On the Detection of Peripheral Cyanosis in Individuals with Distinct Levels of Cutaneous Pigmentation

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***Abstract*— Peripheral cyanosis, the purple or blue coloration of hands and feet, can represent the initial signs of life-threatening medical conditions such as heart failure due to coronary occlusion. This makes its effective detection relevant for the timely screening of such conditions. In order to reduce the probability of false negatives during the assessment of peripheral cyanosis, one needs to consider that the manifestation of its characteristic chromatic attributes can be affected by a number of physiological factors, notably cutaneous pigmentation. The extent to which cutaneous pigmentation can impair this assessment has not been experimentally investigated to date, however. Although the detection of peripheral cyanosis in darkly-pigmented individuals has been deemed to be impractical, data to support or refute this assertion are lacking in the literature. In this paper, we address these issues through controlled *in silico* experiments that allow us to predictively reproduce appearance changes triggered by peripheral cyanosis (at different severity stages) on individuals with distinct levels of cutaneous pigmentation. Our findings indicate that the degree of detection difficulty posed by cutaneous pigmentation can be considerably mitigated by selecting the appropriate skin site to perform the observations.**

***Index Terms*— cyanosis, skin, pigmentation, reflectance, predictive simulation.**

I. Introduction

Peripheral cyanosis refers to the purple or blue coloration of extremities (hands and feet) that becomes apparent when oxygen demand exceeds supply in the dermal tissues [1], [2], [3]. This may result from peripheral circulatory failure (*e.g.*, due to reduce cardiac output), peripheral vasoconstriction (*e.g.*, due to hypothermia), or peripheral vascular occlusion (*e.g.*, due to arterial thrombosis) [2], [3], [4]. In most cases, it is associated with the presence of high levels of deoxygenated hemoglobin (dexoyhemoglobin) in these tissues [1], [4]. However, it may be also prompted by the presence of abnormal amounts of one or more types of dysfunctional hemoglobins, namely methemoglobin (MetHb), sulfhemoglobin (SulfHb) and carboxyhemoglobin (CarboxyHb), in the blood stream [2], [3].

Since peripheral cyanosis may represent the initial signs of serious medical conditions that can lead to a life-threatening situation (*e.g.*, a myocardial infarcation) [2], [3], [4], its effective detection by health-care professionals can play an important role in preventing such an outcome. To achieve this objective, however, it is necessary to account for physiological factors that can affect the manifestation of peripheral cyanosis (Fig. 1 (leftmost)). Among these factors, one can highlight an individual's level of cutaneous pigmentation. In fact, it has been often claimed that the detection of peripheral cyanosis in darkly-pigmented individuals is problematic [1], [2], [4]. However, as stated by Baernstein and Elmore [2], data to support or refute this assertion are not readily available in the literature.

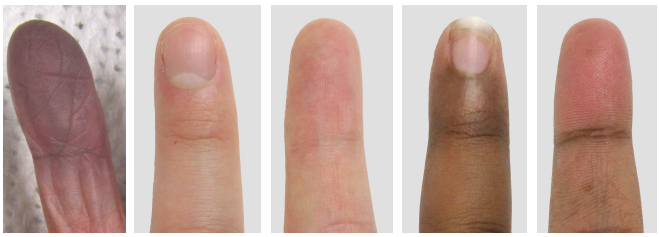

Fig. 1. Photographs depicting a cyanotic and normal skin appearances. Leftmost photograph: a cyanotic palmar fingertip (courtesy of James Heilman, MD). Remaining photographs, from left to right: dorsal and palmar surfaces of fingers belonging to a lightly pigmented and a darkly pigmented specimen, respectively.

This lack of data may be explained by a number of practical limitations associated with *in vivo* experiments. For example, in order to obtain a sufficiently comprehensive volume of data to verify this claim, one would need a variety of test cases that may not be safe to elicit on live subjects. In addition, these test cases would likely involve variations on selected biophysical variables, while other variables would be kept fixed during the different measurement instances. Such controlled *in vivo* experimental set-up might be difficult to attain during "wet" laboratory procedures involving live subjects.

