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SCHREYER HONORS COLLEGE

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pH PROFILES IN CONTINUOUS COUNTERCURRENT HOLLOW FIBER DIALYSIS

BENNETT P THOMA
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Reviewed and approved* by the following:

Andrew Zydney
Bayard D. Kunkle Chair
Thesis Supervisor

Darrell Velegol
Distinguished Professor of Chemical Engineering
Honors Advisor

* Electronic approvals are on file.

ABSTRACT

Pharmaceutical companies are very interested in transitioning their historically batch operations for the production of high-value biological products to continuous processes. Continuous processes can decrease production time, reduce facility sizes, and improve product quality. One critical step for successful continuous biomanufacturing is product formulation to place the product in the desired buffer for storage and delivery. Several recent studies have demonstrated that it can be difficult to control the final pH during batch diafiltration due to Donnan effects and the need to maintain electroneutrality with charged products. The objective of this thesis was to investigate the effectiveness of a continuous dialysis process, as an alternative to batch diafiltration, with a specific focus on evaluating the pH behavior as a function of operating conditions.

Experiments were performed using a Polyflux® 17R countercurrent hollow fiber dialyzer, with serum IgG as a model product and histidine as the desired formulation buffer. The countercurrent dialysis was able to achieve high degrees of buffer exchange. The pH of the final product was a function of the dialysate flow rate, with the best performance obtained using a ratio of dialysate to feed flow rate of approximately 1:1. Under these conditions, very small changes in pH were seen over time, which is ideal for a continuous steady-state process. These results provide the first analysis of the pH shifts in countercurrent dialysis of antibody solutions and are the first step towards the development and application of continuous dialysis processes for antibody formulation.

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Chapter 1

Introduction to Monoclonal Antibodies and Buffer Exchange

1.1 Introduction to Monoclonal Antibodies

Antibodies, also known as immunoglobulins, are Y-shaped proteins made by the immune system, specifically in B lymphocytes, a type of white blood cell. The purpose of antibodies is to bind to antigens on the surface of bacteria, viruses, or cancer cells and prevent them from harming the body [1]. Antibodies are made naturally by the immune system in response to infections. It is now possible to produce antibodies commercially using recombinant DNA technology. These antibodies are typically referred to as monoclonal antibodies (mAbs) since they are all identical and bind to only one antigen epitope [2]. Polyclonal antibodies refer to the collection of antibodies produced within the body by multiple lymphocytes and are capable of binding to a wide range of antigens [3].

Figure 1 shows the structure of an antibody.

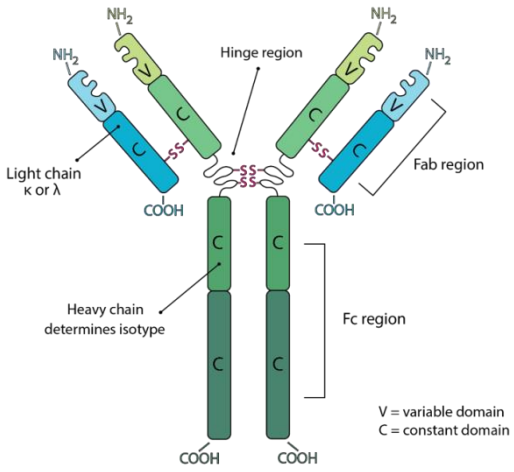

Figure 1. Structure of an Antibody [4]

There are two main regions in an antibody: the fragment antigen binding (Fab) region and the fragment crystallizable (Fc) region. The arms at the top of the antibody represent the Fab regions. Each antibody has a different amino acid sequence in this region, which leads to antibody specificity to the antigen's epitopes (the locations of antibody binding). The trunk of the Y represents the Fc region. It activates killer cells within the antibody, thereby initiating the process of phagocytosis, leading to destruction of the bacteria via ingestion [1]. Unlike the Fab region, the Fc region has a more consistent amino acid sequence among multiple antibodies.

1.2 Buffer Exchange

Monoclonal antibodies are currently produced in mammalian cells, most commonly Chinese Hamster Ovary (CHO) cells. The antibodies are purified using a series of chromatographic steps to remove host cell proteins, DNA, and other impurities. The

optimization of these chromatographic separations typically involves selection of buffers with the appropriate pH and ionic strength to achieve the desired binding of the product or impurity to the chromatographic resin. At the end of the process, the protein product must be placed in a buffer that is appropriate for long-term storage, a step referred to as formulation. The formulation step involves both product concentration and buffer exchange [5]. Buffer exchange simultaneously removes the production buffer from, and inserts the storage buffer into, the product solution.

