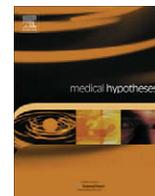




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Harnessing color vision for visual oximetry in central cyanosis

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ABSTRACT

Central cyanosis refers to a bluish discoloration of the skin, lips, tongue, nails, and mucous membranes, and is due to poor arterial oxygenation. Although skin color is one of its characteristic properties, it has long been realized that by the time skin color signs become visible, oxygen saturation is dangerously low. Here we investigate the visibility of cyanosis in light of recent discoveries on what color vision evolved for in primates. We elucidate why low arterial oxygenation is visible *at all*, why it is perceived as blue, and why it can be so difficult to perceive. With a better understanding of the relationship between color vision and blood physiology, we suggest two simple techniques for greatly enhancing the clinician's ability to detect cyanosis and other clinical color changes. The first is called "skin-tone adaptation", wherein sheets, gowns, walls and other materials near a patient have a color close to that of the patient's skin, thereby optimizing a color-normal viewer's ability to sense skin color modulations. The second technique is called "biosensor color tabs", wherein adhesive tabs with a color matching the patient's skin tone are placed in several spots on the skin, and subsequent skin color changes have the effect of making the initially-invisible tabs change color, their hue and saturation indicating the direction and magnitude of the skin color shift.

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Introduction

Skin color modulations have long been realized to be of diagnostic value, and are still important to clinicians today. For example, of the approximately 10,000 medical conditions listed in WrongDiagnosis.com, 644 (or about 6%) list skin color changes as a symptom; and of the 500 most prevalent conditions, 51 (10%) list skin color changes. Of the color-presenting medical conditions mentioned, pallor, cyanosis, and yellow skin make up nearly three-quarters of the skin color-presenting disorders (41%, 24% and 10%, respectively). What underlies this clinical sense color vision bestows? As we will see, although it is not remarkable that dichromats cannot sense clinical skin color modulations, it is remarkable that color-normals *can* sense them. Recent research suggests that trichromatic color vision among primates evolved with cone sensitivities specifically designed to sense oxygenation modulations in the skin. Here we describe how, in light of this research, we can acquire a new appreciation for the mechanisms underlying our perception of clinical color changes such as cyanosis. We then point out how our "oximetric color sense" – while effective at sensing color signals due to emotion or state – is handicapped for sensing clinical skin color changes, such as central cyanosis. Finally, we describe two simple techniques which overcome

the handicap, allowing the full oximetric power of color vision to be brought to bear in clinical settings.

Color vision, oximetry, and cyanosis

Recent research suggests that color vision evolved for the purpose of seeing skin color modulations signaling emotion or mood, like a blush on a face, or receptivity on a chimp rump [1]. The primate trichromatic color vision mechanism is highly optimized for sensing modulations in the oxygenation and concentration of hemoglobin. Fig. 1a illustrates the relationship between blood physiology (oxygenation and concentration of hemoglobin in the skin), the spectrum of skin (after having been filtered by the eye), our cone sensitivities (S, M and L), and the perceived color modulation. The key spectral feature to observe is the "W" in the spectrum near 550 nm. Modulations in hemoglobin concentration raise and lower the "W", modulating the color of skin along a blue–yellow axis (greater concentration being bluer, and lower luminance). Modulations of oxygenation, however, change the salience of the "W", modulating skin color along a red–green axis (greater oxygenation being redder). Notice how the M and L cones have maximal wavelength sensitivities in just the right place for detecting oxygenation modulations, namely, at the first trough and middle peak of the "W", respectively [1].

