



Modeling growth of 60-unit shells in solution: Early results

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Abstract

Current research into supramolecular assembly using molecular dynamics simulation is summarized. Ongoing simulations are aimed at exploring the nature of the growth pathways of larger shells than considered previously, under reversible bonding conditions and in the presence of an explicit solvent. © 2010 Published by Elsevier B.V. Open access under [CC BY-NC-ND license](https://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

The formation of the capsid shells that package spherical viruses [1,2] is an example of self-assembly in the natural world, a phenomenon that exists at the border of biology and chemistry. The highly symmetric capsid shapes are a consequence of their assembly from multiple copies of one or a small number of distinct capsomer proteins [3]. Experimentally, direct observation of growing molecular assemblies is difficult, while the final state reveals little about how it came into being. An approach based on molecular dynamics (MD) simulation [4] of suitably designed models has been developed to provide access to the assembly pathways themselves and as a means for examining whether self-assembly is subject to general organizational principles. What makes capsid assembly suitable for simulation, despite the apparent biochemical complexity, is the fact that it is able to occur reversibly *in vitro* [5–7] without the presence of genetic material. MD simulation is also able to predict, among other things, the time-dependent populations of partial assemblies; this, in principle, provides a link with experiment [8].

MD modeling of capsid self-assembly, based on simple structural models, was introduced in Refs. [9,10]. The major features of the approach are an effective molecular shape formed out of rigidly arranged soft spheres that enables particles to fit together into a closed shell, and multiple interaction sites positioned to stabilize the correct final

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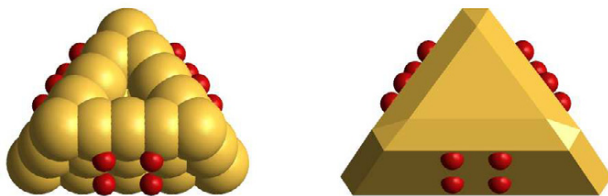


Fig. 1. Details of the model capsomer particle, showing the large spheres responsible for the excluded volume and the small spheres signifying attraction sites; the equivalent truncated triangular pyramid block is also shown.

structure. The initial focus of the simplified approach was on achieving assembly, with the solvent omitted due to computational limitations. Inclusion of an explicit atomistic solvent had to await further increases in computing power [11,12] but, even then, the resulting simulations were limited to icosahedral shells constructed from triangular particles, rather than the larger shells that had been considered earlier. These simulations were able to establish that the self-assembly process involves by a cascade of reversible stages, with a strong preference for low-energy intermediate states, leading eventually to a high proportion of fully assembled shells. Paradoxically, it is the reversibility of the bond formation process that is the key to efficient production, due to its ability to help subassemblies avoid becoming trapped in states not lying on the correct pathway. Early results from ongoing efforts to extend the approach to larger shells are outlined in the present paper.

2. Methodology

The simplified model capsomer particles have an effective molecular shape, based on rigid assemblies of soft-sphere atoms, that ensures they can fit together to form closed polyhedral shells. The particles also include attractive forces, acting between corresponding pairs of precisely positioned interaction sites, that drive self-assembly and maintain the structural integrity of partial and complete shells; bond formation is governed by energetic considerations alone and bonds can break when strained sufficiently. In the present study, the effective shape of the particle, shown in Fig. 1, is a truncated triangular pyramid. Multiple layers of spheres provide a certain amount of steric shielding of the attractive interactions. These particles fit together to form a 60-faced pentakis-dodecahedral shell. The simulations include a solvent, represented by discrete atoms that are identical to the particle spheres and subject to the same soft-sphere repulsion. The remaining technical aspects of the MD simulations, together with additional considerations motivating the overall approach, are described elsewhere [11,12].