The most widely used method for buffer exchange in commercial production is diafiltration (DF). Diafiltration involves a simultaneous dilution (buffer addition) and concentration. The latter is performed by tangential flow ultrafiltration in which filtrate is removed by pressure-driven filtration through a semi-permeable membrane that retains the product while allowing free passage of water and small buffer components [6]. The most widely used process configuration is constant volume batch DF, shown in **Figure 2**. In this configuration, the product solution is continuously recirculated through the tangential flow ultrafiltration module while fresh (DF) buffer is added at a rate equal to the filtrate removal rate.

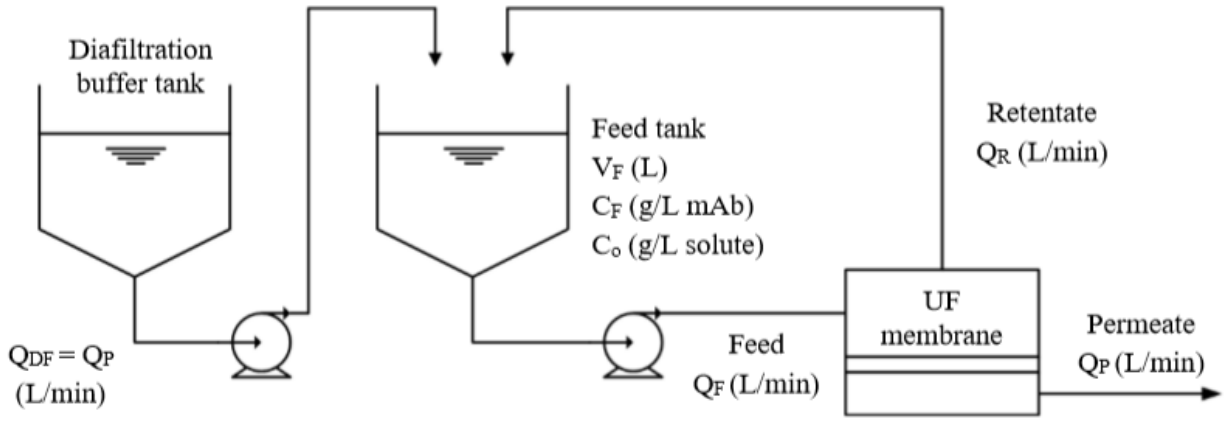

Figure 2. Schematic of batch diafiltration

Nearly all current bioprocesses are performed in batch mode with the membrane modules housed in a large stainless-steel skid. However, there is growing interest in the potential of using continuous bioprocessing for the production of monoclonal antibody products [7], as it could significantly reduce production time, reduce facility size, and improve product quality [8].

1.3 pH During Diafiltration of Monoclonal Antibodies

There is extensive experimental data showing that there can be significant discrepancies between the concentration of buffer components in the final formulated product and those in the diafiltration buffer even after an extended DF (which would be expected to have replaced all of the original buffer with the DF buffer). As a result, the final pH and ionic strength can be significantly different than the targeted pH. These discrepancies have typically been attributed to electrostatic interactions between ions and the charged protein. For example, Bolton et al. [8] found significant shifts in solution pH after DF of a mAb and Fc-fusion protein, with the magnitude of the pH shift depending on the protein charge due to “retention” of oppositely-charged ions by the protein during the diafiltration. A recent study presented a new mass balance model for predicting the pH profiles during DF, which provided an opportunity for pre-selecting the pH and concentration of the DF buffer to achieve the desired product formulation at the end of the DF process. This study will be examined further in Chapter 2.

Yehl et al. [9] recently proposed an alternative to diafiltration for protein formulation. Instead of using simultaneous dilution / filtration for buffer exchange, the formulation was accomplished using countercurrent dialysis in which transport across the semipermeable membrane is due to diffusion driven by the concentration gradient between the product solution

and the dialysate buffer. Data obtained with a hollow fiber membrane module showed that it was possible to achieve high degrees of buffer exchange using less buffer than traditional batch DF processes. In addition, this dialysis process was ideal for use as part of a continuous process, with very stable performance over multiple days of operation with no evidence of membrane fouling, likely due to the absence of any pressure driven filtration.

1.4 Experiment Objectives

The objective of the work described in this thesis was to examine the magnitude of any pH shifts during a continuous countercurrent dialysis process and to compare the behavior of this system to what has been previously observed in batch DF processes.

Chapter 2 provides a brief discussion of the theoretical background on Donnan Equilibrium, including the associated mathematical equations used to describe ion partitioning across a semipermeable membrane. Chapter 3 describes the materials (antibody, starting solution, dialysate buffer), the apparatus (including dialyzers and pumps), and procedures used for all experiments. Chapter 4 presents the experimental results from these studies along with an initial interpretation of the pH shifts observed during countercurrent dialysis for buffer exchange. Chapter 5 provides a summary of the key conclusions from this thesis and provides an overview of next steps for future experimentation.

