An Unusually Slow Self-Assembly of Inorganic Ions in Dilute Aqueous Solution

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Reaching thermodynamic equilibrium states in dilute solution is usually very fast for inorganic solutes. For example, it takes at most seconds for NaCl solution to establish equilibrium after NaCl crystals disappear in water. For the processes involving organic macromolecules, such as the micellization of the block copolymers in solution, it may take a little bit longer, but usually no more than hours. It is very rare to take months for soluble inorganic ions to reach the thermodynamically stable state in dilute solution. Herein such an unusually slow self-association of inorganic ions in aqueous solution is reported.

Since the past decade, a series of giant polyoxomolybdate (POM) molecules were synthesized, represented by the pioneer work of Müller et al.[1] Various POMs, including some wheel-shaped and hollow, spherical "Keplerate" molecules, were synthesized by partially reducing Mo^{VI} to Mo^V via simple inorganic synthesis approaches.[2] The spherical "Keplerate" POM $(NH_4)_{42}[Mo_{72}^{VI}Mo_{60}^V$-$O_{372}(CH_3COO)_{30}(H_2O)_{72}]$·ca.$300H_2O$·ca.$10CH_3COONH_4$($\{Mo_{132}\}$) has a very similar structure to that of C_{60}. Moreover, the 60 Mo^V can be replaced by 30 Fe^{III} ions, leading to the formation of giant molecules $Mo_{72}^{VI}Fe_{30}^{III}O_{252}L_{102}$·ca.·$180H_2O$ with L = H_2O/CH_3CO-O^-/$Mo_2O_{8/9}{}^{n-}$ ($\{Mo_{72}Fe_{30}\}$, Figure 1, left).[3]

Most POMs are quite soluble in polar solvents because they contain a large number of water ligands and they are negatively charged in solution (similar to polyelectrolytes), balanced by small counterions such as Na^+ or NH_4^+. However, these giant molecules usually do not exist as single ions even in dilute solution. Instead, large, uniform aggregates with unknown structures were observed.[4] Recently, by using a combination of static and dynamic light-scattering techniques (SLS and DLS), I showed that the supramolecular structures formed by soluble POM-based giant molecules in solutions were hollow, spherical, "blackberry"-like vesicles (Figure 1, right).[5] Instead, the electrostatic interactions among the negatively charged spheres could be responsible for the vesicle formation. For the samples synthesized in different batches, variable amounts of remaining NaCl led to variable vesicle size (18−45 nm).

The self-association of POM-based giant molecules in solution has more unusual behaviors. Unlike common inorganic ions, which usually reach equilibrium state in dilute solution quickly, these POM giant molecules need months to reach an equilibrium state.

In this study, $\{Mo_{72}Fe_{30}\}$ was again used as the model system. Its single crystals were dissolved in distilled water at room temperature with stirring. A commercial Brookhaven Instrument light-scattering spectrometer was used for both the absolute integrated scattered intensity (SLS) and the DLS (with a BI-9000AT digital correlator) measurements. The CONTIN method[6] was used to analyze the DLS data to calculate the hydrodynamic radius (R_h) of the particles from the characteristic line width Γ. DLS measurements also provide information on the particle-size distribution in solution from a plot of ΓG(Γ) versus R_h.
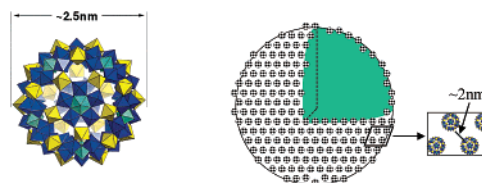

Figure 1. (Left) Structure of $\{Mo_{72}Fe_{30}\}$ "Keplerate" giant molecules. Reprinted from ref 2, page 198, Figure 5, copyright 2001, with permission from Elsevier Science. (Right) "Blackberry" supramolecular structure as determined by laser light-scattering studies.[5]
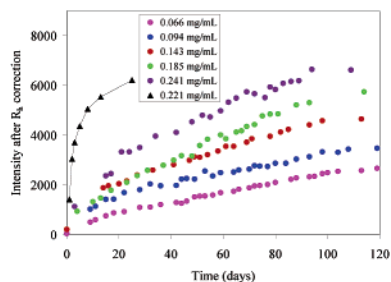
Figure 2. Change of total scattered intensity I of $\{Mo_{72}Fe_{30}\}$ solutions at 90° angle. All solutions were kept at 25 °C except one at 45 °C (the data shown by ▲).

