

Review

Stimulus-Responsive Heteroaggregation of Colloidal Dispersions: Reversible Systems and Composite Materials

Melanie Bradley ^{1,*}, Azwan Mat Lazim ² and Julian Eastoe ¹

¹ School of Chemistry, University of Bristol, Bristol BS8 1TS, UK; E-Mail: julian.eastoe@bristol.ac.uk

² School of Chemical Sciences and Food Technology, Faculty of Science and Technology, University Kebangsaan Malaysia, 43600 Bangi, Selangor, Malaysia; E-Mail: azwani79@ukm.my

* Author to whom correspondence should be addressed; E-Mail: melanie.bradley@bristol.ac.uk.

Received: 16 May 2011; in revised form: 24 June 2011 / Accepted: 29 June 2011 /

Published: 1 July 2011

Abstract: Heteroaggregation is the aggregation of mixed particle systems where the colloidal particles may differ in charge, size and chemical composition. The phenomenon of heteroaggregation is of great relevance in industrial processes and the natural environment. This review will focus on binary heteroaggregation where at least one of the particles is a stimulus-responsive smart particle. Aggregation under various conditions of pH, temperature, light and relative concentration can be induced by the careful manipulation of any one or more of these environmental conditions during the heteroaggregation of smart particles. Stimulus response provides the potential for reversibility from an aggregated to a stable system and exceptional control over inter-particle interactions. The significant fundamental and applied studies that have made an impact in this area will be discussed.

Keywords: microgel; pH; separation; composite; smart particle; heteroflocculation; heteroaggregation

1. Introduction

Over the last two decades, there has been an increasing interest in stimulus-responsive, or *smart*, materials. The definition of a smart material is one that can sense stimulus from its surrounding, e.g.,

temperature or light, and react to it in a useful, reliable, reproducible manner. Smart materials therefore respond to changes in the environment in a rather predictable manner and some have a ‘memory’ as they revert back to their original state once the stimulus is removed. The dispersion behavior of smart particles can be manipulated by external stimuli such as temperature, pH, electric/magnetic fields or light. Such materials are also attractive in many applications since changes in material properties can be triggered which provides an ‘on’ and ‘off’ control. There is growing interest in the preparation and application of mixed smart particle systems and using the method of heteroaggregation in the preparation of new materials and the development of advanced separation technology.

1.1. Defining Heteroaggregation

Heteroaggregation is the aggregation of mixed particle systems where the colloidal particles may differ in charge, size and chemical composition. The aggregation process that occurs in mixed particle systems is known by three different names: heteroaggregation, heteroflocculation and heterocoagulation. The terms heteroaggregation and heteroflocculation are often used interchangeably. Heteroflocculation refers to reversible or temporary contact between particles, whilst heteroaggregation is a general term which refers to particle aggregation [1]. Heterocoagulation is used to describe irreversibility of aggregation due to permanent contact between particles. A coagulated aggregate separates out by sedimentation if it is denser than the medium, or creams and rises to the surface if its density is less than that of the dispersion medium. Smart particles are making their mark in both fundamental and applied heteroaggregation studies. They provide the advantage that inter-particle interactions can be tuned using stimulus during the heteroaggregation process while also providing the possibility for a heteroaggregated system to be reversed to a stable dispersion.

1.2. The Application of Heteroaggregation

The phenomenon of heteroaggregation is of great relevance in industrial processes and the natural environment compared to the analogous process with identical particles (*i.e.*, homoaggregation). Dispersions of fine solid particles in a liquid in the colloidal size range (a few nanometers and less than a few micrometers) are commonly used to manufacture coatings, composite materials and ceramics. They are encountered in foods, pharmaceuticals and biotechnological processes and constitute the bulk of industrial and city effluents. Understanding the stability in these systems with changes in environment is significant as many organic functional groups are stimulus responsive, most notably to pH change.

In separation technology, which may involve either an extraction or purification process, it is necessary to separate the particle matter from the liquid. Techniques have been developed which cause agglomeration of the small particles and thus simplify the separation technique. This is achieved through a variety of industrial processes, including drying, slip casting, pressure filtration, and centrifugation [2]. Generally, in all these processes the success of the operation depends on the control of interactions between particles. These traditional methods of colloid separation are all energy intensive. Consideration of the environmental impact of these techniques is also now much more important and so alternatives are being sought [3]. There is considerable interest in developing

methods, such as heteroaggregation, to aid in phase separation and recovery of colloidal systems with as little energy expenditure as possible. Thus, the heteroaggregation of smart colloidal systems is being investigated in separation technology as a sustainable procedure with low environmental impact in conjunction with control over colloid *instability* and *stability*.

In the preparation of new materials there is an increasing interest in using preformed particles, with well characterized properties, and creating secondary self-ordered structures [4,5]. The structuring of materials on a particle-by-particle basis using heteroaggregation allows intricate structures to be produced and control over the three-dimensional organization of materials as well as the combination of different materials over several length scales. Many of the composite materials made using heteroaggregation have a core-shell structure although other topologies are found in the literature.

This review will focus on the heteroaggregation of smart particles (taken from experimental results) and discusses the techniques used to study heteroaggregation and the stimulus that is used to cause destabilization. In the context of this review, a smart particle has either stimulus responsive surface functionality, or is a microgel particle, which is a cross-linked polymer particle that shows reversible swelling/deswelling behavior depending on local conditions [6,7]. The development of significant heteroaggregation experiments will be discussed, including structural characterization along with a description of the properties and applications of stimulus-responsive heteroaggregation of colloidal particles.

2. Fundamental Techniques for Heteroaggregation Analysis

The study of heteroaggregation is rather more complex than homoaggregation which makes its investigation in routine applications difficult. There are several techniques, the majority of which are indirect, that are used to study both the kinetics of heteroaggregation and the equilibrium properties of the heteroaggregates formed. The parameters adjusted in heteroaggregation studies often include, particle ratio, size and electrolyte concentration.

