**Validating a Novel Bilirubin Quantification Method: A Coupled Computational and In-Vitro Modeling Approach**

(Technical Paper)

**The Costs Associated with Equitable Engineering Design**

(STS Paper)

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## Introduction

Approximately 60% of term and 80% of preterm newborns develop jaundice in the first week after birth (Woodgate et al., 2011). Jaundice is the accumulation of bilirubin in the body which causes a visible yellowing of the skin. The disease is not usually harmful itself, however it is indicative of an underdeveloped liver, and elevated levels of bilirubin in newborns can lead to difficulty waking, high-pitched crying, poor sucking or feeding, and fever. While rare, severe cases can lead to permanent brain damage, which can cause involuntary and uncontrolled movements, permanent upward gaze, and hearing loss (Mayo Clinic, 2022). Current methods of measuring the extent of jaundice in patients include visual examination of skin coloration, transcutaneous measurement with a non-invasive device, and blood testing. The current non-invasive transcutaneous methods of measuring bilirubin in the skin overestimate bilirubin levels in darker skin tones, so the use of invasive heel prick blood sampling is required instead in these cases (Maya-Enero et al., 2021). This invasive method is painful and causes a higher risk of infection due to the underdeveloped nature of newborn immune systems.

Treatment may not be required for mild jaundice, but for more severe cases treatments include phototherapy, intravenous transfusion of an immunoglobulin, and blood transfusion. Phototherapy is a method of treating jaundice by which blue light is applied to the skin leading to the breakdown of bilirubin so that it can be excreted from the body. The goal of the technical project is to develop a computational model that allows for accurate transcutaneous bilirubin measurement in darker skin tones from absorbance measurements and a physical in vitro model that simulates physiological conditions and allows for realistic testing of bilirubin transport in the skin and blood. The goal of the STS project is to research and explore the costs of equitable design in engineering and assess the relative success of these measures.

**Technical Discussion**

The overestimation of bilirubin by non-invasive transcutaneous bilirubinometers is due to the high degree of overlap between the absorption spectra of bilirubin and melanin, which makes it difficult to determine if the variations in readings of reflectance from the bilirubinometers is attributable to bilirubin specifically when in the presence of melanin. This causes challenges in accurately measuring how much bilirubin is present in skin containing higher melanin concentrations. Phototherapy for neonatal jaundice involves the use of blue light as a phototherapeutic treatment to reduce the serum concentration of bilirubin in the blood by photoisomerizing and reducing the concentration of bilirubin in the skin (Woodgate et al., 2015). Through the use of phototherapy, bilirubin is photoisomerized into the much more water soluble compound lumirubin that can diffuse into the bloodstream and be excreted from the body. This project will be a continuation of a previous Capstone group's work which showed that the destruction of bilirubin under blue light can be measured in a controlled laboratory environment and represented by a computational model using exponential regression.

The project will involve the creation of a computational model that can accurately predict bilirubin levels with varying levels of melanin and other physiological factors, as well as a physical model that mimics the mechanics of bilirubin transport in the body. The computational model will integrate the existing absorbance data from previous work to differentiate between melanin and bilirubin absorbance spectra. We will then employ mass balance equations to develop a time-dependent mathematical model for neonatal bilirubin concentration. Finally, we will optimize parameters within the computational model, validated by an in vitro model and the

mass-balance model, to enable realistic testing. The computational model will have predictive power that will allow for accurate bilirubin concentration measurements based on the observed destruction of bilirubin into lumirubin. The in vitro model will serve to simulate physiological conditions that will allow us to analyze bilirubin transport between skin and blood. The information obtained from this model will help reform the computational model and improve its real world application. This physical model will employ a flow dialysis setup that will allow the destruction and diffusion of bilirubin through a membrane from a hydrophobic environment simulating the skin that contains various relevant molecules such as bilirubin, melanin, and albumin, into a circulating flow of fluid representing the blood. The results of this work could be used as part of the development of a prototype treatment and diagnostic medical device, as well as improving the understanding of bilirubin transport in skin and blood. This project will be conducted under the direction of Dr. William Guilford, Department of Biomedical Engineering, and Dr. Brian Helmke, Department of Biomedical Engineering.

**STS Discussion**

The overestimation of bilirubin levels in darker skin tones is an example of racial disparities in healthcare and technology. Implicit biases have been shown to negatively affect people of color when receiving medical care. People of color face more barriers to accessing healthcare, and when they do receive care, they are more dissatisfied with their experience than white people (US Department of Health and Human Services, 2003). The premature death rate from heart disease and stroke is highest among Black Americans. In addition, numerous disparities in health conditions and risk behaviors exist among people of color, including asthma,

diabetes, HIV/AIDS, hypertension, low birth weight, obesity, preterm births, and tuberculosis (Centers for Disease Control and Prevention, 2011). There has been increasing focus on equitable design in technologies over recent years with diversity, equity, and inclusion (DEI) being emphasized throughout companies and universities around the world. The focus on DEI is not solely on the administrative level, as a large majority of those surveyed (78%) say it's important to work at a company that makes diversity and inclusion a priority, and more than 50% consider it to be "very important." Also, employees who were satisfied with their employers' DEI efforts scored higher on the happiness index and reported greater satisfaction with their pay and opportunities for career advancement (*Dei in the workplace: Why it's important for company culture* 2023). The emphasis of DEI is both on the corporate and cultural level, and it is seen as a necessity for many people. Every year companies in the US spend around $8 billion on DEI efforts, according to research by the consulting firm McKinsey & Company (Ellingrud et al., 2023). Does the money and time invested into DEI yield tangible results? Does equitable design cut into profits or increase them? My research will investigate the costs associated with equitable engineering design compared to design without such considerations.

**Conclusion**

The overestimation of bilirubin levels by non-invasive transcutaneous bilirubinometers in patients with darker skin tones disproportionately affects minorities and reinforces the disparity in quality of healthcare received. The development of a computational method to more accurately measure bilirubin levels in skin with higher concentrations of melanin and the in vitro

model described in this proposal will provide patients with darker skin the same level of care and safety received by lighter skinned patients.

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