Quantifying composition of human tissues from multispectral images using a model of image formation

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Abstract. This paper describes a novel method for quantitative interpretation of multispectral images. By constructing an optical model of a tissue and by modelling the image formation process we predict the spectral composition of light remitted from the tissue. The parameters characterising the tissue are varied to represent the entire range of tissue instances. The modelling of image formation is used in place of statistical modelling in which training is performed using measured data with known parameterisation. In this way the method overcomes a common problem in medical imaging where "ground truth" data can be impossible to obtain. The paper shows application of the method to the recovery of histological parameters characterising the skin, the eye and the colon.

1   Introduction

Colour plays an important role in the clinical diagnosis of many conditions. However, the receptors in the clinician's eye, as well as the sensors in a standard RGB camera, provide only a limited representation of the visible spectrum. Research in medical spectroscopy has shown that spectral data can yield information beyond what is possible by observation or photography. One well known example is pulse oximetry which uses two spectral measurements to determine blood oxygenation. Although very useful, spectroscopy is inherently one-dimensional and lacks the ability to show spatial variations, which are an important diagnostic factor. Abnormalities often show themselves as unexpected patterns or distortions of regular features and colours.

Multispectral imaging can combine these two important indicators: spectral signatures and spatial variations. Suitable imaging systems exist, but interpretation of multispectral data is an open problem. One common approach is spectral classification whose objective is to distinguish between the spectra of normal and abnormal tissues. Based on the classification, false-coloured "diagnostic" images are then presented to a clinician. However, there is a well recognised lack of enthusiasm amongst the clinicians for such "black box" systems. Our earlier research has shown that images which reveal information on the basis of which diagnosis can be formed with high confidence, are much more acceptable.

Light which enters the tissue interacts with its components, and through these interactions (mainly absorption and scatter) the spectral composition of light is altered in a characteristic way. Thus remitted light bears an imprint of tissue properties. How can we derive information related to these properties from the spectra? If the parame-

ters describing composition of the imaged tissue were known a priori, the spectral information could be correlated with these known parameter values using statistical analysis (e.g. multivariate techniques). A statistical model constructed through training using this "ground truth" data could be then used to estimate the parameter values associated with the image spectra. However, most tissues are too complex and the parameters of interest, for example the level of blood supply, cannot be easily determined. Moreover, linear methods are not very appropriate in this domain because the light scatter in tissue makes the relationships between the tissue composition and its spectra highly non-linear.

In recent years we have developed a methodology which overcomes the problem caused by the lack of the "ground truth" data. Instead of training a model on known measured spectral data, we train it on the spectral data generated by a physics-based model of image formation applied to an optical model of a tissue. We construct a non-linear multi-dimensional model, parametrised by those tissue components which have been found to affect the spectral variability. Fortuitously, we have found that usually the same parameters carry diagnostically relevant information. Moreover, the analysis of spectral variability as a function of the parameter changes allows us to define a small number of spectral bands which contain the bulk of information pertaining to the parameters. Following image acquisition in these chosen bands, the parameters are recovered from the multispectral image data through the "model inversion". The recovered parameter values are represented in the form of parametric maps, one for each parameter. The maps show both spatial variations and variations in the magnitude of the parameters, and have been found useful in diagnosis.

We have applied this method of quantitative parameter recovery to multi-spectral images of the skin [5], the eye [6] and the colon [2]. This paper draws on that earlier work, explains the general principles of our method and shows examples of the clinical applications.

2   Image formation model

Tissue model. Although in this paper we concentrate on human tissues, our methodology is applicable to any material which is composed of a number of optically homogenous layers occurring in a known and pre-determined order. The generic requirements are that each layer's composition and the optical properties of its components must be known across a range of wavelengths, as must be the typical ranges of the layer thickness and component concentrations. Optical responses from all the layers under consideration must be detectable.

Typical tissue components of interest are pigments (e.g. haemoglobins in the blood) and structural fibres (e.g. collagen), membranes and cells. Their optical properties are specified by the wavelength dependent factors: the refractive index, the absorption coefficient, the scatter coefficient and the anisotropy factor. These properties are treated as the model "constants" and have to be specified a priori. The model variables are typically the quantities of the above components which vary from one instance of the tissue to another, for example haemoglobin concentration, thickness of

a collagenous layer or density of collagen fibrils. These variables are the parameters which we would like to recover from multispectral images of the tissue.

