Bachelor Thesis Research

Computational Modeling of the Sorbent System for Enhanced Efficiency in Peritoneal Dialysis: Investigating the Effects of Model Parameters Modifications on Solute Clearance

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Abstract: A computational model with the aim of exploring strategies for enhancing the efficacy of solute clearance in the sorbent chamber of the peritoneal dialysis system was developed. The sorbent chamber was modeled as a fixed-bed column, and Thomas and Yoon-Nelson were employed to predict the breakthrough curve from experimental data using linear regression analysis. The Thomas model was chosen to perform further study and the impacts of different parameters on the total mass of solute removal were first investigated separately. The results demonstrated that the total mass of solute removal increased with the increase in mass of the sorbent as well as adsorption capacity and decreased with the increase in flow rate. Finally, a combined analysis was conducted to identify the optimal combination of parameters for maximizing solute removal.

I. INTRODUCTION

End-stage kidney disease (ESKD) has become a major public health concern worldwide, with a substantial influence on global morbidity and mortality rates (Kovesdy, 2022). The prevalence of ESKD has escalated in the past few years, and the total number of patients worldwide requiring kidney replacement therapy (KRT) reached a significant 4.8 million at the end of 2022 (Fresenius Medical Care, 2022). Kidney transplantation stands as the preferred method of KRT due to its improved long-term survival and enhanced life quality of patients when compared to chronic dialysis (Medin et al., 2000; Oniscu et al., 2005; Port et al., 1993; Tonelli et al., 2011; Wolfe et al., 1999). However, the availability of donated organs has been insufficient to meet the demand of patients, leading to a prolonged waiting list for many years now (Fresenius Medical Care, 2022; Singh et al., 2019). Furthermore, the increasing elderly, diabetic, and metabolic syndrome patient populations are projected to worsen the problem (Artiles et al., 2023; Cohen et al., 2020; Rysz et al., 2021). In addition, this medical treatment may not be accessible to all individuals as a result of the costly expenses associated with the transplantation procedure and the requirement of lifelong immunosuppressive therapy (Hagenmeyer et al., 2004; Kuppachi et al., 2022; Wojciechowski & Wiseman, 2021).

In light of these challenges, dialysis emerges as an alternative KRT that offers two primary modalities: hemodialysis (HD) and peritoneal dialysis (PD). At the end of 2022, around 3.9 million patients worldwide received dialysis treatment (Fresenius Medical Care, 2022). In HD, the removal of waste products from the body involves the utilization of an extracorporeal circulation system (Elliott, 2000). As explained by Elliott (2000), the patient's blood is directed through an artificial kidney (dialyzer), with the assistance of a blood pump to facilitate the movement of blood through tubing. The study indicates that within the dialyzer, the semipermeable membrane aids in the exchange of wastes and excess fluids between the blood and the dialysate, effectively purifying the blood and restoring the balance of electrolytes and fluids within the body. On the other hand, PD employs a different approach that depends on the natural filtration ability of the peritoneal membrane (Gokal & Mallick, 1999). According to Gokal and Mallick (1999), a sterile dialysis solution (dialysate) is infused into the patient's abdominal cavity via a catheter in PD. The peritoneal membrane, a vascularized and thin layer that covers the abdominal cavity, functions as a semipermeable barrier and allows the movement of solutes, including electrolytes, waste products and fluid between the peritoneal cavity's surrounding blood vessels and the dialysate solution (Solass et al., 2019). PD offers several advantages in comparison to HD, as it does not require blood access, is capable of maintaining residual kidney function, and reduces the risk of hemodynamic instability (Chen et al., 2020; François & Bargman, 2014). However, there are some significant limitations that reduce the usage of PD, such as a low clearance rate and limited technique survival attributed to the deterioration of the peritoneal membrane due to recurrent peritonitis and long-term exposure to hypertonic glucose-based dialysis solutions (Bammens et al., 2003; Krediet, 2022; Nolph et al., 1978; Roumeliotis et al., 2020; Yung & Chan, 2012). In 2022, there were 5,216 patients being treated with HD in the Netherlands, while the number for PD was 958 (Nefrovisie, 2022). A collaborative effort between UMC Utrecht nephrologists and Nanodialysis, a medical device company, is currently underway to develop a novel device for sorbent-assisted peritoneal dialysis (SAPD) with the goal of improving conventional PD (van Gelder, de Vries, et al., 2020; van Gelder, Ligabue, et al., 2020).

The fundamental mechanism of SAPD is that the peritoneal dialysate is continuously recirculated via a single-lumen catheter while the spent dialysate containing uremic toxins is regenerated by a sorbent cartridge (van Gelder, Ligabue, et al., 2020). Under normal circumstances, a healthy kidney would eliminate uremic toxins from the body (Duranton et al., 2012). However, people with ESKD experience an accumulation of these harmful chemicals in the bloodstream, which eventually reach different organs and induce uremic syndrome (Falconi et al., 2021). The study by Falconi et al. (2021) describes uremic compounds as consisting of ions (e.g., phosphate and potassium), small water-soluble solutes (e.g., urea and creatinine), and low-molecular-weight proteins (e.g., β2–microglobulin and leptin). Successful dialysate regeneration is achieved when a sufficient amount of uremic toxins is completely removed by implementing extra sorbents, while crucial nutrients and electrolytes, which are important for maintaining overall physiological balance, are retained (Ash, 2009). In general, the innovative approach of incorporating sorbents into the PD process holds promise for addressing the shortcomings of traditional peritoneal dialysis as it enables a more efficient elimination of uremic wastes, thereby improving the overall effectiveness of the treatment and enhancing the patient's well-being.

A key understanding regarding sorbents is adsorption, a surface phenomenon by which a compound is attracted to the surface of a solid adsorbent and is attached to it by physical or chemical bonds (Foo & Hameed, 2010). Earlier systems such as the automated wearable artificial kidney for PD (AWAK PD™) and the Carry Life System (CLS) use ion-exchangers, which are capable of exchanging harmful ions for bicarbonate, acetate, and other less toxic ions, and activated carbon for adsorbing organic chemicals and middle molecules (Agar, 2010; van Gelder, de Vries, et al., 2020; van Gelder, Ligabue, et al., 2020). The new SAPD device also uses activated carbon to remove organic waste solutes (van Gelder, de Vries, et al., 2020; van Gelder, Ligabue, et al., 2020). The structure of activated carbon provides a highly porous nature and a large surface area, thereby intensifying the interaction between solutes and the adsorbent material and facilitating proficient adsorption and consequent elimination of organic waste, hence augmenting the overall purification of the dialysate and amplifying the efficacy of the SAPD therapy (El-Naas & Alhaija, 2013; Li et al., 2002; Wang et al., 2022). Additionally, ferric oxide hydroxide (FeOOH) is used to remove anions, mostly phosphate, in lieu of ion exchangers in the SAPD system (van Gelder, de Vries, et al., 2020; van Gelder, Ligabue, et al., 2020). Moreover, it was observed in van Gelder et al. (2020) that calcium and magnesium ions can also be eliminated through linking to phosphate molecules that are bound to FeOOH.

The schematic diagrams for the experimental setups of the SAPD system developed by van Gelder et al. (2020) are illustrated in Figures 1 and 2. In the setup for recirculation experiments, the system constantly recycles the used dialysate through a tidal mode, which is a cyclical pattern of dialysate flowing into and out of the SAPD system. The nighttime system is a combination of the daytime system with the addition of a dialysate reservoir. In both systems, the filter is positioned to prevent solutes from entering the peritoneal cavity, or dialysate reservoir. The experimental setup for single-pass experiments includes an extra waste reservoir compartment. In this setup, the dialysate is circulated from the dialysate reservoir through the sorbents into the waste reservoir. In vitro results and studies that have been done on a uremic pig model showed an enhancement in small solute clearance as compared to static dwell (van Gelder, de Vries, et al., 2020; van Gelder, Ligabue, et al., 2020). However, the experiment has used an animal model, and future clinical studies are necessary to show the device's efficacy in humans. To gain an in-depth understanding and optimize the performance of the system, it is crucial to determine the key factors that play a significant role in affecting the solute clearance rate. Identifying these elements can help refine the design and functionality of the device, leading to better treatment outcomes for patients. Additionally, exploring the relationship between the device's parameters and the amount of solute adsorbed, as well as investigating how the device's settings can be adjusted to maximize efficient solute removal are essential. This knowledge will provide valuable insights into the operational dynamics of the system and guide the development of improved strategies for solute removal, leading to enhanced dialysis efficiency. Thus, this study's goal is to develop a computational model to optimize different parameters, aiming to enhance the effectiveness of solute clearances within the SAPD system.

