Electronic Supplementary Information: Water Plays a Diverse Role in a Hydrogen-Bonded, Hexameric Supramolecular Assembly

Ankita Katiyar, Julia C. Freire-Sovierzoski, Paul B. Calio, Anthony A. Vartia, and Ward H. Thompson*

Department of Chemistry, University of Kansas, Lawrence, KS 66045, USA

E-mail: wthompson@ku.edu

Simulation Details

Molecular Dynamics (MD) simulations were performed using the Large-Scale Atomic/Molecular Massively Parallel Simulator (LAMMPS) software.^{1,2} The General AMBER ForceField³ (GAFF) was used to describe the resorcinarene and chloroform interactions while water was represented by the SPC/E model.⁴ A cubic simulation box, with periodic boundary conditions, containing one resorcin[4]arene hexameric assembly, chloroform solvent molecules, and different numbers of water molecules was used for all simulations. The trajectories are initiated with the assembly, including eight structural waters, pre-formed with six encapsulated chloroform molecules.

For eight to sixteen water molecules, the simulation box length was 73.05 Å on each side and 2983 chloroform molecules were included; for forty and fifty water molecules a

larger simulation box, with side length 103.525 Å was used with 7722 chloroform molecules included. Both box sizes were selected to approximate the experimental concentrations of water in the simulation box.^{5,6} Lennard-Jones and electrostatic interactions were evaluated within a cutoff of 12 Å and 12 Å, respectively. The long range electrostatics were included using the damped-shifted force approach⁷ with a damping parameter of $\alpha = 0.2$.

Thirteen 5 ns trajectories were propagated for each system with a 1 fs time step and configurations saved every 100 fs. The trajectories differed in the initial velocities, which were chosen randomly from a Boltzmann distribution. For each trajectory, the temperature was maintained for 0.1 ns using velocity rescaling followed by a 0.15 ns NVT equilibration period and finally a 5 ns NVT data collection stage at 298.15 K. In the latter two NVT periods a Nosé-Hoover thermostat with a time constant of 10 fs was used to maintain the temperature.

The free water diffusion coefficient in chloroform was calculated at two different water concentrations, 49.8 mM and 75.2 mM. The exact water concentration in water-saturated chloroform has been reported to be in this range, but is also dependent on the presence and concentration of the hexameric assembly.⁵ Our simulations find that $D_{w,free}$ decreases with water concentration as the population of larger water clusters increases. To find the number of bound waters, we have used the diffusion coefficient calculated from the 49.8 mM solution for low water content ($N_{tot} = 8$ to 16 waters) and that obtained from the 75.2 mM solution for higher water content ($N_{tot} = 40$ and 50 waters). This choice is made to more faithfully represent the waters that are free, *i.e.*, unassociated in any way with the assembly, in each solution.

The diffusion coefficients were calculated from the mean squared displacement (MSD),

$$MSD(t) = \left\langle |\vec{r}(t) - \vec{r}(0)|^2 \right\rangle,\tag{1}$$

where $\vec{r}(t)$ is the three-dimensional position vector of the particle at time t and $\langle \cdots \rangle$ indicates

a thermal average over all particles. For both the water molecules and the assembly the diffusion of the center-of-mass position was examined. The diffusion coefficient, D, is given by the slope of MSD(t) in the long-time limit,

$$D = \lim_{t \to \infty} \frac{MSD(t)}{6t}.$$
(2)

In practice, D is calculated from the slope of MSD(t) over an interval in which linear behavior is observed, here 75 –175 ps. The diffusion coefficients of both water and the assembly obtained in this way are tabulated in Table S1.

$1a:H_2O$	Diffusion Coefficient (× $10^{-5} \text{ cm}^2 \text{s}^{-1}$)		
ratio	Assembly	Water	
6:8	0.26 ± 0.03	0.41 ± 0.03	
6:9	0.27 ± 0.02	0.81 ± 0.16	
6:10	0.25 ± 0.02	0.99 ± 0.21	
6:11	0.28 ± 0.02	1.50 ± 0.13	
6:12	0.29 ± 0.02	1.50 ± 0.18	
6:13	0.26 ± 0.02	1.64 ± 0.26	
6:14	0.25 ± 0.04	1.67 ± 0.25	
6:15	0.25 ± 0.02	1.78 ± 0.24	
6:16	0.26 ± 0.02	2.04 ± 0.17	
6:40	0.37 ± 0.04	3.42 ± 0.20	
6:50	0.37 ± 0.05	3.68 ± 0.13	
49.8 mM Water Saturated CHCl ₃ (for 8-16 waters)		5.10	
75.2 mM Water Saturated $CHCl_3$ (for 40 & 50 waters)		4.65	

Table S1: Change in diffusion coefficients of the 1a and water for different $1a:H_2O$ ratios.

N_{total}	N _{bound}
8	7.74 ± 0.02
9	7.99 ± 0.32
10	8.49 ± 0.44
11	8.20 ± 0.29
12	9.25 ± 0.70
13	9.28 ± 0.70
14	9.89 ± 0.75
15	10.29 ± 0.77
16	10.11 ± 0.55
40	11.46 ± 1.87
50	11.34 ± 1.56

Table S2: Effect of total water molecules on the number of bounded water molecules.

Table S3: Adsorption isotherm model parameters and free energy change at 298 K for simulated and experimental 5 data.

	K_{eq}	N _{max}	$\Delta G \; (m kcal/mol)$
Simulation	0.093	4.48	-1.4
Experimental ⁵	0.084	6.02	-1.5



Figure S1: Illustration of a long hydrogen-bonded water chain interacting with the assembly. Water molecules are shown as ball-and-stick structure in blue and hydrogen bonds are indicated by black dashed lines.

References

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