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# Molecular dynamics study of DNA damage induced by hydroxyl radicals

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DNA can be damaged by hydroxyl radicals produced in cells through metabolism or radiation [1]. DNA damage by hydroxyl radicals can be classified into two major categories: the addition of hydroxyl radicals to the base and the hydrogen abstraction from the sugar moiety. Previous studies have shown that hydrogen abstraction reactions tend to occur in the following order: C5' > C4' > C3' > C2' > C1', where C1'-C5' represent the carbon atoms in the sugar moiety [2]. Moreover, molecular simulation results indicate that the differences in reactivity between DNA and hydroxyl radicals are mainly due to differences in solvent accessibility to the respective hydrogen site [3]. In this study, the hydrogen abstraction reaction is evaluated based on the accessibility of hydroxyl radicals.

The base sequence of DNA used is d(ATATAT) with 1783 water molecules and 8 hydroxyl radicals. The bsc1 force field of Amber22 was used for DNA and the TIP3P force field for water. Three different models were used for hydroxyl radicals [4-6]. Molecular dynamics (MD) simulations were performed using Amber22. The initial box for the simulation was a truncated octahedron of 45.3 Å with periodic boundary conditions. The cutoff distance for the Lennard-Jones interaction and the electrostatic interaction was set at 8 Å. Ten sodium ions ($Na^+$) were added for electrical neutralization in the particle-mesh Ewald calculation. After equilibration of the system, a 100 ns MD simulation was performed under NPT conditions with an integration time step of 2 fs. Temperature and pressure were set to $T$ = 310 K and $P$ = 1 atm, respectively. The accessibility of hydroxyl radicals was calculated for the hydrogen of each sugar. The number of times a hydroxyl radical approached within 3 Å of the hydrogen of each sugar was counted. To efficiently sample the configuration of hydroxyl radicals, a constraining potential with a flat bottom and a parabolic side up to 8 Å was imposed between the hydroxyl radical and the oxygen atom of the sugar moiety.

The relationship between the number of times a hydroxyl radical approaches the hydrogen atom of each sugar (accessibility) and the rate of hydrogen abstraction measured in previous studies (reactivity) [2] is shown in Fig. 1. From this figure, the number of times the oxygen atom of the hydroxyl radical approaches the hydrogen atom, calculated as in the case of the water molecule in the previous study [3], shows little correlation. This suggests that the mere proximity of a hydroxyl radical to a hydrogen atom does not necessarily result in hydrogen abstraction.

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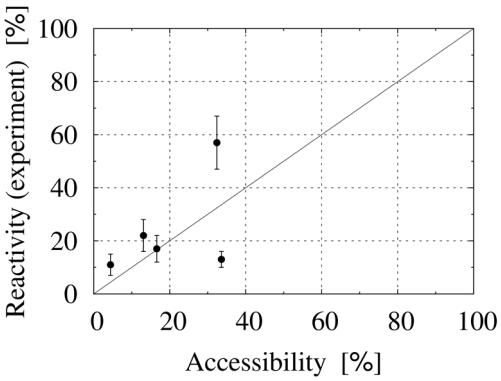


**Figure 1.** Relation between hydroxyl radical accessibilities to each hydrogen atom.