Thesis Project Portfolio

Design of a Skin-Tone Inclusive Technique for the Non-Invasive, Transcutaneous Measurement of Bilirubin

(Technical Report)

Analysis of the Contributors and Implications of the Instillation of Racial Bias into the Infrared-Based Pulse Oximeter

(STS Research Paper)

An Undergraduate Thesis

Presented to the Faculty of the School of Engineering and Applied Science

University of Virginia • Charlottesville, Virginia

In Fulfillment of the Requirements for the Degree

Bachelor of Science, School of Engineering

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Spring, 2023

Department of Biomedical Engineering

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Sociotechnical Synthesis

Racial Bias in Infrared-Based Pulse Oximeters and Transcutaneous Bilirubinometers

The technical work I performed while developing a skin-tone inclusive technique for the non-invasive measurement of bilirubin is closely related—both technically and in its social implications—to my STS research project, where I explored how the overestimation of oxygen saturation by pulse oximeters defined power relations between Black and White patients during the COVID-19 pandemic. Technically, the projects relate in that the primary contributor to their respective shortcomings is largely attributable to melanin—a chromophore in the skin that not only has a particularly wide light absorption spectrum, but is also found in higher concentrations in patients with darker skin tones. The technologies described in both projects have a tendency to marginalize Black patients by reducing their likelihood of receiving quality clinical care. This directly increases mortality rates and reinforces existing race-related socioeconomic disparities by increasing medical care costs for an already vulnerable and largely uninsured population.

Neonatal jaundice is a common condition caused by a build-up of bilirubin—a byproduct of hemoglobin destruction—in the blood. Currently, bilirubin levels in neonates of darker skin tones are frequently overestimated by bilirubinometers, making the predictive utility of this light absorption-based screening method lower in racial populations with higher melanin contents. This is due to the high degree of overlap between the absorption spectra of bilirubin and melanin, which makes it difficult to determine whether variations in the reflectance spectra collected by bilirubinometers are attributable to bilirubin specifically. This issue is addressed by using blue light to stimulate a photoisomerization reaction that converts bilirubin to a colorless substance. My team aims to *prove* that collecting absorption spectra both before, during, and after locally photobleaching the bilirubin in a small patch of skin makes it possible to distinguish the degree of absorption that occurs specifically due to bilirubin by generating a complete decay curve.

My STS research addresses a similar issue, but focuses on the opposite end of the spectrum; it analyzes the implications of the instillation of racial bias into pulse oximeters beyond the narrow scope of clinical care. Current infrared thermometers have a strong tendency to overestimate blood oxygen saturation levels in patients with higher melanin concentrations, and darker-skinned minority patients' resultant 23-29% decreased likelihood of recognition for COVID-19 therapy eligibility relative to Whites played a powerful role in defining power relations between racial groups during the pandemic. My writing corroborates evidence to argue that the overestimation of blood oxygen saturation levels during the COVID-19 pandemic played a notable role in defining mortality rates, perpetuating racially-biased healthcare spending, and ultimately marginalizing minority patients using the framework of *technological politics* developed by Langdon Winner.

The value of addressing these technical and social problems conjunctively lies in the consequences that would arise if I focused on only one. Without consideration of the technical shortcomings that make bilirubinometers and infrared pulse oximeters melanin-dependent, the racial bias in these technologies would persist. My technical work also provided a strong context and background for my understanding of how melanin contributes to the overestimation of oxygen saturation levels in Black patients. Additionally, if the role of pulse oximeters in defining power relations between racial groups were ignored, the issues evident in current technology would remain unacknowledged and the pressure engineers feel to be cognizant of bias in the design of future devices may remain low—leading to the reproduction of unfair devices whose technical shortcomings perpetuate inequality. My STS research informed me of the consequences that would result if the technical issues present in bilirubinometers went unaddressed.

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Van Spinelli

Sam Thapaliya

Cooper Yurish

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.

William H. Guilford, Department of Biomedical Engineering

Design of a Skin-Tone Inclusive Technique for the Non-Invasive, Transcutaneous Measurement of Bilirubin

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Abstract

Neonatal jaundice is a common condition caused by a build-up of bilirubin in the blood; approximately 50% of term and 80% of preterm infants develop jaundice in their first week of life. Relevantly, up to 10% of term and 25% of preterm neonates require phototherapy, which involves the use of blue light as a phototherapeutic treatment to reduce the serum concentration of bilirubin in the blood (TSB) by photoisomerizing the bilirubin in the skin (TcB). Currently, bilirubin levels in neonates of darker skin tones are frequently overestimated by non-invasive, transcutaneous bilirubinometers; this makes the predictive utility of TcB screening lower in this racial population. Overestimation of TcB increases the likelihood that darker-skinned neonates undergo unnecessarily long phototherapeutic treatment protocols that can deplete essential nutrients, disrupt their thermochemical environment, and separate them from the mother. The overestimation is due to the high degree of overlap between the absorption spectra of bilirubin and melanin, which makes it difficult to determine whether variations in the reflectance spectra collected by bilirubinometers are attributable to bilirubin specifically. We address this issue by using blue light to stimulate a photoisomerization reaction that converts bilirubin into lumirubin—a colorless substance. By tracking the rate of decay of bilirubin using changes in absorbance over time, the resultant decay curve makes it possible to determine the original concentration of bilirubin in the skin irrespective of melanin concentration. Our project establishes a proof of concept for the viability of this method. In our research we present valuable background information, collect the UV-Vis spectra of relevant skin chromophores, create and validate a computational model of the rate of change of bilirubin, and construct a simple physical model—all of which provide support for the continued development and refinement of this method.

Keywords: bilirubin, melanin, absorbance, photoisomerization, phototherapy, bilirubinometer

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Introduction

Neonatal jaundice is a common condition caused by a build-up of bilirubin—a byproduct of hemoglobin destruction—in the blood. The build-up of bilirubin concentration (hyperbilirubinemia) is what contributes to many of the common signs regularly associated with jaundiced patients, including notable yellowing of the eyes and skin in patients with lighter skin tones. Approximately 50% of term and 80% of preterm infants develop jaundice in their first week of life[1]. Careful and accurate monitoring of bilirubin concentrations is of critical importance, as untreated or unnoticed hyperbilirubinemia can lead to encephalopathy, hearing loss, and kernicterus—a permanently disabling neurological condition characterized by choreoathetoid cerebral palsy, upward gaze paresis, enamel dysplasia of deciduous teeth, sensorineural hearing loss, and dyssynchrony spectrum disorder[2].

Phototherapy

In order to prevent the sequelae associated with hyperbilirubinemia, up to 10% of term and 25% of preterm neonates require phototherapy for treatment, which involves the use of blue light as a phototherapeutic treatment to reduce the serum concentration of bilirubin in the blood (TSB) by photoisomerizing and reducing the cutaneous concentration of bilirubin in the skin (TcB)[3]. The blue light employed in phototherapy stimulates the photoisomerization of bilirubin into a second conformation of bilirubin termed lumirubin. While bilirubin is typically stored in fatty deposits in the tissue, lumirubin is much more soluble in the aqueous solutions present in the circulatory system. This makes it easier to break down and pass through the body without needing to be processed by the liver, which is not fully developed in neonates and is the primary contributor to hyperbilirunemia[4].

Existing Measurement Methods

Two methods are currently employed for monitoring and diagnosing hyperbilirubinemia. The current gold standard method involves measuring TSB directly by obtaining venous or heel stick blood samples; while accurate, this procedure is painful, invasive, and poses notable health risks such as an increased risk of hospital-acquired infections—particularly in neonates[5]. Other risks of heel pricks include the accidental puncturing of the heel bone or joint disease, which can cause damage to cartilage and bone. To add, in order to continuously monitor TSB and track increases and decreases in its concentration, healthcare workers must often repeatedly prick newborns at the same site, which complicates the healing process in a patient category that is already prone to infection due to their underdeveloped immune systems[6].

Alternatively, to mitigate these health risks, transcutaneous bilirubin screening measures TcB non-invasively by using a handheld bilirubinometer. Transcutaneous bilirubinometry directs specific wavelengths of light into the skin and measures the reflectance spectrum of the light that returns to the device; the reflectance spectrum varies based on the wavelengths of light that are absorbed by components in the skin such as bilirubin, hemoglobin, and melanin[7]. The proportion of light absorbed by the skin is used as an indicator of the concentration of bilirubin present. These transcutaneous measurements work to provide a quantitative risk assessment for infants prone to severe hyperbilirubinemia or bilirubin encephalopathy and allow for timely clinical decisions in areas with limited access to laboratory screenings[8].

