**DNA structural change induced by lesions: a molecular dynamic simulations study based on DEER experiments**

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We use Double Electron-Electron Resonance (DEER) combined to molecular dynamic simulations to study structural changes in DNA duplexes induced by different lesions. We have previously demonstrated that the 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) guanine, a paramagnetic probe, can be used to accurately measure distances in DNA duplex and moreover to follow B-form to A-form DNA conformational changes. The same protocol is here applied on several single damaged DNA duplexes. Due to the fact that the radical probe grafted on guanine can influence both the 3D model building and the calculated distance, we first characterized its conformational properties along with its internal dynamic. Indeed, it is grafted on the N2 amino group of the guanine, which is normally involved in the Watson-Crick pair G-C. Two different base-pairing models have then to be considered for the building of the TEMPOG-C base pair, depending on whether the remaining N2 proton is engaged or not in a hydrogen bond. To select which of base pairing fit the best with experimental data, MD simulations were performed on the undamaged duplex. We observed during these calculations that TEMPOG adopt several conformations due to variations of $\chi$ angle, from anti to high-anti, coupled with a rotation of the (TEMPO) pseudo plan with respect to guanine base plan. These different conformations of the radical probe have a significant influence on the calculated distance fluctuations. MD simulations of 10ns were then performed on DNA duplexes containing nick, gap, 8-oxoG or THF abasic site. Very good agreements between measured and calculated distances were found for all the systems excepted those containing abasic site and gap. The DNA duplex containing THF abasic site, which experimentally differ the most from undamaged DNA (3.5 Å) required additional calculations. In fact, the abasic site and its opposite base could present three different conformations: i) both abasic site and the opposite base are intrahelical, ii) abasic site is extrahelical whereas the opposite base is intrahelical iii) both abasic site and the opposite base are extrahelical. 3D model building and simulation of these different systems allowed us to determine the conformation adopted by our DNA sequence. Duplex containing a gap is the only one for which calculated results differed rather from experimental data. This may be due to the fact that it is the most destabilized system and so that it could adopt many different structural changes during our simulations.



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