Self-Assembly of Calcium Carbonate Nanoparticles in Water and Hydrophobic Solvents

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Abstract

The self-assembly of Ca^{2+} and CO_3^{2-} ions into nanoparticles in water and hydrophobic solvents is investigated using Molecular Dynamics (MD) computer simulation. A new three-stage particle assembly procedure is used which relaxes the structure of the nanoparticle towards a lower energy state. In hydrophobic solvent the bare particle is essentially spherical whereas in water it is ellipsoidally shaped. With surfactant stabilizer the nanoparticles typically exhibit non-spherical cores in model hydrophobic solvents. Binary surfactant systems exhibit synergistic effects were for example a salicylate-sulfonate combination forms a cage which promotes a compact core. Synergistic effects on the shape of the particle were also observed in a hydrophobic solvent for surfactant-stabilized systems with trace water as a third component. The simulations show that rather than being a rigid structure the carbonate core shape and stabilizing shell coverage is sensitive to solvent, surfactant and small polar molecules which act as co-surfactants.

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Introduction

Nanoparticles are increasingly finding applications in important technologies such as chemical production, energy management, as bioactive agents and as additional components in materials science. The solvent, chemical composition of the core and surfactant-stabilizer can affect the performance of these particles in the various applications. For example, the surface charge and hence electrolytic properties of silica nanoparticles depend on the size of the nanoparticle, with potential consequences for cellular uptake.¹ The effectiveness of triangle-shaped nanoplates against *E. coli* is greater than that of spherical or rod-like nanoparticles.^{2,3} Oleic acid stabilizers can affect the reactivity during reduction of Fe₃O₄ nanoparticles used to form ferri- and ferromagnetic materials.⁴ A molecular dynamics study of gold nanoparticles interacting with a polystyrene interface showed that the presence of surfactant-stabilizer can cause significant disordering of the polystyrene chains compared to an uncoated particle, with performance implications for memory-storage devices.⁵

It is therefore important to be able to control the shape and core accessibility of a nanoparticle via suitable choice of surfactant stabilizer and solvent conditions.^{6,7} For example, Wieneke *et al.* carried out experiments on TiO₂ nanoparticles, focusing on the effect of solvent on the size and stability of the structures formed,⁸ finding that the size of the nanoparticle can vary dramatically, with some nanoparticles forming agglomerates between 16 and 800 nm across. Sperling and Parak demonstrated that the chemical nature of the solvent affects the extent of aggregation of the micelle into colloidal nanostructures.⁹

Calcium carbonate, CaCO₃, is found in nature in many morphological forms, and sea life has proved particularly adept at growing it into a variety of shapes. Recent laboratory-based studies have revealed that carbonates can be grown into different structures (e.g. flowers) by altering the chemical environment of the growing front with time.¹⁰ Calcium carbonate is used industrially in ultra fine form via precipitation from solution, in which the particles can range in diameter from a few nanometres to many hundreds of nanometres in the same sample. Control of the rate

of nucleation from solution,^{12,13} and the size distribution and morphology is made using a third component, such as a polymer or another component which forms a core-shell structure.^{11–13} More chemically specific synthetic paths can lead to monodisperse calcium carbonate particles which are typically 2-4 nanometers across, for example by growth inside proteins,¹⁴ or by a microemulsion route to make the so-called overbased detergents used as engine oil additives^{15–17} and medicines¹⁸ where its acid-neutralization properties are exploited. Synthetic routes,^{19,20} and tribological performance,²¹ have been studied extensively. The overbased particles have a reverse micelle structure whose formulation is continually being adapted to satisfy environmental legislation and performance demands.²² Experiments on alkyl sulfonate and alkyl phenate stabilized nanoparticles predict a predominantly amorphous core,^{22–24} a conclusion supported by classical Molecular Dynamics (MD) simulations of Quigley and Rodger.²⁵ Kobylansky found that CaCO_3 nanoparticles stabilized by sulfonate-based surfactants display faster neutralization properties than the corresponding phenate and salicylate systems.²¹

There is widespread interest in establishing chemical architecture- property relationships for these nanoparticles. With continual improvements in molecular modeling software and computational power, MD computer simulations can be used effectively to explore the chemical factors which determine the formation, shape and physical properties of CaCO_3 nanoparticles. This work follows on from previous MD and experimental investigations carried out 15-20 years ago of small (2-4 nm diameter) overbased CaCO_3 nanoparticles in the presence of four different surfactant types.^{16,17,26,27} The total base number (TBN) measures the acid neutralizing ability of an individual particle. The original simulation studies investigated model nanoparticles with a TBN of *ca.* 250, and were close in composition to commercial products. Langmuir trough and Langmuir-Blodgett film characterization carried out in parallel with molecular modelling proved that these particles were 2 – 4 nm in diameter. The original MD simulations used a preformed CaCO_3 core to guide the assembly of the nanoparticles in the gas-phase, but were unable to include the effect of explicit solvent due to computational limitations of the time. As far as we are aware there have been no other MD simulations of overbased detergents in the intervening years. Most of the mod-

elling work in relation to oil additives has been on the surfactants in the oil, using either Density Functional Theory (DFT) [28] or MD [29,30]. With the improved software we are able to explore new aspects of the overbased particles under more realistic conditions.

