

Schematic Models of Molecular Self-Organization

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Summary: Molecular self-organization is central to the formation of numerous biological structures and the emulation of this process through the creation of synthetic counterparts offers great promise for nanofabrication. Our approach to understanding the principles governing this process is inspired by existing models and measurements on the self-organization of actin, tubulin and the ubiquitous icosahedral structures of viral capsids. We introduce a family of simple potentials that give rise to the self-organization of chain-like, random surface ('membrane'), tubular ('nanotube') and hollow icosahedral structures that are similar in many respects to their biological counterparts.

Keywords: nanotube; polymerization transition; self-assembly; simulation; virus capsid

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Introduction

Molecular self-organization is central to the formation of numerous biological structures^[1-3] and the emulation of this process through the creation of synthetic counterparts^[4-9] offers great promise for nanofabrication^[10-15]. The central problems in this field are an understanding of how the symmetry of interacting particles encodes information about the geometrical structure of the organized structure and the nature of the thermodynamic transitions governing this type of organization. Our approach is inspired by a long tradition of modeling and precise experimental observations on biological self-organization of chain-like polymers (actin^[16-19] and crystallin proteins^[20]), fiber-like polymers (tobacco mosaic virus^[21-23], sickle cell hemoglobin^[24-27], type-1 collagen^[28] and amyloid fibers^[29-32]), hollow cylindrical structures such as tubulin^[33-38] and the normally icosahedral structures of plant and animal 'spherical' virus capsids^[39, 40-47] and of clathrin-coated vesicles involved in cellular transport by endo- and exocytosis.^[48, 49] We obtain these structural forms of self-organization based on minimal models involving *equivalent* particles exhibiting an interplay between directional (dipolar and multipolar) and short-range (van der Waals) interactions. (Zhang and Glotzer have recently recently considered other interesting examples of self-organization with directional interactions.^[52])

Specifically, a dipolar potential, having a continuous rotational symmetry about the symmetry axis, leads to chain formation at equilibrium^[50] (*equilibrium polymerization*^[51]), while changing to a potential having a 2-fold and 3-fold discrete rotational symmetries (e.g., square quadrupole interaction or triangular ring of dipoles, respectively) leads to the self-organization of nanotube and icosahedral structures resembling those found in the self-organization of tubular or icosahedral viruses^[1, 3, 40-47]. This type of self-organization is also relevant to a wide range of commercial additive materials called ‘gelators’ that self-organize into nanoscale fiber structures^[53-64] and to synthetic peptide gels promising for tissue engineering applications.^[65-67]

The term ‘self-organization’, and indeed a whole field of scientific inquiry, was initiated by the remarkable observation that the proteins and RNA components comprising tobacco mosaic virus could regenerate into active viruses in vitro^[21-22]. It was soon realized that the RNA was often unnecessary for this process, prompting numerous further investigations into the nature of this highly specific, but apparently equilibrium-based, organizational process. Self-organization of ‘spherical’ viruses under in vitro conditions was later observed in the nearly spherical cowpea chlorotic mottle virus.^[22] These developments were facilitated by developments in electron microscopy that enabled the resolution of the molecular structure of viruses with unprecedented detail (scales on the Å).^[1] It was soon found that while other viruses also had the rod-like form of tobacco mosaic virus, spherical viruses were more common. This is especially true in the case of viruses associated with diseases in humans and other animals.

Spherical viruses often contain only enough genetic material for replicating a few proteins and this led to the notion that the organization must involve particles having ‘equivalent’ structure. This property alone was suggested to be sufficient to understand the formation of closed structures having a tube-like form of rectangular symmetry or closed structures belonging to the family of Platonic polyhedra (cube, octahedron, tetrahedron, icosahedron)^[39]. The formal arguments by Crick and Watson^[39] were soon borne out by observations indicating a particular prevalence for viruses to form icosahedral structures.^[1,40,44] A strict equivalence of molecular environments for identical proteins within viral structures evidently severely limits the size of the virus that can form, however. Caspar and Klug^[3] addressed this issue, and the prevalence for icosahedral symmetry, by allowing for small variations of environment within the organizing virus, such that ‘inequivalent’ particle environments are minimized. Physically, this loose principle of ‘quasi-equivalence’ requires that the ‘frustration energy’ associated with