Time-resolved light scattering techniques, either static light scattering (SLS) or dynamic light scattering (DLS), are used to measure the heteroaggregation rate constant especially at early stage of aggregation [8]. The Rayleigh-Debye-Gans (RDG) approximation is usually applied to calculate the rate constant from light scattering. Ryde and Matijevic [9] have successfully explored RDG theory to support their light scattering data and reported that absolute heteroaggregation rate constants can be determined by analyzing time-dependent multi-angle static light scattering (SLS). Using the RDG theory, Galetto *et al.* [10] have focused on the time resolved simultaneous static and dynamic light scattering (SSDLS) of larger and complex particles. They reported detailed heteroaggregation rate constants of amidine latex particles, sulfate latex particles, and silica particles using different ionic strengths and surface charge densities based on SLS and DLS [11]. This technique is only reliable when heteroaggregation takes place. However, in general homoaggregation and heteroaggregation take place simultaneously, and the separation of both processes is nontrivial [12,13]. One way to tackle this problem is to measure an apparent aggregation rate constant in such a mixed system. If the particles are exactly the same size, then the apparent aggregation rate constant can be shown to be a weighted sum of the homoaggregation and heteroaggregation rate constants, where the weights are the products of the mole fractions of each constituent. Thus, by measuring this apparent aggregation rate constant as

a function of the composition of the binary mixture, homoaggregation and heteroaggregation rate constants can be determined separately [14,15].

Techniques used to study heteroaggregates in equilibrium include turbidity, rheology, electron microscopy and porosimetry. UV-Vis spectroscopy is used to measure turbidity. The changes in turbidity reflect changes in the system stability and are reported as a dispersibility factor (n) based on the wavelength dependence of the turbidity of the particles [16]. In general the more aggregated the mixture the larger the heteroaggregates and hence the lower the turbidity. At low turbidity there is less wavelength dependence on absorbance and the n value is close to zero. Rheology has been extensively used to probe the deformation and flow of heteroaggregates, generally by shear flow measurements. This measurement provides information about the viscoelastic properties of the heteroaggregated dispersion and this is largely related to the interfacial activity of the particles being mixed. Therefore, the key to interpreting rheological data is to first have an understanding of the interactions between the particles that form the heteroaggregates. It is almost universally the case that the rheological properties are determined by controlling the connectivity between the particles. In order to get a more viscous or elastic structure a stronger network is required. Electron microscopy enables imaging of the dry heteroaggregated samples to probe morphology. Mercury porosimetry can be used to calculate a pore diameter, to provide an estimate of pore size within an aggregated structure. Due to the complex analysis of the heteroaggregation procedure and the heteroaggregates produced at least two of these techniques are required for data analysis and interpretation.

3. Heteroaggregation of Smart Systems

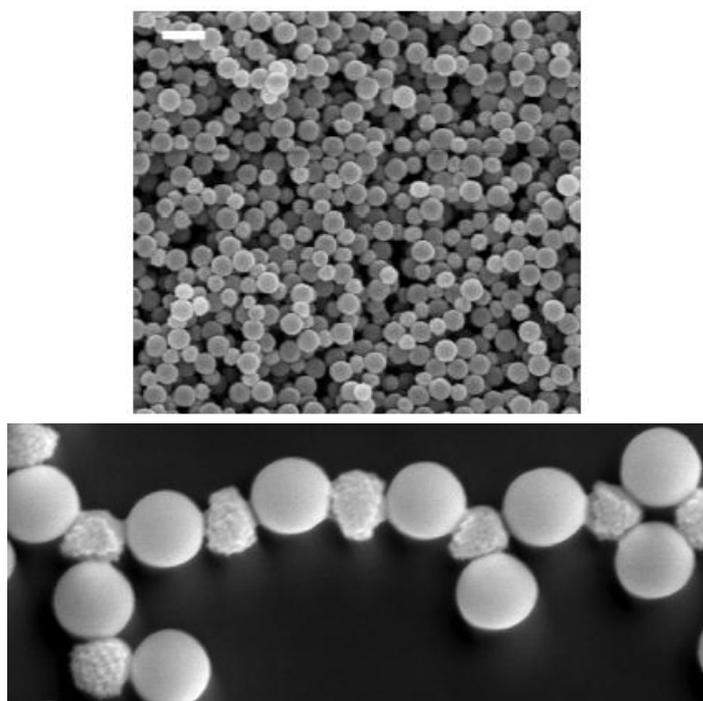
Since the early 1990s, heteroaggregation studies have been carried out on systems containing oppositely charged particles [1,17,18]. Now heteroaggregation and heteroflocculation of smart particles is of increasing interest due to the technological importance of developing materials and separation processes that can be controlled remotely and contain advanced functionality on the nanometer scale.

The early work on heteroaggregation of smart particles focused on the charge heteroaggregation of *soft* microgel particles with *hard* latex particles. Fernandez-Barbero *et al.* [19,20] looked at the heteroaggregation of negatively charged polystyrene particles with positively charged poly(2-vinylpyridine) (PVP) microgel particles, of the same size, in terms of the heteroaggregation kinetics and size of the aggregates formed. They studied the heteroaggregation of these systems, along classical lines, using variable electrolyte concentration. Increasing electrolyte concentration decreases the range of inter-particle interactions from long range electrostatic interaction to short range van der Waals interaction. They observed increase in the fractal dimension of the heteroaggregate formed in this system at high electrolyte concentration (or the heteroaggregates have a more open branched structure), compared to that expected from hard sphere charge heteroaggregation. The result was explained by accounting for differences between the homoaggregation speeds for both systems with the microgels undergoing faster aggregation than the latex particles. They also postulate that weaker van der Waals forces were involved in the particle aggregation because of the presence of the microgel, allowing the possibility for rearrangement within the clusters. This concept of subtly tuning

inter-particle interactions has since been used to control heteroaggregation using stimulus as will be discussed in the next section.

