Relative Stability of Crystal and Amorphous States for Tetrahedrally Coordinated Particles and Nanostructures

by

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Abstract

DNA nanotechnology has blossomed in the last decade, with applications including the creation of biosensors, targeted drug delivery using DNA “packaging”, and the self-assembly of optical materials. Much attention has recently focused on using DNA as a linking agent to engineer nanoparticle (NP) lattices with specific geometries. There has been success generating a broad range of crystal lattices, but the formation of one of the most basic symmetry types, the tetrahedral or diamond lattice, has been particularly challenging. We use molecular simulations to examine a combination of NP uniformly coated with DNA that connect via linking units that incorporate tetrahedral structure. We find that the nonspecific interactions can play an important role in the stabilization of the diamond structure. We test the stability of spherical NP-DNA complexes with tetrahedral linkers in a 1:1 ratio, which allow for a variety of lattices, including a diamond structure. Interestingly, this scheme can result in a diamond ordering of NP by an interpenetrating network of DNA, each with diamond connectivity. The possibility of such interpenetrating structures was recently postulated by research from Wesleyan. Finally, we examine a simplified model for NP with highly directional interactions to provide a general framework to understand the balance between diamond and more densely packed lattice structures.
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Chapter 1

Introduction

1.1 DNA Nanotechnology

Nanomaterials, due to both their small size and unique behavior, have a wide variety of useful properties and novel applications. Nanotechnology, as a field, seeks to study these exact traits. For instance, one can take advantage of novel electronic and optical properties for integrating useful materials into circuits on an ever shrinking scale. Other goals of research include small-scale energy storage in objects such as quantum dots, targeted drug delivery mediated through biosensors, and the creation of hypothetical “invisibility” paints. [1]

Fabrication on such a small scale is not easy, however. The methods that have been developed thus far can be divided into two fundamentally different approaches to creating these nanomaterials. The first is the “top-down” approach, which utilizes macroscopic tools to position atoms or etch guides into surfaces in order to reach the desired structure. While effective, the utility of this approach is limited because of its low-throughput and often prohibitive cost. The alternative approach is to go “bottom-up,” taking advantage of chemical or physical structures to coerce the atoms into “self-assembly.” This approach is advantageous as it is relatively inexpensive, high-throughput, and is only limited in resolution by the fundamental physical limits of the
molecules involved. The challenge with this method is in guaranteeing that units assemble into the desired structure, since there are frequently many low energy intermediate structures. \[2\]

Deoxyribonucleic acid (DNA) serves as an ideal tool for guiding such self-assembly. DNA itself is already on the nanoscale, forming strands with a helical diameter of 2 nm. In addition, the specificity of base-pair bonding makes DNA’s interactions inherently programmable. Each strand of DNA is formed by a sequence of one of four base pairs: adenine (A), cytosine (C), guanine (G), or thymine (T). This means a sequence of \(N\) base pairs has \(4^N\) possible configurations. Further, each base binds with a specific partner during hybridization, A bonds with T and C bonds with G. This means that each strand has a unique complement. By creating appropriate base sequences one can control bonding effectively and efficiently. In addition, DNA has many other useful properties for nanotechnology, such as the ability to reverse bonding through thermal and chemical processes. The relative stiffness of double-stranded DNA (dsDNA) as opposed to single-stranded DNA (ssDNA) also provides a useful tool for controlling the structure of DNA-based materials. This difference can be quantified by the persistence length, \(l_p\), with the \(l_p\) of ssDNA ranging from 1.5 to 25 nm \[3–5\] in various solutions, while under similar conditions dsDNA has an \(l_p\) of 50-100 nm \[6\]. All of these properties, when combined, make DNA an excellent tool for creating self-assembly in nanomaterials. \[7–10\]

1.1.1 DNA-Functionalized Materials

While base sequences can be used to control bonding, additional tools are required to enforce geometric structure beyond that of linear strands. One route to the creation of more complex geometries is to join multiple ssDNA to a single metallic nanoparticle (NP) or molecule. These core NP can then be connected in the desired fashion by appropriately programming the base-pair sequences to create the desired links. These DNA-functionalized materials have been used to create aggregate structures such as nanoscale lattices \[11–15\] as well as closed geometries \[16\]. Using NP for the junctions
Figure 1.1: A schematic illustration of DNA-functionalized nanoparticles in two stages of self-assembly. (a) Two NPs are tethered together with complementary strands of ssDNA. The complementary ends of the strands combine to form dsDNA, linking the two NPs together. (b) When the dsDNA forms links between the NPs, the NP can be arranged into a three-dimensional lattice structure. Figure from Ref. [1].

of these structures is advantageous as it not only creates rigid junction points, compared to the flexible structures made purely from DNA, but also allows the structure of NP to be easily determined with crystallographic methods. These methods take advantage of the larger and more solid nature of the NPs to reflect electromagnetic waves and determine the periodic structure. This process is analogous to the manner in which X-ray diffraction crystallography takes advantage of the heavy nuclei in a traditional solid to determine the structure.

The simplest way to create such links is to assign the same “palindromic” base sequences to each strand of ssDNA on every NP. These strands are self-complementary, creating a system where each ssDNA can bind with every other ssDNA. Such systems create aggregate structures that have little overall specificity due to the universal nature of their bonding. More specificity can be introduced by creating two distinct sequences
of DNA that are complementary with each other. By coating different NPs or different parts of each NP with different strands, one can control which of the NP will bond together. Another route to controlling bonding is by making none of the attached ssDNA complementary, and instead introducing free-floating “linker” ssDNA that can attach to the NPs on both ends. This introduces an additional route to controlling structure, since one can now adjust the linker-NP ratio as well as adjusting the strand sequence.

These processes have been used to successfully generate a variety of lattice structures by multiple research groups. These lattices have demonstrated not just a variety of structures, but also of size and spacing. All of the cubic Bravais lattices (simple cubic, face-centered cubic, and body-centered cubic) have been generated in this manner. Several rectangular and hexagonal lattices have been produced as well. The most basic way to engineer such structures is by simple changes in the primary structure, such as modifying the size of NPs or length of DNA strands. Many more complicated methods have also been used. Such methods include modifying densities of linking strands, creation of binary systems of NPs, and changes in rates of DNA hybridization. The binary systems approach, which mixes two different types of NPs, has also demonstrated the ability of these systems to construct different crystal structures through the introduction of new bases into the Bravais lattices described previously. These results include lattices that are isostructural to materials such as Cr$_3$Si, AlB$_2$, and Cs$_6$C$_{60}$. Given such variety, it is incredible that the relatively simple diamond cubic (DC) structure has remained elusive.

As these DNA controlled crystal structures are a recent development, practical applications have yet to be fully realized. However, there are several theoretical applications that hold great promise. Three-dimensional crystals created with DNA could be used as a scaffold for the arrangement of macromolecules into ordered structures, which can then be used to facilitate X-ray spectroscopy to study the structures of proteins and other important macromolecules. The same approach can also be used for the as-
Figure 1.2: A visualization of lattice structures that have been successfully generated with DNA-functionalized NPs. The lattice parameter and NP size are easily adjusted by changing the length of DNA strands and size of the core particle respectively. Note the structure of each lattice shape represented. On the leftmost side are simple cubic structures; the middle section shows BCC structures; the rightmost edge contains FCC structures. All of these are cubic in nature, no diamond lattices have been generated. Figure taken from Ref [18].

Assembly of nanoelectric components into three-dimensional arrays, a step up from the current approaches that are limited to two-dimensional systems. Our ability to tune the lattice parameters of these systems also allows for a hypothetical metal-insulator transition to occur at a critical spacing, based on previous studies of silver NP. [17] [20] These superlattices could also be integrated with DNA-based computation in order to create powerful DNA computers. [21][25]

### 1.2 The Diamond Cubic Structure

This range of applications makes it important to understand how to create as many of these structures as possible. In this study, we focus on a basic crystal that is important
Figure 1.3: The unit cell of the diamond cubic or DC (left) and zincblende or ZnS structure (right). Note that the ZnS structure is the same as the DC, except that the base sites made up of alternating materials. Because the yellow sites of the ZnS make up a unit cube of the FCC lattice, this visualization also demonstrates the geometric construction of the DC structure as an FCC Bravais lattice with a two element basis.

to other technologies and has yet to be created with structural DNA methods: the diamond cubic (DC) structure.

