Supporting Information for:

Synthetic Ion Channels via Self-Assembly: a Route for Embedding Porous Polyoxometalate Nanocapsules in Lipid Bilayer Membranes

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1 MD Methods

All simulations were performed using the molecular dynamics program NAMD [1]. Water, ions and lipids were parameterized using the CG forcefield developed by Marrink et al. [2], and incorporated

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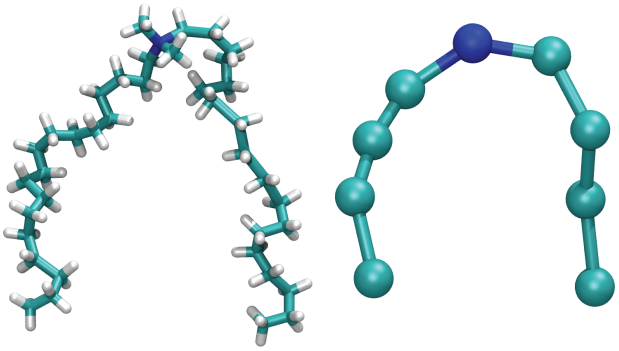

Figure S1: All-atom (left) and CG (right) models of DODA. The blue GC bead represents the nitrogen atom of the DODA head group and its four neighboring carbons. Each cyan CG bead represents four carbons, except for the last bead on each tail representing five carbons.

into NAMD by Shih et al. [3]. A custom forcefield was developed to describe the porous nanocapsule and DODA; the details are presented below. Temperature was kept constant at 310 K by Langevin thermostat using a damping coefficient of 1 ps^{-1}. To maintain pressure constant at 1 bar, the Nosé-Hoover Langevin Piston method was used with a decay period of 200 fs and a damping timescale of 50 fs [4, 5]. Each simulation was initialized through a period of minimization using a conjugate gradients method for 3000 steps followed by a 1560 step warming period to raise the temperature in 1K increments to 310K. SMD was performed using a velocity of 10^{-5} Å/timestep and a spring constant of 5 kcal/mol. The timestep of our CGMD simulations was 20 fs, which corresponds to a physical time of ∼80 fs, which is the time quoted in all our figures [2]. System setup, as well as all figure renderings, were performed using VMD [6].

2 CG model

All our CGMD simulations of water, ions, octane and lipids employed the coarse-grained force field developed by Marrink et al. [2]. In the CG method, groups of atoms are replaced by beads. The beads interact like atoms in all-atom models, through bonds, angles, dihedrals and nonbonded forces. Table S1 and Figure S1 summarize our CG model of DODA. Table S2a lists parameters not included in the Marrink model that were necessary for CGMD simulations of DODA.

CG Bead Name	CG Bead Type	Atom Name
Amo	Qo (charged)	N C1 C2 C5 C6
CTA1	C (apolar)	C4 C8 C10 C12
CTA2	C (apolar)	C14 C16 C18 C20
CTA3	C (apolar)	C22 C24 C26 C28
CTA4	C (apolar)	C30 C32 C34 C36 C38
CTB1	C (apolar)	C3 C7 C9 C11
CTB2	C (apolar)	C13 C15 C17 C19
CTB3	C (apolar)	C21 C23 C25 C27
CTB4	C (apolar)	C29 C31 C33 C35 C37

Table S1: CG model of DODA. This table details the mapping from an atomistic representation of DODA to a CG representation. Hydrogen atoms have been omitted.

a

Angle	K_{angle}	Angle
C C Qo	2.988	180
C Qo C	2.988	134

b

Bond	K_{bond}	Length
M B	75.000	3.297
B L	75.000	3.756
L L	75.000	2.590
L S	75.000	3.484

c

Angle	K_{angle}	Angle
M B L	75.000	112.083
B M B	0.001	72, 144
B L B	75.000	62.085
B L L	75.000	144.776
B L S	75.000	93.154
L B L	75.000	129.683
L S L	75.000	43.638
L L S	75.000	67.548

Table S2: CG parameters. a) DODA parameters not included in the Marrink model. b and c) Bond (b) and angle (c) parameters of the CG model of the porous nanocapsule. Note that the angle BMB has two equilibrium values in the structure, 72° and 144°. To eliminate possible distortions of the structure, the 72° angle term was assigned a negligible force constant.

The porous nanocapsule considered here is made of 12 repeats of a pentagonal unit. Thus, specifying the mapping of one pentagonal unit and its linker units to a CG representation is sufficient to describe the mapping of the entire capsule. As shown in Figure 1, the pentagon's center molybdenum atom and all surrounding oxygens are mapped to the center CG bead (cyan, type M). The five molybdenum atoms forming a pentagon around the center molybdenum are each mapped, with their oxygens, to the corresponding green, type B bead. Each linker molybdenum atom and its oxygens are mapped to the corresponding white, type L bead. Finally, the sulfate linker groups are mapped onto the yellow, type S beads. A full map between all-atom and CG models of the porous nanocapsule is detailed in Table S3. The bond and angle parameters necessary for the MD

simulations of the CG capsule are given in Table S2b and c.

