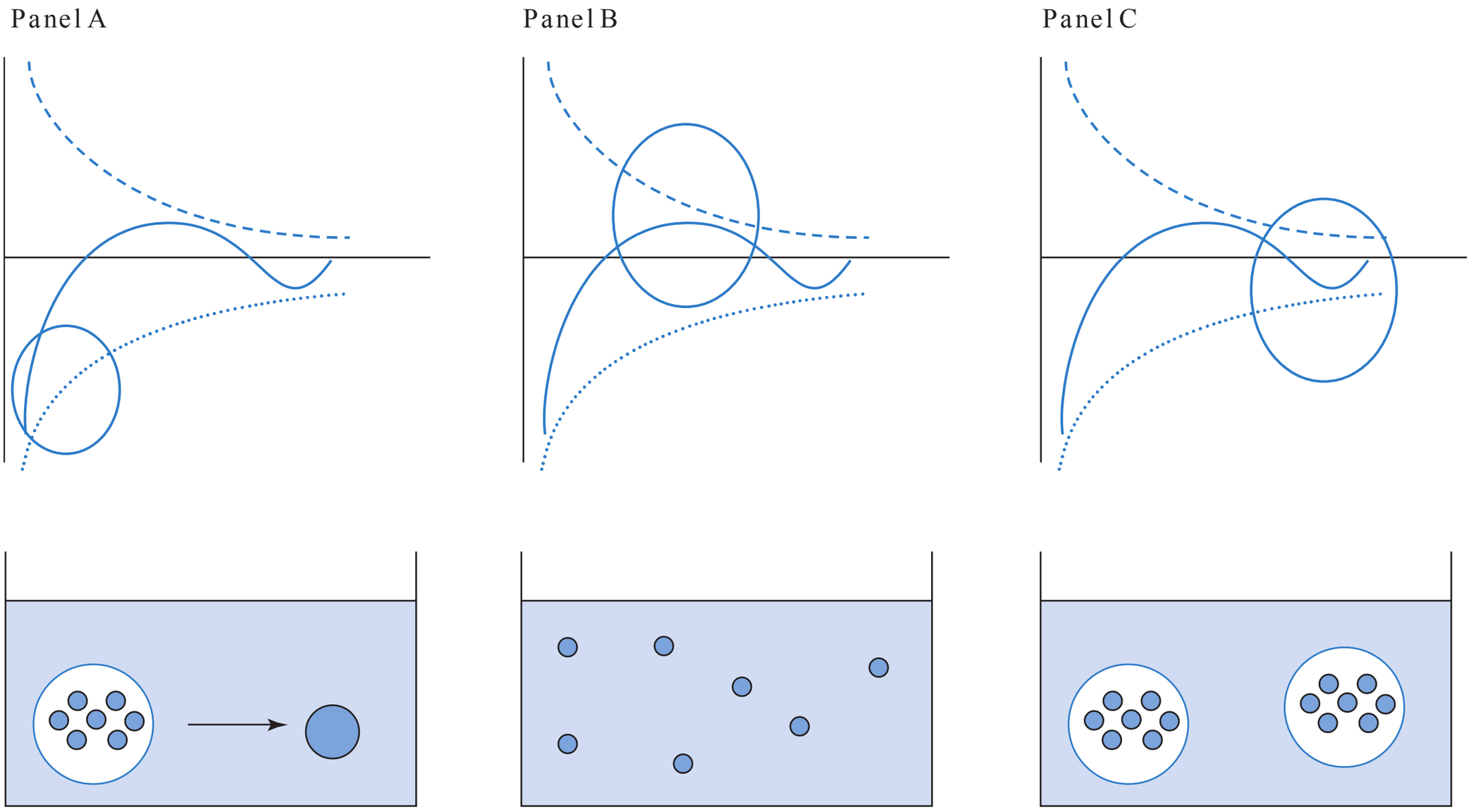

Fig. 26.4 • Flocculation and defocculation consequences of the DLVO theory for pharmaceutical suspensions.

The primary maximum

The naming of the 'primary maximum' zone follows the same conventions as for the primary minimum. The primary maximum zone is described as a 'maximum' because the total energy is calculated to be above zero (using the convention of repulsive energy being positive and attractive energy being negative). It is described as 'primary' because it is the largest positive deviation from zero. Particles in the primary maximum zone show a higher energy of repulsion than attraction and are therefore likely to remain separate or 'deflocculated'. This is illustrated in panel B of Figure 26.4. At first sight, this would appear to be a good formulation strategy for pharmaceutical suspensions, as if the particles can be forced into the primary maximum zone then they should remain independent and hence dosing would be expected to be reproducible. This is true when the kinetic energy of the particles is less than V_T and they are, if anything, more likely to move away from each other, which will have the effect of decreasing the magnitude of V_T but maintaining an overall repulsive effect. However, if the kinetic energy of the particles is high enough, for example if the temperature is increased, then this can overcome the energy barrier imposed by V_T with the result that the particles can then move closer together. In this case, V_T will initially decrease but remain repulsive, so the particles will still exist as independent entities. However, the magnitude of the difference between V_T and the particles' kinetic energy is now greater and therefore they are likely to move even closer together. At some point, the particles will be sufficiently close so that the overall energy of interaction becomes negative, i.e. it is now predominantly attractive, and the particles enter the primary minimum zone with the consequences described above. In summary, therefore, formulating pharmaceutical suspensions so that the particles are in the primary maximum zone can be considered to be risky.

The secondary minimum

Panel C of Figure 26.4, shows the behaviour within the secondary minimum zone. As its name suggests, the 'secondary minimum' gives rise to an overall attractive energy of interaction between particles, but of a lower magnitude than that seen in the primary minimum. The particles here show an overall limited attraction to each other and behave as 'floccules', loose aggregates of individual particles. Depending on the kinetic energy of the particles, their behaviour will vary slightly. If the kinetic energy is less than the V_T, then the particles will