Large-Scale Production of Medical Grade Bioplastic
(Technical Topic)

The Role of Bioplastics in a Circular Plastic Waste Economy
(STS Topic)

A Thesis Project Prospectus Submitted to the

Faculty of the School of Engineering and Applied Science
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements of the Degree
Bachelor of Science, School of Engineering

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Fall, 2020

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

Signature _____Joseph Bledsoe_____

Approved _____ Date _____
Kathryn A. Neeley, Associate Professor of STS, Department of Engineering and Society

Approved _____ Date _____
Eric W. Anderson, Department of Chemical Engineering

INTRODUCTION

The introduction of plastics in the early 20th century gave way to an entirely new consideration for engineering design. A material could be chemically synthesized to satisfy the desired criteria of a design. The popularity of Bakelite, the first chemically synthesized production polymer, arose due to its unique properties such as its high thermal resistance, low electrical conductivity, and molding ability. Decades later, polymers such as polyvinyl chloride (PVC), polyethylene, polypropylene, and polystyrene became commonplace.

All of the aforementioned polymers have unique properties that qualify each as the most suitable choice for different applications. These applications can be generalized into two broad categories of either permanent-use or disposable-use plastics. Permanent-use plastics include items such as PVC piping used in plumbing systems, polyesters used in textiles, and mixed plastics found in electronic components where disposable-use plastics include items such as polyethylene bottles, food packaging, or polystyrene packing peanuts. These categories are similar in that they both are produced from non-renewably sourced petroleum and take an exceptionally long time to degrade. For example, complete degradation of a common high-density polyethylene bottle is estimated to take 500 years in land (Chamas, 2020).

The improper disposal of these plastics, especially in marine environments, is of great concern. “9.25 million to 15.87 million tons of microplastics — fragments measuring between five millimeters and one micrometer — are embedded on the sea floor” (May, 2020). Plastics mechanically break down into small particles that can be mistaken as food for marine life which then propagate through entire ecosystems and therefore endanger the health of humans.

Landfill decomposition, combustion, and recycling are the currently adopted methods for proper disposal of plastics. The previously mentioned in-land decomposition time of plastics

results in a rate of decomposition that is far exceeded by the rate at which plastics are entering landfills. From 1950 to 2015, the production of plastics has risen from 1.3 million tons to over 322 million tons in which 78% was discarded in landfills (Antelava et al.). Although valiant efforts are being made in shifting away from landfill use, the relative rates of disposal still aren't sustainable.

One enticing solution that has recently emerged is the production of bioplastics. Bioplastics are a potential alternative to traditional petroleum sourced plastics and are advantageous in that they degrade much faster. Currently the most promising candidate for a bioplastic alternative is polyhydroxybutyrate (PHA). Previous studies revealed that 85% of PHA were degraded in seven weeks and can degrade in aquatic environments within 254 days. In addition, there are numerous types of bioplastics that offer a wide range of properties (Reddy et al. 2003). The focus of this research will be to explore the opportunities that bioplastics offer in hopes that they may help mitigate the damage currently inflicted by petroleum-based plastics.

TECHNICAL TOPIC: PRODUCTION OF POLY-4-HYDROXYBUTYRATE AS AN AFFORDABLE ALTERNATIVE MATERIAL FOR MEDICAL DEVICES

THE OBJECTIVE

The objective of our technical project is to (1) create an industrial scale process to produce medical grade poly-4-hydroxybutyrate (P4HB) through metabolic pathways in genetically engineered Escherichia coli; (2) evaluate efficiencies of a variety of operating conditions for industrial scale manufacturing; (3) determine the operating conditions that maximize product yield and profitability.

BACKGROUND

Researchers have been seeking alternatives to synthetic plastics that are biodegradable and biocompatible. PHAs are among the more promising replacement candidates, as they have desirable properties such as insulating ability, are biodegradable, have a high tensile strength, and can be biocompatible for surgical use. The extremely high elasticity of P4HB, comparable to ultrahigh molecular weight polyethylene, is one of its most interesting features (Martin and Williams, 2003). After 10 years of clinical trials, P4HB is unique among all types of PHA produced to date, since it's the only PHA-based material with FDA clearances for clinical usage starting with an approval for suture applicable in general soft tissue approximation (Williams, Rizk, and Martin, 2013). Since our society, more than ever, has been searching for alternatives to synthetic plastics, the bio-based, biodegradable, and biocompatible P4HB stands out as a material with both high market value as well as large market potential (Camila, Qun, and Manford, 2020).

