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Brownian dynamics simulation of protein-polyelectrolyte particle formation and growth

The interaction between protein and polyelectrolytes is relevant for the development of protein drug delivery systems [1]. The formation and growth of protein-polyelectrolyte complexes has been monitored experimentally by nanoparticle tracking analysis (NTA) and flow imaging microscopy (MFI) [2]. Although Smoluchowski's theory was able to describe the agglomeration in this system, it can be expected that if systems become more complex (for instance when starting with size distributions instead of a single particle size), finding the analytical solution may not be easy. Therefore we develop here a simulation environment that allows explicit size dependent particle properties to be loaded in a Brownian motion based agglomeration process.

A direct collision (DC) simulation was developed focusing on the perikinetic particle agglomeration. In the simulation, particles are displaced stochastically in short time steps where the displacement distance is shorter than their diameters. Whenever two particles are close to each other within the distance of effective collision diameter, a merge of the two particles is assumed to take place. In order to lift the simulation efficiency, the DC simulation always starts with hundreds of particles in a mini-volume (about 1E-14 – 1E-13 m3) followed by step-by-step expansion into larger volumes while maintaining the particle number concentration constant (typically about 1E15 particles/m3).

The DC simulation was validated through comparisons with analytical solutions of Smoluchowski's model, and with the modelling results on gold particles described in Smoluchowski's own paper [3]. It was found that for the given systems a short displacement distance of maximally ≈1/4 of the particle diameter was necessary for a good fit.

The DC simulation was applied to experimental data on protein-polyelectrolyte particle growth. The DC simulation started with an initial particle concentration of 1.23E15/m3 as reported [2] after 1 min of the mixing of protein and polyelectrolyte. From the fit of the particle size envelope a ratio of effective particle collision radius versus the real particle radius was calculated to be 0.2-0.5. This value is much lower than that was reported by Smoluchowski [3] for gold particles. This short effective collision distance for proteins compared with the real radius of the particle made a shorter displacement distance (≈1/10 of the particle size) in the simulation necessary.

Reference

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