to formation of insoluble aggregates (Patapoff & Esue, 2009). Addition of polysorbate 20 inhibited the aggregate formation and resulted in little change in viscosity after multiple cycles. It was hypothesized that the mAb formed a thin layer at the protein air–water interface that resulted in unfolding and generation of insoluble aggregate species. The addition of the surfactant, as discussed in previous chapters, prevents this aggregation by adsorption to this interface, thus preventing the mAb from exposure to the hydrophobic air–water interface. This example shows that such artifacts can occur and need to be taken into consideration when interpreting the experimental results.

Other methods for determination of viscosity

Microfluidic rheometry using pressure drops to determine viscosity

Recently a rheometer has been developed that uses pressure drop measurements to determine viscosity (Hudson, Sarangapani, Pathak, & Migler, 2014; Pipe & McKinley, 2009). This rheometer generally can meet the need to use small microliter volumes of material, has a wide dynamic range of shear rates (range of ~3 decades), and no air–sample interface, which has been shown to be a potential problem in conventional rotational viscometers (Patapoff & Esue, 2009). This instrument has an uncertainty of only a few percent and its performance was evaluated using monoclonal antibody solutions at different concentrations, pH, and temperature (Hudson et al., 2014).

Viscosity determined using travel time of a magnetic piston

A viscometer that measures viscosity by determining the travel time of a magnetically oscillating piston has been developed. The pistons were calibrated using fluids with viscosity ranges of 0.5–5, 2.5–50, and 5–100 mPa; and used to determine viscosities of monoclonal antibody solutions from 20 to 225 mg/mL (Yadav, Shire, & Kalonia, 2010).

Use of standard capillary electrophoresis instrumentation

It has been shown that using a capillary electrophoresis (CE) instrument without the applied electric field, Newtonian fluid viscosities could be determined by filling the capillary with the protein sample by applying a constant pressure (Allemendinger et al., 2014). A dye such as riboflavin is used to monitor the movement of the dye in the presence of the protein in the capillary. Using the Hagen–Poiseuille equation (Eqn (6.1), Chapter 6) the movement of the riboflavin peak is converted to a viscosity of the solution. Accuracy and precision was verified by comparing the CE determinations with cone and plate measurements. Viscosities in the range of 5–40 mPa s were reliably measured using this technique which has short measurement times (1–15 min), and small sample volume (a few microliter) when using a 20.5 cm length capillary of 50 μm diameter.