Polyoxometalate Macroion Induced Phase and Morphology Instability of Lipid Membrane

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Electronic Supplementary Information (ESI)

Synthesis of {$Se_{16}W_{101}$}. The {$Se_{16}W_{101}$} macroion is synthesized in the University of Glasgow by following the published procedure [1].

Figure S1. a) Structure of $\{Se_{16}W_{101}\}$ macroion ($K_{52}[(H_8W_{100}Se_{16}O_{364})WO(H_2O)_2].174H_2O$), which is synthesized in the University of Glasgow by following the published procedure [1]. **b)** The effect of $\{Se_{16}W_{101}\}$ cluster on the dynamics of single lipid molecules in a supported α-PC bilayer. The diffusion coefficient, *D* of fluorescent lipid probe in α-PC supported lipid bilayer is measured in $\{Se_{16}W_{101}\}$-added buffer solution against $\{Se_{16}W_{101}\}$ concentration by fluorescence correlation spectroscopy (FCS) using a same instrument and procedure reported previously[2]. The buffer solution added with 0.02 M NaAc-HAc (pH 3.80) is used in this work. It is observed that the diffusive dynamics of lipid gradually decreases with increasing $\{Se_{16}W_{101}\}$ concentration, and when the concentration exceeds ~1.0 μM, the lipid diffusive dynamics appears to be significantly suppressed without detectable *D* by our FCS setup.

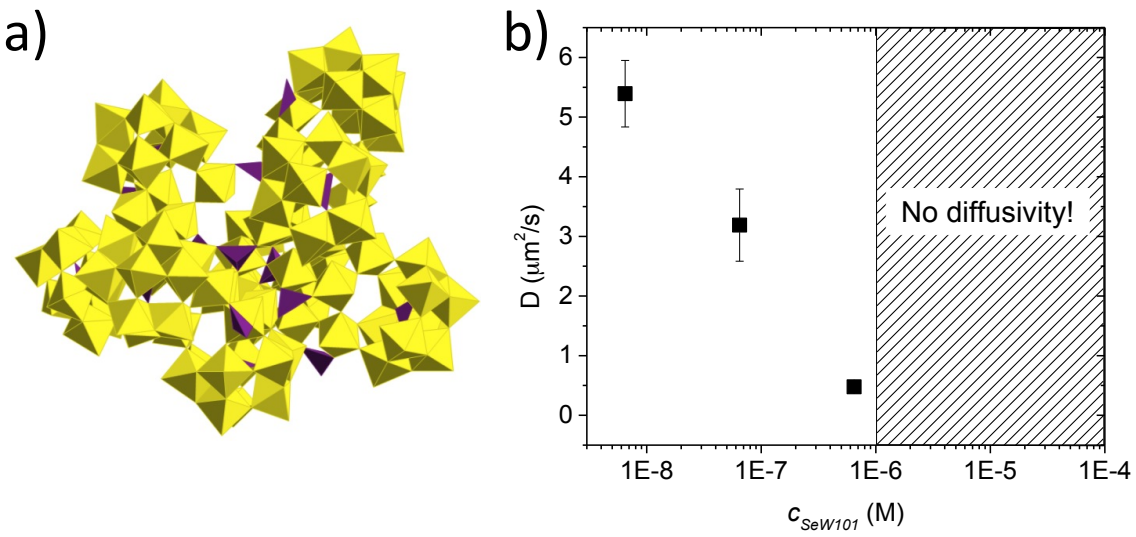


Figure S2. AFM micrographs display **a)** the homogeneous and uniform morphology of supported α-PC bilayer on silicon wafer in the buffer solution of 0.02 M NaAc-HAc (pH 3.80) before adding $\{Se_{16}W_{101}\}$. It should be noted that no liposomes are expectedly observed because they are very soft and can be readily ruptured and spread on the highly hydrophilic silicon surface upon adsorption to form a homogeneous SLB. **b)** The morphology of α-PC bilayer immediately after adding 6.5 μM $\{Se_{16}W_{101}\}$ in the buffer solution, exhibiting $\{Se_{16}W_{101}\}$-induced formation of pores and stacks of multi-lamellar lipid bilayers on the previous uniform lipid bilayer. Section analysis of the AFM micrograph in **b)** shows the height profile of the Inset figure along a black line.

