Physics Based Medical Image Understanding of the Colouration of the Ocular Fundus with Application to Detection of Diabetic Retinopathy

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Abstract.
By analysing the interaction of light with the structures and pigments of the human ocular fundus a model has been developed capable of predicting the colouration of ocular tissue. Variations in the colour of healthy tissue can be attributed to changes in the amount of ocular pigmentation and thus the model is used to generate a range of colouration. Representation of this range within a three-dimensional colour space shows the colouration of healthy fundus tissue to be confined to a relatively small volume and as such enables the detection of tissue abnormalities from digital images.
This approach to medical image understanding has also been employed by Cotton and Claridge [1,2] who have been able to predict the colouration of normal skin and from this developed a technique for the early diagnosis of malignant melanoma. In this paper a technique is described which enables the detection of ocular abnormalities which are known to form in diabetic retinopathy. These abnormalities can be detected as they are observed to lie outside the region of healthy colouration predicted by the model.
It is envisaged that the key ideas in this work could be developed to provide a new generic approach applicable to other areas of medical image understanding.

1 Method

As light propagates through biological tissue it is both scattered and absorbed. Scattering primarily occurs from the underlying tissue structure whilst absorption tends to result from the tissue pigments. The back of the eye, referred to as the ocular fundus, comprises three different layers each of which interact with light in a different way. Moving in the direction of incoming light these layers are: the retina, the choroid and the sclera and are depicted in figure 1. The retina consists primarily of neural tissue, which can be considered transparent to visible light. At the interface

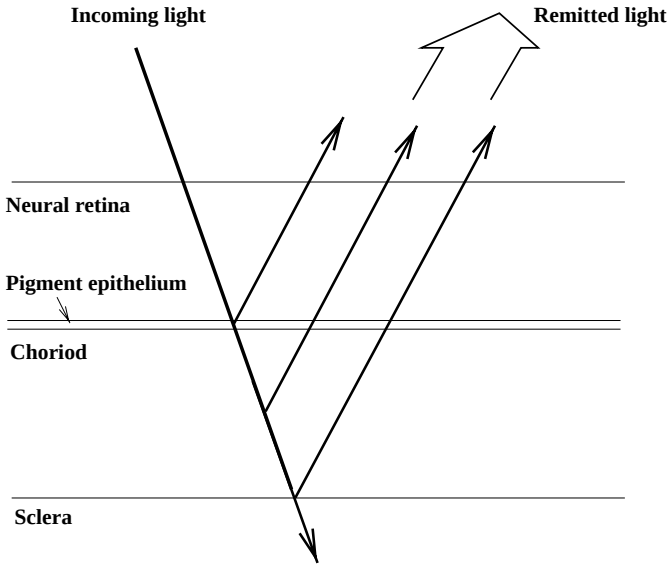

Figure 1. Tissue layers within the ocular fundus

between the choroid and the retina there is a thin layer of cells, know as the RPE (retinal pigment epithelium) which contain a large amount of melanin and as such absorb a significant amount of the incident light. This tissue is also known to scatter light to a degree. The choroidal layer is a very vascular tissue which, as well as containing a large amount of blood, also contains melanin. The concentration of melanin within the choroid is subject to large variations between different ethnic groups and people with different eye colour. Again this layer also scatters light, the scattering originating from the underlying collagen tissue. The scleral layer is made of randomly arranged

collagen fibres which scatter the incoming light to a high degree and as such is known to reflect about 50% of any incident radiation.

If exact scattering and absorption coefficients are known then it is possible to calculate the fraction of incident light remitted from the tissue using the Kubelka- Munk theory [3]. This theory is an approximate solution of the general radiation transport equation and has been shown to work well for other tissue types, for example the skin [4]. Delori and Pflibsen [5] have also applied this theory to the ocular fundus. Using experimental data on the scattering coefficients of the ocular tissue [6] and the absorption coefficients of the ocular pigments [7] the Kubelka-Munk theory is applied at discrete wavelengths and a reflectance spectrum constructed across the whole visible spectrum (400-700 nm). By convolving this spectrum with the appropriate primary response curves it is possible to obtain the RGB values for the spectrum and thus the colour of the tissue.