inequivalent environments to be minimized and led to the specific suggestion that spherical viral capsids should be built up from hexagonal and pentagonal protein clusters and should comprise a specific family of icosahedron-related surfaces ('icosadeltahedra').^[1,3] These surfaces are closed 'geodesic' or 'fullerene-like' structures comprised of 12 pentagonal clusters and varying number of hexagonal clusters that fill in the closed structure. A perfect icosahedron of sixty equivalent vertices (proteins) has 20 faces, while the larger icosadeltahedron contain an integer multiple of 60 vertices, the integer factor being a quantized 'triangulation factor', T . Remarkably, the heuristic arguments of Caspar and Klug and the resulting virus structure classification scheme has been found to apply to all but a small number of 'spherical' viruses^[1]. Unfortunately, these formal arguments do not provide any insight into the thermodynamic factors governing this sort of self-organization, nor is there any specific indication of what the term 'quasi-equivalent' really means in terms of molecular potentials and protein structure.

Stimulated by the philosophical approaches of Crick and Watson^[39] and Casper and Klug^[3], we seek to develop a family of minimal ('schematic') models that can give rise to these types of molecular self-organization processes and that can serve as a testing ground for understanding the principles of self-organization. Our approach builds on our recent systematic investigation^[50] of the Stockmayer fluid (SF) involving a fluid having a competition between dipolar and van der Waals interactions and the formation of equilibrium linear polymers upon cooling. This is a natural starting point for investigating protein self-organization since proteins are often characterized by large dipolar (e.g., the dipole moments of tubulin, collagen and hemoglobin(S) are 1410 D, 1150 D and 545 D, respectively^[68]) or directional hydrogen bonding interactions and it seems likely these highly directional interactions must be part of any explanation of molecular self-organization of proteins in solution ($1 \text{ D} = 3.336 \times 10^{-30} \text{ Coulomb} \cdot \text{m}$). In particular, we consider a *point quadrupole* generalization of the SF that approximately models two side-by-side and head-to-tail dipoles or four charged particles (two plus and two minus charged particles) in a square ring. We also consider a triangular configuration of SF particles at the vertices of triangle in a head-to-tail orientation (See Fig. 1). As opposed to the dipolar SF fluid particles, which have a continuous rotational symmetry about the axis in which the dipoles point, these 'composite particle potentials' exhibit discrete rotational symmetries (two and three-fold symmetries about the plane containing the particles in the discrete particle analogs of our model potentials). It seems plausible to us that many real

physical systems should exhibit potentials with these basic symmetries and we inquire into how these apparently modest generalizations of the SF affect molecular self-organization. At gas phase densities, the simulation of strongly associating systems can present challenges for traditional simulation techniques. The strong binding energies between associated particles and large distances between non-associated particles can make the configuration-space sampling inefficient^[69] since the time required for particles to undergo an association/disassociation transition can be very long compared to typical molecular dynamics simulation times. There are MC algorithms that can overcome this problem, however and in the present work we utilize the Aggregate Bias Monte Carlo algorithm^[70] to improve our sampling of configuration-space. At the heart of this algorithm is an intra-box swap move that is targeted at sampling the formation or destruction of clusters. We also implement the simple translational and rotational moves to explore nearby regions of phase space. The MC computational methods utilized in the present paper have been described in a previous paper^[50] in the case of the SF and their extension to the potentials defined in the next section is straightforward. The simulation boxes contain 256 particles and have a number density of either $\rho^* = 0.001$ or $\rho^* = 0.02$. As with the SF, the interactions between particle pairs are truncated at half the box length and the validation of this procedure is discussed in our previous paper^[50].