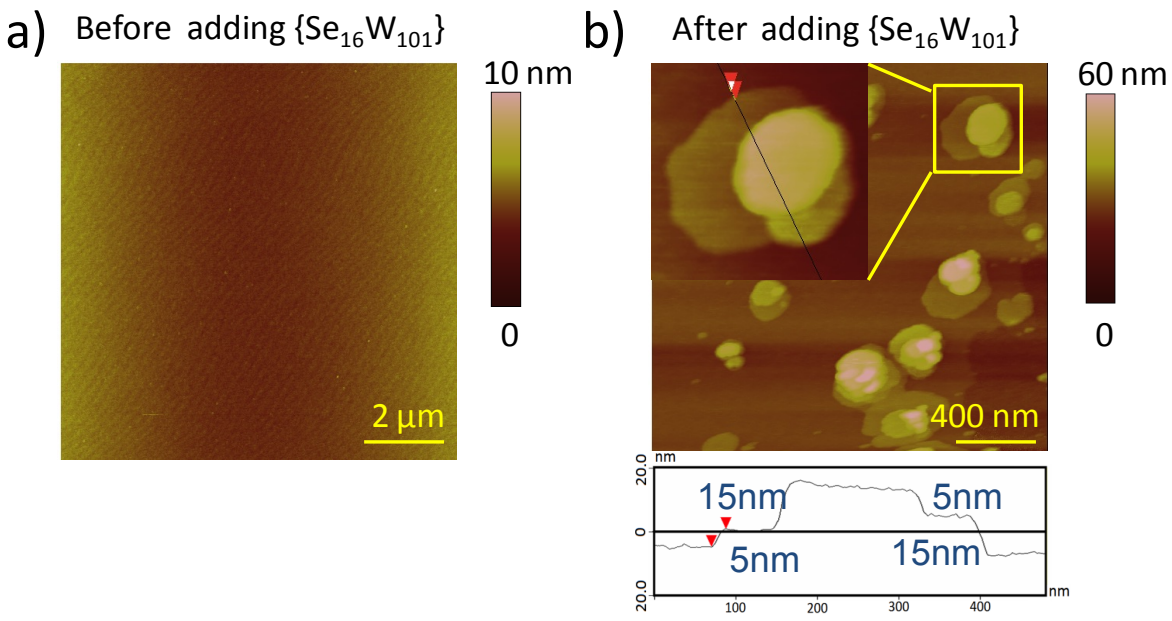


Figure S3. AFM **a)** height and **b)** phase micrographs exhibit the morphological structure of α-PC liposomes added with $\{Se_{16}W_{101}\}$ in the buffer of 0.02 M NaAc-HAc (pH 3.80) at T = 25 °C. The molar ratio of $\{Se_{16}W_{101}\}$ to α-PC is 0.033. Circled regions indicate the $\{Se_{16}W_{101}\}$-induced budding on liposome interface.