This structure is most famously present the crystallized C organization more commonly known as diamond, from which it acquires its name. The diamond cubic structure also occurs naturally in the crystallization of other group 14 elements, such as Si and Ge. [26] Several other molecules can also crystallize into this form, for example solid H$_2$O of the form I$_c$ and the closely related form I$_h$. [27]

DC structures are primarily defined by their tetrahedral bonding angle. For group 14 elements, this angle arises naturally from the four valence electrons that define this group. For ice I$_c$ and I$_h$, this structure instead comes from the tetrahedral alignment of the two valence electrons and the two H in the molecule. The DC is the most simple structure consisting of a single network of fully bonded particles with this tetrahedral symmetry. While it is not a Bravais lattice, it may be defined as a two element basis to the FCC lattice with the two elements separated by the vector $\frac{1}{4} [111]$ relative to the unit
This two-element basis then allows for related structures to be formed by the placement of two distinct particles at opposing sites on the basis. This structure is referred to as the ZnS or zincblende structure, after the most common naturally occurring crystal with this structure. It is geometrically identical to the DC, with alternating sites occupied by the opposite substance so that each particle’s four nearest neighbors are particles of the complementary material. \[20\]

This structure also has several important applications. On a molecular level, these structures are very important in semiconductor manufacture. Both Si and Ge in this form are used industrially as semiconductors. On a nanoscale, colloidal materials arranged in a DC lattice are predicted to have unique optical properties. Of particular note is the photonic band gap expected to exist in such nanomaterials. \[28, 29\]

1.3 Creating a DNA-NP Diamond Cubic

The creation of cubic lattices through uniformly functionalized NPs does not take full advantage of DNA self-assembly. While NP size and lattice parameters are easy to control with these methods, the isotropic nature of the interactions limits the control that can be exerted over the assembled geometry. While the introduction of free-floating ssDNA linkers asserts some regulation over these interactions, the linear shape of these strands still limits their ability to effect any new structure. A better route to controlling the structure is to introduce a linking particle that encodes the desired geometry.

Recent work from Brookhaven National Lab by Dr. Oleg Gang (yet to be published) has demonstrated one way of creating such linkers. To enforce the tetrahedral bonding of a diamond lattice, he introduces tetrahedrons made purely from DNA. These structures are created by using DNA scaffolding to arrange four lengths of ssDNA so that each strand wraps around one face of a tetrahedron. This results in six hybridizations, one for each edge. By adding additional length to each strand so that it extends from one of the vertices, one can then functionalize each vertex. This whole process creates
a tetrathedrally-functionalized linking particle. These linkers can then be used to enforce a diamond geometry on a lattice of NP.

While these particles on their own might be enough to generate the desired structure, a lattice consisting entirely of these linkers would be difficult to work with experimentally. In particular, because these linkers are hollow tetrahedrons consisting of organic molecules it is difficult to detect them using crystallographic techniques. Analyzing the structure of a system consisting entirely of these linkers would be difficult, due to the ineffectiveness of standard techniques. Moreover, it is desirable create diamond organizations of NP due to the previously mentioned applications for such an arrangement. Thus, a system consisting of a combination of these tetrahedral linkers along with isotropically functionalized gold NPs is ideal. Some success has been had with such a mixture, combining linkers with gold NP in a 1:1 ratio. We utilize this experimental set-up as the focus of our modeling and analysis.

1.3.1 Interpenetrating Systems

Previous computational work has shown that systems containing DNA tetramers, such as the linking particles described above, have the potential for novel phase transitions. Because such particles can have relatively long bonding lengths relative to particle size they hold the potential to form interpenetrating states, where multiple independent networks are intertwined within each other. Such a system has demonstrated multiple liquid phases of increasing density and interpenetration, with multiple liquid-liquid critical points separating these phases. [30]

Although our interests in studying systems with DNA tetramers is more focused on ordered states, interpenetrating systems are also viable in these regimes. For instance, solid H$_2$O can form multiple crystal structures with similar interpenetration. Each of the ice forms VI, VII, and VIII contain some level of interpenetration. [27] Similar interpenetrating structures are certainly worth considering and analyzing for the NP-tetrahedron system.
1.4 Topics of This Thesis

This thesis then seeks to understand the fundamental physics associated with these tetrahedrally coordinated linkers and the ordered structures associated with them. While experimental work is fundamental to understanding the realities of such systems and developing applications, it is also limited in scope by the inability to directly access the nanoscopic structures involved. Instead, we focus on the application of computational methods in order to probe the behavior of these systems on the smallest scale. Although the models involved sacrifice some of the physical detail, these simulations allow us direct retrieval of information that would otherwise be obscured. In simulation we are able to directly access velocities, positions and energies in order to elucidate the exact properties of this system.

In our simulations we focus specifically on the stability and favorability of crystal states created by these tetrahedrally coordinated particles. We first use a coarse-grained model of DNA along with molecular dynamics (MD) methods to consider the stability of crystals formed by the DNA tetrahedrons and functionalized NPs. Next, we examine two crystal states created by this system, and demonstrate the favorability of the experimentally created system in our model. We then consider how the presence of Mg$^{2+}$ in solution, known to be important experimentally, can create an electrostatic attraction between the sugar-phosphate backbone of DNA. This attraction would then serve as an isotropic attraction between the NP that can help increase the theoretical favorability of the experimentally generated structure.

To further examine the effects of this isotropic interaction we switch to a more simplistic model where the free energy of various phases can be more precisely evaluated via Monte-Carlo (MC) simulations. This model considers only one type of particle with a single, tetrahedrally-coordinated attraction. Although this model sacrifices much of the detail of the coarse-grained model, it allows us to directly and efficiently probe the effects of the introduction of an isotropic interaction into a system of tetrahedrally attractive particles. By tuning this attractive isotropic potential to the appropriate
length we can heavily favor one crystal state over another. Using this methodology we demonstrate the elimination of a crystal phase for positive pressure via the introduction of an isotropic potential that is only $1/50^{th}$ the strength of the tetrahedral attraction. This demonstrates the great importance of considering the effects of such interactions on any tetrahedrally attractive particles, including the electrostatic attraction in created by Mg$^{2+}$ in the tetrahedron-NP system.
Chapter 2

Coarse-Grained Model for DNA

2.1 Model for DNA Strands

A wide variety of models for DNA exist in the literature with varying degrees of detail. At one extreme there are the fully atomistic models, which contain all the details of the molecules and solvents. \cite{31, 33} Although these simulations retain the most information about the molecules involved, they are also the most computationally expensive. This means that simulations of this nature are limited to a small number of strands over short time scales. Any behavior that is exhibited in bulk or over longer time scales will be completely unobservable in such a simulation. On the complete opposite end of the spectrum are the bead-string models. These models group each nucleotide into a single spherical bead. These models are useful for studying the dynamic properties, such as diffusion and relaxation, of fixed strands of DNA. \cite{34} These bead-spring models are unsuited for our purposes as they completely ignore strand hybridization. In between these two extremes, there exist models of varying complexity that are all capable of simulating double-strand formulation. \cite{35, 37}

This work is primarily interested on the assembly, stability, and dis-assembly of DNA based superlattices. To facilitate such a study we requires a model that is both simplistic enough to simulate DNA on the scale of such a lattice, while still being detailed enough
CHAPTER 2. COARSE-GRAINED MODEL FOR DNA

to capture the formation of dsDNA. Toward this end we use a model that has been previously developed to suit exactly these needs, a simple coarse-grained model capable of capturing strand hybridization. [38, 39]

This model simplifies the sugar-phosphate backbone of DNA to a string of monomers. The Watson-Crick base-pair bonding is then captured by an additional “sticky site” that is attached to the monomer. This site is of type A, C, G or T and can only bond with the appropriate partner sticky site (A with T, C with G) to fully capture the specificity. The small size of the sticky site relative to the monomers also ensures that each site can only bond to a single base to preserve the one to one nature of base pair bonding. While this model does not include all chemical details, such as electrostatic interactions, it has minimal computational cost and allows for study of suitably large systems to study DNA superlattices.

