

Overview

This project is using molecular simulation to investigate the dynamics of two previously synthesized hexameric supramolecular assemblies. The first is composed of six resorcin[4]arene monomer units and eight water molecules (Fig. 1a) while the second consists of six pyrogallol[4]arene monomers and no water (Fig. 1b). Both supramolecular assemblies take on approximately spherical structures (see Fig. 1c,d) with an interior volume of the “capsule” of $\sim 1500 \text{ \AA}^3$. Both assemblies are held together by hydrogen bonds which, while individually weak, combine in larger number (sixty in the case of the resorcinarene capsule) to make the assemblies stable over months or even longer.

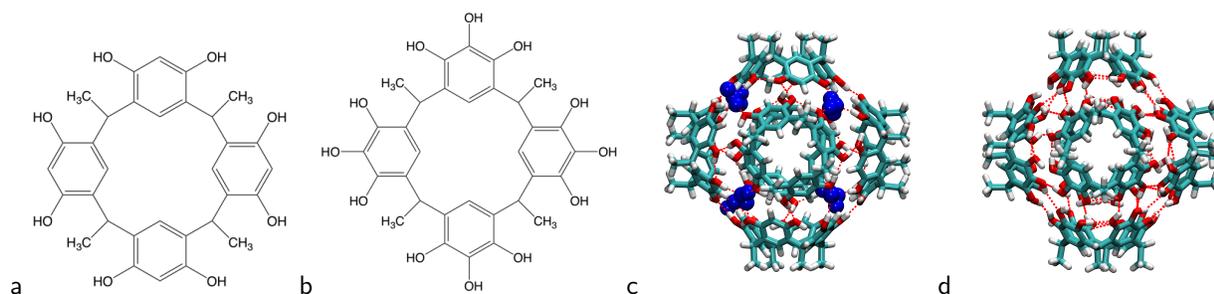


Figure 1: a: Resorcin[4]arene monomer structure, b: Pyrogallol[4]arene monomer structure, and simulation snapshots of c: the hexameric resorcin[4]arene assembly, and d: the hexameric pyrogallol[4]arene assembly. In c and d carbon (cyan), oxygen (red), hydrogen (white), and water atoms (blue) are shown along with hydrogen bonds (dashed lines).

A major goal of the project is to understand the mechanism(s) by which capsules take up and release solvent and solute “guest” molecules and the associated timescales. These events appear to be rate determining in catalyst systems based on such assemblies. We have developed and validated models for both assemblies that are appropriate for molecular dynamics (MD) simulations. As a starting point we first examined the dynamics of water in these systems with an eye to understanding previously reported NMR measurements.¹

Hexameric Resorcin[4]arene Assembly

The primary system studied in this work is the resorcinarene hexameric assembly (Fig. 1). Water is key to this assembly as eight waters are part of the structure and it has been observed that the assembly will not form without water present in solution (the usual solvent is wet $CDCl_3$). Previous NMR measurements of the water and assembly diffusion coefficients as a function of water content in solution¹ provide an opportunity to learn about the water dynamics in these systems.

We have calculated the diffusion coefficient, D , of both the water and the hexameric assembly as a function of total water content in the solution ranging from 8 to 50 water molecules while keeping the concentration of resorcinarene fixed. Our results are shown in Figure 2 and are in excellent agreement with the prior NMR measurements.¹ A standard picture for water in these systems is that it is free in solution or one of the eight waters making up the assembly. This leads to the predicted diffusion coefficient versus water content plotted as the blue line in Fig. 2a, which clearly does not agree with the measured (or simulated) data. Thus, we have posited that waters can additionally attach, or adsorb, to the assembly; this is an equilibrium process that gives rise to varying numbers of adsorbed waters depending on the water concentration in solution. This assumption leads to the predicted diffusion coefficient, D_{pred} , as a function of water content as

$$D_{pred} = \frac{N_{ads}}{N_{tot}} * D_a + \left(1 - \frac{N_{ads}}{N_{tot}}\right) * D_w, \quad (1)$$

where D_a and D_w are the diffusion coefficients of the assembly and free water, respectively, and N_{ads} and N_{tot} are the number of adsorbed and total waters, respectively. This can be used to interpret both the measured and simulated diffusion coefficients and, as seen in Figure 2a, it provides an excellent description of both sets of diffusion results. Further, visual inspection of the simulations indicates that the extra water molecules form linear chains in interacting

