SELF-ASSEMBLY OF POLYOXOMETALATE (POM)-CONTAINING HYBRIDS:
FROM AMPHIPHILICITY TO ARCHITECTURE

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SELF-ASSEMBLY OF POLYOXOMETALATE (POM)-CONTAINING HYBRIDS:
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Thesis

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ABSTRACT

Since the first Polyoxometalate (POM)-based hybrid clusters have been synthesized\textsuperscript{1}, numerous efforts have been invested in designing multifunctional material including such as fluorescent\textsuperscript{2}, thermal stimuli-responsive properties. Unlike normal amphiphilic molecules, these hybrids are highly charged, which makes the solution behavior more complicated.

In this work, two sets of POM-containing hybrids, the POM-Peptide hybrid and the POM- Polyhedral oligomeric silsesquioxane (POSS) hybrids are explored by using Laser light scattering (LLS), Transmission electron microscopy (TEM) and Nuclear magnetic resonance (NMR). Studies reveal the self-assembled behaviors of these hybrids are different from previous POM-based hybrids in our group regarding of their driving force, architecture, amphiphilicity and counterions. This work will help us further understand how various driving forces affect self-assembled structure, morphology changing and size role.
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1.1 Polyoxometalate (POM)

Polyoxometalate is a large group of metal oxide cluster, which is formed by linking metal oxide polyhedra through sharing their corner, edge and face. Usually POM is polyatomic ion and high negatively charged due to the excess oxo ligands over central metal ions. Since the POM is highly negatively charged, it contains counterions (e.g., Na\(^+\), K\(^+\)) distributing around its surface. The size of POM is between 1 to 10nm, these macroions are well-defined, uniform, no intra-molecular interaction and behave completely different from simple small ion and large colloidal particles.
1.2 Polyhedral Oligosilsesquioxanes (POSS)

Polyhedral Oligosilsesquioxanes (POSS) is a class of three-dimensional silsesquioxanes synthesised from the condensation of silanol precursor.\(^5\) Since the first discovery of POSS in 1946,\(^6\) many well-defined POSS molecules have been reported as well as commercialized. They have the same empirical chemical formula with \([\text{RSiO}_3/2]^n\), where \(n\) is the number of element building unit. Among a variety of POSS structure, the cubic T8 (\(n=8\)) POSS is the most common one. Due to the multi-functional sites and groups, POSS is used as a basic building atom to creat novel POSS functional material. Such facile synthesis includes thiol-ene reaction, iodination reaction, metal-catalyzed reaction and so on.\(^7\)

1.3 Polyoxometalate-Containing Hybrids

Incorporating organic part in to inorganic POM is a promising way to enhance the adaptability and property of POM related materials. Usually the POM-containing hybrid can be divided into two groups, the strong interaction (colvalent bonds) and the weak interaction (hydrogen bonding, electrostatic interactions). During the past ten years, a large quantity of POM-containing hybrids have been synthesised reagrding their organic tails, shape, archutecture.\(^8\) For example, Lindqvist type polyoxometalates functional with pyrene fluorescent group,\(^9\) dumbell-like hybrid with two Wells–Dawson-type polyoxometalates.\(^10\) Figure 1 illustrates different architecture of POM-containing hybrids.
1.4 Self-assembly of POM macroion and POM-Containing Hybrid in solution

It has been well studied that the fully hydropholic POM can spontaneously self-assembly into highly ordered blackberry spheric structure with the driving force counterion-mediator attraction. Unlike other micelles and vesicle formation, the blackberry is a kinetic controlled process, the transition from monomer to oligomer is time limiting because this transition needs overcoming high energy barrier. Figure 2 the concept of blackberry formation.
Figure 2. Illustration the formation from monomer to blackberry. Copyright 2005 American Chemical Society

The POM-containing hybrids can also self-assembly into spheric structure. Unlike pure poltoxometalate, these hybrids are double-layer vesicle structure indeed. By appropriately changing solvent, reverse vesicle is observed.
2.1 Sample preparation

All the samples are received from collaborators without further purification. The solvents are purchased from Sigma-Aldrich (HPLC grade).

The solution samples are prepared by first dissolving powder in good solvent then slowly adding another solvent. Then the samples are kept in certain temperature.