In this paper, we systematically investigate the extent to which cutaneous pigmentation can impair the detection of peripheral cyanosis. In order to overcome the *in vivo* testing limitations outlined above, we performed controlled *in silico* experiments. These experiments were carried out using a first-principles light transport model for human skin, known as HyLIoS (*H*yperspectral *L*ight *I*mpingement on *S*kin) [26], and biophysical data provided in the literature. More specifically, we compared cyanotic appearance changes elicited on individuals with distinct levels of cutaneous pigmentation. Besides considering different stages of peripheral cyanosis severity, we also examine its manifestation at skin sites with distinct pigmentation characteristics, namely the dorsal surface of the fingers and the palmar fingertip (Fig. 1). Our findings indicate that the putative masking effects of

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TABLE I

HYLIOS PARAMETERS EMPLOYED IN THE SPECIFIC CHARACTERIZATION OF THE SKIN TISSUES FOUND IN THE DORSAL SURFACE AND IN THE PALMAR FINGERTIP OF THE FINGERS BELONGING TO THE LIGHTLY (LP) AND DARKLY (DP) PIGMENTED SPECIMENS CONSIDERED IN THIS INVESTIGATION.

Parameter	Dorsal Surface		Palmar Fingertip		References
	LP	DP	LP	DP	
Stratum Corneum Thickness (cm)	0.001	0.002	0.013	0.026	[5], [6], [7], [8], [9]
Stratum Granulosum Thickness (cm)	0.0046	0.0015	0.0123	0.006	[9], [10]
Stratum Spinosum Thickness (cm)	0.0046	0.0015	0.0123	0.006	[9], [10]
Stratum Basale Thickness (cm)	0.0046	0.0015	0.0123	0.006	[9], [10]
Papillary Dermis Thickness (cm)	0.02	0.023	0.02	0.023	[11], [12]
Reticular Dermis Thickness (cm)	0.125	0.2	0.125	0.2	[11]
Stratum Granulosum Melanosome Content (%)	0.0	5.0	0.0	0.25	[13], [14], [15]
Stratum Spinosum Melanosome Content (%)	0.0	5.0	0.0	0.25	[13], [14], [15]
Stratum Basale Melanosome Content (%)	1.0	5.0	0.15	0.25	[13], [14], [15]
Stratum Granulosum Colloidal Melanin Content (%)	0.9	5.0	0.06	0.25	[13], [14], [16]
Stratum Spinosum Colloidal Melanin Content (%)	0.9	5.0	0.06	0.25	[13], [14], [16]
Stratum Basale Colloidal Melanin Content (%)	0.9	5.0	0.06	0.25	[13], [14], [16]
Stratum Basale Melanosome Dimensions ($\mu m \times \mu m$)	0.41×0.17	0.69×0.28	0.41×0.17	0.69×0.28	[17]
Melanosome Eumelanin Concentration (g/L)	32.0	50.0	32.0	50.0	[18], [19]
Melanosome Pheomelanin Concentration (g/L)	2.0	4.0	2.0	4.0	[18], [19]
Dermal Oxyhemoglobin Fraction (%)	90.0	90.0	90.0	90.0	[20]
Functional Hemoglobin Concentration in Blood (g/L)	147.0	147.0	147.0	147.0	[21]
Papillary Dermis Blood Content (%)	0.5	0.5	0.5	0.5	[22], [23], [24]
Reticular Dermis Blood Content (%)	0.2	0.2	2.0	2.0	[22], [23], [25]

cutaneous pigmentation, particularly on darkly-pigmented individuals, can be considerably minimized by selecting observation sites more susceptible to the chromatic variations associated with peripheral cyanosis.

II. IN SILICO EXPERIMENTAL SETUP

In the investigation described in this paper, we employed HyLIoS to compute directional-hemispherical reflectance curves (Figs. 2 and 4) for selected skin specimens subjected to different stages of peripheral cyanosis severity. We note that the predictive capabilities of this model have been extensively evaluated through quantitative and qualitative comparisons of its outcomes with actual measured data [26].

Within the HyLIoS' geometrical-optics formulation, a ray interacting with a given skin specimen can be associated with any selected wavelength within a spectral region of interest. Hence, this model can provide reflectance curves with different spectral resolutions. For consistency, however, we considered a spectral resolution of 5 nm in all curves depicted in this work, which were computed using a virtual spectrophotometer [27]. In their computation, we considered an angle of incidence of 10° and 10^{6} sample rays.