Here all-atom MD simulation is used to generate calcium carbonate nanoparticles. Novel aspects of calcium carbonate nanoparticles which are considered here for the *first* time are, (a) a new preparation procedure which produces a more thermodynamically stable particle, (b) use of explicit water and cyclohexane solvents with and without a surfactant stabilizer in both cases, (c) exploration of a binary mixture of stabilizing surfactant molecules, and (d) addition of water as a third component in the hydrophobic solvent case. Because of the strong binding forces between the ions in calcium carbonate particles it is tempting to view them as being relatively rigid structures on the surface of which other chemical constituents just adsorb. By varying the chemical composition of the mixture, the aim of this study is to ascertain to what extent this is true. In addition, this work provides new insights into how nanoparticle shape and geometry can be controlled by solvent and additional chemical components, with potential relevance to applications as discussed in a broad sense at the beginning of this section.

Simulation details

Parametrization

Four different surfactant types, an alkyl sulfonate, sulfurised alkyl phenol (SAP), alkyl salicylate and alkyl calix[6]arate were modeled in this study. Their chemical structures are given in Figure 1. Dodecane alkyl chains were used in each case. The same surfactant systems were studied experimentally and in MD simulations by one of us and co-workers,^{26,27} in a previous set of publications, whose results provide a benchmark and reference for the present simulation study.

There are several key differences between this study and the previous MD simulations. First, the previous MD simulations were conducted in the gas phase, and were commenced from a largely preformed CaCO_3 core. Here the particles were generated in explicit model solvent, either water or cyclohexane, which is closer to the conditions prevailing in the experimental synthetic procedure. Secondly, in this work the calcium and carbonate ions, surfactant and solvent molecules were allowed to self-assemble in solution without bias from random initial positions at the start of the simulation. In some of the simulations trace amounts of water were introduced to reflect more closely conditions prevailing in hydrophobic solvents. The AMBER forcefield was used in the previous study for non-bonded interactions between the surfactant molecules and the core, and a Born-Mayer potential to model the inorganic core. In this work the Gromos53A6 forcefield was used for all species, which is broadly similar to the previous AMBER forcefield and directly compatible with the scheme used to parameterize the surfactants. Finally, the nanoparticle was subjected to an annealing then quenching stage to relax the system towards a lower free energy state. For some of the simulations the number of deprotonated chelating groups in the surfactant was the same as in the previous work. Every other hydroxyl group of the calix[6]arate was deprotonated to give a symmetrical arrangement around the ring and the same charge state as previously modeled.

Self-assembly simulations were performed using GROMACS v4.5.5.^{31,32} Parameters for the sur-

Figure 1: The four types of surfactants modeled in this study

factants, cyclohexane and the carbonate ions were obtained using the online Automated Topology Builder (ATB) server.^{33,34} The ATB uses a knowledge-based approach in conjunction with B3LYP/6-31G* derived geometries to calculate the partial charges for the molecules, and builds a topology which is compatible with the Gromos53A6 forcefield.³⁵

The Gromos53A6 forcefield was parameterized empirically to reproduce accurately the solvation free energies of small polar molecules and amino acids. In order to test the compatibility of the ATB-derived partial charges within the Gromos53A6 forcefield, the solvation free energies of three amino acid sidechains were calculated using charges derived from the Gromos53A6 forcefield, the ATB and the AM1/BCC method³⁶ in antechamber.^{37,38} The three parameter sets produced similar solvation free energies (given in Supporting Information), indicating that there is insignificant force-field dependence on the key system properties and *inter alia* supports the use of the ATB charges in this study.

Self-assembly method

Table 1: Summary of the molecular details of the simulations, including the number of each species. IS is the total number of interaction sites from the surfactant molecules. The SAP and salicylate molecules have two IS per molecule while the sulfonate has one. The calixarate has six IS per molecule. Cyclohexane is the solvent. An extra 3 carbonate molecules were added for the Calix[6]arate system since the total surfactant charge in this system was $-6 e$.