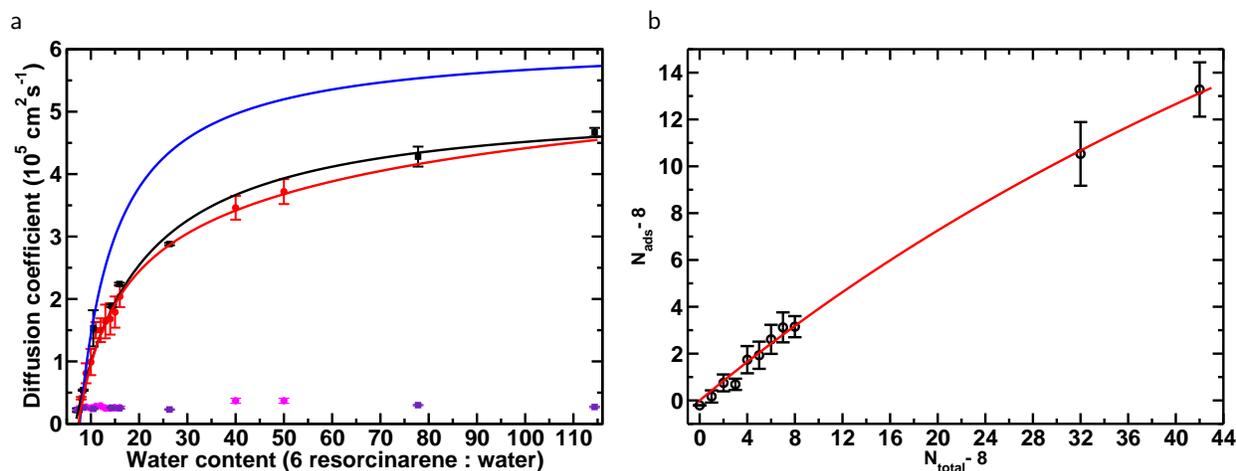


Figure 2: a: Diffusion coefficients of water from experiments¹ (■), our simulations (■) and of the assembly from experiments¹ (■) and our simulations (■) as a function of resorcinarene:water ratio. Predictions are shown assuming only eight waters adsorb to the assembly (blue line) and a variable number of waters adsorb, Eq. (1), for measured (black line) and simulated (red line) diffusion coefficients. b: The number of adsorbed water molecules versus the total number of waters in solution (symbols) along with the Langmuir adsorption isotherm fit (red line).

with the assembly and some of them are also encapsulated in the hexameric assembly cavity. Together these results indicate that the water molecules exhibit complex interactions with the assembly and even a more dynamical role, including perhaps as a promoter for guest exchange processes, than has been previously considered.

The nature of the water adsorption to the assembly is itself interesting as we find that it is well described by a Langmuir adsorption isotherm, as shown in Fig. 2b, which predicts

$$\frac{N_{ads}}{N_{sites}} = \frac{K_{eq}N_{tot}}{1 + K_{eq}N_{tot}}, \quad (2)$$

where we find the number of adsorption sites to be $N_{sites} = 49$. We have further been able to determine the timescales for waters to move between free in solution, part of the assembly, and encapsulated within the assembly. We are currently preparing a manuscript on these results.

Hexameric Pyrogallol[4]arene Assembly

The pyrogallolarene assembly, Fig. 1b,d, provides an interesting point of comparison with the resorcinarene assembly, in that the two share analogous structures but there are no water molecules required for the pyrogallolarene capsules (in fact, water is detrimental to their stability). We have carried out MD simulations on the pyrogallolarene assembly in CHCl_3 solvent with and without water. Such systems have also been the subject of NMR measurements of diffusion coefficients.² Our (preliminary) results indicate that there is a significant difference in the water association with the pyrogallolarene assembly compared to resorcinarene, with the former being considerably weaker. This is consistent with the NMR results.² Understanding the driving forces for this behavior and the dynamics relevant to the water-assembly association processes for both systems will provide additional insight into the role of water in the hydrogen-bonded complexes.

References

- [1] Avram, L. & Cohen, Y. The role of water molecules in a resorcinarene capsule as probed by NMR diffusion measurements. *Org. Lett.* **2002**, *4*, 4365–4368.
- [2] Avram, L. & Cohen, Y., Hexameric capsules of lipophilic pyrogallolarene and resorcinarene in solutions as probed by diffusion NMR: One hydroxyl makes the difference. *Org. Lett.*, **2003**, *5*, 3329–3332.