Scaling of a Suspension Polymerization Process

A Major Qualifying Project

submitted to the Faculty of

WORCESTER POLYTECHNIC INSTITUTE

in partial fulfillment of the requirements for the

Degree of Bachelor of Science

by:

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Abstract

POROS beads are the solid phase used for the separation of chemicals in a packed column. The goal of this project was to successfully develop a new scale of production for one of the more popular POROS lines, R250, at the Bedford site of Life Technologies Inc. This new scale is set to be used in their pilot plant as a way to troubleshoot the large scale 300 gallon batch process if and when any inconsistencies occur with production. This intermediate scale will also be the basis for any scale up procedures of other products on the same line. The project scope included mathematically scaling down the entire process, ensuring that the pilot plant had the necessary validated equipment to run the process, physically designing the initial experimental tests for the pilot plant, and writing a standard operating procedure that could be executed in the future.
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Introduction

The R250 POROS process has been trademarked and is owned by Life Technologies Inc. Therefore it is necessary to omit certain details associated with the process, including proprietary chemicals, temperatures, and ratios. Proprietary chemical names have been replaced with a name representing their function in creating the beads, for example [buffer] or [monomer 1]. Temperatures like [A] °C and [B] °C represent proprietary temperatures that are used in the process. Also the proprietary ratios between aqueous and organic phases at different scales have been replaced with [X:Y] and [Z:Y].

Background

The following gives a background on the applications and production techniques for R250 chromatography beads. R250 is a subset of one POROS bead product line. The R refers to the type of chromatography that the beads are used for (reverse phase) the 2 refers to the 2nd pore structure developed, and the 50 indicates the average particle size of 50 microns. The final pore size for this line of beads is expressed in angstroms and should be on average 1080 Å. The polymerization of these beads is through suspension polymerization.

Chromatography Beads

Chromatography beads are used in analytical separation of chemicals, where liquid is run through the column and various properties of the bead allow for varying flow of varying components, allowing the operator to distinguish between different components. The round
beads themselves are generally made up of a soft particle, most commonly a silica or organic polymer base.

When producing beads it is important to create a bead that can properly function while having a high surface area compared to its volume. The key factors that distinguish that ratio are the particle diameter and pore size. For liquid chromatography applications the particle diameter ranges between 1 µm to 100 µm. The pore structure generally takes up as large a percentage of the total surface area as possible. Pore size is measured in angstroms.

Another factor when making chromatography beads is effectively gauging performance. Performance is dependent on the relationship between two factors, productivity and peak resolution. In laymen’s terms this is the ratio between speed and accuracy of the analysis. Productivity has a number of quantitative measures that control it. The major factors include the rates of adsorption and desorption in the column, the rate of mass transfer between the bead pore and the fluid flowing through, the rate of fluid flow, as well as the volume of beads required to perform effective separation. Resolution, on the other hand, is mainly affected by how effectively the beads can create dispersion between the solutes. But resolution is also notably affected by the inherent tendency of the solutes to separate. So when choosing between productivity and resolution, high productivity is possible for separations of solutes with drastically different physical properties while high resolution is required for solutes that have similar properties and are more difficult to differentiate.

Packed column chromatographic approaches are commonly used to maximize both resolution and productivity. High flow rates, low pressure drops, and minimal bandspeading are
desirable for optimal separations and overall performance. Maximizing the ratio between surface area and volume means that the beads must have microscopic pores to control resolution\(^6\). Particle size on the other hand can contribute to pressure drop across the system, with larger particle size causing a smaller pressure drop. Another important factor in determining performance is bandspeaking. Bandspeaking is caused by three phenomena: longitudinal (molecular) diffusion, the variety of paths fluid can take through a packed column, and the rate of mass transfer in the bead\(^6\). The rate of mass transfer in a particle is related to the pore size and can be expressed by the equation below\(^6\):

\[
H - Cu = \frac{(cd^2u)}{D_{eff}}
\]

where \(H\) represents plate height, \(u\) represents the fluid velocity through the bed, \(c\) is a constant, \(d\) is the particle diameter, \(D_{eff}\) is the diffusion coefficient of the solute through the pore, and \(C\) is the rate of mass transfer of the particle\(^6\). Overall the limiting factor in the creation of the optimal bead is the relationship between pore size and particle size.

