Histological parametric maps of the human ocular fundus: preliminary results

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Abstract. Specific colours observed in images of the ocular fundus depend on the architecture of its layers and the optical properties and quantities of any pigments present. These colours can be predicted from the parameters describing the ocular tissue composition using a physics-based model of light transport. This paper reports preliminary results of the application of the inverse process by which the parameters can be estimated from image colours. This is achieved by relating the colour of each image pixel to the closest matching colour predicted by the light transport model, and hence to the parameters which generated it. The spatial distribution and estimated quantity of each parameter is shown in a separate image called parametric map. The first parametric maps of Retinal Pigment Epithelium (RPE) melanin, choroidal melanin and choroidal blood computed by this method show a distribution of pigments which is generally consistent with physiology.

1 Introduction

The pupil of the eye provides an opening through which the interior of the eye (the ocular fundus) can be examined. This is clearly useful for the diagnosis of eye disorders. However, the fundus is also a unique location at which blood vessels can be directly observed and this makes it valuable for the diagnosis of diseases affecting the vascular system, such as diabetes. Many abnormal conditions are manifested through local changes in the fundus colouration or through the appearance of unusual colours. The long term objective of this work is to relate the colours seen in the fundus to its condition and to any pathological changes.

The colour of the fundus depends on several factors including the architecture of its layers and the nature and density of any pigments present [1]. Quantitative characterisation of these features should be possible if a one-to-one relationship exists between these physiological factors, and the spectral intensity distribution (SID) of the light remitted from the tissue [2] under a given incident light. This approach has been shown to work for the skin [3]. In this work, it is applied to the ocular fundus to create parametric maps of the key ocular pigments. Although this research work is at preliminary stage, the early results for the healthy fundus look promising. It is hoped that in the long term the results of this research will be used to help with the diagnosis of diabetic retinopathy, which is the most common cause of blindness in the UK's working population [4].

2 Outline of the method

The method involves three main steps. The first step is to determine the composition of the ocular tissue and specifically the properties of its optically active components, their spatial arrangement and their physiologically plausible ranges. This information is usually taken from the previously published literature. The next step is to predict the *entire* range of colours which can occur in the healthy tissue and to relate them to tissue parameters. This yields a model of tissue colouration based on a mathematical model of the optical radiation transport. Finally, the tissue parameters for a particular case are estimated from its colours. This is done by relating the colour of each pixel in a colour image to the histological parameters using the model of colouration computed previously. The distribution of each parameter is shown in a separate monochrome image called a parametric map. A collection of these maps was shown to be valuable in diagnosis of skin disorders [5].

3 Methods

3.1 The structure and optical properties of the ocular fundus

The human ocular fundus comprises a number of optically and anatomically distinct layers as shown in Fig. 1. Its colour is determined primarily by the blood in the choroid and further significantly modified by the amounts of pigment melanin in the RPE and in the Choroid. The internal retina is transparent except for a few vessels, thus reflecting little light. Light is highly scattered by the collagen in the choroidal layer. The colour of blood

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is determined by the chromophores present in it. The most important is the haemoglobin which can exist in oxygenated and de-oxygenated form [6]. The two forms have slightly different absorption properties and for modelling purposes are usually combined in the ratios appropriate for a given tissue. Melanin is a dark brown pigment that is present not only in the fundus of the eye but also in the skin, in the hair and in the iris. Within the fundus it can be found in the RPE and in the choroid. In the RPE higher concentrations of melanin occur in the foveal region, whereas in the choroid the distribution is normally fairly even. The levels of choroidal melanin vary with racial group and with eye colour [7]. Macular pigments, including Xanthopyll [8], are localised in the foveal region. They make a small contribution to the colour of the fundus [7]. Although the lens and the intraocular media do not belong to the eye fundus, they affect the observed fundus colouration. Lenses become yellowish with age, thus reducing the amount of light remitted in the blue region of the spectrum [9]. The intraocular media loses its transparency and may increase the scatter, thus decreasing the visibility of fine detail in the fundus [7].

