MEDICAL APPLICATIONS OF BIOPLASTICS

ACTOR NETWORK ANALYSIS OF PETROLEUM PLASTICS

A Thesis Prospectus
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Bachelor of Science in Chemical Engineering

By
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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.

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The production and widespread use of petroleum plastics has led to many disruptions of many marine and land ecosystems as well as daily human life. Its persistence in marine and terrestrial environments and degradation into microplastics has raised concern from a growing portion of the population. Increasing concern for the disposal end of life for plastic because of how long it persists in marine and land environments. Plastics were originally used because of their durability, pliability and other advantageous properties, such as high thermal and electrical resistance,. Bio-based plastics are the future, and will be crucial to the global transition to a self-sustainable, circular economy. The use of plastics is not going away for the foreseeable future, but the microplastics and negative consequences associated with them must be addressed immediately to mitigate widespread damage to the ecosystem.

The intentions of this research are to illuminate potential alleviation to the aforementioned problems using the 4 e's of sustainable engineering practice (Koller, 2017): economic, ethical, environmental, and engineering aspects. The proposed solutions must be economically feasible, meaning that they must have comparable profit margins to compete against the practices currently in place. There must be an environmental advantage compared to current methods. The methods and transactions surrounding the proposed alternatives must be ethically sound. The technical expectations of any proposed process must be within the confines of realistic engineering technologies. Looking at the beginning and end of life of the products that go into making plastics and how the technologies are integrated into a larger network will benefit all humans.

In 2015, 200 million tons of plastic were produced and is going to increase (Jambeck et al., 2015). Upwards of 8 million tons of plastic find their way into ocean(www.WWF.org, 2020). The use of petroleum plastics is not sustainable and has caused many people to look into alternatives. An emerging material that has the potential to replace petroleum plastics are a class of biopolymers call polyhydroxyalkanoates (PHAs). PHAs are produced through metabolic reaction pathways in bacteria. PHA is energy storage mechanism for bacteria which is analogous to fat in the human body. Our technical project aims to develop large-scale production of a specific PHA as a biocompatible plastic for medical applications. The plastic is used in surgical implants, sutures, and skin scaffolding and can be processed by the body converting it into water and carbon dioxide (Utsunomia, 2020). The aim of the technical project is to design a sustainable process for the production of PHAs that will provide evidence for the widespread adoption of PHA as a better alternative to petroleum plastics for applications larger than medical devices.

Eric W. Anderson of the Department of Chemical Engineering is the technical advisor that will guide our team through the design process. The technical team is comprised of three additional fourth year undergraduate students, Joseph Bledsoe, Lia Macera, and Xhesika Sula, in the Department of Chemical Engineering.

Our remaining task for our Fall 2020 semester is to complete the Design Basis Memorandum, which will be submitted to Eric W. Anderson on November 6th. Our final results regarding process variables, viability, and economics will be presented in a final report that will be consistent with scientific publications. The final report will be submitted in the Spring of 2021 along with an oral presentation. The final report resembles a Phase I design package and decision. Throughout Spring of 2021, three progress reports will be presented to various faculty of the Chemical Engineering Department about our current design process to receive feedback and criticisms about how our team is designing a solution to the identified problem. In addition, weekly meetings with Eric W. Anderson are in place for next semester to keep our progress on track.

MEDICAL APPLICATIONS OF BIOPLASTICS

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.

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.

TECHNICAL OBJECTIVES

The motivation behind our project is to take advantage of the properties of P4HB, especially suitable for medical applications, to create a sustainable, cost-effective biomaterial by developing. The optimizing a process by which P4HB is produced from recombinant Escherichia coli, using the metabolic pathways shown in Figure 1.