Reference	Mixture	Surfactant	Cyclohexane	Calcium	Carbonate	Water	IS
A	SAP	6	1361	16	10	0	12
B	Sulfonate	12	1680	16	10	0	12
C	Salicylate	12	1649	16	10	0	24
D	Calix[6]arate	2	2000	16	13	0	12
M1	SAP/Sali	3 : 6	2070	16	10	0	18
M2	Sulf/Sali	4 : 8	1651	16	10	0	20
M3	Sulf/Sali	8 : 4	2036	16	10	0	16
W1	SAP	6	1349	16	10	12	12
W2	Sulfonate	12	1668	16	10	12	12
W3	Salicylate	12	1637	16	10	12	24

Table 1 gives the number of species included in the simulations performed. The number of each species is the same as in the previous work, which corresponds to an experimentally determined TBN of 250 and is directly comparable with commercial overbased detergents.¹⁷ The excess electron charge on the SAP is located on the oxygen of the deprotonated *OH* group. In the case of the sulfonate the electron charge is approximately evenly distributed on the three oxygen atoms of the SO_3 group. For the salicylate the charge is evenly distributed between the two oxygen atoms of the deprotonated carboxylic acid group. In each case all possible headgroup sites were deprotonated.

The molecules were first subjected 1000 steps of conjugate gradient potential energy minimization, followed by short MD equilibration simulations of 100 ps length in the NVT and then NPT ensembles. The particle mesh Ewald method³⁹ was used for the electrostatic interactions, with interactions between atoms within 1.0 nm evaluated after every time step and atom-atom interactions beyond 1.0 nm evaluated every five steps. The non-bonded Lennard-Jones cut-off was 1.2 nm. A leapfrog equation of motion integrator was used with a time step of 2 fs. The bond distances and angles of water molecules were constrained with the SETTLE algorithm⁴⁰ and all other bonds constrained using LINCS.⁴¹ The simulations were performed at 300 K with the temperature regu-

lated using a velocity rescaling thermostat with a coupling time of 0.1 ps.⁴² The original velocity rescaling of Woodcock⁴³ has been shown to produce a canonical ensemble distribution.⁴⁴ Also Heyes *et al.* demonstrated using MD that static and dynamical properties of liquids are statistically indistinguishable using velocity rescaling and Nosé-Hoover thermostats.⁴⁵ The pressure was set to 1 bar and controlled using the Parrinello-Rahman barostat.⁴⁶ Following equilibration a simulation was carried out for 20 ns in the NPT ensemble to observe the self-assembly process. The resultant nanoparticles were simulated for a further 40 ns during which the radius of gyration (R_g) of the CaCO_3 core, the R_g of the whole nanoparticle, the core surface area and the radial distribution function between the surfactant head-group and core atoms were computed.

Core-annealing procedure

A more thorough process of nanoparticle construction than in the early simulations,^{26,27} was carried out. The first stage of the simulation (referred to as ‘Phase I’) allowed the various model chemical components to self-assemble from random starting positions. Once formed the components of the nanoparticle are unlikely to rearrange during a typical simulation timescale because of the strong coulombic forces between the core ions, and between the core ions and the deprotonated surfactant head-groups. It is likely that the nanoparticle is nevertheless in a local minimum rather than the global free energy minimum.

After Phase I the charges on the calcium and carbonate ions were gradually reduced using a modified type of ‘slow-growth’ procedure, termed *coulombic annealing*, which forms Phase II. The rationale for carrying out this procedure is that the ions and surfactant molecules are then given an opportunity to relax towards a structure with a lower free energy as the attractions between oppositely charged ions are weaker. The new procedure is able to achieve a state with a lower free energy than the initial structure which would be closer to that of the global minimum if the free energy landscape is of a funnel form. This procedure at least gives the system an opportunity to seek out a more optimum structure. The coulombic interactions were gradually reduced at a rate of

$d\lambda/dt = 4 \times 10^{-8} \text{ ps}^{-1}$, where λ is the factor which multiplies the original coulombic charges.⁴⁷ A value of $\lambda = 1$ corresponds to the charges in the program library. At regular intervals of λ (0.9, 0.8, 0.7 ...), the coulombic annealing simulation was temporarily halted and the system equilibrated for 5 ns during which the properties of the core were calculated. The coulombic annealing simulations were then restarted until the next equilibration point. For all systems during Phase II the simulation was continued until the nanoparticle was on the verge of breaking apart.

In Phase III of the nanoparticle construction, the core ion coulomb interactions were restored to their initial values by reversing the direction of the slow-growth process. This approach, which we refer to as Slow Quenching (SQ), reversed the direction of the annealing process, at a rate of $d\lambda/dt = -4 \times 10^{-8} \text{ ps}^{-1}$, reintroducing gradually the original interactions within the core, and between the core ions and surfactant molecules. At the end of this annealing-quenching sequence the program library charges on the ions from the input forcefield were restored. Then reported quantities were derived from the last 10 ns of a further 20 ns period of simulation. This slow return to the original force field gives more time for relaxation and equilibration of the core and the arrangement of the surfactant molecules on the surface of the core to take place before the structure becomes too rigid. A schematic diagram of the nanoparticle formation and annealing processes is given in Figure 2.

Figure 2: Schematic diagram of the nanoparticle formation and annealing processes. **PI**) is Phase I, **PII**) is Phase II and **PIII**) is Phase III. Calcium and carbonate ions are represented in yellow and red spheres respectively. The surfactant molecules are represented with blue dots for the headgroup with organic tails.

