LARS Information Note 022277

A MATHEMATICAL BASIS FOR THE DETECTION OF JAUNDICE BY SKIN REFLECTANCE ANALYSIS

BY

EDWARD J. HANLEY

FEBRUARY 1977

The Laboratory for Applications of Remote Sensing

Purdue University West Lafayette, Indiana

1977

ABSTRACT

The objective of this report is to provide a physical basis for the method of optically detecting jaundice. The skin is treated as a homogeneous scattering medium in which the bilirubin is dispersed. The purpose of the model is to determine in what manner the optical properties of the bilirubin affect the observed reflectance of the skin. The model is used to explain the correlation obtained from the 1975 Home Hospital study.

ACKNOWLEDGMENT

This work was supported in part by the National Institute of Health, National Inttitute of Arthritis, Metabolism and Digestive Diseases, Grant Number 1 R01 AM18871-01.

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Introduction

Bilirubin is formed by the breakdown of hemoglobin by the cells of the reticuloendothelial system, and it circulates in the blood in low concentrations. An increase in the bilirubin concentration in the bloodstream results in the clinical condition of jaundice; this increase may be due to a number of causes.

The study of Wiechel [1] sought to empirically determine the relation between skin reflectance and total serum bilirubin concentrations for relatively low ($\leq$ 10 mg/100 ml) bilirubin concentrations. Although total serum bilirubin concentration may not be a good indication of the risk of jaundice [9, 10, 19, 20], this parameter was examined since it is currently the most common measure of the degree of janudice. In the study, *in vivo* reflectance spectra in the visible region were recorded for a number of full term white infants in addition to the total serum bilirubin concentrations.

The skin is far from homogeneous and each of the components has both absorbing and scattering characteristics. In order to properly correlate experimental spectral reflectance measurements with skin physiology, it is desired to determine how the optical properties of the individual components are related to the bulk optical characteristics of the skin. Thus, in this report a mathematical model describing the optical behavior of the skin is presented.

Mathematical Model

The many different scattering and absorbing mechanisms involved in the optics of living human tissue make rigorous modeling of the skin impractical if not impossible. To circumvent this complexity, an approximate approach, phenomenological in nature, will be taken. This approach, which has previously been proposed as a modeling tool for describing the optics of highly scattering materials such as human tissue [2], involves treating light photons as particles

which may be scattered, absorbed or generated by the optical medium. The photons are assumed to obey diffusion and continuity equations and the approach is appropriately termed the photodiffusion method.

From photodiffusion theory (see Appendix A), the density of randomly directed photons, P, within an illuminated material is given as:

$$-D\nabla^2 P(x,y,z) = g(x,y,z) - P(x,y,z)/\tau \qquad (1)$$

where D = diffusion coeff. = $c_o/n(w+2k)$

τ = mean life time = n/wc_o

n = refractive index of medium

w = absorption coefficient

k = scattering coefficient (into one hemisphere)

g = generation function

The generation function describes the rate of generation of randomly distributed photons per unit volume. This function is also used to describe the randomization, by scattering, of collimated photons in cases where the material is illuminated by a beam. If the illuminating flux is diffuse, the generation function is set equal to zero.

The photon flux, F, at any point (x,y,z) within the medium is given by

$$F = -D\nabla P(x,y,z) \qquad (2)$$

Here, due to its actual fine grained complexity, the skin is considered to be homogeneous and isotropic. For the case where the tissue is uniformly illuminated by diffuse light and can be approximated by a semiinfinite slab of thickness, t, the reflectance of the layer is

$$R(t) = \frac{k}{q} \frac{\sinh(qt)}{\cosh(qt) + [(k+w)/q]\sinh(qt)} \qquad (3)$$

where $q = [w(2k+w)]^{\frac{1}{2}}$

For the limiting case of an infinitely thick layer (note that a highly absorbing medium such as a malignant melanoma or mole is optically thick although its physical dimensions may not be large), the reflectance becomes

$$R(\infty) = \frac{k}{q+w+k} \tag{4}$$

The problem has now been reduced to that first considered by Kubelka and Monk [3] with identical results. The Kubelka-Monk theory is, in fact, regarded as a special case of the more general approach [4].

For a mixture of two or more components, where the volume fraction of the individual components is variable and where each component has different absorbing and/or scattering coefficients, it is necessary to modify the absorption and scattering coefficients of the composite layer. The underlying assumptions for the photodiffusion model (see Appendix A) imply linearity in the differential absorption and scattering coefficients and this linearity allows superposition of the optical constants of the various components according to the volume fraction of each component. Thus the optical coefficients of a composite material will be a linear combination of the coefficients of the individual components and can be expressed as:

$$k = \sum_i k_i V_i \tag{5}$$

$$w = \sum_i w_i V_i \tag{6}$$

where k_i = scattering coefficient of component i

w_i = absorption coefficient of component i

V_i = volume fraction of component i

The Optical Detection of Jaundice

In order to test the model and demonstrate its utility in the optical detection of disease, the photodiffusion theory will be used to determine a basis for the optical detection of jaundice; available reflectance data for

jaundiced infants will be presented for verification of the model.

