

# Binding of Calcium and Carbonate to Polyacrylates

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Polyacrylate molecules can be used to slow the growth of calcium carbonate. However, little is known about the mechanism by which the molecules impede the growth rate. A recent computational study (Bulo et al. *Macromolecules* 2007, 40, 3437) used metadynamics to investigate the binding of calcium to polyacrylate chains and has thrown some light on the coiling and precipitation of these polymers. We extend these simulations to examine the binding of calcium and carbonate to polyacrylate chains. We show that calcium complexed with both carbonate and polyacrylate is a very stable species. The free energies of calcium–carbonate–polyacrylate complexes, with different polymer configurations, are calculated, and differences in the free energy of the binding of carbonate are shown to be due to differences in the amount of steric hindrance about the calcium, which prevents the approach of the carbonate ion.

## 1. Introduction

The formation of  $\text{CaCO}_3$  in water is of interest to scientists working in a number of different fields. In biology, calcium carbonate forms the shells and crusts of undersea animals,<sup>1</sup> while in chemical engineering, and for that matter in everyday life, the formation of calcium carbonate in reaction vessels is a menace.<sup>2</sup>

The addition of polyelectrolytes to reaction mixtures has been shown to considerably slow the rate of calcite formation.<sup>3</sup> Both in the presence and in the absence of polyelectrolyte, a strongly hydrated precursor forms. However, the polyacrylate seems to prevent any aggregation of this amorphous phase, such that the large crystals of amorphous calcium carbonate, calcite, and vaterite, observed after 5 min in the absence of the polymer, are no longer formed. Moreover, it seems likely that the remarkable control that sea animals have over the phase and morphology of the  $\text{CaCO}_3$  particles that they use to form their shells arises from the interactions of functionalized polymers with the growing crystals.<sup>4</sup>

Commonly the sodium salts of polyacrylates (see Figure 1) are used as a simple model system to understand polyelectrolyte behavior.<sup>5</sup> This polymer, when in aqueous solution, is assumed to have a stretched configuration and is known to have its sodium ions disassociated and at a distance of approximately 4–5 Å from the negatively charged polymer chains.<sup>5</sup> When divalent cations are added, these, unlike monovalent cations, are known to strongly coordinate to the chain, which is believed to be an entropic effect.<sup>6</sup> It seems likely, therefore, that the polymer's ability to suppress calcite formation stems somehow from the ability of the polyacrylate to bind calcium ions.

Experiments<sup>7–11</sup> have shown that there are a number of different modes of calcium binding to the chain and that at high calcium concentrations one can observe chain coiling and precipitation. Moreover, coarse-grained simulations<sup>12–22</sup> have shown that when large concentrations of calcium are present, the polymer can have a smaller radius of gyration as a consequence of decreased repulsion between monomers resulting

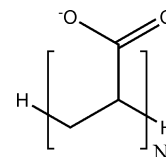


Figure 1. Structure of the polyacrylate polymer.

from charge neutralization. Most recently, atomistic molecular dynamics simulations, by Molnar and Rieger,<sup>5</sup> and metadynamics simulations, by Bulo et al.,<sup>23</sup> on short polymers have shown that at high calcium and polyacrylate concentrations there is little coiling of the polyacrylate chains because of the local rigidity in the stretched chain. As a result, in these conditions the aggregation of chains is initiated by long-range interactions between chains, which arise because of the shielding of the negative charges by the closely bound calcium ions and a related dispersion of the surrounding sodium cloud.<sup>5</sup> In contrast, at low calcium concentrations the polyacrylate chains can coil. In these coiled configurations, many calcium ions cluster together, share several  $\text{COO}^-$  groups, and have local crystal-like features.<sup>23</sup>

The aim of this study is to extend the work of Bulo et al.<sup>23</sup> so as to investigate what effect the carbonate has on the binding of calcium to polyacrylate. Simulations, using the newly developed well-tempered metadynamics method,<sup>24</sup> have been performed to ascertain the relative stability of calcium–carbonate, calcium–polyacrylate, and calcium–carbonate–polyacrylate complexes. A further metadynamics simulation has then been used to investigate how the proximity of carbonate to the polyacrylate chain affects the relative stability of the various modes of the binding of calcium to the polyacrylate chain.