Chapter 2

Introduction to Donnan Effects in Membrane Processes

2.1 Electroneutrality

Although counterintuitive in nature, the concentration of ionic buffer species (including H^+ ions and thus the product pH) after formulation can be different from the pH of the diafiltration buffer, even after an extensive DF process, "due to electrostatic interactions between the charged protein and the charged ions" [10]. These electrostatic interactions are driven by the need to maintain electroneutrality in the product solution, as shown in **Equation 1,**

$$\frac{z*C_{mAb}}{MW_{mAb}} + [His+] - [Cl-] + [H+] - [OH-] = 0 \quad \text{(Equation 1)}$$

where z is the charge of the monoclonal antibody, C_{mAb} is the antibody concentration (in g/L), and MW_{mAb} is the antibody molecular weight (in g/mol). Equation (1) has been written for a protein in a buffer containing only Histidine, its counterion (Cl-), and water (which has both H+ and OH- ions); the terms in brackets are the molar concentrations of these specific ionic species. The electroneutrality equation applies to both the permeate and retentate solutions; in other words, the sum of the charges on each side of the membrane approaches zero. Thus, the concentration of small ions will change depending on the charge of the monoclonal antibody until the sum of the charges in the product solution is zero. In the case of a positively-charged antibody (like most monoclonal antibodies as well as the IgG used in this thesis), the positively-charged His+ and H+ ions will be "pushed" into the permeate, while the negatively-charged ions [Cl- or OH-] are "held back" with the product on the retentate side of the membrane.

The final pH of the product solution is determined by the combination of the electroneutrality constraint with the acid-base equilibrium for the histidine buffer,

$$\boldsymbol{pK_{his} = pH + log\left(\frac{[His^0]}{[His^{+1}]}\right) = 6.0 - 0.5\frac{\sqrt{I}}{1+\sqrt{I}}} \quad \text{(Equation 2)}$$

where I is the ionic strength in mol/L. The final expression on the right hand side of Equation (2) arises from the ionic strength dependence of the equilibrium constant for buffer dissociation, which is a direct result of the non-ideal activity coefficient of the ions. The form of Equation (2) is consistent with the extended form of the Debye-Huckel theory for the activity coefficient [11]. As the solution progresses along the length of the dialyzer, the buffering capability changes since ions are exchanged between the original buffer in the retentate and the dialysate buffer, both of which can have different ionic strength.

2.2 Model Development in Previous Studies

Baek et al. [10] recently developed a model capable of predicting the pH and buffer concentrations throughout a batch diafiltration process by combining Equations (1) and (2) with simple mass balances, e.g.

$$V\frac{dC_i}{dt} = q\left[C_{i,DF} - C_{i,p}\right]$$

where $C_{i,DF}$ is the concentration of species "i" in the DF buffer and $C_{i,p}$ is the concentration of species "i" in the permeate solution. V is the constant volume in the retentate solution and q is the volumetric filtrate flow rate. **Figures 3 and 4** show typical results for the solution pH and histidine concentration as a function of the number of diavolumes during a batch DF process

beginning with the antibody in a pH 7 phosphate / NaCl buffer and using 10 mM histidine (also at pH 7) as the DF buffer. The number of diavolumes is equal to the total volume of buffer processed divided by the constant retentate volume.

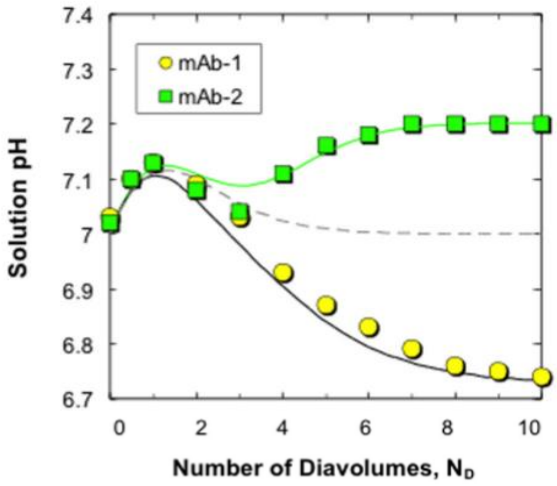

Figure 3. Solution pH vs. Number of Diavolumes for a Batch Diafiltration System [10].