The experimental procedure of Wiechel [1] involved irradiating the blanched skin of an infant and recording the backscattered flux via a bifurcated fiber optic probe. For this physical situation, the skin will be modeled as a semi-infinite slab uniformly irradiated by diffuse light (neglecting edge effects). Although the characteristics of the light source and fiber optic probe used in the investigation are such that the illuminating flux was not truely diffuse, the assumption is justified since, in a highly scattering medium such as skin, any collimated component is rapidly reduced to a Lambertian distribution.

The reflectance of a semi-infinite slab uniformly irradiated with diffuse flux was given by equation (4). This expression may be rearranged to express the so-called Kubelka Monk ratio, ξ, in terms of the reflectance:

$$\xi = \frac{W}{k} = \frac{R}{2} + \frac{1}{2R} - 1 \tag{7}$$

It has been observed that the scattering coefficient of human skin is relatively independent of wavelength in the visible and near infrared regions. Accurate measurements of this coefficient over the entire spectrum are not presently available; however, the scattering coefficient for white skin has been reported as 55 cm^{-1} at 620 nm [5].

The bilirubin-albumen complex in solution has been observed to obey Beer's law [6] and it can be shown that the molecular extinction coefficient, ε, is related to the absorption coefficient, w, as follows [4]:

$$w = \frac{2\varepsilon C}{M} \tag{8}$$

where C = concentration

M = molecular weight

The majority (>97%) of bilirubin in the bloodstream of infants is bound to albumen, a serum protein [7]. The absorption maximum for the protein bound bilirubin occurs at 460 mμ [6,8-10] where the molecular extinction coefficient, ε, has been reported as 4.67×10^4 [6,11].

Now it is of interest to consider the Kubelka Monk (KM) ratio at 460 mμ, the absorption peak for bilirubin-albumen, for the jaundiced condition. Combining equations (8) and (6):

$$\xi_J = \xi_H(1-V_S) + \frac{2\varepsilon C}{Mk} V_S \tag{9}$$

where ξ_J = KM ratio for jaundiced skin

ξ_H = KM ratio for healthy skin

V_S = volume fraction of serum

Superficial blood in human skin will occupy about 5% of the total tissue volume. Thus newborns, whose hematocrit levels are typically 0.50, will have an average volume fraction of blood serum of 2.5%. The effect of blanching the skin is to squeeze blood out of the superficial capillaries and thus further reduce the volume fraction of serum. The magnitude of this reduction is, of course, dependent upon the applied pressure and this parameter could not be accurately controlled in the experiment by Wiechel [1]. For the purpose of the calculation, an estimated average value of 0.15% will be used for V_S.

The variation in the KM ratio due to an increased bilirubin-albumin concentration in the serum can be expressed as:

$$\Delta\xi = \xi_H - \xi_J = \frac{w}{k} - \frac{w}{k}(1-V_S) - \frac{2\varepsilon C}{Mk} V_S$$

or

$$\Delta\xi \simeq \frac{2\varepsilon C}{Mk} V_S \tag{10}$$

Therefore, a linear relation is expected between the change in KM ratio and the concentration of bilirubin in the blood. This relation is plotted in Figure 1 for the coefficients reported at 460 mμ.

In order to correlate the theoretical results with the experimental measurements of Wiechel [1], it is necessary to know the value of ξ_H at 460 mμ. Due to the variability of optical coefficients for individuals, some normalization technique is required. A possible normalization procedure becomes apparent upon examination of the KM ratio for normal individuals in the 400 to 500 mμ range [12,13]. A near linear relation is observed between the KM ratio and wavelength at 400, 440 and 500 mμ; additionally, the value of ξ_H at 460 mμ consistently is found to intersect this line at the 480 mμ level. Thus ξ_H was estimated from the reflectance data at 400, 440 and 500 mμ for each of the measurements on jaundiced infants reported by Wiechel [1] and $\Delta\xi$ then calculated. The resulting values are plotted in Figure 1 for comparison with the theoretical relation.

The datum shown in Figure 1 was analyzed statistically and a correlation coefficient, R^2, of 0.773 was determined for the linear regression of $\Delta\xi$ to the total serum bilirubin concentration, C; this indicates that a strong correlation exists. Considering the effects of uncertainty in the coefficients, experimental error, nonideal boundary conditions and the crude normalization approach used for the model in addition to the possibility that bilirubin was present in the serum while not bound to albumen and/or there was a significant volume of bilirubin absorbed by the superficial tissue, the correlation is more than adequately strong to justify the applicability of the model.