Light interaction model. A spectrum remitted from a tissue is the result of interaction of incident light with the tissue components. Any absorbers (pigments) will attenuate light at specific wavelengths, and the degree to which light is attenuated will depend in part on the pigment concentration. Any scatterers will selectively alter paths of the incident photons at different wavelengths and in this way change the shape of the remitted spectra. These interactions can be modelled and for a given tissue composition (as defined above) the corresponding diffuse reflectance spectrum can be computed by solving a light transport equation, normally using an approximate method (e.g. Kubelka-Munk). In this work we use Monte-Carlo method [4], a stochastic approach which simulates the interactions of a large number of photons (of the order of 10^{4-5}) with tissue. It does so by computing the probability that a photon of a specific wavelength is reflected, absorbed or scattered in a given tissue layer. A reflectance curve is generated by carrying out simulations for all the wavelengths.

Imaging system model. The final step in the model of image formation is the process of image acquisition. The tissue is illuminated using a light source with a given spectral profile ($I_0(\lambda)$). The remitted light is then separated into narrow-band spectral components, normally using filters with known transmission properties ($F_n(\lambda)$). The filtered light is recorded by a camera whose sensors (e.g. CCD) have a particular quantum efficiency characteristics ($Q(\lambda)$). The imaging model can be expressed as

$$\{ \int I_0(\lambda) \, F_n(\lambda) \, Q(\lambda) \, d\lambda \}_{n=1,\ldots,N} \tag{1}$$

3 Tissue reflectance model: the ground truth

Given the optical model of a tissue and a method for modelling of the light interaction we can predict the spectra remitted from the real tissue. Further on, given a model of the imaging system, including spectral filter definitions, we can predict values in the multispectral image data. This *forward model of image formation* provides us with the means of relating tissue parameter magnitudes to image values. In section 4 we shall describe the methods for carrying out the inverse process, that is obtaining the parameter magnitudes from image values. In this section we shall outline the algorithm for computing the tissue reflectance model and discuss the essential details related to its implementation.

Building the model. A generic algorithm for constructing the tissue reflectance model is shown below. In the essence, for a given tissue it computes the range of all possible reflectance spectra, and then their multispectral representations. In order to implement this algorithm we have to choose which tissue components (parameters) to represent in the model; and for each parameter we have to define its range and sampling (discretisation). In the last step we have to define the filters which implement

the transition from spectra to image values through the application of the imaging system model (Eq. 1).

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given
   incident light I_0
   the number and the order of distinct optical layers
   the optically active components within each layer
   absorption and scatter coefficients for all the components
for all values of parameter p_1
   for all values of parameter p_2
  . . .
    for all values of parameter p_K
       compute Reflectance_Spectrum <r_1,...r_M> =
                        Light_Interaction_Model(I_0, p_1, …, p_K)
       compute multispectral image vector <y_1,...,y_N> =
                   convolve(<r_1,...,r_M>, Imaging_System_Model)
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Tissue related parameters. Each tissue has specific and unique composition in terms of the optical layers, their arrangement and quantities. This information is normally obtained from histology textbooks. The composition of superficial tissues is limited to a relatively small number of absorbing pigments and scatter-originating connective tissues. Their optical properties can be found from research publications (e.g. see [8]).

Some quantities stay constant; some quantities vary, but have little effect on the spectra. Prior to making a commitment to a particular parameterisation it is useful to carry out preliminary modelling for *all* the known parameters in order to determine their role as a variable or as a constant: the more of the variable parameters the more complex the model and the subsequent parameter recovery. The choice of granularity for parameter discretisation is not critical as normally the spectra change smoothly as a function of the parameter changes. We have found empirically that having around 5 ± 1 discrete values within a given range gives satisfactory results.

Spectrum related parameters. By acquiring multi-spectral images we represent a continuous spectrum by a set of discrete values. As the image acquisition is implemented through bandpass filtering, it is necessary to define the number and the spectral locations of the filters, and for each filter its bandwidth and transmittance. A simple solution is to choose uniform sampling throughout the entire visible range. However, this may lead to increase in computational effort. We have implemented a method for optimal filter selection which defines a small number of filters, M (for N variable parameters M=N or M=N+1) with the objective to minimise the error with which the parameters can be recovered from image values. The method also ensures that with the chosen filters there is a one-to-one, unique, correspondence between all the parameter vectors and all the image vectors. The details are given in [1,5].

Formalised description of the model. The tissue reflectance model is constructed for N variable parameters which have been found to affect the shape of the remitted spectra. Each specific instance of tissue can thus be defined by an N-dimensional parame-

ter vector $\mathbf{p}=<p_1,...,p_n>$. The range of each parameter is discretised to k_n levels, giving in total $K=k_1 \times k_2 \times ... \times k_n$ parameter vectors which, together, define *all the possible instances* of the given tissue (within given discretisation). Through modelling of the light interaction with tissue and of the image acquisition process we associate with each parameter a spectrum and an M-dimensional image vector $\mathbf{i}=<i_1,...,i_M>$. The parameter vectors together with the image vectors form the tissue reflectance model: $\mathbf{i} = f(\mathbf{p})$. This model is used in the next step to derive parameters from multispectral images of tissue.