To enable the full reproduction of our *in silico* experimental results, we made HyLIoS available online [28] via a model distribution system [29]. This system enables researchers to specify experimental conditions (*e.g.*, angle of incidence and spectral range) and specimen characterization parameters (*e.g.,* pigments and water content) using a web interface [28], and receive customized simulation results. In addition, the supporting biophysical data (*e.g.*, refractive index and extinction coefficient curves) used in our investigation are also available online [30].

In our *in silico* experiments, we considered two skin specimens with distinct levels of cutaneous pigmentation, henceforth referred to as lightly pigmented and darkly pigmented, respectively. In addition, for each specimen, we considered two skin sites, namely the dorsal surface of their index finger and the corresponding palmar fingertip. The datasets used in the specific characterization of these sites are provided in Table I, while the dataset containing the remaining parameters used in the general characterization of these sites is provided in Table II. The selection of values for these datasets was based on physiologically valid ranges provided in related references, which are also listed in Tables I and II.

The datasets mentioned above were employed to compute the baseline reflectances for the four selected skin sites in their normal state. In order to compute their reflectances associated with different stages of peripheral cyanosis severity, we considered the combined impact of the dermal oxygenation fraction (given in %) and the reticular dermis blood content (given in % and denoted by v_{blood}^{rd}) on the manifestation of peripheral cyanotic chromatic attributes [31], [32]. More specifically, the values originally assigned to these parameters (provided in Table I) were replaced by the values depicted in Table II. We note that the former parameter can be represented by $100 - f_{deoxy}$, where f_{deoxy} (given in %) indicates the fraction of deoxyhemoglobin to the total amount of functional hemoglobins present in the dermal tissues. We also remark that, for v_{blood}^{rd} variations, we considered ranges provided in the related literature [24]. Finally, since cyanotic skin appearances prompted by the presence of abnormal amounts of dysfunctional hemoglobin are relatively rare [33], particularly when compared to cyanotic skin appearances associated with the presence of high levels of dexoyhemoglobin, their investigation was deferred to future work.

We also generated skin swatches (Figs. 3 and 5) to complement our investigation. Their chromatic attributes were obtained from the convolution of a selected illuminant's spectral power distribution spectrum, the computed reflectance data and the broad spectral response of the human photoreceptors

TABLE II

HyLIoS parameters employed in the general characterization of all skin specimens considered in this investigation. The acronyms SC, SG, SS, SB, PD and RD refer to the skin layers considered by HyLIoS: Stratum Corneum, Stratum Granulosum, Stratum Spinosum, Stratum Basale, Papillary Dermis and Reticular Dermis, respectively.

Parameters	Values	References
Aspect Ratio of Skin Surface Folds	0.1	[36], [37]
MetHb Conc. in Blood (g/L)	1.5	[38]
CarboxyHb Conc. in Blood (g/L)	1.5	[39]
SulfHb Conc. in Blood (g/L)	0.0	[40]
Blood Bilirubin Conc. (g/L)	0.003	[41]
SC β-carotene Conc. (g/L)	2.1E-4	[42]
Epidermis β-carotene Conc. (g/L)	2.1E-4	[42]
Blood β-carotene Conc. (g/L)	7.0E-5	[42]
SC Water Content (%)	35.0	[43], [44]
Epidermis Water Content (%)	60.0	[43], [45]
PD Water Content (%)	75.0	[43], [45]
RD Water Content (%)	75.0	[43], [45]
SC Lipid Content (%)	20.0	[46]
Epidermis Lipid Content (%)	15.1	[43],[47], [48]
PD Lipid Content (%)	17.33	[43], [47], [48]
RD Lipid Content (%)	17.33	[43],[47], [48]
SC Keratin Cont. (%)	65.0	[49], [50], [51]
SC Urocanic Acid Density (mol/L)	0.01	[52]
Skin DNA Density (g/L)	0.185	[43], [53], [54]
SC Refractive Index	1.55	[55], [56]
Epidermis Refractive Index	1.4	[55], [57]
PD Refractive Index	1.39	[55], [58]
RD Refractive Index	1.41	[55], [58]
Melanin Refractive Index	1.7	[59]
PD Scatterers Refractive Index	1.5	[60]
Radius of PD Scatterers (nm)	40.0	[61]
PD Fraction Occupied by Scatterers (%)	22.0	[22]

TABLE III

Stages of peripheral cyanosis severity considered in this investigation. These correspond to the combined impact of increases in the f_{deoxy} (fraction of deoxyhemoglobin to the total amount of functional hemoglobins present in the dermal tissues) and v_{blood}^{rd} (reticular dermis blood content) parameters.