**Applications of POROS beads**

POROS beads are designed for a wide variety of chromatography applications including cation exchange, anion exchange, hydrophobic interactions, affinity, and reverse phase\(^7\). The beads have a rigid structure that is coated with proprietary polymers to give them the desired separation properties. POROS beads have been optimized for various types of affinity and surface interaction chromatography. They work through a process called perfusion.
chromatography, which differs from diffusion chromatography. With perfusion chromatography, the beads act mainly as a solid support with a large surface area and are designed to have minimal diffusion dependent separation properties. This allows them to be designed to have minimal back pressure and high flow rates. POROS particles possess both large pores and small pores, also known as throughpores and diffusive pores, which minimize the longitudinal diffusion, eddying diffusion, and mass transfer effects common with other particles. The large throughpores have diffusive pores that branch off from them internally. These properties effectively increase the performance overall of the beads while keeping productivity and peak resolution high.

Suspension Polymerization

POROS beads are manufactured by the process of suspension polymerization. For POROS the aqueous phase is a mixture of water and various salts. The organic phase consists of organic solvents, monomers, and initiator. Suspension polymerization is optimal for this process because the goal particle size is to produce a spherical 50 micron particle. Other similar types of multi-stage polymerization, like emulsion, precipitation, and dispersion polymerization are much better for making smaller particle size products. The suspension polymerization process relies on creation of a polymer through the free radical transfer, which is brought about by the thermal decomposition of an initiator, in the case of R250 it is [initiator 1]. It then interacts with the aqueous phase and forms the beads in suspension. The bead particle size is controlled by the addition of [initiator 1], which acts as a catalyst and lowers the energy required to form a single bead. Higher levels of initiator result in smaller beads. Agitation in the polymerization process also plays an important role in particle size.
Physical factors must also be considered when using suspension polymerization. In this process too much agitation can lead to surface shear and particle breakage while too little will lead to separation of the aqueous and organic phases and not allow the entire process to coalesce\(^2\). There is a range of impeller tip speed that is within operating conditions. In that range small adjustments can be made to perfect the particle size. Higher impeller speed leads to smaller particles. Developing the proper ratio between the aqueous and the organic phase is also important. This ratio is an important factor in determining the overall yield of the process. The pilot plant scale process will mimic large scale, which operates at a \([X:Y]\) aqueous to organic ratio\(^2\). The phases are also very temperature sensitive. When combined they must be controlled at \([A]\) °C until polymerization occurs or there will be an adverse effect on the pore and particle size, mainly oversized particles. Suspension polymerization is effected by many factors that alter the bead particle and pore size that are significant in achieving the desirable results.

The aqueous phase of the suspension polymerization is important in developing the base bead material. The solution is made in a glass lined vessel and consists of water, salt, two stabilizers, surfactant, and a buffer. The organic phase brings together some of the chemical properties of the bead and develops the mode of reaction of the overall process. It is mixed in a large glass beaker (22L). \([\text{Porogen 1}]\) and \([\text{porogen 2}]\) are the organic solutes that form the basis of the organic solution. They both have a major effect on the pore size of the beads because they control the suspension of the beads when they are polymerizing. \([\text{Monomer 1}]\) and \([\text{monomer 2}]\) are also added and polymerize in the process to create the individual beads in solution. \([\text{Initiator 1}]\) is also added to the organic phase before polymerization. Polymerization is initiated by heating, after combining and agitating the two phases.
Post Production and Recovery consists of sonication to disperse agglomerated particles, and washes with a variety of chemicals. The product is then dried and converted to finished product by coating with additional polymers.

