25 Spectrophotometric Intracutaneous Analysis (SIAscopy)

Paul J. Matts
Procter & Gamble, Egham, U.K.

Symon D. Cotton
Astron Clinica, Cambridge, U.K.

WHAT IS SIASCOPY?

Spectrophotometric intracutaneous analysis (SIA)scopy is a skin-imaging technique that allows the rapid, noninvasive in vivo quantification and assessment of (eu) melanin, (oxy) hemoglobin, and dermal collagen within human skin. A powerful feature of SIAscopy is that it produces independent linear measurements of each of these endpoints, which can also be mapped over the skin, producing images called SIAscans. SIAscopy was originally developed for the assessment of malignant melanoma (1) where the accurate assessment of melanin, blood, and collagen has been shown to increase diagnostic accuracy (2) for the disease.

SIAscopy measures underlying histological parameters through the use of a model of tissue coloration, providing a cross-reference between spectral measurements and histology. The model is constructed by computing the spectral composition of light remitted from the skin, given parameters specifying its structure and optical properties, providing a unique mapping between the spectral measurements and the histological parameters (3). For each histological component, a parametric image is then created, providing the magnitude of each at all pixel locations. This approach requires two inputs: the first is a set of parameters that characterize a given tissue by specifying its components, their optical properties, their quantities, and their geometry; the second is a method for computing the remitted spectra from the given parameters.

CONSTRUCTION OF THE MATHEMATICAL OPTICAL MODEL OF HUMAN SKIN

The skin consists of a number of layers with distinct functions and optical properties as shown in Figure 1. Light incident to the skin penetrates the superficial layers, and while some of it is absorbed, much is remitted back and can be measured.

The stratum corneum is a protective layer consisting of keratinized squamous cells (corneocytes), and it varies in thickness across the body. Apart from forward scattering of incident light, it is optically neutral (4). The epidermis is composed of several layers of differentiating keratinocytes and also contains pigment-producing cells, melanocytes, and their product, the melanins. The melanins are complex heteropolymers that strongly absorb short-wavelength radiation, i.e., light in the blue part of the visible spectrum and radiation in the ultraviolet (UV) waveband (in the latter case, therefore, acting as a filter to protect the deeper layers of the skin from the well-documented harmful effects of UV radiation). Within the epidermal layer, there is very little scattering and that which does occur is forward directed. This means that all light not absorbed by melanin can be considered to pass into the dermis. The dermis is composed largely of collagen fibers, and in contrast to the epidermis, it contains sensors, receptors, blood vessels, and nerve endings. Hemoglobin, present in blood vessels within the dermis, acts as a selective absorber of light. The dermis consists of two structurally different layers, papillary and reticular, which differ principally in the size of collagen fibers. The scale of the collagen fibers in the papillary dermis (diameter of an order of magnitude less than the incident visible light) makes this layer highly scattering, i.e., any incoming light is scattered with a proportion directed back toward the skin surface. The scatter is greatest at the blue end of the spectrum, decreasing with increasing wavelength

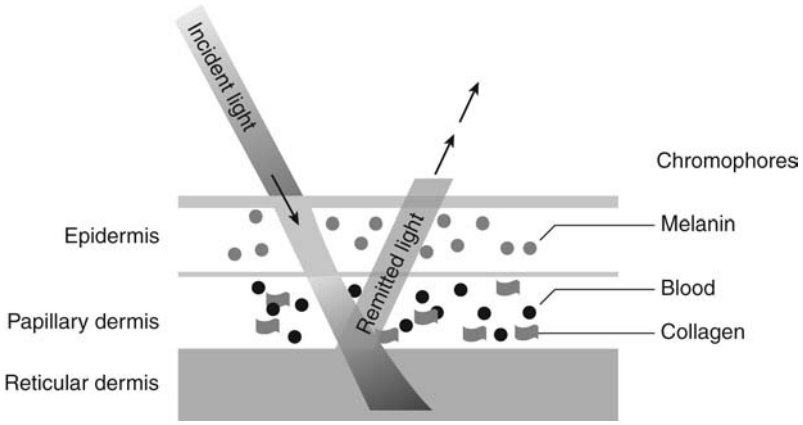

Figure 1 A schematic representation of skin layers (*labels on the left*) and chromophores (*labels on the right*).

(through green and red and into the infrared). Within the reticular dermis, in contrast, the larger scale of collagen fiber bundles causes highly forward-directed scattering (1). Thus, any light reaching this layer passes deeper into the skin and does not contribute to the remitted spectrum.