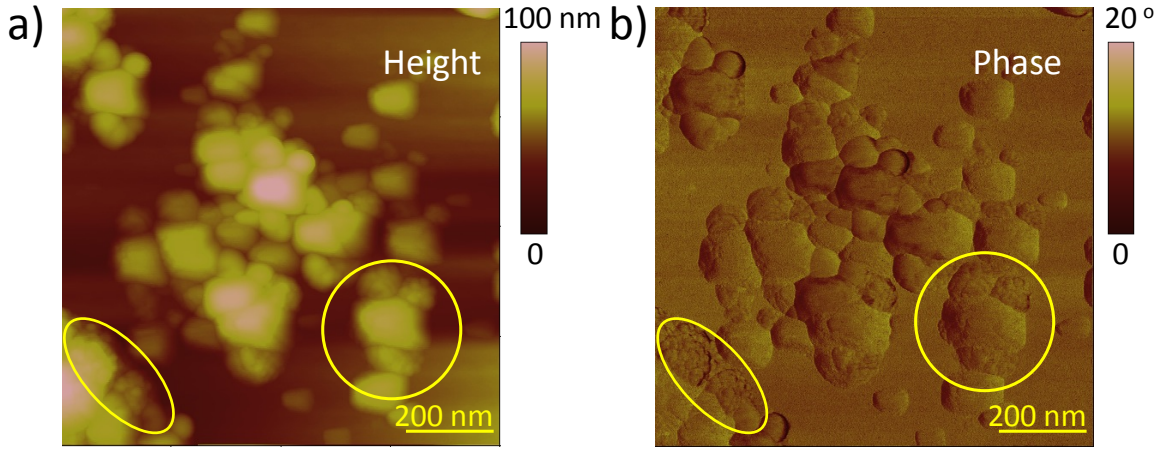


Figure S4. Long-term stability of $\{Mo_{176}\}$ macroion is confirmed by **a)** small-angle X-ray scattering (SAXS) and **b)-d)** UV-vis spectroscopy measurements. Small-angle X-ray scattering (SAXS) data were collected using a Bruker Nanostar equipped with a Cu microfocus source, Montel multilayer optics, and a HiSTAR multi-wire detector. SAXS spectra of 51 μM $\{Mo_{176}\}$ shown in panel **a)** were collected with a sample-to-detector distance of 26.3 cm with the sample chamber under vacuum. **Inset:** the gyration radius of $\{Mo_{176}\}$ macroion measured over varied storage time by fitting the curves in **a)** and the black line is the theoretical gyration radius got by CRYSOL based on single-crystal structure data of $\{Mo_{176}\}$. UV-vis spectra of 13 μM $\{Mo_{176}\}$ were acquired by using a Cary 6000i spectrometer for **b)** or a Cary Varian spectrometer for **c)-d)**. Experiments were conducted in the buffer solution of 0.02 M NaAc-HAc (pH 3.80) at a storage temperature of **b)** 4 °C and **c)** 25 °C. **d)** The time-dependent UV-vis adsorption of 13 μM $\{Mo_{176}\}$ solution at the wavelength of 747 nm and 387 nm at 25 °C and 60 °C.