This explains why skin color changes have historically been so useful in clinical medicine: our eyes *are* oximeters. In fact, the clinical disciplines wherein pulse oximetry is utilized to a greater extent correlates well with the importance of clinical color signs in

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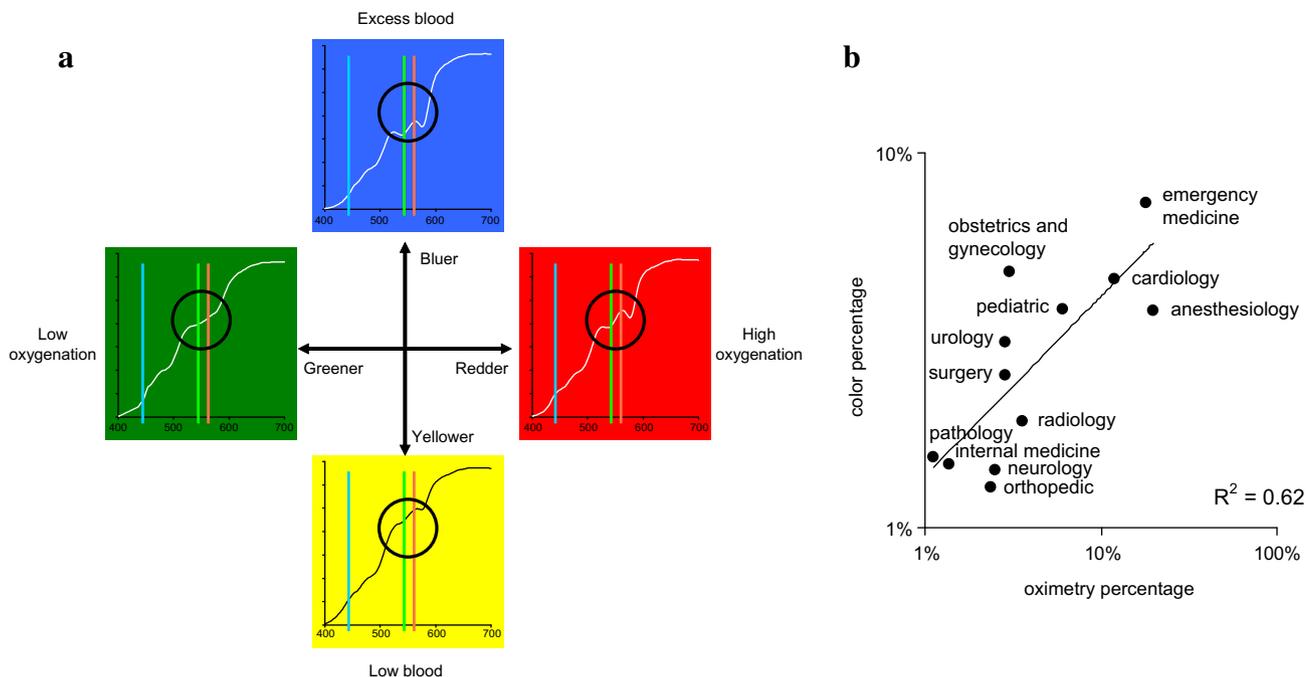


Fig. 1. (a) Model skin spectra (using the model in [42]), as filtered by the eye [43,44], showing how modulations in blood oxygenation and hemoglobin concentration modulates the skin spectrum. The maximal wavelength sensitivity for the three cone types – S, M and L – are shown with vertical lines. Greater concentration lowers the “W” region, enhancing the relative activation of the S cone, which leads to perceptions that are more blue; lowered concentration does the opposite, leading to yellower skin. Greater oxygenation accentuates the “W” feature, raising the activation of the L cone relative to the M cone, which leads to perceptions that are redder; lowered oxygenation does the opposite, flattening out the “W” feature and leading to perceptions that are greener. (b) Plot showing that greater clinical importance of color in a discipline correlates well with the importance of oximetry. The y-axis shows the percentage of books within each clinical discipline that come up on searches with the word “color” in Google Books. The x-axis is the same, but for the word “oximetry”. Dermatology (not shown in the plot) is a counter-example to this trend due to the many skin disorders not due to hemoglobin oxygenation or concentration changes.

diagnosis (Fig. 1b). This also explains why dichromats have such trouble seeing clinical skin color modulations, something noticed more than 200 years ago by Dalton [2–20].

Cyanosis is one of the more important clinical color signs, referring to a bluish discoloration of the skin, lips, tongue, nails and mu-

cous membranes. It can occur due to coldness in the extremities, in which case it is referred to as peripheral cyanosis. Much more seriously, it can be due to poor arterial oxygenation, in which case it is called central cyanosis, and is commonly due to pulmonary disease or congenital heart lesions.