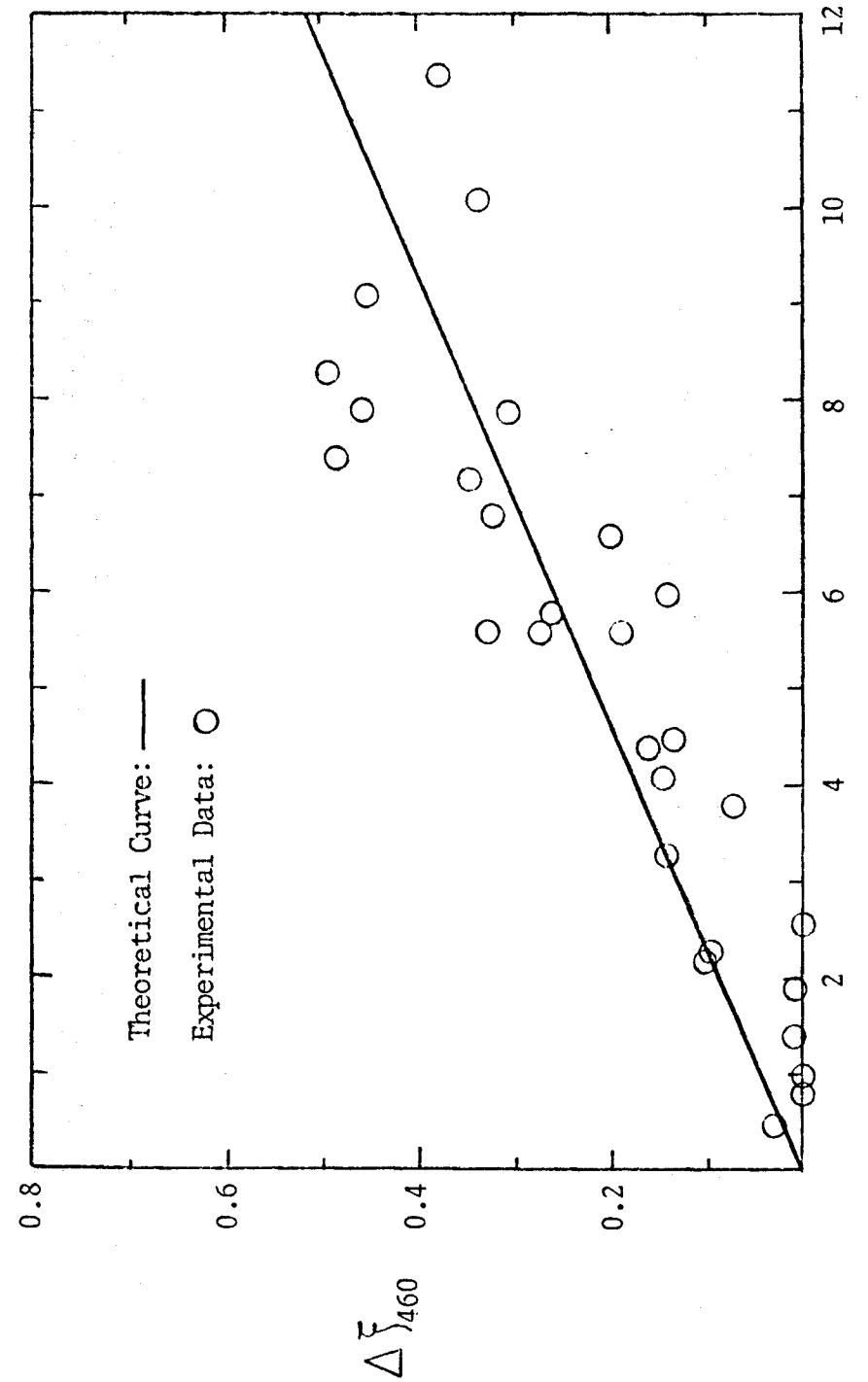

Figure 1. Change in KM ratio at 460 nm, $\Delta\xi_{460}$, vs Total Serum Bilirubin Concentration, C.

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APPENDIX A - PHOTODIFFUSION THEORY

The photodiffusion approach is an approximate method for describing the optical behavior of highly scattering mediums. The basic phenomenological approach can be traced back to Schuster [14] while Kubelka and Monk [3] expanded the theory and determined a solution for the one-dimensional case. The Kubelka-Monk theory was adapted to the problem of electron transport in semiconductors by McKelvey et al. [15], expanded to the general three dimensional case by Shockley [16], and transformed back to optical terms by Longini and Zdrowski [2].