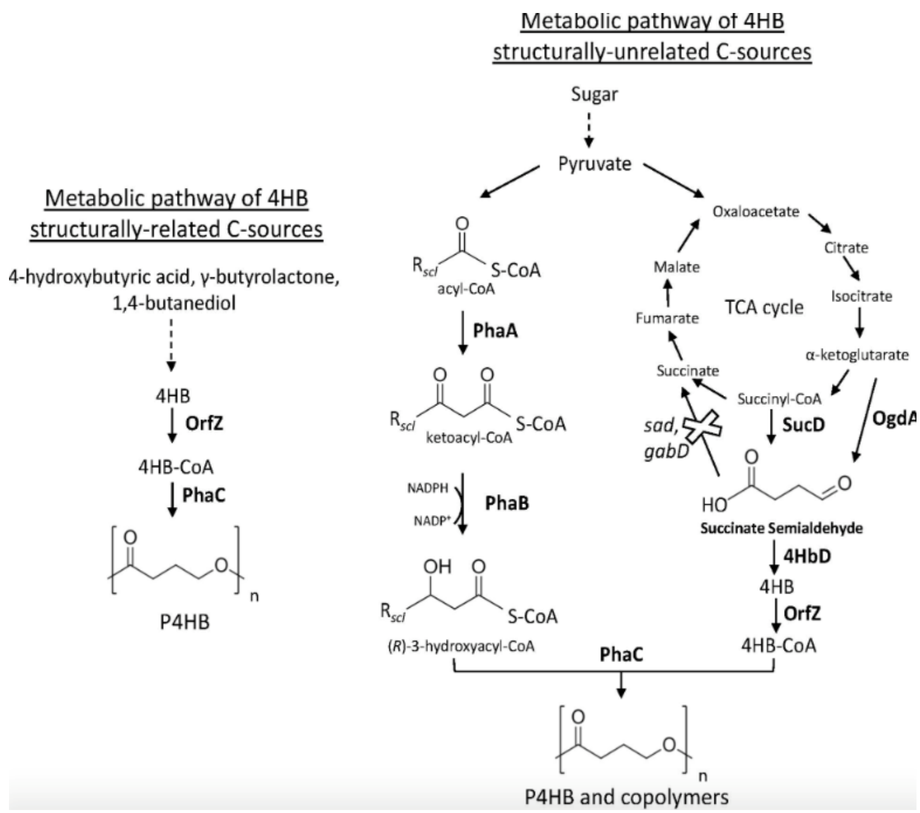

Figure 1: Metabolic pathway heterologously expressed in recombinant bacteria (e.g., E. coli and H. bluephagenesis) for the synthesis of P4HB and copolymers from related and unrelated C sources. The deletion of endogenous sad and gabD both encoding succinate semialdehyde dehydrogenase reinforces the carbon flux toward 4HB-CoA. PhaA, 3-ketothiolase; PhaB, acetoacetyl-CoA reductase; OgdA, 2-oxo-glutarate dehydrogenase; SucD, succinate semialdehyde dehydrogenase; 4HbD, 4-hydroxybutyrate dehydrogenase; OrfZ, 4HB-CoA transferase; PhaC: PHA synthase. (Camila, Qun, and Manfred, 2020).

FERMENTATION PROCESS OF P4HB

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.

SEPARATION AND PURIFICATOIN OF P4HB

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.

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.

ACTOR NETWORK ANALYSIS FOR PETROLEUM PLASTICS

Despite efforts to make petroplastics more circular, they will have effects everywhere. Kevin Loria claims every person might consume up to five grams of plastic per week, or a credit card's amount of plastic, in a Consumer Report magazine article (2020, June). He suggests action calls to reduce the total consumption of plastic. The bioaccumulation of microplastics will continue to compound the affect these materials have on human health over time. The consumption of the microplastics are primarily from the packaging of what we drink and eat. It is also suspended in the air that we breath. Additionally, researchers in the isolated atolls of the Maldives found 0.32 particles per meter cubed of microplastics on the surface of the water (Saliu et al., 2018). Unintended consumption of plastic affects birds, marine animals and plankton in the ocean. There are additives to plastic that make the plastic harder, softer, or flexible.

Researching the growing list of toxic additives and their effects on living organisms will be further researcher next semester. Considering the above-mentioned consequences of plastic waste, my STS research will attempt to narrow down the most promising technological, societal, and regulatory actions that may combat further detriment to the environment.

By looking at the social institutions and roles of key players (Law & Callon, 1988), "a method of social analysis that takes the technical aspects of the engineer's work to be profoundly social." The network analysis will focus on the systems currently in place for the production, waste management, and use of petroleum plastics as well as identify gaps of communication and knowledge between the actors. There will be an emphasis on the unintended consequences on the "linear economy" pattern with petroleum plastic products. The linear-economy pattern is characterized by assuming resources are abundant, available, easy to source, and that waste products are easily disposed. The problem with the linear economy pattern and petroleum plastics is that many of the assumptions are wrong, such as the abundance and ease of disposal.

The biggest fallacy of petroleum plastics waste in a circular economy in the disposal which is a result of its extremely long lifetime (Yadev et al, 2019). It will take at least 500 years to for plastics to degrade completely (Chamas et al., 2020). Up to 58% of plastics are landfilled or enter the natural environment where they accumulate and persist well beyond the human lifespan (Chamas, 2020). Another false assumption of petroleum plastic as a part of a circular economy is the abundance of fossil fuels. In 1970's more research began exploration into alternative sources of plastic not from plastic because in the United states the oil crisis made citizens view oil as nonrenewable resource for the first time (Williams et al., 2016). The aim of the STS topic analyzes the petroleum plastic industry and will make recommendations on how to move closer to a more sustainable circular economy.

Actor network theory (ANT) can be applied to the interactions in the petroleum plastic industry and the adoption of sustainable alternatives. Changes to plastic use for technologies must be accepted by the four main social groups that come in contact with the plastic as well as the regulatory agencies (Figure 2). The molded plastic can take on any form imaginable for consumer packaging products. Some of the biggest names that appear making these plastics products are Coca-Cola, Nestle, and Proctor & Gamble. The consumers in this case, buy these products and very quickly loss the utility in the plastic. The plastic is passed off to waste management systems for disposal of the products in a proper way to the waste management system. The primary regulator agency that interact with the main four actors listed in the United States is the environmental protection agency (EPA). Smaller regulator agencies work on localities such as plastic straw and plastic bag bans. How these agencies interact and listen to the actors will be the primary focus of my STS research.