3. Results

The systems used for the initial explorations contain 2750 triangular particles; the remainder of the total of 125 000 bodies in the system are solvent atoms. Although this is sufficient to form 45 complete 60-unit shells, the actual yields are expected to be much

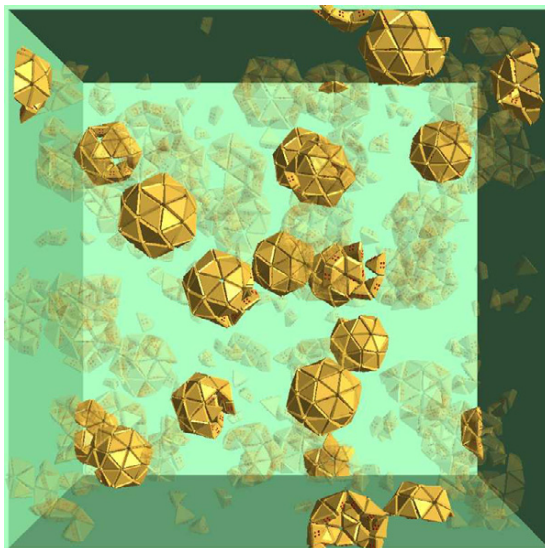


Fig. 2. Shells growing in solution, including three that have reached completion (size 60); clusters with size < 50 and monomers are shown semi-transparently, the solvent is omitted, and some of the structures appear fragmented due to periodic boundary conditions.

lower. Several parameter combinations (e.g., interaction strength, particle concentration, density) were examined, following the choices that proved successful in the earlier work with icosahedral shells. From these runs, the one that appeared most promising at an intermediate stage was followed for an extended period of time, and the results obtained for this run are summarized here.

The state of the selected run after 60 million time steps is shown in Fig. 2. The yield at this point is three closed shells, with a total of 17 clusters of size ≥ 50 . While this is only a small fraction of the maximum possible, it is likely that additional shells will achieve completion if the simulations are extended further. The shells are three times the size considered previously (with solvent), and since most growth steps involve unit size changes, growth times are increased by at least this amount.

The evolving cluster distribution for this run, expressed as the mass fraction of clusters of each size as functions of time (time step 0.005), is shown in Fig. 3. There are several features of this graph worth noting. The small peak at size 60 corresponds to the completed shells. There is a transient peak at, or just below, size 70; this corresponds to a larger incorrect structure in which a second layer began to form, but eventually broke away leaving a smaller, nearly-complete shell and another much smaller subassembly. The steadily declining monomer population is also apparent, as is the gradual overall shift of the cluster distribution to larger sizes.

These very limited results can be contrasted with the high yields and extensive growth statistics obtained in the simulations of icosahedral cluster growth under similar conditions and investment of computational effort. To obtain analogous results for the larger

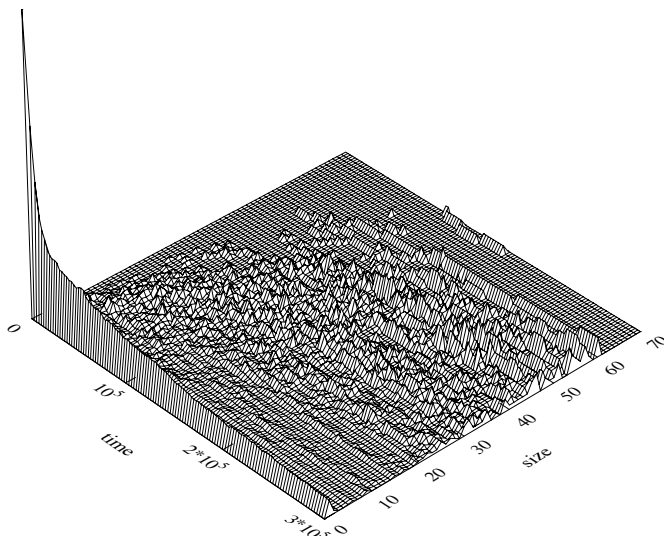


Fig. 3. Cluster size distribution (including monomers) as a function of time (MD units).

shells of the present system, including quantitative data on the intermediate states such as the preference for maximal bonding, as well as the lifetimes of intermediate states and the prominent role of reversibility in the bonding process, will require extensive simulations of systems nearly an order of magnitude larger in overall size.

4. Conclusion

The approach used for simulating the self-assembly of icosahedral shells in solution is clearly capable of extension to larger shells. The present work, while hinting at this capability, indicates that larger systems are needed, both in order to provide additional space for shells to grow and more particles for increased yield. Hopefully, substantial performance enhancements promised by harnessing the computational power of commodity graphics processing units (GPU) [13] will make such simulations feasible in the not too distant future.

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