**Vessel Scaling**

When scaling a process an important factor that needs to be adjusted for the new scale is impeller speed. Matching impeller types involves comparing the curvature and the length of the impeller relative to the sides of the vessel. The type or quality of the mixing done by each type of agitator is different. For example, directly scaling a paddle agitator and a three blade propeller agitator would create issues because a comparable level of agitation can be achieved with 50 RPM on a paddle agitator that would take 400 RPM on a three-blade propeller agitator. So it is important when scaling a process to have a similar type of agitation for both scales.

Matching impeller speed requires comparing the type of impeller used in a vessel and the relative size of the impellers to achieve equal liquid blending. Depending on what process is being scaled equal liquid blending might correspond to, equal liquid motion, equal suspension of solids, or equal rates of mass transfer. Initially it is important to develop the ratio of volumes between the two reactors. Assuming that the tank is standard cylinder, volume, $V_1$, can be expressed as:

$$V_1 = \left( \frac{\pi D_{T1}^2}{4} \right) (H_1) = \left( \frac{\pi D_{T1}^3}{4} \right)$$

$V_1$ equals to volume, $D_{T1}$ equals diameter of Vessel 1 and $H_1$ equals the vessel height. Now a ratio of two volumes can be determined using the following equation:

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\[ \frac{V_2}{V_1} = \frac{\pi D_{T2}^3 / 4}{\pi D_{T1}^3 / 4} = \frac{D_{T2}^3}{D_{T1}^3} \]

And the ratio, R, can be expressed as:

\[ R = \left( \frac{V_2}{V_1} \right)^{1/3} = \frac{D_{T2}}{D_{T1}} \]

Based on R it is possible to calculate the new agitator diameter for the volume that is required in the same geometrically shaped vessel.

So to compare agitator speeds \( N_1 \) and \( N_2 \) the following equation applies:

\[ N_2 = N_1 \left( \frac{1}{R} \right)^n = N_1 \left( \frac{D_{T1}}{D_{T2}} \right)^n \]

For this equation \( n = 1 \) for equal liquid motion, \( n = 3/4 \) for equal suspension of solids, and \( n = 2/3 \) for equal rate of mass transfer. It is important to account for the difference in the ratio of \( D_a \) to \( D_T \) in the vessels that are being scaled.

**DeltaV Automation System**

DeltaV is a digital automation system designed to create an easy to use interface for plant operations. At the Bedford site of Life Technologies it is used primarily to interface between temperature control units, vessels, and agitators. In the pilot plant it is used to manage four main vessels on three temperature control units. The pilot plant is designed so that any of the four vessels can be attached to either temperature control unit. DeltaV will recognize the vessel and
adjust the desired flow rates and pressures it operates under. Besides a general interface it also provides a process history view, which monitors a variety of factors over time. This tool is very helpful when troubleshooting issues with programs because it can compare set points and process variables. This allows an operator to see how the DeltaV changes the jacket temperature on a vessel when a product set point is programmed.
**Methodology**

This methodology section looks at the process taken for engineering the R250 polymerization process at the pilot plant scale. This includes viewing of the large and small scale versions of the process and steps taken to develop an intermediate, pilot scaled process.

Differences between the large scale and pilot plant scale processes should be minimized in order to fully understand how changes made to the pilot plant scale would affect the large scale.

**Small Scale Process**

The goal of viewing the small scale process was to gain a more intimate understanding of the chemistry of R beads and to help conceptualize what chemicals were responsible for affecting specific qualities of the beads. This was important because it provided an idea of how to react to issues that might arise in making the material in the pilot plant.