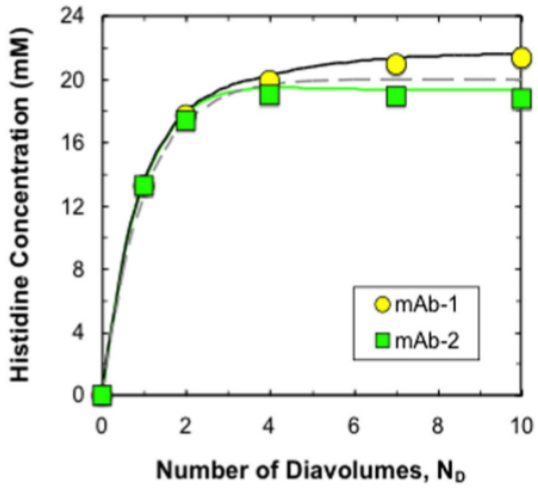

Figure 4. Histidine Concentration vs. Number of Diavolumes for a Batch Diafiltration System [10].

The symbols show experimental data for two different monoclonal antibodies, one of which is positively-charged (mAb-2) and one of which is negatively-charged (mAb-1). The solid black and green lines are the model predictions developed by numerical solution of Equations (1) to (3); the only difference between the model for mAb-1 and mAb-2 was the value of the antibody charge in Equation (1) which was evaluated independently based on zeta potential measurements. The model predictions are in excellent agreement with the experimental data over the entire DF process, demonstrating that the equations and principles used to develop this model were able to successfully describe the pH and buffer profiles. The initial increase in pH seen with both antibodies was due to the reduction in ionic strength of the starting phosphate buffer, which caused an increase in pK_a value of the phosphate and a corresponding increase in pH. The pH at

large diavolumes was dominated by the antibody charge. The positively-charged mAb-2 caused a preferential reduction in H+ ions, leading to a higher pH = $-\log_{10}[H+]$, with the opposite behavior seen with mAb-1. The pH and ion concentrations all approach steady-state values after approximately 10 diavolumes, with the final pH being considerably different than the pH 7 of the histidine buffer used for the diafiltration.

The objective of the studies outlined in Chapter 3 is to examine the pH shifts in a continuous countercurrent dialysis process. Although **Equations (1)** and (**2)** apply to any membrane process, the mass balances used to describe the time dependent variation in the species concentrations in the batch process (**Equation (3)**) will clearly not be applicable to the dialysis process in which the concentrations in the product and dialysate solution both vary with axial position throughout the hollow fiber dialyzer. Although the development of a new model to describe the pH and buffer concentrations in countercurrent dialysis was beyond the scope of this thesis, **Equations (1)** and **(2)** still provide an appropriate framework for thinking about the performance of the dialysis process.

Chapter 3

Materials and Methods

3.1 Materials

Membranes

All continuous dialysis experiments were performed using a countercurrent hollow fiber dialyzer (Polyflux® 17R, Surface Area = 1.7 m^2) obtained from Baxter (Figure 4). The dialyzer has approximately 12,000 fibers, each 25 cm in length and 210 µm in inner diameter. A new dialyzer was used for each experiment.

Figure 3. Polyflux 17R hollow fiber hemodialyzer

Model Protein

Human serum immunoglobulin G (IgG ~150 kDa molecular weight) was obtained from NovaBiologics (Oceanside, CA) as a lyophilized powder and used as the model protein in all experiments. Serum IgG is a polyclonal solution containing a wide range of antibody molecules; it is much less expensive and more readily available than commercial monoclonal antibodies.

Starting Solution

The IgG was initially dissolved in 20 mM phosphate buffer containing 58 mM NaCl at pH 7 with an IgG concentration of 60 g/L. The phosphate buffer was prepared by diluting a concentrated 1M phosphate buffer solution (Sigma-Aldrich) with deionized water, then adding drops of concentrated NaOH until the pH reached 7. The pH was measured using a 420APlus pH meter from Thermo Orion (Beverly, MA). All starting solutions were centrifuged at 4800 g and then pre-filtered through 0.2 μm mixed cellulose ester and/or 0.45 μm polyvinylidene fluoride (PVDF) membranes before use to remove any insoluble aggregates.

Formulation Buffer

The dialysis was performed using 20 mM histidine buffer solutions at pH 7, prepared by dissolving 12.41 g of L-histidine (Molecular weight = 155.15 g/mol) in deionized water. Drops of HCl were added until the pH reached 7, then deionized water was added until there was 4 L of solution.

3.2 Continuous Countercurrent Dialysis

Apparatus

The experimental setup for all continuous diafiltration experiments is shown in **Figure 6**.

