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Q-Sense | [Application Note] 16

QCM-D viscosity analysis for microlitre protein samples

High concentration protein solutions are common in pharmaceutical applications. For example, solution formulation of monoclonal antibodies for therapeutic purposes often necessitates preparation of high concentration solutions of these proteins. Since high concentration solutions are expensive, sample volume is critical. This application note demonstrates how Q-Sense QCM-D instruments can be used to measure viscosity in microliter volumes.

Introduction

The Quartz Crystal Microbalance with Dissipation (QCM-D) measures viscosity with a shear oscillation technique. The change in the resonance frequency (Δf) of the oscillating sensor and the dampening of the sensor movement (ΔD) are monitored when the sample is injected into the sensor chamber. The evaluation software QTools* allows for calculations of viscosity for both Newtonian and non-Newtonian fluids.

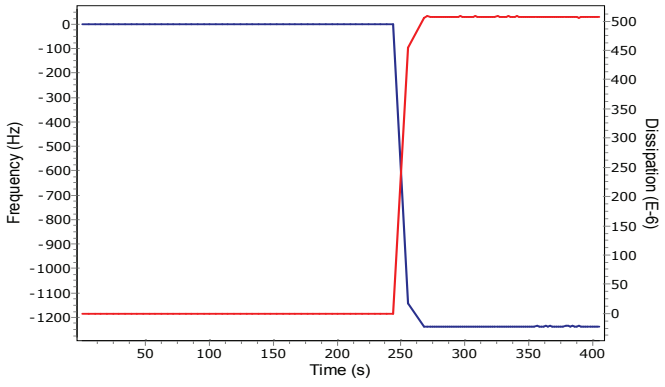
Approach

To prove the use of QCM-D as a viscometer, two viscosity standards, S3 and S6, were measured at different temperatures. Viscosity standards are well characterized Newtonian fluids used for calibration of viscometers and were purchased from Paragon Scientific, UK. Next, sucrose solutions of different concentrations were measured. These results were verified by comparison to other published data on viscosity of the same fluids. To demonstrate the usefulness of the QCM-D viscometer in protein applications, viscosities of concentrated BSA (bovine serum albumin) solutions were measured. Sample-to-sample variations were measured by testing 3-4 samples under the same conditions at the same time for all studies.

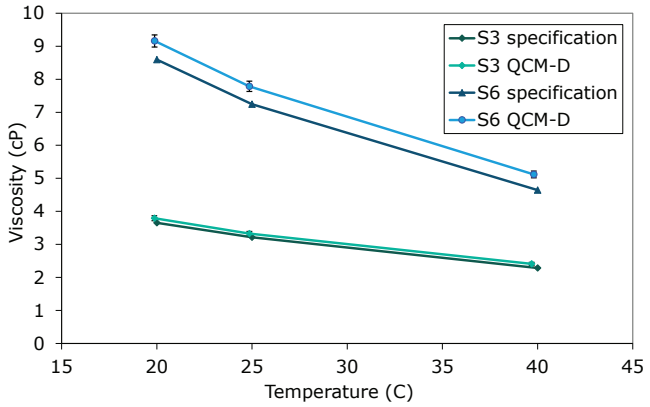
Results and discussion

Figure 1 shows a typical QCM-D data output of a viscosity measurement. The reading starts with an empty chamber, followed by inflow of fluid (indicated by arrow in figure 1). The f and D data were then modeled in QTools to obtain viscosity data. For the modeling in QTools, literature values for density were used.