The small scale process was performed on sight in Bedford under the supervision of a PhD engineer who works on research and development for the R process. He provided a great deal of insight into the process as well as a base model for calculating masses of each of the components. A spreadsheet provided the molecular weights and densities of each of the components. That made it possible to look at an SOP for the process and calculate the percent mass of each component. The spreadsheet was then altered to calculate masses for all components by inputting a volume and an aqueous/organic ratio.
The small scale process was performed in a total of 1.05 L and done in glass vessels, which afforded a much better physical understanding of the chemistry.

The phase ratio was a key difference between the small and large scale processes. The small scale process operates at a phase ratio of \([Z:Y]\) aqueous to organic, while the large scale is \([X:Y]\). The difference in phase ratios is due to the percent loss associated with agglomerations of the aqueous phase during synthesis on the large scale. The \([X:Y]\) ratio is preferred in order to mimic the large scale, but it might need to be lowered if a proper suspension does not form when running the process.

First the aqueous phase was mixed. There were some key factors that were addressed in the small scale viewing. First there was a major difference in agitation speeds in the small scale and the large scale SOP. That meant there was going to have to be a comparable measure developed and it was tip speed. There was also a significant difference between the % of [surfactant] in the small and large scale. Based on previous runs the surfactant has shown to be a major factor in the aqueous phase that controls particle size. This meant that when making adjustments to particle size, surfactant would be an easy option. After the addition of water, polyvinyl alcohol, and [natural product 1] there was a temperature ramp and hold for a few hours. The temperature ramp is necessary to allow polyvinyl alcohol and [natural product 1] the necessary conditions to dissolve fully in water. The large scale SOP provided a peak temperature, \([B]^{\circ}\text{C}\) but did not outline the ramp time to get there.
Large Scale Production

Part of the research on the production of R250 was viewing the large scale process. Fundamentally this gave a look at the ergonomics of doing a process on the pilot plant scale and an understanding of what equipment would be necessary to make the process work in the pilot plant.

The vessels used for the large scale process were a glass lined vessel and two stainless steel vessels.

Pilot Plant Preparation

Another integral part to the successful production of R250 in the pilot plant involved the preparation of all the necessary equipment in the pilot plant facility at the Life Technologies site in Bedford.

The first step was to designate the optimal equipment for production of the R250. The large scale process showed it would be best to use a glass lined reactor for the aqueous portion and a stainless steel for both the organic and polymerization portions. The pilot plant had a 30 gallon glass lined vessel which was appropriate. They also had a 30 gallon stainless steel reactor as well as a 10 gallon pressure can, which was an acceptable size for the organic phase. Appendix 2 includes photographs of the various vessels and the walk-in hood in the pilot plant.

It was also necessary to configure the plant and note any equipment for transfer of materials. Large scale had a few scales set up in a lab under a hood, which could be used to weigh out all of the components less than 10 kg. The pilot plant was set up with a walk-in hood,
which could be used to weigh out any of the liquids. The stainless steel and glass lined vessel also had to fit in the walk in hood, so the organic phase was moved into a smaller hood located next to the walk in. It would provide the necessary space and would allow us to work with organic solvents without having as much direct contact with the material. The transfer of organics from their designated drums to a pressure can on a scale was done with a plastic hand pump, and pressure was used to transfer the material into the production vessel. The initial choice was that all of the vessels could connect with quick connect hosing. The area also had pressure, air, and nitrogen lines that were readily available to make connections. The combination of those two areas provided all of the necessary space and was within the safety guidelines for handling and production of chemicals. A Product Hazard Analysis was also done by the Life Technologies’ Environmental Health and Safety group to ensure that operators were not being exposed to any harmful materials.