Inherent Inadequacy of Bilirubinometers

Currently, bilirubin levels in neonates of darker skin tones (with higher cutaneous melanin concentrations) are frequently overestimated, making the predictive utility of TcB screening lower in this racial population[9]. This can be explained by the high degree of overlap between the absorption spectra of bilirubin and melanin as seen in *Figure 1*; the relative absorption due to melanin is noticeably high near the peak absorbance of bilirubin—which is near the ideal wavelength at which bilirubin concentration would be most easily detected or monitored. Even considering other locations along the spectra, the relative absorption due to melanin is higher

at all locations. As a result, higher cutaneous melanin concentrations can effectively mask fluctuations in bilirubin absorption and make it more difficult to accurately determine bilirubin concentrations in the skin[10,11]. The overlap typically leads to the overestimation of TcB, since the increase in absorption is generally interpreted as a higher bilirubin concentration by most bilirubinometers[7].

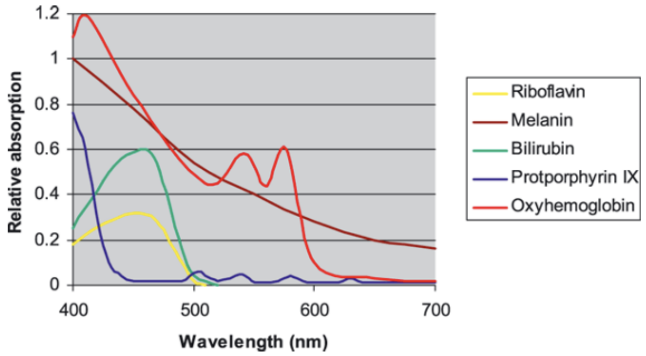

Figure 1: Relative absorption spectra of common cutaneous chromophores at wavelengths between 400 and 700 nm (Mahmoud et al., 2008).

The overestimation of bilirubin measurements poses several risks, including an increased propensity to be prescribed phototherapeutic treatment to treat hyperbilirubinemia. While historically this treatment has been considered generally safe, recent studies have indicated that various side effects may have gone unaccounted for. These include notable short-term effects such as imbalances in the neonatal thermal environment, water loss, electrolyte disturbance, induction of modified liver function and development of cholestasis known as "bronze baby syndrome," and disordering of the newborn's circadian rhythm, and effects associated with the reduction of early-stage maternal-infant interactions[12]. To add, some studies have suggested that long-term side effects and impacts may be at play, such as melanocytic nevi and skin cancer, allergic diseases, and retinal damage[12].

Considering the aforementioned overestimation of bilirubin concentration in neonates of darker skin tone, their increased likelihood of being prescribed phototherapeutic treatment indicates the unintentional implementation of racial bias into bilirubinometers. The racial bias ingrained into the current method used to attain efficient transcutaneous bilirubin measurements disproportionately affects these individuals, limits their access to equivalent quality care, and contributes to macroscale problems with race-based health disparities in the United States.

Overview of Solution

The goal of this research is to provide a proof of concept for a non-invasive, skin-tone-inclusive method for measuring TcB. The overlap in absorbance between melanin and bilirubin makes it difficult to determine whether modulations in the reflectance spectra collected by bilirubinometers can be attributed to bilirubin specifically. Our data suggest that a combination of photobleaching bilirubin—as is done in phototherapy—and traditional reflectance-based measurements can be used to remedy the negative influence of melanin on TcB measurements.

This novel procedure involves continuously photoisomerizing the bilirubin at a small test site on the skin, likely on the pinna of the ear, similar to a bilirubinometer currently on the market—the Bilicare device[13]. The photoisomerization of bilirubin in response to phototherapeutic light causes it to convert to lumirubin. While phototherapy is typically employed in an effort to help neonates easily excrete excess concentrations of bilirubin, the conversion of bilirubin to lumirubin is also recognized for its role in "photobleaching" newborns [14]. Lumirubin is not only more soluble in aqueous solutions, but also absorbs significantly less light. The method described capitalizes on this change in absorbance; at specified time intervals throughout the photobleaching process, the transmittance of 460 nm light will be recorded through the pinna of the ear. As the bilirubin in the skin decreases at the measurement site, the transmittance plot is expected to reach a horizontal asymptote as the bilirubin is fully photoisomerized to lumirubin. Computational analysis of the decay curve and final horizontal asymptote should make it possible to determine the initial cutaneous concentration of bilirubin—TcB. The concentration of

bilirubin in the skin of the pinna correlates significantly with TSB; TcB values determined using our proposed method should therefore make it possible to accurately approximate serum concentrations of bilirubin and help physicians make clinical decisions regarding the requirement of phototherapeutic treatment[13].

We here describe a series of physical and computational experiments that were performed to corroborate a proof of concept for this method. The most important of these included the development of a computational framework to theoretically describe and predict the rate of conversion of bilirubin to lumirubin and the collection of spectrophotometric data for relevant skin chromophores—especially bilirubin, lumirubin, and melanin. The latter task involved determining the absorption spectrum of lumirubin by first fully photoisomerizing bilirubin, and comparing the collected spectra of all chromophores to published spectra available in the literature when available. Lastly, a simple physical model was built in order to validate/adjust the aforementioned computational model, confirm the relationship between absorption and actual bilirubin concentration, and perform other tests to assess the potential clinical viability of the technique.

The differentiating factor between our proposed method and existing devices is that our technical solution accounts for the absorbance of light due to melanin and other skin chromophores so that race and complexion are not determinants of healthcare quality.

Results

The first approach was to verify the absorbance spectra of the three main chromophores of interest (melanin, bilirubin, oxy-hemoglobin) that we would review in the literature. By creating solutions of the three chromophores we were able to read their absorbance spectra using the ThermoFisher NanoDrop oneC. The figure below showed the comparison between our collected results and the literature values. The melanin data match very well (Figure 2). The bilirubin data varies but at the important range of wavelengths (445-480 nm) the data does match (Figure 3). The hemoglobin was excluded because the extinction coefficient of hemoglobin and the concentration in the skin are so small that any physiological concentrations of melanin and bilirubin would wash out any effect in the absorbance spectrum of all the chromophores combined.

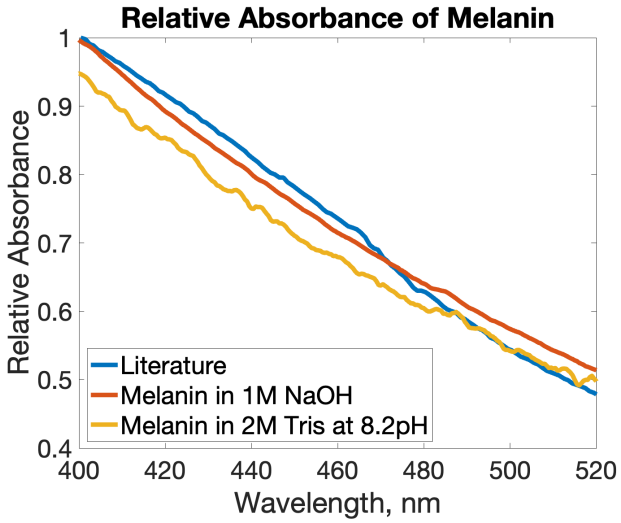

Figure 2. Absorption spectra of melanin in NaOH and Tris buffer solutions. Literature spectrum from Mahmoud et al., 2008[10].

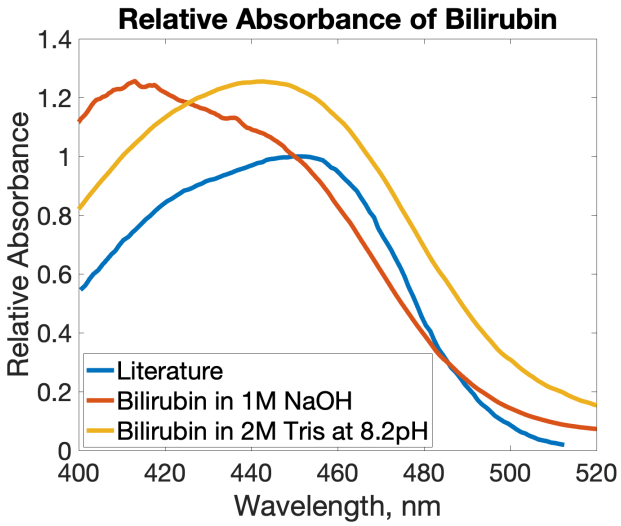

Figure 3. Absorption spectra of bilirubin in NaOH and Tris buffer solutions. Literature spectrum from Mahmoud et al., 2008[10].

We selected a 253 mW, 470nm LED array from Thorlabs to use as our light source. We found that 470 nm light would maximize the amount of light that converts

bilirubin to lumirubin. This LED array is 38mm in diameter which was big enough to light an entire cuvette without needing a lens.

We needed to create solutions of bilirubin and melanin that were closer to physiological concentrations, so the introduction of a tris-buffer was added to lower the pH to 8.2. Then, to verify how stable bilirubin was in an 8.2 pH solution 2 different storage conditions were tested simultaneously (Light and No light). The figure below shows the decay of the bilirubin's absorbance over time. With this information, we concluded that the buffered bilirubin solution does not rapidly degrade in a buffered solution (Figure 4).