Stage	f_{deoxy} (%)	v_{blood}^{rd} (%)
Cyanotic I	25.0	5.0
Cyanotic II	50.0	10.0
Cyanotic III	75.0	15.0

[34]. This last step was performed by employing a standard XYZ to sRGB conversion procedure [35] and considering three CIE standard illuminants, namely D65, D50 and A [34]. Since the resulting qualitative observations remained unchanged regardless of which one we used, we elected to present in this paper the swatches generated using the D65 (daylight) illuminant to conserve space.

III. Results and Discussion

As peripheral cyanosis becomes noticeable with increases in f_{deoxy} and v_{blood}^{rd}, the corresponding spectral reflectance curves of the affected skin sites asymptotically converge to a reflectance curve with a markedly low magnitude. This curve, henceforth referred to as the reflectance minima (R_{min}) curve, varies from one skin site to another. More specifically,

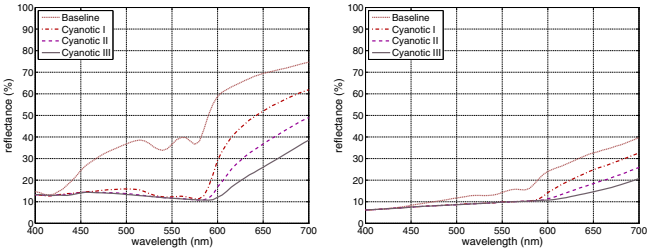

Fig. 2. Reflectance curves computed for the dorsal surface of the fingers belonging to the lightly (left) and darkly (right) pigmented specimens considered in this investigation. These curves were obtained using the datasets provided in Tables I and II. However, for the computation of the cyanotic curves, we have modified the values assigned to the f_{deoxy} and v_{blood}^{rd} parameters in order to elicit the distinct stages of peripheral cyanosis considered in this investigation (Table II).

Fig. 3. Skin swatches depicting hue transitions on the dorsal surface of the fingers belonging to the lightly (top) and darkly (bottom) pigmented specimens considered in this investigation. From left to right, these transitions correspond to increasing degrees of peripheral cyanosis severity, namely from baseline to cyanotic stages I, II and III (Table II), respectively. These swatches were generated considering a D65 illuminant [34] and using the corresponding skin spectral responses computed using the HyLIoS model (Fig. 2).

the more abundant is the presence of melanin (either in the eumelanin or pheomelanin form) in a given site, the faster is the convergence (notably in 400 to 580 nm region) and the lower is the overall magnitude of the corresponding R_{min} curve. These aspects can be observed in the reflectance graphs presented in Figs. 2 and 4.

Accordingly, the fastest convergence to the lowest R_{min} curve verified in our experiments was elicited at the dorsal surface of the finger belonging to the selected darkly pigmented specimen (Fig. 2 (right)). As a result, while one can observe the characteristic transition from a typical skin coloration to cyanotic hues in the skin swatches generated for the selected lightly pigmented specimen (Fig. 3 (top)), the same cannot be observed for the selected darkly pigmented specimen (Fig. 3 (bottom)).