2.2 Instruments and characterization

Both dynamic light scattering (DLS) and static light scattering (SLS) are performed by using a commercial Brookhaven Instrument LLS spectrometer equipped a 532 solid-state laser. DLS data is collected by a BI-9000AT multichannel digital correlator and then analyzed with CONTIN software. The hydrodynamic radius ($R_h$) value is got from Stokes-Einstein equation: $R_h = K T / (6 \pi \eta D)$. SLS data is collected at scattering angle between 30 degree to 90 degree using 2 degree intervals then processed with Zimm model.
1D NMR spectra is obtained on Varian NMRS 500 spectrometer. 2D NOESY NMR spectra is obtained on Varian INOVA 750 spectrometer. 2D DOSY spectra is obtained on Bruker 500 spectrometer.
CHAPTER III
RESULTS AND DISCUSSION

3.1 POM-Peptide Hybrids

In this section, the POM-peptide hybrids will be discussed in detail in term of amphiphilicity, self-assembled structure, driving force.

3.1.1 Evidence of peptide hybrids self-assembly studied by Laser Light Scattering (LLS)

The solution study of POM-peptide hybrid is performed in acetonitrile/water mixture solvent. The sample is first dissolved in pure acetonitrile with concentration 2mg/ml and then slowly added water to reach certain volume fraction. Dynamic Light Scattering is applied to monitor this self-assembly process. As figure 3 shows, this process has a lag phase around 5-10 days and will reach thermodynamic equilibrium after one month. Compared with the initial scattering intensity, the final intensity is several hundred times higher, which strongly suggests large self-assembled structure formed in solution.
Figure 3. (A) Chemical structure of POM-Peptide Hybrids. (B) Total intensity change during the self-assembly.

NMR also confirms the self-assembled process, the peaks becomes broad after several weeks due to the slow diffusion resulting from large self-assembly.
Figure 4. (A) NMR spectra of DiPhen Peptide after self-assembly. (B) NMR spectra of DiPhen Peptide before self-assembly. (C) Zoom in spectra of A. (D) Zoom in spectra of B.

3.1.2 determine self-assembled morphology by Laser Light Scattering (LLS) and Transmission electron microscopy (TEM)

After the intensity reach equilibrium, DLS is used to measure hydrodynamic radius (Rh) at different angle. From CONTIN analysis, the Rh doesn’t have angular dependence, which demostrates its spheric morphology. Moreover, Rg value from SLS is close to Rh, suggests the hollow spheric structure.

Figure 5. (A) CONTIN result of Phen-Peptide in acetonitrile/water mixture. (B) TEM image of hollow spheric blackberry

3.1.3 Insight the detail molecule structure of self-assembly by 2D-NOESY NMR study
Some of peptide tails are fully hydrophilic, unlike amphiphilic POM-containing hybrids, which form vesicle structure in solution, they don’t have hydrophobic part to fill the hydrophobic layer. So it is interesting to explore what exactly spheric structure of these hybrids. 2D-NEOSY NMR is a geart technique to determine spatial association based on distance ($< 3\,\text{Å}$). If these hybrids really form vesicle, the counterion tetrabutyl ammonium (TBA) should be strongly associate with peptide tails to fill the hydrophobic layer, resulting the strong NMR signal in NOESY spectra. Based on the spectra, the peaks is rather weak even after self-assembly, suggests the TBA doesn’t close associate with peptide tails. In order to form hollow shpere, they should self-assemble into single layer blackberry instead of double layer vesicle.

![2D-NOESY spectra of Ala-Peptide after self-assembly](image)

Figure 6. 2D-NOESY spectra of Ala-Peptide after self-assembly, the red rectangular peaks are signals from counterion TBA
More evidence comes from the concentration and temperature study, it is found that the blackberry size is concentration and temperature dependent, which means the end functional carboxylic acid plays an important role in this blackberry formation. So the carboxylic acid group prefers to extend outside responding to the effect of concentration and temperature.

![Figure 7. (A) Temperature dependence of Ala-Peptide. (B) Concentration dependence of Ala-Peptide](image)

3.1.4 Explore the driving force balanced by electrostatic interaction and hydrogen bonding

Since the peptide hybrids contain charge, electrostatic interaction should be a common driving force. In acetonitrile/water mixture solvent, when increasing the volume fraction of water, the blackberry size will be smaller because polar water can induce counterion TBA disassociation from the POM surface, which favors higher surface charge density. 2D-DOSY experiment is applied to support this idea. As figure shows, when introducing water into acetonitrile, the difference of diffusion coefficient between TBA and peptide tails becomes larger. On other
words, TBA is looser associated with POM when adding water.

