The Hydrophobic Topographies of Cyclodextrins and Some Non-Glucose Cyclooligosaccharides and Their Properties in Aqueous Solution

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Molecular dynamics simulations of α-cyclodextrin (**1**) in water were used to analyze hydrogen-bonding, hydration properties, and water exchange phenomena in detail (Fig. 1 and 2). Of the approx. 105 - 115 water molecules contained in the first hydration sphere of α-CD, an average of 34.2 ± 2.5 are engaged into 37.3 ± 2.8 hydrogen bonding interactions with the solute; the cavity itself is filled with an average of 6.2 H_2O molecules.

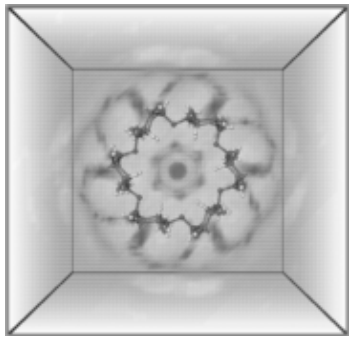
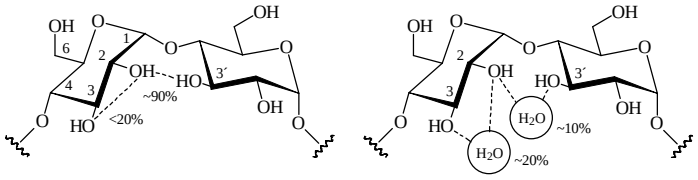


Fig. 1: MD-derived relative water densities around α-CD in solution: dark shading indicates enhanced water probabilities, whereas light areas correspond to low or bulk phase water densities (*left*: front view perpendicular to the CD macrocycle, *right*: side view)

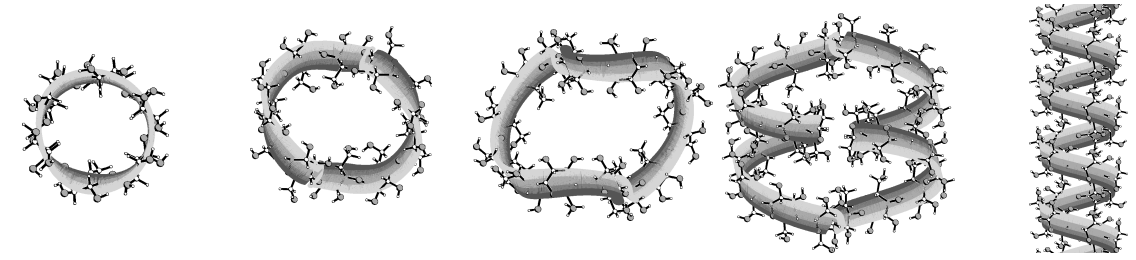
Fig. 2: 120 ps partial MD trajectory of the diffusion of a single water molecule through the CD cavity.

All hydroxyl groups are engaged in extensive H-bonding interactions with the surrounding solvent. Preferred are interresidue interactions of the 2-O ⋯O-3' type between adjacent glucose units, but water-mediated hydrogen bond bridges (i.e. water molecules H-bonded to two hydroxyl groups simultaneously, cf. Fig. 3) were also found to persist with high significance.

Fig. 3: In α-CD interresidue hydrogen bonds of the 2-O ⋯O-3' type occur with high probability and long life-spans of around 30 ps, whereas the intra-residue interaction is disfavored. Water-mediated H-bond bridges are observed with probabilities of around 10 - 20 %.



The hydrophobic characteristics of small- and large-ring CDs (cf. ribbon models shown below) were studied by molecular modeling and color-coded projection of the molecular lipophilicity patterns onto the solvent-accessible surfaces of the cyclodextrins[1].



CD_6 (α-CD, **1**) CD_{10} CD_{14} CD_{26} V_H-amylose