inductance shift, L_2. The inductance shift and crystal resonance frequency, ω, are used to calculate the reactance shift, X_2, by

$$X_2 = \omega L_2 \tag{9.12}$$

For Newtonian fluids R_2 and X_2 are equal and related to the viscosity, η, by

$$\eta = 2R_2^2 / \left(A^2 \rho \omega\right) \tag{9.13}$$

where A is a crystal constant and ρ the solution density.

For a viscoelastic fluid the storage modulus, G', related to the elasticity of the solution, and G'', related to the viscosity of the solution, are expressed as

$$G' = \left(R_2^2 - X_2^2\right) / \left(A^2 \rho\right),\ G'' = \left(2R_2 X_2\right) / \left(A^2 \rho\right) \tag{9.14}$$

Both the storage and loss modulus contribute to the complex viscosity of the solution, η^*, by the relationship

$$\eta^* = \left[\left((G')^2 + (G'')^2\right)^{1/2}\right] / \omega \tag{9.15}$$

The storage modulus, G', determined by ultrasonic rheology has been shown to be an important parameter for the analysis of protein–protein interactions at high protein concentrations (Saluja, Badkar, Zeng, Nema, & Kalonia, 2007). This was demonstrated by determining G' at a frequency of 10 MHz for an IgG_2 mAb between pH 3 and 9 at 4 mM ionic strength. A comparison of the pH and ionic strength dependency of G' with the DLS interaction parameter, k_D, shows similar trends (Figure 9.2). In this publication data were also presented for determination of B22 but was incorrectly done with the DLS instrument. This issue has been thoroughly discussed and is related to detector saturation in the DLS instrument (Yadav, Scherer, Shire, & Kalonia, 2011).

The DLS k_D parameter is determined by plotting the diffusion coefficient determined by DLS as a function of concentration. The mutual diffusion coefficient, D_m, at any given concentration depends on the diameter d_H of the protein/mAb and the interactions between the molecules (Eberstein, Georgalis, & Saenger, 1994; Mandel, 1993). At high dilution the diffusion coefficient, D_s, is the diffusion coefficient for a single molecule with a particular diameter. The concentration dependency of D_m can be determined by (Zhang & Liu, 2003)

$$D_m = D_s\left(1 + k_D c\right) \tag{9.16}$$

where c is the mass concentration of protein or mAb and the slope k_D is the interaction parameter which can be expressed as

$$k_D = 2B_{22}M_w - \zeta_1 - 2\nu_{sp} \tag{9.17}$$