The structural analysis was performed using the inbuilt GROMACS packages `g_sas`, `g_gyrate`, `g_dist` and `g_rdf`. The shape of the nanoparticle was characterized in terms of an asphericity order parameter, A_3 ,^{48,49} derived from the moment of inertia tensor which was accumulated during the simulation,

$$A_3 = \frac{\left\langle \sum_{i \neq j} (\lambda_i - \lambda_j)^2 \right\rangle}{2 \left\langle \left(\sum_{i=1}^3 \lambda_i \right)^2 \right\rangle} \quad (1)$$

where $\langle \dots \rangle$ denotes a time average and λ_i are the principle moments of inertia of the core or total nanoparticle. A value of $A_3 = 0$ indicates a sphere and 0.25 an infinitely thin circular disk. The accessibility of the core to small molecules was estimated using the dimensionless parameter, S , defined by

$$S = \frac{\langle SA \rangle}{\langle R_g \rangle^2} \quad (2)$$

where SA is the actual time-average surface area of the core (or whole particle) calculated in the program using a standard program routine employing a ‘probe’ molecule of diameter, 1.4 Å. The denominator in the equation is proportional to the surface area of the nanoparticle assuming it is a sphere with radius, R_g . Given two cores with the same radius, a larger S indicates a larger accessible surface area. The time averaged radius of gyration, R_g of the core and whole nanoparticle were calculated routinely.

Self-Assembly of Nanoparticles

CaCO₃ particle formation in solvent without surfactant.

Self-assembly simulations were made of the formation of a CaCO₃ nanoparticle *without surfactant* in water and cyclohexane starting from randomly positioned ions in the solvent. These model nanoparticles act as reference states for the CaCO₃ particles formed in the presence of other molecules. The ions aggregate to form a nanoparticle because of the strong coulombic forces between the ions when compared with their interactions with the solvent molecules. The coulombic annealing process was not used to relax these particles since, in the absence of surfactant, it was observed that a low free energy state spontaneously formed during the MD simulations which did not change upon annealing.

Figure 3 shows snapshots of the ions in the cores formed in water, and Figure 4 gives a snapshot of the particle formed in cyclohexane. Only the solvent molecules within 3 Å of the core surface are shown.

Figure 3: Side-on **a)** and top-down **b)** representative snapshots for the self-assembled CaCO₃ particles in water.

Figure 4: A representative snapshot of the self-assembled CaCO_3 nanoparticle in cyclohexane. The hydrogen atoms of the cyclohexane molecules have been removed, and only the first layer of cyclohexane molecules shown for clarity.

Figure 3 shows that in water the nanoparticle is not spherical, as it would be if formed in a vacuum. The particle would also be statistically spherical in a continuum representation of water with the appropriate relative permittivity. A discrete molecule representation of the solvent is therefore necessary in this case to produce a realistic result. The water molecules penetrate part way into the core, forcing it to adopt a non-spherical shape which presumably maximizes the polar interactions between the core ions and the solvent molecules, thereby making the total energy of the system more negative. The nanoparticle formed in cyclohexane, shown in Figure 4 is essentially spherical as it just needs to minimize the surface area. There are no energetic advantages to be derived from a reorganized structure involving the solvent molecules penetrating the core as there are no large attractive energy terms in this interaction. Such a process would be thermodynamically unfavorable. The average value of the asphericity parameter, A_3 , of the particle in cyclohexane is 0.04 and 0.14 in water, indicating that it is less spherical in water than cyclohexane, which is consistent with the snapshots in Figures 3 and 4. Therefore the polarity of the solvent can affect significantly the shape of a bare calcium carbonate nanoparticle.

The effects of surfactant on the nanoparticle are considered in the next section.

Self-assembly process with surfactant

Without a surfactant stabilizer the nanoparticles generated in the previous section would over time aggregate to minimize the surface area and free energy of the system. Experimentally, calcium carbonate nanoparticles are synthesized with surfactant stabilizer making them at least kinetically stable and only marginally thermodynamically unstable. The previous simulations,^{26,27} showed that surfactants with polar head-groups can distort the shape of the nanoparticle core away from the stabilizer-free reference states, a feature explored further below .

Figure 5 shows snapshots of the carbonate-surfactant system in cyclohexane for the four surfactant types after 20 ns of simulation. The figure reveals that the final nanoparticle structure depends on the surfactant type. A comparison between the final nanoparticle structures reveals that after 20 ns the micelle formed using model SAP is disc-shaped, with the alkyl chains directed outwards from the micelle core. The sulfonate nanoparticle as a whole is more spherical, but the surfactant is somewhat unevenly distributed around the core in patches. The salicylate nanoparticle is more cylindrical than the other nanoparticles, which may be due to a two-stage assembly process (evidence for this is presented in the Supporting Information). The salicylate surfactant exhibits the same patch-like features as the sulfonate nanoparticle, with the alkyl chains extending into the solvent.