Schematic model potentials and associated patterns of self-organization

A. Stockmayer Fluid

First, we briefly recall some basic aspects of self-organization in the Stockmayer fluid (SF)^[50], which is a minimal model exhibiting an interplay between directional (dipolar) and isotropic (van der Waals) interactions. Specifically, two particles interact via a Lennard-Jones (LJ) potential and an additional point dipole potential placed the center of each particle (Fig. 1a). The interactions between particle pairs are truncated at half the box length and the validation of this procedure is discussed in our previous paper^[50]. The dipolar contribution to the interaction potential is given by,

$$u_{\text{dipole}} = (\boldsymbol{\mu}_i \cdot \boldsymbol{\mu}_j) / r_{ij}^3 - 3 (\boldsymbol{\mu}_i \cdot \mathbf{r}_{ij}) (\boldsymbol{\mu}_j \cdot \mathbf{r}_{ij}) / r_{ij}^5 \quad (1)$$

where $\boldsymbol{\mu}_i$ is the dipole moment of particle i and $\mathbf{r}_{ij} = \mathbf{r}_i - \mathbf{r}_j$ is the separation vector between particles i and j and the LJ contribution equals,

$$u_{\text{LJ}} = 4 \epsilon [(\sigma / r_{ij})^{12} - (\sigma / r_{ij})^6], \quad (2)$$

where the van der Waals (vdW) interaction energy strength ϵ controls the magnitude of the

potential minimum, and σ is the separation at which the vdW energy vanishes. The total potential of the SF fluid equals, $u_{\text{SF}} = u_{\text{LJ}} + u_{\text{dipole}}$. In the literature, it is conventional to define the magnitude of the dipole relative to the vdW energy, $(\mu^*)^2 = \mu^2 / \epsilon \epsilon_D \sigma^3$ where ϵ_D is the dielectric constant of the medium. Physically, the self-energy of a dipole ($\mu^2 / \epsilon_D \sigma^3$) equals the Coulombic interaction energy between two charged hard spheres of common diameter σ and valence that are in contact where μ equals the charge magnitude q times the charge separation σ , i.e. $\mu = |q| \sigma$. The dipole-dipole interaction of two hard spheres in head-to-tail configuration is larger in magnitude by a factor of 2 so that the dipolar self-energy sets the energy scale also for describing the mutual interactions of dipoles^[50]. For all of the simulations discussed below, we take $\mu^* = 6$, unless otherwise stated. With this choice of dipole strength, the dipolar contribution to the minimum in the potential is roughly 100 times the LJ contribution so that the directional interaction predominates.^[50] The anisotropy in the potential is illustrated in Fig. 1 of ref. [50], which shows the minimum of the SF potential as a function of fixed relative orientations of the two particles for $\mu^* = 6$. There is a deep minimum in the interparticle potential corresponding to a head-to-tail alignment of the dipoles and a particle separation $r = 0.829 \sigma$. The potential at this minimum for this choice of μ^* equals $u_{\text{min}} = -100 \epsilon$. All densities ρ reported in this paper are number densities density and T is normalized by the van der Waals energy ϵ / k_B , where k_B is Boltzmann's constant.

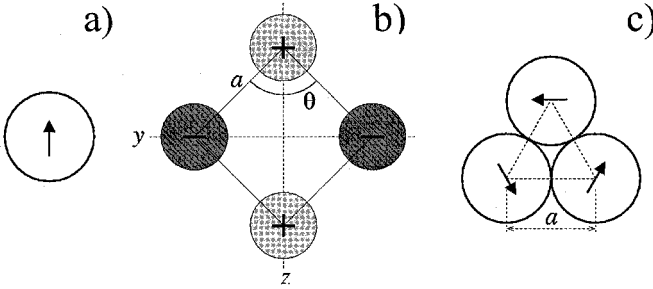


Figure 1. Multipole potentials. a) dipole, b) quadrupole, c) 'hexapole' or dipole triangle.

