)*eye(ny+1);
B1(end-ny:end,end-ny:end) = (-2-4*dx/dt)*eye(ny+1);
%Matrices C1 and C0 (to solve system)
C1 = eye(nx*(ny+1))-delta*D1-gamma*A-gamma*alpha2*beta2*B1;
C0 = eye(nx*(ny+1))+delta*D0+gamma*A+gamma*alpha2*beta2*B0;
M = inv(C1);
N = M*C0;
%Dirichlet boundary data
phiLeft = zeros(ny+1,nt+1);
for ll = 1:nt+1
    phiLeft(:,ll) = (1-exp(-(ll-1)*dt/Te))*ones(ny+1,1);
end
Results(1:ny+1,:) = phiLeft;
%Variables at each time step
phi = zeros(nx*(ny+1),1);
%Solving temporal evolution
for ll = 1:nt
    phi  = N*phi+(-delta+gamma*alpha2*beta2)*M*([phiLeft(:,ll);zeros((nx-1)*(ny+1),1)]+[phiLeft(:,ll+1);zeros((
    Results(ny+2:end,ll+1) = phi;
end
save('Results.mat','Results')
```

11.2 Relative Error Analysis

11.2.1 Convergence Codes

```
close all
clear
clc
for ny = 2.^[2:6];
    %Physical Parameters
    Pe = 1; %Peclet number
    He = 1;
    Te = 1;
    alpha2 = 1; save('alpha2.mat','alpha2')%ratio of the squares of the length and width
    %Length of simulation
    Tend = 4; save('Tend.mat','Tend')
    %Numerical parameters
  %   ny = 40; save('ny.mat','ny') %number of intervals in the y direction
    nx = ceil(ny/sqrt(alpha2));% save('nx.mat','nx') %number of intervals in the x direction
    ndelt = ny;
    nt = round(Tend*ndelt);
    %Resulting discretisation
    dx = 1/nx;
    dy = 1/ny;
    dt = 1/ndelt;
    beta2 = (dy/dx)^2;
    %Variables to store results
    Results = zeros((nx+1)*(ny+1),nt+1);
    %System constants
    delta = -dt/(4*dx);
    gamma = Pe*dt/(2*dy^2);
    %System Matrices
    %D0 and D1
    D0 = zeros(nx*(ny+1),nx*(ny+1));
    D0(1:ny+1,ny+2:2*(ny+1)) = eye(ny+1);
    for kk = 2:nx-1
        D0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = -eye(ny+1);
        D0((kk-1)*(ny+1)+1:kk*(ny+1), kk   *(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
    end
    D1 = D0;
    D0(end-ny:end,end-ny:end) =  4*dx*eye(ny+1)/dt;
    D1(end-ny:end,end-ny:end) = -4*dx*eye(ny+1)/dt;
    %A
    A = zeros(nx*(ny+1),nx*(ny+1));
    Adiag = -2*eye(ny+1)+diag(ones(1,ny),-1)+diag(ones(1,ny),1);
    Adiag(1,2) = 2;
    Adiag(end,end-1) = 2;
    Adiag(end,end) = Adiag(end,end)-2*dy*He;
    for kk = 1:nx
```

```
        A((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:kk*(ny+1)) = Adiag;
    end
    % B0 and B1
    B0 = zeros(nx*(ny+1),nx*(ny+1));
    B0(1:ny+1,1:ny+1) = -2*eye(ny+1);
    B0(1:ny+1,ny+2:2*(ny+1)) = eye(ny+1);
    for kk = 2:nx-1
        B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = eye(ny+1);
        B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:(kk  )*(ny+1)) = -2*eye(ny+1);
        B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk  )*(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
    end
    B0(end-ny:end,end-(2*ny+2)+1:end-(ny+1)) = 2*eye(ny+1);
    B1 = B0;
    B0(end-ny:end,end-ny:end) = (-2+4*dx/dt)*eye(ny+1);
    B1(end-ny:end,end-ny:end) = (-2-4*dx/dt)*eye(ny+1);
    %Matrices C1 and C0 (to solve system)
    C1 = eye(nx*(ny+1))-delta*D1-gamma*A-gamma*alpha2*beta2*B1;
    C0 = eye(nx*(ny+1))+delta*D0+gamma*A+gamma*alpha2*beta2*B0;
    M = inv(C1);
    N = M*C0;
    %Dirichlet boundary data
    phiLeft = zeros(ny+1,nt+1);
    for ll = 1:nt+1
        phiLeft(:,ll) = (1-exp(-(ll-1)*dt/Te))*ones(ny+1,1);%(sin(pi*(ll-1)*dt/Te))*ones(ny+1,1);%
    end
    Results(1:ny+1,:) = phiLeft;
    %Variables at each time step
    phi = zeros(nx*(ny+1),1);
    %Solving temporal evolution
    for ll = 1:nt
        phi  = N*phi+(-delta+gamma*alpha2*beta2)*M*([phiLeft(:,ll);zeros((nx-1)*(ny+1),1)]+[phiLeft(:,ll+1);zer
        Results(ny+2:end,ll+1) = phi;
    end
    save(['ResultsN',num2str(ny),'.mat'],'Results')
end
```

11.2.2 Error Comparing

