Optical Measurement of Glucose Content of the Aqueous Humor

Dan Daly and Graeme Clark, Lein Applied Diagnostics

Many diabetics must measure their blood glucose levels regularly to maintain good health (Appendix 1). In principle, one way of measuring the glucose concentration in the human body would be by measuring optically the glucose content of the aqueous humor in the eye. Lein Applied Diagnostics wish to assess how feasible this is,

1. purely by a system using a linear confocal scan (Appendix 2) with an LED source, as described below; and
2. by supplementing such a system with other suitable measurements.

The sensitivity of the refractive index of the aqueous humor to the glucose concentration is of the order of one part in 10^5 for a change in glucose concentration of 5mg/dl, and concentrations of between 50mg/dl and 400mg/dl need to be detected reliably.

Confocal Scanning: The use of a confocal scanning technique enables one to measure the optical depth of the aqueous humor to this required accuracy. The optical depth, D, is given by L/n where L is the physical depth of the anterior chamber and n is the refractive index of the aqueous humor. This direct measurement cannot be made in practice as the real depth of the anterior chamber changes due to corneal swelling and accommodation of the ocular lens.

Problem 1: Is it possible to use other information obtainable from the confocal microscopy to resolve this point. In particular the measurement detects retro- reflections from the front and back of the cornea, and from the front and back of the lens, in addition to the measurements giving the location of the various surfaces. Do these retro- reflections provide the necessary information?

Problem 2: If the scan can only tell us the optical depth, what else could be measured that would enable the refractive index to be obtained to the required accuracy? In particular, can this be achieved by any of (or some combination of) the following:

1. Taking measurements at different wavelengths of light. Two wavelengths allow the measurement of the dispersion of the aqueous humor, which is a function of the glucose concentration.

2. Taking several measurements, say one when the subject is focusing on infinity and one when he or she is focusing in the near- field.
3. Use of polarization (since glucose is optically active).
4. Use of spectroscopic techniques.
5. Other suggestions

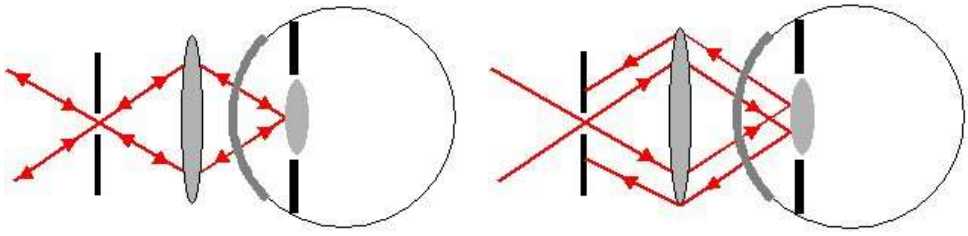
Appendix 1

Diabetes is a large and growing problem. The International Diabetes Federation estimates that some 194 million people worldwide have diabetes today. In the UK, 3.9% of the adult population in the UK is diabetic. By 2025, the number of diabetics is forecast to jump to 333 million worldwide. In this market, glucose self- monitoring is essential for identifying when a diabetic's blood sugar level is too low, in which case they may have seizures, or too high, which can lead to blindness and invalidity in the longer term.

The current 'finger stick' method of measuring blood glucose is a multi- step process that is particularly difficult for young and elderly patients, or those with impaired vision or motor control. The user pierces her skin with a lancet to draw blood, applies the blood to a test strip, and then inserts the strip into a meter from which the glucose value is read. This process is painful, risks infection, can damage nerves and is unpopular, especially with young children and teenagers.

Appendix 2

The confocal technique works as shown in Figure 1.



(a). Eye in focus ***(b). Eye out of focus***

Figure 1. Principle of confocal measurement

The principle of the process is that if the surface of one of the components of the eye is at the focal point of the measurement lens (as

in Figure 1(a)) light will be retro- reflected along its original path and will pass through the small pinhole. This light will then fall on a detector and a large intensity signal is seen. If no surface is at the focal point (as in Figure 1(b)) the reflected light diverges and hardly any makes it back through the pinhole. The detector therefore registers a low intensity signal.

This technique can be applied to the measurement of the refractive index as described below. An outline concept of a test system is shown in Figure 2.

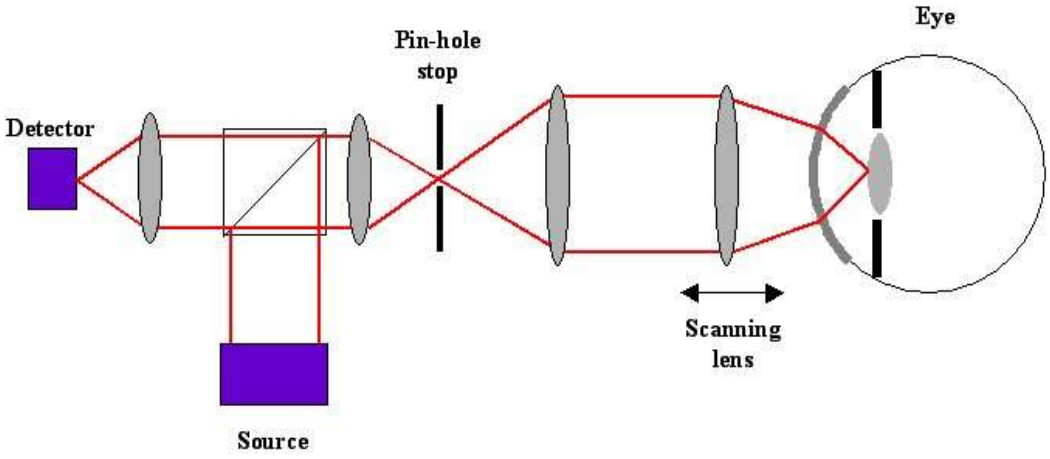


Figure 2. Confocal arrangement to measure the refractive index of the aqueous humor

As the scanning lens is moved backwards and forwards a bright image will be seen on the detector when the returning light reflected from the eye is focussed through the pinhole stop. At each interface (cornea/aqueous humor, aqueous humor/lens etc.) there will be light reflected such that during the scan the intensity profile shown in Figure 3 will be generated.

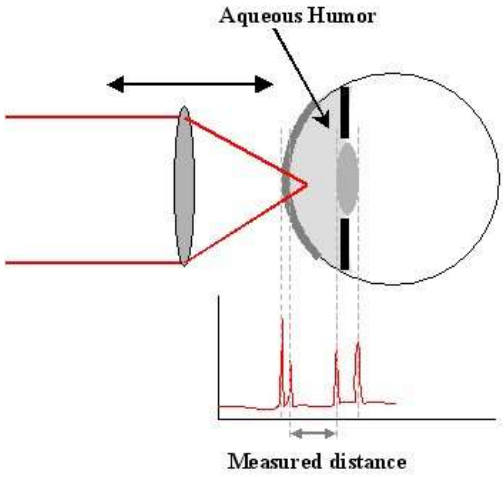


Figure 3. Intensity profile seen during the scan.

The physical distance moved by the scanning lens between the two central intensity peaks is directly related to the refractive index of the aqueous humor. The glucose concentration can therefore be calculated by knowing the position of the scanning lens when a bright image is seen on the detector.