The most common interaction in this model is the shifted-force Lennard-Jones (LJ) potential $U_{sf}(r)$:

$$U_{sf}(r) = \begin{cases} U_{LJ}(r) - U_{LJ}(r_c) - (r - r_c) \frac{dU_{LJ}(r)}{dr} \bigg|_{r=r_c} & \text{if } r \leq r_c \\ 0 & \text{if } r \geq r_c \end{cases}$$  \hspace{1cm} (2.1)

Here, $r_c$ is a cutoff distance, above which the potential is a constant zero that allows contributions to the force and energy at long range to be ignored and greatly simplifying computation. Note also that the potential is defined so that both force and energy go continuously to zero at the cutoff distance, which prevents problematic behavior. We further define the LJ potential $U_{LJ}(r)$ in equation 2.1 between particles $a$ and $b$ as:

$$U_{LJ} = 4\epsilon \left[ \left( \frac{\sigma_{ab}}{r} \right)^{12} - \left( \frac{\sigma_{ab}}{r} \right)^6 \right] \hspace{1cm} (2.2)$$

In the above equation $\epsilon$ is the minimum value of the potential well and $\sigma_{ab}$ is an interaction length associated with the radius of particles $a$ and $b$. We then define a unit of length, $\sigma = \sigma_{mm}$, the length for the interaction between two monomers. The smaller radius sticky site interactions, both between each other and with monomers, are given
an interaction length $\sigma_{ss} = \sigma_{sm} = 0.35\sigma$. For all interactions, other than those between complementary sticky sites, the force needs to always be repulsive. In order to ensure this we set $r_c = 2^{1/6}\sigma$, the minimum of the potential well for these values. For the attractive base pairs we set $r_c = 2.5\sigma$, significantly larger than the minimum value, to allow the particles to attract each other. While a completely chemically accurate model would have C to G interactions that are stronger than the A to T interactions, such details are not important for our purposes.

To ensure connectivity between the monomers, we combine the repulsive LJ potential with a finitely-extensible, nonlinear elastic (FENE) spring potential:

$$U_{\text{FENE}} = -\frac{kR_0^2}{2} \ln \left[ 1 - \left( \frac{r}{R_0} \right)^2 \right]$$

In the small $r$ limit this potential approaches a harmonic spring potential, while still preventing the bond length from ever exceeding $R_0$. These properties make it a useful potential for studying tightly bound particles. This potential, in combination with the truncated LJ potential, is a common choice for modeling coarse-grained polymers. As in similar models for polymers, we set $k = 30\epsilon/\sigma^2$ as the bond strength and $R_0 = 1.5\sigma$ as the maximum length of extension. [40] [41] These choices of parameters create an average separation of $r_{avg} \approx 0.96\sigma$, the value that minimizes the potential $U(r) = U_{ss}(r) + U_{\text{FENE}}(r)$.

In order to ensure rigidity of the DNA strands we also introduce a three-body angular potential:

$$U_{\text{lin}}(\theta) = k_{\text{lin}}(1 + \cos \theta)$$

where $\theta$ is the angle created between three consecutive monomers. The minimum of this potential is at $\theta = \pi$, encouraging straight configurations of monomers. For our simulations we set $k_{\text{lin}} = 0.7$, giving an experimentally accurate persistence length $l_p \approx 15$ nm. [42] Torsional terms that would enforce helical geometry in the strands are also neglected for simplicity.
Figure 2.1: A schematic of the coarse-grained model for DNA. (a) The atomic structure of DNA. The sugar-phosphate backbones are shown in blue, while the bases are shown in green. The red lines represent possible hydrogen bonds between complementary base pairs. (b) A representation of how our model grains the different parts of DNA into two force sites, blue for the backbone and a green “sticky site” for the base. (c) An image taken directly from simulation of two strands “zipped” together at low T to form a strand of dsDNA.

The sticky sites are also attached to the monomer with the same $R_0$ and $k$ values. Because $\sigma_{sm} = 0.35\sigma$ this results in an average separation between bonded sticky sites and monomers of $r = 0.38\sigma$. The sticky sites are thus almost completely contained within the repulsive shell of the monomer, excluding more than one sticky site from connecting to the same partner. The sticky sites are also kept at a right angle with the backbone monomers with a modified three-body angular potential:

$$U_{\text{angular}}(\theta) = k_{\text{angular}}(1 - \sin \theta)$$

Where $\theta$ is the angle created between the vectors from the center of each monomer to the sticky site and to its neighbors. Note that this potential thus exists twice for each sticky site, once for each neighbor. We set $k_{\text{angular}} = 30\epsilon$, making this potential very rigid and strictly enforcing that each particle stay at a right angle to the monomer backbone.

Overall, this model is well suited for simulations of DNA-functionalized NP. Because
each nucleotide is represented by two force sites, the model keeps computational costs at a minimum while still capturing the behavior of reversible hybridization. It also does so with only three types of potentials, counting eqn. 2.5 as eqn. 2.4 with a phase shift. This is in contrast to models which rely on artificial selection rules or explicitly defined base pair bonds, which would be both more complicated to implement and more computationally expensive.

Assigning all force sites a mass \(m\) then fully defines a set of units with length defined by \(\sigma\), energy defined by \(\epsilon\), and entropy defined by Boltzmann’s constant \(k_B\). Unless otherwise noted, all data based on this model will be presented in terms of these fundamental units. This means time will be in units of \(\sigma\sqrt{m/\epsilon}\) and temperature will be in units \(\epsilon/k_B\).

### 2.2 Functionalized Nanoparticles and Tetrahedral Linking Particles

For the tetrahedral linking particles introduced in section 1.3, we approximate the DNA tetrahedron as a rigid tetrahedron. We create one strand of ssDNA for each vertex of the tetrahedron, four total, each attached to a core monomer. Each of these monomers is then attached to its neighbors through an extended FENE bond (eqn. 2.3) and repulsive LJ potential (eqn. 2.2), except with \(r\) replaced by a shifted separation \(r - r_0\). For the bonds between the vertices of the tetrahedron, we set \(r_0 = 17.94\ \sigma\), meaning the average bond length is \(18.9\ \sigma\). With the approximation \(\sigma \approx 0.65\ \text{nm}\), the average separation between two base pairs of ssDNA, this gives an edge length of \(12.3\ \text{nm}\), the same as the experimental value.

A similar approximation is used for the gold NPs. While in an experiment these particles can be created with hundreds of strands of DNA attached to each particle, we approximate them as 20 strands that are uniformly spread across the surface of the NP. In order to create this structure we again use a rigid polyhedral approximation, except
Figure 2.2: A simple schematic of the experimental makeup of the tetrahedral linker and AuNP. (a) The Au NP are uniformly coated in ssDNA. The DNA strands are 20 bases long with 10-15 of the bases forming the active sequence that connects to the tetrahedral DNA. Manufactured NP have a diameter of ranging from 7-17 nm. Best assembly was observed experimentally with a NP diameter of 7 nm and a recognition site of 10 bases. (b) The tetrahedral linkers are created from four strands of ssDNA that wrap around each face and hybridize to form the 6 edges of the structure. The length of the hybridization along the edges is 37 base pairs long, resulting in a tetrahedral edge length of 12.3 nm. The ssDNA extending from each vertex can be made with a non-active connecting region of 1-10 bases and an active hybridizing region of 8-15 bases. Best assembly was observed with a linking length of 2 bases and a hybridizing length of 8 bases. Figure courtesy of Dr. Oleg Gang this time we use a dodecahedral shape in order to allow for the necessary 20 vertices. In the bond between two adjacent vertices we fix \( r_0 = 3.84 \sigma \) to create a radial distance of \( 5.36 \sigma \approx 3.5 \) nm, mimicking the experimental NP radius.

Finally, we introduce an additional repulsive force from a force site at the center of both particles. This repulsion prevents the unphysical situation of a NP or linker moving through the essentially empty space at the center of a tetrahedral linker in simulation. While to truly accurately represent the shape of these particles would require occupying space in a line between the vertices, this would require the introduction of
Figure 2.3: A snapshot from simulation of a gold NP (the gold sphere) tethered via hybridized DNA to a tetrahedral linker. Bonds are represented by blue cylinders, the backbone monomers are represented by red spheres, and the sticky sites are represented by the small gray spheres. The volume that would be occupied by the NP is filled in with the gold color for illustrative purposes.

a large number of particles and additional force calculations. By instead introducing a central force site and adding a repulsive force we exclude the unphysical situations with much less computational expense. This repulsion is implemented by creating an extended LJ repulsion from linker to linker and from linker to NP, eqn. 2.1 with $r$ shifted appropriately for the radius. The repulsion is set to exclude the volume based on the insphere of the tetrahedron, with a repulsive radius $r \approx 3.8\sigma$.