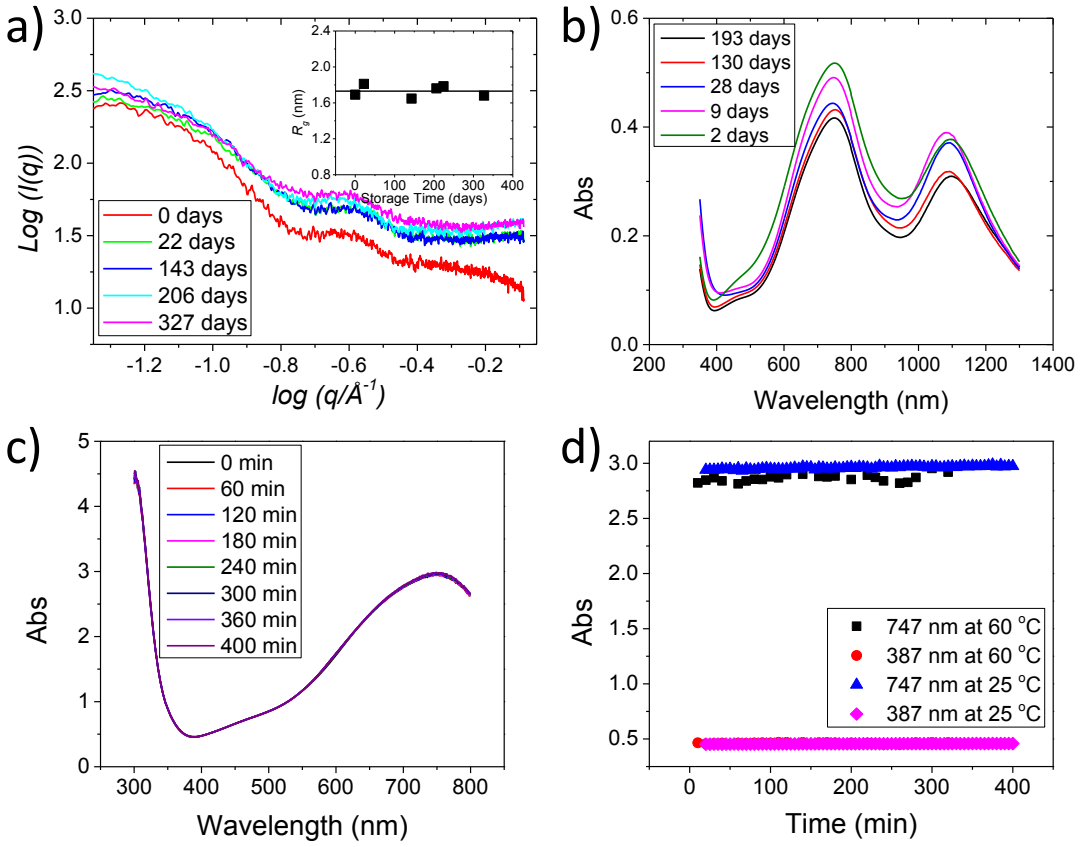


Figure S5. **a)** Schematic illustration of the electrostatic interaction between lipid bilayer, depicted in a red dashed cylinder of r_o = 2.05 nm in radius, and a {Mo_{176}} macroion, which is cylindrical coordination of (r, ϕ, z) with respective to the electric field generated by a {Mo_{176}} macroion. The permanent dipole of α-PC lipid is depicted with a length of l and a tilting angle of 25° with respective to the normal of the lipid bilayer plane. **b)** Computed electrostatic attraction potential (unit: thermal energy, k_BT at T = 298 K) of lipid bilayer with a {Mo_{176}} macroion as a modeled as a disk of R in radius and negligible thickness and whose 32 negative charges are uniformly distributed along its spherical rim over the azimuth angle, ϕ' = [0, 2π], in a cylindrical coordination system. The planes of a {Mo_{176}} and lipid bilayer are considered to be parallel to each other. The polar head group of a lipid in the zwitterionic α-PC bilayer is placed in the function of separation distance, z.

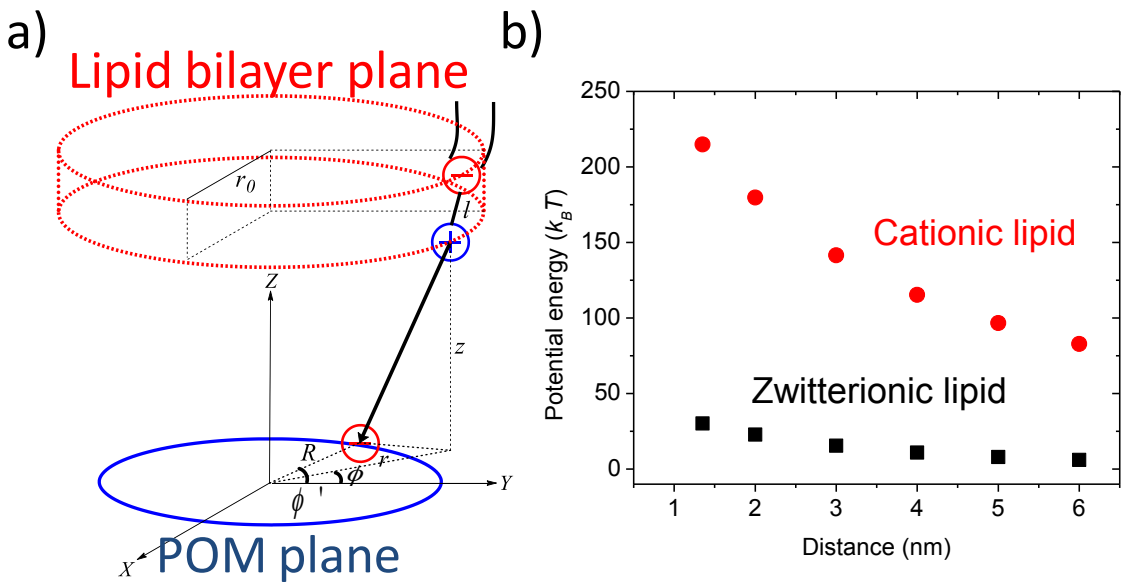


Figure S6. Photographs show the evolution of the mixing of {Mo_{176}} macroions in the volume ratio 1:2 water and chloroform mixed solution added with α-PC lipids. The molar ratio of added {Mo_{176}} to α-PC in the water-chloroform is 1:32. The photographs from left to right are obtained with the mixture before sonication, immediately after sonicating for 10 min and 21 hours after sonication. The photograph taken in 21 hours after sonication indicates the phase separation between the aqueous phase and chloroform phase, the latter of which also exhibits a color change in comparison to the photograph in the middle, indicating the formation of the {Mo_{176}}-lipid complex in chloroform.