From these first principles, therefore, the mathematical optical model for normal skin has three layers corresponding to epidermis, upper papillary dermis (with prevalence of blood), and lower papillary dermis. The range of wavelengths used by the SIAscope technique, from 400 to 1000 nm, covers the entire visible spectrum and a small range of near infrared. Recently, the model has been verified by comparing its output to that generated by a stochastic Monte Carlo method using a public domain implementation (Figs. 2 and 3) (5). Q2

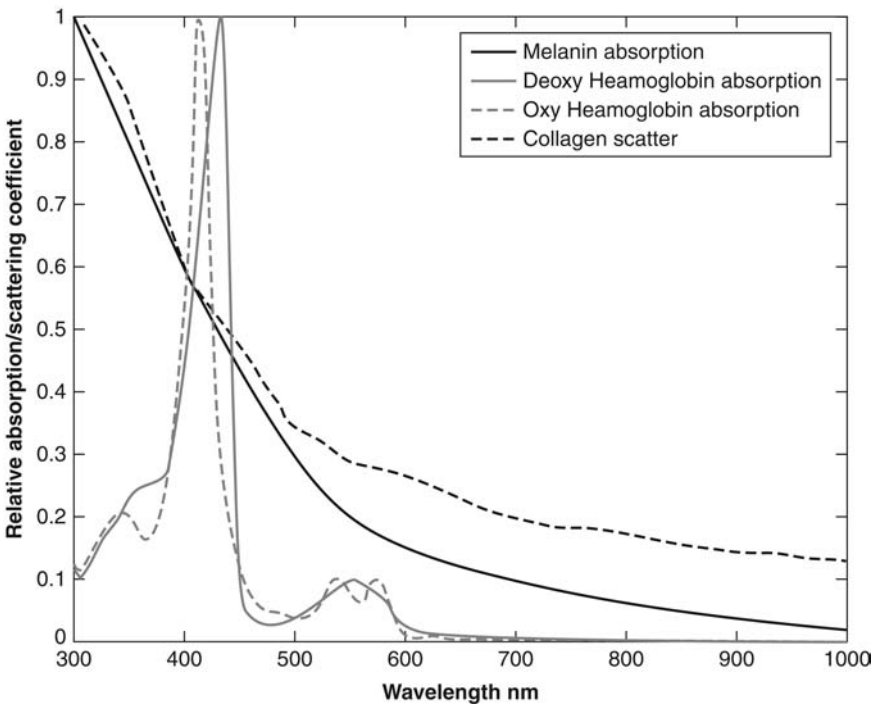

Figure 2 Absorption coefficients of principal components of human skin.

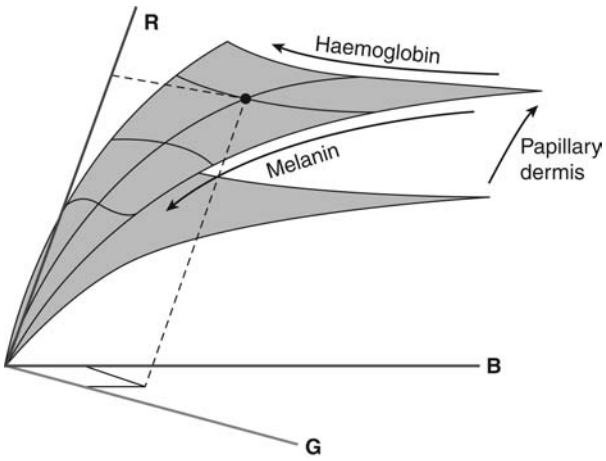

Figure 3 Schematic relationship between two reference systems: color system, with axes R, G, and B; and the histological components hemoglobin, melanin, and collagen.

CONTACT SIASCOPY

Contact SIAscopy uses a small handheld scanner (Fig. 4), which is placed in contact with the skin. This contact ensures that the distance of the skin from the lens is known and fixed, which allows exact calibration of the spectral imaging used. This control of imaging geometry allows the synthesis of accurate gray scale concentration maps each of (oxy) hemoglobin, (eu) melanin, collagen, and the position of melanin relative to the dermo-epidermal junction (Fig. 5). A small

Figure 4 SIAscope.

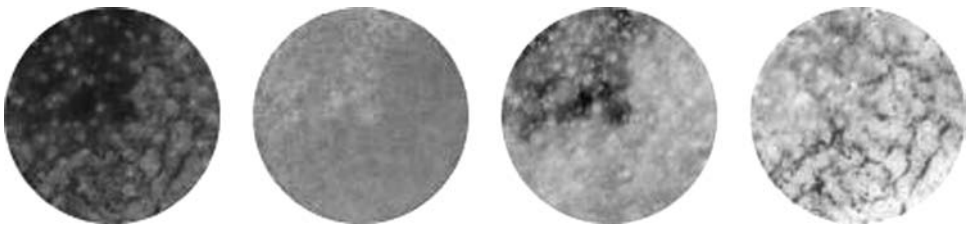

Figure 5 SIAscans showing, from left: color, collagen, melanin, and hemoglobin.

amount of matching fluid is used to ensure that optical aberration due to the refractive index of air is removed effectively.