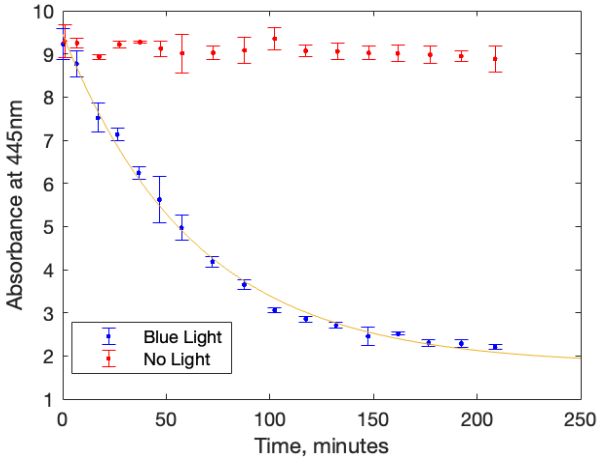

Figure 4. Sample of bilirubin in 2M Tris buffer at 8.2pH being exposed to the blue light array (blue light) and in the dark (no light). Bilirubin does not rapidly degrade over time.

To create a way to predict the bilirubin concentration in a solution, buffered bilirubin solutions of varying concentrations were prepared (0.011, 0.05, 0.1 mg/ml). These concentrations cover the extreme variation in the actual physiological concentration of bilirubin in the skin. Then these solutions were aligned into a 3-D printed chamber that placed the ThorLab's light array with a cuvette of 4ml of each solution.

Each of the solution's absorbance spectra decreased at the 460 nm wavelength. We selected 460nm since our computational model indicated that this wavelength had the greatest change in absorbance in melanin and bilirubin solutions. The computational model was based on findings from Nii et al. which indicated that the conversion from bilirubin to lumirubin could be modeled as a simple, first-order differential equation (see Methods and Material for an in-depth description). This change in absorbance at 460 nm is then plotted over time. Noticing that the curves generated show an exponential decay, we fitted exponential decay curves to the data using Matlab and noted the alpha, or initial degree of absorbance—which we expected to relate closely with concentration. The alpha value represents the amount of change in absorbance due to photoconversion bilirubin if you complete phototherapy for an infinite amount of time. We also directly took the delta in absorbance between the starting and ending concentrations, which will be referred to as the 'delta' technique. We were able to generate a linear regression model for both the alpha and delta values. Both models had a high R^2 value (>.99).

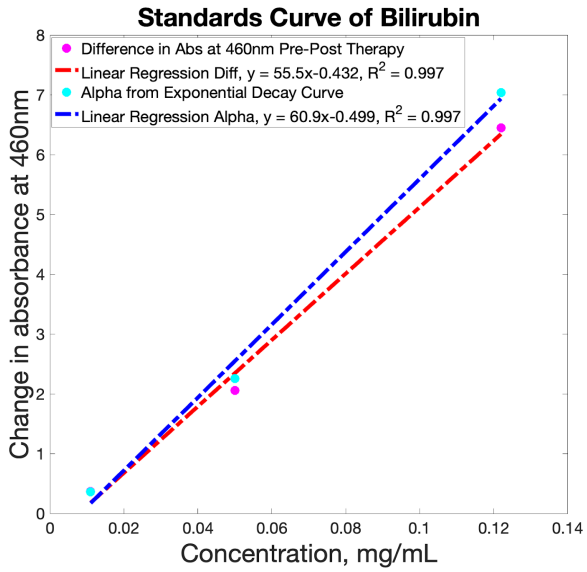

Figure 5. Linear standard curves that relate initial bilirubin concentration to change in absorbance at 460 nm and the initial absorbance, alpha, from a fitted exponential decay curve. These will be used to estimate bilirubin concentration from the phototherapy procedure.

The next step in validating the novel procedure was adding varying mixtures of both melanin and bilirubin to verify the regression could accurately predict the bilirubin concentration independent of the melanin concentration. To accomplish this validation we created

4 mixtures of high/low (0.05mg/ml and 0.2mg/ml) melanin and high/low (0.05mg/ml and 0.1mg/ml) bilirubin. These concentrations were decided since they represent the range of concentrations that are expected physiologically. Ideally, more combinations should be tested with higher concentrations of melanin but this research was focused on proof of concept and struggled to dissolve melanin at concentrations greater than 0.5mg/ml (see Challenges & Limitations section). After the four solutions were photobleached, exponential decay curves were fitted (see Figures 4 & 5).

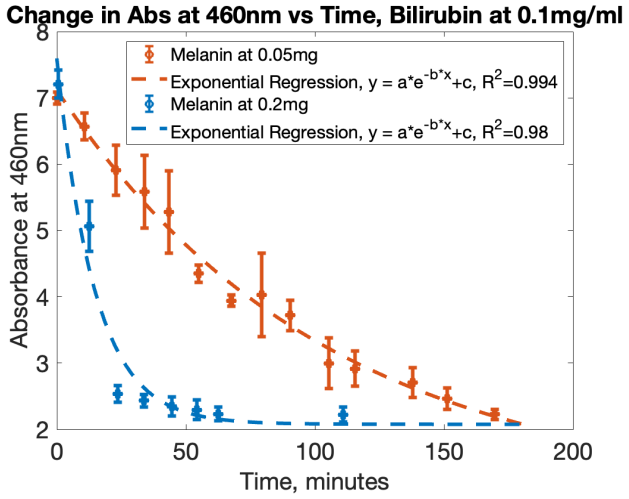

Figure 5. Absorbance at 460 nm during blue light exposure. Bilirubin concentration is 0.1mg/mL

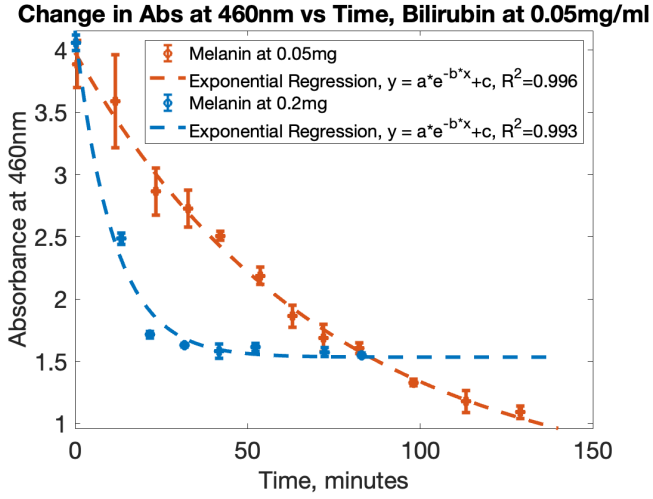

Figure 6. Absorbance at 460 nm during blue light exposure. Bilirubin concentration is 0.05mg/mL

Both the high melanin solutions photobleach much more rapidly than we have seen in both when generating the standards curve and in the low melanin groups (b coefficient mean: Low 0.01 vs High 0.08). We are currently unsure of the cause of this; our first guess would be due to the tris buffer breaking down and the pH of the solution being much more basic, which may catalyze the degradation process.

The alpha and delta values were used to estimate the initial concentration by the standard curves (see Table 1). Overall, the percent error was 9.44%+/-10.3%. However, this was mostly due to the low melanin/low bilirubin solution, which photo bleached much quicker than expected and seems to be an outlier in this group. Excluding that solution the percent error goes down to 4.5% +/-2.9%. The fitted alpha value was expected to perform better than directly measuring the delta because it should be more representative of the total absorbance due to bilirubin. In the small sample size, it is difficult to confirm this hypothesis but the alpha value is twice as accurate in the high concentration of melanin. Additionally, there does not appear to be a difference in accuracy in the high melanin concentration solution, which gives us hope that localized phototherapy could be used as a bilirubin measurement technique.

		Melanin Concentration			
		0.05 mg/ml		0.2 mg/ml	
Bilirubin Concentration	0.05 mg/ml	Delta	0.0582 (16.3%)	Delta	0.053 (5.9%)
		Alpha	0.0661 (32.1%)	Alpha	0.0513 (2.5%)
	0.1 mg/ml	Delta	0.0937 (6.3%)	Delta	0.0976 (2.4%)
		Alpha	0.1086 (8.6%)	Alpha	0.0988 (1.2%)

Table 1. Estimated concentration of bilirubin using both methods. The delta method takes the difference in absorbance at 460 nm before and after phototherapy. The alpha method fits an exponential decay curve to the data and the initial amount coefficient, alpha, is used. The percent error accompanies the estimated concentration.