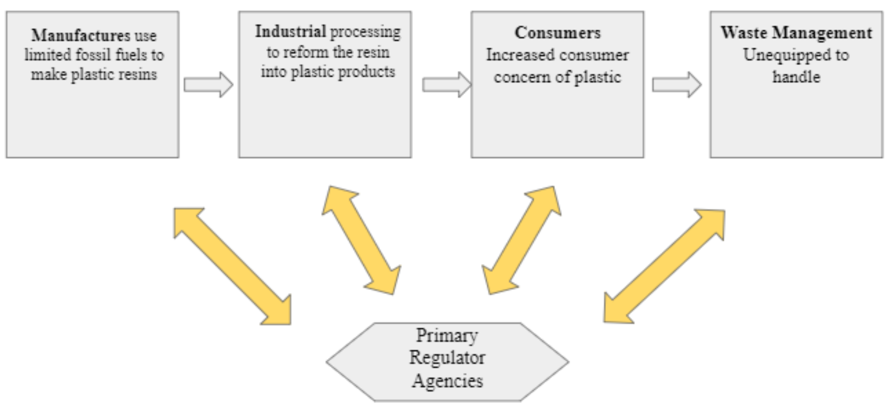

Figure 2: Key actors in the petroleum plastics life cycle: The network contains manufactures of plastic resins from refined crude oil products, industrial manipulations of the plastic for consumer products and the waste management system. Governmental agencies communicated and impose regulations on the use of plastics with each actor. (Created by CJ Hall, 2020)

The waste management system of plastics has multiple avenues to deal with municipal plastic waste which include landfills, recycling, incineration, and composting (Figure 3). Unfortunately, the majority of the waste plastic is sent to the landfills where it will stay indefinitely. Another disadvantage of landfilling plastics is the amount of plastic finds its way into our environment (Ritchie & Roser, 2018). Bioplastics are an emerging technology that will allow for the composting of plastics in land and marine environments. The adoption of bioplastics as an alternative to single-use plastics will be a focus of the STS research.

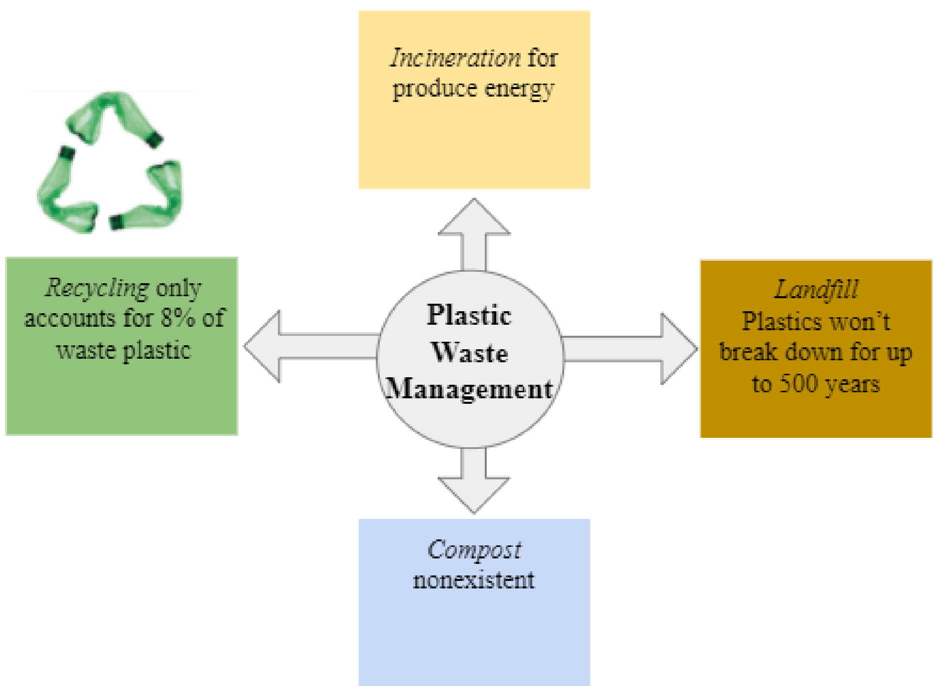

Figure 3: Benefits and drawbacks of the current waste management system for petroleum plastics: Landfills, recycling centers, incinerators for energy recovery, but most of the plastic produced ends up in a landfill. (Created by CJ Hall, 2020)

MOVING FORWARD USING PLASTICS

Solutions to the plastic waste problems will require a cumulative effort across regulatory agencies, industrial actors, and most importantly how society, specifically consumers interact with plastic. My STS project will present an ANT analysis of the connections between these relevant groups, how they may collaborate to counteract consequences of and eliminate plastic waste. Prioritizing the health of living organisms and the efficiency of affected industries, several case studies and prior research will be utilized to make arguments for potential solutions. The rapid growth of plastic production and consequential waste accumulation that is currently observed.

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