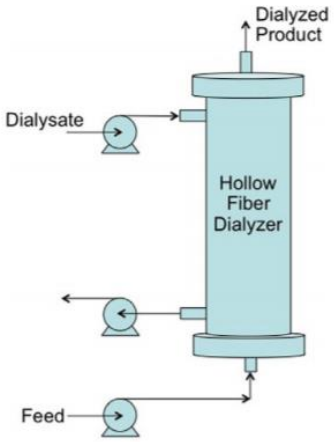

Figure 4. Experimental Setup of Continuous Countercurrent Dialysis System [9]

The dialyzer was mounted in a vertical orientation with the dialysate buffer introduced into the shell side from the top port. The IgG feed solution was introduced into the lumen-side inlet at the bottom of the dialyzer to achieve countercurrent flow. Masterflex L/S 16 (1/8" ID) platinum-cured silicone tubing (Cole-Parmer) was used for pumping and connections due to its smooth surface and low protein binding property. Masterflex L/S peristaltic pumps (Cole-Parmer) controlled the feed and dialysate flow rates. The dialysate inlet and outlet flows were controlled using a single pump fitted with two pump-heads; a separate pump was used for the feed inlet. The pumps were calibrated before each experiment by timed collection using a digital balance. Dialyzers were flushed with dialysate buffer solution before each experiment.

The experiment was started with the feed and dialysate flows beginning to fill the dialyzer simultaneously. The IgG feed was kept at a constant flow rate of 4 mL/min for all experiments based on previous studies performed using a similar system [9]. The dialysate flow rate was varied between experiments, with data obtained at low (4 mL/min), medium (9 mL/min), and high (27 mL/min) dialysate flow rates to evaluate the effect of this parameter on

the pH of the dialyzed product. Experiments were performed at room temperature (21 +/- 2 C) without any external temperature control.

Sample Collection

Dialyzed product samples of approximately 10 mL were collected at five different time points after the start of the experiment: 15, 30, 40, 50, and 60 minutes. The pH of each sample was measured using a 420APlus pH meter.

Chapter 4

Experiment Results and Discussion

4.1 Experimental Data and Trend

Yehl et al. [9] demonstrated that countercurrent hollow fiber dialysis could provide a 99.9% buffer exchange for a serum IgG product. The extent of buffer exchange was determined experimentally by tracking the removal of a model impurity, vitamin B-12, which was easily assayed due to its strong absorbance 550 nm wavelength. The ratio of the initial impurity concentration to the final concentration of impurity remaining in the IgG solution after the dialysis was defined as the fold removal *R*. Experimental data for the fold removal were obtained over a range of dialysate flow rates while keeping the feed flow rate constant at 4 mL/min with results shown in **Figure 7.** The solid curve in Figure 7 is a model calculation developed using the

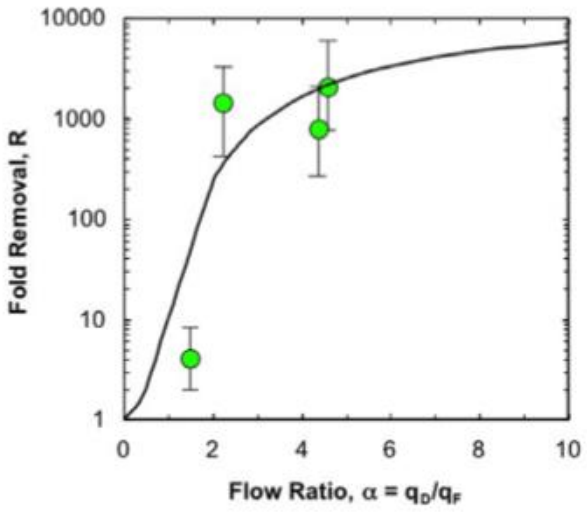

Figure 5. Fold-removal of vitamin B12 as a function of the ratio of the dialysate to feed flow rates (α) for data obtained with the Optiflux F180B dialyzer using a feed flow rate of 4 mL/min.

standard equations for countercurrent mass transfer (analogous to the equations for a countercurrent heat exchanger). The data obtained from this study demonstrated that countercurrent hollow fiber dialysis can provide high levels of buffer exchange appropriate for use in bioprocessing applications; this work served as motivation for the experimental studies conducted in this thesis.

Typical experimental data for the product pH as a function of time during countercurrent dialysis using the hollow fiber Polyflux 17R dialyzer are shown in **Figure 8**. The experiments were all conducted at the same feed flow rate (4 mL/min) but with different values for the dialysate flow rate (4, 9, and 27 mL/min). In each case, the feed was a 60 g/L solution of IgG in a 20 mM phosphate + 58 mM NaCl buffer at pH 7, using a 20 mM histidine buffer at pH 7 as the dialysate solution. Even though the feed and dialysate were both at pH 7, the pH of the product stream varied between 6.7 and 7.4; this is discussed in more detail subsequently. In each case, the pH increased with increasing time, with the values at 9 mL/min clearly approaching an asymptote at long times. This increase is likely due to the washout of the dialysate buffer that was originally present in the dialyzer at the start of the experiment coupled with the time constants associated with the approach to steady-state of the concentration profiles within the hollow fiber dialyzer.

