Abstract

Frequent monitoring of blood glucose levels is an essential part of diabetes care, but the invasiveness of current devices deters regular measurement. Non-invasive glucose measurement techniques are painless to implement and rely on changes in sample properties to estimate glucose concentration. The use of near infra-red (NIR) photoacoustic spectroscopy (PAS) for continuous non-invasive blood glucose measurements is explored through simulation studies, followed by experiments on different sample media. The theoretical background of the technique is outlined and verified through simulation, and experimental studies are performed using a photoacoustic measurement setup. The apparatus is used to obtain dual-wavelength photoacoustic measurements *in vitro* from aqueous glucose solutions, solutions of glucose and hemoglobin, and whole blood samples, and the results show the values of the signal features to vary with the change in sample glucose concentration. However, the measurements are affected by the presence of other biomolecules, resulting in an increased estimation error and necessitating calibration to obtain accurate glucose concentration estimates. A kernel based calibration algorithm using multiple features of the photoacoustic signal is used to estimate glucose concentration from photoacoustic measurements. The calibration of photoacoustic measurements from glucose solutions using Gaussian kernel-based regression results in a Root Mean Square Error (RMSE), Mean Absolute Difference (MAD), and Mean Absolute Relative Difference (MARD) of 7.64 mg/dl, 5.23 mg/dl, and 2.07% respectively. Kernel-based calibration also performs well on solutions of glucose and hemoglobin, and whole blood samples, resulting in lower estimation errors than that of previous efforts and with glucose estimates being in the acceptable zones of a Clarke Error Grid (CEG). It allows for individual calibration of photoacoustic measurements in vivo, resulting in a RMSE, MAD, and MARD of 19.46 mg/dl, 10.79 mg/dl, and 7.01% respectively with 89.80% of the estimates being within Zone A of the CEG. The use of polynomial kernel-based calibration also provides better performance over previous efforts with a mean absolute relative difference (MARD) of 8.84% and Clarke Error Grid distribution of 92.86% and 7.14% over Zones A and B of the grid. The improvement in the estimation accuracy with the use of dual glucose-specific excitation wavelengths for photoacoustic measurements along with kernel-based calibration would enable continuous non-invasive glucose monitoring, facilitating better diabetic care and improved treatment outcomes.

Keywords: Diabetes, Glucose Monitoring, Noninvasive Measurement, Photoacoustic Spectroscopy, Calibration, Kernel Methods