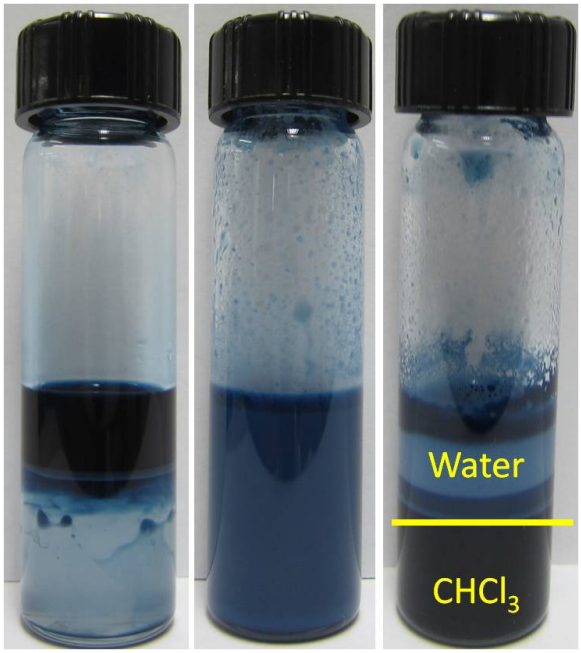


Figure S7. AFM micrographs display the morphological change of supported α-PC bilayer on a clean and smooth silicon wafer suspended in the buffer solution added with 12.7 nM $\{Mo_{176}\}$ and 0.02M NaAc-HAc (pH 3.80) over repeated continuous scanning over an area of 2 μm × 2 μm, except the last one over a scanning area of 5 μm × 5 μm. The destruction of α-PC supported lipid bilayer by AFM scanning tip indicates that the lipid bilayer remains very mobile possibly owing to too low surface coverage of adsorbed $\{Mo_{176}\}$, suggesting the fluid phase of lipid bilayer with adsorbed $\{Mo_{176}\}$ at sufficiently low $\{Mo_{176}\}$ concentration; it is in sharp contrast to the robust morphology of lipid bilayer at high $\{Mo_{176}\}$ concentrations as shown in **Figure 1c**, in which $\{Mo_{176}\}$-induced gelation of lipid bilayer is suggested.

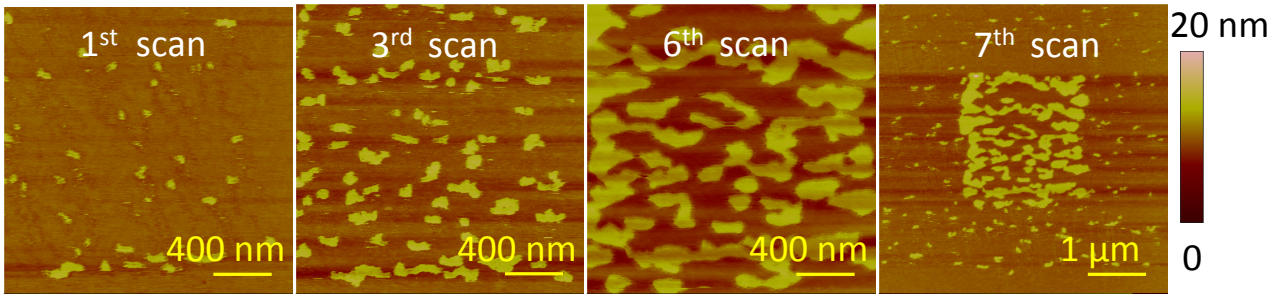
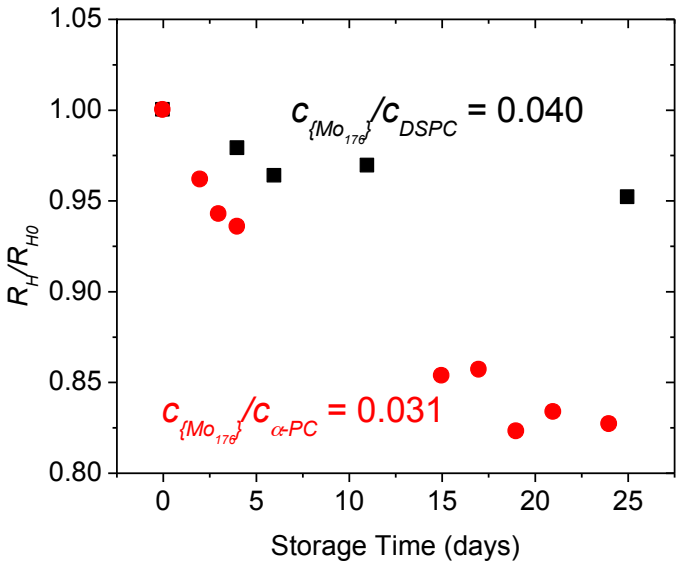


Figure S8. Size change of α-PC (red circles) and DSPC (black squares) liposomes added with $\{Mo_{176}\}$ macroions against storage time is determined by dynamic light scattering (DLS). The measured liposome radius of liposome is normalized by the one of freshly made liposome-POM mixture in the buffer solution of 0.02 M NaAc-HAc (pH 3.80). All the liposome samples are stored at a constant temperature, $T = 4.0$ °C.



References

(1) Yan, J.; Long, D.-L.; Cronin, L. *Angew. Chem. Int. Ed.* **2010**, *49*, 4117-4120.
(2) Jing, B.; Zhu, Y. *J. Am. Chem. Soc.* **2011**, *133*, 10983-10989.