Methods & Materials

Optimal Light Wavelength for Photobleaching

Below, Equations 1 and 2 were derived to find the expected extinction of bilirubin for a given wavelength (λ). The percent absorbance for bilirubin is based on

summing the total relative absorbances at a given wavelength, as in Figure 1. Then, the absorbance of bilirubin at the given wavelength is divided by the

$$1.\ E_{Br}(\lambda) = A_{\%Br}(\lambda)\phi_{Br}(\lambda)N_p$$

$$2.\ A_{\%Br}(\lambda) = \frac{A_{Br}(\lambda)}{\Sigma_i^M A_i(\lambda)}$$

Equations 1&2: Two derived equations for calculation the expected extinction rate of bilirubin ($E_{Br\%}(\lambda)$).

summation yielding the percent absorbance of the bilirubin at a specific wavelength. This percentage is multiplied by the quantum yield of the conversion of bilirubin to lumirubin for a given wavelength as seen in Equation 2. The quantum yield is the ratio between the number of isomerization events for a specific conversion and the total number of possible isomerization events possible (i.e. based on the number of photons). Finally, these two values are multiplied by the number of photons. The product is the total number of bilirubin molecules converted into lumirubin for a specific wavelength of light. In order to find the optimal wavelength for maximal bilirubin extinction, we used quantum yield data from Agati et al and absorbance data from Mahmoud et al. Since the number of protons is independent of wavelength, the term is unnecessary for the optimization of the equation. By plotting the product of the percent absorbance of bilirubin and the quantum yield of bilirubin with respect to wavelength and finding the maximum value gave approximately 470 nm as the optimal wavelength as seen in *Supplemental Figure 1*.

Bilirubin and Melanin Stock and Test Solution Preparation

Using stock solution protocols found on Sigma Aldrich, we used a 1M NaOH solution to dissolve both bilirubin and melanin. An ultrasonic bath was used to dissolve bilirubin into the basic solution. A rotating mixer in a cold room was used to dissolve melanin into solution. However, small aggregates of melanin remained even after 50x dilution. Therefore, the concentration of the melanin stock solution was estimated using an extinction coefficient spectrum from the Oregon Medical Laser Center in Portland[15]. The 10mm absorbance at 300 nm was used to estimate the concentration of the melanin stock solution. The test solutions were created by dissolving the stock solution in a 2M Tris buffer at 8.2pH.

Confirmation of Absorbance Spectra of Melanin and Bilirubin

Solutions of bilirubin at 1 mg/ml and melanin at 0.5ml/ml were created using the above procedure. Then these solutions were diluted by 5 times into the Tris buffer. After obtaining absorbance spectrums of all 4 solutions using 5uL from a ThermoScientific NanoDrop OneC spectrophotometer, the absorbance data was exported into Matlab. To generate the absorbance spectra plots, the data from the NaOH solutions was scaled to a relative absorbance of 1 at 450 nm for bilirubin and 400 nm for melanin. The absorbance data for the Tris solutions was multiplied by 5 after being scaled. This adjustment was done to understand the shape of the spectra, not the absolute magnitude. These were compared to spectra found in Mahmoud et al[10].

Phototherapy Procedure

Fill a spectroscopy cuvette with 4mL of a test solution and place it within the 3D printed holder, which places the cuvette directly against the LED array. The LED array is a 4.0 mW/cm^2 array centered at 470 nm purchased from Thorlabs. Once the test solution is inserted into the holder, 5uL is removed and tested on ThermoScientific NanoDrop OneC. Full absorbance spectrum data, from 200 nm to 800 nm, is generated 3 times for each time point. Between measurements, the device was covered to be shielded from ambient light.The test is continued until the absorbance spectrum stops changing between time points. Then the data is imported into Matlab. The change in absorbance is calculated by subtracting the last reading from the initial reading. The decay curves were created by determining the average times and absorbance values at 460 nm. The error bars represent the standard deviation of the 3 absorbance values. Exponential decay curves are fitted using Matlab's built-in fitting function. The function is “a*exp(-b*x)+c”, with the starting values a=4, b=0.05,

and c=1. Bilirubin is estimated using a linear standard curve which was created after photobleaching 3 solutions of bilirubin, 0.011mg/ml, 0.05mg/ml, and 0.122mg/ml. Linear regressions were performed on both the fitted exponential decay alpha value and the difference in 10mm absorption at 460 nm before and after phototherapy.

Computational Model

The computational model is a time-iterative model that estimates the concentrations of the differing chromophores during phototherapy: hemoglobin, melanin, and bilirubin's photoisomers[10]. The computational model uses a reaction rate found in Nii et al[16]., which is derived from a simple reaction equation: d[LR]/t='k' [EZ-BR]. Then using the relative absorbance spectrums of each chromophore, composite absorbance spectrums were created using the relative concentration to weigh each chromophore. The model estimates the skin absorption spectra at time intervals and creates concentration vs time curves (see *Supplemental Figure 2*). It also generates absorbance decay curves at specific wavelengths which can be compared to our experimental data.

Discussion

Significance & Innovation

Up until now, a lack of consideration for the influence of melanin on transcutaneous bilirubin measurements led to the perpetuation of inequality in healthcare by selectively marginalizing patients with darker skin tones. Existing bilirubinometers have a tendency to overestimate bilirubin concentration, resulting in a variety of consequences—most notably the prescription of excessive phototherapeutic treatments, which is associated with several (aforementioned) consequences. The only present means of avoiding this involves repeated heel stick blood samples—which also carry notable negative consequences, such as increasing the risk of hospital-acquired infections. In either case, hyperbilirubinemic neonates of darker complexions (especially Black patients) are currently left severely disadvantaged.

The significance of finding a solution to this problem is clear, and the results are very promising for future endeavors to remedy the negative relationship between skin color and neonatal healthcare. Overall, the results suggest that bilirubin concentrations can be accurately estimated by detecting changes in absorbance in response to the photoisomerization of bilirubin at a small test site. In our physical model, this remained true even after the addition of influential skin chromophores such as melanin that contribute significantly to the existing technical issues associated with bilirubinometers.

The novel combination of phototherapy and traditional spectrometry described offers several notable value propositions, such as:

- Mitigating the impact of race and skin tone on TcB measurements.
- Reducing the likelihood that neonates are prescribed phototherapeutic treatment unnecessarily as a result of overestimated TcB.
- Introduces a fundamentally new diagnostic method that employs common treatment-oriented technologies in a non-traditional way. This introduces a new methodology for solving future diagnostic issues attributable to variable patient demographics.
- Generating new knowledge regarding the rate of photoisomerization and decay of bilirubin in the skin that may be applied to solve other problems—such as difficulties measuring TcB non-invasively after phototherapy due to the dissonance between TcB and TSB concentrations. Currently, TcB is no longer representative of TSB after phototherapy due to the photobleaching of the skin.
    - Much of the information related to bilirubin, its conversion to lumirubin, and its processing out of the body is treated as a "black box" in engineering.

Challenges and Limitations

One of the most notable challenges faced while generating the data presented involved dissolving skin chromophores such as bilirubin and melanin under

physiological conditions—let alone physiological pH. This is largely attributable to the fact that most of the skin chromophores considered (especially bilirubin and melanin) are not naturally found in aqueous solutions, but rather in subcutaneous fat stores. Working with melanin was particularly difficult, and small specks or aggregates were extremely difficult to dissolve in melanin stock solutions regardless of the pH or concentration—even in strong bases. Even in cases where the skin chromophores were fully dissolved, the applicability of the results may be limited by the fact that the testing occurred under conditions that were distinct from physiological conditions.

The influence of the buffer spectra on the chromophore stock solutions also presented notable hurdles when collecting absorbance data. This is largely because the buffers considered—including Tris—often had relatively strong absorption peaks within the UV-Visible light range.

Another area of consideration is the relatively small sample size. This is in part attributable to the time scale associated with the full photoisomerization of bilirubin to lumirubin. While it was expected to be on the order of minutes, the multiple hours required for each test limited the number of samples the team was able to run within the time allotted for the project. The regular variance in absorption data collected using the ThermoFisher NanoDrop oneC may also be important to consider. It proved difficult to pipette the same volume of the solution onto the reader for every experiment, mainly due to the scale and sample size. Furthermore, bubbles in the liquid sample may have impacted data as well.

Future Work

The apparent exponential decay observed as bilirubin was photoisomerized into lumirubin is of particular relevance. The estimated bilirubin concentrations showcased in the results section were calculated either using the total change in absorbance by bilirubin before and after phototherapy, or by using values based on the full exponential curves fitted to the decay data. Contrary to the relatively short time frame expected, the photoisomerization of bilirubin regularly took several hours to fully convert to lumirubin and reach a horizontal asymptote in the decay curve. However, in the future, it would be ideal to be able to measure TcB within a much shorter time frame. An ideal method would use a smaller number of data points collected during the first few minutes of blue light therapy in order to predict the entire exponential decay curve in real time and estimate TcB on a shorter timescale. Alternatively, a brighter light could be used to accelerate the rate of photoconversion. However, more research needs to be done regarding the potential negative impacts associated with brighter light; a safety limit for the timescale employed in this technique has not yet been established.

