Supporting Information

Counteracting Influence of 2-hydroxypropyl Substitution and the Presence of Guest on the Shape and Size of β-Cyclodextrin Cavity

Avilasha A. Sandilya and M. Hamsa Priya*

Department of Biotechnology, Bhupat and Jyoti Mehta School of Biosciences
Indian Institute of Technology Madras, Chennai-600036, India

Conformation	α_1	α_2	α_3
$^4C_1$	-35	-35	-35
$^1C_4$	35	35	35
$B_{3,O}$	30	-60	30
$B_{2,5}$	30	30	-60
$B_{1,4}$	-60	30	30
$^{3,O}B$	-30	60	-30
$^{2,5}B$	-30	-30	60
$^{1,4}B$	60	-30	-30
$^1S_3$	60	-60	0
$^1S_5$	60	0	-60
$^3S_5$	0	60	-60
$^3S_1$	-60	60	0
$^5S_1$	-60	0	60
$^5S_3$	0	-60	60

Table S1: Pickett Strauss parameters describing glucose conformations [1, 2]
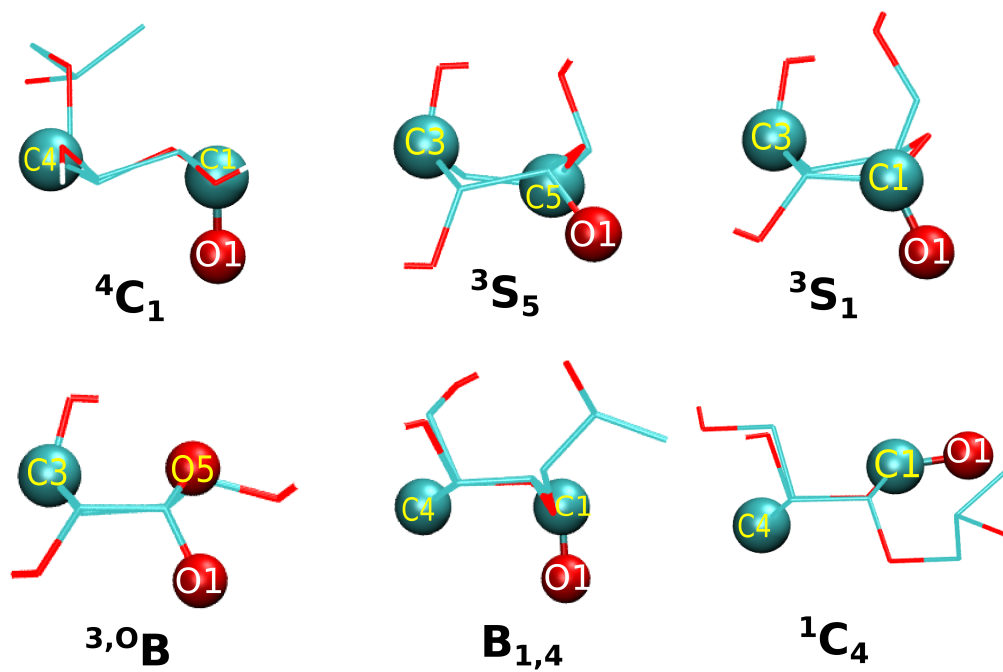
*Corresponding author: hamsa@iitm.ac.in