The heteroaggregation of charged particles, which may include a microgel component, is a method for producing porous materials. Experimentally, the time evolution of the size, structure and porosity of oppositely charged *soft* microgel particles with *hard* latex particles was investigated by Snoswell *et al.* [21] at low electrolyte concentration to produce open fractal heteroaggregate structures, as shown in Figure 1. By adjusting the electrolyte concentration, they were able to control the aggregation time, giving a series of desired pore sizes and morphologies. The use of deformable microgel particles produces heteroaggregates with greater contact area between oppositely charged particles resulting in aggregates with much greater mechanical strength than those formed from mixing hard spheres. The other potential benefits of using swellable microgels in the production of porous materials are mechanical flexibility and reversible changes in porosity, using stimulus such as pH, all of which expand the application of these novel materials.

Figure 1. Porous microgel-latex heteroaggregate. The scale bar in the top image denotes 1 μm (reproduced with permission from reference [21]).



3.1. The Types of Stimuli Used to Prompt Heteroaggregation of Smart Particles

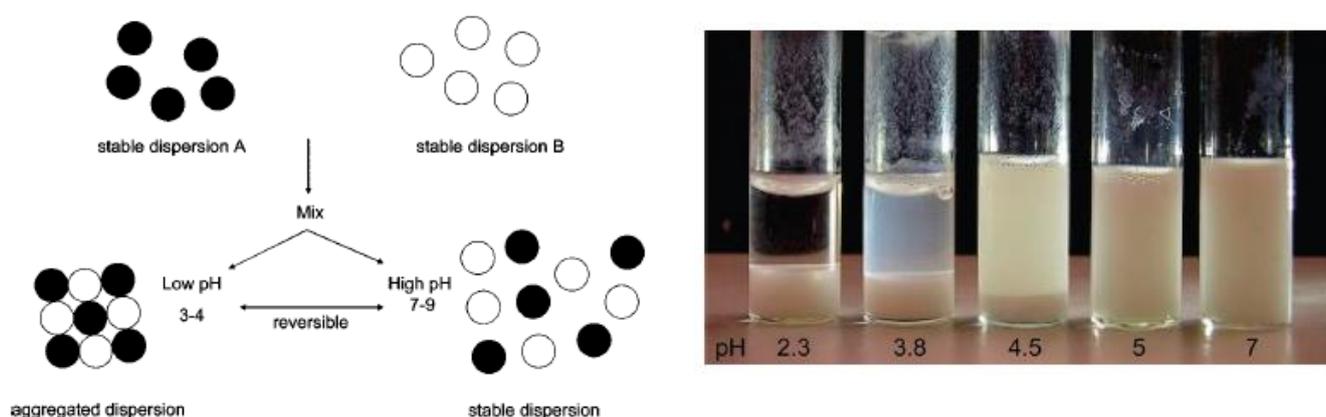
One of the most important parameters to control during the heteroaggregation process is the rate. There is also advantage in having a trigger than can “turn off” stability initiating aggregation in mixed particle dispersions. In this section we focus on the different types of stimuli that have been used to control the heteroaggregation of smart particles.

3.1.1. H-Bonding

The best way to obtain well-ordered heteroaggregated structures is by slowing the rate of heteroaggregation and having an external influence over the inter-particle interactions in the mixed systems. Hydrogen bonding can be used to provide mutual interactions among colloidal components. Typically for hydrogen bonding to take place one set of particles provides an H-bonding proton and the other set an H-bond acceptor. H-bonding is a short range interaction, thus, electrolyte has to be present in the system to screen the electrostatic repulsion between the two sets of particles, which both carry the same charge *i.e.*, negative or positive. Starck *et al.* [22] studied the heteroflocculation of mixtures of particles carrying carboxylic acid surface groups and others carrying poly(ethylene oxide) surface functionality (PEO). The carboxylic acid provides the H-bonding proton and the PEO contains ether oxygen as the H-bond acceptor. Heteroflocculation was observed at pH 3 when the carboxylic acids on the surface of the particles remain associated. No heteroflocculation was observed at pH 9 when the carboxylic acid are ionized and thus do not provide an H-bonding proton.

In a subsequent study by Starck *et al.* [23], H-bonding was used to drive the reversible heteroaggregation of silica particles containing surface carboxylic acid groups and PEO groups. The motivation of this study was to produce ordered and uniformly structured composite materials (shown by the schematic in Figure 2). The authors reported that heteroflocculation occurred in the pH range 3.0–4.5 and beyond pH 5 no flocculation was observed (Figure 2). The rate of heteroaggregation was controlled by pH through reducing the inter-particle interactions which avoids rapid coagulation that tends to produce low density and disorganized particle arrangements. The stimulus responsive nature of this heteroaggregation, using pH to control the H-bonding interaction, provides the advantage that binary particles can co-exist in dispersion prior to heteroaggregation. This also enables greater manipulation of the particle structure within the heteroaggregates formed which is not possible using the classical technique of co-mixing the particle dispersions.