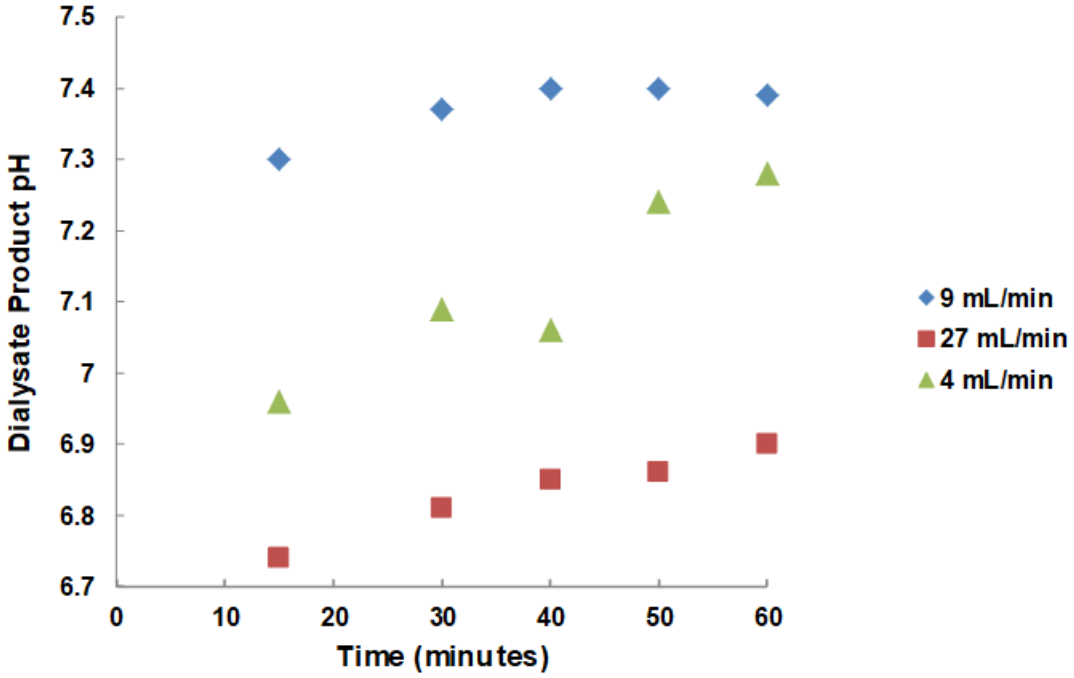

Figure 6. Product pH as a function of time at various dialysate flow rates for countercurrent dialysis of 60 g/L IgG in a 20 mM phosphate 58 mM NaCl buffer at pH 7 using a 20mM histidine buffer at pH7 as the dialysate solution

Based on **Equations (1)** and **(2),** there are two separate effects that govern the product pH when removing phosphate and adding histidine. First, removing phosphate lowers the ionic strength *I*, which increases the pK_a of the phosphate buffer and in turn increases the pH according to **Equation (2)**. Second, the rate of addition of histidine is a function of the electrical charge of the IgG. A recent paper by Yang et al. [12] gave the charge of human IgG as -6.3 in a pH 7.4 phosphate buffer. A negative charge will tend to lower the solution pH according to **Equation (1)** since additional H+ and His+ ions will be required to maintain electroneutrality in the protein solution.

The data in Figure 7 suggest that at low dialysate flow rates, the reduction in ionic strength dominates the pH behavior, leading to the increase in pH seen at long times. In contrast, the behavior at a dialysate flow rate of 27 mL/min appears to be dominated by the electroneutrality constraint. This is consistent with the results for mAb-1 shown in **Figure 4** as part of the discussion in the Introduction to Electroneutrality section in Chapter 2. In the batch diafiltration, the pH increases at small numbers of diavolumes, corresponding to a small degree of buffer exchange, due to the shift in pK_a of the phosphate associated with the lower ionic strength. The presence of the negatively charged IgG changes the concentration of small ions, as the sum of the charges in the retentate solution must remain equal to zero. This leads to the low pH (pH < 7) at large numbers of diavolumes in **Figure 3**, analogous to the low pH seen at the high dialysate flow rate in Figure 7.

The slow approach to steady-state in Figure 8 is another key observation from these experiments; this will be discussed more in Chapter 5. The pH data have been replotted in **Figure 9** as a function of the cumulative dialysate volume pumped through the dialyzer. The data at dialysate flow rates of 4 and 9 mL/min tend to collapse to a single curve when plotted in this fashion, with the steady-state pH achieved at around 300 mL of cumulative dialysate volume. The blood volume in the Polyflux 17R dialyzer can be estimated directly from the dimensions of the hollow fiber membranes as:

$$V = \frac{1}{4} N \pi d^2 L$$

where N = 12,000 is the number of fibers, d = 210 μm is the fiber inner diameter, and L = 27 cm is the fiber length [13]. This gives V = 110 mL for the fiber lumens, which corresponds to a 30 min residence time for the product solution. The data in Figure 8 indicate that the residence time for dialysate is also important in determining the approach to steady-state. The volume for the

dialysate flow-path can be estimated by subtracting the fiber volume from the total cartridge volume, giving $V_{dialysate} \approx 300$ mL, which is in good agreement with the results in Figure 9. Further experiments should be conducted over a broader range of dialysate flow rates to validate that the residence time is one of the key factors controlling both the final product pH and the approach to steady-state in the continuous hollow fiber dialysis process.