Given the fact that P4HB is biodegradable and yields 4-HB, which is a normal compound in the human body and proven to be biocompatible, P4HB has become a prospective material for medical applications, which is the only FDA approved PHA for medical applications (Camila, Qun, and Manfred, 2020). The motivation behind our project is to take advantage of the properties of P4HB such as increased flexibility, a moderate resorption rate, and completely neutral degradation biocompatibility. These properties set P4HB apart from other PHAs for medical scaffolding as it can be used to produce a high strength biomaterial without sacrificing 2 elasticity to yield strong, pliable monofilament fibers (www.GalateaSurgical.com). We aim to create a sustainable, cost-effective biomaterial by developing and then optimizing a process by which P4HB is produced from recombinant Escherichia coli.

UPSTREAM

The upstream process we are designing starts with the cultivation of the recombinant E. Coli in a stirred tank bioreactor. Seed cultures will be prepared in glycerol stock before inoculation into the growth medium. A stirred tank bioreactor consists of a vessel, a head plate to close the vessel, feed lines, sensors, and a control system. The bioreactor is mixed via an impeller shaft allowing the suspension of cell cultures. Use of a bioreactor allows for optimal cell growth due to constant mixing and controlled through sensors.

Current methods of producing P4HB primarily use sugar-based feedstocks. Given that feedstocks account for a large portion of production costs, specifically in regards to the cost of carbon, identifying the most efficient feedstock is crucial for financial viability. Several published studies, in which PHAs were synthesized from E. Coli using various feedstocks, will be used to determine the most effective, sustainable, and economically feasible process.

The most influential reactor parameters we will investigate will be reactor size, mixing configuration, oxygen transport, and temperature control. The reactor volume will greatly influence capital costs, production rate, and energy usage. Economic analysis will determine the optimal reactor volume that satisfies our target market demand. Using power to reactor volume data from existing literature, we will choose mixing parameters that optimize cellular oxygen uptake and minimize energy consumption. Oxygen transport will heavily impact the cell growth rate and will be determined by the oxygen feed rate and mixing parameters. Maintaining the optimal temperature for cell growth will be crucial in assuring a maximum growth rate and production. The optimal temperature according to literature will be used and maintained via sensor-controlled cooling.

DOWNSTREAM

The downstream processes will be designed such that the final P4HB produced remains below a threshold of 20 endotoxin units (EU) per medical device, and 2.15 EU per device that contacts the cerebrospinal fluid standards set by the F.D.A. and United States Pharmacopeia (F.D.A. 1997). The stream leaving the bioreactor will be fed to a centrifuge to harvest the P4HB from the cells. Our project will compare the results from several published studies to determine optimum and sustainable extraction techniques. One study suggests a temperature-controlled method where precipitation of poly(3-hydroxyoctanoate-co-3-hydroxyhexanaote) (PHO) was triggered 3 by cooling the hot solution to a particular temperature. N-hexane and 2-propanol were found to be optimal solvents for such procedures.

Quantitative extraction with n-hexane took place at 50°C and optimal precipitation occurred between 0 and 5°C. The purity was >97% (w/w) and the endotoxicity between 10 and 15 EU/g PHO (Furrer, Panke, and Zinn, 2007). Another method we plan to investigate was conducted by Wampfler et al (2010) using active charcoal at the beginning of polymer extraction with ethyl acetate, where synthesized PHA material had less than 2 EU per gram of polymer. The final purity of the P4HB will be evaluated by third party compositional analysis, ensuring F.D.A. specifications are met.

FURTHER RESEARCH

To ensure our first objective is accomplished, we plan to compare several studies in which P4HB was produced using recombinant E. Coli. This data will then be analyzed to create an optimum industrial scale process for the production of P4HB. We can achieve our second goal of analyzing the cost effectiveness of process methods by manipulating the process variables suggested by the industrial scale process that we developed with our primary objective. We will

analyze the costs associated with various process variables such as the source of feedstock, size of the bioreactor, cell disruption methods, centrifugation design, or the impact that lyophilization has on the final product of extracted P4HB. To attain our third goal of optimization, we will analyze the cost effectiveness of the process variables determined by our secondary objective in comparison to process yields, published literature, and viability of implementation.

Modeling of published data, through Python, AspenTech, and Microsoft Excel, will allow for us to optimally design a method to produce bioplastics. To accomplish our goals of creating a sustainable and optimal process, the following design considerations will be addressed. One of the largest operational costs comes from the carbon source to feed the cells. We will use published research to model and determine the most economic carbon source. We will look at the effect of different feed stocks as well as the size and type of bioreactor to determine optimum operational conditions.

