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Interaction of β-Cyclodextrin with DNA-Bases

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Complexes of β-cylodextrin with five nucleotides of adenine (A), thymine (T) guanine (G), cytosine (C), and 5-methylcytosine have been investigated using Hatree-Fock (HF) and density functional theory (DFT) calculations of different quality.

This work was inspired by recent technological advances made in single-molecule sequencing of DNA. One molecule of single-stranded DNA can be sequenced by using nanopores made of α-hemolysin as the sequencing device. An exonuclease enzyme attached to the top of the pore cleaves bases from the DNA strand so they can traverse the pore one at a time. The different nucleotides then bind to cyclodextrin attached to the inside of the pore [1]. The different bases are discriminated by the change they induce in the amplitude of the current carried by aqueous ions passing through the pore. Several variants of this method are currently developed by different companies and will be marketed soon.

We calculated low energy conformations of complexes of β-cyclodextrin with the five different nucleotides mentioned above, using different methods (HF, DFT). The interaction energy with β-cyclodextrin was estimated from the energy difference between a complex and the molecules it consists of. The presented results show, that it is possible to discriminate all five nucleotides very clearly.

Because one can easily distinguish between cytosine and 5-methyl-cytosine, this method can be used to sequence methylated DNA directly in one step which might be an advantage compared to other similar sequencing methods.

[1] Clarke J, Wu HC, Jayasinghe L, Patel A, Reid S, Bayley H. Continous base identification for single-molecular nanopore DNA sequencing. Nat Nanotechnol. 2009; 4: 265–270. doi:10.1038/nnano.2009.12