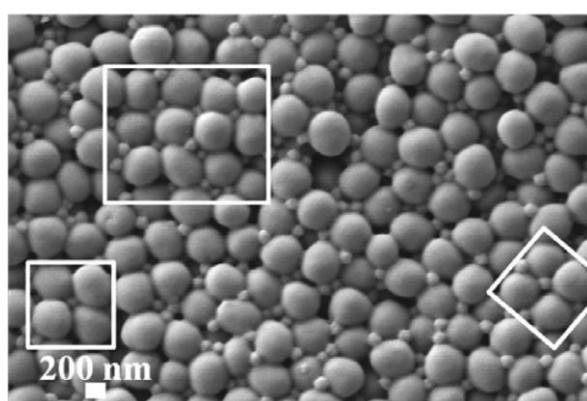
Figure 2. Schematic of the heteroaggregation process (left) and dispersions of mixed carboxylic acid functionalized and poly(ethylene oxide) surface functionality (PEO) functionalized silica particles over the pH range 2–7 (reproduced with permission from reference [23]).



The use of a binary colloidal system to generate a binary composite material with specific stoichiometry in analogy to chemical compounds was the premise of work by Huber *et al.* [24]. The

binary colloidal system was made up of one set of polystyrene particles with surface phenol residues (PSOH) as H-bond donors (with hydrodynamic radius of 270 nm) and the other set with 4-vinylpyridine (PS4VP) as the corresponding H-bond acceptors through the nitrogen (with hydrodynamic radius of 140 nm). Upon mixing these particles, in chloroform, heteroaggregation was observed immediately with little influence over the rate. In order to control the rate of heteroaggregation in a dispersion prepared with a 1:1 number ratio of binary particles a phenol capping agent was used which forms H-bonds with the PS4VP particles. The weakening of the inter-particle H-bonds due to the capping agent gives the particle more time to order into the desired cubic arrangement shown in Figure 3.

Figure 3. Cubic arrangement of heteroaggregated particles formed through H-bonding interactions (reproduced with permission from reference [24]).



3.1.2. Variable Temperature

In an early paper investigating the heteroaggregation of microgel/latex dispersions the novel concept of using stimulus to control stability was investigated. When combining microgels with a latex dispersion made up of oppositely charged particles, ionic interactions result in heteroflocculation. Islam *et al.* [25] reported the interactions between a cationic poly(N-isopropylacrylamide) (PNIPAM) microgel and anionic latex as a function of temperature at approximately equal microgel/latex particle concentration. Colloidal PNIPAM microgel particles swell and shrink in response to temperature and have a volume phase transition temperature (VPTT) around 32 °C. Interestingly, heteroaggregation only occurred in the mixed dispersion when the temperature was raised above the VPTT of the microgel. At room temperature the charge density of the microgel is believed to be sufficiently low, and the density of the surface hairy layer high enough, to provide steric stabilization and prevent aggregation via electrostatic attraction between the two particles.

Heteroaggregation of mixed microgel systems can be controlled by temperature which can be used as a trigger to switch “on” or “off” the heteroflocculation mechanism. The heteroaggregation of negatively charged PNIPAM and positively charged PNIPAM-*co*-4-vinylpyridine (P4VP) have been studied in detailed by Hall *et al.* [26]. They used pH to change the inherent properties of the P4VP microgel particles and used temperature to study the heteroaggregation upon mixing different ratios of PNIPAM/P4VP microgel dispersions. They demonstrated that heteroaggregation in these systems is a complex balance between diffusion effects, repulsive and attractive forces as well as van der Waals forces—all of which are influenced by the microgel ratio, the magnitude of the particle surface charge

and microgel particle size. In general increasing the mixed dispersion temperature increased the Hamaker constant and surface charge density of both sets of particles which favored heteroaggregation. The two significant findings in this article are: (1) it is possible to re-disperse heteroaggregates upon cooling, and (2) temperature influences the type of heteroaggregates formed. In one example heteroaggregates formed at room temperature appeared to re-stabilise upon heating due to the formation of hetero-microparticles, which comprise an inner anionic PNIPAM microgel core surrounded by cationic P4VP microgel particles. The net charge of these heteroaggregates is positive and a disperse hetero-cluster is formed.

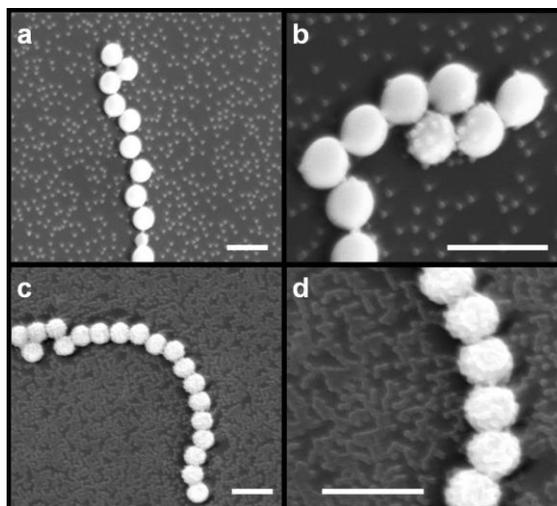
3.1.3. Adjustable pH

The preparation of pH responsive smart particles involves the inclusion of acidic or basic functional groups. A demonstration of using pH-triggered formation of heteroaggregates between mixed pigment/polystyrene (PS) dispersions was reported by Hui *et al.* [27]. PS particles contained surface carboxylic acid functional groups, and the pigment particles had both carboxylic acid and a steric stabiliser on the surface. They found that individual pigment and PS dispersions have critical pH values of 1.9 and 3.45 respectively, and below this pH value the individual dispersion homoaggregates. However in dilute mixed dispersions between pH 2.2 and 3.3, with a pigment volume fraction below 0.08 of the total particle volume fraction, heteroaggregation occurs due to pH-triggered electrostatic attractions between the oppositely charged pigment/PS particles. In a concentrated dispersion of similar pigment volume fraction gel formation was observed due to summation of these heteroaggregates into larger networks. Therefore, these findings provide some insight into the adjustable pH window for transitions from liquid to gel forms in heteroaggregated dispersions for possible application in ink jet printing.