CG Bead Name	CG Bead Type	Atom Name
C1	M(Qo)	M1 O1 O2 O3 O4 O5 O6 O7
B2	B(Qo)	M2A O8 O9 O10 O11
B3	B(Qo)	M3A O12 O13 O14 O15
B4	B(Qo)	M4 O16 O17 O18 O19
B5	B(Qo)	M5A O20 O21 O22 O23
B6	B(Qo)	M6A O24 O25 O26 O27
L7	L(P)	M7 O28 O29 O30 O31
L8	L(P)	M8 O32 O33 O34 O35
L9	L(P)	M9 O36 O37 O38 O39
L10	L(P)	M10 O40 O41 O42 O43
L11	L(P)	M11 O44 O45
S1	S(P)	S1 O85 O86
S2	S(P)	S2 O87 O88
S3	S(P)	S3 O89 O90

Table S3: CG model of the porous nanocapsule. This table details mapping between the atomistic and CG representations of one pentagonal unit of the porous nanocapsule. In the CG Bead Type column, each entry is followed in parentheses by the Marrink bead type that was used to compute the nonbonded interactions.

3 Capsule-DODA-octane simulations

To test our CG model of the porous nanocapsule and DODA, self-assembly of DODA with the capsule in a simple nonpolar solvent (octane) was simulated. Figure S2 presents the results of a typical simulation. Starting from an initially random distribution, Figure S2a, DODA molecules adhere to the surface of the capsule with their positively charged head groups, Figures S2b-d, eventually forming a steady-state hydrophobic spheroid, Figure S2e. Such simulations were performed at three DODA concentrations (0.35, 0.54 and 0.8 mmol/L), three times for each concentration. A stable assembly similar to that shown in Fig. 2e was observed at the end of each simulation.

The structure of the steady-state assembly is characterized in Figure S3. As previously shown by Kurth and co-workers [7] for the porous CH_3COO-linker nanocapsule, DODA tends to aggregate near the capsule; its concentration decreases with the radial distance from the capsule's surface. In

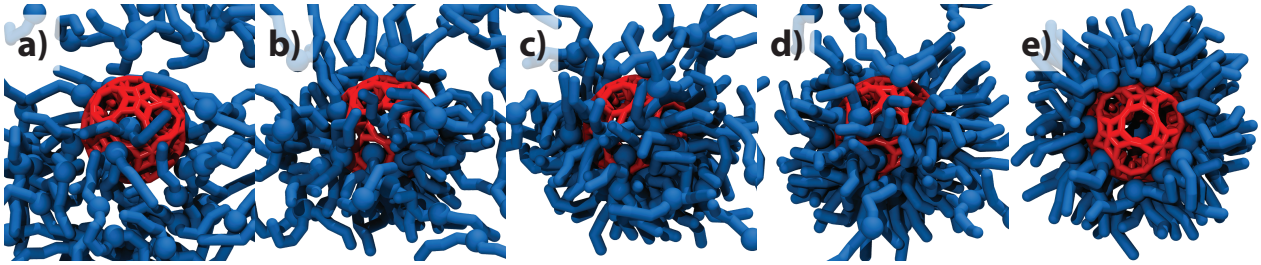

Figure S2: Self assembly of the porous nanocapsule (red) with DODA detergent (blue) in a nonpolar solvent (not shown). The snapshots illustrate the progress of a CGMD simulation in a cut-away view. The snapshots correspond to 0 (a), 1.6 (b), 3.2 (c), 4.2 (d), and 164.0 (e) ns of the simulation. An animation illustrating the self-assembly is available.

a steady state, DODA molecules form a spherical shell around the capsule, with their positively charged headgroup facing the negatively charged capsule and their hydrophobic tails facing the octane solvent, Figure S3a. The structure of the steady-state assembly could be reproduced in nine independent simulations performed at three different DODA concentrations, Figure S3b. The kinetics of the assembly is quantitatively characterized in Figure S3c.