Colour of the ocular tissue is known to vary considerable from person to person and with position in the individual fundus. This difference in coloration has been attributed to the amount of the ocular pigment present [5, 8]. Thus, to generate a model capable of predicting all possible colours, it is necessary to calculate colouration for an appropriate range of concentrations of each of the ocular pigments. If this range of colouration is represented in a three-dimensional colour space (the RGB values being plotted on orthogonal axes) then it can be seen to occupy a well defined volume which is bounded by physiologically meaningful axes. These axes represent the concentration of melanin in the RPE, blood in the choroid and melanin in the choroid. This volume describes the colouration of all healthy ocular tissue and as such can be used to differentiate between normal and abnormal tissue, which is likely to lie outside this volume.

1.1 Diabetic Retinopathy

Diabetic retinopathy is a disorder of the small blood vessels of the outer retina from which leakage of plasma often occurs. Initially this exuded plasma seeps into the surrounding tissue where it collects. The structure of the surrounding tissue is such that water can pass unimpeded to the inner layers of the fundus but the larger molecules, lipids and lipoproteins, become trapped and build up to form semi-solid residues described as exudates. If left untreated these exudates can cause loss of visual acuity and in some cases even blindness. Indeed diabetic retinopathy is the most common cause of blindness in the working population of the Western world and a significant cause of blindness among the elderly [9].

The colouration of an eye affected by diabetic retinopathy spans the whole range of colours between that of healthy tissue, which is a red-orange colour and that of exudates which are a whitish colour. The explanation for this can be found by considering the directionality of the remitted light. The remitted light is not specularly reflected due to the curvature of the back of the eye and the non-collimation of the incident light. This multi-directionality of the remitted light causes light from healthy tissue to become mixed with that from the exudate boundaries and thus gives the observed range of colours.

By normalising the model with the digital images of the fundus it is possible to use the model predictions to identify any areas which contain abnormal tissue and thus detect the presence of exudates. The errors inherent in the model are calculated giving a region of uncertainty outside of which all tissue colouration is deemed to be from abnormal tissue. The results of this technique are shown in the next section.

2 Results

Figure 2 shows a comparison between the range of colouration predicted by the model and that found in a fundus known to be affected by diabetic retinopathy. The pixels in the right hand image are mostly seen to lie within the region predicted by the model apart from a small proportion which have larger red and green components. Figure 3 shows how the model can be used to detect the presence of exudates within the ocular fundus. The left hand image shows a fundus affected by diabetic retinopathy, the white areas indicating the presence of exudates. In the right hand image tissue which has been detected as being abnormal by the model has been coloured black. A visual inspection of the two images demonstrates the effectiveness of the model.

The acquisition of normalised images of the ocular fundus proves to be a difficult problem. For the purposes of comparison in this investigation an approximate method has been employed which relies on two reference points. At the optic disc there is no pigment and thus no variation in colour between different fundi. The absolute brightness has been measured experimentally by Delori and Pflibsen [5]. A second reference point of a blood

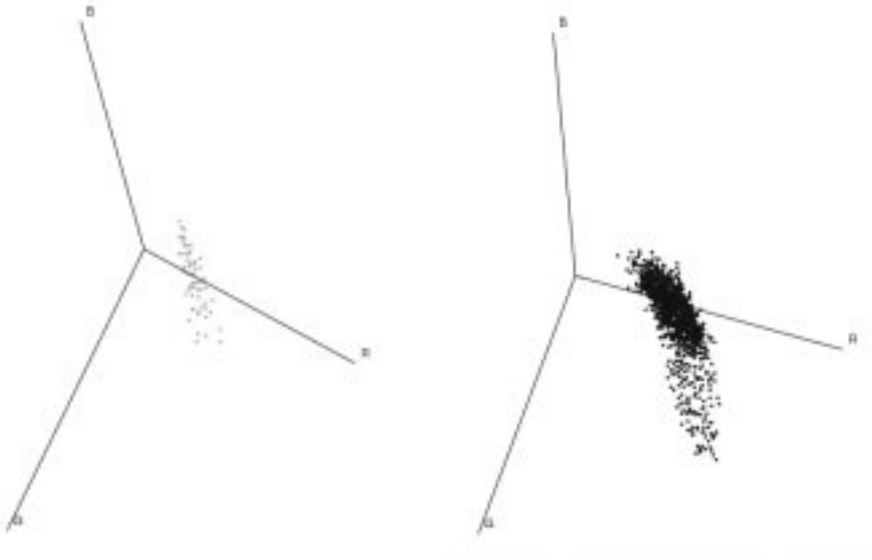

Figure 2. Comparison between the model prediction of colouration and that found in a fundus known to be affected by diabetic retinopathy: The model data is shown on the left and the image data shown on the right