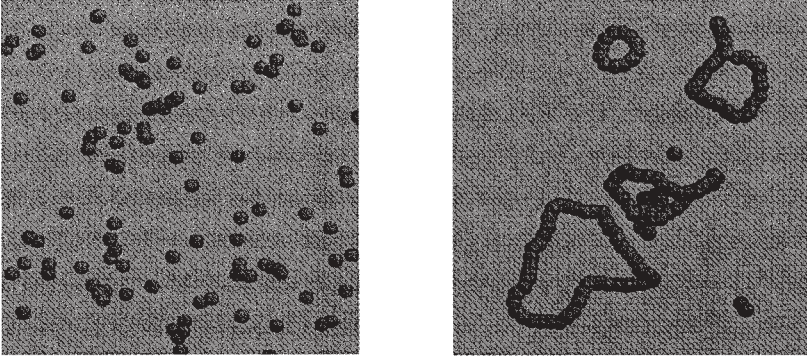


Figure 2. Polymerization transition in the Stockmayer fluid (SF) upon cooling.

a) $T = 7.6$, b) $T = 5.95$. The density is constant, $\rho = 0.001$.

In a previous computational investigation^[50], we studied the SF as a model of self-organization and mapped out the thermodynamic transition lines for this fluid as a function of concentration and temperature. Upon cooling, there is a polymerization transition where the dipoles chains form and disintegrate in a state of *dynamic equilibrium* (Fig. 2). The location of the transition curves defining this transformation are found to be well-described^[50] by the theory of equilibrium polymerization^[51], where the sticking energy is uniquely fixed by the minimum in the intermolecular potential between two SF particles^[50]. At low temperatures, the long-range dipolar interaction causes the chains to form ring structures that minimize the field energy of the polymeric structures. This topological transition occurs despite the entropic energetic cost of confining the free ends of the chain. Figure 2 shows the change in organization as T is lowered through the transition temperature ($T_\phi = 9.8$ at this concentration). This transition temperature T_ϕ is defined by an inflection point in the T dependence of the extent of polymerization Φ (fraction of particles in the clustered state)^[50]. T_ϕ increases monotonically with concentration ρ and the shape of this transition line (Arrhenius temperature dependence of ‘critical concentration’ for polymerization^[50]) and measurement of this transition line provides fundamental information about the basic energetic parameters (entropy and enthalpy of polymerization) governing this thermodynamic transition.

The self-organization of dipolar particles into chains upon lower T below T_ϕ leads to the steady growth of polymer chains, although fluctuations do occur as chains associate and dissociate in dynamic equilibrium. Raising the temperature within the polymerized regime leads to a steady decrease in the average size of the chains, the system reverting to largely monomers for $T > T_\phi$. The growth upon cooling and the shrinking of the chains upon

heating are quite reversible and no nucleation seems to be required to affect this process. Fluctuations in thermodynamic variables (average energy E , extent of polymerization Φ , chain length L , etc.) become large and long-lived near T_Φ and the specific heat C_p shows a maximum near T_Φ , reflecting these fluctuations. The T where the maximum occurs providing an alternative definition of the polymerization transition temperature. We shall see that the smooth and reversible nature of the polymerization in the SF is completely altered by changing to potentials with discrete rotational symmetries.

B. Quadrupole/vdW Fluid

The inclusion of a quadrupole interaction (Fig. 1b) superimposed on the van der Waals interaction is a direct formal generalization of the SF.^[71-72] The LJ component of the potential is the same as in Eq. (2). The *point quadrupole* interaction between two *linear* quadrupoles ($\theta = 0$ in Fig. 1b) of magnitude Q_i and Q_j whose orientations are described by the unit vectors $\bar{e}_i$ and $\bar{e}_j$ can be written as,

$$u_{ij} = \frac{3}{4} \frac{Q_i Q_j}{r_{ij}^5} \left(1 - 5 \cos^2 \theta_i - 5 \cos^2 \theta_j - 15 \cos^2 \theta_i \cos^2 \theta_j + 2 (\cos \gamma_{ij} - 5 \cos \theta_i \cos \theta_j)^2 \right) \quad (3)$$

$$\cos \theta_i = \frac{\bar{e}_i \cdot \bar{r}_{ij}}{r_{ij}}, \quad \cos \theta_j = \frac{\bar{e}_j \cdot \bar{r}_{ij}}{r_{ij}}, \quad \cos \gamma_{ij} = \bar{e}_i \cdot \bar{e}_j.$$