Improvements could be made to the physical model employed, such as using a photodiode that measures the transmittance of light at a particular wavelength rather than using the Nanodrop oneC to reassess the entire spectrum at specific time intervals. This is beneficial because it would not only help generate more data points for future decay curves, but also be more representative of the eventual (ideal) handheld prototype device this technique is being designed for. Having more data points would likely make it easier to accurately predict complete decay curves on a shorter timescale. It is also worth considering a wider range of bilirubin and melanin concentrations in future tests to confirm that the proposed method remains viable for “edge” cases—at particularly high or low concentrations. Future tests should also consider the influence of the other known skin chromophores present in the skin—especially hemoglobin. Monitoring changes in the pH of the test solution may also be useful to ensure that the cuvette conditions remain as representative of physiological conditions as possible.

It may also be worth establishing that the decay rate of bilirubin observed is best represented by an exponential decay curve. Other curves were not strongly considered (such as polynomial decay curves) and may yield values that more accurately measure TcB.

Acknowledgments

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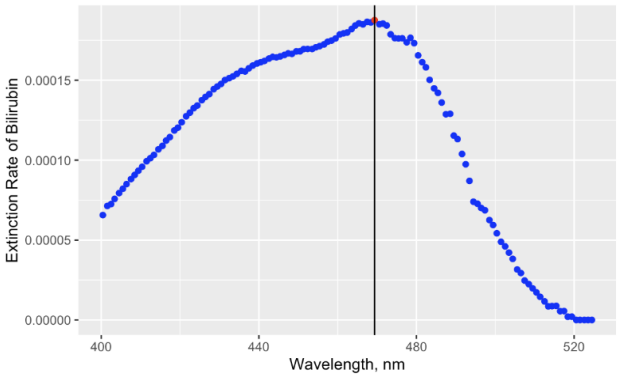
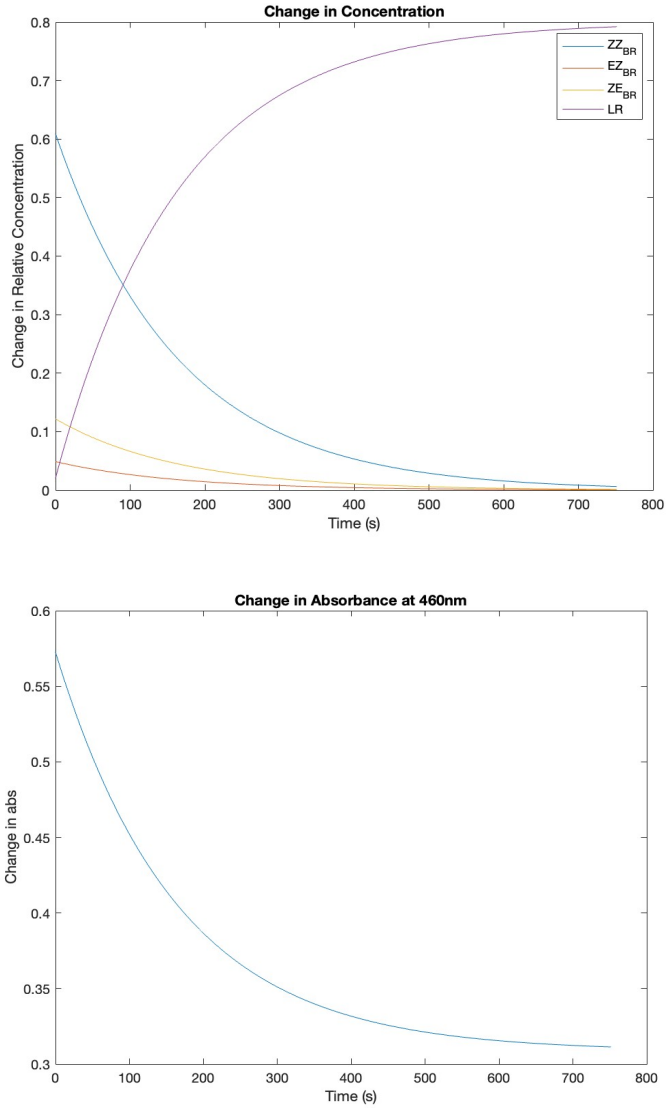
Supplemental Figures



Supplemental Figure 1. Calculated extinction rate of bilirubin plotted against wavelength. Relevant data sourced from *Quantum yield and skin filtering effects on the formation rate of bilirubin*[17].



Supplemental Figure 2. Both figures were created using the computational model of the phototherapy reaction in Matlab. (Top) Plot of the relative concentrations of ZZ_BR, ZE_BR, EZ_BR, and LR throughout a simulated phototherapy duration. (Bottom) Change in absorbance at 460 nm throughout the duration of a simulated phototherapy duration. 460nm was selected because it has the greatest change in absorbance and thus will be the easiest to detect in a physical model.

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Analysis of the Contributors and Implications of the Instillation of Racial Bias into the Infrared-Based Pulse Oximeter

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Bachelor of Science, School of Engineering

Eddy A. Trujillo

Spring, 2023

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

Advisor

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Introduction

While often unintentional, macroscale disparities—such as the 24% higher all-cause mortality rate among Black populations relative to Whites in the United States—can often be reproduced and explained by the structural inequalities that influence the development of health-related technologies (Benjamins et al., 2021). As biomedical technology becomes increasingly integral to the widespread provision of quality healthcare, careful consideration of the rules, biases, policies, and cultural influences that contribute to the racial discrimination evident in technological design today is undoubtedly vital for mitigating future healthcare disparities.

In order to illustrate the political and social consequences that result from a lack of attention to unique racial differences during the development of biomedical devices, I will focus on how the overestimation of oxygen saturation by pulse oximeters led to Black patients being 29% less likely to be prescribed COVID-19 therapy relative to Whites throughout the pandemic—a clear indicator of the role of a biomedical device in perpetuating racial inequality (Fawzy et al., 2022). The racial bias of pulse oximeters is well-documented and a variety of its implications within the medical environment have been thoroughly discussed—such as its impact on reducing the likelihood that Black patients are recognized as eligible for COVID-19 therapy. While recognizing its immediate healthcare impacts is important, current approaches generally fail to recognize the social and political implications of the bias, such as its immediate impact on mortality rates and its role in reinforcing existing socioeconomic disparities by increasing medical care costs for an already vulnerable and largely uninsured population.

Technological politics argues that the role of technological devices extends far beyond the technical work they perform (Winner, 1980). Drawing on this framework makes evident that *if* the role of biomedical devices in defining power relations between racial groups is ignored, the issues evident in current technology will remain unacknowledged and the pressure engineers feel to be cognizant of bias in the design of future devices may remain low—leading to the reproduction of unfair devices whose technical shortcomings perpetuate inequality. Understanding the widespread social implications of the infrared pulse oximeter adds pressure to address the device's technical deficiencies and stresses the role engineers can play in mitigating social injustice. To illustrate the influence of pulse oximeters on defining politically-relevant factors such as power relations between different groups and the perpetuation of racial injustice, I will analyze how the instillation of racial bias into the infrared-based pulse oximeter marginalizes Black and Hispanic patients by reducing their likelihood of receiving adequate COVID-19 therapies using a framework based on *technological politics*.

Background

Ever since the development of the first commercially available red and infrared light-based pulse oximeter by Dr. Takuo Aoyagi and Nihon Kohden in 1974, pulse oximetry has increased in popularity and accuracy over time (Bhattacharya, 2020). The technology was developed with the ultimate goal of quickly detecting blood oxygen saturation levels non-invasively—saving time and reducing the health risks associated with serum-based methods that require blood extraction.

Currently, the process for measuring oxygen saturation requires calculating the ratio between the amounts of 660 nm (red) and 940 nm (infrared) wavelength light transmitted through a thin piece of tissue; the most common location of measurement is through the finger.

Each wavelength corresponds with the peak absorbance wavelengths of oxyhemoglobin and reduced hemoglobin, representing oxygenated and deoxygenated blood, respectively (Jubran, 2015). Calculations using these measurements ultimately yield the percent oxygen saturation values used in clinical settings to make diagnostic and treatment decisions. Because of its design, infrared-based pulse oximetry is less accurate in individuals with darkly pigmented skin. This inaccuracy is particularly noticeable at hypoxic arterial oxygen saturation levels (Sao2); a study employing three different pulse oximeters found that Sao2 was overestimated at 60-70% oxygen saturation levels (hypoxic conditions) by 3.56 ± 2.45% in darkly pigmented subjects relative to lightly pigmented subjects (Bickler et al., 2005).

This inaccuracy has notable implications, as evidence suggests that accurate pulse oximetry can curtail mortality rates, reduce the lengths of emergency department visits, and increase the rate of detection of otherwise unnoticed hypoxemia (Enoch et al., 2016). Excluding these benefits from a population that already showcases increased mortality rates only further inflates existing disparities. The historical lack of consideration of minorities in healthcare and clinical studies, the locations and time periods in which the current infrared-based design was developed (in Japan during the 1970s and 1980s), and the priorities of the researchers developing this non-invasive method all contributed to the observed disadvantages individuals with darkly-pigmented skin experience with pulse oximetry.