Pilot Plant Run Overview

The pilot plant runs all entailed a similar protocol. The aqueous phase was prepared in the glass lined reactor in the walk-in hood in the pilot plant. The vessel is connected to one of the three TCU’s in the walk-in hood. The salts were weighed out on a lab scale and added through a large port on the top of the vessel through a funnel. The organic was prepared under a smaller hood in the pilot plant. The organics were weighed out in the walk-in hood, while the operator wore a full face respirator for safety. They were transferred into the 22L glass flask through one of the ports on the top of the vessel, using a funnel. The 22L flask sits in a water bath at a constant temperature.
The transfer phase was conducted as follows. The glass lined vessel was pressurized and
the aqueous contents were pumped through a closed system into the stainless steel
polymerization vessel. The organic was pulled out through a hose connected to a pressure can
that was under vacuum. The pressure can was then attached to a filter that was then connected to
a port on the stainless steel vessel and pumped in the vessel. All vessels were either purged or
sparged with nitrogen in order to prevent vessel contents from reacting with air.

There were multiple variations between the final version of the process and the initial
batch that was run. The process was run in the pilot plant through the polymerization step.
Afterwards it was transferred to small scale for sonication and recovery due to the lack of
verification documentation on the sonicator that is going to be used in the pilot plant. After
polymerization and a soak, 4 liters of product were washed on the small scale so it could be
tested. Another key difference is the stripping of [monomer 2]. A column in the pilot plant for
[monomer 2] stripping had not arrived in time to process this batch, so the large scale column
was used for stripping [monomer 2]. This required coordination with large scale production,
which will need to be avoided in the future because of the pilot plant’s increasingly tight
schedule. Another key difference is the vessel that was used to mix together the organic phase.
The initial plan was to use a 10 gallon mixing can, but it was determined that the motor on the
can was not to the correct safety specifications. So a back-up was identified, a 22 L glass flask
with an air driven motor. This vessel was not the same type of material the large scale uses, but
it was acceptable. An explosion proof motor was never found that could fit onto the mixing can,
so the 22 L flask is the permanent option for the organic phase production. For the next run
verifications for the sonicator will be completed and the entire SOP will be appropriate for the pilot scale process.

**Results and Discussion**

**Batch One Production**

From the dates March 14, 2012 to March 19, 2012 the first batch of R250 ran. The following summarizes the general run and any issues that were encountered with the initial production.

The aqueous phase was formulated on Wednesday March 14th. The general run went as planned; there were no major issues with the Standard Operating Procedure. The only note was that a longer stem is required for the funnel, when adding components some of the salts got stuck to the inside around the port. They needed to be washed off with water so additional steps were added to the SOP that require small water washes after the two major additions in order to prevent losses of material. Also there was a note about the level of foam due to a tendency of bubble formation after additions of certain salts; issues of large foam increase are not encountered in the pilot plant.

The 2nd day was the organic phase preparation and the polymerization of the product. Various issues arose with the SOP while going through these steps. The set up for the 22L flask was not optimal and caused slight wobbling of the vessel during the addition of each chemical. If there is a need to use the 22L flask again the set up will be altered to be safer and more secure.
Also the SOP was written for the use of the 10 gallon mixing can, so initially a chemical was charged to a pressure can and then into a port on the glass vessel. The issue was that vessel did not have any way to attach the hose so we had to slowly add the chemical, controlling the flow manually. This could have led to issues, so for the other chemical additions we deviated from the SOP and poured the chemicals into the 22L flask. The deviation will not be an issue in the future if the 10 gallon mixing can is used. Next the aqueous and then the organic were transferred into the stainless steel polymerization vessel. The aqueous solution was pumped into the polymerization vessel through its bottom port under nitrogen pressure. The addition went well until the end of the charge. Once the solution was transferred and the line was no longer full, nitrogen began nitrogen into the system, causing the aqueous phase to bubble. The bubbles filled the entire vessel and started slowly leaking out of the top. We were able to stop the increase of bubbles, but there was a minor spill. Next the organic was transferred in through a top port. This transfer was very successful and caused the bubbles to dissipate almost immediately. The issue then became starting the program for the temperature ramp. The DeltaV operating system did not recognize the communication link between the temperature control unit that controlled the jacket temperature and the temperature control unit that controlled the product temperature. So it was impossible to run the program that had been set up for this process. Fortunately a member of the maintenance staff was able to help get a connection between TCU’s, but it would still not run the program. So a program was entered through the TCU that should have produced a proper ramp into the system. The ramp should have worked, based on the ramps that had run in the past, but there was an issue with continuity and the ramp was not linear, there was a bump
in the initial temperature increase which made the slope of the higher temperature shallower, which has a major effect on particle size (see Graph 1 in Appendix 2).