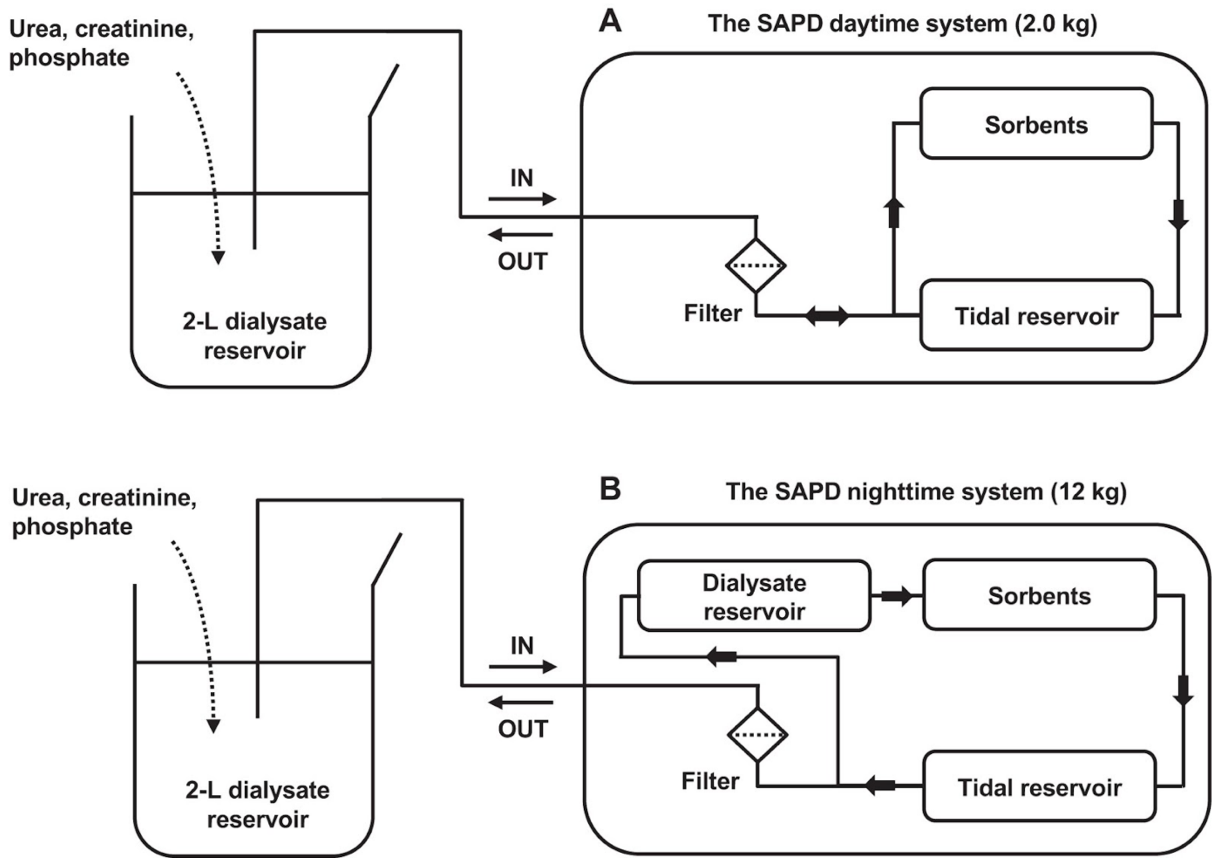

Figure 1. Experimental setup for recirculation experiments with the sorbent-assisted peritoneal dialysis (SAPD) daytime (A) and nighttime (B) system (van Gelder, Ligabue, et al., 2020).

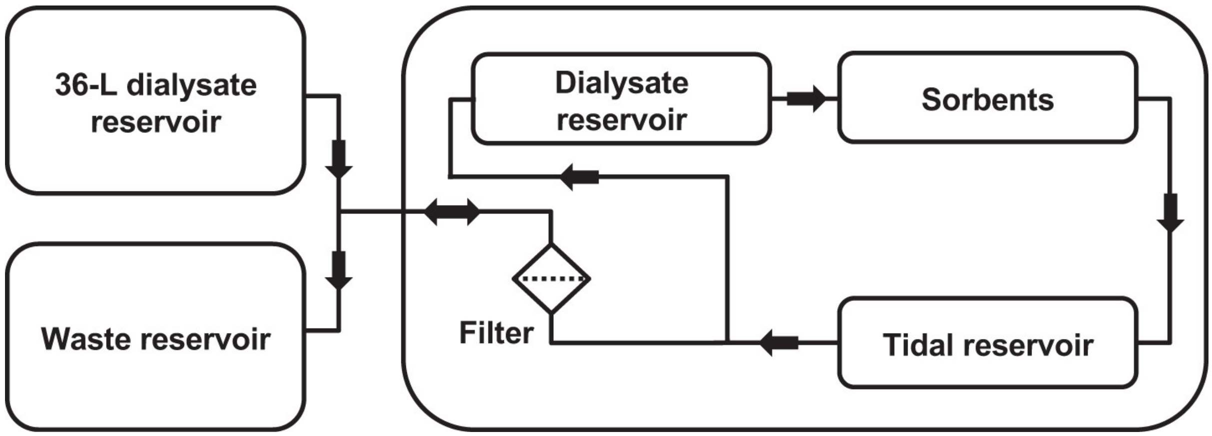

Figure 2. Experimental setup adapted for single-pass experiments with the sorbent-assisted peritoneal dialysis (SAPD) nighttime system (van Gelder, Ligabue, et al., 2020).

Computer models are valuable tools in contributing to the understanding of how to improve the effectiveness and efficiency of PD systems. For many years, computational modeling has been utilized to investigate various aspects of the development of PD treatment. For instance, Seames et al. (1990) developed a mathematical model to explore peritoneal fluid and solute transfer in PD; Rippe and Levin (2000) predicted the ultrafiltration profiles in continuous ambulatory PD under different experimental conditions; the review paper of Waniewski (2006) explains many different approaches to modeling the transport process in PD; Öberg and Rippe (2017) studied and optimized a computational model of automated PD by simulating it in a clinical problem; and Lee et al. (2020) have used computational simulations to explore the effectiveness of steady concentration peritoneal dialysis in comparison to conventional PD. In the current study with the SAPD system, computational modeling can act as an excellent instrument to provide advanced comprehension regarding the associated properties of sorbents and their direct impact on solute removal. Through computational modeling, various scenarios can be simulated and analyzed to examine the effect of different parameters on solute clearance. By leveraging the predictive capabilities of computational models, it is possible to identify specific parameters that have a significant impact on solute clearances. Additionally, the model in a virtual environment can be manipulated to explore how modifications in the sorbent system's parameters can contribute to improving clearance rates. By combining computational models with experimental data, researchers can validate the model and enhance its predictive accuracy. Hence, this iterative process of modeling and experimentation allows for a deeper understanding of the underlying mechanisms and interactions involved in SAPD.

The aims of the present work are to first develop a computational simulation of the sorbent cartridge in the SAPD system. The model needs to incorporate sorbent material properties and device parameters that contribute to the enhancement of solute clearance. The sorbent chamber was selected to be modeled since it is the only component responsible for the adsorption process in the SAPD system. Second, the effect of dialysate flow rate and mass of the sorbent on the amount of solute adsorbed was investigated. Previous systems, including AWAK PD™ and CLS, used relatively low rates of dialysate flow, which were 33 ml/min and 17 ml/min, respectively (van Gelder, de Vries, et al., 2020). As discussed in van Gelder, de Vries, et al. (2020), both show solute clearances that are comparable to conventional PD. Meanwhile, the system of van Gelder et al. (2020) had higher dialysate flow rates of 81 ± 11 ml/min. Hence, one of the goals is to explore whether a higher dialysate flow rate results in higher clearances and what the optimal flow rate is. For the sorbent weight, several studies have illustrated that increasing the adsorbent dosage for the sorbent weight results in an increase in the removal efficacy; however, the adsorption capacity decreases (Djelloul et al., 2017; Mosoarca et al., 2020; Mu'azu et al., 2020). Consequently, it is necessary to examine how these parameters can improve the efficacy of the SAPD system for solute clearance. The third objective of this research endeavor encompasses the optimization of parameters and the determination of the synergistic combination of all variables that can lead to an optimal clearance rate.