```
close all
clear
clc
nyVec = 2.^(2:6);
compareCell = cell(1,length(nyVec));%Storing the resulting matrices
count = 0;
for ny = nyVec
    count = count+1;
    load(['ResultsN',num2str(ny),'.mat'],'Results')
    xVec = 0:1/ny:1;
    yVec = 0:1/ny:1;
    tVec = 0:1/ny:4;
    CompareMat = zeros(nyVec(1)^2,4*nyVec(1));
    for kk = 1:4*nyVec(1)
        [~,indexT] = min(abs(tVec-kk/(4*nyVec(1))));
        for jj = 1:nyVec(1)
            [~,indexX] = min(abs(xVec-jj/nyVec(1)));
            for ii = 1:nyVec(1)
                [~,indexY] = min(abs(yVec-ii/nyVec(1)));
                CompareMat((jj-1)*nyVec(1)+ii,kk) = ...
                    Results((indexX-1)*(ny+1)+indexY,indexT);
            end
        end
    end
    compareCell{count} = CompareMat;
end
error = zeros(1,length(nyVec)-1);
for pp = 1:length(nyVec)-1
    error(pp) = norm(compareCell{pp}-compareCell{length(nyVec)},1);
end
plot(log(nyVec(1:end-1)),log(error),'LineWidth',4)
m = polyfit(log(nyVec(1:end-1)),log(error),1);
hold on
plot(log(nyVec(1:end-1)),m(1)*log(nyVec(1:end-1))+m(2))
grid on
```

11.2.3 Video Recording For One Sided Model

```
clear
clc
load('Results.mat')
load('nx.mat')
load('ny.mat')
dx = 1/nx;
dy = 1/ny;
xvec = 0:dx:1;
yvec = 0:dy:1;
vidObj = VideoWriter('Solution','MPEG-4');
open(vidObj);
for ll=1:size(Results,2)
    surf(xvec,yvec-1,reshape(Results(:,ll),ny+1,nx+1),'LineStyle','none','FaceColor','interp')
    set(gca,'zlim',[0 1.2])
%     view([30+ll 60])
    currFrame = getframe(gcf);
    writeVideo(vidObj,currFrame);
%     pause
end
close(vidObj);
```

11.2.4 Codes For Two Sided Model

```
    close all
clear
clc
%Physical Parameters
Pe = 1;
He = 1;
Te = 1;
De = 1; %Ratio of Diffusivities
Ve = -1.1; %Ratio of velocities
alpha2 = 1; %ratio of the squares of the length and width
%Length of simulation
Tend = 5; %total time to be simulated measured in the time units used for non-dimensionalisation
%Numerical parameters
ny = 20; save('nyCoupled.mat','ny')
nx = ceil(ny/sqrt(alpha2)); save('nxCoupled.mat','nx')
ndelt = 100; %Number of time steps per unit time
nt = Tend*ndelt; %number of total time steps
%Resulting constants
dx = 1/nx;
dy = 1/ny;
dt = 1/ndelt;
beta2 = (dy/dx)^2;
%Variables to store results
Results = zeros(2*(nx+1)*(ny+1),nt+1);
%System constants
delta = -dt/(4*dx);
gamma = Pe*dt/(2*dy^2);
mu = delta*Ve;
lambda = gamma*De;
%System Matrices
%D0 and D1
D0 = zeros(nx*(ny+1),nx*(ny+1));
D0(1:ny+1,ny+2:2*ny+2) = eye(ny+1);
for kk = 2:nx-1
    D0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = -eye(ny+1);
    D0((kk-1)*(ny+1)+1:kk*(ny+1), kk   *(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
end
D1 = D0;
D0(end-ny:end,end-ny:end) =  4*dx*eye(ny+1)/dt;
D1(end-ny:end,end-ny:end) = -4*dx*eye(ny+1)/dt;
%A
A = zeros(nx*(ny+1),nx*(ny+1));
Adiag = -2*eye(ny+1)+diag(ones(1,ny),-1)+diag(ones(1,ny),1);
Adiag(1,2) = 2;
Adiag(end,end-1) = 2;
Adiag(end,end) = Adiag(end,end)-2*dy*He;
for kk = 1:nx
    A((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:kk*(ny+1)) = Adiag;
end
% B0 and B1
B0 = zeros(nx*(ny+1),nx*(ny+1));
```

