

Glucose content monitoring with time-of-flight technique in aqueous Intralipid solution imitating human skin: Monte Carlo simulation

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ABSTRACT

Glucose content monitoring is of great importance today due to a number of people suffering from diabetes. In this paper, laser pulses propagation in a sample of aqueous Intralipid solution with glucose is simulated by Monte Carlo method. Effect of glucose is based on refractive index matching of Intralipid vesicles and surrounding water if glucose is added. Temporal profiles of femtosecond pulses (906 nm) diffusely scattered within a 2-mm thick plain glass cuvette with a skin phantom are registered in backward direction by fiber-optics detectors 0.30 mm in diameter with numerical apertures of 0.19, 0.29, and 0.39. It is revealed that glucose content within the physiological range (100-500 mg/dl) can be detected because of the effect of glucose on the peak pulse intensity and on the area under the pulse temporal profile (energy of the registered pulse).

Keywords: light propagation, skin phantom, optical diagnostics, medicine, time-of-flight technique.

1. INTRODUCTION

A problem of diabetes is one the most acute nowadays. More than 140 million people worldwide suffer from it. As it is reported¹, this number will increase up to 300 million by the year 2025. The disease develops due to either lack of the hormone insulin created by pancreas in the organism or inability of cells to accept it. These two mechanisms cause two kinds of diabetes (I and II respectively). It could lead to increased amount of glucose in blood resulting in coma and even death of an individual. That is why determination of glucose content in blood and skin is of great importance. Currently, glucose diagnostics is carried out mostly by finger prickling. Such unpleasant procedure can prevent diabetic patients from monitoring the glucose content as often as necessary. In order to avoid psychological problems, novel non-invasive, in particular, optical methods should come into practice.

Many optical approaches have been suggested: NIR absorption and scattering²⁻⁵, polarimetry⁶⁻⁷, Raman spectroscopy⁸, photoacoustics⁹, and time-of-flight technique¹⁰. However, all of them suffer from the lack of sensitivity within the physiological range of glucose (100-500 mg/dl). In particular, in¹¹ due to rather long pulses used (30 ps) only very high concentrations of glucose could be detected in transillumination geometry both experimentally and by simulations (4-8 mass %, i.e. 4000-8000 mg/dl).

In this paper, we show by means of Monte Carlo simulations that method of optical time-resolved spectroscopy applied for backward detection geometry is a promising tool for this task.

2. MATERIALS AND METHODS

In this paper, we simulate propagation of laser pulses within a 2-mm plain cuvette filled with 2% Intralipid solution as the best phantom for skin in NIR range¹². The setup modelled in our study is represented in Fig. 1. As a light source, a

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laser with the wavelength of 906 nm is considered. Related to this, optical properties of Intralipid solution are calculated basing on published data¹³, namely: anisotropy factor $g = 0.57$, scattering coefficient $\mu_s = 4 \text{ mm}^{-1}$, absorption coefficient $\mu_a = 0.007 \text{ mm}^{-1}$ (as it is for water because Intralipid is non-absorbing in NIR), refractive index $n_{int} = 1.325$. The cuvette is supposed to be made of glass with $n_{glass} = 1.5$. Laser pulses of zero duration (temporal delta-function) are injected into infinitely small (point-like) spatial region. The scattered pulses are registered in backward direction by round detectors 0.3 mm in diameter (mimicking the optical fibres with numerical aperture NA of 0.19, 0.29, and 0.39) with temporal resolution of 0.1 ps. Such detection corresponds to *in vivo* conditions. Each probing pulse contains 500 million photons providing reasonable compromise between the statistical error and computational time (about 10 hours for P-IV 1700 MHz, 512 MB RAM).

