Fully automated capillary viscometer

An instrument that measures viscosity of protein solutions automatically by varying solute concentration and shear rate has been described (Grupi & Minton, 2012). By measuring the pressure difference between the two ends of the capillary filled with a protein solution flowing at a known rate, enables determination of the viscosity using the Hagen–Poiseuille equation. A volume of as little as 0.75 mL can provide the viscosity as a function of concentration and shear rate. Viscosities as high as 500 mPa s and as low as 1 mPa s at shear rates between 10 and 2×10^3/s have been determined with good accuracy and precision.

Use of dynamic light scattering

Diffusion coefficients determined by dynamic light scattering (DLS) measurements can be used to compute viscosities of protein solutions (He et al., 2010) by using the Stokes–Einstein equation:

$$D = kT/6\pi\eta R \tag{9.11}$$

where D is the diffusion coefficient, k the Boltzmann's constant, T the temperature, R the radius of a particle, and η the viscosity of the solution. Using polystyrene beads with known values of R allows for the determination of the viscosity of the protein solution that the beads are suspended in. The size of the beads is larger than that of the protein molecules, and thus the DLS signals can easily be separated. This method was used to determine viscosities of two mAb solutions and the results when compared with cone and plate measurements showed good agreement. Using a DLS instrument with plate reader allowed for rapid determination (~5 times less than cone and plate) using ~10 times less sample.

Determination of viscoelastic properties using a quartz crystal microbalance

Many of the most used methods to measure viscosities of protein solutions require fairly large volumes (3–5 mL), which may be difficult to obtain for high-concentration protein/mAb formulations during early stages of development. A technique based on the use of piezoelectric quartz crystals showed that this technique could be used to obtain viscoelastic data in 2-3 min with as little as 8–10 µL of solution. The basic theory and use of quartz impedance analysis were used to generate viscosity values at 25 °C for liquid solutions of sucrose, urea, PEG-400, glucose, and ethylene glycol, all Newtonian fluids, and found to be reproducible and consistent with literature values (Saluja & Kalonia, 2004). This initial work was extended to determine full rheological properties of protein solutions at high concentration (Saluja & Kalonia, 2005). The main properties of the vibrating quartz crystal used to compute viscoelastic properties of solutions are the measured shifts ± solution of the series resistance, R_2, and