transportation. This motion can therefore affect the inter-particulate distance and by consequence the values of $V_A$, $V_T$ and $V_R$ (above), potentially affecting the flocculation status of the suspension. When considering the effects of movement, it must be remembered that deflocculated systems behave as individual small particles, whilst flocculated systems behave as individual large particles with a porous structure. Flocculated and deflocculated systems will show different particulate behaviour as a result.

## Diffusion

Brownian motion (Chapter 5) is the irregular movement of particles through the medium and is shown by particles up to approximately 1 to 2 μm radius. The result of Brownian motion is diffusion of the particles throughout the medium, from an area of high concentration to one of low concentration. Diffusion (Chapter 3) will therefore result in an improved, more homogeneous distribution of the particles throughout the system. It can be described by the Stokes-Einstein diffusion equation (Eqn 3.30). From Equation 3.30, it can be seen that reducing the particle size will increase the diffusion constant and, conversely, increasing the particle size will reduce it. There is an effective size range above which diffusion will be negligible, and for particles of radius greater than approximately 1 to 2 μm, diffusion can be ignored. As pharmaceutical suspensions may contain particles in the sub-micrometre range, diffusion may be an important contributor to particle movement. However, it is most likely to be observed with deflocculated systems, as these behave as independent particles, and less likely to be seen with flocculated systems. The latter behave as larger particles due to their agglomerated status, and they are therefore likely to be of a size above the effective cut-off for diffusional movement. Diffusion can be reduced by increasing the viscosity of the medium, with a value of 5 mPa s effectively reducing diffusion to zero. For comparison, water at 20°C has a viscosity of 1 mPa s and a 2%w/v solution of low molecular weight hydroxypropyl methylcellulose (HPMC) has a viscosity of 5 mPa s at 20°C.

## Sedimentation

Sedimentation (also discussed in Chapters 5 and 6) is the downward movement of particles under gravity, and is observed for particles with radii of approximately 0.5 μm and greater. The vast majority of pharmaceutical suspensions will contain particles in this size range, so sedimentation is a significant cause of particle motion. Sedimentation is described by Stokes' sedimentation equation (Eqn. 26.3), with the sedimentation velocity, $v$, predicting the speed of settling expected under particular conditions; higher values of $v$ suggest greater likelihood of sedimentation. Here, the Stokes equation has been given in two equivalent forms, defined by the particle radius and diameter:

$$v = \frac{2a^2 g(\rho - \rho_o)}{9\eta} = \frac{d^2 g(\rho - \rho_o)}{18\eta} \qquad (26.3)$$

where $v$ is the sedimentation velocity, $a$ and $d$ are the particle radius and diameter respectively (the particle is assumed to be spherical), $g$ is the acceleration due to gravity, $\rho$ and $\rho_0$ are the densities of the particles and the medium respectively, and $\eta$ is the viscosity of the medium.

In the context of suspension formulation, Equation 26.3 shows that reducing the particle size will reduce the sedimentation rate, and conversely increasing the particle size will result in increased settling. Both flocculated and deflocculated systems will show sedimentation. Due to their relative sizes, flocculated systems will settle quickly whereas deflocculated systems will settle more slowly. Increasing the viscosity of the medium will reduce sedimentation, as will reducing the difference in density between the medium and the particle.

## Controlling particulate movement in suspensions

Diffusion and sedimentation of particles within the suspension formulation will have opposite, but not equal, effects; sedimentation leading to increased proximity of particles and diffusion leading to greater dispersion of particles within the system. Particulate movement is almost inevitable in a liquid suspension system, with the overall result of a variation in the separation distance between particles, which has a direct consequence on the energies of interaction between particles and hence their flocculation behaviour. Increasing the separation distance will initially move particles away from the primary maximum zone into the secondary minimum