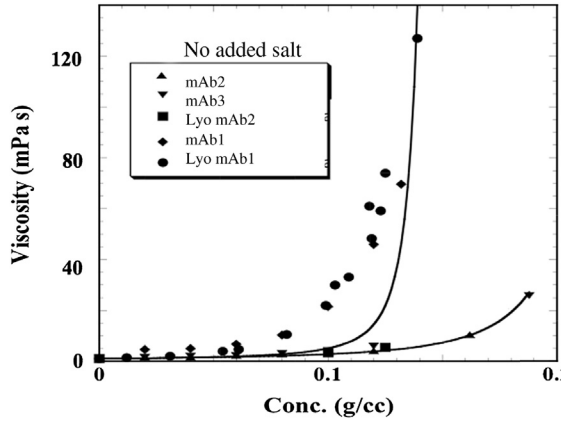

Figure 9.3 Viscosity at 25 °C as a function of protein concentration for lyophilized and TFF concentrated mAb1. The TFF nonlyophilized samples of mAb1, mAb2, and mAb3 and reconstituted mAb1 lyophilized samples are in 266 mM sucrose and 16 mM histidine at pH 6 and 0.03% polysorbate 20. The lyophilized mAb2 samples are in either 240 mM trehalose, 40 mM histidine, 0.04% polysorbate 20 at pH 6 or in 300 mM trehalose, 50 mM histidine, and 0.05% polysorbate 20 at pH 6. The solid line is the result of fitting of the data to the modified Mooney equation as described in the text.
Composite of figures from Liu et al. (2005).

molecule the size of a monoclonal antibody is less negative than −5.34 mL/g, then the net interactions are repulsive, whereas if the value is more negative than −5.34 mL/g the net interactions are attractive (Yadav, Shire, et al., 2010).

The dependence of viscosity on attractive protein–protein interactions

As shown and discussed previously in Chapter 7 the reconstitution time for a lyophilized mAb was dependent on the viscosity after addition of diluent (Figure 7.5). A viscosity–concentration profile for three IgG1 mAbs that were constructed using the same human IgG1 framework is shown in Figure 9.3. These profiles were analyzed using the modified Mooney equation for quasi-spherical particles (Ross & Minton, 1977):

$$\eta = \eta_0 \exp\left([\eta]\, c / (1 - k/v)\, [\eta]\, c\right) \tag{9.18}$$

where η_0 is the solvent viscosity, $[\eta]$ the intrinsic viscosity of the protein or mAb, k is a "crowding factor," and v is the Simha parameter related to the ellipsoid of revolution used to model the protein (Mehl et al., 1940). A typical value for $[\eta]$ of 6.3 cm^3/g for an IgG_1 (Hall & Abraham, 1984; Kilar et al., 1985) (strictly speaking this will be a function of the solvent parameters) and a determined η_0 of 1.1 mPa was used for the