The molecular basis of high viscosity of monoclonal antibodies (mAbs) at high concentration

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What is viscosity?

Although viscosity has been discussed in previous chapters in context of how it impacts pharmaceutical development of mAbs, it was never clearly defined. In general viscosity is understood by many to be related to the flow of a liquid and its "stickiness to surfaces." Here we discuss some formal definitions for viscosity and what methodologies have been used to determine viscosity of protein solutions.

The viscosity of a liquid is essentially a measure of the resistance of fluids to flow. This can be expressed quantitatively by imagining that the fluid is broken up into several volume elements where a volume element's movement relative to another volume element is as shown in Figure 9.1. If the volume element, at a distance dx (center to center), is moving with a relative velocity du relative to the second element then the frictional force, F_f, will be proportional to this relative velocity and the contact surface area, dA, between the volume elements. The force should also be inversely proportional to the distance dx between the centers of the volume elements (Tanford, 1967, pp. 317–336). Thus,

$$F_f \sim (du/dx)\, dA \tag{9.1}$$

And the proportionality constant, η, is the viscosity, so that

$$F_f = \eta\, (du/dx)\, dA \tag{9.2}$$

From this, the viscosity has units of g/cm s. In honor of Jean Léonard Marie Poiseuille this combination of units is called 1 Poise or 1 P. Recently the convention has been to express the units of viscosity in terms of units of pressure, which is Newtons/m^2 or kg/m s and is called 1 Pa in honor of the physicist Blaise Pascal. Thus, 1 Pa s has the dimensions kg/m s or 0.1 Poise, and therefore 1 centiPoise (cP) is equivalent to 1 milli Pa sec or 1 mPa s. Fluids can vary widely in their viscosities as shown in Table 9.1, ranging from 0.02 mPa s for air to that of 1×10^6 mPa s for window putty.

Another important aspect of viscosity is the difference between a "Newtonian" and "Non-Newtonian" fluid. Essentially the viscosity as defined by Eqn (9.2) is defined as a simple proportionality constant that is independent of the velocity of flow of the fluid. This is not always the case since for some fluids the flow gives rise to an orientation of the molecules, which then alters the frictional force between the adjacent volume elements. A practical determination of whether a fluid is "non-Newtonian"

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