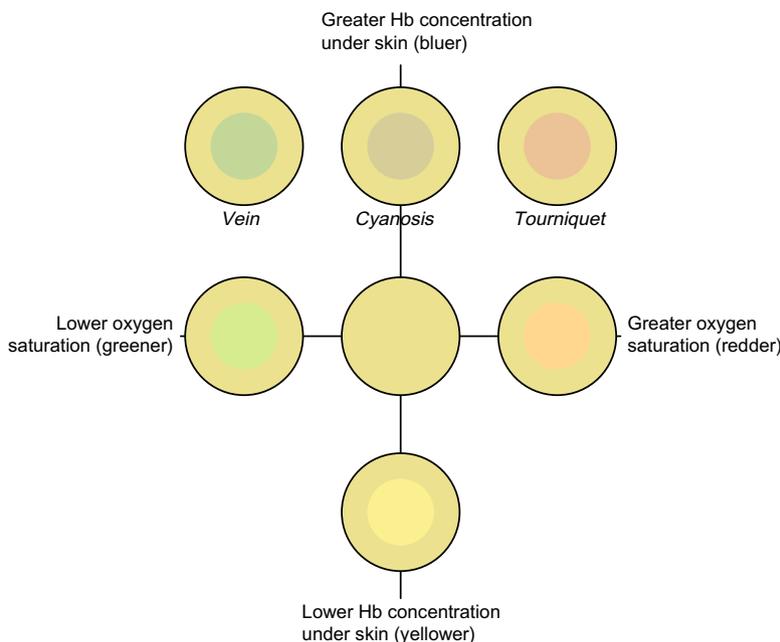


Fig. 2. Schematic illustration of how the skin conditions for cyanosis (blue) relate to those for blue-green veins and purplish skin (as when a tourniquet is briefly applied).