All of the numerical values above are based on the experimental values that gave the best assembly results, described in 2.2. The base pair sequences attached to each particle are similarly chosen. For the tetrahedral linkers we attach ssDNA with 2 non-linking base pairs and then an 8 base pair chain with the sequence A-A-G-C-A-G-G-G to form the active connecting region. We then assign the complementary 8 base pair sequence C-C-C-T-G-C-T-T to the strands on the NP, along with a 10 inactive monomers that link this active region to the NP.
2.3 Simulation Methods

Numerical calculations are performed in the isothermal-isobaric ensemble (fixed $N$, $P$, and $T$). $N$ is easily fixed by keeping the force sites contained in the system fixed. $T$ and $P$ are then held constant through a Nosé-Hoover integration scheme in order to maintain the determinacy allowed for by our use of molecular dynamics. [43] Time integration is performed by a three-cycle velocity Verlet version of the rRESPA integration scheme. [44] This integration method separates the forces that have high variation for small changes in position, such as the FENE and angular potentials, from those that vary more gradually, such as the LJ potential. The more quickly varying forces are updated more frequently than the more slowly varying forces, with time steps ranging from 0.001 to 0.006 in LJ units.

For all of the molecular dynamics simulations we fix $P = 0$. While a more chemically accurate model would include solvent effects and be able to relate these to an experimental pressure, we neglect such details to reduce computational expense. Instead, we treat the system as “free-floating” particles in a vacuum. This representation is similar to the experimental case where units float in water with little to no external pressure. The assignment of $P = 0$ is also convenient as it greatly simplifies several calculations by eliminating the $PV$ term.

Simulations are performed with periodic boundary conditions in order to allow for macroscopically periodic structures such as lattices as well as to minimize the impact of finite size effects.
Chapter 3

Stability of DNA-linked Lattices

3.1 Possible Ordered Structures

We analyze two possible ordered structures that can be formed by the linker-NP system. While in theory many more structures are possible, the two we consider are the most simple that preserve both the tetrahedral shape of the bonding as well as the 1:1 ratio of linker to NP.

The most simple and obvious of these structures is the regular NP-linker DC structure. This is identical to the zincblende structure discussed in section 1.2 with the tetrahedrons and NP making up the two complementary particle types. These two particles then serve as a basis on the FCC Bravais lattice, with each particle type forms an FCC when considered individually. Unfortunately, this means that the NPs do not form a DC in this structure.

Since the most basic ordering does not result in a DC structure for the NP, we also consider a slightly more complex ordering. Because of the potential for DNA tetramers to form interpenetrating structures, discussed in 1.3.1, it makes sense to choose as our second structure the lattice consisting of two unconnected, interpenetrating DC structures. This structure is the same as two of the structures described in the preceding paragraph, except each is offset and rotated so that each network occupies the gaps in
Figure 3.1: An idealized visualization of the relationship between the orderings considered. From top left, clockwise: (a) The locations of the Au NP, represented by the gold spheres, in the single connected network. The positions are identical to the unit cube of the FCC. (b) The same structure as a, but with the positions of the tetrahedral linkers (purple) added in and the connections shown by the blue lines. The tetrahedral bonding results in a DC structure for both sites combined. (c) The full structure formed by two independent and interpenetrating versions of the structure described in (b). The more lightly colored spheres and connections represent the second network added to the diagram. Two unit cubes of the overall BCC structure are also observable here, with either set of purple spheres making up four corners of one of these cubes. (d) The same diagram shown in (c) with the tetrahedrons and connections removed. This shows the DC structure of the Au NP in the interpenetrating system, created by the two offset FCC lattices made by the darker and more pale particles respectively. The DC structure of the NP is most easily observed by considering the oppositely shaded nearest neighbors of any particle in this system, each set of which forms a tetrahedron.
the other network. This means that each particle has four nearest neighbors on its own network as well as four nearest neighbors on the opposite network, positioned in a cube around each particle. In this way the linkers and NPs of the interpenetrating structures, when considered together, form a BCC lattice.

In addition, if we consider only the NP or only the tetrahedrons in the interpenetrating structure, we are left with two FCC lattices displaced by \( \frac{1}{4} \frac{1}{4} \). This displacement functions exactly as the \( \frac{1}{4} \frac{1}{4} \) displacement and results in the linkers and NP each forming a DC structure.

For the sake of simplicity we will refer to both of these orderings by the shape that the NPs alone form within the structure. This nomenclature lines up nicely with the structures that will show in experimental scattering results, since the NP are the only particles that will be detected by these techniques. In this chapter, the FCC lattice will refer to the ordering where the NP and tetrahedrons each form an FCC lattice while both considered together form a DC. Similarly, we now use DC to refer to the ordering that forms two interpenetrating DC structures overall.

Since these structures are constructed in experiment through self-assembly, these same orderings should be reproducible in simulation through the same processes. This would then allow us to easily determine the structure that should be formed experimentally. Unfortunately, the time scales of self-assembly are significantly longer than the time scales we are able to access in simulation. Instead, we artificially construct the orderings directly then analyze their characteristics. In this way, we determine which tetrahedral orderings fits with experimental data and explain through thermodynamics why this ordering is favored.

### 3.2 Melting Temperature

After identifying the most likely structures to be formed by the linker-NP mixture, the first step in analyzing the structures is identifying their melting temperature of the crystal state, \( T_M \). We do this by heating the system from a fully bonded crystal state
Figure 3.2: The average potential energy between base pairs per force site, $U$ in units of $\epsilon$, as a function of temperature, $T$ in units of $\epsilon/k_B$, as well as the derivative of this function. The value of $U$ rises slowly from a minimum of $\approx 0.038 \epsilon$ until it gets close to the melting temperature, $T_M$, where the DNA hybridization begins to break and energy sharply increases. This results in the sharp peak in $\frac{dU}{dT}$ that is maximized at $T_M$, giving values of $T_M = 0.126$ for the FCC and $T_M = 0.128$ for the DC.

and measuring the temperature at which the bonds between the linkers and NP break. While in theory this same value could also be calculated by starting from an amorphous state and cooling it into the crystal structure, the crystallization process is substantially longer than melting process and it is far more practical to heat the system than cool it.

We quantify the amount of links that are present in the system by measuring the attractive energy between the base pairs in the system. For a 1:1 mixture of linkers to tetrahedrons in which all of the tetrahedron’s arms are fully connected to a complementary strand of DNA, this attractive energy should total to an average of $U \approx 0.038 \epsilon$ per force site. This $U$ increases slowly as $T$ increases, up until $T_M$ is approached and $U$ rapidly jumps to 0 as all of the bonds are broken. $T_M$ is thus best observed by noting the point at which $U$ increases rapidly toward 0 and $\frac{dU}{dT}$ is sharply peaked, i.e. the value for $T$ where $\frac{dU}{dT}(T)$ is maximized. Under the definition the we calculate the values $T_M = 0.126 \epsilon/k_B$ for the FCC structure and $T_M = 0.128 \epsilon/k_B$ for the DC.

The melting temperature provides two useful pieces of information about these two
organizations of NP. For one, it provides a hint about the relative stability of these two structures. While a higher $T_M$ does not guarantee favorability for all temperatures, it does provide one regime where we know the DC to be more stable than the FCC: $0.126 \epsilon/k_B < T < 0.128 \epsilon/k_B$. In addition, the fact that the DC is more resistant to heating than the FCC means that the DC is more stable to kinetic disturbances than the FCC. These two factors both provide some qualitative evidence that the DC is a generally more stable configuration, but the small difference in $T_M$ and the inconclusiveness of this methodology make this argument very weak.

$T_M$ also provides a useful guideline for the ideal $T$ to run simulations at. Because all of the connections between DNA break at $T_M$, simulations above this temperature will fail to hybridize and we are left with a bunch of free-floating NP and linkers. In simulations significantly below $T_M$ any base pairs that bond will be energetically trapped and the system will remain locked into the first bonds that it forms. Thus in order to effectively study the properties and dynamics of the system we operate at a $T = 0.115 \epsilon/k_B$, slightly below $T_M$.