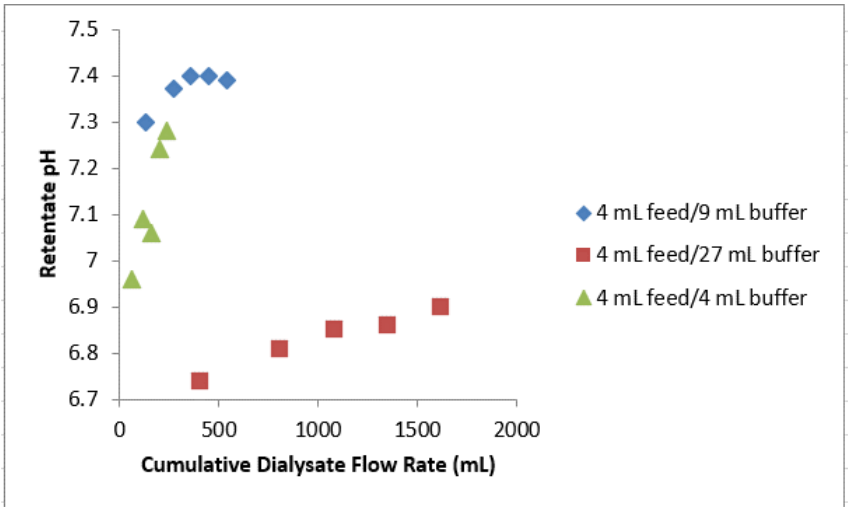

Figure 7 Product pH as a function of the cumulative dialysate volume processed

The results in Figures 8 and 9 indicate that it should be possible to achieve a targeted pH value for the formulated product by adjusting the flow rate of the dialysate solution. It would obviously be best if one could also achieve steady-state operation quickly with minimal variation in pH behavior over the course of the process. This would insure more consistent product, while facilitating the implementation of appropriate process monitoring and control. The results at a dialysate flow rate of 9 mL/min yielded the most stable pH curve, although this run also had the largest deviation from pH 7 (the pH of the dialysate solution). Additional studies will be required to identify the optimal conditions for design and operation of this type of continuous

countercurrent hollow fiber dialysis system for formulation of protein products like monoclonal antibodies.

Chapter 5

Conclusions and Next Steps

5.1 Summary of Findings

Significant investments of time and money are currently being made by large pharmaceutical companies to transition operations of high-value biological products from batch to continuous processes [14]. There are several motives to this transition. The benefits of a continuous process include reducing production time, reducing facility sizes, and improving product quality. One critical step of the downstream operations that has been a challenge to transition to a continuous format is the final formulation step, which is currently performed using batch diafiltration. Recent work by Yehl et al. [9] has demonstrated that countercurrent dialysis could provide an attractive approach for continuous formulation, but there has not been any previous study examining the presence and / or magnitude of any pH shifts that might occur during such a process due to Donnan effects associated with satisfying the electroneutrality constraint when dealing with electrically-charged proteins.

The data presented in this thesis show the first experimental results for the pH of a formulated IgG product generated by countercurrent dialysis. Experiments were performed using a Polyflux® 17R countercurrent hollow fiber dialyzer, serum IgG as the antibody, and histidine as the exchange buffer. The results showed significant pH shifts depending upon the magnitude of the dialysate flow rate. For example, data obtained using a buffer exchange flow rate of 9 mL/min yielded a final product pH of nearly 7.4 even though the IgG feed and the dialysate were both at pH 7. This increase in pH was likely due to the shift in the pK_a of the phosphate buffer

caused by the reduction in ionic strength as phosphate and NaCl diffuse out of the IgG feed solution and into the low ionic strength histidine buffer used as the dialysate. The results also demonstrate that a significant time was required to achieve steady-state behavior in this system due to the low flow rates used and the relatively large volume in the dialysate chamber of the hollow module ($V_{dialysate} \approx 300$ mL). At least one dialysate volume needed to be passed through the system for the product pH to reach an essentially steady-state value.