In the photodiffusion theory, randomly distributed photons are assumed to obey diffusion and continuity equations. The density of randomly directed photons, P, within an illuminated material can be written as [17]:

$$-D\nabla^2 P(x,y,z) = g(x,y,z) - \frac{P(x,y,z)}{\tau}$$

where D = diffusion coefficient = $c_o/n(w+2k)$

τ = mean life time = n/wc_o

n = refractive index of medium

w = absorption coefficient

k = scattering coefficient (into one hemisphere)

g = generation function

Although the subscripts have not been included, the above equation can be considered on a per wavelength or frequency basis.

The generation function describes the rate of generation of randomly distributed photons per unit volume. This function is also used to describe the randomization, by scattering, of collimated photons in cases where the media is illuminated by a collimated flux (if the illuminating flux is diffuse, the generation function is set equal to zero).

The underlying assumptions of the photodiffusion approach, as presented by Longini and Zdrowski [2], are listed below on a one dimensional basis but have also been shown to be applicable to three dimensions [16].

(i) The material is considered to be divided by planes into many thin elementary sheets parallel to the surface of the sample.

(ii) If many different scattering and absorbing mechanisms are involved, these elementary sheets must be thick enough to completely include any of these mechanisms.

(iii) The elementary sheet must be thin enough so that both scattering and absorption are linearly dependent on thickness.

(iv) The optical properties of one elementary sheet are not correlated with those of the next.

Under these assumptions, differential equations may be set up and solved for transmission and reflection relations for the layer. Note that "differential" now refers to the minimum thickness of an elementary sheet and thus the minimum allowable sample thickness for which the equations will be correct.

The quantities w and k may be identified with the physical parameters of mean free path between scattering, S, and the mean total optical path before absorption, L, as follows [15]

$$k = 3/4S$$

$$w = 3/4L$$

For a mixture of two or more components where the volume fraction of the individual components is variable and where each component has different scattering and/or absorption coefficients, the coefficients of the composite layer need be modifed. The basic assumptions imply linearity in the differential absorption and scattering processes and this linearity allows superposition of the optical constants of the various components according to the volume fraction

of each component. Linearity in a "granular" structure, such as human tissue, is achieved if the scatterting and absorption of one elementary sheet are uncorrelated with those of the next. If the graulations are small enough, then the entire graules can be included in an elementary layer according to the second assumption. Because of the linearity, each coefficient is linear and the optical coefficients of the composite material will be a linear combination of the coefficients of the individual components and can be expressed as [2]:

$$k = \sum_i k_i V_i$$

$$w = \sum_i w_i V_i$$

where k_i = scattering coefficient of component i

w_i = absorption coefficient of component i

V_i = volume fraction of component i

The solution to the photodiffusion equation for the one dimensional case where a slab is uniformly irradiated with diffuse light (g = 0) is presented as follows. The photodiffusion equations reduces to

$$\frac{d^2P}{dx^2} - \frac{1}{D\tau} P = 0$$

which has the general solution

$$P(x) = C_1 e^{qx} + C_2 e^{-qx}$$

where

$$q = \sqrt{1/D\tau} = \sqrt{w(2k+w)}$$

Considering the slab to be of finite thickness, a, the boundary conditions associated with the photon flux, F, are as follows:

$$\text{(a) at } x = 0,\ F = -D\frac{dP}{dx}\bigg|_o = F_o[1-R(a)] = -Dq(C_1-C_2)$$

$$\text{(b) at } x = z,\ F = -D\frac{dP}{dx}_a = F_oT(a) = -Dq(C_1e^{qa}-C_2e^{-qa})$$

where R(a) and T(a) are the reflection and transmission coefficients for the layer of thickness a.

The following boundary conditions are derived from consideration of the photon density

$$\text{(c) at } x = 0,\ P(0) = P_o = C_1 + C_2$$

$$\text{(d) at } x = 0,\ P_o = F_o[1+R(a)]/C$$

$$\text{(e) at } x = a,\ P(a) = C_1e^{qa} + C_2e^{-qa}$$

$$\text{(f) at } x = a,\ P(a) = F_oT(a)/C$$

where C is the velocity of light in the medium.

These equations can now be solved with the following results:

$$T(a) = \frac{1}{\cosh(qa) + \frac{k+w}{q}\sinh(qa)}$$

$$R(a) = \frac{k\sinh(qa)}{q\cosh(qa)+(k+w)\sinh(qa)}$$

As the slab thickness is increased to infinity, the reflectance becomes

$$R(\infty) = \frac{k}{k+w+q}$$

It has been tacitly assumed that the medium bounding the slab is non-reflecting and has the same index of refraction as the slab. Solutions to more complex geometries are available in the literature [17,18,5].