II. MATERIAL & METHODS

1. Experimental setup

1.1. Materials

The experimental setup involved the utilization of various materials and equipment. A precision balance (VWR, RMCU) was employed for accurate measurements. The dialysate reservoir, with a capacity of more than 40 liters, consisted of a polypropylene container (approximately 45 liters) in a gray color, while the waste reservoir, with a similar volume, was a polypropylene container (approximately 45 liters) in the same color. The chemicals used in the study included the following substances: distilled water (40 liters), glucose (Sigma; molecular weight: 180.16 g/mol), phosphate (Sigma, Lot#SLCK2210, S5011-500g; molecular weight: 119.98 g/mol), sodium chloride (NaCl) (Sigma, Lot# STBK1741, 31434-1kg-M; molecular weight: 58.44 g/mol), sodium bicarbonate ($NaHCO_3$) (Sigma, Lot#SLCD6141, S6014-500g; molecular weight: 84.01 g/mol), calcium chloride dihydrate ($CaCl_2$ dihydrate) (molecular weight: 111.56 g/mol), magnesium chloride hexahydrate ($MgCl_2.6H_20$) (molecular weight: 203.3 g/mol), and a potassium compound (molecular weight: 74.55 g/mol).

1.2. Single-pass experiments

The experimental setup consisted of a total dialysate volume of 40 L, incorporating a daytime cartridge containing sorbents. A sample of the dialysate reservoir was collected for subsequent clinical laboratory analysis. A device equipped with a conditioned cartridge, which included a mixture of 100 g of FeOOH and 200 g of activated carbon, was prepared. The device was then connected to the 40-liter dialysate reservoir and the waste container before starting. The flow rate was set to 60 mL/min, and the duration of the experiments was 4 hours. During the course of the experiment, samples were periodically obtained from the waste container and the outgoing line at scheduled time points. Once the dialysate reservoir was completely depleted, a final sample was collected from the waste reservoir for subsequent chemical analyses.

1.3. Preparation of protocol dialysis

The calculated amount of glucose was placed into a 50-mL Greiner tube. The calculated amount of NaCl was added to a weighing boat. Subsequently, the chemicals from steps 1 and 2 were combined in a 5-liter beaker. Following this, 5 L of distilled water was added to the beaker using a graduated cylinder of 1 L. The mixture was thoroughly stirred using a magnetic stirring bar until complete dissolution was achieved. In the next steps, the solution obtained from the previous process was added to a reservoir containing 30 L of distilled water. The reservoir was then thoroughly mixed. Additionally, the calculated amount of NaHCO3 was placed into a weighing boat, and it was subsequently added to a separate 5 L beaker. Similar to the previous step, the mixture was stirred using a magnetic stirring bar until complete dissolution occurred. The bicarbonate solution obtained from this process was then added to the reservoir, and the reservoir was once again mixed. Finally, a sample was collected from the reservoir.

2. Mathematical description and computational modeling

2.1. Breakthrough curve analysis

The sorbent chamber was modeled as a fixed-bed column in order to study the contact between adsorbate and adsorbent occurring in the adsorption system. In fixed bed adsorption, an adsorbent material is placed within a stationary bed or column, and a fluid containing the waste solute is then circulated through the bed, allowing for adsorption to occur (DiChiara et al., 2015). A breakthrough curve, which is a plot of the ratio of the effluent to influent solute concentration (C_t/C_0) as a function of time or effluent volume, specifies the performance of fixed-bed adsorption (Patel, 2019). It illustrates how the concentration of the solute changes as it passes through the sorbent bed or column. Initially, the solute concentration in the effluent is low as the sorbent has not yet reached its adsorption capacity. However, as time progresses, the concentration of the solute gradually increases until it reaches a breakthrough point, where the solute concentration in the effluent sharply rises, until an arbitrary point is reached when the column approaches saturation (El-Naas & Alhaija, 2013). Breakthrough curve characteristics such as the breakthrough time and the shape of the curve are extremely important for the design of the adsorption column (Xu et al., 2013). The breakthrough time is the duration of time required for the solute to reach the point of breakthrough on the breakthrough curve. The curve commonly exhibits an S-shape pattern, albeit with different degrees of steepness and the position of the breakthrough point (El-Naas & Alhaija, 2013).

In the present work, the breakthrough curves were plotted based on the results of the single-pass experiment, and subsequent analysis was conducted using the Thomas and Yoon-Nelson models. The Thomas model is a widely used model for describing the adsorption dynamics in fixed-bed adsorption systems (Patel, 2019). According to Patel (2019), the underlying assumption is that the adsorption process adheres to the Langmuir kinetics of adsorption-desorption, and that the driving force for the process complies with second-order reversible reaction kinetics. The Langmuir isotherm assumes that the adsorbent surface has a fixed number of sites available for adsorption, and that the processes of adsorption and desorption occur independently and reversibly, meaning that molecules can both attach to and detach from the surface (Foo & Hameed, 2010; Latour, 2015). The linearized form of the Thomas model is given below:

$$ln\left(\frac{C_0}{C_t}-1\right)=\frac{k_{Th}q_e x}{Q}-k_{Th}C_0 t \tag{1}$$

where k_{Th} is the Thomas rate constant (mL/min mg), q_e is the adsorption capacity (mg/g), x is the mass of the adsorbent (g), Q is the volumetric flow rate (mL/min), and t is the effluent time (min). By plotting $\ln\left(\frac{C_0}{C_t}-1\right)$ versus t for a given flow rate using linear regression analysis, the value of k_{Th} and q_e can be determined. The Yoon-Nelson model proposes that the probability of adsorption for each of the adsorbate molecules decreases at a rate proportional to both the probability of adsorbate adsorption and the probability of adsorbate breakthrough on the adsorbent (Patel, 2019). The Yoon-Nelson model is expressed in a linear form as:

$$ln\left(\frac{C_t}{C_0-C_t}\right)=k_{YN}t-\tau k_{YN} \tag{2}$$

where k_{YN} is the rate constant (min-1), and τ is the time required for 50% solute breakthrough. Similar to the Thomas model, the parameters of the Yoon-Nelson model were determined using linear regression analysis. A determination of coefficient (R^2) values was calculated for both models in order to determine the goodness of fit.

2.2. Model description

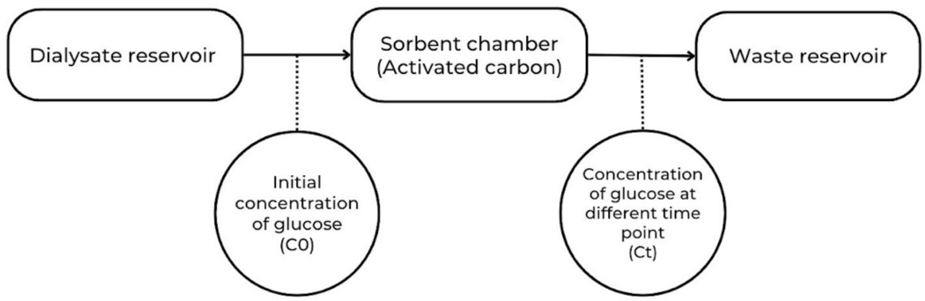

Figure 3. Schematic diagram of the computational model.