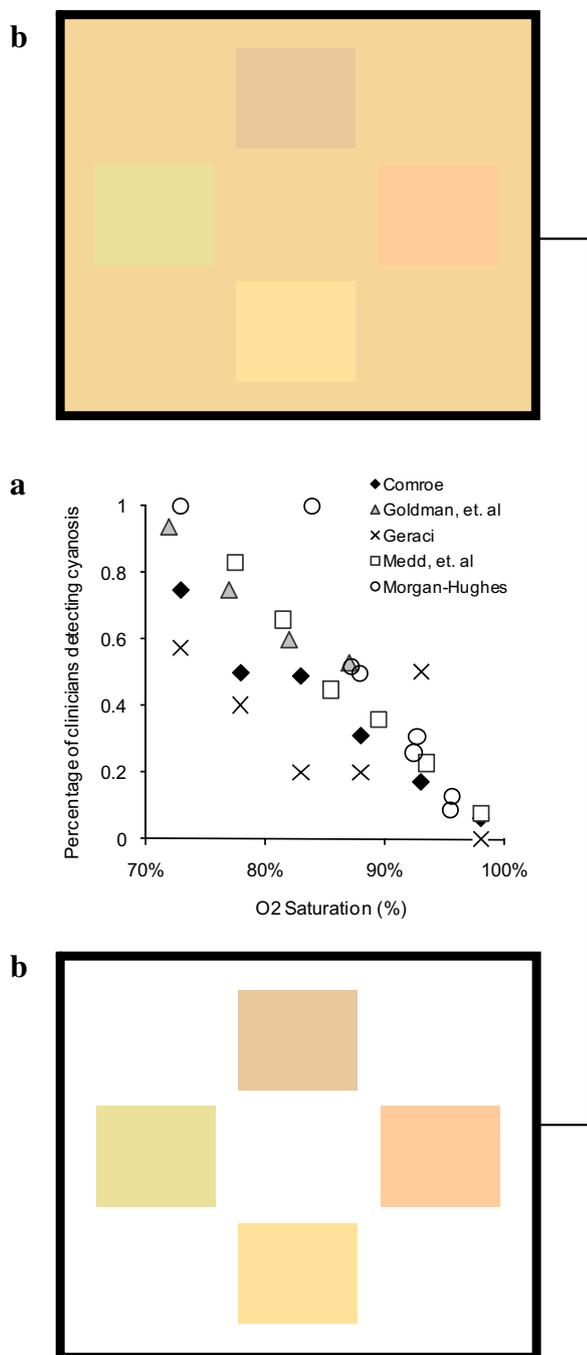


Fig. 3. (a) Percentage of observers who see cyanosis on a patient, as a function of oxygen saturation, from Refs. [29–31,33,34] (In middle). (b) Illustration of how perceived color depends on the background. The four colored squares at the top are identical to those at the bottom, but at the top they appear to be the four primary hues, whereas the bottom ones appear to be similar skin-toned colors. Perceived color on skin crucially depends on the background unchanged skin color, akin to the top here. Cyanosis is difficult to detect because it tends to lead to fairly uniform skin color shifts, and so there is no baseline skin for contrast (top and bottom) (the images in (b) are physically separated to reduce the effect of one perceptually affecting the other).

Why does cyanosis appear blue? There appear to be vasomotor mechanisms which respond to the lower oxygen saturation by slowing capillary blood flow and increasing cell uptake of oxygen (a mechanism hypothesized as far back as Campbell et al. [21]; see also [22]). This increases the hemoglobin concentration under the skin, which leads to bluer skin (see Fig. 1a). Note that veins

are also cases of high hemoglobin concentration, and are thus shifted towards blue; but the hemoglobin in veins is mostly reduced, and so is shifted towards green, which is why veins appear blue-green. And, note that brief application of a tourniquet also raises the hemoglobin concentration in the skin, thus shifting skin color to be bluer; but in this case the hemoglobin tends to be relatively oxygenated and so is shifted toward red, which is why tourniquets initially turn skin blue-red, or purplish. Cyanosis is therefore similar to veins and tourniquets in that there is also a raised concentration of hemoglobin, and thus bluer skin. But cyanosis differs from veins and tourniquets in that it is more oxygenated than venous blood, and less oxygenated than tourniquet-induced blood in the skin. Thus, cyanosed skin shifts very little along the red-green axis, lying in between blue-green and blue-red in color space, i.e., it is just bluer (see Fig. 2). (Note that the blue of cyanosis is *not* because deoxygenated blood is blue, as is often surmised. Deoxygenated blood seen through a transparent tube appears red, and is shifted only slightly toward green relative to oxygenated blood (see also [23]).)

Overcoming color vision's clinical handicap

There has been considerable attention to the visibility of cyanosis over the last century, going back to the studies of [24–27]. The standard conclusion is that color-normals are poor at detecting cyanosis [24,28–34]. Fig. 3a shows a compilation of the results from some of these papers, showing how the probability of a clinical observer detecting cyanosis varies as a function of oxygen saturation. One apparent feature from these plots is that observers are very often not confident there is cyanosis until oxygen saturation has fallen to around 80% or below, which is dangerously low.

We are left with a paradox. In the previous section we concluded that our color vision serves as a highly sensitive oximeter, but in the previous paragraph we noted the difficulty observers have in detecting cyanosis. If our eyes are oximeters, why is central cyanosis difficult to detect?

In order to resolve this paradox, we must recognize that what our eyes are good at is sensing spatial variations in skin color. The skin color modulations for emotions tend to have strong spatial color gradients, allowing the observer to see the signal, such as detecting blushes [35] or the many other color signals primates have long been known to display [36–39]. The perceived color relies upon its contrast with the spatially proximal unchanged baseline skin color. Our perception of blue-green veins, for example, crucially depends on its contrast with the baseline skin color surrounding it: blue-green veins seen through an aperture do not appear blue-green at all, but, rather, skin colored. Veins deviate only slightly from baseline skin color, and deviate in the blue-green direction. This small deviation from baseline suffices for our visual system to elicit the perception of a strongly qualitatively different color perception. Fig. 3b illustrates this well-known perceptual effect. Our ability to see skin color modulations so well depends on our cone sensitivities being tuned for sensing hemodynamic changes, but it *also*, therefore, depends on there being a spatial spectral gradient with which our visual system can elicit large perceptual differences for even small spectral differences.

