Simulations of DNA brick self-assembly

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We show that DNA brick structures can successfully self-assemble within a narrow temperature window in brute-force simulations using a minimal interaction potential, and we demonstrate that the process is initiated by nucleation. Given the minimalist nature of our DNA model, our work implies that other systems, such as colloids, could also be designed to assemble into truly complex structures.

1 What we are doing and why

- Ke *et al.* have shown that large structures can self-assemble from a pool of well-designed building blocks, not unlike Lego bricks.[1] This behaviour is particularly intriguing given that the same degree of complexity has never before been realised in a colloidal system. DNA bricks appear to be able to avoid the problem of self-poisoning, and can self-assemble in high yields.
- This fact is even more surprising since the bricks of Ke *et al.* were made using 'positive' design only.
- Ke *et al.* suggest that in their system, seeding is slower than the subsequent growth of the desired structure, but it is not immediately obvious that this should be the case.[2]
- Simulating this system is difficult because it is very large: coarse-graining is essential.
- Our ultimate goal is to understand the process of DNA brick self-assembly and to determine the underlying design principles that govern which structures can assemble and which ones cannot.

2 Brute-force simulations

Lattice simulations with a simple 'patchy' DNA interaction, where each patch has a distinct DNA sequence and the interaction energy is determined using the nearest-neighbour parameterisation of the hybridisation free energy,[3] can result in complex structure assembly in a narrow temperature window.[4]

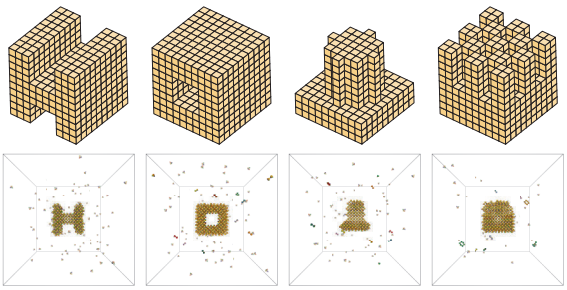


Figure 1: 'Complex' target structures. The first row shows the designed structure, and the second row the final assembled structure in simulations. A self-assembly trajectory for the H-shaped structure is shown in the central column.

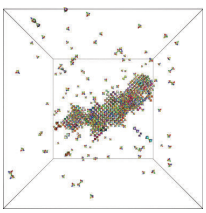


Figure 2: At low temperatures, ever larger aggregates of clusters in which patch bonding is not perfectly complementary form, which then frustrate the system.

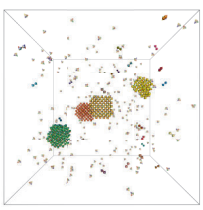
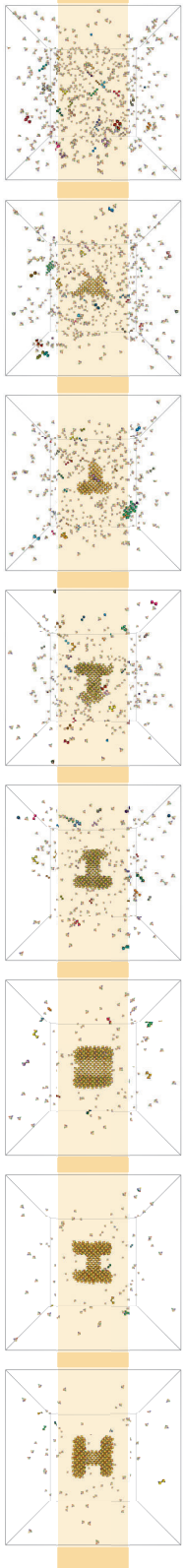


Figure 3: Multiple target structures can also be assembled within the same simulation box. This figure shows three nearly full-assembled cubes and a further cube that is beginning to form.



3 A nucleation-initiated process?

The time evolution of the largest cluster size for a particular set of simulations at different temperatures is shown in figure 4(a); at high temperatures, no clusters form; at intermediate temperatures, clusters can grow to large sizes; and at low temperatures, the largest cluster does not grow considerably after an initial growth stage, as other clusters have formed and misbonded, and these 'incorrect' bonds do not dissociate readily.

Additional simulations at intermediate temperatures have varying 'lag' times prior to fast growth, implying that the self-assembly might be nucleation-initiated. To quantify this, we have calculated the free-energy profile for the self-assembly of a brick cube at a temperature where spontaneous self-assembly occurs (figure 4(b)).

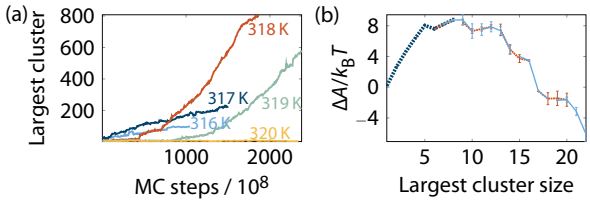


Figure 4: (a) The size of the largest correctly-bonded cluster is shown as a function of time for several temperatures for a particular set of trajectories. (b) The free-energy profile at $T = 319.5$ K.

The free-energy barrier to nucleation at this temperature is small, consistent with the fact that spontaneous growth is observed in brute-force simulations. At lower temperatures, where the nucleation free-energy barrier is very small, several nuclei can form simultaneously and form aggregates. To achieve successful self-assembly, nucleation barriers should be sufficiently high to suppress such in-growth aggregation.

4 The next steps

We have now developed an off-lattice model which exhibits analogous behaviour.

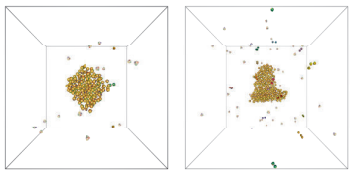


Figure 5: A cube and semi-cylinder self-assembled in simulations using an off-lattice potential.

In future work, we propose to

- verify that our off-lattice model reproduces certain features of the experimental system,
- study the effect of sequence and bonding patterns on the design rules, for example by explicitly calculating the free energies of 'crystalline' structures, and
- extend the model to allow us to study the self-assembly behaviour when non-DNA molecules are present.

EPSRC Engineering and Physical Sciences Research Council

erc European Research Council

[1] Y. Ke, L. L. Ong, W. M. Shih, and P. Yin, Science **338**, 1177 (2012).
[2] K. V. Gothelf, Science **338**, 1159 (2012).
[3] J. SantaLucia Jr and D. Hicks, Annu. Rev. Biophys. Biomol. Struct. **33**, 415 (2004).
[4] A. Reinhardt and D. Frenkel, Phys. Rev. Lett. (2014), accepted, arXiv:1402.6228