The basis of the SLS data analysis is the Rayleigh−Gans−Debye equation.[7] Here the scattered intensities were measured at a fixed scattering angle (90°) to get the relative change of intensity with time. In this case, the scattered intensity $I \propto C \cdot M$ with C and M being, respectively, the concentration and the molecular weight of the solutes (Figure 2). It is reasonable to assume that for the vesicles at different stages, the intermolecular distance in the vesicles is a constant, to make the whole system stable. Therefore, the number of $\{Mo_{72}Fe_{30}\}$ molecules in each vesicle is proportional to the square of the vesicle's R_h, i.e., $M \propto R_h^2$ and then $I \propto C \cdot R_h^2$.

The scattered intensity I from a homogeneous solution containing newly dissolved $\{Mo_{72}Fe_{30}\}$ was very weak (42K total counts for 0.185 mg/mL solution, including 26K contributed from pure H_2O). By using the Rayleigh−Gans−Debye equation, it can be estimated that at this moment the $\{Mo_{72}Fe_{30}\}$ molecules basically exist as unimers or oligomers. I continued to increase with time. After several days, DLS measurements showed two modes with average R_h of 1.3 nm and ∼20 nm, which should be attributed to the single $\{Mo_{72}Fe_{30}\}$ molecules and supramolecular aggregates, respectively. CONTIN analysis of DLS measurements at different time is shown in Figure 3. In day 4, the contribution to the total scattered intensity (the relative peak areas) from two modes was comparable. Considering that large particles scatter the incident beam more strongly (here 10^4 vs size) than small particles, it could be concluded that over 99% of $\{Mo_{72}Fe_{30}\}$ still exists as single molecules. I drastically increased within the next several weeks to over 6000K counts, indicating a continuous formation of larger aggregates. At
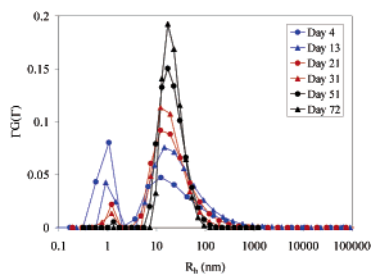
Figure 3. CONTIN analysis of DLS study on {Mo$_{72}$Fe$_{30}$} aqueous solution at different times.

the same time, in CONTIN analysis the peak due to {Mo$_{72}$Fe$_{30}$} single molecules became smaller and smaller while the peak due to vesicles became much larger, also suggesting a continuous formation of aggregates from {Mo$_{72}$Fe$_{30}$} molecules. After day 72, the mode due to single molecules could no longer be detected by CONTIN analysis due to the dominant contribution from the vesicles, although there should still be certain amount of single molecules in solution. The total scattered intensity I still kept increasing, but the increment became smaller and smaller until finally the change was negligible (Figure 2). The average R_h of the aggregates obtained from DLS basically did not change during the whole period, but the size distribution of the aggregates became narrower. The average radius of gyration (R_g) of the aggregates was measured as 20 nm (by SLS), which is the same as the R_h value. As discussed in earlier work, this result confirmed that the aggregates were hollow vesicles.[5] Very similar results were obtained on other samples. The samples from different batch might form vesicles with a little different R_h, which will affect the comparison of I from samples with different concentrations. To solve this problem, in Figure 2 all the intensity data was corrected to the same R_h condition so that the intensities from different concentrations can be directly compared with each other.

