

The Study of the Dielectric Response of Red Blood Cells to Sugar Exposure – *In vitro* Basis for Non-invasive Glucose Impedance Monitoring

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Introduction

Monitoring glucose levels non-invasively would probably be the most attractive option for patients with diabetes [1,2]. Because of the specific reactions of blood and tissue cells to varying glucose concentrations, the electrolyte balance across the membranes of blood cells and underlying tissue is changed [3]. This in turn results in a change in the membrane's electrical properties that can be effectively monitored by dielectric spectroscopy (DS). Such *in vitro* characterization can provide an essential basis for further understanding and development of non-invasive glucose monitoring methods for *in vivo* application [2]. In this research, we propose possible biophysical underlying mechanisms.

Methods

The general principles of Time Domain Dielectric Spectroscopy (TDDS) and a detailed description of the experimental measurement method and procedure have been previously described [4-5]. Dielectric measurements of the cell suspensions were provided with the TDDS set-up with a recording system at non-uniform time-scale up to 5 μ sec (frequency range from 200 kHz up to 2 GHz) [6]. After isolation and pretreatments, the cells were re-suspended in PBS with varying sugar concentrations and measured by TDDS. The part of the dielectric permittivity spectra, corresponding to the Maxwell-Wagner relaxation process, was fitted by a modified approach for spheroid particle suspensions. The volume fraction and size of the suspended cells were concurrently measured.

Results

An almost monotonic increase of the erythrocyte's membrane capacitance was observed with increasing D-glucose concentration. No associated change in membrane capacitance was indicated for an increasing non-permeable L-glucose concentration. Similar to D-glucose dose-response, membrane capacitance variance was found when the cells were exposed to fructose. This could mean that the observed capacitance changes are possibly coupled to glycolytic processes and related regulation. Furthermore we found a significant discrepancy in the membrane response to 2-deoxyglucose, which is a non-metabolized D-glucose derivative. This leads us to suggest that the source of the observed alterations is associated with glycolytic processes. Additional, *in-direct* support for this proposal comes from the DS study of Na⁺ and K⁺ roles on D-glucose-induced membrane responses. We observed a strong correlation between ion arrangements and membrane capacitance changes. The effect became more pronounced at "hyperglycemic" D-glucose

levels (>12mM). Finally, we present possible mechanisms to account for the observed RBC membrane alterations.

Conclusions

DS has shown to be a sensitive method for monitoring cellular responses on transport of sugars that differ in transport ability, kinetics and transport mediators. These results will further help to facilitate and continue the development of sensitive miniaturized tools aiming at in vivo glucose monitoring techniques, based on the characterization of the dielectric properties of tissues and blood.

References:

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