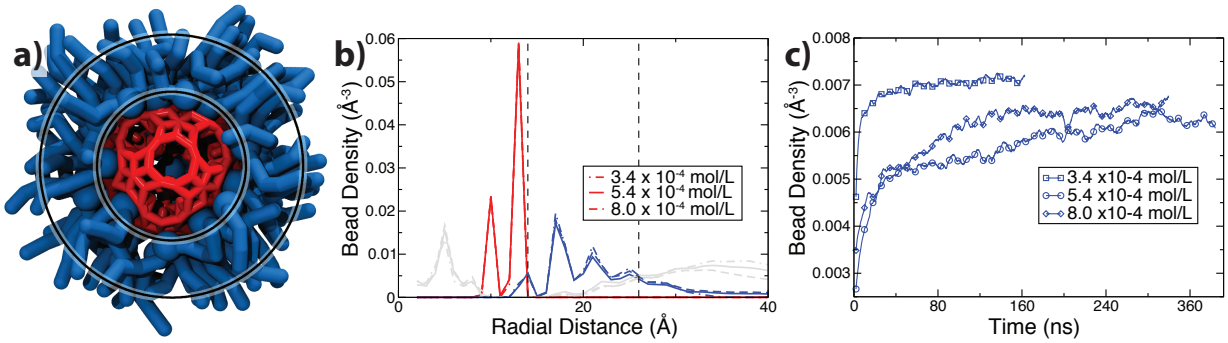

Figure S3: Structure and kinetics of the DODA/capsule assembly in hydrophobic solvent. a) Steady-state structure of the DODA-capsule assembly. The capsule (red) is surrounded by a shell of DODA (blue). The inner and outer rings indicate the transition from the porous nanocapsule to DODA, and from DODA to solvent, respectively. b) Density of CG beads versus radial distance from the center of the capsid. Blue, red and grey indicate the density of the porous nanocapsule, DODA and octane, respectively. The transition between the domains is defined as the distance at which the corresponding bead densities become equal and is shown as dashed lines. c) Density of DODA versus time in three CGMD simulations. The density of DODA was computed in the region defined by the inner and outer rings, see panels a and b. The aggregation at 3.4×10^{-4} mol/L occurs much faster than in the other simulations because this simulation was performed having long-range electrostatics enabled via Particle Mesh Ewalds method [8].

[DODA]	[Cl^-]	[Na^+]	Simulation Steps	Comment
0.045	0.016	0.0	3,340,000	Partial liposome
0.060	0.029	0.0	2,120,000	Liposome (after 1,140,000 steps)
0.076	0.043	0.0	2,460,000	Liposome (after 1,870,000 steps)
0.076	0.043	0.0	2,030,000	Liposome (after 1,240,000 steps)
0.11	0.092	0.022	1,857,000	Interconnected network of POPC and DODA
0.059	0.26	0.23	1,974,000	Partial lipsome; lipids aggregate without capsule

Table S4: Summary of all simulations of the porous nanocapsule in a solution of DODA, POPC, water and ions. Concentrations are given in mol/L. Concentrations for POPC are omitted, as the concentration of POPC was fixed at a 1:2.2 DODA:POPC ratio. Liposome formation times are estimations based on the kinetics of the self-assembly process. For the last simulation, the concentrations of Na^+ and Cl^- differ from 0.25 mol/L because extra ions were added or subtracted to neutralize the system.

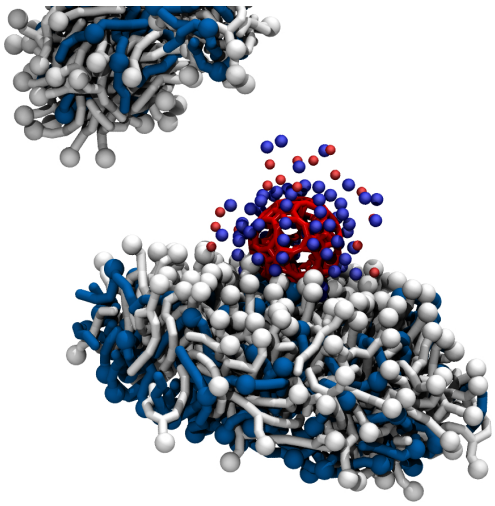

Figure S4: Incomplete assembly of a DODA/POPC/capsule liposome. This simulation was carried out at 0.25 M concentration of NaCl. The competition between Na^+ (blue) and DODA (blue) for neutralizing the capsule (red) prevented assembly of the capsule liposome. POPC molecules are shown in white and Cl^- ions in red.

4 Animations

NonpolarSelf-assembly.mpg: Self-assembly of DODA around the porous nanocapsule in a hydrophobic solvent (octane). The nanocapsule is shown in red, DODA is shown in blue, the octane solution is not shown. This animation corresponds to 164 ns of the CGMD simulation.

LiposomeSelf-assembly.mpg: Self-assembly of DODA, POPC and the porous nanocapsule into a capsule liposome. The nanocapsule is shown in red, DODA in blue, POPC in white, water and ions are not shown. The animation corresponds to 100.24 ns of the CGMD simulation.

LiposomeSelf-assembly_Cut-away.mpg: Cut-away view of the above simulation.

Fusion.mpg: Fusion of the capsule liposome with a lipid bilayer membrane. The DODA, POPC, and the nanocapsule forming the capsule liposome are shown in red, blue, and while, respectively. The lipids comprising the upper and bottom leaflets of the bilayer are shown in green and red, respectively. Water and ions are not shown. During the course of the simulation, some of the lipids from the top leaflet are inserted into the bottom leaflet to flatten the membrane. This animation corresponds to 940.4 ns of the CGMD simulation.

Fusion_Cut-away.mpg: Cut-away view of the above simulation.

IonChannel.mpg: Exposed to electrolyte solution nanocapsule interacts with inorganic cations and water. The nanocapsule is shown in yellow, DODA in dark gray, POPC bilayer in green, Na^+ and Cl^- ions in blue and red, respectively, water molecules are shown as white spheres. The animation provides a cut-away view of a 32-ns fragment of the 351-ns CGMD simulation.

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