More generally, the energy between two *pure quadrupoles* i and j is given by^[73],

$$u_{ij} = \frac{1}{9} \bar{Q}_i : \bar{T}_{ij} : \bar{Q}_j \quad (4)$$

where $\bar{T}_{ij} = \bar{\nabla} \bar{\nabla} \bar{\nabla} \bar{\nabla} \frac{1}{r_{ij}}, \quad r_{ij} = (\bar{r}_{ij} \cdot \bar{r}_{ij})^{1/2}, \quad \bar{r}_{ij} = \bar{r}_i - \bar{r}_j.$

A pure quadrupole charge configuration is defined to have a zero net charge (monopole strength is zero) and dipole and multipole moments higher than quadrupole also vanish. An example of such an ideal quadrupole configuration of *discrete charges* is shown in Fig. 1b. The quadrupole moment tensor for a molecule i consisting of N_i discrete (point) charges of charge q_i is given by,

$$\bar{Q}_i = \sum_{j=1}^{N_i} q_j (3 \bar{r}_j \bar{r}_j - r_j^2 \bar{\delta}) \quad (5)$$

More specifically, for the four particle configuration shown in Fig. 1b, consisting of four point charges of common charge magnitude q and charge separation a between plus and minus charges, the quadrupole moment tensor reduces to the matrix representation,

$$\overline{\overline{Q}} = 4a^2q \begin{bmatrix} -\frac{\cos\theta}{2} & 0 & 0 \\ 0 & \frac{\cos\theta-3}{4} & 0 \\ 0 & 0 & \frac{\cos\theta+3}{4} \end{bmatrix} \quad (6)$$

This represents the quadrupole moment tensor for a pure quadrupole in it's principle axis frame where the matrix becomes diagonal. The limit $\theta \rightarrow 0$ recovers the case of a linear quadrupole oriented along the z-axis where we have,

$$\overline{\overline{Q}}_{linear} = 4a^2q \begin{bmatrix} -1/2 & 0 & 0 \\ 0 & -1/2 & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad (7)$$

Given that Eqns. (3) and (4) for $\theta = 0$ are equivalent if $Q = 4a^2q$, we write the quadrupole moment tensor for a pure quadrupole in it's principle frame as,

$$\overline{\overline{Q}} = Q \begin{bmatrix} -\frac{\cos\theta}{2} & 0 & 0 \\ 0 & \frac{\cos\theta-3}{4} & 0 \\ 0 & 0 & \frac{\cos\theta+3}{4} \end{bmatrix} \quad (8)$$

where $Q = 4a^2q$ is taken to be a general 'strength parameter' of the quadrupole interaction. However, the interaction energy between two pure quadrupoles also depends on the 'quadrupole angle parameter' θ so that two-parameters are required to specify this potential. Similar to the SF, we define a reduced quadrupole interaction strength relative to the van der Waals interaction as, $Q^* = Q/(4\pi\epsilon_D\sigma^5\epsilon)^{1/2}$.

Although the local symmetry associated with the ability of SF particles to freely rotate and translate in space is broken when linear polymer chains begin to form upon cooling, the freedom of these the particles to rotate about the local chain axis between the particles remains preserved in the organized structure. This rotational freedom causes the resulting structures to be floppy and one-dimensional by nature. The discrete rotational symmetry of the Quad/vdW fluid (Fig. 1b) gives rise to structures that likewise exhibit this discrete two-fold local symmetry within the organized structure. In Fig. 3, we show a representative two-dimensional or random surface polymer that spontaneously organize in the Quad/vdW fluid at low temperatures. These structures are evidently invariant under discrete two-fold rotations within the sheet so that this symmetry of the individual particle is likewise preserved in the organized structure. We also observe that the 'dipoles' comprising the quadrupole have a strong tendency to form closed loops as in the SF. The

reason is the same, minimization of the energy of the resulting cluster. Thus, the organization of both the SF and the Quad/vdW fluids are both driven by directional interactions and the preservation of local symmetries in the single particle potential.