## 2. Forcefield

Previous simulations<sup>23</sup> of polyacrylate, calcium, and water have been carried out using the CHARMM forcefield.<sup>25</sup> However, it has been shown that nonpolarizable models of the carbonate ion provide a poor description of the solid phases of calcium carbonate.<sup>26</sup> Recently, a new transferable shell model forcefield for calcium carbonate has been developed<sup>27</sup> by combining the model of Archer et al.<sup>28</sup> for calcium carbonate, the SWM4-NDP<sup>29</sup> model for water, and the mineral water interaction from the de Leeuw and Parker

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**TABLE 1: Gas Phase Binding Energies and Equilibrium Distances of Pairs Calculated Using MP2/6-311+G\* and the Empirical Forcefield<sup>a</sup>**

	MP2/6-311+G*		classical forcefield	
	$U$ , eV	$d_{eq}$ , Å	$U$ , eV	$d_{eq}$ , Å
$\text{Ca}^{2+} + \text{C}_3\text{H}_5\text{O}_2$	-13.471	2.19	-13.448	2.19
$\text{H}_2\text{O} + \text{C}_3\text{H}_5\text{O}_2$	-0.826	2.04	-0.776	2.00

<sup>a</sup> The equilibrium distance,  $d_{eq}$ , is the shortest distance between the oxygens of the functional group and the calcium ion or the shortest distance between these oxygens and the hydrogen of a water molecule.

potential.<sup>30</sup> This forcefield provides a good description of the solid phases of  $\text{CaCO}_3$ , the hydrated phases of  $\text{CaCO}_3$ , and the solvation of  $\text{Ca}^{2+}$  ions.<sup>27</sup>

The aim in this paper is to model the interplay among polymer, calcium, and carbonate. The interactions between these species are unlikely to be well described if a CHARMM description of the polymer is mixed with a different forcefield<sup>27</sup> for the water, carbonate, and calcium. Ideally, though, one would wish to avoid fitting a new potential for the polyacrylate to make its description consistent with that of the calcium, carbonate, and water in ref 27. Chemically, it seems likely that the polymer–calcium and polymer–water interactions will be dominated by their interactions with the functional group. Moreover, the functional group in a polyacrylate is very similar to a carbonate ion. As such, one simplistic way to obtain a new potential for the polyacrylate would combine the terms for the intramolecular interactions and intermolecular backbone interactions from CHARMM with a description of the functional group water–calcium–carbonate interactions taken from the shell model potential for the carbonate. As Table 1 shows, this potential, with a small rescaling of the Buckingham terms, reproduces well the gas phase geometries and binding energies of calcium–monomer and water–monomer clusters as calculated using MP2/6-311+G\* optimizations in Gaussian 03.<sup>31</sup>

### 3. Methods

The simulations were carried out using a modified version of dl\_poly\_2.16<sup>32</sup> and used well-tempered metadynamics<sup>24</sup> to increase the frequency of rare events. This method uses a number of order parameters to describe the system and adds a history-dependent term to the potential to encourage the system to explore a larger region of phase space. However, unlike previous flavors of metadynamics,<sup>33,34</sup> well-tempered metadynamics uses Gaussian “hills” whose heights are no longer constant. Instead, the height depends on the histogram of previously visited configurations, which ensures a more rapid and smoother convergence of the free energies obtained.