Literature Review

A myriad of articles and research journals have addressed the now well-known issues inherent to the technology behind infrared-based pulse oximeters. Their analyses generally focus on the immediate, short-term implications of erroneous measurements without strong consideration of their overarching impacts—most of which extend far beyond the immediate

medical and healthcare-oriented atmosphere. To add, these analyses are generally outdated and fail to account for the inequitable impact that pulse oximeters have had on the diagnosis and treatment of Black and Hispanic patients, specifically during the eminent COVID-19 pandemic.

Importantly, in *Racial and Ethnic Discrepancy in Pulse Oximetry and Delayed Identification of Treatment Eligibility Among Patients With COVID-19*, Fawzy et al. work to establish the existence of systemic racial and ethnic biases in pulse oximetry during the COVID-19 pandemic specifically. This retrospective cohort study collected data from over 7000 COVID-19 patients across 5 different medical centers around the Baltimore and Washington, D.C. area. Predictions such as the consistent overestimation of oxygen saturation levels among Black and Hispanic patients relative to White patients were supported by the dissonance between measurements collected via infrared-based pulse oximetry and arterial blood gas measurements; arterial blood gas measurements were employed in the study as a gold standard technique that returns oxygen saturation levels irrespective of skin color. Fortunately, the team took their research a step further in an effort to formally establish an association between biased pulse oximetry measurements and their association with unperceived or delayed recognition of eligibility for oxygen threshold-specific therapy. Among 6673 patients with available pulse oximetry measurement data and other relevant, covariate data, the predicted overestimation of oxygen saturation levels among 1903 patients was linked to a systematic failure to identify Black and Hispanic patients who technically met the requirements for eligibility for oxygen threshold-specific therapy. The study also found a statistically significant delay in recognizing *when* patients met the clinically recommended threshold for initiating therapy (Fawzy et al., 2022). In summary, the data confirmed the aforementioned racially-biased findings—pulse oximeters overestimated blood oxygen levels by 1.2% in Black patients and 1.1% in Hispanic

patients. While 1.2% is a seemingly undaunting number, this led to Black and Hispanic patients being 29% and 23% less likely to be prescribed COVID-19 therapy, respectively. While this study does important work in recognizing the clinical relevance of racially-biased infrared pulse oximeter measurements during the recent and irrefutably relevant pandemic, its analysis fails to engage in the discussion of the politically-relevant implications of the findings.

Other articles, such as *An Overdue Fix: Racial Bias and Pulse Oximeters* focus primarily on the main contributors to the perpetuation of racial bias in pulse oximetry (Wickerson, 2022). For example, much of the discussion is dedicated to describing the inadequate requirements set by the Food and Drug Administration (FDA)—such as not requiring diversity in medical device evaluation. As a result, many pulse oximeter manufacturers elect not to test their medical devices on diverse populations. In the article, Wickerson also describes other issues with the medical device approval process, such as the streamlined 510(k) application process that allows manufacturers to gain approval to legally produce and market devices based on establishing that their new device is "substantially similar" to pulse oximeters that have been approved in the past. As a result, the racial bias that has been instilled into the technology since its approval in the 1980s has retained the ability to continue pervading the new devices that are marketed today. After describing the impacts that FDA regulations have had on modern pulse oximeters, Wickerson moves away from a pure research approach and engages in applied research—making many suggestions that may help eliminate bias in health technology in the future. Wickerson's discussion deviates from the purpose of this pure research paper—which is primarily to consider the societal, racial, and political factors that are largely defined by the racial bias present in pulse oximeters. Other articles, such as *Eliminating racial bias in medicine is an obligation we all share* by Ehrenfeld, follow a similar trajectory—focusing on the responsibility of the FDA, the

issues with the underlying processes for 510(k) clearance, and the lack of diversity in testing populations. He also considers the role that the device's development in Japan during the 1980s may have played in the lack of consideration and calibration for patients of darker skin tones. However, this article is similar to Wickerson's in that it engages in applied research and focuses largely on the determinants that help perpetuate racial bias in pulse oximetry measurements, but lacks notable discussion of the societal implications of the racial bias itself. Wickerson and Ehrenfeld do important work by identifying notable contributors to the persistence of racial bias in pulse oximeters, all of which help explain the complexity of the issue and how the pulse oximeter was able to have such an inequitable impact during a pandemic 40 years after its technology was first developed. In combination, these pieces of literature lay out much of the groundwork that is necessary for understanding—and in the future—addressing the problem by not only identifying existing contributors, but also the way these unaddressed contributors have had modern-day implications.

The rest of this paper is aimed at filling in the gaps necessary to extend the relevance of the issues with racially-biased pulse oximeters beyond the immediate technical, federal, and medical environments discussed above in order to expose the life-and-death social and socioeconomic implications of the problem.

Conceptual Framework

The *technological politics* framework accounts for societal, racial, and political factors that are largely defined by the development, approval, and popularization of technology. In his writing, Langdon Winner argues that technological artifacts have *politics*—which he defines as "arrangements of power and authority in human associations"—that extend beyond the limits of the mere technical work they perform. He expresses that the influence of technical design

choices on relations of power and privilege between groups cannot be ignored, as they can advantage some while significantly marginalizing others—regardless of the intentionality behind the design choices (Winner, 1980).

In this research project, I intend to use technological politics to provide an in-depth analysis of the political and social relevance of racially-biased pulse oximeter measurements. If we assume that pulse oximeters merely perform technical work, we fail to acknowledge their role in defining the quality of care, mortality rates, and racial inequity they have perpetuated during an unprecedented pandemic. I argue that pulse oximeters play an undoubted role in defining power relations between White and Black populations—significantly advantaging Whites. To accomplish this, I will hone in on the influence of overestimated oxygen saturation levels in Black patients on the decreased likelihood of receiving life-saving COVID-19 therapies in Baltimore, which consequentially has even greater political and social implications such as defining mortality rates and distributing medical financial burdens unequally—all clear indicators of the role of racially-based pulse oximetry in perpetuating racial inequality.

Analysis

The role of the bias instilled into the technology of pulse oximeters extends far beyond the immediate medical and healthcare-oriented atmosphere. The 1.2% and 1.1% average overestimations of oxygen saturation levels in Black and Hispanic patients, respectively, and the resultant 29% and 23% decreased likelihoods of treatment eligibility recognition relative to Whites play a powerful role in defining the power relations between minority groups and Whites, especially in the Baltimore and Washington, D.C. area (Fawzy et al., 2022). Evidence suggests that reliable pulse oximetry measurements can curtail mortality rates, reduce the lengths of emergency department visits, and increase the rate of detection of otherwise unnoticed

hypoxemia (Enoch et al., 2016). My writing focuses on corroborating evidence to provide a convincing analysis of the role racially-biased oxygen saturation measurements, reduced detection of hypoxemia, limited access to life-saving COVID-19 therapy, and extended hospital stays play in the social and political atmosphere by defining power relations. These inequitable technological solutions inevitably deepen the socioeconomic divide *and* gap in mortality rates between Whites and minority groups such as Blacks and Hispanics.

The Role of the Pulse Oximeter in Defining Mortality Rates

One of the statistics that best supports the importance of perceiving pulse oximeters as true social and political contributors is their definitive role in influencing mortality rates. This is arguably where pulse oximeters are most effective in defining power relations between White, Black, and Hispanic patients. The legally and clinically approved technology employed in clinics disadvantages patients of darker skin tones and reduces their *power* relative to White patients by reducing their likelihood of retaining their most valuable asset—life. Empirical data suggests that hospitalization and death varied greatly by race and ethnicity, as indicated by Table 1, which highlights the rate ratios of hospitalization and death due to COVID-19 in Black and Hispanic patients relative to Whites (CDC, 2022). While both figures are daunting, the starkly increased death rates of *1.6x* and *1.7x* indicate that Black and Hispanic populations died at nearly twice the rate of White populations without any notable biological contributors—suggesting that the determinants of these figures are unlikely to be genetically induced. The role that racially biased pulse oximeters may have played in defining these figures can be at least partially explained by

Table 1: Ratio of Hospitalization and Death Rates of Black and Hispanic Patients Relative to White Patients Due to COVID-19

	White Patients	Black Patients	Hispanic Patients
Hospitalization	1.0x	2.1x	1.8x
Death	1.0x	1.6x	1.7x

Note. Data from "Hospitalization and Death by Race/Ethnicity" Published by the CDC, on December 28, 2022. (CDC, 2022)

the aforementioned and well-established association between race-based overestimation of oxygen saturation levels and unrecognized eligibility for oxygen threshold-specific therapy (Fawzy et al., 2022).