5.2 Suggestions for Future Work

In order to further pursue the development of a continuous countercurrent dialysis process for formulation of biotherapeutics, it would be interesting to:

- Investigate the pH behavior over a wider range of dialysate flow rates to determine if it is possible to more accurately control the final pH of the dialyzed product. These experiments would need to be performed for sufficiently long times to insure that the data reach the true steady-state behavior, requiring the washout of at least one dialysate volume from the hollow fiber cartridge.
- Evaluate the effect of different feed (product) flow rates on the product pH, both at a constant value of the dialysate flow rate and at fixed values of the ratio of the feed to dialysate flow rate. These data would help define the operating space for the countercurrent dialysis process, while also demonstrating the robustness of this method for product formulation.

- Examine the effect of different dialysate buffers on the pH shifts. This would include histidine buffers at different molarity (ionic strength) and pH as well as buffers with different buffering capacity, e.g., acetate instead of histidine.

In all of the above experiments, it would be important to measure the histidine, phosphate, and NaCl concentrations in the final formulated product, in addition to the pH, to provide additional insights into the performance of the buffer exchange process. It would also be very useful to repeat the experimental studies performed with serum IgG with other proteins having very different electrical charge, similar to the positively-charged and negatively-charged antibodies examined by Baek et al. [10].

In parallel with these experimental studies, it would also be helpful to develop a mathematical model for the countercurrent dialysis process, building upon the model framework used by Baek et al. [10] to describe pH shifts during batch diafiltration. This would require simultaneous solution of the mass balances for the different solutes in both the product and dialysate streams accounting for the countercurrent flow in the hollow fiber dialyzer.

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Bennett P. (Ben) Thoma

Education:

The Pennsylvania State University, University Park, PA

B.S. in Chemical Engineering | *May 2020*
Minor in Spanish

Centro Internacional de Estudios de Español, Ronda, Spain | *May 2017 – June 2017*
- Completed a 9-credit Spanish grammar & composition curriculum instructed by native Andalusians
- Presented Pablo Picasso's *Guernica* to guests at the Reina Sofia Art Museum in Madrid

Professional Experience:

Phillips 66 Company, Houston, TX
Lubricants Intern | *May 2019 – August 2019*
- Created methodology to assess $8 million of a Specialties Lubricants Plant's socialized costs in order to evaluate customer profitability
- Developed an Alteryx workflow to evaluate $2.3 million in packaging labor costs on 1,700 products, creating a continuous and more efficient profitability evaluation
- Built a Tableau Dashboard that visually compares profitability at both the customer and product levels, then implemented this dashboard into the plant's new product evaluation process for the Plant and Sales Managers
- Defined and composed the company's first sales battlecards by collaborating with a sales & marketing firm, then implemented the battlecards to standardize a product's sales pitch amongst all Territory Sales Managers

ExxonMobil Chemical Company, Baton Rouge, LA
Intermediates, Aromatics, and Synthetics: Technical Co-Op | *January 2019 – May 2019*
- Scoped a process modification to Baton Rouge's Plasticizer unit, which would save $400,000 in filters, waste disposal, and raw materials per year
- Created a new model that accurately predicts fouling on the Department's phase-change heat exchangers
- Managed a wireless instrumentation initiative that saved $130,000 per year in mechanical reliability without modifying existing piping
- Installed air-operated valves to eliminate operator risk of silica-containing dust accumulation

Instructional Aide, *Chemical Engineering (CHE) 210: Material Balances* | *August 2018 – December 2018*
- Held 2 office hours per week to assist over 75 students enrolled in their first chemical engineering class
- Observed all CHE 210 classes so that challenging concepts can be reinforced during office hours
- Assisted in re-designing and grading the individual final project, "Assessing the Economic Value of Propylene Glycol Production"

Leadership:

Penn State IFC/Panhellenic Dance Marathon (THON) Donor & Alumni Relations: Development
Third-Party Fundraising Coordinator | *April 2017 – April 2018*
- Advised the efforts of 70 fundraisers that raised over $750,000 by approving applications, providing starter kits, answering follow-up questions, and sending thank-you notes
- Co-published a column in THON's annual program, *Diamond Guide*, to highlight and promote outstanding fundraising, which resulted in a new campaign, "THON Nation"

Penn State Engineering Ambassadors | *March 2017 – Present*
- Present contemporary engineering topics to over 4,000 middle and high school students annually
- Enhanced presentation and communication skills using Assertion-Evidence theory at EA's Mid-Atlantic Conference at the University of Connecticut

- Provide tours and presentations of Penn State's College of Engineering to accepted and prospective students

Awards:

- Penn State Graziani Honors Scholarship in Chemical Engineering | *August 2019*
- Society of Plastics Engineers Color & Appearance Division Scholarship | *August 2016-Present*
- American Association for Drilling Engineers Scholarship | *August 2016*
- Institute for Supply Management Scholarship | *August 2016-Present*