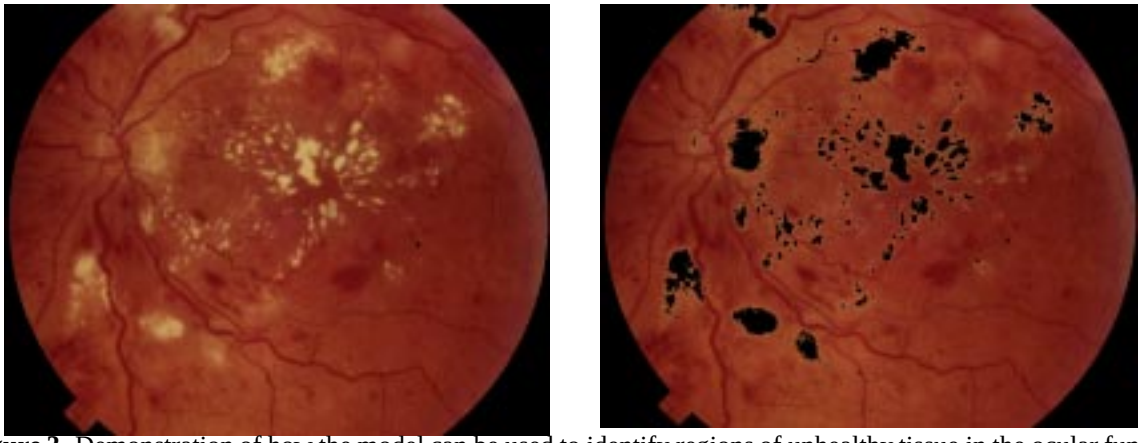

Figure 3. Demonstration of how the model can be used to identify regions of unhealthy tissue in the ocular fundus

vessel lying over the optic disc was employed, for which the intensity could be estimated using a simple model. The brightness of the whole image was then adjusted to fit with these reference points. Work is currently being undertaken to develop a system which will utilise some computational methods of brightness correction [10–12] so that the model data can be compared directly with images.

Another important difficultly which must be overcome is one of uniform illumination across the fundus during image acquisition. Again techniques are currently being developed to combat this problem. At the moment only the image shown in figure 3 is known to satisfy this condition and so it is not possible to demonstrate the model on other images.

3 Discussion

The work described in this paper uses the methodology developed by Cotton and Claridge [1,2] with modifications to the computational solution of the Kubelka-Munk theory. Their work has been a huge success and a system has been developed which is now being tested clinically. The preliminary studies described here have shown the technique to be applicable to the ocular fundus and models are currently being developed for the many different types of tissue abnormality which are known to occur. It is hoped that this will enable accurate differentiation between healthy and abnormal tissue which, in turn, will enable more general diagnostic techniques to be developed to assist ophthalmologists in their clinical practice.

It is envisaged that the key ideas in this work could be developed to provide a new generic approach applicable to

other areas of medical image understanding. These ideas are effectively a combination of three separate techniques. Firstly data must by acquired across a range of wavelengths. Secondly the underlying physics must be understood so that a forward mathematical model can be constructed and thirdly the image data and the model results must be represented so as to provide an effective mapping between measurable quantities and histological parameters.

Cotton and Claridge , in their model of skin colouration, are able to map between measured colour and the concentration of melanin and blood. From this they make accurate deductions on the nature of the tissue. It is hoped that such a mapping can be developed for the ocular fundus. In particular it would be of great clinical value if precise histological data could be obtained in the region of the optic disc as this would enable early detection of glaucoma.

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