The next day there were visible beads in the reactor and samples were taken to view under a microscope. The resultant beads looked to be in the ballpark range for what you might expect to see under a microscope, however, it was noted that the flow rate of liquid through a packed bed of the beads was significantly faster than that of the normal beads, which implied a larger size.

The results of the first batch were very positive considering the temperature variation in the ramp. Most importantly, a stable suspension formed which meant it would be possible to imitate the ratio of aqueous to organic phase at the pilot plant scale. The pore size came back at 969 Å, fairly close to the 1080 Å required, and the particle size came back at 40.73µm average. 40.73µm is actually slightly large and corresponds to about a 55 µm final particle diameter. The coulter size that needs to be achieved is between 33 and 38 µm. The results of other QC tests backed up results from the coulter analysis and functional testing, showing a larger bead. The bad pore size was associated with non linear ramp and the bad particle size was associated with an improper amount of [surfactant 1] or improper impeller speeds. But even though Experimental Run 1 was off, it proved the theory of the process application.

**Batch Two Production**

The goal of the second run was to get a successful product after making changes to the process based on the first run experience. The only compositional change in the process was made to the [surfactant 1]. The mass % in the total aqueous phase was increased by 0.08% based
on tests previously done that compare different amounts of surfactant with particle size. That amount should have allowed a decrease in the particle size to very close to 50 µm. Once the particle size can be obtained with the right range, it would be easiest to merely adjust the agitation speed up or down a few RPMs to get the desired bead size.

The second batch was run from 10Apr2012 to 13Apr2012. The aqueous phase preparation once again went very well. A new funnel allowed proper additions of all the salts and the protocol added a section that noted washing of port after each major addition, steps 2h and 2t. The organic phase had been remedied to better use the round bottom flask. Appropriate safety was taken when transferring the organics and the additions went well.

Unfortunately there were once again issues with the DeltaV program. The system had thought the polymerization reactor was still physically connected when it was not and it read that the product temperature was lower than its set point. So it increased the jacket temperature to [C]°C. This caused the jacket to heat up when the polymerization vessel was connected and the aqueous and organic phases were added (see Graph 2 in Appendix 2). The reactor heated up prematurely and caused a failure of the batch. We continued with the process anyway in order to gauge success of the washes. The Nutsche that is used for washing does work for filtering, but the run was ultimately a failure because the premature heating. Preliminary testing put the particle size at 44.08 µm coulter and 2,682 Å, well out of spec.

**Batch Three Production**

The third experimental batch began on 23April2012. This run will entail completing the entire run with pilot plant equipment from start to finish. It will include process qualifications
for a sonicator and a validation of all the equipment associated with the process. There have been edits made to the SOP that note the need for constantly monitoring DeltaV’s settings and that should prevent the issue that arose in Batch Two to repeat itself.

**Conclusions and Recommendations**

The project shows that it is possible to make an R bead in the pilot plant at Life Technologies in Bedford. The specifications have not been met for the 250 product, but they are very close. The fundamentals for the production are sound. Going forward the results of Batch Three production should be much closer to the range required for R250.