The computational model used in this study was specifically designed to simulate the breakthrough curve and analyze the adsorption behavior of glucose. Hence, it is important to note that the analysis focused solely on the adsorption of glucose, excluding the consideration of other substances present in the adsorption of sorbents. Relevant conditions and variables were carefully considered in the design of the computational model to ensure accuracy and specificity. It is important to note that the model only incorporated the mass of the activated carbon that was used in the single-pass experiments since glucose was absorbed by this adsorbent material, as recorded in the experimental results of the SAPD system, which was studied by van Gelder et al. (2020). The best-fit model, determined through analysis and comparison with the experimental results, was employed as the foundation to develop the simulation. The schematic diagram for the model is demonstrated in Figure 3. It simulates the glucose removal process, beginning with the downstream dialysate reservoir, passing through the downstream sorbent, and reaching the waste reservoir. Glucose concentrations in the downstream sorbent and waste reservoirs, as well as the overall mass of glucose adsorbed were predicted and the results were compared to experimental data. The concentration of glucose in downstream sorbent was calculated (Equation 4), which is deduced from a nonlinear equation of Thomas model (Equation 3).

$$\frac{C_t}{C_0} = \frac{1}{1 + exp\left(k_{Th}q_e x/Q - k_{Th}C_0 t\right)} \tag{3}$$

$$C_{ds} = C_{ddr}\left(\frac{1}{1 + exp\left(k_{Th}q_e x/Q - k_{Th}C_0 t\right)}\right) \tag{4}$$

In this equation, c_{ddr} represents the initial concentration of glucose in the downstream dialysate reservoir, while c_{ds} is the annotation for glucose concentration in the downstream sorbent. Additionally, the concentration of solute in the waste reservoir is updated at each time step t based on the following equation:

$$C_{w,t} = \frac{1 \times Q \times c_{ds} + V_{waste} \times c_{w,t-1}}{Q + V_{waste}} \tag{5}$$

In this equation, $c_{w,\,t}$ represents the concentration of waste solute at time t, 1 is the timestep, V_{waste} is the volume of waste accumulated up to time t which increases as more fluid flows through the system, and $c_{w,t-1}$ is the concentration of solute at the previous time step. The calculation of solute concentration in the waste reservoir adheres to the principle of mass conservation (Tamir, 2013). This principle ensures that the rate of change in solute concentration within the system should be equal to the net rate of solute influx and efflux. In this case, the influx is determined by the incoming current, while the efflux is driven by the accumulation of waste volume. The equation ensures that the concentration in the waste reservoir is adjusted to maintain mass balance.

2.3. Optimization

Using the developed simulation above, each parameter was individually examined to understand its influence on the total amount of solute removal. The parameters of interest are flow rate, mass of the sorbent and an extra parameter of Thomas model which is the adsorption capacity. The model randomly generated values for each of the parameters within a defined range while keeping other values constant throughout the simulation, and it calculated the corresponding amounts of glucose adsorbed. To ensure a comprehensive analysis, the code was executed 10 times, generating different values of the parameters with each iteration. The resulting data was then plotted, with the values of the parameters arranged in ascending order, allowing for a clear visualization of the relationship between each parameter and the total amount of solute removal. The optimal combination of these parameters that maximizes the quantity of solute adsorbed was then determined by incorporating all the parameters into a single simulation.

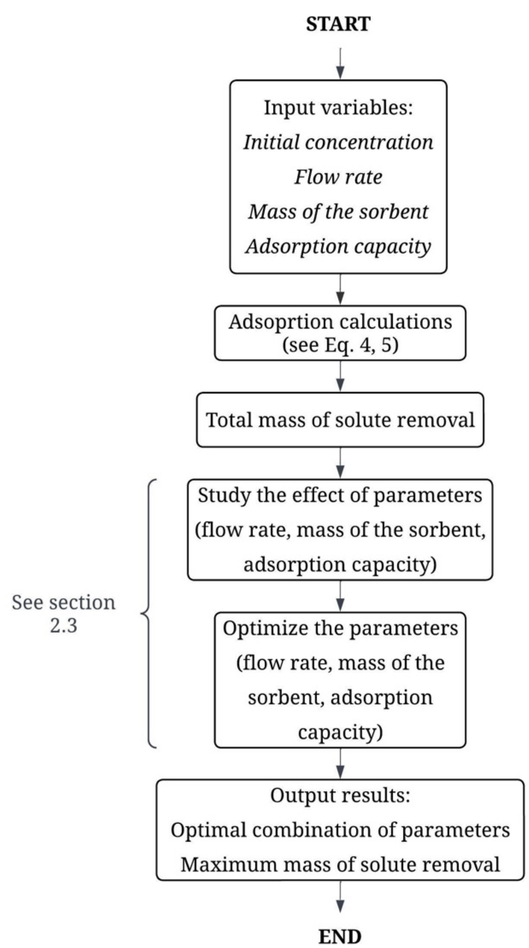

Figure 4. Flow chart of the computational model.

2.4. Software used

In this study, Python, a versatile programming language, was utilized to develop and simulate the computational model. Several key packages were employed to facilitate various aspects of the modeling process. For plotting and visualizing data, the matplotlib.pyplot package was utilized, enabling the generation of clear and informative graphs. To perform linear regression analysis, the sklearn.linear_model package was used, providing the determination of the best-fit line to the experimental data. Curve fitting was conducted using the scipy.optimize.curve_fit package, which allowed for the estimation of model parameters by fitting the model to the experimental data. Optimization tasks were accomplished using the scipy.optimize and scipy.interpolate packages, which are robust tools for optimizing the model parameters and interpolating data points, respectively. Furthermore, the method employed in the scipy.optimize package was the Sequential Least Squares Programming (SLSQP) method. The SLSQP method is an optimization algorithm commonly used to solve constrained nonlinear optimization problems that aims to minimize a given objective function subject to a set of constraints (Kraft, 1988). The SLSQP method combines the concepts of sequential quadratic programming (SQP) and least squares minimization and iteratively updates the decision variables to find the optimal solution by minimizing the objective function while satisfying the constraints. (Fu et al., 2019).

III. RESULTS

1. Breakthrough curve analysis

Breakthrough curves plotted from the results of the single-pass experiment are shown in Figure 5. The model focused on analyzing the data on glucose removal by the sorbent chamber. It is illustrated that the breakthrough curves plotted from both the Thomas and Yoon-Nelson models are identical, with the same R^2 value of 0.704945. The parameters of each model were calculated and shown in Table 1.

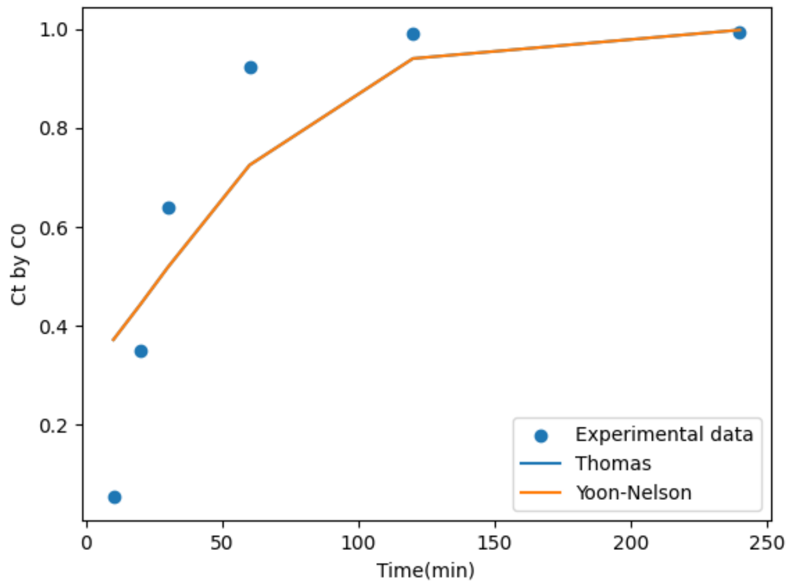

Figure 5. Breakthrough curve for glucose with the Thomas and Yoon-Nelson model.

C_o (mg/mL)	Q (mL/min)	Thomas		Yoon-Nelson	
		k_{Th} (mL/min mg)	q_e (mg/g)	k_{YN} (min^{-1})	(min)
19.26	60	0.00155042	159.049	0.0298611	27.5266

Table 1. Parameters of Thomas and Yoon-Nelson.

The Thomas model was selected to generate the simulation process. Solute concentrations in the downstream sorbent and waste reservoir were calculated, and the results were plotted with the experimental data for comparison purposes, as shown in Figure 6. The total amount of glucose throughout the 240-minute duration of the experiment is illustrated in Figure 7. The cumulative sum of the total amount of glucose removed in 240 minutes was approximately 45.442 g.