We note that specifically rectangular symmetry of the square quadrupolar potential significantly impacts the self-organization geometry. Changing the angle θ of the quadrupole potential from $\pi/2$ can break this symmetry, making it difficult for this potential to organize the particles into a sheet morphology as in Fig. 3 and a disordered network structure forms instead^[73]. Previous simulations for linear quadrupole interactions with anisotropic hard-core interactions likewise led to 'branched equilibrium polymers'.^[74]

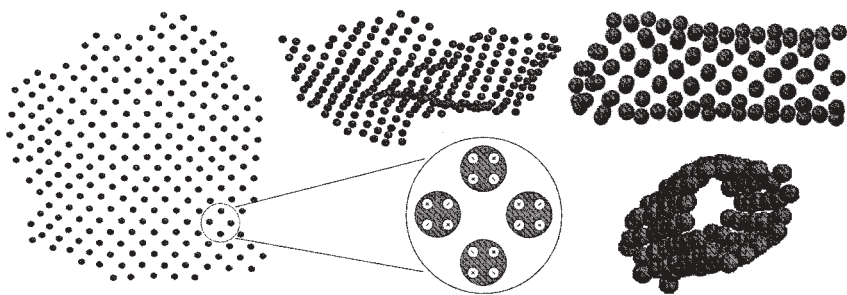


Figure 3. Sheets and tubes formed by square Quadrupole/van der Waals fluid. Left indicates a top view of a representative sheet polymer ($T = 1.35$, $Q^* = 1.0$, $\rho = 0.001$) and a profile view is shown in top middle. 'Local charge orientation' is indicated in the middle bottom. Right shows side and view of self-organized tubes ($T = 1.7$, $Q^* = 2.0$, $\rho = 0.001$).

The tendency for SF chains to curl up into rings^[50] from dipolar interactions has its counterpart in the Quad/vdW fluid. The first stage of this process^[73] involves the formation of a bilayer sheet (a structure that we refer to as 'pita bread'). There multilayers close-off at their edges and then open up to form a hollow structure. It is through this process that our nanotubes 'nucleate' or initiate growth. Once formed, the tubes continue to grow from their ends (See Fig. 3). It is also possible to preferentially select tubular growth through the introduction of a 'seed' and we illustrate this process below.

The local rectangular symmetry of the self-organized nanotubes is apparent in Fig. 3, but the development of some helicity is also suggested in this morphology. Note that that this emergent helical symmetry is *not related to molecular chirality*, but derives from the staggering of the particles within the surface to minimize the field energy (This mechanism of the emergence of chiral symmetry from non-chiral molecules in naotubes and ribbon self-organization has been discussed before by Schnur^[13]). We remark that

tubulin forms nanotubes with a similar rectangular symmetry as a characteristic feature of its self-organization^[36] and the general tendency to form helical cylinders was suggested on general grounds by Crick and Watson.^[39]

C. Hexapole Fluid with van der Waals Interaction

It is evident that many self-organizing structures do not have the rectangular symmetry exhibited by the Quad/vdW fluid model and otherwise do not form one-dimensional polymeric structures as in the SF fluid. Many structures exhibit 3-fold and 5-fold and even higher order *discrete rotational symmetries*. A three-fold symmetry is evident for example in the faces of icosahedral capsid structures^[1] and the hexagonal lattice structure of certain tubular virus structures^[75]. Three-fold symmetry is also apparent in the three-arm star structure of clathrin trimers ('triskelions') before they self-organize into icosahedral frameworks about vesicles.^[49] We next introduce a schematic model of the multipole class that provides some insights into these growth forms.

Three-fold symmetry in our self-organization process can be generated by simply placing SF particles at the vertices of triangles in a head-to-tail configuration (Fig. 1c) to obtain a 'hexapole' or 'triangular dipole potential, augmented by van der Waals interactions (Hex/vdW model). For simplicity, the dipole strength, van der Waals radius and other parameters are taken to be exactly the same as in SF (Fig. 1a). Triangular configurations of proteins have been directly observed in the capsid structures of proteins^[76], so that this structure is plausible for modeling virus assembly.