3.2 Model of colouration for the fundus

The forward Monte Carlo (MC) model of fundus colouration used in this work was originally proposed and validated by Preece and Claridge [10]. Its construction requires information about the structure and optical properties of the fundus and a model of light transport. The fundus structure is shown schematically in Fig. 1. This structure is valid only for young Caucasian subjects and for the perifoveal areas of the fundus. Pigments in each layer are characterized by an absorption coefficient $\mu_a(\lambda)$, a scattering coefficient $\mu_s(\lambda)$ and an anisotropy factor g. The absorption coefficients for melanin and blood are well studied and widely available (e.g. [10] [11]). The availability of scattering coefficient data is more limited and has been taken here from Hammer *et al* [12]. Given the

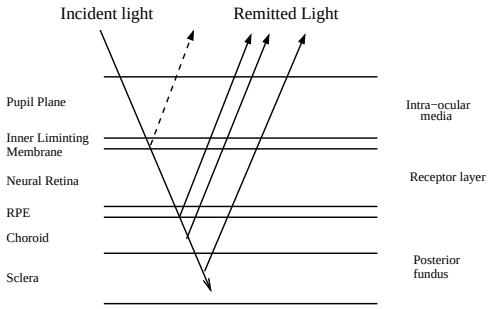

Figure 1. A model pathway of light remitted from the ocular fundus. Figure reproduced from [10].

above information, a mathematical model of light transport, hence capable of solving the general radiative transfer equation (RTE), is required to predict all the potential spectra resulting from the different combination of parameter values. MC simulation [13] provides the most accurate stochastic solution to RTE, and it has been shown to generate spectra which agree well with experimental observations [10]. This process can be denoted by a mapping function from the parameter space, **P**, to the remitted spectra space, **S**. The parameter space $\mathbf{P}$ must be suitably discretised.

$$f : \mathbf{P} \longrightarrow \mathbf{S} \tag{1}$$

The image acquisition process is then simulated by applying optical filter functions to the predicted spectra. This can be denoted by a function from the spectra space **S** to the image space, **I**, whose values are colour vectors, such as for example [R G B].

$$b : \mathbf{S} \longrightarrow \mathbf{I} \tag{2}$$

Figure 3.2 depicts the two stages of the forward modelling process which generates a colour vector for every possible combination of histological parameters. In this way a systematic relationship between image values $\mathbf{I}$ and parameters $\mathbf{P}$ can be established. This relationship is known as the model of colouration.

3.3 Inversion process

The objective of the analysis can now be re-stated as follows. Given a colour image $\mathbf{I}$ and the model of colouration determine the parameter values $\mathbf{P}$. The corresponding mapping function is

$$d : \mathbf{I} \longrightarrow \mathbf{P} \tag{3}$$

This inversion problem does not have to be solved algebraically. Instead a discrete look-up table can be used. For those colour vectors for which the look-up table does not have direct entries, parameter values can be interpolated.

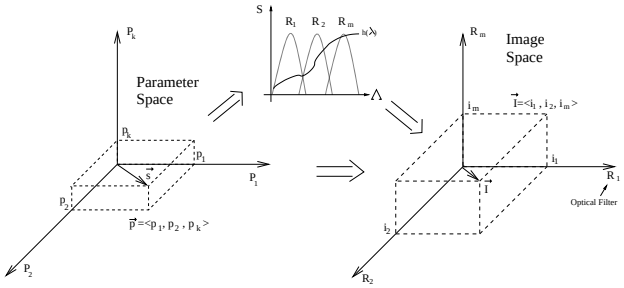

Figure 2. Parameter Space to Image Space

4 An experiment

This section describes a preliminary experiment carried out to get an initial indication of the method's performance. An image of a healthy fundus was scanned from a 35mm slide. The image was uncalibrated and nothing was known about the photographic processes that had produced it. This represents a major problem for the algorithm because the inversion process assumes the calibrated data. Calibration is the subject of further work. In an attempt to reduce the illumination dependence, the original image was normalised by the average local brightness, but in future work the use of calibrated data is envisaged. The image was cropped to show only the part of the fundus which received fairly uniform illumination. This includes the foveal region in which the mapping is expected to fail, since the current model is only valid for the perifoveal region (the additional pigments in the foveal region are not modelled at present). The parameter space $\mathbf{P}$ was very coarsely discretised to a set of $5 \times 5 \times 5$ equally spaced values between the plausible ranges of concentrations of the histological components shown in Table 1.

	Lower Bound	Upper Bound
RPE Melanin	4.0	7.5
Blood Haemoglobin	4.0	7.0
Choroidal Melanin	0.8	2

Table 1. Plausible ranges of concentrations of the histological components (mmol/l) [10].