The contact SIAscope provides a rapid and convenient method for assessing and characterizing intrinsic and extrinsic skin aging and also assessing the effects of cosmetic products, for example, the reduction of solar lentigines (6,7).

CHROMOPHORE MAPPING

We have given the term "chromophore mapping" to the synthesis and subsequent analysis of the gray scale molecular concentration maps produced by SIAscopy. These maps are readily accessible by a wide range of image analysis techniques, allowing sophisticated analysis of the arrangements of chromophores within them. We used these techniques in a study performed on 400 female Caucasian subjects aged 10 to 70 years, recruited in equal five-year cohorts (7), and demonstrated remarkable relationships for the melanin, hemoglobin, and collagen endpoints (obtained using a contact SIAscope) with age, consistent with ingoing hypotheses relating to the extent and timetabling of expression for each of these optical skin components. Moreover, sufficient dynamic range was present within the data to allow the use of this technique to track changes in these chromophores because of treatment.

SURFACE ANALYSIS

Further development of the contact SIAscope method has yielded an analysis of fine surface topograhical features ("microtexture" and fine lines and wrinkles) (8). This technique uses the fact that light returning from the skin is a blend of deeply scattered light and direct surface reflection resulting from the stacked nature of the stratum corneum. If the deeply scattered light is isolated and removed, the remaining directly reflected light carries information pertaining to the skin surface. Other workers have used this phenomenon by acquiring separate images taken in different polarization states (9). This is a useful technique, but requires specialist hardware and can suffer from registration problems between image sets.

Highly detailed information regarding the surface of the skin can be obtained using contact SIAscopy because the instrument polarizers operate only within the visible region of the spectrum and do not interact with infrared light (Fig. 6). This results in suppression of surface reflection in the visible spectrum only (which is why a matching fluid is required to obtain accurate collagen measurements). By using a technique described in (8), a prediction of

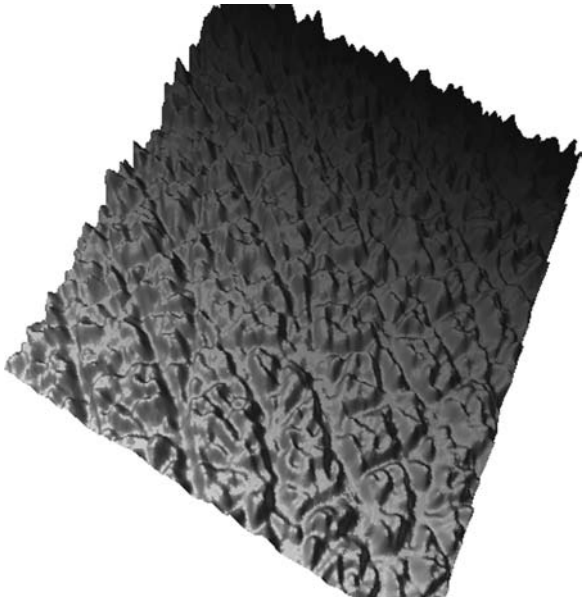

Figure 6 Skin surface micro architecture measured with a SIAscope.

what the polarized infrared signal should be is made from the polarized-visible spectra and then compared with the actual unpolarized infrared measurement. The difference is then converted into a measurement of direct surface scatter. The result is a detailed map of skin topology, which is both rapid and simple, lending itself naturally to large scale cosmetic testing and development.

HYDRATION

An adaptation of the surface analysis technique can also be used to assess skin hydration levels in vivo, allowing investigation into the effects of skin moisturizers and also diseased skin conditions such as eczema. This technique operates on the principle that direct surface reflection measured by the surface analysis technique is lower in hydrated stratum corneum. An example of skin moisturization changing over time following the application of a topical moisturizer is shown in Figure 7, with the false color images showing the spatial changes in hydration over a 10-minute period.

NONCONTACT SIASCOPY

Noncontact SIAscopy (NCS) uses a digital camera as a broad-band spectrometer to recover chromophore information over a wide area. The same mathematical model underpinning contact SIAscopy is used to create a mathematical model of the camera response to varying amounts of hemoglobin and melanin (10). The mathematical model is based on the Bayer filter response curves, the light-sensitive array that sits at the focal point of a digital camera, and the spectral power distribution of the light source (usually a flash) used with the camera. To measure the response curves of the Bayer filter, a double-monochromator is used to illuminate it with specific and highly calibrated narrow (<10 nm) wavebands of light.