An isotactic sodium polyacrylate chain of five monomer units, a  $\text{Ca}^{2+}$  ion, and a  $\text{CO}_3^{2-}$  ion were placed in a box of 895 water molecules. The polymer used is considerably shorter than the 20mer used in the work of Buló et al.<sup>23</sup> However, on the basis of the work of Buló et al.,<sup>23</sup> a 5mer with one calcium ion would not be expected to agglomerate and precipitate. Furthermore, coiling of a longer chain would be highly unfavorable with a single calcium ion.

The system was equilibrated for 1 ns using the Berendsen thermostat to maintain the temperature at 300 K and the Berendsen barostat to ensure that there is zero applied pressure. The relaxation times of the thermostat and barostat were 0.5 and 2.0 ps, respectively. The final configuration from this run, from which the constant volume metadynamics calculations are

commenced, has a concentration of 61 mmol  $\text{dm}^{-1}$ . Subsequent metadynamics calculations were run at constant volume and used a thermostat recently developed by Bussi et al.<sup>35</sup> to maintain constant temperature. A 0.2 ps relaxation time was used with this thermostat. In both equilibration and production runs, a 1 fs time step was used, and quaternions were used to describe the orientations of the rigid water molecules. The rigid body equations of motions were integrated using the NOSQUISH algorithm of Miller et al.,<sup>36</sup> and long ranged electrostatics were treated using the smoothed particle mesh Ewald sum.<sup>37</sup>

All well-tempered metadynamics simulations were run at a temperature of 300 K, for 6 to 8 ns, until the free energy differences between the states of interest were converged to within  $0.3 k_B T$ .  $T + \Delta T$ , the notional temperature at which the space of collective variables is explored,<sup>24</sup> was set to 3000 K, and the initial rate of deposition of energy was 0.1 eV  $\text{ps}^{-1}$ . The Gaussian widths used were 0.2 Å for all distances and 0.05 units for all coordination numbers. Gaussians were added at a rate of 1 for every 0.1 ps of simulation time. For all distance-based collective coordinates, a harmonic wall was added at 8.0 Å with a force constant of 1.0 eV Å<sup>-2</sup> to prevent sampling of uninteresting regions of the free energy surface.

The order parameters defined below were used in this study:

$S_a(R)$ , the separation between the calcium ion and the carbon of the carbonate ion.

$S_b(R)$ , the separation between the calcium ion and the nearest oxygen of the polyacrylate chain.

$$S_b(R) = \min(r_{\text{Ca}} - r_{\text{O}(\text{CO})}) \quad (1)$$

$S_c(R)$ , the coordination number of the calcium ion with the carboxylate units on the chain defined as a sum of switching functions on  $\text{Ca}-\text{O}(\text{CO}^-)$  distances.

$$S_c(R) = \sum_{i \in N} f_i \quad \text{with} \quad f_i = \frac{1 - \left( \frac{r_{\text{Ca-fg}}}{r_0} \right)^n}{1 - \left( \frac{r_{\text{Ca-fg}}}{r_0} \right)^m} \quad (2)$$

Here  $r_{\text{Ca-fg}}$  is the separation between the calcium and the nearer of the two oxygen atoms of the functional group. The parameters  $n$ ,  $m$ , and  $r_0$  were set to 8, 16, and 3.5 Å, respectively, which have been shown elsewhere<sup>23</sup> to be optimal for this system.

$S_d(R)$ , the maximum contact order of the  $\text{Ca}^{2+}$  ion to the carboxylate units of the chain. This is a dimensionless quantity, which is defined as the maximum distance, along the chain, between two monomers coordinated to one  $\text{Ca}^{2+}$ .

$$S_d(R) = \max(f_i \times f_j \times \text{dist}) \quad (3)$$

Here,  $f_i$  is defined in the same manner as in eq 2, but the parameters  $n$ ,  $m$ , and  $r_0$  are now 6, 12, and 3.5 Å, respectively.<sup>23</sup>

