Scientific report for the period 30.11.2018 – 29.11.2019

During the end of the first stage and the second stage of the project (01.12.2018-31.12.2018, and 01.01.2018-31.12.2019), the following activities have been carried out:

1. Expansion of the computing architecture of the group

We acquired a high performance server with capacity of up to 10 GPUs, and our budget allowed the acquisition of 6 GPUs with it. Our computing infrastructure now contains 62 CPU cores and 9 GPUs in total.

2. Models for colloidal Goldberg polyhedra

We managed to find the optimal parameters for a minimalistic model that is both experimentally realisable, and theoretically well-behaved, capable to form a whole range of polyhedral shells, depending on the composition of the binary particles. The concept is very simple, and the two types of particles ('metal' and 'ligand') form the vertices and edges of these polyhedra. The interaction between them is purely ionic and repulsive Lennard-Jones.

We investigated the energy per M particle in M:L 1:2 ratio clusters up to M₃₁L₆₂, for different bend angles of the L particles. Smaller bend angles (larger bend) increase the preferred curvature, hence smaller symmetric shells can form as magic number clusters. We also find that increasing the relative strength of Coulombic interactions affects the whole organization of the landscape, and therefore its selfassembling character.



Energy/'metal' particle diagram for different cluster sizes, with M:L ratio 1:2. Right panel: using the same principles, various other symmetries can be created for other M:L ratios.



Disconnectivity graphs for $M_{24}L_{48}$ for three different bend angles. For the largest bend angle (a), we find a simple single transition-state rearrangement (top right panel) through which the pseudorhombicuboctahedral structure B can interconvert into the global minimum A. Increasing the Coulombic interaction strength creates a separate funnel for competing structure C higher up in the landscape.

Our findings about the stability of such shells have been confirmed by preliminary molecular dynamics simulations using the HOOMD-Blue simulation toolkit from the Glotzer group. The M₂₄L₄₈ system readily self-assembles shells (forming the into symmetric entropically more accessible pseudorhombicuboctahedral structure instead of the global minimum) on sufficiently low temperatures. Larger simulations of M₃₀₈L₅₉₂ in bulk show the spontaneous aggregation of these particles into curved partial shells so far. We will increase the concentration of the particles in the next step to see if that facilitates the closure of shells. In every simulation, we are working with a slight excess of M particles, in order to replicate experimental conditions for which such shells were observed.

Preliminary data shows that even when starting from a non-random configuration, ondulations appear spontaneously in the sheets that form in the first stage. This is a highly nonequilibrium configuration, and is quenched to low temperatures, but the spontaneous curvature is nevertheless there. Once we optimize the necessary temperature that allows proper equilibrium dynamics, we will equilibrate the system at high temperature, and do parallel cooling runs to evaluate the efficiency of shell formation in bulk, for different bend angles of the 'ligand' particles.

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Simulation snapshot of 900 particles after 124 million time steps



Example of an ongoing simulation with 7200 particles.

We are currently finishing writing up a paper about the Goldberg model, to be submitted to Nanoscale.

3. Investigating interactions between macroions in explicit solvent

In order to gain a better insight into the behaviour in bulk of polyoxometalate anions capable of assembling into hollow shells in dilute solutions, we created an atomistic model of these shells using Gromacs. The models were parameterised to have the same charge as the experimental polyoxometalate anion (-42, containing 132 Mo atoms and 372 oxygens). We then solvated configurations containing 2, 6 and 12 particles, respectively, using a mixture of TIP4P water and acetone in different sized boxes, simulating different concentrations, added the appropriate number of Na⁺ counterions and ran npT molecular dynamics on the system. These systems are very difficult to study in experimentally relevant concentration ranges. The most dilute system, which is about 10x more concentrated than the one in experiments, contains 12 macroions and altogether almost 10 million atoms. The speed of MD simulations on such a sized system is about 0.26 ns/day on one GPU. In order to get physically meaningful results for such a size, several hundreds of nanoseconds are necessary. Currently we stand at 19 ns simulation time, which is well equilibrated, but no aggregation of macroions is observed yet.

For the 6-particle system, computation is much faster. We currently have 380 ns of simulations, during which we observe spontaneous formation of a dimer which is stable throughout the simulation, and temporary formation of trimers from this dimer, but these structures dissociate easily.

We also constructed a hollow icosahedral structure of 12 particles, in a smaller box, and are working currently to find whether it is possible to relax the structure in a way that the icosahedral arrangement stays stable at 300 K.



Typical radial distribution function of Na^+ ions from the centre of the macroion, compared to that of oxygen atoms from the macroion itself. Distances are in nm.

We constructed various radial distribution functions to evaluate the position of the Na⁺ counterions relatively to the macroions and found no significant difference between the different sized systems. All counterions prefer positions close to the macroion shell for all simulations considered.



Comparative radial distribution functions for Na+ ions in the three different systems: icosahedral arrangement of 12 macroions, random arrangement if 12 macroions in a bigger box, and a long simulation of 6 macroions in which dimers and trimers are observed.

4. Continued evaluation of the physical differences between CCMV dimer interfaces in dimers and pentamers of dimers



Change in alpha carbon RMSD during long simulations of various ss-CCMV dimer interfaces. The most stable interface is type 1 (blue), which is relevant for capsid assembly nucleation. The type 2 interface is also stable during the 2 microsecond long simulation.

Investigating the physical reasons that govern macromolecular self-assembly is important not only from the electrostatics point of view (as in the case of macroions), but also in systems where the hydrophobic interactions are more important. With this in mind, we continued simulating for longer the dimers and pentamers of dimers of salt-stable CCMV capsid proteins. We analysed results of two microsecond long simulations for each dimer (that for the type 3 dimer is still ongoing). Our results show that the angles between the dimers in the type 2 configuration are significantly different from those in the pentamer of dimers structure. The type 1 dimer on the other hand is flexible by itself, and the five dimers in the pentamer do retain some of that flexibility.

It seems that the specific orientation-dependence of ss-CCMV capsid proteins cannot be traced to the stability of the dimers themselves, but it is relevant in the pentamer of dimers structure. The significant difference between angles in the type 2 dimers when standalone or in a pentamer shows that this dimer might exist in solution, but possibly could not incorporate itself into a pentamer of dimers as easily as a type 1 dimer.



Comparison of the change in the angle between protein chains in T1 dimers (left, D1-D5 are the five dimers in the pentamers of dimers structure), and T2 dimers (right).

Sfantu Gheorghe, on 29.11.2019

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