This difference in thermal stability is best explained by the differing densities of the two structures. Ideally, the DC structure should have twice the density of the FCC. In simulations, the DC is only around 20% more dense than the FCC. This large discrepancy can be explained by the highly flexible nature of the DNA bonding. This flexibility allows the systems to bend and vibrate easily. Because of the high density from the two interpenetrating systems in the DC case, this vibrational motion and deviation from ideal lattice spacing is restricted by steric interactions. In the FCC lattice there is no such restrictions. This means that the FCC lattice is much more free to bend in on itself, creating a large deviation from the idealized density. This also explains the lower $T_M$ of the FCC lattice. Because of the increased tendency to bend and greater freedom to do so, the vibrational energy of the FCC will be higher than that of the DC. This increased vibrational energy then explains the proclivity of the system to dehybridize at lower $T$. 
3.3 Structure Factor

After determining an appropriate $T$ to run these simulations at, we then have sufficient information to compare the structures in simulation with those created experimentally. Experimentally, the structure of these systems is most easily determined through the use of crystallographic methods to compute the structure factor $S(q)$. The same function can also be determined for our computational systems from positions of particles in simulation. The periodic boundary conditions of the simulation do limit the maximum $q$ for which we calculate $S(q)$, since for $q$ greater than the simulation box size the periodic boundary conditions will dominate.

Since experiments are only able to calculate the $S(q)$ of the NP cores, we focus on this data from simulation as well. This data is presented in fig. 3.3. Normalizing $q$ by the first peak location, $q_0$, and comparing to experimental data shows a fit for the peak locations in the simulated DC lattice. The peaks in experiment and simulation line up closely and are located close to the peaks of $S(q)$ for an idealized DC structure.

The FCC lattice presents a much poorer fit for experimental data. The ideal peaks of the FCC lattice contain all of the peaks of the DC lattice. But the two peaks that should be present in an FCC but not DC lattice are missing entirely from the experimental data. The second peak of the ideal FCC lattice in particular is problematic, as it is placed at a point that is essentially a minimum in the experimental data while for the simulated FCC lattice this peak is visible as a noticeable broadening of the first peak location.

The broad peaks in $S(q)$ also help demonstrate the flexible nature of these crystals. Because DNA connections are much looser than conventional bonds, the connections in these systems are much more flexible and the particles are more free to deviate from their ideal positions. This phenomenon presents itself as a broadening of the peaks in $S(q)$ as these deviations cause the periodicity of the system to be less exact. The exceptionally broad peaks of the FCC lattice show this behavior very clearly. Although the bonding of the system is completely ordered, the first two peaks are nearly indistinguishable,
Figure 3.3: The structure factor, $S(q)$ for both organizations in computation as well as experimental results. The data is horizontally scaled by the first peak location, $q_0$, and vertically shifted to distinguish the three data sets. The vertical lines are used to show the peak locations for the ideal lattice, with the peak locations that are shared by both lattices in turquoise. Note that the first peak location that is unique to the ideal FCC lattice matches up poorly with the experimental results, while three peaks of the DC lattice line up with experiment. This data also shows that the lower density FCC state structure is much more flexible, as demonstrated by the broad peaks that meld together.

combining to a single broad peak. Beyond that, the system looks essentially amorphous. This reflects the large amount of empty space in this ordering. In comparison, the DC structure remains relatively stable due to the fact that the two interpenetrating structures are able to help hold each other in position.

3.4 Free Energy

While $T_M$ provides some information about the stability of these structures, we are interested in a better way to quantify the favorability of these organizations relative to
each other. To do this we take advantage of the fact that, because we are working in
the isothermal-isobaric ensemble, the system will be thermodynamically stable where
the Gibbs free energy, $G$, is minimized. Since absolute free energy calculations can be
computationally demanding, we instead calculate the difference in $G$ between the FCC
and DC organizations. This provides sufficient information to determine which of these
crystal states has a lower free energy and is thus more thermodynamically stable.

\[
G = E + PV - TS
\]  

The internal energy, $E$, and volume, $V$, are easily calculated from simulation. Pressure,
$P$, and temperature, $T$, are fixed by the Nosé-Hoover algorithm as described in
section 2.3. This just leaves the entropy, $S$, as the only piece of information necessary
to calculate $G$ from eqn. 3.1. While there is no easy way to calculate the total $S$ for a
given system, we can easily calculate the entropy difference from a given reference state
by taking advantage of the fact that $P = 0$ for the following derivation:

\[
\left(\frac{\partial S}{\partial E}\right)_N = \left(\frac{\partial S}{\partial E}\right)_{N,V} + \left(\frac{\partial S}{\partial V}\right)_N \left(\frac{\partial V}{\partial E}\right)_N
\]
\[
= \frac{1}{T} + \frac{P}{T} \left(\frac{\partial V}{\partial E}\right)_N
\]
\[
= \frac{1}{T}
\]

The above relation then lets you calculate $\Delta S$ from internal energy function $U(T)$
connecting any two states with eqn. 3.2

\[
\Delta S = \int_{T_0}^{T_f} \frac{1}{T} \frac{\partial E}{\partial T} dT
\]  

We then take advantage of the energy functions created in the melting process. Upon
heating to $T$ significantly greater than $T_M$, all of these systems expand to an incredibly
low density gas that we treat as a reference state. Eqn. 3.2 can then be used to calculate
Figure 3.4: $\Delta G$ per NP, in units of $\epsilon$ for the FCC and DC structures relative to the low density state at $T = 0.135 \epsilon/k_B$. Free energy then increases as we lower temperature up to the values at $T = 0.115 \epsilon/k_B$, the temperature at which we fix the crystal states in simulation. While $G$ increases for both orderings, it increases more for the FCC state. This results in the DC state having a lower free energy by $G_{FCC} - G_{DC} = 0.25 \epsilon$ per NP.

the $\Delta S$ for each configuration relative to the high $T$ state, and thus $\Delta S$ between the orderings.

Using this method we then calculate $\Delta G$ for both states relative to the high $T$ state. This computation, shown in figure 3.4 reveals that the DC state has a lower free energy by 0.25 $\epsilon$ per NP. This translates into the ratio $G/k_B = 2.17$, meaning that the free energy of the DC state is lower than that of the FCC by multiple times the kinetic energy of the particles involved. Thus the DC is significantly more thermodynamically stable than the FCC and is the most likely tetrahedral organization at this temperature.

3.5 Effects of Mg$^{2+}$ in Solution

While this model captures the basic features of DNA-based self-assembly, there is an important feature from experiments that is missing. The NP-tetrahedron mixture actually fails to organize in experiment without the presence of Mg$^{2+}$ in solution. Without
these ions, the NP tetrahedron mixture instead stays in an amorphous, fluid-like state. It is well known that the presence of cations in solution, such as Mg$^{2+}$, is capable of inducing screened electrostatic attractions between DNA backbones in solution.\cite{45-47}

It is likely this effect that provides a key attraction to stabilize the FCC structure in experiment. This fact is further evidenced by the fact that at sufficiently high concentrations of Mg$^{2+}$ the NP precipitate from solution although at higher density than for the lower concentration, signaling that the attraction induced by these ions is overwhelming the interaction due to DNA hybridization.

Since our coarse-grained model completely neglects solvent effects, these screened electrostatic interactions are obviously not present in the data from the simulations that has been presented so far. However, we can still make use of our simulations to try and understand how the Mg$^{2+}$ stabilizes the FCC lattice.

First we consider where in the NP-tetrahedron system these DNA-DNA backbone attractions would occur. Because the four ssDNA attached to each tetrahedron are complementary with all of the ssDNA that are coating the entire surface of the NP, the strands attached to the tetrahedrons are all fully hybridized in the connected system. The ssDNA on the NP are in the exact opposite case. Because the concentration of these strands is much higher than that of the complementary strand, there is a large number of these strands that remain unconnected in solution. So we focus on the large number of these un-complimentary, un-hybridized ssDNA that are connected to the NP when considering the effects of the Mg$^{2+}$ concentration.

If it is truly the backbones of the ssDNA attached to the NP that are creating an attraction through this mechanism, then we should be able to observe a noticeable overlap in the locations occupied by the backbone monomers in our simulation. To confirm this, we calculate the average density of DNA backbone sites ($\rho$) attached to a given NP as a function of separation from that particle ($r$). We then consider the overlap of the functions $\rho(r)$ and $\rho(r_0-r)$ where $r_0$ is the average separation between NP. This overlapping area then corresponds to the amount of monomers that will interact...
Figure 3.5: Graphs of the monomer density function around each NP, $\rho$, as a function of distance from the NP, $r$. These are then compared with $\rho(r_0 - r)$ to determine the extent which monomers from NP separated by a distance $r_0$ will interact with each other. The above graphs are shown with $r_0$ equal to the average separation corresponding to that of the first neighbor for the NP in the DC (left) and FCC (right) structures, while the shaded gold region corresponds to the excluded volume from the NP. The higher density of the dc structure results in a much smaller separation, greater overlap of these functions, and increased monomer-monomer interaction between NP.