Figure S1: Molecular representation of the observed glucose conformations. The glycosidic oxygen (O1) and the atoms whose relative position defines the conformations are labelled and shown as spheres.
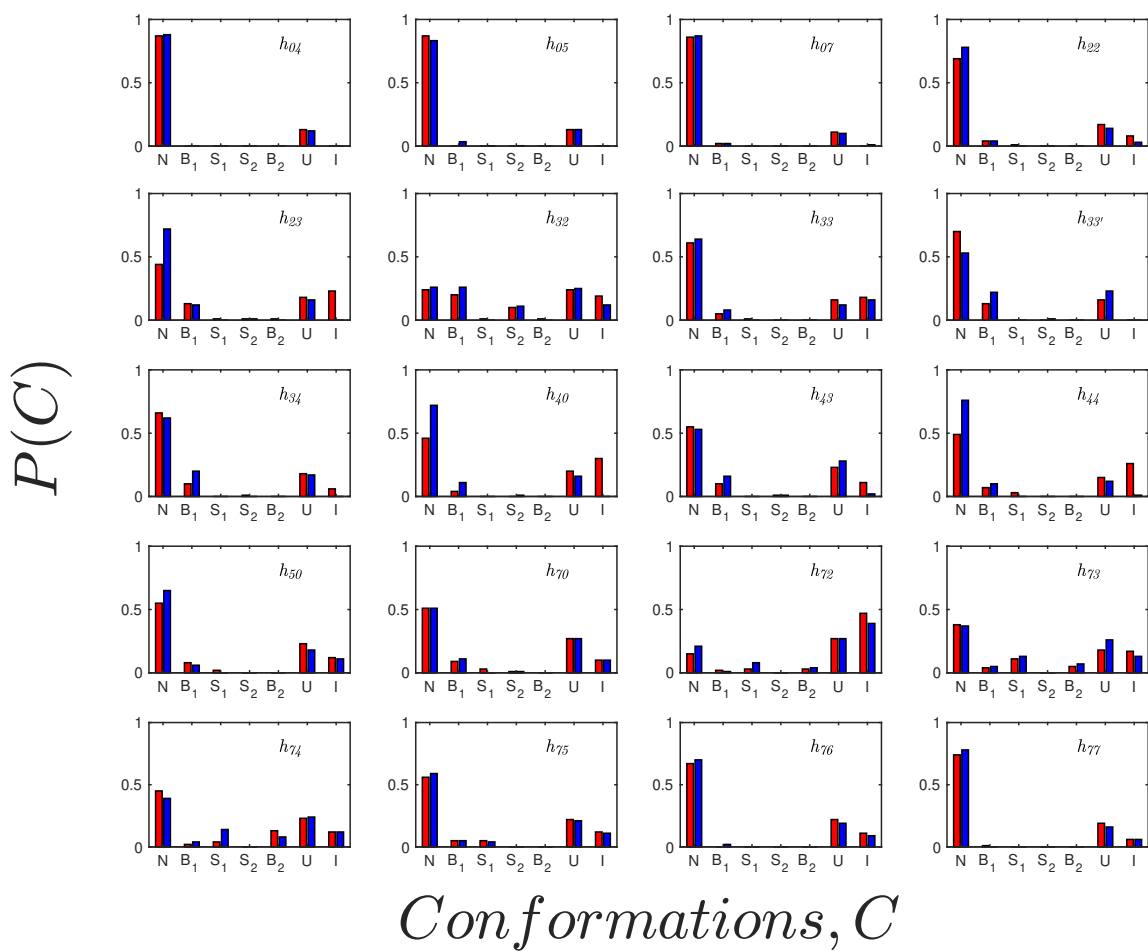
Figure S2: Probability of finding a glucose unit in a given conformation in HPβCDs in the absence (red bars) and the presence (blue bars) of the guest p-nitrophenol. Conformations: N – $^4C_1$; B$_1$ – ^{3,O}B; S$_1$ – $^3S_1$; S$_2$ – $^3S_5$; B$_2$ – B$_{1,4}$; I – $^1C_4$; U – undefined

Table S2: Statistics on the hydrogen bonding and CD–water interaction energy of HPβCDs