A problem still exists, however, because the geometry of the scene being imaged is not known and, therefore, calibration of the measured information is difficult. To overcome this problem, a ratio of different Bayer filter wavebands forms the input to the mathematical model. The use of ratios removes the artifacts of geometry, as they are present equally in all wavebands. From first principles, this approach reduces the number of chromophores that can be measured, such that NCS is able to measure only hemoglobin and melanin. NCS is, however, extremely flexible allowing imaging of full faces, or, indeed, any body part (if the

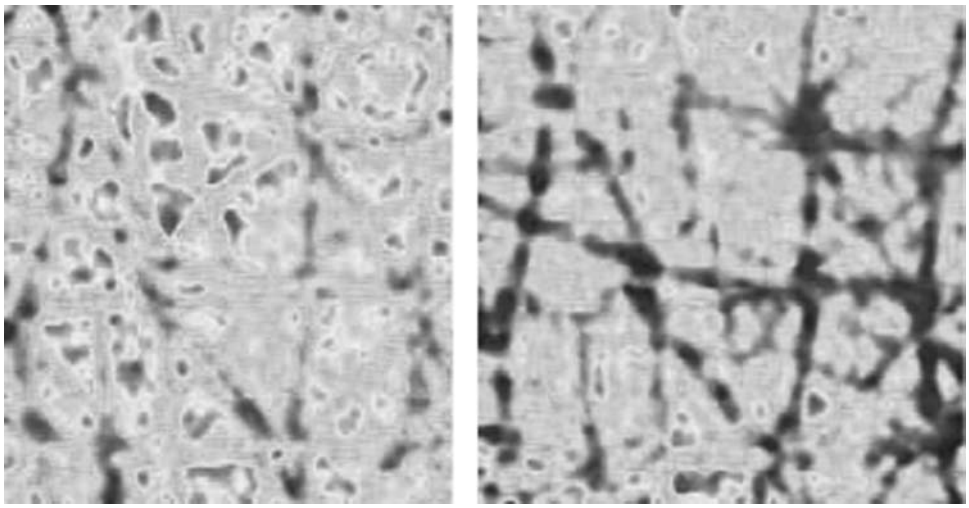

Figure 7 Changes in hydration levels in human skin (same area) following application of a topical moisturizer (before and 10 minutes after application). "Dry" skin (*left*) and "moisturized" skin (*right*) with pseudocolor scale indicating hydration state.

Figure 8 Noncontact SIAscopy in use.

Figure 9 NCS images with (*left to right*) cross-polarized color, melanin, and hemoglobin maps.

camera is used apart from the stand). Apart from the ability to measure large fields, NCS also has the advantage of eliminating the potential artifacts of pressure "blanching" that can potentially occur with any skin contact measure (Fig. 8).

Figure 9 shows NCS melanin and hemoglobin SIAscans. Localized subsurface hyperpigmentation can clearly be seen in the melanin SIAscan and telangiectasia in the hemoglobin SIAscan.

Because the NCS technique now allows routine acquisition of full-face melanin and hemoglobin chromophore maps, the method has proven an ideal clinical partner in assessing the effects of cosmetic treatments. In a recent double-blinded study, NCS was used to provide a quantitative means of measuring the effect of a vehicle containing 2% *N*-acetyl glucosamine (NAG) and 4% niacinamide (N) versus a vehicle control, applied topically, full-face, twice-daily for eight weeks, to two groups of 100 females aged 40 to 60 years, respectively, on melanized hyperpigmented spots (11). Analysis of the NCS melanin maps demonstrated clear treatment effects for the NAG + N combination versus vehicle control, resulting in a significant ($p < 0.05$) reduction in melanin spot area fraction and a significant ($p < 0.05$) increase in melanin evenness.

Finally, it should be noted that a separate study has shown an excellent correlation between NCS-derived melanin concentrations and eumelanin concentrations in human skin biopsies, spanning Fitzpatrick skin types I-VI (12). It must be concluded, therefore, that large-field chromophore mapping by NCS brings a new level of sensitivity and specificity to measurement of human skin color.

CONCLUSION

Whereas even modern high-resolution imaging still only describes skin appearance, SIAscopy explains it by separating the molecular components responsible for that appearance in the first place. In this way, SIAscopy provides the clinician and researcher alike with a powerful new tool to both measure and characterize human skin.

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Contributors : Paul J. Matts[1], Ph.D. and Symon D. Cotton[2], Ph.D.

Affiliation :
Address :
Phone :
Fax :
Email : **matts.pj@pg.com**

Affiliation :
Address :
Phone :
Fax :
Email : **symon.cotton@astronclinica.com**

Lead Author : Paul J. Matts