This analysis reveals that an attractive force between the backbones, such as that created by the Mg$^{2+}$, should result in an isotropic attraction between NP at the first neighbor distance of the DC structure. At the same time, this attraction should drop off to negligible values at ranges equal to the first neighbor distance of the FCC lattice. This effective force could prove to be a key factor for the stability of the DC structure.
CHAPTER 3. STABILITY OF DNA-LINKED LATTICES

3.6 Approximating the Effective Attraction

To actually understand the effects of this screened electrostatic interaction on the crystal structures, we need to introduce a potential to our model that replicates these solvent interactions that are missing from our model.

One approach to recreating this interaction would be to directly add an attractive pair potential between the backbone force sites. This would most directly simulate the attraction between DNA backbones that is induced by the Mg$^{2+}$. The problem with this approach is that our model has no way of excluding this interaction in the case where the monomers have already been hybridized together through base-pair bonding. This means that any such potential would also increase the attractive strength of hybridization. This is completely in contrast to the real physical behavior of these ions, which does not affect the attraction between hybridized strands. Moreover, including such a potential for each backbone site substantially increases computation time, since there are many such sites and the electrostatic interaction (even screened) is relatively long-ranged.

While this problem could be solved by excluding monomers that have been hybridized from this pair potential, this solution would involve a great deal of additional computation in order to introduce a method of keeping track of these bonds. To simultaneously solve both problems, we introduce a force between the NP cores that has the long range behavior we expect to be created by the electrostatic attraction. This can be taken as a reasonable substitute to including interactions at each base, since the NP are nearly uniformly coated by ssDNA. Specifically, we want to introduce an attractive potential that strictly decreases in strength as $r$ increases, eventually becoming negligible. This reflects the fact that the density of monomers decreases as distance from the NP increases and is nonexistent past the ends of all of the ssDNA.

We choose a Yukawa potential, given in eqn. 3.3.

$$U_{\text{Yukawa}}(r) = A \frac{e^{-\kappa r}}{r}$$

(3.3)
to model this behavior. This potential not only has the traits that we require to model
the NP-NP interaction, but also is the potential that we would expect from the screened
electrostatic interaction induced by the Mg$^{2+}$. We set the inverse interaction range
$\kappa = 0.1 \sigma^{-1}$ to match the expected range at which the ssDNA on different NP should
interact. A cutoff distance, $r_c$, is also introduced as in equation 2.1 so that the potential
and force smoothly decay to 0 at $r_c$. We set $r_c = 40 \sigma$, approximately the length at
which $\rho(r)$ goes to 0. The strength of the screened interaction, $A$, increases as the
concentration of Mg$^{2+}$ increases. We then treat $A$ as a free parameter whose effects on
the system we explore.

By examining how the behavior of the structure factor changes as $A$ is adjusted,
we determine that for values of $A > 35 \epsilon \sigma$ the structure of the FCC breaks down
into an amorphous state. The DC behaves similarly, except that its organization holds
until $A > 50 \epsilon \sigma$. Similarly to the experiment, the crystalline orderings only hold for
concentrations of Mg$^{2+}$ below a critical value at which this interaction dominates and
forces the NP into a disordered state. The fact that this critical $A$ value is higher for the
DC ordering also provides evidence that this potential is increasing the thermodynamic
stability of the DC relative to other states.

To fully understand the affect of $U_{\text{Yukawa}}$, we calculate the the response of the Gibbs
free energy as a function of potential strength for both states, $\Delta G(A)$. To do this we
take advantage of eqn. 3.4:

$$\left( \frac{\partial G(\lambda)}{\partial \lambda} \right)_{N,P,T} = e^{-\beta PV} \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{\lambda}$$  \hspace{1cm} (3.4)$$

the thermodynamic identity for the derivative of the free energy, $G$, with respect to
$\lambda$, some parameter of the potential energy function. An analogous identity for the
canonical ensemble is discussed in ref. [43]. For the specific case of our simulation we
set $U = U_{\text{Yukawa}}$, $\lambda = A$, and $P = 0$ and this equation simplifies to:

$$\left( \frac{\partial G(A)}{\partial A} \right)_{N,P,T} = \frac{1}{A} \left\langle U_{\text{Yukawa}}(A) \right\rangle_A$$  \hspace{1cm} (3.5)$$
Figure 3.6: Change in Gibbs free energy, $\Delta G$ in units of $k_B T$ as a function of NP-NP interaction strength $A$. Although the free energy of both structures decreases as we increase $A$, the free energy of the DC structure drops more steeply. This corresponds to an increased stability of the DC structure relative to the FCC through the strengthening of this interaction. Both graphs terminate at the value of $A$ for which the structure breaks down into an amorphous state.

Since $\langle U_{\text{Yukawa}}(A) \rangle_A$ is the average energy contribution of the Yukawa potential for some fixed $A$, we can use eqn. 3.5 to easily compute the value of $\frac{\partial G(A)}{\partial A}$ for various $A$. This derivative can then be integrated numerically to determine the value of $\Delta G(A)$.

The results of this computation are shown in figure 3.6. While the free energy of both structures decreases with increasing $A$, it decreases more quickly for the DC structure. This means that the free energy gap between the DC and FCC state increases with the introduction of this potential, further increasing the thermodynamic stability of the DC state with $G_{\text{FCC}} - G_{\text{DC}}$ increasing from about 2 times $k_B T$ to 3 times $k_B T$.

The eventual breakdown into a disordered state then corresponds to a $G$ that increases even more quickly than that of either of the ordered states. This also explains
the fact that the FCC devolves into this state more quickly; it has a higher $G$ and is thus more quickly overtaken by this rapidly decreasing $G(A)$. 

### 3.7 Summary of Results from Molecular Dynamics Simulations

Using these methods we have demonstrated that the proposed DC structure is thermally more stable than the more simple FCC structure due to it’s higher $T_M$ as well as thermodynamically favorable due to its lower $G$. These factors help explain why it is the more structurally complex DC organization that appears in experiment, rather than the simpler FCC.

We also consider the effects of Mg$^{2+}$ in solution, a factor that is known to be necessary in experiment. By creating a screened electrostatic interaction between the backbones of DNA, these ions produce an isotropic attraction between NP. Such an attraction further favors the dc over the FCC lattice by increasing the free energy difference between the two states.

Although we are able to recreate the breakdown of the crystalline ordering at high concentrations of Mg$^{2+}$, these methods still fail to explain the experimental necessity of the ions to produce any ordering whatsoever. To fully examine the effect of these ions, we require a better understanding of the phase diagram for these materials.
Chapter 4

Monte-Carlo Simulations of the Tetrahedral Kern-Frenkel Model

The aim of this chapter is to examine in a precise way how changes to the isotropic potential affect the relative stability crystal states of tetrahedrally coordinated “patchy” particles. To this end, we examine a very simple hard sphere model with the addition of a weak isotropic potential and directional patches. Without the isotropic interaction, this is known as the Kern-Frenkel model, and its phase diagram has been carefully studied, making it an ideal system to explore the effects of adding isotropic terms.

4.1 Monte-Carlo Simulations

Since we want to explore the full phase diagram of tetrahedrally coordinated particles, we choose to switch methodology. We no longer use the deterministic integration of molecular dynamics. Instead we use stochastic Monte-Carlo algorithms that are optimized for the purpose of phase coexistence calculations.

The Monte-Carlo methods rely on statistical mechanics to generate probabilistic rules that can be used to govern the arrangement and motion of a set of particles. In particular we focus on the the canonical ($NVT$), isobaric-isothermal ($NPT$), and
grand canonical ($\mu VT$) ensembles to generate appropriate statistical laws. By sampling configurations in a manner consistent with these rules, we can thus sample the behavior of a given model. For more detail on these methods, see ref. [43].

While these methods lose the deterministic behavior of molecular dynamics, they also have several advantages. These algorithms do not require explicit force or velocity evaluations, which frees up a lot of computational power and increases efficiency. The lack of force evaluation also allows for discontinuous approximations of potential energy functions to simplify computation.

Monte-Carlo methods are also particularly well-suited to studies of phase behavior, as sampling techniques can be biased in order to hasten lengthy phase transition processes. The statistical effects of these biasing methods can then be corrected with the use of appropriate calculations.

### 4.2 Kern-Frenkel Model

In order to effectively study the influence of the Mg$^{2+}$ on the phase diagram of the tetrahedron-NP system we require a model with the following properties:

1. Sufficient simplicity to allow for efficient reproduction of phase coexistence.
2. The ability to reproduce the four bonding sites of the DNA tetrahedrons.
3. The ability to reproduce the isotropic attraction between NP created by Mg$^{2+}$.