| Molecule | # Hydrogen Bonds | | Interaction Energy, kJ/mol | | |
	CD–CD	CD–Water	$\langle \epsilon_{elec} \rangle$	$\langle \epsilon_{disp} \rangle$	$\langle \epsilon \rangle$
βCD	5.6±0.1	32.1±0.2	-970±5	-156±1	-1125±4
h_{04}	5.6±0.1	32.2±0.2	-931±6	-198±1	-1130±5
h_{05}	5.1±0.4	33.2±0.5	-960±17	-207±8	-1167±9
h_{07}	5.1±0.7	35.2±1.3	-1042±42	-232±10	-1273±34
h_{22}	3.2±1.1	39.1±2.4	-1196±83	-183±22	-1379±61
h_{23}	2.4±0.2	40.5±1.1	-1240±34	-151±19	-1391±53
h_{32}	2.5±0.2	38.5±0.3	-1208±2	-165±1	-1372±6
h_{33}	2.6±0.2	39.7±0.2	1205±2	-181±6	-1386±4
$h_{33'}$	3.8±0.2	38.3±0.2	-1195±4	-186±1	-1382±4
h_{34}	3.4±0.9	39.2±1.5	-1192±41	-188±22	-1381±21
h_{40}	1.1±0.4	43.2±1.1	-1328±33	-154±11	-1483±22
h_{43}	3.0±0.5	40.1±0.8	-1239±33	-177±5	-1417±22
h_{44}	3.3±0.2	39.7±0.5	-1257±25	-202±7	-1460±18
h_{50}	1.8±0.3	41.6±0.9	-1290±21	-158±8	-1448±29
h_{70}	2.3±0.1	41.8±0.2	-1330±2	-165±4	-1496±2
h_{72}	1.6±0.4	44.1±1.3	-1408±49	-198±4	-1605±54
h_{73}	1.3±0.1	41.1±0.1	-1288±7	-224±1	-1512±8
h_{74}	1.1±0.1	43.2±0.1	-1321±6	-232±2	-1554±5
h_{75}	2.3±0.1	43.8±0.2	-1368±12	-255±1	-1623±9
h_{76}	0.9±0.1	45.1±0.1	-1363±3	-286±1	-1645±3
h_{77}	1.2±0.2	46.2±0.4	-1394±3	-291±11	-1685±15

$\langle \epsilon \rangle$ is the average CD–water interaction energy; $\langle \epsilon_{elec} \rangle$ and $\langle \epsilon_{disp} \rangle$ are the electrostatic and dispersion contributions to the CD–water interaction energy, respectively. The average and standard deviations are obtained from block averaging by dividing the simulation trajectory into three equal blocks

Table S3: Statistics on the hydrogen bonding and CD–water interaction energy in the presence of the guest p-nitrophenol in the cavity of HPβCDs

| Molecule | # Hydrogen Bonds | | | Interaction Energy, kJ/mol |
	CD–CD	CD–guest	CD–water	$\langle \epsilon^{np} \rangle$
βCD	5.9±0.0	0.0	30.7±0.1	-1067±3
h_{04}	6.0±0.1	0.1±0.0	31.4±0.2	-1106±6
h_{05}	5.5±0.4	0.1±0.1	32.4±0.6	-1143±21
h_{07}	5.7±0.4	0.1±0.1	34.0±0.5	-1236±16
h_{22}	4.5±0.6	0.2±0.2	35.3±1.2	-1264±40
h_{23}	4.3±0.0	0.2±0.0	35.8±0.1	-1284±6
h_{32}	2.1±0.1	0.4±0.2	37.0±0.4	-1317±10
h_{33}	3.3±0.2	0.5±0.1	37.4±0.2	-1356±6
$h_{33'}$	3.4±0.2	0.1±0.0	38.0±0.2	-1360±2
h_{34}	3.5±0.2	0.1±0.1	37.8±0.4	-1322±6
h_{40}	3.3±0.1	0.3±0.1	37.2±0.1	-1315±5
h_{43}	3.2±0.1	0.1±0.0	38.7±0.2	-1373±5
h_{44}	3.2±0.1	0.3±0.1	38.3±0.1	-1401±1
h_{50}	2.9±0.0	0.2±0.0	38.4±0.1	-1364±4
h_{70}	2.7±0.3	0.1±0.1	40.9±0.4	-1467±9
h_{72}	1.7±0.1	0.4±0.3	42.7±0.8	-1550±27
h_{73}	1.9±0.4	0.6±0.3	39.2±0.7	-1481±9
h_{74}	1.5±0.1	1.0±0.2	41.3±0.1	-1548±3
h_{75}	2.3±0.1	0.0±0.0	43.4±0.1	-1597±4
h_{76}	1.1±0.1	0.2±0.1	44.3±0.4	-1630±1
h_{77}	1.3±0.0	0.2±0.01	45.3±0.1	-1662±5