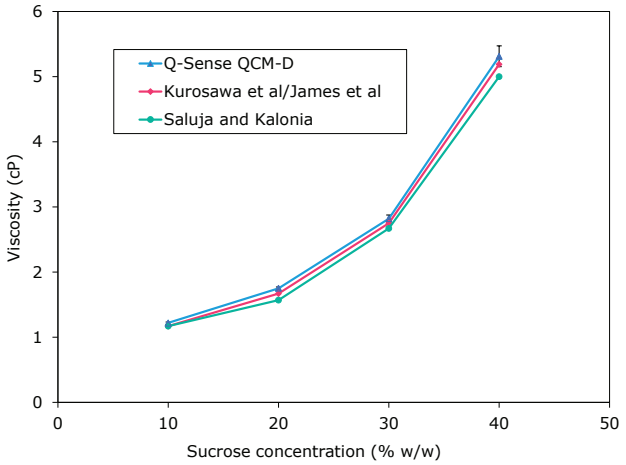
The results for the viscosity standards are shown in Figure 2. The viscosities measured with QCM-D agreed with the specifications. It can be noted that the total deviation was higher at higher viscosities, but the percentage difference was not as significant. The deviation between the QCM-D measurements was very low as can be seen from the error bars. Results from the sucrose study



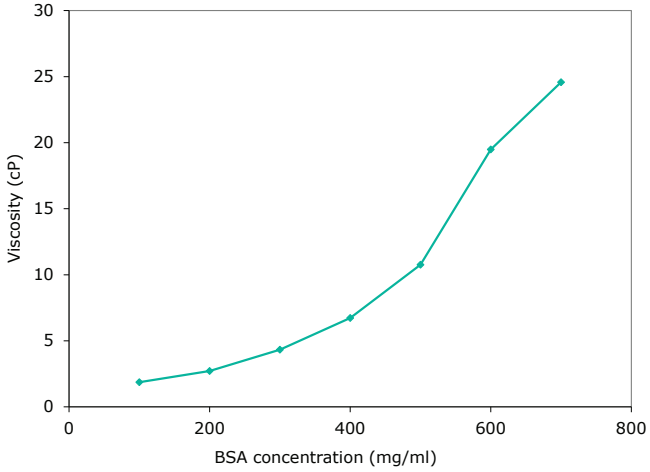
[Figure 1]: Typical example of f and D data from a QCM-D viscosity measurement going from air to fluid.



[Figure 2]: Viscosities of viscosity calibration standards acquired with QCM-D compared to specified viscosities from the manufacturer.



[Figure 3]: Comparison of sucrose solution viscosities acquired with different techniques.



[Figure 4]: Viscosity of BSA solutions acquired with QCM-D at 20°C.

are presented in Figure 3. The viscosities obtained with QCM-D agreed with data by Kurosawa et al, James et al and Saluja and Kalonia and the low error bars show that the measurement reproducibility was very good.

To investigate the viscoelastic properties of the BSA solutions, the viscosities were modeled with both the Newtonian model and the Maxwell viscoelastic model. The shear thinning properties were also investigated as well as the influence from surface adsorption to the sensor. It was found that the fluids were Newtonian and that other properties made negligible contribution to the results. Figure 4 shows the viscosities produced with the Newtonian model. The viscosities were found to increase dramatically with the concentration. This was not further investigated since it was outside the scope of this study.

Conclusions

QCM-D is a suitable tool for viscosity analysis of solutions, such as high concentration protein, where low sample volume and non-destructive analysis is preferable. The study shows that QCM-D can be used for viscosity measurements of fluids of varying character. It can also be used to study other parameters like frequency dependence and surface adsorption processes associated with the properties of the sample.

References:

1. QCM-D measurements by Q-Sense AB and Q-Sense, Inc in cooperation with Pomona College, USA. Detailed reports are available from Q-Sense AB.
2. Oscillating frequency of piezo-electric quartz crystal in solutions. Anal Chim Acta. 1990; 230; 41-49. Kurosawa et al.
3. Viscometer calibration standards: viscosities of water between 0 and 60 degree C and of selected aqueous sucrose solutions at 25 degree C from measurements with a flared capillary viscometer. J Phys D Appl Physiol. 1984; 17; 225-230. James et al.
4. Measurement of fluid viscosity at microliter volumes using quartz impedance analysis. AAPS PharmSciTech 2004; 5; 47. Saluja and Kalonia.

*) QTools is an analysis software included in your Q-Sense QCM-D system used for viscoelastic modeling of QCM-D data.

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