Two factors could contribute to the increase of I in {Mo$_{72}$Fe$_{30}$} solutions: the increase of vesicle number C and the increase of the vesicles' mass M (reflected by R_h). Considering that the R_h of the vesicles basically remains unchanged during the whole period, the increase of I should be mainly due to the increase of C.

It is very unusual for inorganic ions to take months to reach equilibrium in dilute aqueous solution. There are two possible reasons: the free energy difference between single molecules and the vesicles is very small or the single molecules have to overcome a high energy barrier to form the vesicles, which is also suggested by the DLVO theory. The latter can be supported by the fact that the vesicle formation is an endothermic process. At higher temperatures (e.g., 45 °C), most of the vesicles formed within few weeks (data in triangles, Figure 2).

The common driving force for a self-assembly process in solution is the hydrophilic−hydrophobic interaction, such as the behaviors of surfactants and amphiphilic block copolymers. The current case could be different, because the POM-based giant ions do not have obvious hydrophobic parts, and in the vesicles the giant {Mo$_{72}$Fe$_{30}$} ions still keep certain distance with each other, while the hydrophobic interaction is effective only in a very short range. The hydrophilicity of the {Mo$_{72}$Fe$_{30}$} is mainly due to the large amount of water ligands attached to the molecules and the net negative charges on the {Mo$_{72}$Fe$_{30}$} in solution. However, aside from the ligands and the charges, the neutral part of the giant molecule must be less hydrophilic. Thus, we cannot rule out the effect of hydrophobic interactions. Therefore, the driving force could be very complicated; it is probably mainly due to the balance between the attractive van
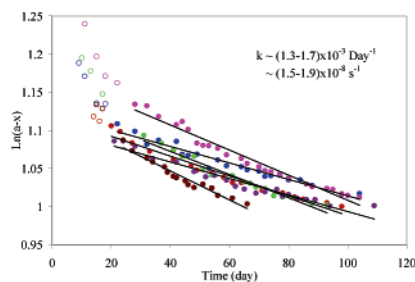
Figure 4. Determination of the "reaction" constant of the vesicle formation at 25°. The linear relationship for each sample suggests first-order "reaction".

der Vaals force and the repulsive electrostatic interaction among adjacent molecules, but the hydrophobic interaction could also play a role. Such a unique and complicated driving force could also be responsible for the slow association process.

Another evidence in support of the electrostatic interaction plays an important role in the formation of the vesicle structure is the effect of additional electrolytes. Adding salts, such as NaCl, into the solution will have an immediate impact on the vesicle structure. The details will be reported separately.

The slow process makes it possible to study the details of the "reaction" dynamics by LLS. According to the basis of reaction dynamics, a first-order chemical reaction should follow the equation: $\ln(a - x) = -kt + \text{const}$ with a and x being the starting reagent concentration and the product concentration at time t, respectively. The slope k denotes reaction rate. Here the product concentration x can be determined by I in Figure 2. Such data treatment is plotted in Figure 4, where linear relations can be found for all concentrations, except the data from first several days (open circles). Therefore, the slow self-assembly of {Mo$_{72}$Fe$_{30}$} possibly follows the rule of a first-order reaction. Due to some unknown reasons, the reaction was delayed during the first several days. The magnitude of k represents the reaction speed. In Figure 4, all the k values are in the range of $\sim(1.3-1.7) \times 10^{-3}$ day^{-1}, or $(1.5-1.9) \times 10^{-8}$ s^{-1}, indicating very slow "reactions".

In summary, an unusually slow self-association of {Mo$_{72}$Fe$_{30}$} ions in dilute aqueous solution is reported. At room temperature, the whole process needs months to complete. On the basis of LLS measurements, the {Mo$_{72}$Fe$_{30}$} ions slowly form supramolecular vesicle structures. More and more vesicles form during the whole period, while the size of the formed vesicles basically remains unchanged with time. The vesicle formation "reaction" roughly follows the rule of first-order reaction.

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