Our remaining task for the Fall 2020 semester is to complete the Design Basis Memorandum, which will be submitted to Professor Anderson on November 6th by 5 pm. Our final results regarding process variables, viability, and economics will be presented in a final report that will be consistent with scientific publications and will be submitted in the Spring of 2021 along with an oral presentation.

STS TOPIC: THE ROLE OF BIOPLASTICS IN A CIRCULAR PLASTIC WASTE ECONOMY

The current dominant system in which plastics are produced, utilized, and disposed of relies on large quantities of easily accessible resources, causes environmental degradation, and threatens competitiveness of countries (Di Maio 2015). The described system is known as a linear economic model and clearly is not a sustainable option for the future. The popularized ideal, the circular economy (CE) model, provides a more robust alternative that may increase the longevity of our society that has become so heavily reliant on plastics. "CE models maintain the added value of products for as long as possible and minimize waste, keeping the resources within the economy when products no longer serve their functions, so that materials can be used again and generate additional value." (Pearce and Turner, 1990)

The use of actor network theory (ANT) will help illuminate the underlying relationships that dictate the development and changes surrounding the plastic waste economy. ANT can be thought of as a framework for conveying the functions and entities related to a sociotechnical system. The semantically dense vocabulary provided by ANT will allow for concise expressions of the complex concepts proposed and will be drawn from Venturina (2010). The sociotechnical network that plastic waste is entangled is broad and complex, so for the purpose of this research, the systems described must be kept fairly abstract.

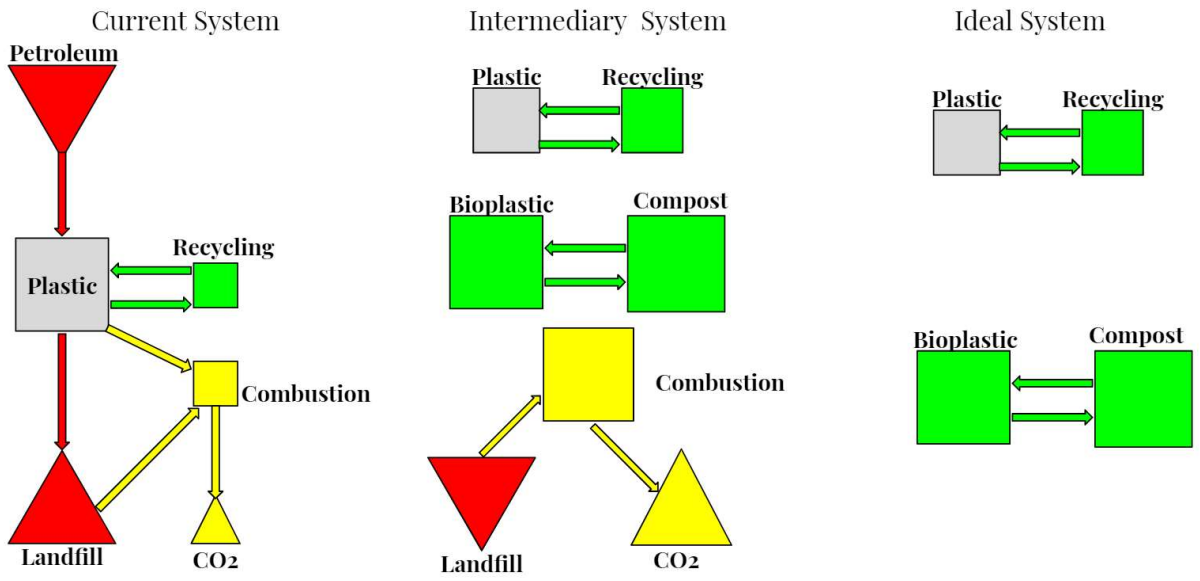
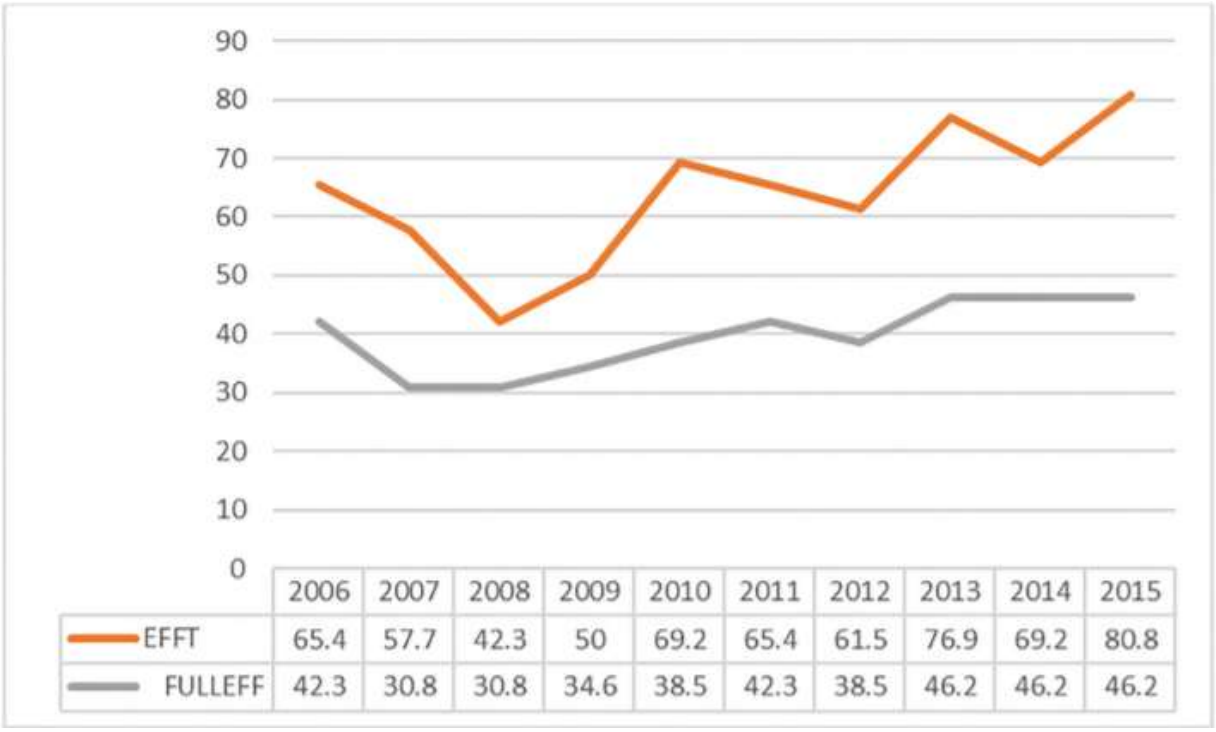