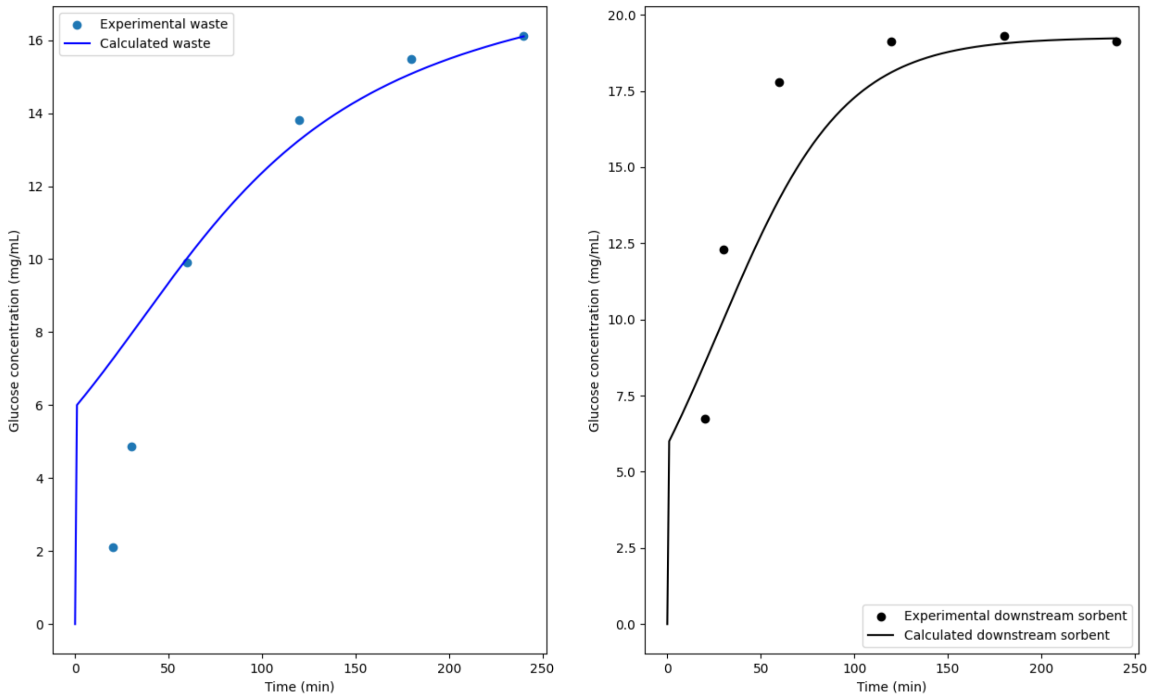

Figure 6. Glucose concentration in the waste reservoir and downstream sorbent in experimental and calculated data.

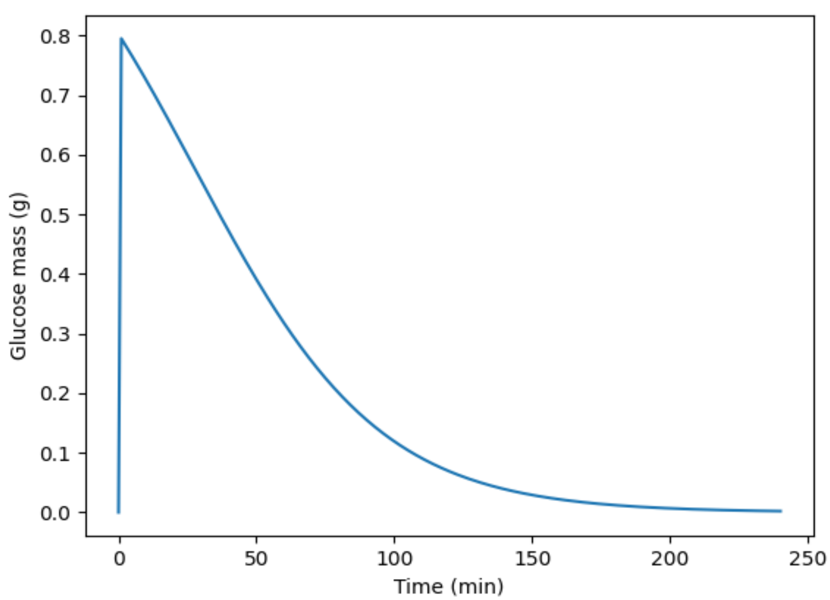

Figure 7. Total mass of glucose adsorbed.

2. Effect of each parameter on the total amount of solute adsorbed

In the Thomas column adsorption model, the kinetic coefficient (k_{Th}) is typically assumed to be constant for a system under specific operating conditions. Hence, each flow rate corresponds to a distinct value of the k_{Th}, which requires the establishment of a function that represents this relationship. This function could be used for the calculation of k_{Th} when the flow rate is known. Subsequently, the effluent concentration of the sorbent could be estimated based on influent concentration, flow rate, and Thomas kinetic coefficient. Hence, a comprehensive understanding of the relationship between flow rate and the Thomas kinetic coefficient facilitates the prediction of effluent concentration in fixed-bed adsorption systems. In the attempt to find the best fit function, multiple equations were evaluated and systematically applied to fit the experimental data, and their goodness of fit was assessed based on the determination of the coefficient. Through this rigorous analysis, it was determined that one particular equation exhibited the highest R^2. The quadratic equation, as displayed in Equation 6, represents a second-degree polynomial equation, which allows for a nonlinear relationship between the variables. It provides flexibility in capturing complex behaviors and variations in the kinetic coefficient kTh as a function of the flow rate Q. As a result, it was selected as the optimal equation to represent the relationship between the Thomas kinetic coefficient and the flow rate in the subsequent analysis and modeling.

$$k_{Th} = aQ^2 + bQ + c \tag{6}$$

By utilizing the relationship between Thomas kinetic coefficient and the flow rate, the impact of the flow rate on the total amount of glucose removal was examined. The simulation was run multiple times to determine the general trend, and one of the results is illustrated in Figure 8. Flow rates within the range of 50 to 250 ml/min were randomly assigned as part of the experimental setup. Despite some noise appearing in the results, the finding reveals a general trend that an increase in flow rate corresponds to a decrease in the total amount of solute adsorbed, indicating that higher flow rates promote a lower efficiency of solute clearance. However, upon testing the simulation using the flow rate value which was set in the single-pass experiment, specifically 60 mL/min, a discrepancy emerged between the predicted total mass of glucose adsorbed and the corresponding experimental result (45.442 g).

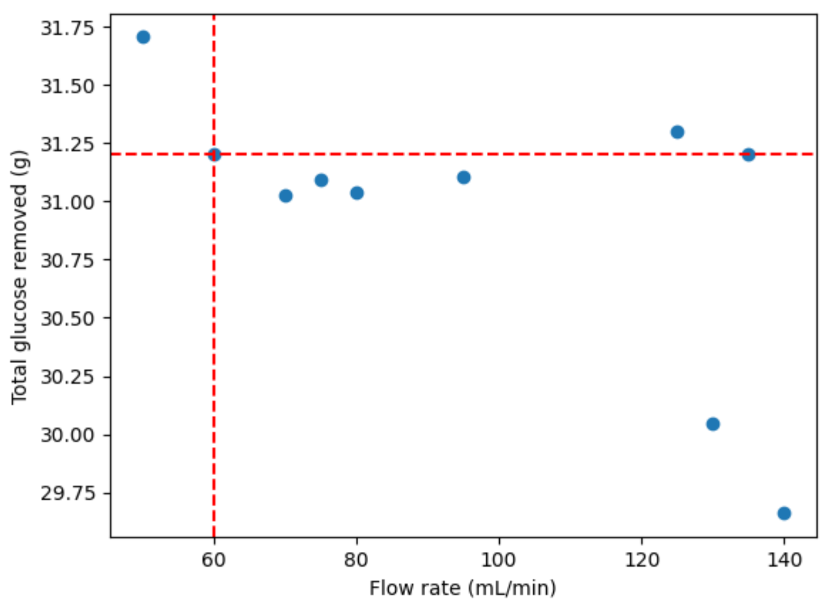

Figure 8. One of the results from studying the effect of flow rate. The intersection of the red dashed lines represents the experimental baseline with a flow rate of 60 mL/min.

Regarding the effect of sorbent weight on the total amount of glucose removal, one result from multiple runs of the simulation is depicted in Figure 9. The mass of the sorbent was randomly varied within the range of 100 to 500 g. An increase in sorbent mass was observed to enhance the total amount of solute adsorbed, indicating that a greater sorbent mass facilitates improved solute clearance. In addition to exploring the effects of flow rate and sorbent weight, the impact of

Thomas adsorption capacity (q_e) was also investigated, as shown in Figure 10, with values that were randomly generated from the defined range of 80 to 320 mg/g. This parameter was later combined with the aforementioned device parameters to optimize the sorbent system's performance. Moreover, extra simulations were performed on solely varying the adsorption capacity to explore its effect on solute concentration in the waste reservoir and downstream sorbent. The result is presented in Figure 11, wherein the adsorption capacity was set to 300 mg/g. When compared with the experimental Thomas adsorption capacity, it is observed that a high adsorption capacity results in a reduction of concentration in the downstream sorbent and a lower accumulation of solute in the waste reservoir, and there is an extended time for the waste reservoir to reach its capacity.

