Electronic Supplementary Information for

“Emergence of Non-Monotonic Deep Cavity Cavitand Assembly with Increasing Portal Methylation”

Alexander Saltzman¹, Du Tang¹, Bruce C. Gibb², Henry S. Ashbaugh¹.*

¹Department of Chemical and Biomolecular Engineering, Tulane University, New Orleans, LA, 70118
²Department of Chemistry, Tulane University, New Orleans, LA, 70118

In this supporting information we illustrate the positioning of the dummy atoms used to align the cavitand hosts with the guests, provide a detailed derivation of eq. (3) from the paper, and describe the topology files provided.

* Dummy atom positioning within the cavitand. As indicated in the paper, two dummy atoms were placed in the host to align the host and constraint the guests along the potential of mean force reaction coordinate. The first “bottom” dummy atom was determined by the average position of the four atoms connecting the four feet of the cavitand to the bottom row of aromatic rings, while the second “top” dummy atom was determined by the average positions of the four carbon atoms on the second row of aromatic rings closest to the cavitand portal. Figure S1 illustrates the positioning of these two dummy atoms in side and top views of deep cavity cavitand octa-acid. The positioning within the other hosts considered is the same.

* corresponding author. email: hanka@tulane.edu.
Derivation of eq. (3). The competitive equilibrium between the hosts and guests to assemble into distinct complexes can be rationalized via a reaction network model. The set of four reactions that describe assembly equilibrium between alkane guests ($G$) and distinct complexes (1:0, 1:1, 2:0, 2:1, and 2:2 assemblies) are

\[
1:0 + G \rightleftharpoons 1:1, \quad (S1a)
\]
\[
1:0 + 1:0 \rightleftharpoons 2:0, \quad (S1b)
\]
\[
1:1 + 1:0 \rightleftharpoons 2:1, \quad (S1c)
\]

and

\[
1:1 + 1:1 \rightleftharpoons 2:2. \quad (S1d)
\]
For completeness we consider the formation of 2:0 complexes, eq. (1b), despite the fact empty dimers are not observed experimentally. The corresponding equilibrium reaction quotients are

\[
\frac{[1:1]}{[1:0][G]} = K_{1:1}, \quad (S2a)
\]
\[
\frac{[2:0]}{[1:0]^2} = K_{2:0}, \quad (S2b)
\]
\[
\frac{[2:1]}{[1:1][1:0]} = K_{2:1}, \quad (S2c)
\]
and
\[
\frac{[2:2]}{[1:1]^2} = K_{2:2}. \quad (S2d)
\]

Rearranging eqs. (S2), the concentrations of the 1:1, 2:0, 2:1, and 2:2 assemblies can be expressed in terms of the guest and empty host concentrations as

\[
[1:1] = K_{1:1}[1:0][G], \quad (S3a)
\]
\[
[2:0] = K_{2:0}[1:0]^2, \quad (S3b)
\]
\[
[2:1] = K_{2:1}K_{1:1}[1:0]^2[G], \quad (S3c)
\]
and
\[
[2:2] = K_{2:2}K_{1:1}^2[1:0]^2[G]^2. \quad (S3d)
\]

The total cavitand concentration, \([1]_{\text{total}}\), is given by the balance equation

\[
[1]_{\text{total}} = [1:0] + [1:1] + 2([2:0] + [2:1] + [2:2]). \quad (S4)
\]

Substituting the expressions for the assembly concentrations (eqs. (S3)) into this balance and rearranging yields

\[
2(K_{2:0} + K_{2:1}K_{1:1}[G] + K_{2:1}K_{1:1}^2[G]^2)[1:0] + (1 + K_{1:1}[G])[1:0] - [1]_{\text{total}} = 0, \quad (S5)
\]
which determines the free host concentration, $[1:0]$, as a quadratic equation in terms of the equilibrium constants and free guest concentration, $[G]$. This expression corresponds to eq. (3) in the paper.

**GROMACS Topology Files.** We have uploaded GROMACS topology files for simulating all the cavitands considered here. The topology files for hosts 0, 1, 2, 3, and 4 are named OA-host0.top, MEMOA-host1.top, DEMOA-host2.top, TrEMOA-host3.top, and TEMOA-host4.top, respectively.