To fulfill the first two criterion we use the Kern-Frenkel model to reproduce the tetrahedral bonding. [48] This model has been used effectively to study the phase behavior of tetrahedrally attractive particles in the past and is thus well suited to study the behavior of our tetrahedrons. This model also has the advantage of having been used to successfully generate both BCC and DC phases. [49][50] Because this model considers all particles identically instead of distinguishing between NP and tetrahedrons, the BCC state in this model is analogous to the overall structure of the DC described
Figure 4.1: A cartoon of a particle with a tetrahedral Kern-Frenkel potential. The red sphere fills in the excluded volume of a single particle, a sphere of radius $\sigma$. The blue cones show tetrahedrally organized attractive patches. These patches extend a distance $\delta$ from the surface of the sphere and extend up to an angle of $\pm \theta$ from the center of the patch. Image taken from reference [49].

Similarly, the DC state in this model is analogous to the FCC state in the coarse-grained model. For this reason, we examine the BCC and DC phases in this model to compare with our earlier results for the DC and FCC phases respectively.

The Kern-Frenkel potential is given in equation 4.1 for particles $i, j$.

$$U_{kf}(\mathbf{r}_{ij}, \Omega_i, \Omega_j) = U_{sw}(r_{ij})f_\theta(\hat{r}_{ij}, \Omega_i, \Omega_j)$$

This potential is based on the radial square well potential:

$$U_{sw}(r_{ij}) = \begin{cases} 
\infty & \text{if } r_{ij} < \sigma \\
-\epsilon & \text{if } \sigma < r_{ij} < \sigma + \Delta \\
0 & \text{if } \sigma < r_{ij}
\end{cases}$$

This square well defines an attractive energy $\epsilon$ as well as a length of interaction $\delta$. 
This potential is then modulated by an angular function based on the orientation of the two particles involved.

\[
f_\theta(\hat{r}_{ij}, \Omega_i, \Omega_j) = \begin{cases} 
1 & \text{if } \hat{e}_a \cdot \hat{r}_{ij} > \cos \theta \text{ for some patch } a \text{ on particle } i \\
& \text{and} \\
0 & \text{otherwise}
\end{cases}
\]

This function limits the interactions to orientations where \(\hat{r}_{ij}\) points through the surface of both spheres within \(\theta\) of an attractive patch on the particle.

In the above equations the vector \(\mathbf{r}_{ij}\) is used to denote the position of particle \(i\) relative to the position of particle \(j\). We also define the orientation of particle \(i\), \(\Omega_i\). This orientation is defined by the unit vectors, \(\hat{e}_n\), that point from the center of the particle to the location of the attractive patches on the sphere. By affixing four patches at a tetrahedral angle to each particle we can then use this function to create a tetrahedrally attractive potential.

This potential is then easily supplemented by an isotropic square-well potential, equation 4.2 with out any modification, that can be used to study the effects of the Mg\(^{2+}\). This gives a total energy function 4.4 for each pair of particles.

\[
U(\mathbf{r}_{ij}, \Omega_i, \Omega_j) = U_{kf}(\mathbf{r}_{ij}, \Omega_i, \Omega_j) + \alpha U_{sw}(r_{ij})
\]

While this model lacks almost all of the detail of the coarse-grained model, its simplicity allows us to efficiently study the interplay between tetrahedral and isotropic attractions. While the introduction of a second particle type would better reflect the details of the NP-tetrahedron system, the choice of a single species of particle still allows us to understand the behaviors we are interested in. This choice of one type of particle also provides a convenient starting point for our studies, as this system has already been studied in detail without the isotropic attraction. [49] [50]
CHAPTER 4. MONTE-CARLO SIMULATIONS OF THE TETRAHEDRAL KERN-FRENKEL MODEL

Figure 4.2: The $P$-$T$ phase diagram of the tetrahedral Kern-Frenkel model for $\alpha = 0$, $\cos \theta = 0.92$, and various $\delta$. Both $P$ and $T$ are in reduced units. We choose to modify $\alpha$ starting from the parameters in graph (d), $\delta = 0.24$. This gives a large difference in $P$ between the FCC-BCC and BCC-DC coexistence lines, as well as a non-trivial a liquid-gas $T_c$. Graphs from reference [49].

4.3 Choice of Parameters

We fix the square well $\sigma$ and energy $\epsilon$ then define the Kern-Frenkel interaction length $\Delta_{kf}$ and the square well interaction length $\Delta_{sw}$. We then fix our fundamental unit of energy as $\epsilon$ and our fundamental unit of length as $\sigma$. Temperature, $T$, is then measured in units of $\epsilon/k_B$ and pressure, $P$, is given in units of $\epsilon/\sigma^3$. This leaves us with four unitless parameters for study: $\theta$, $\delta = \Delta_{kf}/\sigma$, $d = \Delta_{sw}/\sigma$, and the potential coupling parameter $\alpha$.

If we consider the case where $\alpha = 0$ then we recover the pure tetrahedral Kern-Frenkel potential, whose phase diagram has been studied throughly for various parameters of $\delta$ and $\theta$. [49] [50]. Since our interest lies in the effect that the introduction of the
isotropic potential, i.e. an increase in $\alpha$, has on the phase diagram we choose fixed values of $\delta = 0.24$ and $\cos \theta = 0.92$ from the literature. These choices allow us to examine the effect that $\alpha$ has on the BCC-DC phase coexistence line without having to worry about the FCC phase, which occurs at much higher values of $P$. This combination of values also geometrically excludes the possibility of the same patch attracting multiple particles, reflecting the exclusivity of the DNA system. The assignment of $\delta = 0.24$ also gives a non-trivial liquid-gas $T_c$. \cite{19}

Recalling the tetrahedron-NP system, we were interested in an isotropic potential that stabilized the overall BCC state over the overall DC state for all particles. To this end, we choose a value of $d = 0.3$. This guarantees that the interaction from $U_{sw}$ picks up both the first and second neighbor for each particle in the BCC lattice but only the first neighbor in the DC. This means that an increase in $\alpha$ should decrease the free energy of the bcc state relative to the DC state, meaning that an increase in this parameter should cause the BCC-DC phase coexistence line to encroach on the DC phase.

This fixes all parameters except $\alpha$, which we leave free in order to study its effect on the system.
Chapter 5

Effects of Increasing Isotropic Attraction on Tetrahedral Particles

5.1 Hamiltonian Gibbs-Duhem Integration

We then need a method for determining the phase diagram of eqn. 4.4 for any \( \alpha \) starting from the case where \( \alpha = 0 \). We perform this process using Hamiltonian Gibbs-Duhem integration. This is a general method for integrating the phase coexistence lines for a changing potential, which we detail below.

Given a potential energy function \( U \) that depends on some coupling parameter \( \lambda \), we can calculate the \( P-\lambda \) phase coexistence line from some point along the coexistence line through the derivative \( \frac{dP}{d\lambda} \). It can be shown that along the phase coexistence line between states \( A \) and \( B \), this derivative can be computed through eqn. 5.1.

\[
\frac{dP}{d\lambda} = -\frac{\langle \partial U(A)/\partial \lambda \rangle_{N,P,T,\lambda} - \langle \partial U(B)/\partial \lambda \rangle_{N,P,T,\lambda}}{V(A) - V(B)}
\]

(5.1)

For our case, where \( U \) is given by eqn. 4.4 and \( \lambda = \alpha \), eqn. 5.1 simplifies to eqn. 5.2.
where $U_{sw}$ is defined by eqn. 4.2

\[ P = 0 \]
\[ = 0.004 \]
\[ = 0.008 \]
\[ = 0.012 \]
\[ = 0.016 \]
\[ = 0.02 \]

\( \alpha = 0 \)
\( \alpha = 0.004 \)
\( \alpha = 0.008 \)
\( \alpha = 0.012 \)
\( \alpha = 0.016 \)
\( \alpha = 0.02 \)