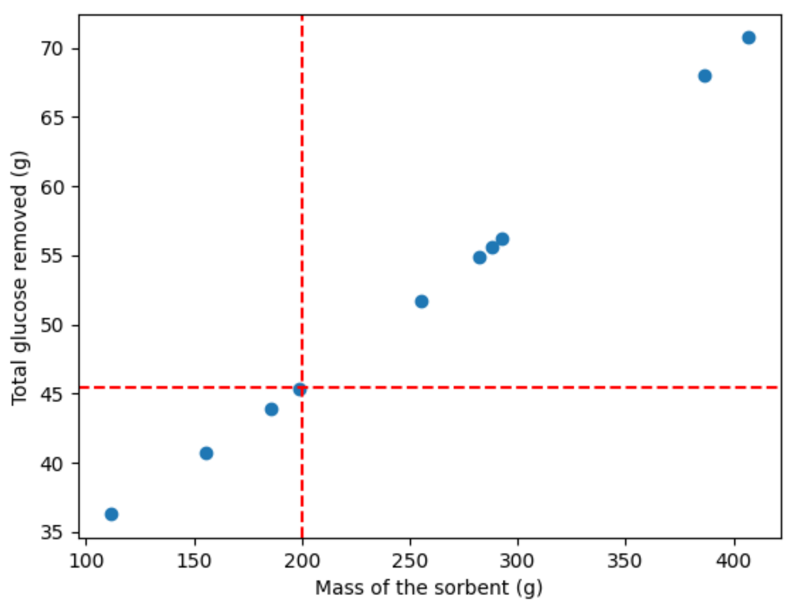

Figure 9. One of the results from studying the effect of the mass of the sorbent. The intersection of the red dashed lines represents the experimental baseline with the mass of 200 g.

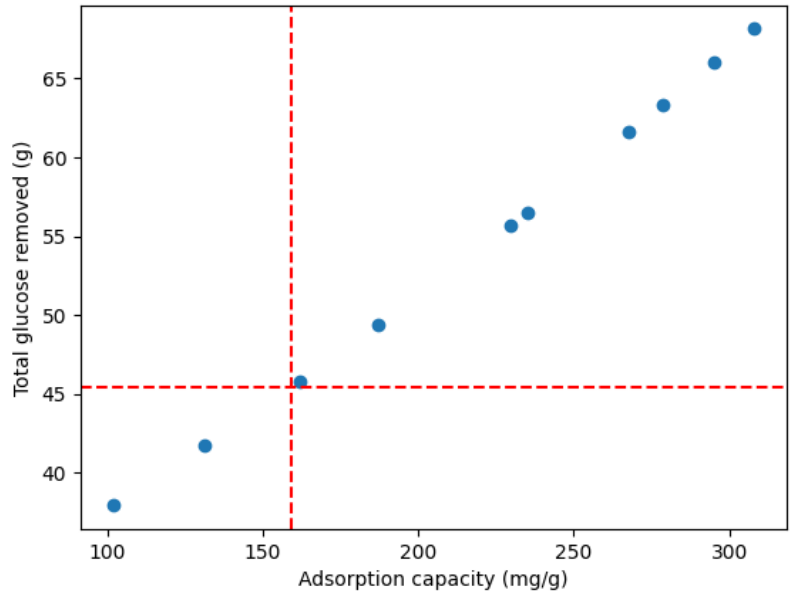

Figure 10. One of the results from studying the effect of Thomas adsorption capacity. The intersection of the red dashed lines represents the experimental baseline with an adsorption capacity of 159.049 mg/g.

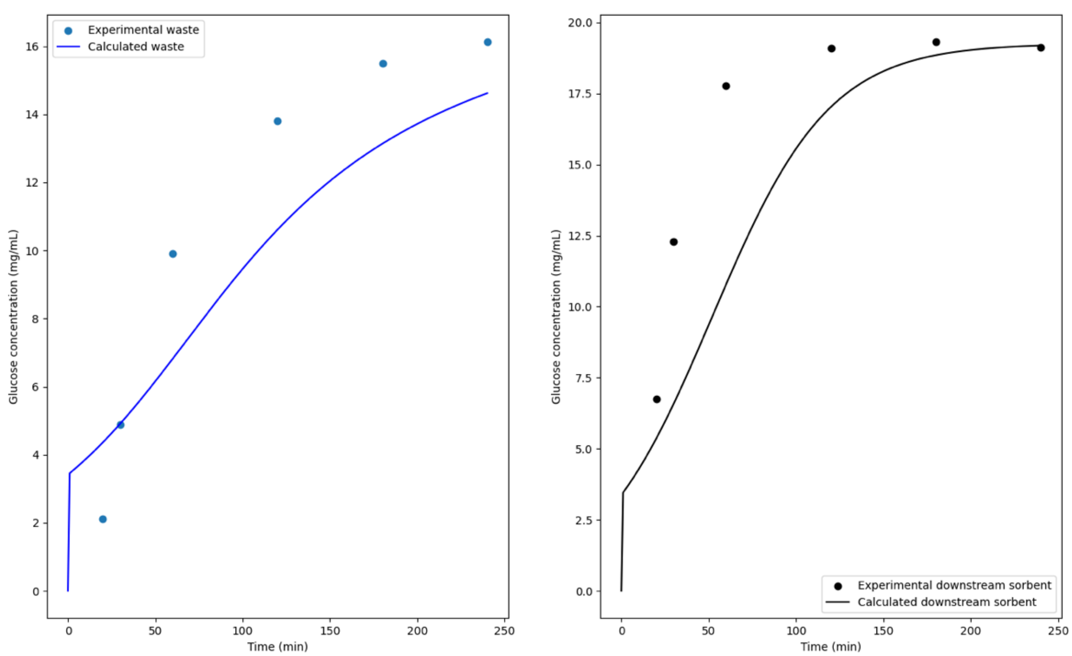

Figure 11. Glucose concentration in the waste reservoir and downstream sorbent in experimental and calculated data, with an adsorption capacity of 300 mg/g.

3. Simulation combining all parameters

The simulation conducted with the aim of identifying the optimal combination of three influential parameters, namely flow rate, adsorption capacity, and the Thomas kinetic coefficient, fulfilled its objective of achieving enhanced performance in solute removal. By systematically varying these parameters within predetermined ranges, the simulation effectively converged towards the combination that yielded the highest performance. The findings demonstrate a significant improvement in the cumulative amount of glucose adsorbed compared to experimental data. The optimized simulation consistently achieved a total glucose removal of approximately 160 g, irrespective of multiple simulation runs. Regarding the sorbent weight and adsorption capacity, it is noteworthy that in multiple simulation runs within the specified range (e.g., 100 to 500 for the mass of the sorbent, and 80 to 320 for the adsorption capacity), the optimal value consistently reaches the upper limit (e.g., 500 and 320, respectively). This observation implies that the optimization process prioritizes maximizing the sorbent weight and adsorption capacity to enhance solute removal efficiency. However, specific values for flow rate varied in each simulation run, highlighting the challenge of determining an ideal value for this parameter within the studied range.

IV. DISCUSSION

The present study aims at investigating how to improve the efficiency of solute clearance in sorbent-assisted peritoneal dialysis by varying different device parameters through computational modeling of the sorbent chamber. The findings of the study demonstrate that by modifying different device parameters through computational modeling of the sorbent chamber, significant enhancements in solute clearance efficiency in sorbent-assisted peritoneal dialysis were achieved.

Regarding the breakthrough curve analysis, the value of R^2 indicates that the models can be considered to have a reasonably good fit and capture a substantial portion of the variability in the data. Additionally, both the Thomas and Yoon-Nelson models have the same R^2 values, and there are two possible explanations for this. On the one hand, it may specify that both models provide an equally good fit to the data, which implies that they are able to explain the same amount of variation in the experimental results. Working with each model separately would help to investigate whether the models produce similar predictions or if there are any differences in their estimates of solute clearance and relevant parameters. On the other hand, both the Thomas and Yoon-Nelson models having the same R^2 value could be due to the limited amount of experimental data available for analysis, which was the case for this project. When the dataset is small, it may limit the ability of the models to capture the full variability of the data and differentiate between their performances. Consequently, it is challenging to draw a definitive conclusion about which model provides a better fit. The small sample size might not provide enough information to fully evaluate the models' performance and accurately distinguish between them. Due to the constraints of time and resources, it was not feasible to implement and analyze both the Thomas model and the Yoon-Nelson model within the scope of this research study. Consequently, a decision was made to prioritize the utilization of the Thomas model as the primary focus of investigation while deferring the implementation of the Yoon-Nelson model to future research endeavors.