Of all the points I attempt to establish in my analysis, the connection between the increased mortality rate and lack of treatment with COVID-19 therapy is likely the clearest and most straightforward. Fortunately, some treatments for COVID-19 like antiviral medications and antibody-related therapies are primarily dependent on factors that are unlikely to be susceptible to variations in race and skin tones—such as body temperature, pre-existing risk factors such as being immunocompromised, and other body metrics (CDC, 2020). However, treatment with oxygen therapy is typically only applied in particularly severe late-stage cases—such as in acute hypoxemic respiratory failure—and *is* primarily determined using blood oxygen saturation levels (*Oxygenation and Ventilation for Adults*, 2022). While this metric works appropriately for patients of lighter skin tones, the overestimation of oxygen levels by ~1.1-1.2% in Black and Hispanic patients by transcutaneous pulse oximeters works directly to disadvantage this population (Fawzy et al., 2022). The link between the race-based overestimation of oxygen saturation levels and unrecognized eligibility for oxygen therapy is well-established; this, combined with factors such as the almost exclusive employment of oxygen therapy in severe, high-risk, hypoxemic, late-stage cases works conjunctively to exacerbate their influence on the mortality rates of minority groups. The overestimation of blood oxygen saturation and the resultant decreased likelihood of receiving oxygen therapy under typically life-threatening conditions explain how pulse oximeters can act as determinants for the quality of healthcare received and increase mortality rates in patients of darker skin tones—both of which are concerning and inherently social and political issues.

The Link Between Racially-Biased Measurements and Healthcare Spending

The role of pulse oximeters in defining power relations goes beyond simply defining mortality rates. Even in cases where the delayed treatment of minorities with darker skin tones did not result in death or have a direct impact on the rates displayed in Table 1, the social implications of the overestimations were still incredibly significant; they instead acted to continue disadvantaging Black and Hispanic patients beyond the scope of the immediate clinical environment by indirectly increasing their healthcare-related financial burden. In a study that discussed general racial and ethnic disparities throughout the COVID-19 hospitalization process, it was found that among ~150,000 patients with data regarding race and ethnicity, ICU admission rates were 252.9 for Hispanics or Latinos, 190.7 for Blacks, and only 60.2 for Whites per 100,000 in the U.S. population (Acosta et al., 2021). This means that Hispanic and Black patients are 3.2-4.2 times more likely to be admitted to the ICU due to COVID-19.

The social relevance of these statistics becomes more significant when financial and economic factors are accounted for. The median cost of a typical COVID-19-related hospital stay is currently an egregious $1,772 per day. For patients admitted to the ICU, the median cost rises to $2,902 per day (Tucker, 2022). In culmination, these statistics indicate that Hispanic and Black patients are not only 3.2-4.2 times more likely to be admitted to the ICU, but therefore much more likely to be responsible for paying an additional $1,130 per day upon admission.

Some may argue that the implications of these figures cannot be interpreted properly without also comparing the lengths of time spent in each hospital admission type. Statistics indicate that for COVID-19, the average length of stay in the hospital was 6 days with a median total cost of $11,267. In contrast, the median length of stay in the ICU was 5 days with a median total cost of $13,443 (Tucker, 2022). While this diminishes the starkness of the cost difference,

other social factors play into the social significance of the issue—such as the fact that minorities in the Baltimore and Washington D.C. area are far more likely to be uninsured. Hispanic adults—with the highest admission rates to the ICU—bear the greatest financial burden of the increased costs with a 19% uninsured rate in 2021. Black patients, with an 11% uninsured rate, also bear a greater financial burden than White patients, with a 7% uninsured rate (Artiga, 2022). In culmination, this stands to show that even when the length of stay is accounted for, not only is the median total cost *still* higher, but the percentage of the Black and Hispanic patients responsible for bearing the full cost of their stay is *also* significantly higher. This speaks volumes, especially considering the widespread, pre-existing disparity in socioeconomic status between minority groups such as Blacks and Hispanics in the United States relative to Whites. Pulse oximeters unfairly increase the financial burden minority patients face, perpetuate socioeconomic disparity, and intensify the already present gap in financial and social power between Black, Hispanic, and White patients.

Conclusion

By employing technological politics, I have analyzed the role of racially-biased pulse oximeter measurements in defining socially-relevant power relations between Whites and minority populations such as Blacks and Hispanics. By impacting diagnostic and treatment decisions in the medical atmosphere—such as reduced recognition of hypoxemia and ultimate eligibility for COVID-19 therapy—pulse oximeters have directly impacted mortality rates during the COVID-19 pandemic and played a role in deepening the already prevalent socioeconomic gap between Whites and minority populations by increasing healthcare costs for an already financially vulnerable population.

Recognizing the implications of biases is imperative to achieving equitable healthcare outcomes and reducing disparities between racial groups; without analyses of the notable social and political contributions of biomedical devices, future changes in healthcare policies are unlikely to be effective at combatting resultant disparities. If the role of biomedical devices in defining power relations between racial groups is ignored, the issues evident in current technology will remain technically unaddressed and the pressure engineers feel to be cognizant of bias in the design of future devices may remain low—leading to the reproduction of unfair devices whose technical shortcomings perpetuate inequality. By analyzing the technological politics of biomedical devices, policy setters & public health workers, FDA regulators, and engineers alike can effectively (and simultaneously) work across various sectors to reduce racial disparity and work towards the provision of equitable healthcare.

Words: 3295

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Design of a Skin-Tone Inclusive Technique for the Non-Invasive, Transcutaneous Measurement of Bilirubin

Analysis of the Contributors to the Instillation of Racial Bias into the Infrared-Based Pulse Oximeter

A Thesis Prospectus
In STS 4500
Presented to
The Faculty of the
School of Engineering and Applied Science
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In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Biomedical Engineering

By
Eddy A. Trujillo

October 27, 2022

Technical Team Members: Van Spinelli, Sam Thapaliya, Cooper Yurish

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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Introduction

While often unintentional, macroscale disparities—such as the 24% higher all-cause mortality rate among Black populations relative to Whites in the United States—can often be reproduced and explained by the structural inequalities that influence the development of health-related technologies (Benjamins et al., 2021). Jaundice—yellowness of the skin that occurs as a result of the buildup of cutaneous bilirubin—is a condition observed in approximately 80% of preterm infants in their first week of life (Woodgate & Jardine, 2011). The current most common, economically feasible, and efficient method for measuring bilirubin levels in newborns non-invasively is less accurate in babies with darkly pigmented skin—a clear indicator of racial bias in an incredibly relevant piece of biomedical technology. My technical team will be developing a proof of concept for a racially-inclusive bilirubinometer using a novel combination of two existing technologies—showcasing the positive impact of considering *all* skin tones at the start of a biomedical device's development. Similar racial biases are also prevalent in other biomedical devices such as pulse oximeters, respirator masks, and spirometers (Davis, 2021). As biomedical technology becomes increasingly integral to the widespread provision of quality healthcare, careful consideration of the rules, biases, policies, and cultural influences that contribute to the racial discrimination evident in technological design today is undoubtedly vital for mitigating future healthcare disparities. In order to illustrate the political and social consequences that result from a lack of attention to unique racial differences during the development of biomedical devices, I will focus on how the overestimation of oxygen saturation by pulse oximeters across five hospitals in Baltimore led to Black patients being 29% less likely to be prescribed COVID-19 therapy relative to Whites—a clear indicator of the role of a biomedical device in perpetuating racial inequality. (Fawzy et al., 2022)

The significance of addressing these technical and social problems conjunctively lies largely in the negative consequences that would arise if engineers focused on only one. Without careful consideration of the raw technical shortcomings that make bilirubinometry melanin-dependent, the racial bias in this piece of technology would persist—further contributing to observed race-based healthcare disparities. However, if the role of biomedical devices in defining power relations between racial groups is ignored, the issues evident in current technology will remain unacknowledged and the pressure engineers feel to be cognizant of bias in the design of future devices may remain low—leading to the reproduction of unfair devices whose technical shortcomings perpetuate inequality.

To reduce and prevent racial bias in biomedical technologies, both the technical and social contributors to these biases must be considered. In the technical section of this prospectus, I propose a novel method that combines phototherapeutic techniques with traditional absorbance-based bilirubinometry to account for the influence of melanin on transcutaneous (through-the-skin) bilirubin measurements. To illustrate the influence of pulse oximeters on defining politically-relevant factors such as power relations between different groups and the perpetuation of racial injustice, I will analyze how the instillation of racial bias into the infrared-based pulse oximeter marginalizes Black patients and affects the likelihood of receiving adequate COVID-19 therapies using a framework based on *technological politics* (Winner, 1980).

Technical Research Project

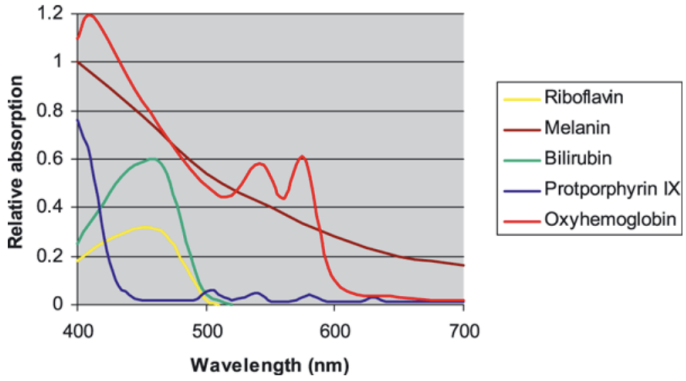
Neonatal (newborn) jaundice is a common condition caused by a build-up of bilirubin—a byproduct of hemoglobin destruction—in the blood; approximately 50% of term and 80% of preterm infants develop jaundice in their first week of life (Woodgate & Jardine, 2011). If left

untreated, jaundice can cause severe brain damage (Kernicterus), athetoid cerebral palsy, and hearing loss (CDC, 2020). Relevantly, up to 10% of term and 25% of preterm neonates require phototherapy for treatment, which involves the use of blue light as a phototherapeutic treatment to reduce the serum concentration of bilirubin in the blood (TSB) by photoisomerizing and reducing the cutaneous concentration of bilirubin in the skin (TcB) (Sarici et al., 2004).