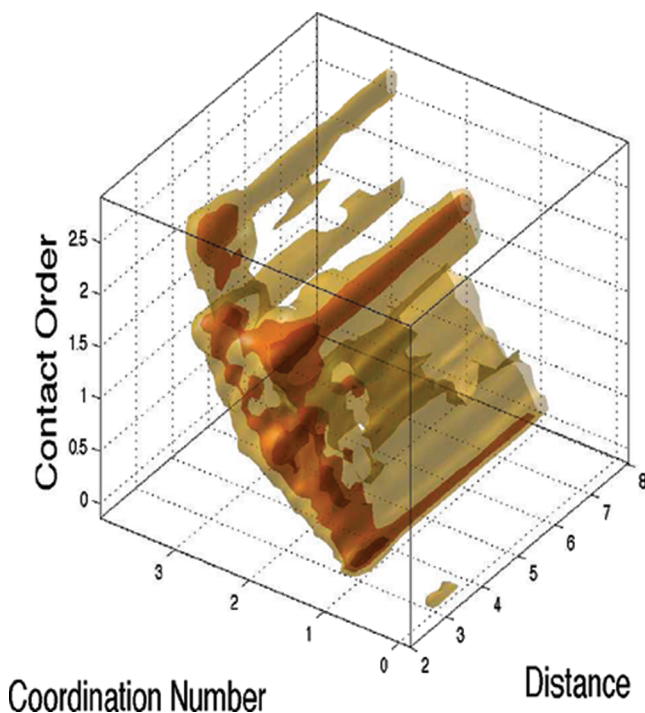
### 4. Results and Discussion

**4.1. Single Polymer Studies.** Buló et al.<sup>23</sup> used the minimum distance between the  $\text{Ca}^{2+}$  ion and the oxygens of the polyacrylate chain ( $S_b(R)$ ) and the number of carboxylate groups to which the  $\text{Ca}^{2+}$  ion is attached ( $S_c(R)$ ) as collective coordinates in a metadynamics simulation to investigate the free energy associated with binding a calcium ion to a polyacrylate chain. Here, in addition to these two collective coordinates, the distance between the  $\text{Ca}^{2+}$  ion and the carbon of the carbonate ( $S_a(R)$ ) has been used in a metadynamics simulation to establish whether simultaneous binding of both the calcium and the carbonate to the chain is desirable. Table 2 gives the free energies integrated over the regions corresponding to the binding of calcium to just

**TABLE 2: Integrated Free Energies of the Basins Corresponding to Calcium Bound Only to the Polymer, Calcium Bound Only to the Carbonate, and Calcium Bound Simultaneously to Both Polymer and Carbonate<sup>a</sup>**

	free energy, $k_B T$
calcium bound to carbonate	-19.57
calcium bound to polymer	-25.55
calcium bound to both	-35.68

<sup>a</sup> These numbers are quoted relative to the integrated free energy for a state in which the calcium, carbonate, and polymer are all dissociated.

**Figure 2.** Isosurfaces of the free energy surface (at values of -0.85, -0.54, -0.23, and 0.08 eV) for the coordination of calcium and carbonate to a 5mer as a function of the calcium carbonate distance (in Å), the number of functional groups attached to the calcium, and the maximum contact order.

the polymer, the binding of calcium to just the carbonate, and the simultaneous binding of calcium to both the polymer and the carbonate. It is clear from this table that by far the most stable configuration in solution is to have both calcium and carbonate bound to the polyacrylate chain. However, it is also apparent that coordination of carbonate with a calcium bound to the polyacrylate comes with a far smaller free energy gain than coordination with a free calcium. This is almost certainly due to electrostatic repulsion between the chain and the carbonate as are the differences between the free energy changes on binding carbonate observed for the different configurations.