4   Image interpretation

The model captures the relationship between the tissue parameters and the corresponding image vectors. In this sense it is equivalent to a statistical model obtained by training using images with known ground truth. We now can proceed with the main objective of this work, which is to find the parameters given multispectral image values. We shall refer to this process of parameter recovery as the "model inversion". In general, this is a very difficult task, especially when the model is highly non-linear. We have explored three different inversion methods, as described below.

Direct spectral matching. The simplest method of inversion is to find a model spectrum which best matches the given measured spectrum. The parameters used to generated the model spectrum are then assumed to correspond to the parameters which represent the measured spectrum. The method of finding the best match was implemented as a distance minimisation problem. In addition to the parameter values, this method can return additional useful quantities, for example the scale factor, which is a function of the distance between the camera sensor and the imaged tissue and which helps to appreciate the shape of the colon surface.

Model inversion via multidimensional interpolation. As the forward model is constructed using a numerical solution to the radiative transport equation, it is not possible on its basis to formulate an analytical inverse function which would return the parameters given the spectra. We can exploit the fact that, formally, the model is a vector-valued function on a vector domain ($\mathbf{i} = f(\mathbf{p})$, see Sec. 3). If a given measurement vector $\hat{\mathbf{i}}$ corresponds exactly to a model image vector $\mathbf{i}$, the parameter vector $\mathbf{p}$ can be obtained via a simple look-up. In all other cases we need to find an approximate solution. Given that the mapping between image vectors and parameter vectors is unique, and the density of the data points is sufficiently high, we can employ the inverse function theorem and compute parameter vector $\hat{\mathbf{p}}$ for an arbitrary measurement vector $\hat{\mathbf{i}}$ using a truncated Taylor expansion.

Neural network. Using the discretised model we have trained a two-layer, radial-basis neural network. The image vectors generated by the model were used as inputs, and the corresponding model parameter vectors were provided as the target outputs

[7]. After training, the input to the network were the measurement vectors obtained from the image, and the output were the estimated parameter vectors.

5   Experimental results

The parameter recovery methods described above were applied to a range of multispectral medical images [2,5,6]. In this section we show examples of applications for three tissues: the skin, the eye and the colon.

Before showing the results we briefly outline a typical image acquisition process. Multispectral imaging is implemented using a liquid crystal tuneable filter VarSpec (C.R.I., USA) which allows the selection of narrow Gaussian shaped filters of half-width 5-7nm in the range from 400 to 700nm. The filter is mounted on front of a high sensitivity monochrome camera Retiga Exi 1394 (QImaging, Canada). The individual spectral images forming the multi-spectral data set are acquired serially. The acquisition time is chosen to ensure that the images are correctly exposed.

Prior to quantitative interpretation the acquired image data is pre-processed to remove the effects of the image acquisition system. Individual images are normalised to an exposure time of one second, a gain of one and offset of zero. Spectrum at each pixel is then deconvolved with the imaging model spectrum to give a "pure" tissue reflectance spectrum which can then be compared to the model spectrum.

Skin. The skin imaging work was carried out with the purpose of early detection of skin cancers, and in particular malignant melanoma. The skin model comprises three layers, and variable parameters include the haemoglobin concentration, melanin concentration in the epidermal and the dermal layers, and the thickness of the dermis [5,6]. Only small areas of the skin are imaged and for this reason the imaged skin area can be assumed to be flat and thus to get uniform illumination. This removes the need to carry out spatial normalisation of the illuminant, resulting in a fairly simple model where spectra are represented by four optimally selected spectral bands [5]. The four parameters are derived from the model using linear interpolation. Figure 1 shows an example of quantitative parametric maps of a skin cancer. The parameter recovery method has been used clinically for several years and it has proved to be a powerful tool for cancer diagnosis and other applications [3].

Eye. We have developed a four-layer model of the eye structure, parametrised by five parameters: the concentration of the haemoglobins and the melanins (separately) in different layers, and the concentration of the macular pigment. The back of the eye (ocular fundus) is imaged through an ophthalmic microscope (called a fundus camera). The passage of light through the eye, including the pupil, and the curvature of the fundus, make it impossible to determine the spatial distribution of the incident light. For this reason the model uses the normalised spectral representation (image quotients [5,7]). Each spectrum is represented by six narrow spectral bands, one of which acts as a normalising factor. As the eye cannot stay still during image acquisition, the images in the individual spectral bands have to be registered prior to the parameter extraction. Inconsistent illumination caused by the movement sometimes

causes problems with the parameter recovery, and is the subject of work in progress. The two parameters of clinical interest, the levels of the retinal blood and the levels of the macular pigment, are derived from the image data using neural networks. Figure 2 shows the examples of the parametric maps of retinal blood and Macular Pigment.