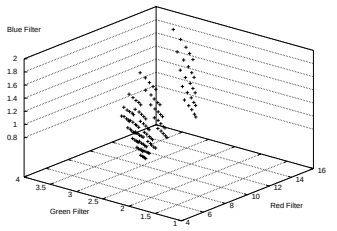

Figure 3. Model of colouration. The main axes correspond to the standard RGB optical filters applied, whereas the sparsity of points reveal the virtual axes for the three parameters considered. Any point in the model of colouration is linked to a unique set of parameters, or concentrations of the histological components considered by the model.

Standard RGB optical filters were modelled as non-overlapping Gaussian functions with central wavelengths located at 650, 550 and 450 nm respectively and full width at half maximum (FWHM) of 40 nm. A schematic representation of the model of colouration is shown in Figure 3 as a cloud of points in the image space $\mathbf{I}$. The individual points are located at the RGB coordinates computed by applying the optical filters defined above to the spectra predicted by the model. Each point in this space has an associated vector of parameter values, indicating the original set of concentrations that have yielded that point in the image space. It can be seen from the figure (Figure 3) that the model of colouration forms a volume within the image space. The sparsity of points shown in the figure helps one to observe the three virtual axes corresponding to quantities of the three histological components. Once the relationship between estimates of the parameters from the image data have been established, the variation of each parameter across the fundus can be displayed in the form of a grey level image. Such image is called a parametric map and may be computed very simply. The RGB values of each pixel in the fundus image provide the index to the model of colouration. The parameters at this location are looked up in (or interpolated from) the model. A set of new grey level images is created in which the colour of the pixel is substituted by a value

representing the magnitude of the given parameter.

5 Results and discussion

Preliminary results are shown in Figure 4. Although the mapping is very crude, the maps exhibit a distribution of pigments which is generally consistent with physiology. The RPE melanin levels increase towards the foveal region. In the central foveal area the incorrectly low levels of melanin are most likely caused by the presence of macular pigments which are not represented by the model. The levels of choroidal melanin do not show much spatial variation across the fundus, as expected. Blood levels are shown in two maps, one focusing on large and medium retinal vessels, the other on blood level variations in the choroid. It can be seen that the retinal vessels are picked up well. When contrast is stretched, some variations in the choroidal blood start showing up, however, their interpretation would be premature because the lack of image calibration certainly introduced large mapping errors. Both maps show high levels of blood in the centre of foveal region, which is incorrect. This is likely to have been caused by the macular pigments, similarly to the RPE melanin map discussed above.

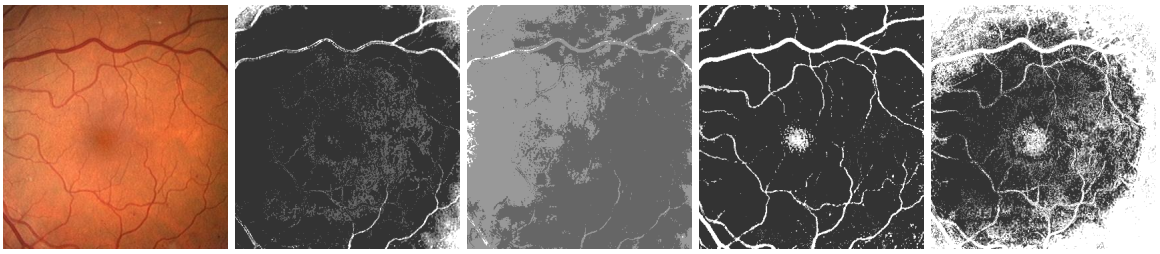

Figure 4. From left to right: Original Image; RPE Melanin Parametric Map; Choroidal Melanin Parametric Map; Blood Parametric Map (Main vessels); Blood Parametric Map (Choroidal variations).

6 Conclusion

The preliminary results reported in this paper indicate that a physics-based interpretation of the colours in the ocular fundus is feasible. The first parametric maps of RPS melanin, choroidal melanin and choroidal blood computed by this method generally show the distribution of the above pigments consistent with physiology. Further work is in progress to include additional ocular pigments in the model, to calibrate or normalise the input image data, and to increase the resolution with which the physiological parameters are discretised.

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