After completion of multiple experimental runs it seems that the pilot plant needs a few more pieces of equipment dedicated to R250. Mainly the vessel used to prepare the organic phase is being used in the pilot plant and occasionally in a second location. In order to prevent cross contamination, purchasing another 22 L round bottom flask should effectively manage that risk. Also an attachment needs to be purchased that can connect to a port in the round bottom flask that directs any dangerous organics into the top of the hood that it is being operated in. Currently, while sparging, a great deal of dangerous gas is exiting one of the ports which makes it difficult to add any additional material if an operator is not wearing a full face respirator. Also to make the pilot plant more “lean”, denoting certain pieces of equipment with a certain color that stands for the R process might help differentiate between lines that can be used for other processes and those that should be dedicated just for the R process.
The major issue with the completion of batches of R250 in the pilot plant was the interface between DeltaV, the temperature control units, and vessel thermal monitors. This prevented the successful completion of both of the batch runs and raised concerns about being able to pinpoint a root cause in experimental runs. The problems that occurred for the experimental runs had not been documented thoroughly so the full scope of their effect on the finished product was unknown. The problem is not necessarily with DeltaV. DeltaV works very well in large scale production on vessels and lines that are static and not being disconnected. But the pilot plant was designed to be mobile and more of an experimental set up that would allow operators to be more creative in the space. The system is objectively stymieing the productivity and creating a great deal of issues for operators and maintenance, which have to address issues within DeltaV or hire out a contractor to come in and make fixes. Some of these issues arise for unknown reasons. The bottom line seems to be that DeltaV thinks it is connected when it is not or vice versa.

The DeltaV issues can be addressed in various ways. The best result would be that operators would be able to use DeltaV as an interface in the pilot plant without hindering success of production. One way to do this would be to objectively eliminate DeltaV and find a way to do manual interface in the pilot plant. That option would lead to the best results, but it would definitely be the most expensive. Another option would be training more people in the inner workings and programming of DeltaV. Those people would most likely be engineers that have to use DeltaV regularly or additional maintenance or staff. This would alleviate some of the stress that it puts on the few people well versed on the subject. It might also be possible to develop a standard operating procedure for using the DeltaV interface in the pilot plant that outlines...
stepwise the order which vessels, TCUs, hoses, and communication should be established. This would help minimize issues and help troubleshoot problems in the future if they arise. Ultimately it is imperative that when operating in DeltaV, operators must check and double check all interfaces and connections in order to assure that basic issues do not arise.

Because there are still some unknowns on how and when particles and pores form in POROS beads it would be helpful to purchase an instrument that would be able to analyze production more closely. There are multiple instruments available that would measure formation of beads while in process. Lasentec® PVM® by Mettler Toledo is an example of that type of device. The device when placed in a reactor records video that looks at a multitude of particles simultaneously. It can then measure the size of these particles and create a graph over time that compares the number of various size particles over time. Because POROS product formation is not fully understood this type of instrument would be critical in forming a more complete analysis of bead formation. A piece of equipment like similar to the Lasentec® PVM® would be a valuable asset to Life Technologies, creating a stronger understanding of POROS formation.

Overall this paper outlines the creation of a new scale process in the pilot plant at Life Technologies, in Bedford. The completion and successful testing is very close to completion and it should be a fully validated pilot plant process in the very near future. The author will continue advising and working at Life Technologies toward a successful experimental and validation run until his project contract expires.
Bibliography


Appendix 1

General Process Overview

Aqueous:

- Addition of water, salt, surfactant, buffer, and stabilizers. They proceed to go through agitation and soaking.

Organic:

- Addition of monomers, porogens, and initiator. They then proceed through agitation.

Polymerization

- Combination of the aqueous and organic. They then enter an initial hold. There is then a temperature ramp and a soak of the product.

Post processing

- The final step includes filtering, washing, and drying of finished product.
Appendix 2

Graph 1: Batch 1 Temperature Ramp Discrepancy

Graph 2: Batch 2 Temperature Ramp Discrepancy
Figure 1: The DeltaV interface in the pilot plant and the 0.1 m Nutsche reactor in the walk-in hood
Figure 2: The 30 gallon Nutsche reactor used for filtering and cleaning of products.
Figure 3: The 30 gallon stainless steel vessel used for the aqueous phase.
Figure 4: The 30 gallon stainless steel vessel used for the polymerization phase