Colon. The colon has three optically distinct layers. The layers are parameterised by haemoglobin concentration and its saturation, and by three parameters characterising the connective tissue: the size of collagen fibres, their density and the layer thickness. As the colon surface is uneven, an additional parameter estimates the distance between the point on the surface and the CCD sensor and acts as a scaling factor on the magnitude of each spectrum. The images are obtained from ex-vivo colon samples and 33 narrow band spectra are recorded. The parameters are recovered using the direct spectral matching. Figure 3 shows the parametric maps of the colon in which clear differences between the normal and the cancerous tissue can be seen.

6   Discussion and conclusions

This paper has described a novel method of quantitative interpretation of multispectral images and showed its application to the recovery of histological parameters from images of the skin, the eye and the colon. The novelty of the method lies in the way it constructs and encodes the relationship between the parameters of interest and the image data. In traditional statistical methods such relationships are constructed experimentally. This requires the availability of the "ground truth", which most often is a physical entity (object) for which parameter values are known. The object properties, such as for example its spectral reflectance, are measured and related to the known parameters through a statistical model. In our work, which involves imaging of living human tissues, it is virtually impossible to obtain the ground truth through measurements. In their place we have constructed a virtual experimental set-up which is based on a detailed model of image formation. The optical model of tissue provides the required ground truth for the subsequent inversion process through which the quantitative tissue parameters can be recovered.

One disadvantage of our method is that it requires a great deal of a priori information, including detailed parametrisation of tissue properties, as well as the development of high-fidelity light propagation models. However, if quantitative results are required, the effort in researching parameters and refining models is worthwhile.

As the method is based on physics, it is genuinely quantitative. The images shown in this paper provide visual representation of the recovered data, but behind the pixels there are true physical quantities for concentration, density and thickness of the tissue components. We believe that such results provide objective information about tissues, even in the presence of inevitable errors, and are more clinically valuable than, for example, classification based on spectral data.
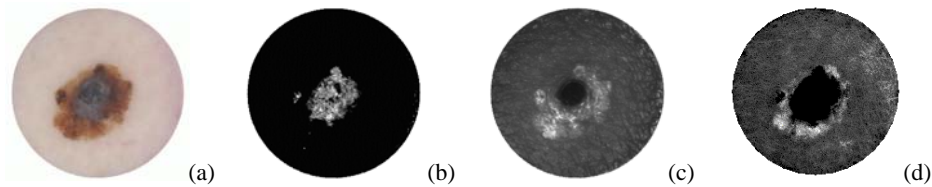
Fig. 1. (a) Colour image of a skin cancer melanoma; parametric maps showing levels of (bright=more) (b) dermal melanin, (c) collagen thickness and (d) dermal blood
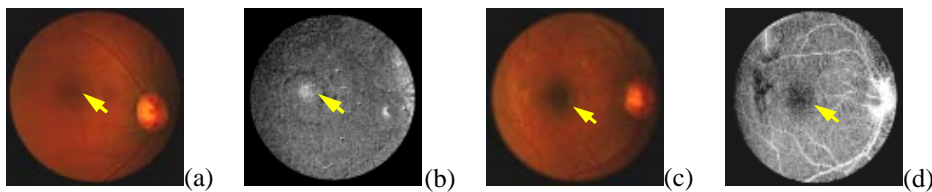

Fig. 2. (a) and (c): RGB images and their parametric maps (bright=high level) showing (b) Macular Pigment; arrow points to fovea where elevated levels of MP can be seen. (d) retinal blood; retinal vessels can be clearly seen; arrow points to fovea with decreased levels of blood
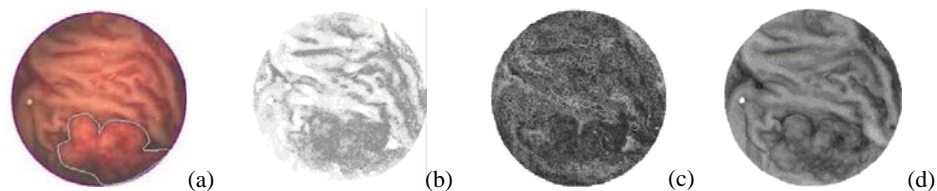

Fig. 3. (a) RGB image of the colon with cancerous area outlined; parametric maps showing levels of (dark=high level) (b) haemoglobin in mucosa, (c) thickness of mucosa and (d) the scaling factor (proportional to the elevation)

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