Electric field induced heteroaggregation of large negatively charged latex particles and small positively charged pH-responsive microgel particles was demonstrated by Snoswell *et al.* [28] in the formation of pH-responsive particulate strings. The microgel particles were used to bridge the latex particle strings formed in the presence of an electric field allowing them to remain intact once the electric field was removed, as shown in Figure 4. The flexibility of the string was shown to be dependent on the microgel cross-linker concentration, with low concentration producing flexible strings as a result of better adhesion to the latex particles and the ability of the microgel particles to undergo larger pH-triggered swelling. Particulate strings such as these may find application in microscopic mechanical actuators or sensors.

We have developed a simple method to disperse and recover gold nanoparticles (AuNPs) based on pH-induced heteroaggregation of mixed positive/negative aqueous microgels [29]. AuNPs were adsorbed onto the surface of cationic pH-responsive microgel particles to form positively charged composite inorganic-organic particles. The stability of these composite systems was readily and reversibly controlled by using pH upon the addition of negatively charged microgel dispersion. Solution pH was used to control the electrostatic interaction between the mixed microgel dispersion affording flocculated (pH 3) or re-dispersed (pH 10) Au-NPs as desired. It was demonstrated that good recovery efficiency of the AuNPs was achieved after pH-induced separations under acidic conditions.

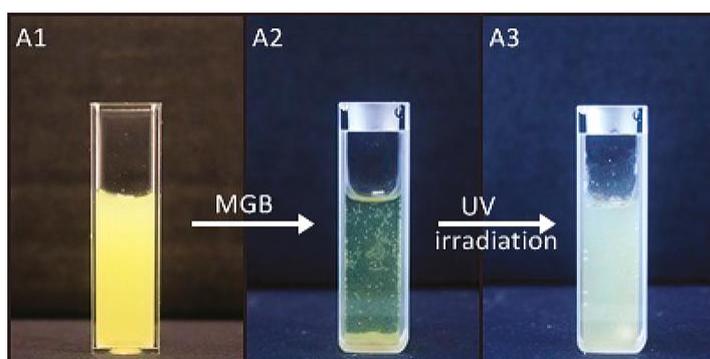
Figure 4. Colloidal strings formed by electric-field induced ordering of latex particles that are glued together through heteroaggregation with microgel particles. The scale bars represent 2 μm (reproduced with permission from reference [28]).



3.1.4. Light

Light is a non-intrusive stimulus and when used in heteroaggregation allows the ability to tailor electrostatic interactions between colloids in the absence of chemical additives. The general concept of microgel heteroflocculation in combination with photo-responsive surfactants (PRS) was applied by us to access new light-sensitive materials [30]. With these PRS-microgel complexes, stability was controlled by both charge and light. Firstly, anionic PRS was complexed with cationic microgels to form stable but shrunken PRS-microgel complexes, which are negatively charged (image A1 in Figure 5). The addition of another cationic microgel sequestered some of the PRS surfactant, which induced instability by driving a co-flocculation with the PRS-microgel complexes (image A2 in Figure 5). UV-irradiation was used to photolyze the complexed PRS, reinstating the original positive charges on the microgel, re-swelling that microgel component, and also stabilizing the mixed microgel dispersion (image A3 in Figure 5).

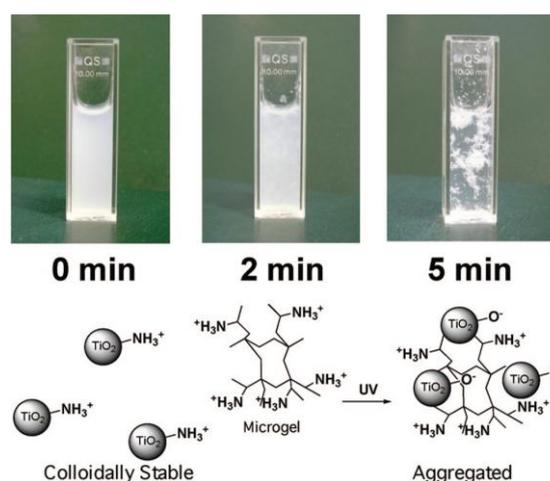
Figure 5. Light triggered reversible co-flocculated a mixed microgel system (reproduced with permission from reference [30]).



A photo-induced phase transition in a binary heteroaggregate was demonstrated by Plunkett *et al.* [31]. Silica particles were coated with a cationic self-assembled monolayer that undergoes charge inversion upon photo-cleavage, to access light-sensitive colloidal particles. A binary colloidal suspension was prepared between the photo-sensitive silica particles and negatively charged silica particles. Heteroflocculation in this system produced chain-like aggregates comprised of alternating charged particles. A change in the colloidal packing after UV-irradiation was observed by a decrease in the sediment height, consistent with a gel-to-fluid phase transition.

Photocatalysis has been used to trigger the heteroaggregation between titanium dioxide (TiO_2) and polyvinylamine microgel. Ye *et al.* [32] functionalized TiO_2 with an aminosilane coating which undergoes photodecomposition, upon which the particle surface charge changes from positive to negative *in situ*, as shown by the reaction scheme in Figure 6. When these initially cationic particles are mixed with cationic microgels, of similar size, the suspension is stable as shown in the first photograph in Figure 6. Heteroflocculation is subsequently triggered by UV-irradiation as shown in the last photograph.

Figure 6. Light-triggered heteroflocculation of a binary titanium dioxide/microgel dispersion (reproduced with permission from reference [32]).



4. Application of Smart Particle Heteroaggregates

There are many important processes which are controlled by heteroaggregation. Paper making is a classic example whereby the final product is produced from initial slurry through the heteroaggregation of cellulose fibers and filler particles. Mineral flotation processes [33] water purification [34,35], pigment manufacture, biological tissue growth [36], printing and the synthesis of coated particles [37] or nanostructured materials [38] also utilize the principles of heteroaggregation.