```
B0(1:ny+1,1:ny+1) = -2*eye(ny+1);
B0(1:ny+1,ny+2:2*ny+2) = eye(ny+1);
for kk = 2:nx-1
    B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = eye(ny+1);
    B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:(kk  )*(ny+1)) = -2*eye(ny+1);
    B0((kk-1)*(ny+1)+1:kk*(ny+1),(kk  )*(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
end
B0(end-ny:end,end-(2*ny+2)+1:end-(ny+1)) = 2*eye(ny+1);
B1 = B0;
B0(end-ny:end,end-ny:end) = (-2+4*dx/dt)*eye(ny+1);
B1(end-ny:end,end-ny:end) = (-2-4*dx/dt)*eye(ny+1);
%Matrix E0 and E1
E0 = zeros(nx*(ny+1),nx*(ny+1));
for kk = 2:nx-1
    E0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = -eye(ny+1);
    E0((kk-1)*(ny+1)+1:kk*(ny+1), kk   *(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
end
E0(end-ny:end,end-2*(ny+1)+1:end-(ny+1)) = -eye(ny+1);
E1 = E0;
E1(1:ny+1,1:ny+1) = -4*dx/(dt*Ve)*eye(ny+1);
E0(1:ny+1,1:ny+1) =  4*dx/(dt*Ve)*eye(ny+1);
%Matrix F
Fdiag = -2*diag(ones(ny+1,1))+diag(ones(ny,1),-1)+diag(ones(ny,1),1);
Fdiag(1,2) = 2;
Fdiag(end,end-1) = 2;
Fdiag(1,1) = Fdiag(1,1)-2*dy*He/De;
for kk = 1:nx
    F((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:kk*(ny+1)) = Fdiag;
end
%Matrices G1 and G0
G0 = zeros(nx*(ny+1),nx*(ny+1));
for kk = 2:nx-1
    G0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-2)*(ny+1)+1:(kk-1)*(ny+1)) = eye(ny+1);
    G0((kk-1)*(ny+1)+1:kk*(ny+1),(kk-1)*(ny+1)+1:(kk  )*(ny+1)) = -2*eye(ny+1);
    G0((kk-1)*(ny+1)+1:kk*(ny+1),(kk  )*(ny+1)+1:(kk+1)*(ny+1)) = eye(ny+1);
end
G0(end-ny:end,end-(2*ny+2)+1:end-(ny+1)) = eye(ny+1);
G0(end-ny:end,end-ny:end) = -2*eye(ny+1);
G0(1:ny+1,ny+2:2*ny+2) = 2*eye(ny+1);
G1 = G0;
G0(1:ny+1,1:ny+1) = (-2-4*dx/(dt*Ve))*eye(ny+1);
G1(1:ny+1,1:ny+1) = (-2+4*dx/(dt*Ve))*eye(ny+1);
%Matrices C1 and C0 (to solve system)
C0 = eye(nx*(ny+1))+delta*D0+gamma*A+gamma*alpha2*beta2*B0;
C1 = eye(nx*(ny+1))-delta*D1-gamma*A-gamma*alpha2*beta2*B1;
H0 = eye(nx*(ny+1))+mu*E0+lambda*F+lambda*alpha2*beta2*G0;
H1 = eye(nx*(ny+1))-mu*E1-lambda*F-lambda*alpha2*beta2*G1;
%Coupling Matrices
%K matrix
K = zeros(nx*(ny+1),nx*(ny+1));
for kk = 1:nx-1
    K(kk*(ny+1),kk*(ny+1)+1) = 2*dy*gamma*He;
end
%L matrix
L = zeros(nx*(ny+1),nx*(ny+1));
for kk = 2:nx
    L((kk-1)*(ny+1)+1,(kk-1)*(ny+1)) = 2*dy*gamma*He; %which happens to be the same as 2*dy*lambda*He/De
end
%Block system matrices
M1 = [C1,-K;[-L,H1]];
M0 = [C0,K;[L,H0]];
M = inv(M1);
N = M*M0;
%Dirichlet boundary data
%PhiLeft
phiLeft = zeros(ny+1,nt+1);
for ll = 1:nt+1
    phiLeft(:,ll) = (1-exp(-(ll-1)*dt/Te))*ones(ny+1,1);
end
%PsiRight
psiRight = zeros(ny+1,nt+1);
%Initial values of variables
phi = zeros(nx*(ny+1),1);
psi = zeros(nx*(ny+1),1);
%Storing results
Results(1:ny+1,:) = phiLeft; %Dirichlet BC to the left
Results(end-ny:end,:) = psiRight; %Dirichlet BC to the right
```

