

## Chapter 3

# A New, Non-Invasive *in vivo* Optical Blood Glucose Measurement Technique Using Near-Infrared Radiation (“*Pulse Glucometry*”) and a Proposal for “*Pulse Hemo-Photometry*” Blood Constituent Measurements

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### ABSTRACT

*A recently proposed optical method for a non-invasive in vivo blood glucose level (BGL) measurement named “pulse glucometry” is introduced. This method is based on near-infrared living body spectroscopy to accurately obtain blood information. The remarkable feature of the method is the measurement of both the total transmitted radiation spectra in wavelength  $\lambda$  ( $I^{\lambda}$ ) and the cardiac-related pulsatile component ( $\Delta I^{\lambda}$ ). When  $\Delta I^{\lambda}$  is superimposed on  $I^{\lambda}$ , the differential optical density ( $\Delta OD^{\lambda}$ ), which includes only arterial blood information, is obtained, thus avoiding interference from living tissues other than arterial blood. Another feature is the ability to measure the differential optical density ( $\Delta OD^{\lambda}$ ) in multiple wavelengths to avoid interference from blood constituents other than the target blood chemical (glucose).*

*To support this methodology, a very fast near-infrared spectroscopic system was developed to obtain a photoplethysmographic cardiac signal with a resolution of 8 nm over a wavelength range of 900 to 1700 nm at a 100 Hz sampling frequency. An example of an in vivo BGL measurement is shown and indicates good prediction capabilities. This method can be expanded to the measurement of other blood constituents.*

## **INTRODUCTION AND BACKGROUND**

Knowing the levels of blood constituents and chemicals is very important in the medical field for monitoring the status of patients. Thus, the non-invasive measurement of blood constituents has been a desirable technique for a long time. *In vivo* blood glucose measurement is the primary example of a blood constituent measurement discussed in this study.

The measurement of blood glucose levels (BGL) has long been considered an essential and crucial need for self-care in diabetes and screening in pre-diabetes, as well as for routine health care in normal subjects. In particular, frequent BGL measurements are of the utmost importance in the care of diabetes (Lawton, Peel, Douglas, & Parry, 2004). Many types of portable blood glucose self-monitoring devices (SMBG), sometimes simply called blood glucose meters, using different technologies have been commercialized by different manufacturers. However, almost all of the currently used SMBG devices are based on the user's piercing their own skin with a small needle or lancet and drawing a blood sample. Although the amount of blood sampled is small, this procedure has severe limitations, as frequent monitoring is necessary and the repeated painful puncturing of the skin is troublesome and, furthermore, can cause an infection. These limitations have led to the search for alternative, non-invasive BGL measurements.

To date, the FDA has only approved the non-puncturing GlucoWatch Biographer, which uses reverse-iontophoresis to draw glucose molecules out *via* the inner skin and an electro-chemical electrode (Tierney *et al.*, 2000). Although the GlucoWatch Biographer could sometimes be considered as a minimally invasive blood glu-

cose meter, its measurement procedure can still cause skin irritation after repeated measurements (Eastman *et al.*, 2002). Thus, a truly non-invasive BGL measurement is still desired and has been explored by many research groups and companies worldwide. For example, a surface plasmon resonance technique using ATR prism (Aslan, Lakowicz, & Geddes, 2004; Berger, Itzkan, & Feld, 1997) and an optical coherence tomography (Maier, Walker, Fantini, Franceschini, & Gratton, 1994) were proposed for obtaining blood glucose information from the body's surface. However, in theory, the measurable region for those methods should be too shallow to obtain the blood information directly, especially when using the surface plasmon resonance technique. These methods can only obtain information from the epidermis or dermis. Photo-acoustic techniques and an electrical impedance spectroscopic method were also applied as non-invasive measurement methods (Caduff *et al.*, 2006; DeVries, Wentholt, Zwart, & Hoekstra, 2006; MacKenzie *et al.*, 1999); however, the theoretical backgrounds of the measurements are still unclear. For example, A. Caduff *et al.* (2006) reported that glucose variations affect the electrical properties of cellular membranes and that this can be measured by the electrical impedance spectroscopic method (Caduff *et al.*, 2006). However, this simultaneously shows that the impedance spectroscopic method cannot measure glucose concentrations directly. Because diabetes mellitus is a disease of abnormal glucose sensitivity, it is unclear if the glucose-dependent electrical properties of cellular membranes are not altered in diabetes. Unfortunately, reliable and clinically acceptable measurement methods have not yet emerged, despite considerable attempts for more than four decades.

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