Structural and spectroscopic in vivo imaging of the human retina with scanning light ophthalmoscopy

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Ophthalmic imaging has been an active area of clinical investigation that has been expanding steadily, providing scientists and doctors with valuable information. New diagnostic and therapeutic methods have been established in this field, driven by an overall need to advance clinical care in ophthalmology. New scanning and imaging technologies have had a significant impact on ophthalmology. Structural imaging techniques help in visualising the retina in great detail and helps in assessing retinal health. However, the structure does not always provide information on the tissue health, and thus techniques which can provide a quantitative, functional aspect of living tissue is required in many cases. The work presented in this thesis aims to develop new devices and techniques which can perform imaging of the retina and to apply them for non-invasive imaging of structure and function in the *in vivo* human retina.

To extract structural and functional information from the retina using an SLO, it is essential to understand it's design, construction, and working. For this purpose, **chapter 2** of this thesis discusses the principle of scanning based ophthalmic imaging systems, gives a brief explanation of various design considerations for constructing an SLO, and introduces the retinal oximetry and its importance in diagnosing various retinal diseases. Laser safety considerations for intentional exposure of the retina to the laser light is also described in detail. The knowledge from this chapter forms the basis of the scientific work presented in chapters 3 to 6.

In **Chapter 3**, a novel digital micromirror device (DMD) based SLO is presented. Concentric circle patterns were implemented as a scanning scheme to image the retina and provide fixation at the same time. The DMD was used *in lieu* of traditional scanning mirrors and offered flexibility in terms of speed and confocality. The concentric circles improved the fixation and reduced motion artefacts compared to previously implemented parallel line scanning design. An annulus was used to reduce the corneal reflections from the retina and thereby to increase the signal to noise ratio. *in vivo* imaging was demonstrated by performing non-mydriatic imaging on two subjects at a speed of 7 frames per second with a maximum 20° (diameter) field of view. The images were shot noise limited and clearly show various anatomical features of the retina with high contrast. The images were comparable to images from a commercial SLOs but at a fraction of the cost.

Chapter 4 describes a detailed analysis of the error propagation of measurement noise in retinal oximetry, to identify optimal wavelengths which will yield the lowest uncertainty in saturation estimation for a given measurement noise

level. The effect of haemoglobin packing in discrete blood vessels (pigment packing) is also introduced in this chapter. Pigment packing may result in a non-negligible bias in saturation estimation if unaccounted for under specific geometrical conditions, such as sub-diffuse sampling of smaller blood vessels located deeper within the retina. To validate the analysis, an SLO was developed to produce high contrast images. Confocal reflectance measurements were then conducted on a tissue-mimicking scattering phantom with optical properties similar to retinal tissue, including narrow channels filled with absorbing dyes to mimic blood vessels. By imaging at three optimal wavelengths, the 'saturation' of the dye combination was calculated.

In **Chapter 5**, construction of an SLO based on a double-clad fibre coupler and a supercontinuum source is described in detail. Implementation of a balanced detection scheme to suppress the relative intensity noise of the supercontinuum source is also described with experiments validating the improvements in the signal to noise ratio with the use of balanced detection. The optimum wavelengths for accurate *in vivo* oximetry estimation using two wavelengths are established with an *in silico* analysis. The SLO produced dual-wavelength, high-quality images at 10 frames / second with a 20° imaging field of view. The blood oxygen saturation in retinal blood vessels was mapped from the images.

The eye provides a unique location in the human body with visual access to blood vessels. The blood vessels in the eye are regarded as highly superficial and thus is a desirable access point for Hb concentration estimation due to the lack of thick overlying tissues present elsewhere in the body. In **Chapter 6**, a non-invasive spectrophotometric method to image the retina simultaneously at two 'isosbestic' wavelengths, and then to extract the haemoglobin concentration values from the two images is described.

Finally, in **Chapter 7**, the discussion on the results obtained from the scientific work in chapters 3-6 is presented with an outlook for future research. The concluding remarks of the thesis are also given in this chapter.