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Heteroaggregation processes in colloidal particle and cell systems

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Motivated by the selective adsorption of functionalised drug carrier particles to certain cell types for medical applications this thesis investigates fundamental heteroaggregation phenomena under special consideration of the dynamic behaviour in physical and biological model systems. The adsorption of antibodies as possible functional moieties to receptors on cell surfaces represents an essential first step in a series of further transport limitations for the cellular uptake of functionalised drug carrier particles. To establish suitable scientific methods for the analysis of selective and competitive heteroaggregation processes, the specific interaction and heteroaggregation of multiple colloid constituents was studied in physical particle systems first. Experimental methods primarily include flow cytometry and diverse microscopic techniques, while simulations are based on population balance equations with kernel models rooting in classical colloid science. Both approaches were transferred to biological systems to achieve a more rigorous description of drug delivery dynamics and efficiency. This could prove valuable for future optimisation efforts.

Flow cytometry was established as a very powerful and convenient tool to characterise cluster composition and its dynamics in heteroaggregation processes. It enables an independent and very detailed resolution of multidimensional distributions by a reliably automated single particle analysis. Investigations in binary and ternary particle mixtures focus on electrostatic de- and restabilisation phenomena, that can be tailored by the choice of suitable particle species and their mixing ratio. Experimental results were reconstructed by multivariate population balance simulations in which the internal coordinates represent the particle number of the respective species inside an aggregate. The physically discrete property state space was adaptively reduced by a semi-heuristic approach, so that only property coordinates featuring high aggregate concentrations were considered in the model. The applied aggregation kernels are based on deterministic models from colloid science, in particular DLVO theory, and connect interactions on the single-particle level with the macroscopic behaviour of multiple particle populations. The methods established for particle systems were successfully transferred to a systematic, model-based investigation of preferential aggregation processes in a ternary system of antibodies and two human tumour cell lines (KARPAS-299 and U-937). Despite the assumed instantaneous aggregation following receptor-ligand collisions, the low receptor expression on cellular surfaces causes a rate limited aggregation process (RLCA). Population balance simulations with kernels that consider the strong surface heterogeneities of the aggregating species (patchy particles) confirm the experimental results. The targeted administration of pharmaceutical compounds by functionalised carrier particles to specific cells under minimisation of adverse effects represents a potential area of application of these results.