And therein lies the problem: clinical color changes are not color signals, per se, and (probably) are not evolutionarily selected to be seen. In clinical cases the entire skin can sometimes more *uniformly* shift in color, and an observer will just assume that the current skin color is that patient's baseline color (because there is large variability in baseline skin color across individuals). *In clinical cases there can at times be little or no spectral gradient on the skin and our color perception will – despite its oximetric capabilities – be little help in detecting that the skin color has deviated from baseline.* The

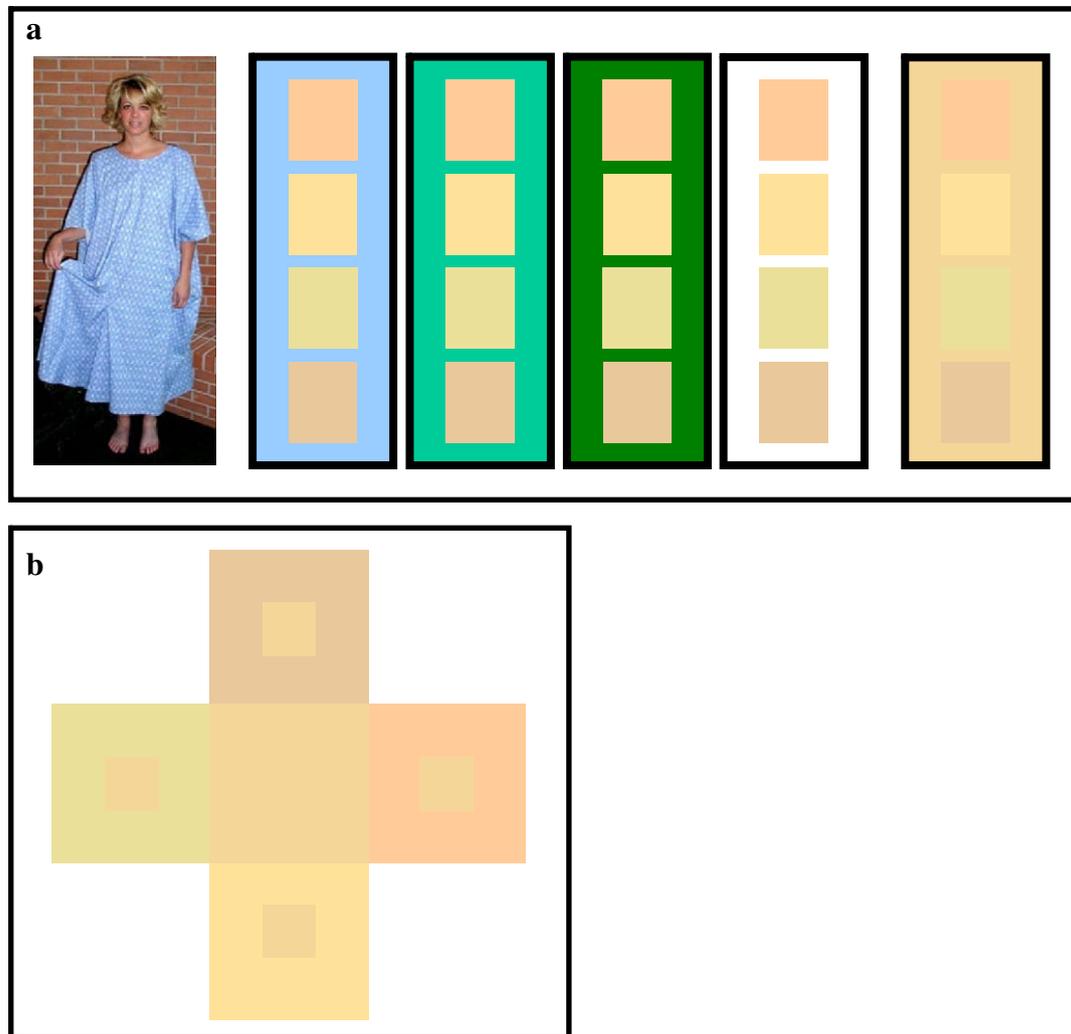


Fig. 4. Two techniques for harnessing color vision's oximetric capabilities in clinical settings. (a) On the left is a standard hospital gown, strongly saturated in color. To its right are four different skin tones placed next to four strongly colored gowns, blue, blue-green, green and white. The differences between the skin-tone colors are difficult to detect. The same four skin tones become easy to detect when placed next to a gown with color very close to these colors, as shown on the right. (b) A skin color-tab biosensor is simply a uniformly colored tab matching the baseline skin color of the patient (the center color). As the skin modulates its color (the larger square regions), the perceived color of the tab (the small squares, each having identical RGB values on the page) dynamically appears to change in a direction opposite to the skin color modulation. A clinical observer can sense the skin color change from baseline by determining the current perceived color of the tab.

difficulty clinicians have in detecting central cyanosis is in large part due to this.

In this light, we describe two simple new techniques that make it easier for color-normal clinical observers to detect central cyanosis (and other clinical color changes). (Note that people of all skin colors undergo the same spectral skin modulations, and thus the techniques below are applicable on any patient population [1,40].)

The first is called “skin-tone adaptation”, and relies on the long known fact that our ability to discriminate color modulations is optimized when the spatially proximal background color is very similar to the colors to be discriminated (this is what Fig. 3b demonstrates). It immediately suggests the following straightforward prescriptive advice for patient care: *sheets, gowns, walls and other material visually near a patient should be skin-toned, preferably closely matched to the skin tone of the patient.* Walls and sheets in hospital and clinic rooms today are typically white, and patient gowns are often blue or green. As Fig. 4a shows, four different skin tones can look practically identical when adjacent to colored gowns (shown are blue, blue-green, green and white), but look radically different when the gown is skin-toned (Fig. 4a, right).

