Optimising Multivariate Models for Glucose Measurements in an ATR-FTIR Spectrometer

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Introduction

Blood glucose monitoring is essential for diabetes management, and contributes substantially to the world's biosensor market [1]. Most glucose sensors used today utilise enzymatic reactions. Some are used for continuous glucose monitoring (CGM), but due to the need for reagents they suffer a loss of accuracy and reliability over time. Optical spectroscopy may be a better alternative for CGM, as it is reagent-free [2].

Principal component regression (PCR) and partial least squares regression (PLSR) modelling are two common methods used to analyse spectroscopic data. PCR and PLSR models often use the entire available spectrum, although wavelength selection can improve model performance [3]. An example of how to choose the best spectral ranges can be found in [4,5], where moving-window (MW) PLSR was implemented for near-infrared spectroscopy of glucose solutions. With the MW-method, a series of multivariate models are built in a window that is moved over the entire spectrum. Optimal spectral ranges are then chosen for the model, using the error levels and number of components to evaluate the model.

This work aims to compare PCR and PLSR directly for glucose concentration measurements in mid-infrared (MIR) spectroscopy, using both the full spectrum and MW-search. These results will also be used to assess the viability of using MIR spectroscopy for CGM.

Methods

Measurements

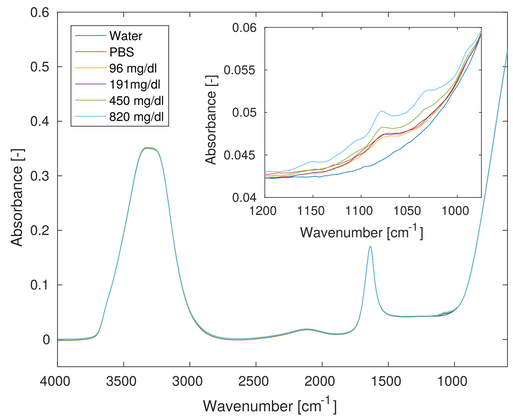
- 22 solutions with phosphate-buffered saline (PBS) and glucose concentrations 36-820 mg/dl (2.0-45.5 mmol/l)
- Data acquisition with an ATR-FTIR spectrometer from Bruker Optics
- Spectra in the 4000-600 cm^{-1} range
- Each measurement consists of 128 scans with a resolution of 4 cm^{-1}

Data analysis

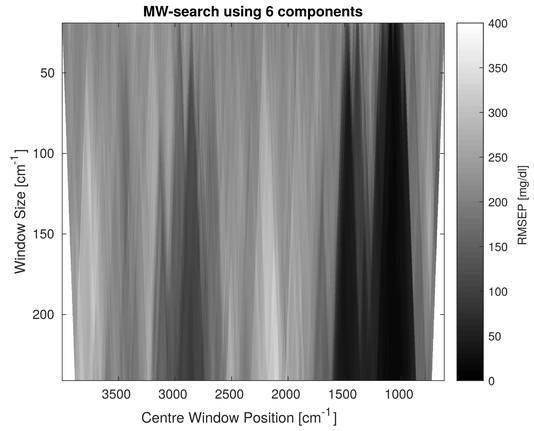
- PLSR and PCR methods were implemented in MATLAB
- 84 measurements are used for calibrating (training) the models and 33 measurements are used for validation
- The MW-search scans the entire spectrum with window sizes 20-240 cm^{-1} and 2-20 components (regression coefficients) for both methods
- Root-mean-square errors of calibration and prediction (RMSEC and RMSEP) are used to evaluate the models

Results

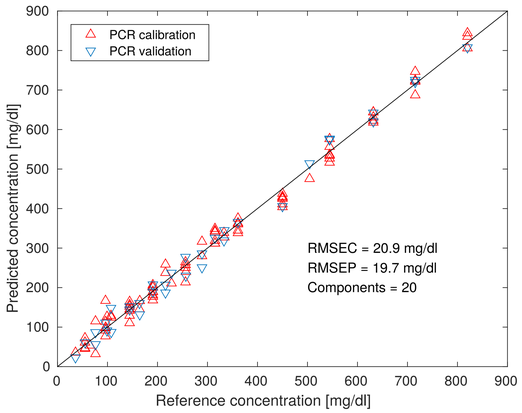
- Different absorbance spectra in FTIR:

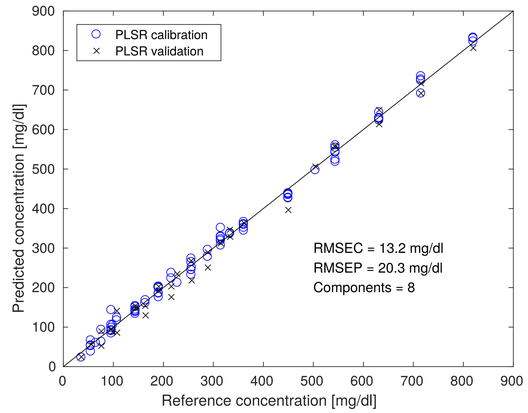


- Example of variation in RMSEP for PLSR modelling:

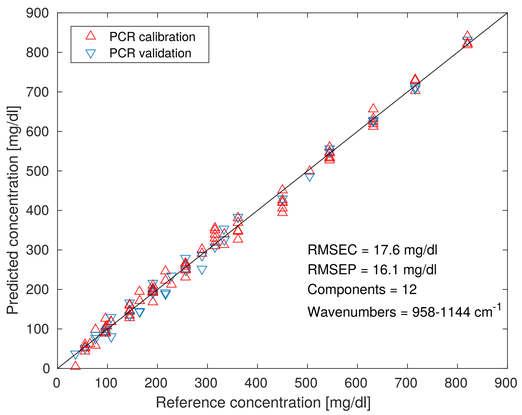


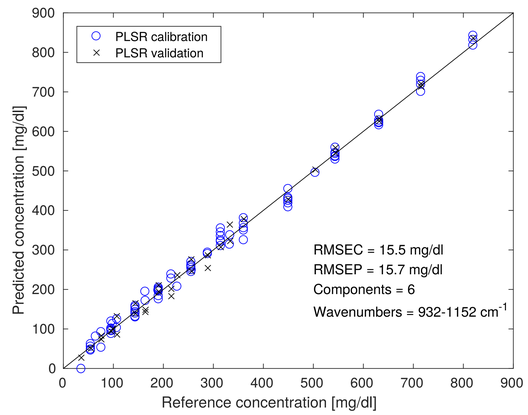
- Results from PCR and PLSR using the full ATR-FTIR spectrum:





- Results from PCR and PLSR using the MW-search for wavelength selection:





Discussion

- Glucose concentrations can be predicted from measurements in the mid-infrared range, down to physiologically relevant levels
- Regression methods are more suitable than e.g. measuring peak intensities, due to complex spectral features and a relatively low glucose signal
- Prediction of glucose concentration is consistently improved with proper wavelength selection
- PLSR and PCR performances are similar, with PLSR attaining a slightly better RMSEP than PCR after the wavelength selection
- Wavelength selection reduces the number of required components, decreasing the complexity of the models
- PCR requires more components than PLSR
- The high linearity indicates that MIR spectroscopy is suitable for glucose measurements, and with wavelength selection it can be seen that a small range around 1000 cm^{-1} should be sufficient

Future Work

- Develop transmission-mode glucose monitoring system
- Using a tunable quantum cascade laser as a source
- Testing in relevant biofluids

References

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