As evidenced by the results of simulation for each parameter, the total amount of glucose adsorbed decreases when the flow rate increases, while the increase in the mass of the sorbent and the adsorption capacity have a positive effect on the removal efficiency. Higher flow rates lead to decreased contact time between the solute and the sorbent material, limiting the opportunity for solute molecules to interact with and adsorb onto the sorbent surface. Hence, the rapid transport of solute molecules through the sorbent chamber at higher flow rates restricts their effective adsorption. The consistent pattern concerning the influence of flow rate on the total amount of solute adsorbed has been widely documented in numerous studies of fixed-bed adsorption systems (Babu & Gupta, 2005; Biswas & Mishra, 2015; Marzbali & Esmaieli, 2017; Saad et al., 2015; Sylvia et al., 2018). Despite the utility of the function that describes the relationship between the Thomas kinetic coefficient and flow rate in predicting the overall impact of flow rate on the removal efficacy, the observed discrepancy between the experimental and calculated mass of glucose removal obtained from simulations incorporating this function highlights a significant problem in accurately characterizing this relationship. In addition, there were some unexpected results, as shown in Figure 8, as the total amount of mass removal did not always decrease when the flow rate increased. Consequently, the function used is considered inadequate, and it is necessary to explore alternative functions that better capture the true relationship between these variables.

Meanwhile, as the mass of the sorbent material increases, there is a larger surface area available for solute molecules to interact with and be adsorbed onto. With a greater sorbent mass, more adsorption sites are present, allowing for a higher capacity to adsorb solute molecules. This leads to an increased likelihood of solute molecules coming into contact with the sorbent surface and being captured through adsorption. The same impact of the adsorbent dosage on the removal efficacy was recorded in other adsorbent materials that adsorbed different solutes (Djelloul et al., 2017; Han et al., 2007; Hor et al., 2016; Mosoarca et al., 2020; Shakoor & Nasar, 2016). The last parameter, which is adsorption capacity, refers to the maximum amount of solute that can be adsorbed by a given amount of sorbent material under specific conditions (Mokhatab et al., 2019). When the adsorption capacity is increased, the sorbent material has a higher capability to bind and retain solute molecules on its surface. This allows for a greater number of solute molecules to be captured and removed from the dialysate during the adsorption process. The additional simulation with the modified adsorption capacity confirms that with a great adsorption capacity, more solute molecules can be effectively captured and retained by the sorbent, reducing their accumulation in the waste reservoir. The increased adsorption efficiency of the sorbent with a higher adsorption capacity allows for a more effective removal of solute from the system, leading to a slower buildup of solute in the waste reservoir. Consequently, the waste reservoir takes a longer time to reach its capacity due to the enhanced adsorption capabilities of the sorbent. Moreover, a high adsorption capacity results in a low solute concentration in the downstream sorbent, indicating effective adsorption and removal of the solute by the sorbent. Conversely, when the adsorption capacity is low, the solute concentration in the downstream sorbent is higher, indicating that a smaller fraction of the solute is being effectively adsorbed and removed by the sorbent. A notable advantage of a high adsorption capacity lies in its potential to extend the operational lifespan of the device encompassing the waste reservoir and sorbent. As discussed, a higher adsorption capacity enables efficient removal of solute from the dialysate, leading to reduced accumulation of solute in the waste reservoir. Consequently, the extended time required for the waste reservoir to reach its capacity allows for prolonged usage of the device before it needs to be emptied or replaced. This advantage of a high adsorption capacity contributes to the overall durability and longevity of the device, facilitating longer-term applications of sorbent-assisted peritoneal dialysis without the need for frequent device maintenance or replacement.

The optimized simulation with the combination of the device's parameters, including flow rate and the mass of the sorbent, as well as the Thomas adsorption capacity, showed results of an increase in the amount of total glucose removal when compared to the experimental data. However, the model failed to determine an ideal value for flow rate, while the optimal values for mass of the sorbent and adsorption capacity were constantly determined as the maximum value in the predetermined range. Moreover, despite the variation of the optimal value for flow rate in multiple iterations, the simulation shows a consistent value for the maximum mass of glucose removal, which is contrary to the fact that flow rate has an effect on the total amount of solute adsorbed. As mentioned above, the function for Thomas kinetic coefficient and flow rate did not correctly reflect the relationship between these two parameters. As a result, the function did not calculate precise values for the Thomas kinetic coefficient when providing the input flow rate. As the simulation model relies on parameter values that are obtained through estimation, if the calibration process is not accurate or if the estimated parameter values do not accurately reflect the real system, it can lead to discrepancies between the simulated and experimental data. Inaccurate parameter values could impact the flow rate optimization and the overall accuracy of the simulation. Furthermore, the model's performance heavily relies on the quality and availability of the data used for calibration and validation. In this project, the experimental dataset was limited in size, therefore, it may not fully capture the system's behavior, making it challenging for the simulation model to accurately reproduce the experimental results. Hence, the model requires further calibration and modification to resolve the issue and improve the simulation process in order to obtain accurate results.

Additionally, the computational model demonstrated that the maximum amount of glucose removal was achieved when utilizing the maximum sorbent weight, as indicated by the optimal value consistently appearing as the maximum number in the experimental setup range. However, it is essential to minimize the mass of the sorbent due to the practical constraints imposed by the SAPD device's weight or the size limitations of the dialyzer. While the model's results highlight the potential benefits of employing a larger sorbent mass for enhanced glucose removal, the implementation of such a design must consider the practical implications associated with the device's weight and dialyzer dimensions. This necessitates a comprehensive optimization approach that accounts for both the desired glucose removal efficiency and the restrictions imposed by the weight of the device and the size of the dialyzer. Hence, the ultimate objective is to strike an optimal balance between efficient glucose removal and the practical feasibility of the device. Furthermore, as mentioned previously, several column adsorption studies have shown that the increase of adsorbent dosage decreases the adsorption capacity (Djelloul et al., 2017; Mosoarca et al., 2020; Mu'azu et al., 2020. Djelloul et al. (2017) explained the decrease in adsorption capacity is due to the adsorbent sites become unsaturated during the adsorption process. Therefore, it is crucial to uphold a harmonious equilibrium between these parameters in order to ensure optimal results. This equilibrium can be achieved by delineating and analyzing the relationship between the adsorption capacity of the device and the mass of the adsorbent utilized. Such an analysis allows for the determination of the ideal adsorption capacity required to achieve the desired level of glucose removal while considering the practical constraints posed by the weight and size of the device. Moreover, delving into the relationship between adsorption capacity and adsorbent mass not only facilitates the evaluation and enhancement of the device's performance but also paves the way for further research and development. It offers valuable insights into potential strategies to improve the adsorbent materials or optimize the dialyzer design, thereby maximizing the device's glucose removal efficiency. Additionally, comprehending this relationship is pivotal in assessing the feasibility of scaling up the device for commercial production or adapting it to diverse clinical settings.

In addition, there is a potential interplay between flow rate, mass of the sorbent and adsorption capacity, which may have a crucial role in the optimization of glucose removal in the context of dialysis systems. The adsorption capacity of the sorbent material determines its ability to capture and remove glucose from the dialysate. Increasing the mass of the sorbent generally enhances the rate glucose removal, however, it decreases the adsorption capacity. Moreover, this needs to be balanced with the flow rate of the dialysate, since a higher sorbent mass can impact the flow dynamics within the system. Higher flow rates may be desirable to achieve efficient removal of glucose, but they can also limit the contact time between the dialysate and the sorbent, reducing the overall adsorption efficiency. Thus, there exists a delicate trade-off between sorbent mass, flow rate, and adsorption capacity, where increasing the sorbent mass may enhance removal efficacy but may also necessitate adjustments in the flow rate to maintain sufficient contact time for optimal glucose removal. Achieving an optimal balance between these factors is critical to designing efficient dialysis systems that maximize glucose removal while considering practical limitations such as the weight of the device and the size of the dialyzer.