Upon lowering temperature in Hex/vdW model, we observe the self-organization of sheets similar to those in Fig. 3, except that they have a *hexagonal* local symmetry. This local symmetry derives from the 3-fold rotational symmetry of the particle potential and the tendency of the dipoles within the sheets to form closed ring dipolar paths^[73] (See Fig. 3). In addition to these structures, we also observe the spontaneous formation of hollow icosahedral structures with remarkable similarities to spherical virus organization. These structures coexist with the sheet polymers.^[3,41-48] An example of one of these icosahedral structures is indicated in Fig. 4a and in Fig. 4b we show a cut through this object to reveal its hollow interior. A rendition of this structure is also given in terms of the triangles defining the hexapole/vdW particles (Fig. 4c) and we compare this structure to an ideal icosahedron (Fig. 4d). Notably, each particle in Fig. 4a exhibit 'equivalent interactions' and fulfills the formal requirements of Crick and Watson^[39] and Caspar and Klug^[1,3].

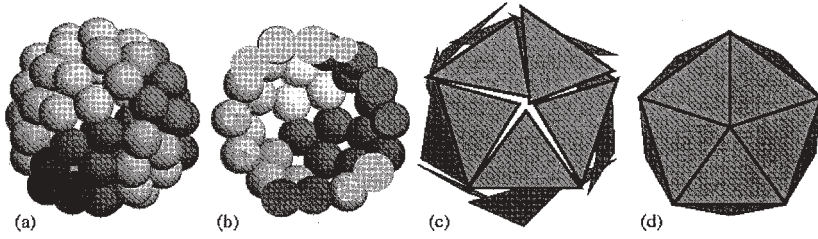


Figure 4. Self-organized icosahedron in the Hex/vdW fluid. a) icosahedron formed from triangular clusters of SF particles, b) slice through icosahedron revealing cluster interior, c) representation of icosahedron emphasizing position of faces of triangular particles composing the cluster, d) ideal icosahedron. Conditions: $\mu^* = 6.0$, $T = 7.75$, $\rho = 0.001$.

The formation of icosahedral particles illustrates a new phenomenon regarding how symmetries of the particle potential encodes information about the symmetry self-organized species. In addition to the 3-fold symmetry of the icosahedron faces, the icosahedron is characterized by twelve 5-fold symmetry axes around the vertices of the icosahedron. How did this symmetry arise that is not shared by the single particle potential? The answer to this question is apparent by following the course of the hexagonal symmetry sheet and icosahedron self-organization process. In the case of the sheet with the local hexagonal symmetry, the growth pattern is *nucleated through the formation of a hexagonal seed* composed of six Hex/vdW particles in a planar configuration (Fig. 5), while the icosahedron is *nucleated by the formation of a pentagonal seed* with a 5-fold symmetry and these fundamental ‘seed’ structures are shown in Fig. 5. It is apparent that these additional higher order (hexagonal and pentagonal) symmetries of the organized structure are shared by their nuclei. The pentagons form by tilting their orientation with respect to their basal plane yielding a lower potential energy per particle than for 5 particles in an ‘unsatisfied’ flat configuration. The energy per particle becomes lower for the flat configuration for which there are 6 particles, but the five-fold symmetry ‘sticks’ once the growth process has nucleated or is slow to revert to hexagonal form. (This process of kinetic direction of capsid organization has been suggested before by Caspar^[77] and has been observed in the assembly of polyomavirus capsids.^[78])

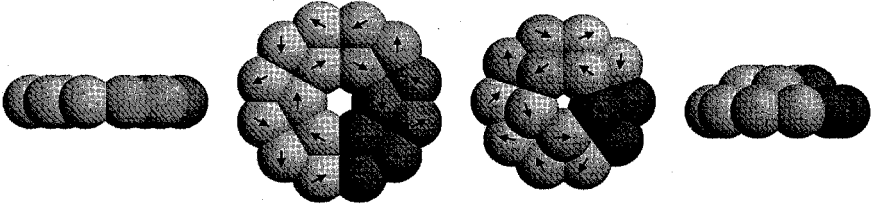


Figure 5. Formation of hexagonal and pentagonal seeds in the Hex/vdW fluid (HF). Left images show side and top view of the hexagonal seed, while the right images show side and top views of the pentagonal seed. Note that the Hex/vdW particles tilt out of the plane to create a surface of near constant mean curvature.