Glucose affects the refractive index of water decreasing its mismatch with Intralipid vesicles resulting additional fraction of $\Delta n = 1.515 \times 10^{-6}$ for each additional mg/dl of glucose. The value of g increases by 0.007% per C/18, where C is glucose concentration in [mg/dl].¹⁴ Due to possible cell volume change the scattering coefficient may decrease by 0.22% per C/18, where C means the same as earlier.¹⁵

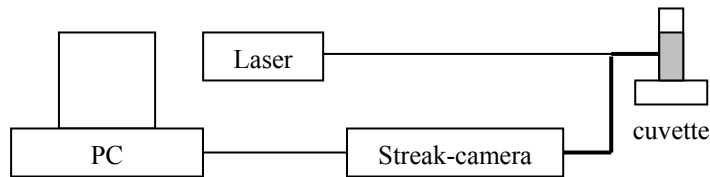


Fig.1: Setup mimicked in the Monte Carlo simulations.

3. RESULTS AND DISCUSSION

The effect of five concentrations of glucose was simulated: 0, 100, 300, 500, and 1000 mg/dl. The second one corresponds to a normal value typical to human blood (70-160 mg/dl)¹⁵, while the larger ones are related to the increased level, with 500 mg/dl causing coma; 1000 mg/dl is considered to see the effect clearer. Typical temporal responses of the turbid medium used in the simulations, are represented in Fig. 2. Decrease in the value of μ_s and increase in that of g (resulting from an increase in glucose content) cause less detected photons in the backward direction. Curves are processed with adjacent averaging over 5 points (otherwise 0.5 ps). It is seen that the curves are distinguishable within the first 3 ps of detection.

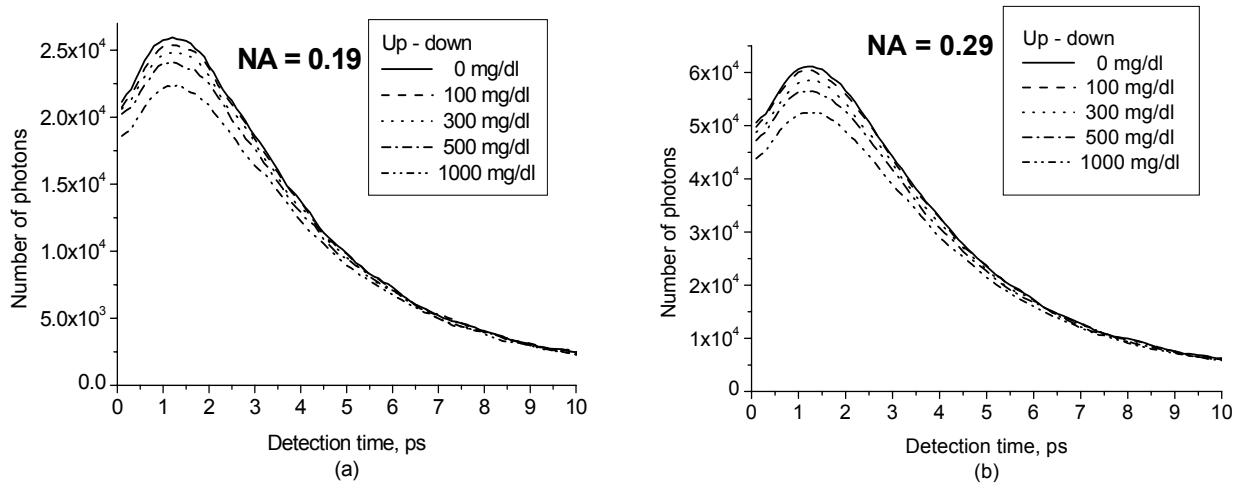


Fig. 2: Temporal diffuse reflected profiles (smoothed by 5 points) of δ -pulses (injected at zero-time) registered by fiber-optics detectors with numerical apertures NA = 0.19 (a) and 0.29 (b) at different glucose content.

Peak intensity and area under the curves derived from these plots are depicted in Fig. 3. A larger numerical aperture of the detecting optical fiber causes more registered photons. For practical reasons the higher is the detected intensity – the better because the useful signal is more distinguishable at the background of noise. The better difference (steeper line) between different glucose content is obtained also for higher NA. This can be observed in both Fig. 3 (a) and Fig. 3 (b).