Figure 5: Self-assembly snapshots after 20 ns for the four detergents in cyclohexane. **a)** SAP, **b)** Alkyl-sulfonate, **c)** Alkyl-salicylate, **d)** alkyl-calixarate. The calcium ions are shown in yellow. Cyan and red colored atoms represent the carbon and oxygen atoms of the carbonate ions, respectively

The nanoparticle formed by the alkyl-calixarate is quite different from those of the other three detergent types. Bearchell *et al.* generated a sandwich-shaped complex with the core, in which the two calixarene molecules capped two ends.²⁷ Here however the core is more or less split in two between the two macrocyclic rings of the calixarene. This is perhaps not a surprising feature as calixarenes are widely used as ion hosts and show promise as ion transporters.⁵⁰ It is possible that

for longer simulation times than feasible at the time, this structure would have also developed in the study of Bearchell *et al.* Once assembled, each system was evolved for a further 20 ns, and then annealed. The following section describes the effects of the annealing process, and presents a structural analysis of the nanoparticles formed

Coulombic annealing and reforming of the nanoparticle

The behavior of the system during the annealing (Phase II) and reforming (Phase III) stages of the nanoparticle construction process are discussed in this section. Figure 6 illustrates the effects of the coulombic annealing process on the SAP nanoparticle system in cyclohexane. The coulombic interactions were gradually reduced, and when they were 50 %, of their initial values (*i.e.* when $\lambda=0.5$), the nanoparticle began to fragment and the simulation process was halted. The coulombic interactions were then restored gradually from the $\lambda=0.6$ structure using the SQ method (Phase III).

Figure 6: Representative snapshots of the SAP nanoparticle during the coulombic annealing process (Phase II). **a)** for $\lambda=0.9$, **b)** for $\lambda=0.8$, **c)** for $\lambda=0.7$, and **d)** for $\lambda=0.6$. Calcium ions are shown in yellow. The cyan and red spheres represent the carbon and oxygen atoms of the carbonate ions, respectively

Figure 6 shows through frames (a) to (d) that the SAP-CaCO₃ core elongates as the coulombic interactions are weakened. As the value of λ was decreased the average distance between the head-group of the surfactant and the core center of mass increased and the surfactant tails progressively wrapped around the core which produced a more cylindrical structure than the disc shape displayed at the start of this process. This trend is reflected in an increased value of A_3 . The structural effects of the coulombic annealing process on the initially formed nanoparticle are summarized in the Supporting Information.

The next stage in the nanoparticle preparation was to restore the coulombic interactions to their library values (Phase III). Since both the Phase II and III procedures are based on a type of ‘slow-growth’ procedure, they can be treated as a free energy difference simulation and used to establish whether the final quenched state has a lower free energy than the initial structure. Figure 7 shows the thermodynamic cycle used to establish the overall free energy change upon the relaxation process, ΔG_{relax} .

Figure 7: Thermodynamic cycle used to calculate the free energy change upon annealing, ΔG_{relax} . State A is the initially formed state at the end of Phase I, state B is the state at the end of Phase II and A* is the final state at the end of phase III. ΔG_{II} and ΔG_{III} are the free energy changes associated with the Phase II and Phase III simulations, respectively.

Taking the SAP nanoparticle as an example, the values of ΔG_{II} (corresponding to the A-B transition, i.e. coulombic annealing) and ΔG_{III} (corresponding to the B-A* transition, i.e. slow-quenching) were found by thermodynamic integration to be $+2362 \pm 43$ and -3349 ± 55 kJ/mol respectively, which corresponds to $\Delta G_{relax} = -987 \pm 98$ kJ/mol, where the (standard) errors were obtained from three independent simulations.

This change indicates that the final relaxed state has a lower free energy than the initial structure. The relaxation process has therefore been proved to cause the system to adopt a lower free energy state through this cycle. Analysis of the individual enthalpic components reveals that the change in free energy ($A-A^*$) is predominantly due to more favourable interactions between the calcium and carbonate ions. The relaxed state is not necessarily a global minima, but it provides a state which is more thermodynamically stable than the one formed spontaneously during the initial stages of the MD simulation. The values of ΔG_{relax} for the alkyl-sulfonate, alkyl-salicylate and alkyl-calixarate were -1226 ± 90 , -1373 ± 165 and -1168 ± 105 kJ/mol respectively, proving that the relaxation process forms a lower free energy state for all surfactant types. Phases II and III of the nanoparticle construction process is therefore a significant improvement in methodology.

Table 2 shows the effect of carrying out Phases II and III on the surface area and radius of gyration, R_g .

Table 2: Comparison between the physical properties of SAP nanoparticles before the coulombic annealing and quenching processes (Phases II and III) with those at the end of the initial formation stage (Phase I) or 'pre-annealing'. The standard deviation of the radius of gyration is given in parentheses. Surface area is denoted by SA. S_c and S_n is the accessibility to the core and the whole nanoparticle respectively.