While glucose plays an essential role in balancing the osmotic environment in the body, it is necessary to achieve maximum removal of glucose from the dialysate during peritoneal dialysis for several reasons (Hantzidiamantis & Lappin., 2022; Triplitt, 2012). Firstly, excessive glucose in the dialysate can lead to increased glucose absorption into the bloodstream during the dialysis process. This can result in an increase in blood glucose levels, which is particularly concerning for individuals with diabetes or impaired glucose tolerance (Kim et al., 2013). By maximizing the removal of glucose from the dialysate, the potential risk of hyperglycemia or glucose-related complications can be minimized. Secondly, maintaining a proper osmotic balance is crucial for peritoneal dialysis efficiency. Glucose is commonly used as an osmotic agent in dialysate to facilitate the removal of waste products and excess fluid from the body (Holmes & Mujais, 2006; Kim et al., 2013). However, if glucose is not adequately cleared from the dialysate, it can contribute to an imbalance in the osmotic gradient, impairing the effectiveness of fluid and waste removal (Sbrignadello et al., 2016). By maximizing the removal of glucose, the osmotic equilibrium can be maintained, ensuring optimal fluid and solute removal during peritoneal dialysis. Furthermore, prolonged exposure to high glucose levels in the dialysate can have detrimental effects on the peritoneal membrane. Hyperglycemia in the peritoneal cavity can lead to structural and functional changes in the membrane, compromising its integrity and potentially affecting the long-term success of peritoneal dialysis treatment (Kim et al., 2013). By achieving maximum removal of glucose, the potential for harmful effects on the peritoneal membrane can be reduced, promoting better long-term outcomes for patients.

In general, the study has several limitations. As already mentioned, analysis of experimental breakthrough curves illustrates the equal fit of both the Thomas and Yoon-Nelson models. If it is impossible to conduct more experiments in order to obtain data for validating the models, there is another method for future studies to address this limitation. It is important to consider the reliability and robustness of the models by conducting further analyses, such as cross-validation or sensitivity analysis. These additional procedures can help assess the stability and generalizability of the models' performance and provide a more comprehensive evaluation of their goodness of fit. Nevertheless, a large dataset would be more beneficial to obtain a more rigorous comparison between the models. Increasing the sample size can provide a more accurate estimation of model parameters and improve the assessment of their goodness of fit, helping to determine if there are any meaningful differences between the Thomas and Yoon-Nelson models in terms of their ability to explain the observed data. Other limitations are the insufficient function for indicating the relationship between the kinetic coefficient and flow rate and the significant impact that this inaccurate estimation has on the final optimization. As discussed, a large dataset would help to improve the estimation of parameters since it provides a broader range of observations and can potentially uncover patterns, trends, or correlations that might not be evident in smaller datasets. This increased sample size allows for more robust statistical analyses and enhances the generalizability of the findings. Despite the limitations discussed, the optimized simulation results demonstrate an increase in total glucose removal in a sorbent system, which hold significant implications for improving the efficiency of glucose removal in this context. Enhanced glucose removal has the potential to positively impact the outcomes of peritoneal dialysis treatments by facilitating the effective clearance of glucose from the peritoneal cavity, which can contribute to improved patient outcomes. Moreover, the implications of the research findings have the potential to extend beyond the specific context of the SAPD system and can be applied to other artificial kidney devices. The findings contribute to the knowledge on adsorption processes of peritoneal dialysis and offer valuable insights for the development of a more efficient system for solute clearance. By studying how to optimize glucose removal in sorbent cartridges of peritoneal dialysis devices, this research contributes to the advancement of the field and the development of innovative solutions that improve the overall efficiency and efficacy of peritoneal dialysis treatments.

In conclusion, the current study developed a computational model to investigate strategies for enhancing the efficacy of the solute clearance of the sorbent chamber in the peritoneal dialysis system. The model incorporated flow rate, mass of the sorbent, and adsorption capacity as key parameters of interest. The analysis utilized the Thomas model, which enabled the examination of experimental breakthrough curves and subsequent optimization of the system. Initially, each parameter's individual impact on the total mass of solute removal was examined in isolation, providing insights into their respective contributions. Subsequently, a combined analysis was performed to identify the optimal combination of parameters that would yield the maximum amount of solute removal. However, the final simulation aimed at determining this optimal combination encountered challenges in determining the value of the optimal flow rate and other parameters. Despite this setback, the study contributes valuable insights into the design and optimization of peritoneal dialysis systems, shedding light on the complex interplay of flow rate, sorbent mass, and adsorption capacity on solute clearance efficacy. These findings have implications for improving the performance and efficiency of peritoneal dialysis treatments and may guide future research in the development of innovative approaches to enhance solute clearance in these systems.

CRITICAL REFLECTION

Throughout the course of conducting the bachelor thesis research, a range of personal experiences and valuable lessons have been gained. Firstly, the significance of a strong working ethic became evident as the project progressed. Maintaining a thorough and concentrated approach to research tasks proved critical in finishing experiments, data analysis, and the writing process on time. The commitment to consistently meeting deadlines and managing time effectively is important to enhance productivity and foster a deeper sense of personal responsibility towards the project. As I progressed through the various stages of my thesis, I acknowledged that adhering to deadlines was crucial for maintaining a smooth workflow. Meeting the assigned deadlines allowed staying on track and prevented any unnecessary delays. It ensures that there is sufficient time to conduct thorough research, analyze the data, and present research findings in a coherent manner. Secondly, effective planning emerged as a crucial factor in navigating the complexities of the research journey. Developing a comprehensive research plan enabled the setting of clear objectives and prioritizing tasks efficiently. However, it is important to acknowledge that unforeseen challenges and obstacles were encountered along the way, highlighting the necessity for adaptability and flexibility within the planning process.

While I aimed to meet all the assigned deadlines, I encountered a minor deviation during one phase of the project. There were constraints of time and limited allocation for the final simulation of optimization, hence, it became apparent that the computational model necessitates further improvement to enhance its performance and achieve the desired outcomes. However, this experience served as a valuable lesson for me. It highlighted the need for better planning and allocating sufficient time to each task in order to avoid such delays in the future. It is important to take immediate action to address the situation and restructure my timeline accordingly. I dedicated extra effort and time to catch up, ensuring the issue did not have a significant impact on the overall completion of my thesis. This experience has taught me the importance of being flexible and adaptable when faced with unexpected challenges or delays. It has reinforced the notion that even with meticulous planning, unforeseen circumstances can arise, and it is crucial to handle them effectively. By acknowledging and learning from this, I have developed a greater understanding of the potential obstacles that can arise in any project and the need to proactively manage them.

Another crucial skill that I have learned during the course of my bachelor thesis research is effective communication. Throughout the research process, engaging in regular communication with the research supervisors proved to be instrumental in shaping the trajectory of the study and ultimately influencing its outcomes. Moreover, the regular communication with the supervisors allowed me to seek their feedback and input on the progress of my research. In addition to the academic benefits, engaging in effective communication with my supervisors fostered a collaborative learning environment. It established a relationship based on trust and mutual respect, where I felt comfortable sharing my ideas, concerns, and progress. Furthermore, effective communication with my supervisors also honed my ability to articulate my research findings and ideas clearly. Through discussions and presentations, I learned to convey complex concepts in a concise and coherent manner, which is an essential skill in academic and professional contexts.

Finally, I had the opportunity to develop and refine my presentation skills, which proved to be a valuable asset. The experience of presenting my research findings to academic audiences allowed me to cultivate this skill and enhance my ability to effectively communicate complex information in a clear and concise manner. One notable area of improvement in my presentation skills was the development of a structured and coherent delivery. Furthermore, the experience of presenting my research findings provided me with a platform to receive feedback and engage in constructive discussions. This not only helped me refine my research but also improved my ability to handle questions and criticisms with professionalism and confidence. Through this process, I learned to actively listen to questions, provide thoughtful responses, and effectively address any concerns or uncertainties raised by the audience. This skill was particularly valuable in fostering a collaborative learning environment, as it allowed me to engage in meaningful discussions with my peers and supervisors, ultimately leading to a deeper understanding of my research topic.

In conclusion, the journey of conducting my bachelor thesis research has provided me with invaluable personal experiences and valuable lessons that have shaped my academic and professional growth. The significance of a strong work ethic, effective planning, and adaptability in managing deadlines and overcoming challenges became evident throughout the research process. Furthermore, effective communication, both with research supervisors and through presentations, has played a vital role in shaping the trajectory of my study and enhancing my ability to convey complex ideas and findings. The experience of presenting my research findings has not only improved my presentation skills but also allowed me to receive feedback and engage in constructive discussions, fostering a collaborative learning environment. Overall, this journey has equipped me with essential skills and qualities that will undoubtedly serve me well in my future academic and professional pursuits.

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