The average and standard deviations are obtained from block averaging by dividing the simulation trajectory into three equal blocks
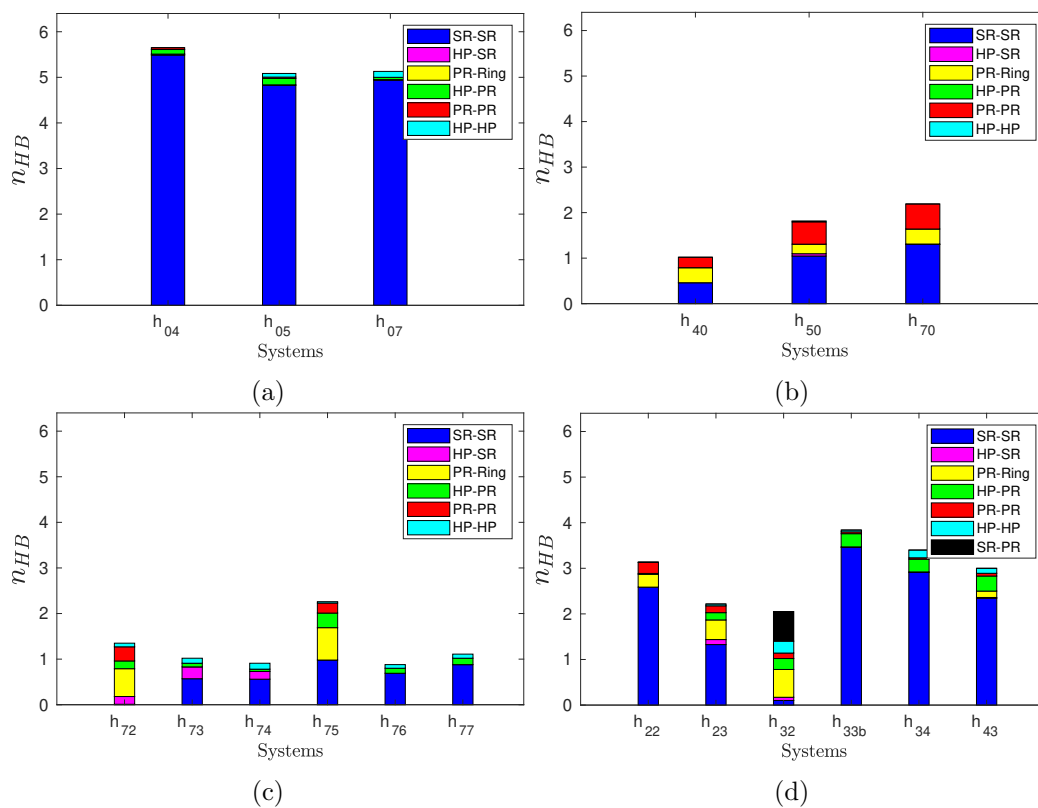
Figure S3: Statistics on the various CD–CD hydrogen bonds in HPβCDs: a) substitution only in the primary rim; (b) substitution only in the secondary rim; (c) increase in the substitution in the primary rim when all the glucose units in the secondary rim are substituted; (d) when glucose units are substituted either at the primary or the secondary hydroxyl rim but not both. Notation in the legends: SR - secondary rim oxygen atoms (O2/O3) ; PR - primary rim oxygen atoms (O6); HP - oxygen atoms of 2-hydroxypropyl; Ring - glucose ring oxygen atom (O5).

References

[1] Herbert L. Strauss and Herbert M. Pickett. Conformational structure, energy, and inversion rates of cyclohexane and some related oxanes. *J. Am. Chem. Soc.*, 92(25):7281–7290, 1970.

[2] Halvor S. Hansen and Philippe H. Hünenberger. Using the local elevation method to construct optimized umbrella sampling potentials: calculation of the relative free energies and interconversion barriers of glucopyranose ring conformers in water. *J. Comput. Chem.*, 31(1):1–23, 2010.