State	Core SA / nm ²	R_g -Core / nm	R_g -Total / nm	S_c	S_n
End of Phase I	8.20	0.53 (0.01)	1.09 (0.02)	29.2	6.9
End of Phase III	8.06	0.55 (0.02)	1.11 (0.03)	26.6	6.5

Table 2 indicates that the SQ process produces a core which has a structure which is similar to the pre-annealed state, but a lower free energy state mainly due to a reorganisation of the core. The core and micelle radii are essentially the same, while the surface area (SA) of the core underwent a slight reduction, and there is a reduced S value suggesting a more uniform distribution of the surfactant molecules around the core making it less accessible to a potential test particle. The surfactant molecules after the quench in Figure 8 look more uniformly distributed around the core than before, which should shield it better from solvent and any other small impurity molecules.

Although the initially-formed and further-equilibrated structural properties are almost the same in this case, this will not necessarily be the case for other classes of surfactant.

To conclude, the annealing-quenching procedure provides the nanoparticle with a facility to relax its structure further after initial formation by mutual diffusion of the species. It has been demonstrated that for all four surfactant types Phases II and III lower the free energy of the nanoparticle.

Figure 8: Representative snapshots for the SAP nanoparticle pre (**left**) and post annealing (Phase II) (**right**). A reference calcium ion is shown in yellow, which helps to align the viewpoint of the two snapshots.

Analysis of Nanoparticle Structure

Radial Distribution Functions

Figure 9 presents the radial distribution functions (RDF) between the oxygen atoms of the surfactant head-group (HG) and the calcium, carbon and oxygen atoms in the core. The figure shows that the distribution of ions around the surfactant head-group differs with surfactant type, as might be expected from the snapshot structures of Figure 1. The architecture of the surfactant molecule has an impact on the organization of the core atoms around the head group. The position of the first peak in the HG-O $g(r)$ is similar for SAP and the salicylate but is further out and more diffuse for the sulfonate and (especially) calixarate cases. The phenolic oxygen on the SAP surfactant has a more localized negative charge than the other three surfactant types, facilitating its stronger interaction with and penetration through the core surface, as revealed by the intense peak in the RDFs. In comparison, the negative charge on the sulfonate surfactant is delocalized around a trigonal head group, sterically prohibiting it from interacting and penetrating as much into the core. The macrocyclic nature of the calixarate places unique constraints on the structure of the core, which is reflected in the RDFs.

Figure 9: Radial distribution functions, $g(r)$, for the four self-assembled CaCO_3 nanoparticles. The RDF between the oxygen atom of the surfactant head-group and **a)** the calcium, **b)** carbon and **c)** oxygen atoms in the core are shown for SAP, sulfonate, salicylate, and calix[6]arate systems.

Nanoparticle size and shape

Table 3 presents key structural parameters for the four types of nanoparticle after the quenching stage. The radius of gyration of the cores ranges from 0.48 nm for the sulfonate to 0.63 nm for the calixarate system which reflects differences in the interaction between the core and surfactant molecule in each case. The sulfonate headgroup penetrates the core least, so that it can occupy

Table 3: Structural parameters of the nanoparticles formed after the annealing and reformation stages. The asphericity, A_3 and the surface area, SA_r , refers to the $CaCO_3$ core, and standard deviations are in parentheses. The radius of gyration, R_g , of the core and total particle are given.

Detergent	R_g -core / nm	R_g -total / nm	A_3	SA_r / nm ²	IS
A SAP	0.55 (0.01)	1.11 (0.02)	0.11	8.06 (0.23)	12
B Sulfonate	0.48 (0.01)	1.18 (0.04)	0.07	7.56 (0.20)	12
C Salicylate	0.61 (0.02)	1.22 (0.03)	0.15	8.26 (0.17)	24
D Calix[6]arate	0.63 (0.01)	1.07 (0.02)	0.12	8.64 (0.21)	12
M1 (SAP-Sulf 3:6)	0.58 (0.02)	1.21 (0.03)	0.09	8.50 (0.21)	6:6
M2 (Sulf-Sal 4:8)	0.62 (0.01)	1.23 (0.04)	0.15	9.09 (0.20)	4:16
M3 (Sulf-Sal 8:4)	0.53 (0.01)	1.20 (0.03)	0.07	8.51 (0.18)	8:8

the smallest volume and retain a more spherical shape. The SAP headgroup is more effective in penetrating the core which in the process expands it and distorts its shape. The salicylate and calix[6]ate also distort the core from a sphere which results in a larger radius of gyration than for the sulfonate. The sulfonate can therefore be considered to be a ‘reference’ state for this class of nanoparticle. The calix[6]arate surfactant traps the core inside its hydrophilic cavity. Table 3 confirms what can be inferred from the snapshot figures, that all four of the nanoparticle cores are not spherical as the average asphericity parameter is greater than zero in all cases (A_3 is 0.15 for the salicylate, 0.11 for SAP and 0.07 for sulfonate). The surface area (‘ SA_r ’) of the core is approximately the same for each type, with differences being consistent with the relative values of the core radii of gyration.