Figure 5.1: The $P$-$T$ phase diagram for the combined Kern-Frenkel and isotropic square well potential, eqn. 4.4 with $0 \leq \alpha \leq 0.02$. The $\alpha = 0$ line is courtesy of Francesco Sciortino and is presented in ref. [49]. We fit coexistence curves to the calculated points that are shown as circles along BCC-DC, squares along DC-fluid, and diamonds along BCC-fluid. Most notable in this graph is the rapid drop in pressure along the BCC-DC line, which causes the DC phase to be completely excluded for $P > 0$, $\alpha \geq 0.02$. This decrease also lets us observe the movement of the liquid-gas $T_c$ into the BCC phase, making liquid-gas separation only a metastable phenomenon. While the BCC-fluid line also decreases in pressure, it does so at a reduced rate and has less of an overall effect on the phase diagram. Note that the BCC in this model is analogous to the DC in the coarse grained model for reasons described in the text. Similarly, the DC phase here should be compared to the FCC results for the coarse-grained model.
\[
\frac{dP}{d\alpha} = -\frac{\langle U(A)_{sw} \rangle_{N,P,T,\alpha} - \langle U(B)_{sw} \rangle_{N,P,T,\alpha}}{V(A) - V(B)}
\] (5.2)

We then use this derivative to integrate the phase diagram in the \( P-T \) plane from ref. [49] into three dimensional \( P-T-\alpha \) space. Performing this calculation, we show that by fixing \( \alpha \geq 0.02 \) the DC phase can be excluded from the phase diagram for positive pressure. Increases in \( \alpha \) with fixed \( T \) cause decreases in \( P \) along the BCC-DC phase coexistence line, eventually causing the line to drop below the \( P = 0 \) line. This means that the BCC becomes the only thermodynamically stable crystal phase for small positive pressure. In summary: by supplementing the directional attraction with an isotropic attraction of only 2% of the strength of the directional potential, we completely eliminate a phase from the \( P-T \) phase diagram.

Increasing \( \alpha \) with fixed \( T \) also decreases the \( P \) along both the fluid-BCC and the fluid-DC coexistence line, however the drop along the fluid-DC line is essentially negligible. This coexistence is actually more affected by the change in the BCC-DC line. This change results in much of the DC-fluid coexistence line being absorbed by the BCC state and reduced to metastability.

While the decrease in \( T \) along the BCC-fluid line is at a slower rate than that along the BCC-DC line, it is large enough to have some effect on the phase diagram. Because \( \partial P/\partial T \) is so high along this coexistence line, this effect is still relatively small. Overall, this effect amounts to a small area in the low \( T \) and high \( P \) region in the fluid phase shifting to the BCC phase.

Applying these results to the systems discussed in section 3.1 gives results that are consistent with our predictions for the NP-tetrahedron system. When placed at an appropriate range, a small isotropic attraction was indeed able to greatly increase the thermodynamic favorability of the overall BCC phase over the DC. Experimental results could also be explained by the small shift from a fluid to a crystal BCC phase slightly above \( T_m \). This shift could provide a mechanism for the stabilization of a crystalline ordering from an amorphous state through the introduction of the \( \text{Mg}^{2+} \).
CHAPTER 5. EFFECTS OF INCREASING ISOTROPIC ATTRACTION ON TETRAHEDRAL PARTICLES

Figure 5.2: A closeup of the DC-fluid interface in fig. 5.1. Note the fact that there is essentially no change in the points along the DC-fluid coexistence line, shown as squares on this graph. This means that the rapidly changing BCC-DC lines and BCC-fluid lines cause most points on the DC-fluid line to move into the interior of the BCC phase, representing the change from stability to metastability of the DC-fluid coexistence. A similar phenomenon occurs with the liquid-gas phase coexistence line when \( \alpha \geq 0.02 \). For these values the the unchanging critical point, \( T_c \), is interior to the BCC phase and thus liquid-gas separation only exists as a metastable phenomenon for these values.

5.2 Fluid-Gas Coexistence from Successive Umbrella Sampling

In addition to more broad effects on the phase diagram, we also study the effect of the isotropic interaction strength on the liquid-gas critical temperature, \( T_c \). We find this temperature using successive umbrella sampling to find the probability distribution \( P(N) \) for various fixed \( \mu \) and \( T \).

This methodology revolves around the fact that \( P(n+1)/P(n) \) can be quickly and
accurately computed for a fixed $\mu$ and $T$ in a Monte-Carlo simulation by artificially constraining the number of particles to either $n$ or $n + 1$. We then use the product of these ratios to calculate $P(N)/P(0)$ for all $N$, eqn. 5.3. $P(0)$ can then be computed using normalization, giving us our normalized probability function, $P(N)$.

$$\frac{P(N)}{P(0)} = \frac{P(1)P(2)P(3)}{P(0)P(1)P(2)} \cdots \frac{P(N-1)P(N)}{P(N-2)P(N-1)}$$  \hspace{0.3cm} (5.3)

From $P(N)$ we calculate $P(N, \mu)$ through histogram reweighting. This process takes advantage of the fact that given some initial $P(N, \mu_0)$, $P(N, \mu_1)$ may be calculated up to a multiplicative constant by eqn. 5.4.

$$P(N, \mu_1) = \frac{Z_0}{Z_1} P(N, \mu_0) \exp[\beta(\mu_1 - \mu_0)]$$  \hspace{0.3cm} (5.4)

The constant $Z_0/Z_1$ may then be calculated by normalization, giving us easy access to $P(N, \mu)$ at any given $T$. Below $T_c$ the value of $\mu$ at phase coexistence will then maximize $\langle N^2 \rangle$. By continuing to set $\mu$ in order to maximize $\langle N^2 \rangle$ while increasing $T$, we find the value at which $P(N)$ ceases to have distinct peaks for the gas and liquid phases: $T_c$. [52]

These coexistence points may further be located on the $P$-$T$ axis by calculating pressure from $P(N, \mu)$ through eqn. 5.5.

$$P = \frac{-k_B T}{V} \ln P(0)$$  \hspace{0.3cm} (5.5)

Performing this computation at various values of $\alpha$ we find negligible change in $T_c$ and $P_c$ from the $\alpha = 0$ case presented in refs. [49, 50]. This still has significant impact on the existence of distinct gas and liquid phases, due to the fact that the fluid-BCC coexistence line is changing. For $\alpha \geq 0.02$ this line actually passes through the critical point, as shown in fig. 5.1. This reduces gas liquid separation to a metastable phenomenon within the BCC phase regime for high enough $\alpha$. 


Chapter 6

Conclusions

We have used two computational approaches to consider the behavior of the 1:1 mixture of DNA tetrahedrons and functionalized NP.

The first approach was to use molecular dynamics methods along with a coarse-grained model to consider the interaction of these particles in detail. Using this model we demonstrate the viability of two ordered phases of the NP. The less dense phase had an overall DC shape when considering both particle types and an FCC structure for just the NP. The other phase was an interpenetrating structure that formed a BCC lattice for both particle types with the NP forming a DC lattice. We then demonstrated that the structure factor of the simulated DC structure of NP matches up with the experimental data.

We also performed calculations to explain the experimental preference for the more complicated interpenetrating phase over the simpler ordering. We show that the DC ordering of the NP has both a lower free energy and higher $T_M$ than the FCC ordering, suggesting that it is more thermodynamically stable in our model and helping to explain it’s experimental favorability.

We also considered the effects of Mg$^{2+}$ in solution with this system. We know that these ions are required for the system to reach an ordered state experimentally, however our model is capable of forming ordered states without this interaction. Nonetheless, we
demonstrate a mechanism that would cause these ions to create a long-range isotropic attraction between NP and show that such an attraction would decrease the free energy of the DC lattice for the NP. This suggests one way that the ions may play a key role in formation of this lattice.

To more fully consider the fundamental physics of such isotropic interactions in concert with tetrahedral attractions, we take a second approach to computational analysis of this system. Instead of the coarse-grained model in a molecular dynamics simulation, we use the Kern-Frenkel model in a Monte-Carlo simulation. Starting from a model known to make the overall DC and BCC phases studied in our MD model, we study the effects on the phase diagram of the introduction of a small isotropic interaction.

This isotropic interaction has a pronounced effect on the phase diagram of tetrahedrally attractive particles. At only 2\% of the strength of the directional attraction, the lower density crystal phase is excluded for positive $P$. Additionally, the higher density crystal state is also made more stable within regimes that were fluid without the isotropic interactions.

This results replicates the behavior observed in the NP-tetrahedron system. The isotropic attraction greatly stabilizes the BCC structure over the DC structure for all particles. At the same time, this attraction also helps create crystallization from fluid in certain regimes. This provides a mechanism for the stabilization of the interpenetrating crystal from an otherwise fluid state through the introduction of Mg$^{2+}$ in solution, exactly as observed in experiment.
Bibliography


[50] F. Romano, E. Sanz, and F. Sciortino, .