Polyacrylates have multiple carboxylate groups, which can all, in theory, bind strongly to the calcium ion. Thus, the statement “binding to the polyacrylate” refers to a huge variety of different calcium binding modes. Buló et al.<sup>23</sup> used the number of functional groups attached to the calcium ( $S_c(R)$ ) and the maximum contact order ( $S_d(R)$ ) as collective coordinates to investigate the free energies of these various binding modes. Here, to investigate what effect the proximity of a carbonate ion has on the mode of binding, the calcium carbonate distance ( $S_a(R)$ ) has been used in addition to Buló’s coordinates for a second metadynamics simulation. The 3D free energy surface output from this simulation is shown in Figure 2.

**TABLE 3: Integrated Free Energies of the Basins Corresponding to the Different Modes of Binding Calcium to the Polyacrylate<sup>a</sup>**

	Relative free energy / $k_B T$		
	Bind	No CO <sub>3</sub>	CO <sub>3</sub>
<b>A</b>	8.09	4.23	4.55
<b>B</b>	10.08	1.72	0.05
<b>C</b>	8.41	0.0	0.0
<b>D</b>	6.81	7.18	8.78
<b>E</b>	9.80	11.21	9.82

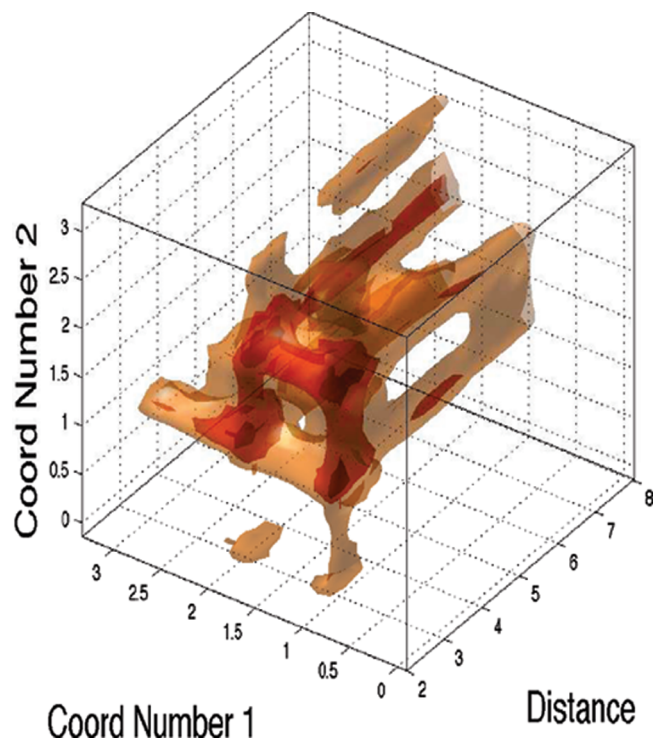
<sup>a</sup> The first column gives the free energy increase for the removal of the carbonate from the configuration. The second and third columns are the free energies relative to the integrated free energy of state C for the coordination of just the calcium and the calcium and the carbonate, respectively. The figures show a representative configuration, from the trajectory, with each binding mode. To maintain clarity, the backbone hydrogen atoms are not shown.

A number of things become apparent on examination of Figure 2. The first is that the free energies of all of the calcium binding modes are lowered by the presence of carbonate. However, the lowest free energy calcium–carbonate distance for a given configuration is strongly correlated with the number of carboxylate groups coordinating to calcium. This observation is not that surprising: if calcium is coordinated to numerous carboxylates, the region about the ion is crowded, and thus the approach of the carbonate is made more difficult.

Using Figure 2 as a guide, the free energies of the basins corresponding to different modes of calcium binding with and without carbonate have been obtained by integrating the free energy in the vicinity of each minimum. The results of this analysis are shown in Table 3.