```
Results(ny+2:(nx+1)*(ny+1),1) = phi;
Results((nx+1)*(ny+1)+1:(2*nx+1)*(ny+1),1) = psi;
%Solving temporal evolution
for ll = 1:nt
    vector = N*[phi;psi]+...
        M*[(-delta+gamma*alpha2*beta2)*(phiLeft(:,ll)+phiLeft(:,ll+1));zeros((nx-1)*(ny+1),1);...
        zeros((nx-1)*(ny+1),1);(mu+lambda*alpha2*beta2)*(psiRight(:,ll)+psiRight(:,ll+1))]+...
        2*dy*gamma*He*M*[zeros(nx*(ny+1)-1,1);(psiRight(1,ll)+psiRight(1,ll+1));...
        (phiLeft(ny+1,ll)+phiLeft(ny+1,ll+1));zeros(nx*(ny+1)-1,1)];
    phi = vector(1:nx*(ny+1),1);
    psi = vector(nx*(ny+1)+1:end,1);
    Results(ny+2:end-(ny+1),ll+1) = [phi;psi];
end
save('ResultsCoupled.mat','Results')
```

11.2.5 Video Recording For Two Sided Model

```
close all
clear
clc
load('ResultsCoupled.mat')
load('nxCoupled.mat')
load('nyCoupled.mat')
dx = 1/nx;
dy = 1/ny;
xvec = 0:dx:1;
yvec = 0:dy:1;
vidObj = VideoWriter('SolutionCoupled','MPEG-4');
open(vidObj);
for ll=1:size(Results,2)
    surf(xvec,yvec-1,reshape(Results(1:(nx+1)*(ny+1),ll),ny+1,nx+1),'LineStyle','none','FaceColor','interp')
    hold on
    surf(xvec,yvec,reshape(Results((nx+1)*(ny+1)+1:end,ll),ny+1,nx+1),'LineStyle','none','FaceColor','interp')
    set(gca,'zlim',[0 1])
    currFrame = getframe(gcf);
    writeVideo(vidObj,currFrame);
    hold off
%     pause
end
close(vidObj);
```

12 Appendix F: Nomenclature

Table 5: Nomenclature: notations and meanings used in the report

symbols	Description (Units)
C	Solute molar concentration (mol/m^3)
Θ	Pollutant molar concentration in blood (mol/m^3)
η	Pollutant molar concentration in dialysate (mol/m^3)
$\mathcal{D}$	the constant of proportionality: diffusion coefficient or diffusivity (Units (Length)$^2/time$)
$\mathcal{D}_B$	diffusivity in blood phase
$\mathcal{D}_{CO_2,B}$	diffusivity of CO_2 in blood phase(m^2s^{-1})
$\mathcal{D}_D$	diffusivity in dialysate phase
$\mathcal{D}_{CO_2,D}$	diffusivity of CO_2 in dialysate phase
h_{CO_2}	Membrane permeability of CO_2 (m^2s^{-1})
$\mathbf{J}$	diffusion molar flux of the solute (Units $moles/area - time$)
$\mathbf{L}$	length of tube where diffusion can happen (m)
$\mathcal{P}\rceil$	Peclet number $(=u_{max}R/D_B)$
r_b	radius of blood channel (m)
r_d	radius of dialysate channel (m)
u_b	velocity at blood inlet
u_d	velocity at dialysate inlet (ms^{-1})
S	Surface area of the fixed volume system (Units m^2)
$\mathbf{n}$	outward normal vector on a surface
V	Fixed volume of a system (Units m^3)
ρ	Solute density concentration (kg/m^3)
Δ	the gradient operator
Δt	the small interval in change of time (unit s)
Δy	the small interval in change of distance in direction of y axis