Clearly, the presence of melanin can mask variations on spectral responses associated with changes in the contents of other pigments found in the cutaneous tissues such as the different types of hemoglobin. Accordingly, the noninvasive measurement of blood related properties (*e.g.*, oxygen saturation levels [1]) is usually performed at hypopigmented sites, such as the palmar fingertips, characterized by a reduced melanin content (more than fivefold lower than

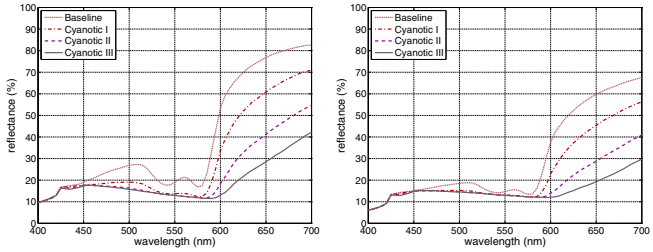

Fig. 4. Reflectance curves computed for the palmar fingertips of the lightly (left) and darkly (right) pigmented specimens considered in this investigation. These curves were obtained using the datasets provided in Tables I and II. However, for the computation of the cyanotic curves, we have modified the values assigned to the f_{deoxy} and v_{blood}^{rd} parameters in order to elicit the distinct stages of peripheral cyanosis considered in this investigation (Table II).

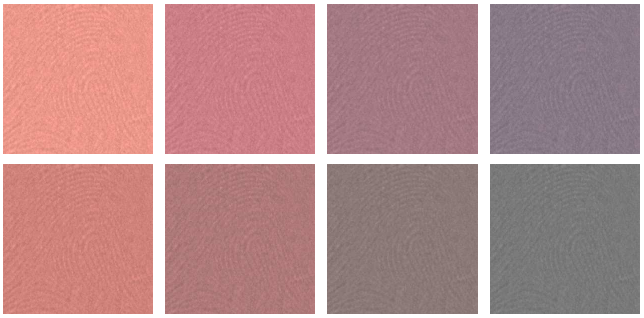

Fig. 5. Skin swatches depicting hue transitions on the palmar fingertips of the lightly (top) and darkly (bottom) pigmented specimens considered in this investigation. From left to right, these transitions correspond to increasing degrees of peripheral cyanosis severity, namely from baseline to cyanotic stages I, II and III (Table II), respectively. These swatches were generated considering a D65 illuminant [34] and using the corresponding skin spectral responses computed using the HyLIoS model (Fig. 3).

in the nonpalmoplantar regions [14]) and increased blood content [62]. These characteristics also make these sites more susceptible to the chromatic variations associated with peripheral cyanosis. For these reasons, we have also examined the spectral responses of the selected specimens' palmar fingertips.

Indeed, the spectral responses elicited at the palmar fingertip of the selected lightly pigmented specimen resulted in the slowest convergence to the corresponding R_{min} curve (Fig. 4 (left)). In addition, this curve is marked by the highest overall magnitude among the R_{min} curves computed during our experiments. Consequently, one can again observe the characteristic transition from a typical fingertip coloration to cyanotic hues in the swatches generated for this specimen's palmar site (Fig. 5 (top)). More importantly, the convergence of the reflectance curves computed for the selected darkly pigmented specimen' palmar fingertip (Fig. 4 (right)) is considerably slower than that of the reflectance curves computed for the nonpalmar surface (Fig. 2 (right)). Moreover, we remark that the curves for the darkly pigmented specimen's palmar fingertip converged to a R_{min} curve with a higher magnitude than the corresponding R_{min} curve computed for the nonpalmar surface. Hence, by selecting the palmar fingertip as the observation site, one may be also able to detect cyanotic hue variations in darkly pigmented specimens as illustrated by the swathes depicted in Fig. 5 (bottom)).

In summary, our findings demonstrate that it may not be possible to visually detect peripheral cyanosis in darkly pigmented individuals when one selects a palmar surface as the observation site. Our *in silico* experiments indicate that this detection difficulty is largely associated with dominant role played by melanin on the absorption of visible light, particularly in the 400 to 580 nm region. However, our findings also show that the masking effects of melanin can be substantially mitigated by selecting a hypopigmented area, such as the palmar fingertip, as the observation site.

IV. Concluding Remarks

The importance of detecting peripheral cyanosis is directly associated with the life-threatening risks posed by the medical conditions that can trigger it. Since these conditions are not exclusively associated with a specific level of cutaneous pigmentation, efforts should be directed toward making the effective detection of peripheral cyanosis universal, *i.e*, less dependent on a patient's pigmentation characteristics. These efforts will likely require pairing *in vivo* observations with *in silico* experiments such as those reported in this work.

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