Table 3 shows that coordination of carbonate and calcium is highly favorable for all polymer configurations. Furthermore, the free energetic ordering of different polymer binding modes is the same both when the calcium is simultaneously bound to the polymer and carbonate and when it is just bound to the polymer. There are, however, some slight perturbations in the relative free energies of the various conformations, which appear correlated with the differences in the free energy of the binding of carbonate. It was previously asserted that differences in the free energy of the binding of carbonate could be explained in terms of differences in the electrostatic interaction between polymer and carbonate. As an example of this, take configurations B and C: configuration C is the lowest energy configuration, while B is a relatively close second. In the presence of carbonate the free energy difference between these two states is markedly decreased, which can be understood to be a consequence of the fact that the free energy of the binding of carbonate to the calcium in state B is markedly larger. This, in turn, can be understood to be because the electrostatic repulsion between polymer and carbonate in state C is 2.18 eV larger than the interaction in state B.





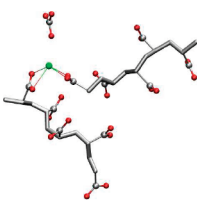

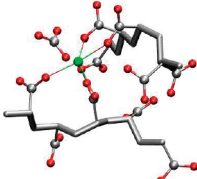
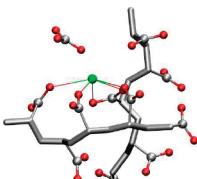
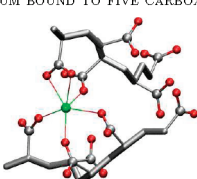
**Figure 3.** Isosurfaces of the free energy surface (at values of  $-0.74$ ,  $-0.55$ ,  $-0.37$ , and  $-0.18$  eV) for the coordination of calcium and carbonate to two 5mers as a function of the calcium carbonate distance (in Å), the number of functional groups belonging to 5mer 1 attached to the calcium, and the number of functional groups belonging to 5mer 2 attached to the calcium.

A similar observation can be made for states D and E. In state D, the electrostatic repulsion between carbonate and polymer is 1.63 eV larger than the interaction in state E. However, it is also interesting to note, from an examination of the figures in Table 3 and the trajectory, that in state D the ion is more effectively surrounded by the polymer, and so the options for carbonate approach to the calcium are reduced. This observation that steric hindrance around calcium lowers the favorability of complexation by carbonate is an interesting one. Buló et al.<sup>23</sup> have shown that, in the presence of larger concentrations of calcium and longer polymers, coiling becomes more energetically feasible and coiled clusters with local crystal-like features are observed. Furthermore, Molnar and Rieger<sup>5</sup> have shown that calcium ions can shield the electrostatic, repulsive forces between polyacrylate molecules, which allows the polymers to approach each other, stick together, and precipitate. In these two situations, one would expect the calcium ion to be very effectively surrounded by polyacrylate, which would perhaps prevent it from binding to carbonate.

**4.2. Two Polymer Studies.** To investigate whether or not calcium can become so encapsulated in polymer that it no longer binds to carbonate, a further metadynamics simulation was carried out. This time, two 5mers, a single calcium and a carbonate, were simulated in a box containing 850 water molecules. Three order parameters were used in the metadynamics: the distance between the calcium and the carbon of the carbonate ( $S_a(R)$ ) and two separate measures of the number of functional groups attached to the calcium ( $S_c(R)$ ), one from each of the polyacrylate molecules. The free energy surface obtained is shown in Figure 3.

Figure 3 shows that in the presence of two polymers the most stable states are those in which the calcium is bound to both polymers and to the carbonate (particularly remarkable is the fact

**TABLE 4: Free Energy Increase Associated with Unbinding Carbonate from a Calcium That Is Itself Bound to Two Polyacrylates<sup>a</sup>**

		Free energy gain / $k_B T$
CALCIUM BOUND TO ONE CARBOXYLATE FROM EACH POLYMER		
I		13.53
CALCIUM BOUND TO THREE CARBOXYLATES, TWO FROM A SINGLE POLYMER		
II		10.46
CALCIUM BOUND TO TWO CARBOXYLATES FROM EACH POLYMER		
III		6.45
CALCIUM BOUND TO FOUR CARBOXYLATES, THREE FROM A SINGLE POLYMER		
IV		9.24
CALCIUM BOUND TO FIVE CARBOXYLATES, THREE FROM A SINGLE POLYMER		
V		-4.50