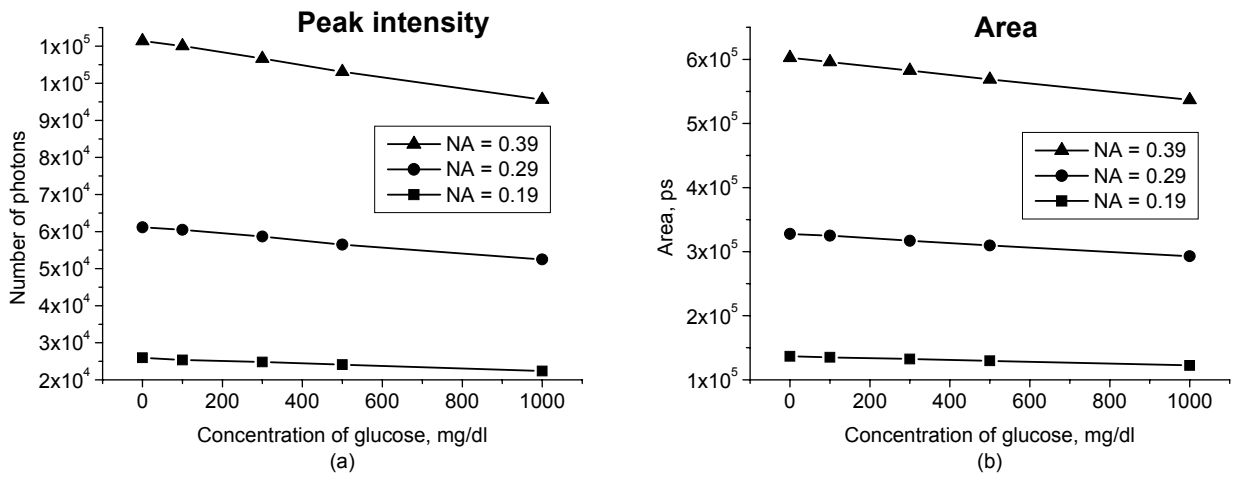


Fig. 3: Peak intensity (a) and area (b) of the backward-scattered pulses at numerical apertures of 0.19, 0.29, and 0.39 versus glucose concentration.

Figure 4 also illustrates the influence of glucose but in regard to intensity of scattering inside the sample. Pulses enter at zero depth. As the scattering coefficient decreases, photons undergo less scattering acts. Maxima in the curves are caused by diffuse scattering. They are located under the surface of the layer. More detailed analysis shows that the peaks even shift a bit to deeper positions as the glucose concentration increases.

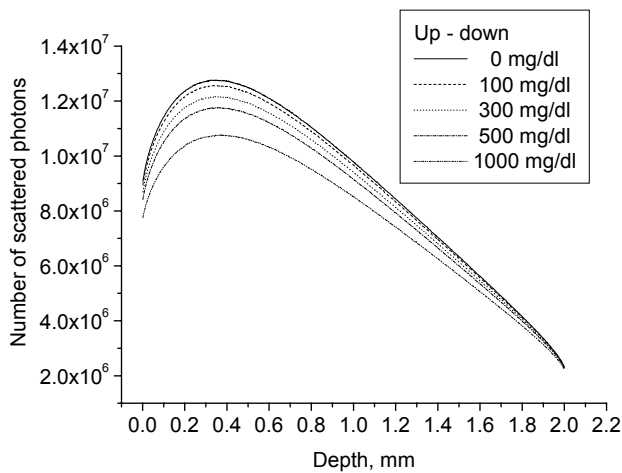


Fig. 4: Profiles of in-depth scattered light intensity inside the sample at concentration of glucose within a range of 0-1000 mg/dl.

4. CONCLUSIONS

We studied a possibility of glucose sensing in an Intralipid-2% skin phantom with femtosecond pulsed laser radiation (satisfactory approximation for delta-function shaped pulses) at a NIR wavelength of 906 nm. Detecting the backscattered radiation with an optical fibre, changes in the glucose level within the physiological range can be detected.

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