Figure 1. Current and Future Plastic Production Lifecycles: A broad generalization of the current life cycle of plastics today including the strong reliance on petroleum for plastic, landfill accumulation, and proposed life cycles to rely more heavily on biodegradable plastics and recycling. (Bledsoe, 2020)

Each object in figure 1 is a fundamental actor of the plastic lifecycle and their size roughly compares their relative quantities. Cube shape actors represent a quasi-steady-state in which their associated quantities may fluctuate, increase, or decrease over time, but remain constant relative to neighboring actors. The triangles represent accumulation meaning that the quantity relative to other actors is not constant. Moreover, upward and downward triangles indicate an increasing or decreasing rate of change respectively. Green, yellow, and red are used to indicate the net environmental impact associated with each actor as sustainable, semi-sustainable, or unsustainable. Each of these presented actors may then be defined as subsystems in which the social behavior, technological implications, and political aspects influencing them can be researched independently.

Achieving a global circular economy will require a series of transitional periods. The three systems laid out in figure 1 will likely take decades to transition between and the progress of each transition will vary for different areas of the world. Figure 3 showcases multiple nations'

cumulative progression towards an intermediary plastic lifecycle over the course of one decade. The metrics used, EFFT and FULEFFF, represent nations that are efficient or fully efficient and nations that have Multidirectional Efficiency Analysis (MEA) scores equal to 1 for that year.



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
EFFT	65.4	57.7	42.3	50	69.2	65.4	61.5	76.9	69.2	80.8
FULLEFF	42.3	30.8	30.8	34.6	38.5	42.3	38.5	46.2	46.2	46.2

Figure 2. EFFT and FULEFFF Yearly Evolution (%): Signifies the progress in intermediary life cycle transitions for European nations (Adapted by Joe Bledsoe from Robaina et al., 2020)

CONCLUSION

The purpose of this research will be to evaluate the efficacy of bioplastics by thorough investigation of all the key human and non-human actors that make up the plastic waste economy network. The findings on bioplastic efficacy will be drawn from technical research surrounding the properties and economic feasibility of PHA's as well as their societal and regulatory adoptability via STS research and analysis of case studies. The primary focus will be to provide supplemental material and supporting evidence for the existing circular plastic waste economy research of Yadav et al. 2020.

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