A second technique for overcoming our clinical color handicap concerns something called “biosensor color tabs”. A clinician places these adhesive tabs at several places on the skin of the patient, and, crucially, the clinician can choose tabs from a large palette of skin-toned colors, and is thus able to find a match to the patient's current skin tone. Just as a clinician may use a marker-pen to encircle a rash in order to better see whether the rash has enlarged or receded at a later time, placing a skin-tone colored tab on skin serves to record the patient's skin tone, allowing the clinical observer to see whether it has changed at a later time. If, for example, the skin uniformly shifts a small amount toward blue, then an initially uncolored, nearly invisible (because it was matched to the earlier skin color), skin tab will suddenly appear yellow and bright (Fig. 4b). The greater the skin color shift, the stronger the perceived saturation of the tab. These spectrally static tabs, then, actually serve as *perceptually dynamic biosensors*. Central cyanosis will thereby become visible at much higher (and safer) levels of oxygen saturation than without such biosensors.

One may wonder if these two techniques for harnessing color vision for oximetry are relevant in modern medicine, given the

availability of pulse oximetry. Recall from Fig. 1b that the clinical disciplines most utilizing pulse oximetry are also the disciplines that most often refer to the patient's clinical skin color in diagnosis: thus, the actual practice of medicine appears to value our human color capabilities, despite the presence of pulse oximetry. There are several potential explanations for this: (a) color perception provides redundant detection of oxygen saturation (e.g., if the oximeter becomes unattached), (b) observation of skin color modulations may lead to a faster behavioral response by the clinician (the "look" of sickness may be more psychologically engaging than numbers or beeps from an oximeter), and (c) our color perception is capable of sensing the spatial *gradients* in skin color across the body, and the nature of those gradients can impart information to a clinician. Furthermore, there are circumstances where pulse oximetry is not used today, but where the "color oximetry" techniques above would be of great value: (i) in certain parts of the hospital (e.g., in transit, or the emergency department waiting room), (ii) in third world hospitals, where it is still not part of standard care [41], (iii) in the field (e.g., for athletes or soldiers), and (iv) in the home (e.g., for SIDS detection).

Conflicts of interest statement

The authors declare that there are no conflicts of interest.

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