Two methods are currently employed for monitoring and diagnosing hyperbilirubinemia. One method measures TSB directly by obtaining venous or heel stick blood samples; while accurate, this procedure is painful, invasive, and poses health risks such as an increased risk of infection—particularly in neonates (Onesimo et al., 2011). Alternatively, to mitigate these health risks, transcutaneous bilirubin screening measures TcB using a handheld *bilirubinometer*. Transcutaneous bilirubinometry directs specific wavelengths of light into the skin and measures the reflectance spectrum of the light that returns to the device; the reflectance spectrum varies based on the wavelengths of light that are absorbed by components in the skin such as bilirubin, hemoglobin, and melanin (Okwundu et al., 2017). These transcutaneous measurements work to provide a quantitative risk assessment for infants prone to severe hyperbilirubinemia or bilirubin encephalopathy (ABE) and allow for timely clinical decisions in areas with limited access to laboratory screenings (Sarici et al., 2004). Currently, bilirubin levels in neonates of darker skin

Figure 1

Absorbance Spectra of Common Skin Components



Note. From "Effects of Visible Light on the Skin," by B. Mahmoud, C. Hexsel, I. Hamzavi, and H. Lim. Copyright © 1999-2022 John Wiley & Sons, Inc.

tones are frequently overestimated, making the predictive utility of TcB screening lower in this racial population (Varughese et al., 2018). This can likely be explained by the high degree of overlap between the absorption spectrums of bilirubin and melanin as seen in Figure 1; higher cutaneous melanin concentrations can effectively ‘wash out’ minor fluctuations in bilirubin absorption and make it more difficult to accurately determine bilirubin concentrations in the skin (Mahmoud et al., 2008). The racial bias engrained into the current method used to attain efficient transcutaneous bilirubin measurements disproportionately affects darker skin-toned individuals, limits their access to quality care, and contributes to macroscale problems with race-based health disparities in the United States.

The overlap in absorbance between melanin and bilirubin makes it difficult to determine whether modulations in the reflectance spectra collected by bilirubinometers can be attributed to bilirubin specifically. Our team proposes that a combination of photobleaching bilirubin—as is done in phototherapy—and traditional reflectance-based measurements can be used to remedy the negative influence of melanin on TcB measurements. If reflectance spectra are collected both before and after locally photobleaching the bilirubin in an area of skin being measured, the differences observed between the two spectra could be attributed to local reductions in TcB specifically. This makes it possible to distinguish the level of absorption attributed to melanin from the absorption occurring due to bilirubin, enabling us to quantitatively account for the influence of skin tone on TcB measurements. Our ultimate goal is to generate evidence for a proof of concept that corroborates the clinical viability of this method.

This will be accomplished by focusing on three specific objectives, each of them important to elucidating the viability of our solution. Our first objective is to develop a computational framework that describes the relationship between bilirubin photoisomerization

and the input of specific wavelengths of light energy. In essence, this computational model should be capable of predicting changes in bilirubin concentration in response to a light energy input. Second, our team will construct a physical model to validate and/or adjust the aforementioned computational model. We will use an experimental setup that will allow us to analyze the absorption spectra of a glass cuvette filled with specified concentrations of melanin and bilirubin before and after phototherapeutic stimulation. Third, we will verify the clinical viability of our results by investigating the maximum intensity of light that can be used to safely, but efficiently photoisomerize bilirubin without cutaneous damage.

STS Research Project

Ever since the development of the first commercially available red and infrared light-based pulse oximeter by Dr. Takuo Aoyagi and Nihon Kohden in 1974, pulse oximetry has increased in popularity and accuracy over time (Bhattacharya, 2020). The technology was developed with the ultimate goal of quickly detecting blood oxygen saturation levels non-invasively—saving time and reducing the health risks associated with serum-based methods that require blood extraction.

Currently, the process for measuring oxygen saturation requires calculating the ratio between the amounts of 660 nm (red) and 940 nm (infrared) wavelength light transmitted through a thin piece of tissue; the most common location of measurement is through the finger. Each wavelength corresponds with the peak absorbance wavelengths of oxyhemoglobin and reduced hemoglobin, representing oxygenated and deoxygenated blood, respectively (Jubran, 2015). Calculations using these measurements ultimately yield the percent oxygen saturation values used in clinical settings to make diagnostic and treatment decisions. Because of its design, infrared-based pulse oximetry is less accurate in individuals with darkly pigmented skin. This inaccuracy is particularly noticeable at hypoxic arterial oxygen saturation levels (Sao2); a study employing three different pulse oximeters found that Sao2 was overestimated at 60-70% oxygen saturation levels (hypoxic conditions) by 3.56 ± 2.45% in darkly pigmented subjects relative to lightly pigmented subjects (Bickler et al., 2005).

This inaccuracy has notable implications, as evidence suggests that pulse oximetry can curtail mortality rates, reduce the lengths of emergency department visits, and increase the rate of detection of otherwise unnoticed hypoxemia (Enoch et al., 2016). Excluding these benefits from a population that already showcases increased mortality rates only further inflates existing

disparities. In order to illustrate the aforementioned general implications of racially-biased pulse oximetry measurements in a modern example, my analysis will be focused on the decreased likelihood of Black and Hispanic patients to be recognized as eligible for COVID-19 medications (Pérez Ortega, 2022). Data from 7000 COVID-19 patients treated across five hospitals in Baltimore confirmed the aforementioned racially-biased findings—pulse oximeters overestimated blood oxygen levels by 1.2% in Black patients. While 1.2% is a seemingly undaunting number, this led to Black patients being 29% less likely to be prescribed COVID-19 therapy (Fawzy et al., 2022). The unfortunate overestimation of arterial oxygen saturation levels was closely tied to a systemic failure to identify minority groups that should have qualified for treatment. Current considerations of the social relevancy of racially-biased pulse oximetry measurements focus primarily on clear indicators of racial bias in measurements, and occasionally on the perpetuation of racial disparities that the current technology induces (Bridger, 2022). While these factors are important, current approaches do not account for or fully describe the social and political ramifications the instillation of racial bias into the pulse oximeter has; it plays a critical role in defining the "arrangements of power and authority in human associations" (Winner, 1980).

The historical lack of consideration of minorities in healthcare and clinical studies, the locations and time period in which the current infrared-based design was developed, and the priorities of the researchers developing this non-invasive method all contributed to the observed disadvantages individuals with darkly-pigmented skin experience with pulse oximetry. The *technological politics* framework accounts for societal, racial, and political factors that are largely defined by the development, approval, and popularization of technology. In his writing, Langdon Winner argues that technological artifacts have politics; he expresses that the influence

of technical design choices on relations of power and privilege between groups cannot be ignored, as they can advantage some while significantly marginalizing others (Winner, 1980). In this research project, I intend to use technological politics to provide an in-depth analysis of the political and social relevance of racially-biased pulse oximeter measurements. If we assume that pulse oximeters merely perform technical work, we fail to acknowledge their role in defining the quality of care, mortality rates, and racial inequality they have perpetuated during an unprecedented pandemic. I argue that pulse oximeters play an undoubted role in defining power relations between White and Black populations—significantly advantaging Whites. To accomplish this, I will hone in on the influence of overestimated oxygen saturation levels in Black patients on the decreased likelihood of receiving life-saving COVID-19 therapies in Baltimore—a clear indicator of the role of a biomedical device in perpetuating racial inequality.

Conclusion

The primary deliverables for the technical problem discussed in this prospectus are a computational model that describes the relationship between light absorption and bilirubin concentration and a functioning physical model that shows the *in vitro* feasibility of our proposed solution. The STS research project will employ a framework based on technological politics to analyze the influence of racially-biased pulse oximeter measurements on the quality of care, mortality rates, and overarching inter-race power relations between Black and White patients during the COVID-19 pandemic. In combination, these deliverables will contribute to the future mitigation of healthcare disparities by addressing specific technical problems in an existing racially-biased biomedical device, and by highlighting the notable negative impacts that arise when the potential bias in biomedical devices is overlooked. Insights from the STS research project will showcase the importance of considering the impacts of the instillation of bias in

biomedical technology, and emphasize the importance of the melanin-dependent considerations being made in the technical project.

Word Count: 2061

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