Once the system has formed a pentamer of Hex/vdW particles, it has two options. It can either form a flat hexagon having a lower energy per particle or continue growing with the pentagonal seed intact. Continued growth of the pentagonal seed leads to an icosahedron or other closed structure due to the curvature induced by this ‘defect’ structure. The completed icosahedron is composed of 12 pentagonal clusters situated at the its vertices (Fig. 4). By varying the relative propensities of the formation of the 5-fold (pentagons) and six-fold (hexagons) particle clusters, we should be able to create larger icosahedron family surfaces that include locally hexagonal symmetry faces. Such structures would be consistent of the intuitive notion of quasi-equivalence since the hexagonal and pentagonal particles involve the coexistence of slightly different local particle environments. The presence of 12 pentagonal clusters in these generalized geodesic structures (including spherical capsids, clathrin, fullerenes and many other closed self-organizing structures composed of pentagons and hexagons) is required by Euler’s theorem so that topological constraints largely dictate the extent to which 5-fold symmetry is expressed in the final organized structure.^[79] In a number of viruses it has been directly observed that the viral capsid assembles directly from preformed pentamer and hexamer units^[42, 45, 78, 80]. Moreover, an admixture of hollow icosahedra and hexagonal sheets has also been observed in capsid protein self-organization in vitro where there is apparently an absence of nucleation control^[81,82]. Spherocylindrical tubes similar to buckytubes have also observed,^[75] although we have not seen these in our simulations.

The high sensitivity of the growth morphology to seed geometry by inserting seeds of specific symmetry provides an important means to control the geometry of self-organization and the kinetics of growth. Seeding can give rise to growth form symmetries that are not shared by the interaction potential of the assembling particles and to growth forms that would otherwise not occur with any appreciable probability. This templating

process^[83] is utilized many biological systems to regulate self-organization into a unique or nearly unique growth forms and this templating will undoubtedly be important for synthetic nanofabrication (Inappropriate templating can be expected to toxic structures, providing a potential explanation of prion and other neurodegenerative diseases.). Figure 6 illustrates the growth of a hollow cylinder nucleated from a seed having the form of a ring of hexagons. This heterogeneous nucleation process leads to the propagating growth of a cylinder with hexagonal local symmetry, a structure that otherwise would not readily form. We have also found^[73] that by making the seed anisotropic (by making particles on one side of the hexagon ring simple vdW particles) we could obtain *directional growth along one direction* and an example of this phenomenon (figure not shown). Such ‘polarized growth’ growth is characteristic of many biological self-organization processes such as microtubule growth emanating from the centrosome in the course of mitosis^[36].

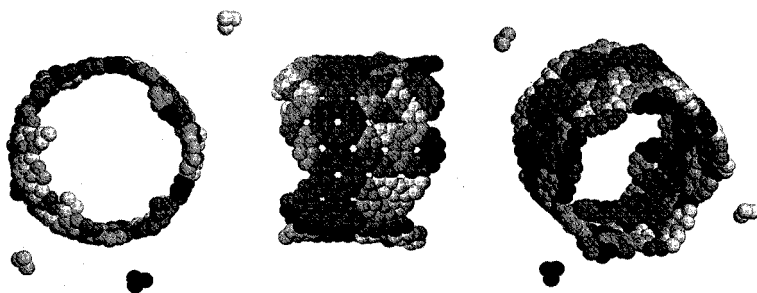


Figure 6. Seeded tube formation in the Hex/vdW fluid. Image shows from left to right the end-on. Side-view and profile view. Conditions: $T = 7.85$, $\mu^* = 6.0$, $\rho = 0.001$.

Conclusions

We have sought to understand how the symmetry properties of the interaction potential of model fluids influence the geometrical structure of self-organization. Our potentials specifically involve a combination of directional (multipole) interactions with isotropic van der Waals interactions, but similar structures can be expected for other highly directional interactions^[9] (hydrogen bonding, hydro-phobic interactions, π - π interactions of aromatic species, metal chelation, etc.) in competition with van der Waals interactions. Biological molecules characteristically exhibit large Coulombic, dipolar and multipole interactions so that the class of potentials that we investigate is promising for understanding certain broad trends in biological and synthetic self-organization.

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