Electronic Supplementary Information for

"Emergence of Non-Monotonic Deep Cavity Cavitand Assembly with Increasing

Portal Methylation"

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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.

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Figure S1. Positioning of the dummy atoms along the C4-axis used to align the cavitand and define the reaction coordinate for binding guests into the host pocket. The host pictured here in licorice representation in deep cavity cavitand octa-acid. The dummy atoms a represented by the pink van der Waals atoms along the centerline of the cavitand. Side and top views are provided.

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

$$1:0 + G \rightleftharpoons 1:1, \tag{S1a}$$

$$1:0 + 1:0 \rightleftharpoons 2:0,$$
 (S1b)

$$1:1 + 1:0 \rightleftharpoons 2:1,$$
 (S1c)

and

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

$$\frac{[1:1]}{[1:0][G]} = K_{1:1},$$
(S2a)

$$\frac{[2:0]}{[1:0]^2} = K_{2:0},$$
 (S2b)

$$\frac{[2:1]}{[1:1][1:0]} = K_{2:1},$$
(S2c)

and

$$\frac{[2:2]}{[1:1]^2} = K_{2:2}$$
(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

$$[1:1] = K_{1:1}[1:0][G], (S3a)$$

$$[2:0] = K_{2:0}[1:0]^2,$$
(S3b)

$$[2:1] = K_{2:1}K_{1:1}[1:0]^2[G]$$
(S3c)

and

$$[2:2] = K_{2:2}K_{1:1}^{2}[1:0]^{2}[G]^{2}.$$
(S3d)

The total cavitand concentration, $[1]_{total}$, is given by the balance equation

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

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

$$2(K_{2:0} + K_{2:1}K_{1:1}[G] + K_{2:1}K_{1:1}^{2}[G]^{2})[1:0]^{2} + (1 + K_{1:1}[G])[1:0] - [1]_{total} = 0,$$
(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.