Langmuir-Blodgett film experiments,¹⁷ gave a diameter of 2.2 nm for a SAP nanoparticle with 250 TBN, which is in excellent agreement with the value of 2.22 ± 0.04 obtained in this study. The diameter of the sulfonate-based nanoparticle in this work, 2.36 ± 0.08 , is in good agreement with small angle X-ray scattering (SAXS) experiments which give values between 2.3 and 3.6 nm.⁵¹ The quantitative accuracy of the computer model for single component surfactant systems suggests that the structural aspects of mixed surfactant nanoparticles should be predicted reasonably well.

Mixed surfactant nanoparticles

In order to explore further the influence of the surfactant architecture on the nanoparticle morphology, three mixed surfactant systems were modeled. The first, **M1**, contained three SAP and six sulfonate surfactant molecules. In this system the number of primary interaction sites (IS), from the SAP (3 molecules $\times$ 2 sites) and the sulfonate molecules (6 molecules $\times$ 1 sites) were equal. The second system, **M2**, contained four sulfonate surfactant molecules (4 IS) and 8 salicylate surfactants (16 IS), therefore giving a potential bias towards the pure salicylate morphology. System, **M3**, contained eight sulfonate and four salicylate molecules, giving a total of eight primary interactions for each surfactant type. The total surfactant net charge in each case was $-12e$. The number of species in each simulation is given in Table 1. Table 3 shows the calculated nanoparticle properties, after the annealing procedures (Phases II and III) described previously.

It might be expected that the properties of the mixed surfactant nanoparticle should broadly follow that of the single surfactant nanoparticle formed from the dominant surfactant in the mixed system, although there is no formal proof of this. The results here for the three mixed systems show deviations from a weighted mean of the properties of the nanoparticles formed from the individual detergents. The core radius and surface area of **M1** are closer to that of the pure SAP (System A) compared to that of the pure sulfonate (System B), despite the number of IS being the same for each detergent type. System **M2** has almost the same core radius as the pure salicylate (System C), although the accessible surface area is larger. System **M3** has a core radius which is close to the mean of those formed from the two surfactant molecules separately, but the core accessible surface is a little higher. A key parameter in governing these trends may be the extent of delocalization of the net charge around the surfactant head-group. The sulfonate and salicylate-carboxylate head-groups both have their negative charge delocalized around several oxygen atoms, resulting in a similar diffuse charge distribution, in marked contrast to the SAP head-group on which the charge is localized on one oxygen atom. The similar charge distribution allows the salicylate and sulfonate surfactants to bind in broadly the same way when the number of IS is the same, so in the case of the

(**M3**) core a weighted mean behavior of the hybrid nanoparticle is obeyed reasonably well.

Analysis of the mixed surfactant nanoparticles shows that the distribution of surfactant molecules around the core is not necessarily uniform, and that different surfactant types can interact synergistically to give a core accessible surface area which is not obviously predictable in advance from the two single surfactant nanoparticles. Figure 10 shows the surfactant distribution around the CaCO_3 core for the **M2** system. Patches of sulfonate surfactants can be seen towards the bottom of Figure 10, which are similar to those seen for the pure sulfonate nanoparticle in the previous studies.²⁷ The hydroxyl group on the salicylate moiety can hydrogen bond directly to the sulfonate head-group and other salicylate surfactant molecules (shown in black). This presumably stabilizes the patches on the surface of the core which are more accessible to a potential test particle. One side of the core is distinctly more accessible than the other in sharp contrast to the accessible surface area profiles of the individual components (shown in Table 3). The simulations carried out with mixed-surfactant systems demonstrate that the properties are typically not additive to varying extents. Therefore, to conclude, system-specific synergistic cross interactions between the head-groups can have a pronounced effect on the amount of accessible surface area of the nanoparticle, which will possibly impact on the reactivity and solubility of the particle in different solvents.

Figure 10: Visualization (viewed from above, **a**) and below, **b**) of the M2 nanoparticle formed with a sulfonate and salicylate surfactant mixture, showing the asymmetry in the distribution of the surfactants around the core. Calcium ions are shown in yellow, and cyan and red indicate the carbon and oxygen atoms of the carbonate ions, respectively. The carbon surfactant chains are shown in blue. Hydrogen-bonds between the hydroxyl group of the salicylate and the sulfonate head-group are shown as short black lines.

Water as a third component

Roman has shown that the rate of formation and final size of sulfonate-based nanoparticles in oil depends on the amount of water in the reaction mixture.^{51,52} Nanoparticles rarely exist in purely hydrophobic environments as it is difficult to remove the last traces of water, and any water molecules present will preferentially associate with the polar carbonate nanoparticle cores, which could affect the structure of the nanoparticle. The original simulation studies of Griffiths¹⁷ and Bearchell²⁷ did not incorporate water in the computer model.