The heteroflocculation of microgels may be exploited to enhance the efficiency of crude oil recovery [26]. Thermo-sensitive PNIPAM systems exist as stable dispersions at room temperature, however, can be triggered to flocculate in response to the higher temperatures prevalent in oil-bearing rock, and the presence of highly concentrated electrolyte in the pumping material, e.g., seawater. Microgel heteroaggregation can consequently block off channels of high permeability, thus enabling the oil in the less permeable areas to be mobilized. This process however depends on the strength of

the aggregates, which must bear huge shear forces resulting from the high pressure. Charge induced heteroaggregates of microgel particles display better rheological properties for this application than homoaggregated systems.

The application of microgels in rheology control has found use in ceramic processing and coating technology. In coatings technology microgels provide desirable shear thinning properties. Microgels have been investigated as alternative processing aids for aqueous ceramic suspension [39]. Ceramics are substances that have to be chemically and thermally stable. Agents are added to ceramic suspensions to enhance the strength and ease of processing. Polyelectrolyte coated alumina was mixed with microgels of like charge or opposite charge and the properties of the sintered product investigated. It was found that ceramic bodies were better formed when similarly charged microgel particles to the alumina were added. The system containing oppositely charged microgel particles to the alumina formed products that crumbled on handling. This was due to charged heteroaggregation producing large macro-pores in the sintered materials and thus a poor microstructure, whereas systems containing those made from like charged microgel particles had a much better microstructure.

Microgels have recently been identified as promising in the design of highly functional bioactive scaffolds in regenerative medicine due to a combination of their rheological properties, drug delivery capability and synthesis from biodegradable and biocompatible polymers [40-42]. In tissue engineering gels are used as a supporting matrix for the delivery of cells. Gelatin nanospheres have been used to form biodegradable colloidal gels by mixing oppositely charged nanospheres under physiological conditions [43]. Elastic gels were formed at low solid content as a result of electrostatic self-assembly between the nanospheres as well as additional stabilization of the gels caused by intimate contact between the nanospheres owing to the deformable nature of the particles. The gelatin nanosphere-based gels were shear-thinning and self-healing which makes them suitable for extrusion and injection by syringes.

A large problem with injecting microgel particles, encapsulating regenerative medicines, into target tissue to aid regeneration, is the displacement of particles by external mechanical deformation. Heteroaggregation of microgel particles was investigated by DeVolder and Kong to overcome this challenge and improve therapeutic efficacy [44]. Oppositely charged microgels were mixed to form a colloidal gel, and its structural strength was modulated through the ratio between oppositely charged microgels as well as the charge on the particles, which was controlled by the type and concentration of ionic unit incorporated into the microgels. The *in vivo* testing, through implantation, of these gels containing a vascular growth factor was shown to significantly increase the vascular density.

Receptor-mediated heteroaggregation of bioconjugated particles is the basis for agglutination tests, used in biological assays, where the presence of visible agglomerates determines the presence of antigen. Using modified responsive polystyrene latex, easy to use pregnancy test kits have been developed. The probe was built based on binary heterocoagulation of polystyrene latex particles where each set of particles contained a specific antibody that binds to human chorionic gonadotropin (HCG) present in the blood and urine of pregnant women [45].

Heteroaggregation of small latex particles onto baculovirus has been used to protect the virus from UV-irradiation [46]. Baculovirus is used to protect soybean plants from being defoliated, however, exposure of the virus to sunlight seriously affects its biological activity. The electrostatic adsorption of

the small latex particles onto the much larger virus particle provides a physical barrier against UV-radiation.

Current particle technology is using the concept of heteroaggregation to produce composite functional materials. Magnetizable silica composite particles from heteroaggregates of large carboxylic acid stabilised latex and much smaller iron oxide nanoparticles has been reported by Lu *et al.* [47]. Heteroaggregation in this system was pH dependent occurring under acidic conditions where the Fe_3O_4 and latex particles were oppositely charged. Fe_3O_4 particles were deposited on the latex particles, and after formation, the heteroaggregate was stable over a wide pH range due to coordination of Fe^{3+} ions and carboxyl groups at the interface. The heteroaggregates were then coated in silica and the latex core removed to produce the final particles. It is envisioned that these particles will find application in biotechnology and field induced assembly.

The preparation of a magnetorheological fluid, by the design of magnetic particles composed of a clay core covered by a shell of magnetite nanoparticles in aqueous suspension, was described by Galindo-Gonzalez *et al.* [11]. To achieve this they used heteroaggregation between small positively charged magnetite and larger negatively charged colloidal clay. These composite particle suspensions display a magnetorheological effect due to a fluid-solid transition, characterized by a high yield stress when an external magnetic field is applied. This is the result of particle chaining in the field.

5. Conclusions

This review has discussed the versatility of heteroaggregation of smart particles, which is much richer from a conceptual point of view than classic particle heteroaggregation because of the inherent control over the particles properties using environmental stimuli, such as pH, temperature and light. Aggregation under various conditions of pH, electrolyte, temperature, charge density and relative concentration can be induced by the careful manipulation of any one or more of these environmental conditions. For each kind of stimulus involved, procedures including physical and chemical methods that led to heteroaggregation have been discussed. In general, heteroaggregation occurs when there is an attractive interaction between particles in mixed dispersions. It has been shown that heteroaggregation in systems of variable charge and charge density are also heavily influenced by a complex balance of forces, both electrostatic and steric, and can be affected significantly by the environment of the particles. The flexibility offered by oppositely charged microgels and their heteroaggregation have numerous advantages, most notably increased structural strength and rheological properties. The underlying principles shown here rely on strong surface interactions which can be altered and monitored. Although the heteroaggregation process of smart particles is still an emerging science, significant fundamental and applied studies have provided understanding of colloidal interactions in these systems. This holds much promise for the development of new smart technology and materials.