<sup>a</sup> Pictures show a sample configuration from each of the integrated minima with all of the water molecules, and the hydrogens on the polymer backbones are omitted for the purpose of clarity.

that the binding to carbonate is still favored when the calcium is bound to two functional groups from each polymer). From the figure, it would appear that the most stable configuration is to have the calcium bound to one functional group from each of the two polymers and also to the carbonate. Furthermore, as would be expected, those states in which one of the polymers coils up so as to achieve more calcium carboxylate contacts have high free energies, and thus low stabilities, both when the calcium is bound to the carbonate and when it is not.

Figure 3 also shows that calcium ions bound to the same number of polyacrylate molecules have different free energies for the binding of carbonate. This adds further weight to the suggestion that it is steric hindrance about the calcium ion and

not just repulsion of the carbonate by the negatively charged polyacrylate chain that lowers the affinity of calcium to carbonate. Integrating the various free energy basins in Figure 3, the results of which are shown in Table 4, confirms this suggestion. Of particular note is the large difference in binding free energy between the situation where the calcium is bound to three carboxylate groups from one polymer and one from the other (IV) and the situation where the calcium is bound to two carboxylates from each of the polymers (III). The free energy gain in the second case is almost  $3 k_B T$  smaller than the first, which is almost certainly because when the contacts are shared equally between the two polymers, the carboxylate groups have more freedom to surround the calcium and thus block approach to the calcium by the carbonate ion.

The strength of the calcium–carbonate attraction is such that only by forming extreme coils, to maximize the number of calcium–carboxylate contacts, can polyacrylates effectively prevent the formation of the calcium–carbonate complex. Admittedly, the strength of the binding of calcium to carbonate can be lowered by more effectively surrounding the calcium ion by carboxylate groups, but even when the calcium is bound to four carboxylate groups, the binding of the carbonate still comes with a free energy decrease.

One suggestion as to how the polymer retards calcite growth is that it mops up calcium ions from solution and thus prevents them from encountering carbonate to form the crystal. Our results make this seem unlikely and suggest instead that calcium carbonate will form in the vicinity of the polymer, which must have some effect at a later stage of calcite growth.

## 5. Conclusions

Atomistic simulations of very short polyacrylates in the presence of calcium and carbonate have been carried out, using well-tempered metadynamics to increase the frequency of rare events and to reconstruct the free energy surface. These have shown that the binding of calcium to polyacrylate is preferable to the binding of calcium to carbonate only and that polyacrylate chains strongly bind calcium carbonate complexes. With that said, the binding free energy of a calcium to a carbonate is lowered when said calcium is bound to polyacrylate. This is because of strong electrostatic repulsion between the carbonate and the polyacrylate chain, which is itself dependent on the geometry of the polymer and in particular how effectively the calcium ion is surrounded by polymer. Even so, a great deal of unfavorable polymer coiling is required before the binding of calcium to carbonate becomes unfavorable. It thus seems highly unlikely that any slowing down of the rate of growth of calcium carbonate in the presence of polyacrylate can be attributed solely to a sequestration of calcium ions by the polyacrylate.

The large free energies of formations of calcium–carbonate–polyacrylate complexes suggests an alternative mechanism for the hindrance of crystal growth. One suggestion could be that the polymers' complexing of calcium and carbonate forces these molecules into an arrangement which does not match the crystal structure. However, given that it is known that calcium carbonate nucleates via an amorphous precursor, this also seems unlikely. A more likely proposition is that polyacrylate strongly binds calcium–carbonate pairs from solution, thereby preventing their further diffusion and the growth of crystal or amorphous material.

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**Supporting Information Available:** The parameters of the potential used in this study and the functional forms are provided. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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