To explore the consequences of this effect, a set of simulations was carried out in which some model water molecules were added to previously formed carbonate nanoparticle systems (i.e. *post* phase III). Each nanoparticle was simulated from self-assembly in a box of cyclohexane. Twelve randomly dispersed water molecules were then introduced and the simulation continued for a further 20 ns. In another set of simulations the water molecules were added at the beginning of Phase I. These two types of simulation procedure are denoted by **A** and **B**, respectively.

The key structural parameters for the SAP, sulfonate and salicylate nanoparticles are shown in Table 4, with the number of species for each simulation given in Table 1.

Table 4: Key structural characteristics of the nanoparticles with additional water molecules formed in cyclohexane. In the simulation reference code in the first column, ‘A’ indicates that the water molecules were added post Phase III, and ‘B’ is when they were added at the start of Phase I. The top three rows are for simulations carried out without water. The standard deviation of each quantity is given in parenthesis.

System	R_g -Core / nm	SA / nm ²	SA % change
SAP	0.55 (0.01)	8.06 (0.23)	
Sulfonate	0.48 (0.02)	7.56 (0.20)	
Salicylate	0.61 (0.01)	8.26 (0.17)	
W1A SAP	0.56 (0.02)	8.09 (0.22)	0
W2A Sulfonate	0.48 (0.01)	7.42 (0.21)	2
W3A Salicylate	0.59 (0.02)	8.10 (0.15)	2
W1B SAP	0.64 (0.03)	8.28 (0.16)	3
W2B Sulfonate	0.67 (0.02)	9.20 (0.18)	22
W3B Salicylate	0.65 (0.03)	8.74 (0.21)	6

The surface area and radius of the core are largely unaffected when the water molecules are added to the preformed nanoparticle after phase III (A). The water molecules were unable to change the shape of the carbonate core during the simulation timescale and instead resided on the surface of the core (see Figure 11, *a*) and *b*)). In contrast, water molecules present at the start of the self-assembly process (stage I (*b*)) significantly altered the properties of the core, particularly for the sulfonate nanoparticle (Figure 11, *d*)). The surface area of the sulfonate nanoparticle underwent a large expansion, indicating that the water molecules penetrated and interacted with the core to a greater extent than for the other two surfactants. The behavior is similar to that of the ‘bare’ nanoparticles in water solvent as discussed above. SAXS experiments performed by Roman also showed an increase in the size of sulfonate-based nanoparticles on the addition of water, by *ca.* 20 % in that case.⁵¹ The sulfonate surfactant does not penetrate the core as much as the SAP and salicylate surfactant molecules, allowing the water molecules to exploit the ease of access to the core. The increase in surface area and radius of gyration radius of the SAP and salicylate nanoparticles is smaller as these head-groups penetrate the core significantly and therefore can dominate any distorting effect due to the water molecules.

To conclude this section, these simulations show that the presence of water can have a significant effect on the morphology of the nanoparticles, to an extent, which depends on the chemical architecture of the surfactant. This is another synergistic effect.

Figure 11: Snapshots of the SAP (**a**, **c**), and sulfonate (**b**, **d**) nanoparticles formed in the presence of water molecules (**Class A**: a), b). **Class B**: c), d)). The core ions are shown in blue, with the surfactant head-groups shown as yellow spheres. The water molecules are represented by red and white colored trimers.

Conclusions

This study has shown that the shape and size of calcium carbonate nanoparticles in a solvent can be controlled quite significantly by its chemical environment, particularly by small polar molecules such as water and surfactant which can bind to the surface and act as stabilizers in hydrophobic media. Strong synergistic effects are observed by competing species and the final structure is the balance between the chemical binding demands of the various species. This is why it is quite difficult to predict in advance even incremental changes in nanoparticle structure by change of formulation. The molecular modeling approach adopted here is well suited to this task, and has been shown to generate nanoparticle properties whose dimensions are in good agreement with experiment, and provide insights into the synergistic effects. There is evidence from the simulations that hybrid systems composed of mixtures of stabilizing surfactant types can be a useful way of fine-tuning and optimizing the structure (and hence physical and chemical properties) of the nanoparticles. It has been shown here that water molecules as another component can have a significant impact by the swelling of the CaCO_3 core, in good agreement with experiment.⁵¹

The methodology used in this work could be applied to the rational design of various types of calcium carbonate nanoparticle, such as the so-called overbased nanoparticles which are used as engine oil additives. The prediction of the physical properties on atomistic detail using these techniques could be used to help guide the synthesis strategy of nanoparticles for specific applications.

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Supporting Information Available

Calculated solvation free energies of amino acid sidechains using different force fields. Self assembly snapshots for the different surfactants as a function of time. Changes in the structural properties for the SAP nanoparticle during the coulombic annealing process.

This material is available free of charge via the Internet at <http://pubs.acs.org/>.

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