Acknowledgments

M.B. acknowledges funding from the Royal Society for a Dorothy Hodgkin Fellowship.

References

1. Islam, A.M.; Chowdhry, B.Z.; Snowden, M.J. Heteroaggregation in colloidal dispersions. *Adv. Colloid. Interface Sci.* **1995**, *62*, 109-136.
2. Myakonkaya, O.; Eastoe, J. Low energy methods of phase separation in colloidal dispersions and microemulsions. *J. Adv. Colloid Interface Sci.* **2009**, *149*, 39-46.
3. Hollamby, M.J.; Eastoe, J.; Chemelli, A.; Glatter, O.; Rogers, S.; Heenan, R.K.; Grillo, I. Separation and purification of nanoparticles in a single step. *Langmuir* **2010**, *26*, 6989-6994.
4. van Blaaderen, A. Colloids get complex. *Nature* **2006**, *439*, 545-546.
5. Edwards, E.W.; Wang, D.; Mohwald, H. Hierarchical organization of colloidal particles: From colloidal crystallization to supraparticle chemistry. *Macromol. Chem. Phys.* **2007**, *208*, 439-445.
6. Bradley, M.; Rowe, J. Cluster formation of Janus polymer microgels. *Soft Matter* **2009**, *5*, 3114-3119.
7. Fan, K.; Bradley, M.; Vincent, B.; Faul, C.F.J. Effect of chain length on the interaction between modified organic salts containing hydrocarbon chains and poly(N-isopropylacrylamide-co-acrylic acid) microgel particles. *Langmuir* **2011**, *27*, 4362-4370.
8. Yu, W.L.; Matijevic, E.; Borkovec, M. Absolute heteroaggregation rate constants by multiangle static and dynamic light scattering. *Langmuir* **2002**, *18*, 7853-7860.
9. Ryde, N.; Matijevic, N.R. Kinetics of heterocoagulation. Part 4.—Evaluation of absolute coagulation rate constants using a classical light scattering technique. *J. Chem. Soc. Faraday Trans.* **1994**, *90*, 167-172.
10. Galletto, P.; Lin, W.; Borkovec, M. Measurement of heteroaggregation rate constants by simultaneous static and dynamic light scattering. *Phys. Chem. Chem. Phys.* **2005**, *7*, 1464-1471.
11. Galindo-Gonzalez, C.; de Vicente, J.; Ramos-Tejada, M.M.; Lopez-Lopez, M.T.; Gonzalez-Caballero, F.; Duran, J.D.G. Preparation and sedimentation behavior in magnetic fields of magnetite-covered clay particles. *Langmuir* **2005**, *21*, 4410-4419.
12. Lin, W.; Kobayashi, M.; Skarba, M.; Mu, C.; Galletto, P.; Borkovec, M. Heteroaggregation in binary mixtures of oppositely charged colloidal particles. *Langmuir* **2006**, *22*, 1038-1047.
13. Yu, W.L.; Borkovec, M. Distinguishing heteroaggregation from homoaggregation in mixed binary particle suspensions by multiangle static and dynamic light scattering. *J. Phys. Chem. B* **2002**, *106*, 13106-13110.
14. Kihira, H.; Matijevic, E. Kinetics of heterocoagulation. 3. Analysis of effects causing the discrepancy between the theory and experiment. *Langmuir* **1992**, *8*, 2855-2862.
15. Puertas, A.M.; Fernandez-Barbero, A.; de las Nieves, F.J. Charged colloidal heteroaggregation kinetics. *J. Chem. Phys.* **2001**, *114*, 591-595.
16. Snowden, M.J.; Gracia, L.H.; Nur, H. Heteroflocculation studies of colloidal poly(NIPAM) microgels with polystyrene latex particles: Effect of particle size, temperature and surface charge. In *New Frontiers in Colloid Science*; Biggs, S., Cosgrove, T., Dowding, P., Eds.; RSC: Cambridge, UK, 2008; p. 148.
17. Anzai, C.; Furusawa, K. Heterocoagulation behaviour of polymer latices with spherical silica. *Colloid. Surface.* **1992**, *63*, 103-111.