Figure 8. Left: 2D-DOSY spectra of Phen-Peptide in 60% water/acetonitrile mixture. Right: 2D-DOSY spectra of Phen-Peptide in pure acetonitrile. The red rectangular peaks are from peptide tails, the black rectangular peaks are from TBA, the other peaks are from solvent.

Despite the fact that the electrostatic interaction is the driving force in self-assembled process, the size rule of these samples seems to be more complicated. As the figure shows, adding water will introduce larger blackberry size, however, continuously-adding water will result into smaller size indeed. This size rule implies other driving forces may affect the blackberry size including hydrophobic interaction, hydrogen bonding and so on.
Figure 9. Blackberry size corresponds to the solvent volume fraction in acetonitrile/water mixture.

Because the short peptide tails are fully hydrophilic, it rules out the possibility that hydrophobic interaction will affect the blackberry size. And in order to explore the influence of hydrogen bonding, salt effects in both water and deuterium oxide are studied. As the result shows, more salt is need to trigger the self-assembly in deuterium oxide because of the weaker hydrogen bonding to screen the electrostatic repulsion. Meanwhile, the size difference becomes larger at high salt concentration. Because salt can also screen the electrostatic, in which case the hydrogen bonding will be more and more dominant. So in this POM-peptide
self-assembly, both strong electrostatic interaction and weak hydrogen bonding will affect the size rule.

Figure 10. Blackberry size corresponds to the salt concentration in H2O and D2O

3.2 POM-POSS/PS hybrids

In this section, the POM-POSS hybrids will be discussed in terms of architecture, counterion.

3.2.1 Effect of molecule rigidity and packing parameter on the self-assembly of Keggin mono-functional hybrids (Keggin-POSS, Keggin-PS)
In this section, two important factors in amphiphilic hybrids, packing parameter and rigidity will be discussed. As the figure shows, two amphiphilic POM-containing hybrids samples are studied in acetonitrile/water mixture solvent.

![Figure 11. Left: Representation of the molecular structure of POM-POSS/PS. Right: CONTIN result of POM-POSS during self-assembly process](image)

Laser Light Scattering (LLS) and Transmission electron microscopy (TEM) are applied to determine their self-assembled morphology. Interestingly, although these two hybrids have almost the same architecture and amphiphilic nature, their solution behavior is completely different.
Two possible reasons may account for this difference. First, the similar size between Keggin POM and POSS prefers the nanobelt-like packing. However, when introducing water into acetonitrile, the molecule will perform microphase separation to form metastable multilayer vesicle. Then a transition form multilayer vesicle to nanobelt is observed after several days. Compared to POSS, PS tail is
relatively larger in size, which will affect the packing parameter. As a result, it can only form vesicle structure. Another reason may come from their difference in rigidity since PS tail is more flexible than POSS, in order to minimize free-energy, it will form more stable normal vesicle rather than unstable multilayer vesicle.

3.2.2 effect of molecule architecture on the self-assembled structure of Keggin POM-POSS hybrids

Architecture is another important factor to influence the hybrids’ self-assembly. Compared to Keggin POM-POSS hybrid, Keggin POM-DiPOSS has the same amphiphilic nature. But since the architecture of these two hybrids is different (2POSS Vs 1POSS), which will also affect the packing parameter finally. Their behaviors in solution are dramatically unlike.
Figure 13. (A) Representation of the molecular structure of POM-POSS. (B) Representation of the molecular structure of POM-DiPOSS. (C) TEM image of POM-POSS at 10th day. (D) TEM image of POM-DiPOSS
In summary, two sets of hybrids, the Anderson POM-Peptide hybrids and Keggin POM-POSS/PS hybrids are explored in solution by Laser Light Scattering. Various self-assembled structure, including single layer blackberry, double layer vesicle, multilayer vesicle, nanobelt are observed with regard to their amphiphilicity, architecture, driving force, conformation, counterion association. The study will further help us understand the behavior of some more complicated complex (e.g., DNA, protein) in solution state.
REFERENCES