18. Harley, S.; Thompson, D.W.; Vincent, B. The adsorption of small particles onto larger particles of opposite charge. *Colloid. Surface.* **1992**, *62*, 163-176.
19. Fernandez-Barbero, A.; Loxley, A.; Vincent, B. Heteroaggregation between charged hard and soft particles. *Prog. Colloid Polym. Sci.* **2000**, *115*, 84-87.
20. Fernandez-Barbero, A.; Vincent, B. Charge heteroaggregation between hard and soft particles. *Phys. Rev. E* **2000**, *63*, 011509-1.
21. Snoswell, D.R.E.; Rogers, T.J.; Howe, A.M.; Vincent, B. Controlling porosity within colloidal heteroaggregates. *Langmuir* **2005**, *21*, 11439-11445.
22. Starck, P.; Vincent, B. Heteroflocculation of particle mixtures by a coacervation mechanism. *Langmuir* **2006**, *22*, 5294-5300.
23. Starck, P.; Ducker, W.A. Simple method for controlled association of colloidal particle mixtures using pH-dependent hydrogen bonding. *Langmuir* **2009**, *25*, 2114-2120.
24. Bayer, F.M.; Hiltrop, K.; Huber, K. Hydrogen-bond induced heteroassembly in binary colloidal systems. *Langmuir* **2010**, *26*, 13815-13822.
25. Islam, A.M.; Chowdhry, B.Z.; Snowden, M.J. Temperature-induced heteroflocculation in particulate colloidal dispersions. *J. Phys. Chem.* **1995**, *99*, 14205-14206.
26. Hall, R.J.; Pinkrah, V.T.; Chowdhry, B.Z.; Snowden, M.J. Heteroaggregation studies of mixed cationic co-polymer/anionic homopolymer microgel dispersion. *Colloid. Surface. A Physicochem. Eng. Aspects* **2004**, *233*, 25-38.
27. Hui, D.; Nawaz, M.; Morris, D.P.; Edwards, M.R.; Saunders, B.R. Study of pH-triggered heteroaggregation and gel formation within mixed dispersions. *J. Colloid Interface Sci.* **2008**, *324*, 110-117.
28. Snoswell, D.R.E.; Brill, R.K.; Vincent, B. pH-responsive microrods produced by electric-field-induced aggregation of colloidal particles. *Adv. Mater.* **2007**, *19*, 1523-1527.
29. Lazim, A.M.; Eastoe, J.; Bradley, M.; Trickett, K.; Mohamed, A.; Rogers, S.E. Recovery of gold nanoparticles using pH-sensitive microgels. *Soft Matter* **2010**, *6*, 2050-2055.
30. Lazim, A.M.; Bradley, M.; Eastoe, J. Controlling gold nanoparticle stability with triggerable microgels. *Langmuir* **2010**, *26*, 11779-11783.
31. Plunkett, K.N.; Mohraz, A.; Haasch, R.T.; Lewis, J.A.; Moore, J.S. Light-regulated electrostatic interactions in colloidal suspensions. *J. Am. Chem. Soc.* **2005**, *127*, 14574-14575.
32. Ye, L.; Miao, C.; Brook, M.A.; Pelton, R. Photoflocculation of TiO₂ microgel mixed suspensions. *Langmuir* **2008**, *24*, 9341-9343.
33. Bandini, P.; Prestidge, C.A.; Ralston, J. Colloidal iron oxide slime coating and galena particle flotation. *Miner. Eng.* **2001**, *14*, 487-497.
34. Findlay, A.D.; Thompson, D.W.; Tipping, E. The aggregation of silica and haematite particles dispersed in natural water samples. *Colloid. Surface. A Physicochem. Eng. Aspects* **1996**, *118*, 97-105.
35. Rubio, J.; Souza, M.L.; Smith, R.W. Overview of flotation as a wastewater treatment technique. *Miner. Eng.* **2002**, *15*, 139-155.
36. Place, E.S.; Evans, N.D.; Stevens, M.M. Complexity in biomaterials for tissue engineering. *Nat. Mater.* **2009**, *8*, 457-470.

37. Lee, J.-H.; Mahmoud, M.A.; Sitterle, V.B.; Sitterle, J.J.; Meredith, J.C. Highly scattering SERS metal nanoparticle coated polymers prepared via combined swelling-heteroaggregation. *Chem. Mater.* **2009**, *21*, 5654-5663.
38. Grzelczak, M.; Vermant, J.; Furst, E.M.; Liz-Marzan, L.M. Directed self-assembly of nanoparticles. *ACS Nano* **2010**, *4*, 3591-3605.
39. Greenwood, R.; Kendall, K.; Ritchie, S.; Snowden, M.J. The use of poly (N-isopropylacrylamide) microgels as a multi-functional processing aid for aqueous alumina suspensions. *J. Eur. Ceramic Soc.* **2000**, *20*, 1707-1716.
40. Saunders, J.M.; Tong, T.; LeMaitre, C.; Freemont, A.J.; Saunders, B.R. A study of pH-responsive microgel dispersions: from fluid-to-gel transitions to mechanical property restoration for load-bearing tissue. *Soft Matter* **2007**, *3*, 486-494.
41. Liu, R.; Milani, A.H.; Freemont, T.J.; Saunders, B.R. Doubly crosslinked pH-responsive microgels prepared by particle inter-penetration: swelling and mechanical properties. *Soft Matter* **2011**, *7*, 4696-4704.
42. Jia, X.; Yeo, Y.; Clifton, R.J.; Jiao, T.; Kohane, D.S.; Kobler, J.B.; Zeitels, S.M.; Langer, R. Hyaluronic acid-base microgels and microgel networks for vocal fold regeneration. *Biomacromolecules* **2006**, *7*, 3336-3344.
43. Wang, H.; Hansen, M.B.; Lowik, D.W.P.M.; van Hest, J.C.M.; Li, Y.; Jansen, J.A.; Leeuwenburgh, S.C.G. Oppositely charged gelatin nanospheres as building blocks for injectable and biodegradable gels. *Adv. Mater.* **2011**, *23*, H119-H124.
44. DeVolder, R.J.; Kong, H.-J. Three dimensionally flocculated proangiogenic microgels for neovascularization. *Biomaterials* **2010**, *31*, 6494-6501.
45. Ouali, L.; Stoll, S.; Pefferkorn, E.; Elaissari, A.; Lanet, V.; Pichot, C.; Mandrand, B. Coagulation of antibody-sensitized latexes in the presence of antigen. *Polym. Adv. Technol.* **1995**, *6*, 541-546.
46. Lessa, M.M.; Medugno, C.C. Heteroflocculation of sulfate polystyrene latex and Anticarsia Gemmatalis Nucleopolyhedrovirus as a model system for studying sunlight protection. *J. Colloid Interface Sci.* **2001**, *239*, 328-333.
47. Lu, Z.; Qin, Y.; Fang, J.; Sun, J.; Li, J.; Liu, F.; Yang, W. Monodisperse magnetizable silica composite particles from heteroaggregates of carboxylic acid stabilised PS latex and iron oxide nanoparticles. *Nanotechnology* **2008**, *19*, 055602.